EMPATHY IN A BROADER CONTEXT: DEVELOPMENT, MECHANISMS, REMEDIATION

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EMPATHY IN A BROADER CONTEXT: DEVELOPMENT, MECHANISMS, REMEDIATION

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EDITORIAL
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Editorial: Empathy in a Broader Context: Development, Mechanisms, Remediation

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Keywords: empathy, neurobiology of empathy, phenomenology of empathy, positive empathy, empathy and age

Editorial on the Research Topic

Empathy in a Broader Context: Development, Mechanisms, Remediation

Empathy has long been a subject of interest of social sciences, starting with the concept of Einfühlung ("in-feeling" or "feeling into") as the human capacity to feel the emotions that the artist or writer had worked to represent (1).

Later on, Theodor Lipps transformed Einfühlung from a concept of aesthetics into a central category of the philosophy of the social and human sciences and postulated that Einfühlung meant the "experience of another human" underpinned by "inner imitation" or instinctive kinaesthetic sensations in the observer as felt by the observed target (2). The word empathy was introduced to English-speaking world by E.B. Titchener (3) who translated Einfühlung by using Greek *em-* ("in'") and *pathos*, ("feeling", "suffering", or "pity"). This heralded the beginning of new, psychological research into the phenomenon, followed by operationalising the concepts of empathy thus firmly rooting it in the fields of sociology and psychology.

The empathy is considered as a multifaceted construct encompassing (1) affective empathy, i.e., affective sharing, (2) empathic concern: motivation to caring for another's welfare, and (3) perspective taking or cognitive empathy, the ability to consciously put oneself into the mind of another and understand what that person is thinking or feeling (4). Through the recent advances in neuroscience, researchers have begun to identify possible biological mechanisms of empathy (5) that human beings may share with higher mammals (6).

The papers in this Research Topic present novel neuroscience research in addition to socially diverse research examining skills, psychology, and interpersonal factors that modulate empathy in specific contexts.

Despite more than a century of descriptive research into empathy, the definition, and phenomenology of the empathy are still evolving and inquiry is broadening. One of the interesting lines of inquiry centers on whether or not cognitive and affective empathy are part of the same concept. This question is addressed in a paper in this Research Topic (Stietz et al.) where the authors argue that the aspects of perspective-taking and affective empathy should not be blended into unifying ("umbrella term") concept of empathy; but rather consider as distinct neurobiological and phenomenological processes.

Sindermann et al.'s study lends support to the above notion by demonstrating sexual dimorphism between cognitive and affective empathy. The authors explored the relationship

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between various self-report measures of empathy, e.g., Empathy Quotient (EQ) (7), Interpersonal Reactivity Index (IRI) (8), Autism Spectrum Quotient (AQ) (9), and Systemizing Quotient-Revised (SQ-R) (10) in a large sample of healthy adults. Apart from gender-neutral associations, the study uncovered differential associations between the above measures in females vs. males. In particular, both EQ and IRI measure of Perspective-taking were negatively associated with Autism Spectrum Quotient in female and male participants. However, in females there was a negative correlation between the IRI scales Perspective-Taking and Personal Distress which contrasted with a weakly positive correlation in the male sample.

A hypothesis paper (Thiriou et al.) considers another aspect of relationship between perspective-taking and empathy. The authors present a bold idea of linking cognitive perspective-taking with emotional/empathic understanding of others' point of view. The authors postulate that this complex association may underlie the insight in people with psychiatric disorders. According to the proposal, affectively experiencing the position of another person about oneself reinforces the insight, i.e., ability to recognise the disorder. This new perspective would certainly warrant an empirical validation.

The Perspective article by Light presents a re-conceptualization of empathy concept by emphasizing a possible change in emotional state of the observer that could be of any, e.g., either negative or positive, or even contrasting valence (contrasting empathy). This latter addition could be considered as controversial by empathy researchers who usually conceptualise empathy as an emergence of a matching, rather than contrasting emotion as is the case of, e.g., *Schadenfreude* (which is not considered as empathetic response). We are looking forward to any comments on this topic by the research community. In the same paper, the author provides their definition of slightly neglected part of empathy, e.g., positive empathy. By positive empathy the author understands our ability to respond to the negative and positive emotion of others with appropriate positive affect. In line with this proposal, another paper (Light et al.) presents a validation of a brief self-report measure of "positive-valence empathy". Apart from excellent psychometric properties, this measure appears to be a significantly better predictor of overall depressive symptomatology than anhedonia.

The study of Heym et al. examined the relationship between Dark Triad traits and distinct facets of empathy in a large sample (301 participant) from two UK University participant pools and *via* general online participation schemes. The authors addressed two main issues: (1) whether impaired empathy represents a common "dark core" binding Machiavellianism, narcissism, and psychopathy, and (2) this core explains associations between the dark traits and indirect relational aggression (IRA). The study results did not support the notion that an unempathic core may underpin all Dark Triade traits. The authors postulated that the Dark Triade traits are best viewed as three independent personality traits, rather than a joint (latent) dyad or triad core, at least in the prediction of these specific empathic deficits and indirect relational aggression.

Several papers in this Topic were focused on developmental aspects of empathy.

The review paper by Beadle and de la Vega considered age-related aspects of empathy. To summarize, across studies, there is little evidence that emotional empathy is lower in older than younger adults. However, older adults tend to show reduced performance and report lower levels of cognitive empathy. The authors also provide for a useful review of studies on neural bases of empathy in aging that showed (counterintuitively) reduced brain activation in older adults to tasks involving *both* cognitive and affective empathy.

Shapira et al.'s study examined genetic and environmental influences on children's emotion recognition, for the first time adding vocal to facial cues of emotion. The authors report shared environmental (rather than genetic) effect on emotion recognition abilities in this cohort.

Kanie et al. report results of social cognition and interaction training (SCIT) in a sample of patients with schizophrenia. SCIT was developed by Penn and colleagues, as a program for social cognitive rehabilitation in schizophrenia (11) The authors reported that the training proved feasible and was well tolerated by patients with schizophrenia in real-world outpatient settings. Statistical analysis showed a significant change in social cognitive outcome measure between the baseline and 3-month interim assessments, and also between the baseline and 6-month endpoint assessments, only in the SCIT but not in treatment as usual (TAU) group. However, the interaction between timepoint and group failed to reach significance, which suggested that the effect of SCIT was no different from that of TAU.

Sinval et al. present the results of a validation study of the Portuguese version of the Oldenburg Burnout Inventory (12). This version of OLBI is characterised by good internal validity and sex-invariance, therefore providing researchers with a useful free tool to measure burnout in Portuguese-speaking populations. Although, not directly examining empathy, this study gives a helpful reference for empathy researchers who investigate potential associations between empathy and burnout.

This Research Topic includes substantive original research that explores neural correlates of empathy among people with autism spectrum disorder (ASD) borderline personality disorder (BPD), conduct disorder (CD), eating disorders (ED), and posttraumatic stress disorder (PTSD) and comparative neurotypical control populations.

There are three studies that focus specifically on autism spectrum disorder (ASD) examining cognitive empathy, perspective taking, and interpersonal motivations. Findings from Komeda et al. suggest that individuals with ASD empathize with, and are more motivate to help, other people with ASD than neurotypical people. Whereas a study by Neufeld et al. found that, compared to neurotypical controls, the association between reward and mimicry is reduced in people with high autistic traits, and mimicry-related brain responses are less modulated by learned reward value in individuals with autism spectrum disorder. A third ASD study in this issue by Stroth et al. examined females with high functioning ASD and found they are able to share another person's physical or social pain on the neural systems level. However, female participants with ASD also have hypoactivation of the anterior insula when compared to neurotypical female subjects. The measurement of neural correlates provides objective measures and insight into neuro-cognitive empathy among people with ASD.

A study by Gaffney et al. which focused female participants with anorexia nervosa (AN) drew some analogies with ASD. They found lower cognitive empathy and intact affective empathy profiles among female participants with AN that are similar to that found in other psychiatric and neurodevelopmental conditions, such as autism spectrum disorder (ASD). These findings add to the literature characterizing the socio-emotional phenotype in eating disorders.

There are two neuroimaging studies that focused on borderline personality disorder (BPD). A study by Flasbeck et al. found that people with BPD showed less activation in the left supramarginal gyrus when viewing angry facial expressions compared to healthy controls. Flasbeck et al. also found differential activation of the left anterior insula among people with BPD in response to the emotional context of facial expressions. Thus, concluding that empathy for pain becomes selectively enhanced among people with BPD. Ducque-Alarcón et al. used fMRI to examine the influence of child abuse on the etiology and neurobiological substrates of BPD. They found hypoconnectivity between the structures responsible for emotion regulation and social cognitive responses in the frontolimbic circuitry (i.e., amygdala) among the BPD group. They concluded that there were differential levels of neural connectivity associated with the types and levels of abuse people had experienced. Another interesting neuroimaging study focused on neural basis of empathy in children and adolescents with early onset conduct disorder (CD). von Polier et al. studied the important role of the amygdala in empathy-related emotional processing among boys with CD. They noted that diminished amygdala responses and their association with low empathy and high callous unemotional traits suggest a pivotal influence of impaired amygdala processing in early-onset CD with notable deficits in empathic behavior. Their study found elevated response in the medial prefrontal cortex in boys with CD which point towards increased demands on self-referential processing to solve empathy tasks, and more cognitive biased processing strategies required for boys with early-onset CD.

The study by Levy et al. is timely in its focus on mothers exposed to wartime trauma who have posttraumatic stress disorder (PTSD). They found that chronic stress takes a toll on the mother's empathic ability and indirectly impacts the neural basis of empathy by disrupting the coherence of both brain and behavior. These findings have important implications for interventions that may not only address PTSD among women but may help address the long term or intergenerational impact of wartime trauma.

In conclusion, we believe that this Research Topic provides for an interesting collection of papers covering a wide variety of emotional, cognitive, and neurobiological processes involved in empathy. We hope this will give the readers useful guidance in their research of this fascinating phenomenon.

AUTHOR CONTRIBUTIONS

SS conceived the idea of the Research Topic, was involved in editing of submitted manuscripts and writing up the Editorial. DB-C was involved in editing of submitted manuscripts and writing up the Editorial.

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SYSTEMATIC REVIEW
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Cognitive and Affective Empathy in Eating Disorders: A Systematic Review and Meta-Analysis

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Background: Recent models of eating disorders (EDs) have proposed social and emotional difficulties as key factors in the development and maintenance of the illness. While a number of studies have demonstrated difficulties in theory of mind and emotion recognition, little is known about empathic abilities in those with EDs. Further, few studies have examined the cognitive-affective empathy profile in EDs. The aim of this systematic review and meta-analysis was to provide a synthesis of empathy studies in EDs, and examine whether those with EDs differ from healthy controls (HC) on self-reported total, cognitive, and affective empathy.

Methods: Electronic databases were systematically searched for studies using self-report measures of empathy in ED populations. In total, 17 studies were identified, 14 of which could be included in the total empathy meta-analysis. Eight of the 14 studies were included in the cognitive and affective empathy meta-analyses.

Results: Meta-analyses showed that while total empathy and affective empathy scores did not differ between those with anorexia nervosa (AN) and HC, those with AN had significantly lower cognitive empathy scores compared to HCs (small effect size). Meta-analyses of Interpersonal Reactivity Index sub-scores revealed that AN had significantly lower Fantasy scores than HC (small effect size), indicating that those with AN have more difficulty in identifying themselves with fictional characters. Only 3 studies examined empathy in those with bulimia nervosa (BN) or binge eating disorder (BED).

Conclusions: The lowered cognitive empathy and intact affective empathy profile found in AN is similar to that found in other psychiatric and neurodevelopmental conditions, such as autism spectrum disorder (ASD). These findings add to the literature characterizing the socio-emotional phenotype in EDs. Future research should examine the influence of comorbid psychopathology on empathy in EDs.

Keywords: empathy, eating disorders, anorexia nervosa, autism, self-report, insight

INTRODUCTION

Rationale

Empathy refers to our ability to understand and identify the mental states of others, as well as our ability to share the feelings of others (1). It is considered a key component of social cognition, cooperation, and prosocial behavior, as it allows us to make sense of and respond appropriately to other people's behavior (2). Empathy can be separated into two major facets. Cognitive empathy refers to the ability to recognize and understand another's mental state (part of theory of mind (ToM) or mentalising) while affective empathy is the ability to share the feelings of others, without any direct emotional stimulation to oneself (3). As an illustrative example, sharing the excitement of a close friend's job offer is fundamentally different from understanding that your friend must be having thoughts and feelings, and what these feelings might be. These two aspects of empathy rely on different brain structures and take different developmental pathways, with affective empathy developing much earlier than cognitive empathy (1).

Differences in empathic abilities have been observed in a number of psychiatric disorders including schizophrenia (4, 5), autism spectrum disorder [ASD; (6, 7)], borderline personality disorder [BPD; (8)], and depression (9). Importantly, far from there being a universal deficit in empathic abilities, research in these psychiatric disorders shows that there is often a difficulty in a specific aspect of empathy, while other empathic abilities remain intact. For example, it has been found that those with ASD have problems with cognitive empathy, but do not differ from neurotypical controls in affective empathy (10). Reduced attention to informative social information may provide one explanation for the problems in cognitive empathy seen in those with ASD. For example, it is reported that individuals with ASD pay less attention to faces, and especially eyes (11), and this is associated with poorer emotion recognition and ToM ability (12–14), as well as lower social competence (15). Similarly, while healthy controls (HCs) show significantly higher levels of cognitive empathy compared to affective empathy, those with BPD show significantly poorer cognitive empathy than HCs, and slightly increased levels of affective empathy (16). In bipolar disorder (BD), this cognitive/affective empathy distinction is further complicated by clinical state. In both manic and depressive phases of illness, there is an impairment in cognitive empathy compared to HCs. However, during the manic phase, affective empathy is significantly higher than in HCs and patients in the depression phase of BD, who did not differ from one another (17). Increased affective empathy in BPD and BD may be related to disturbances in emotion inhibition.

Recent models of eating disorders (EDs) have put forward social and emotional difficulties as key factors in the development and maintenance of the illness (18, 19). However, relatively little is known about the specific empathy profile in those with EDs. Based on longitudinal research in a community sample from Sweden, Gillberg et al. published a number of papers reporting a subgroup of AN patients with "empathy disorders"—those that had severe problems in social understanding and communication, consistent with ASD (20). Poorer outcomes were found in this group (21, 22). Since then, a growing body of evidence has documented overlap between symptoms in ASD and AN. For example, both groups show high levels of social anxiety (23, 24) and alexithymia (25, 26), differences in social attention (11, 27, 28), and poorer emotion recognition (29, 30) and ToM ability (31, 32). Reduced social networks have been documented in AN and bulimia nervosa (BN) (33, 34), as well as difficulties in understanding the concept of friendship (35). It is possible that reduced empathic abilities, along with communication difficulties, may contribute to the diminished social networks and isolation that characterize EDs. Given that interpersonal difficulties are associated with more severe ED psychopathology (36, 37), understanding mechanisms that may contribute to these problems may be helpful in improving outcomes in those with these EDs.

Objectives

The aim of this systematic review and meta-analysis is to provide a synthesis of empathy research in EDs. Previous reviews on social processes in EDs have ascribed relatively little attention to the topic, and focus on emotion recognition rather than other aspects of empathy such as affect sharing [e.g., (31)]. In addition, new studies have been published in the intervening years. An additional aim is to examine potential differences between those with EDs and HCs in the specific types of empathy (self-reported cognitive and affective empathy), to permit better comparisons with other psychiatric populations. Self-reported empathy measures will be the focus of this review, in order to elicit patients' views and self-assessment of their skills.

Research Questions

The research questions are as follows: (1) do levels of self-reported empathy differ in those with EDs compared to HCs? (2) do levels of cognitive and affective empathy differ between EDs and HCs? (3) are empathy levels associated with any psychopathological or clinical variables?

METHODS

Systematic Review Protocol

The review and meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (38).

Eligibility Criteria

Studies using a self-report measure of empathy were included. Inclusion criteria were: (1) means and standard deviations reported for empathy scores in at least one clinical ED group and a HC group (2) the clinical ED group met criteria for any ED diagnosis, according to DSM or ICD criteria (3) full article available in English (4) published in a peer reviewed journal. Articles that examined disordered eating samples rather than a clinical ED were not included.

Data Sources and Search Strategy

The electronic databases SCOPUS, Web of Science, PsycInfo, and PubMed were searched for papers up to September 2018. The following search terms were used: anorexia nervosa OR bulimia nervosa OR eating disorder AND empathy OR emotional empathy OR empathic concern OR interpersonal reactivity. No other search limits were applied, with the exception of Web of Science, where results were filtered by the ED term for relevance. Reference lists were also searched for relevant papers.

Study Selection

The selection process for studies is displayed in **Figure 1**. In total, the search generated 644 records. After removing duplicates, 122 records were assessed for relevance based on article titles. If titles were ambiguous or potentially relevant, records were retained and their abstracts screened against the eligibility criteria. This resulted in 61 abstracts being screened, 19 of which were excluded as they did not meet eligibility criteria. After screening of abstracts, 42 potentially eligible full-text articles were identified. One study included a sample of participants with BN, however at the time of publication, BN was not yet included in the DSM. The study was included in the review as participants had a clinical diagnosis of BN. If means and standard deviations for individual groups were not reported, study authors were contacted. If no response was received, studies were excluded. Evaluation of these full texts resulted in 25 studies being excluded, and 17 studies being included in the review.

Data Extraction

The following data was extracted from each paper that met all eligibility criteria: number of participants in each group, mean age, mean body mass index (BMI), percentage of female participants, empathy measure used, mean empathy scores, and any subscale scores, if they were reported. Where studies reported sub-scale scores only, total, cognitive, and affective empathy scores were calculated so that studies could be included in meta-analyses.

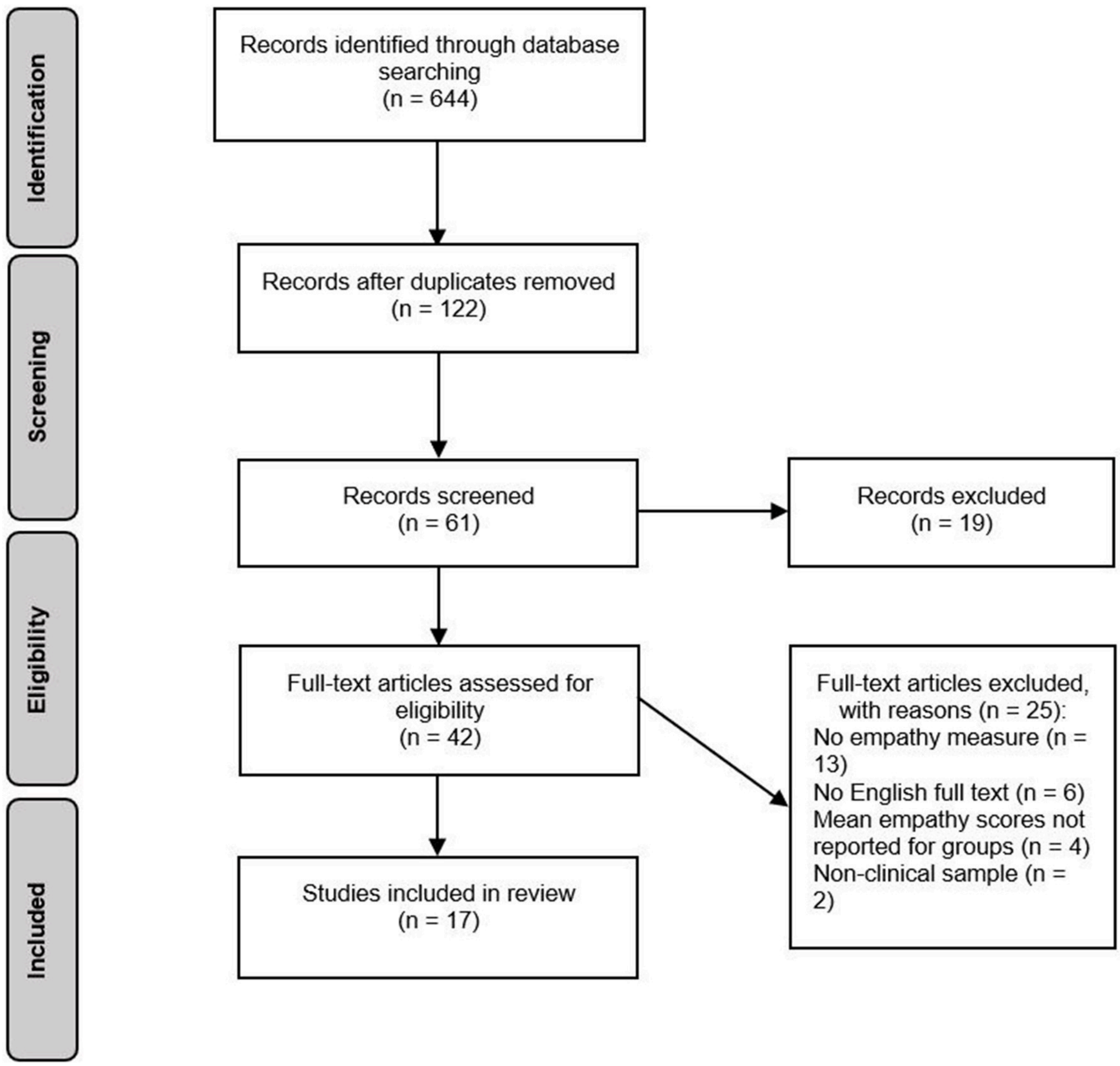

FIGURE 1 | Systematic review search process.

TABLE 1 | Characteristics of studies.

References	Group	Mean age (SD)	Mean BMI (SD)	% female	Empathy measure	Mean (SD) total empathy	Subscales reported?	
							Mean (*SD*) cognitive empathy	Mean (*SD*) affective empathy
Adenzato et al. (45)	30 AN	19.73 (6.06)	15.06 (1.74)	100	EQ	**44.17 (11.47)**	NR	NR
	32 HC	20.47 (2.72)	20.21 (1.45)	100		**50.72 (8.35)**		
Aloi et al. (46)	22 BED	43.8 (10.7)	36.9 (4.2)	81.4	EQ	41.8 (14.9)	NR	NR
	16 sub-threshold BED	42.5 (11.3)	37.5 (4.5)	68.8		50.5 (11.6)		
	20 obese controls	50.6 (8.6)	38.2 (6.5)	45		50.1 (12.4)		
Baron Cohen et al. (47)	66 AN	17.85 (0.39)	NR	100	EQ (adult and adolescent versions)†	**Younger: 44.7 (16.4)** Older: 49.6 (9.7)	NR	NR
	1609 HC	18.56 (3.99)	NR	100		**Younger: 51.2 (14.3)** Older: 48.0 (11.3)		
Butler and Montgomery (48)	15 AN	27.9 (9.9)	NR	100	I_7	15.40 (2.61)	NA	NA
	16 HC	28.4 (8.3)	22.75	100		14.19 (2.74)		
Calderoni et al. (49)	32 AN	14.78 (1.75)	15.07 (1.54)	100	IRI	*5.13 (6.98)*	**0.44 (6.87)**	4.69 (7.08)
	41 HC	14.02 (1.69)	NR	100		*9.44 (5.66)*	**5.24 (6.45)**	4.20 (4.75)
Courty et al. (50)	15 AN	23.9 (4.7)	16.4 (1.7)	93.33	EQ-short	23.0 (6.8)	NR	NR
					IRI	*70.8 (4.83)*	*34.1 (4.85)*	*36.7 (4.8)*
	15 HC	24.0 (4.9)	21.0 (1.8)	93.33	EQ-short	21.1 (7.4)	NR	NR
					IRI	*73.09 (3.79)*	*38.3 (3.31)*	*35.6 (4.22)*
	15 ASD	28.1 (7.5)	23.2 (5.0)	13.33	EQ-short	10.1 (5.7)	NR	NR
					IRI	*65.5 (4.77)*	*32.6 (4.73)*	*32.9 (4.81)*
	15 HC	28.1 (7.3)	22.2 (3.0)	13.33	EQ-short	19.9(3.4)	NR	NR
					IRI	*67.0 (3.39)*	*34.7 (2.75)*	*32.3 (3.93)*
Duchesne et al. (51)	60 BED	NR	38.1	100	IRI	*81.4 (4.04)*	*42.4 (4.40)*	*39.0 (3.65)*
	60 obese controls	NR	37.9	100		*81.3 (3.95)*	*42.7 (3.36)*	*38.6 (4.46)*
	54 HC	NR	21.4 (1.6)	100		*80.6 (4.02)*	*43.4 (4.30)*	*37.2 (3.72)*
Feldman and Eysenck (52)	45 BN	25.13 (6.59)	NR	100	I_7	14.73 (3.17)	NA	NA
	761 HC	NR	NR	100		14.39 (2.87)		
Gramaglia et al. (53)	39 AN	30.59 (3.0)	16.3	NR	IRI	*82.93 (3.81)*	*41.19 (4.48)*	*41.74 (2.99)*
	48 HC	33.19 (3.37)	21.82	100		*80.48 (3.78)*	*41.9 (4.15)*	*38.58 (3.37)*
Guttman and Laporte (54)	28 AN	22	NR	100	IRI	*72.7 (5.60)*	*35.1 (5.51)*	*37.6 (5.69)*
	26 BPD	32	NR	100		*78.9 (5.45)*	*34.7 (5.56)*	*44.2 (5.35)*
	27 HC	21	NR	100		*71.9 (4.83)*	*35.9 (4.61)*	*36 (5.04)*
Hambrook et al. (55)	22 AN	26.73 (4.77)	15.27 (1.22)	100	EQ	45.9 (12.5)	NR	NR
	45 HC	32.51 (9.63)	23.36 (3.76)	100		46.2 (11.1)		
Jermakow and Brzezicka (56)	11 AN	26.80 (4.3)	NR	100	EQ	44.60 (8.58)	NR	NR
					IRI	**63.10 (3.39)**	*34.9 (6.22)*	*28.2 (4.46)*
	33 female HC	21.33 (1.4)	NR	100	EQ	42.42 (9.84)	NR	NR

(Continued)

TABLE 1 | Continued

References	Group	Mean age (SD)	Mean BMI (SD)	% female	Empathy measure	Mean (SD) total empathy	Subscales reported?	
							Mean (*SD*) cognitive empathy	Mean (*SD*) affective empathy
					IRI	**70.03 (2.13)**	*38.52 (4.40)*	*31.52 (4.40)*
	10 ASD	28.30 (9.5)	NR	0	EQ	30.00 (5.05)	NR	NR
					IRI	57.90 (2.20)	*33.5 (5.59)*	*24.4 (3.64)*
	27 male HC	21.76 (2.0)	NR	0	EQ	32.63 (9.97)	NR	NR
					IRI	62.70 (2.33)	*33.38 (5.60)*	*29.33 (5.21)*
Lule et al. (57)	15 AN	16.2 (1.26)	17.07 (1.44)	100	IRI	121.14 (11.25)	NR	NR
	15 HC	16.5 (1.09)	21.06 (1.57)	100		118.50 (10.20)		
Morris et al. (58)	28 AN	26.3 (7.9)	15.5 (1.3)	100	SEQ	**18.8 (2.5)**	NA	NA
	25 AN-REC	29.5 (9.2)	20.1 (1.9)	100		19.8 (3.0)		
	54 HC	29.4 (9.6)	23.1 (3.9)	100		**20.4 (2.4)**		
Nandrino et al. (59)	23 AN	19.64 (1.82)	15.2 (1.07)	100	BES	79.57 (6.70)	35.57 (3.45)	44.00 (5.44)
	23 HC	20.65 (1.90)	21.05 (1.78)	100		80.78 (6.04)	36.78 (3.19)	44.00 (4.93)
Peres et al. (60)	41 AN	16.2 (1.4)	79.78 (8.71) %IBW	100	IRI	*74.44 (4.30)*	35.5 (6.99)	**39.0 (6.45)**
	38 HC	15.84 (1.83)	100.5 (11.71) %IBW	100		*73.1 (4.1)*	37.6 (7.18)	**35.6 (5.21)**
Redondo and Herrero-Fernandez(61)	38 AN	21.9 (5.30)	NR	100	EQ-short	23.42 (7.25)	11.26 (4.84)	7.11 (2.68)
					IRI††	NR	NR	NR
	321 HC	NR	NR	100	EQ-short	25.79 (7.21)	11.03 (4.63)	7.55 (2.35)
					IRI††	NR	NR	NR

Significant differences between ED and HCs are indicated in bold. Italics indicate where scores were not reported in the study, but could be calculated from subscale scores. Potential significant differences could therefore not be reported for calculated scores. AN, anorexia nervosa; AN-REC, recovered anorexia nervosa; ASD, autism spectrum disorder; BED, binge eating disorder; BES, Basic Empathy Scale; BMI, body mass index; BN, bulimia nervosa; BPD, borderline personality disorder; EQ, Empathy Quotient; HC, healthy control; I_7, Impulsiveness, Venturesomeness, and Empathy questionnaire; IRI, interpersonal reactivity index; NA, not applicable; NR, not reported; SD, standard deviation; SEQ, Socio-Emotional Questionnaire.

†*Groups were split into groups depending on age and EQ version used.*

††*Only the PT subscale of the IRI was used.*

Data Analysis

All analyses were performed using R Studio (39) using the metafor package (40). Cohen's d was used to estimate effect sizes and is reported with 95% confidence intervals (CIs). Effect sizes are interpreted using Cohen's (41) definitions of small (0.2), medium (0.5), and large (0.8). Negative effect sizes indicate lower empathy scores in the ED group compared to HC. Separate meta-analyses were performed for different components of empathy. Where two measures of empathy were used in the same study (and therefore on the same group of participants), a multivariate meta-analysis was performed using the rma.mv command. Between-study heterogeneity was calculated using Cochran's Q test. Where heterogeneity was found ($p < 0.05$), meta-regressions were performed using age and empathy measure as moderators.

Risk of Bias

Publication bias was assessed through visual inspection of funnel plots, where the absence of studies in the bottom right corner indicates publication bias. The symmetry of the funnel plots was formally assessed using Begg's rank correlation test (42). Publication bias was also assessed using Rosenthal's fail-safe N (43), which estimates the number of unpublished studies required to change the significant effect size into a non-significant one.

Risk of bias in individual studies was assessed using the Clinical Appraisal Skills Programme checklist for case–control studies (44). The checklist considers how methodological features of studies may have impacted the results, e.g., exclusion and inclusion criteria, recruitment sources, and whether potential confounding variables were included in analyses. Studies can receive a maximum score of 17.

RESULTS

Study Characteristics

Study characteristics are shown in **Table 1**. Fourteen of the included studies compared AN and HC groups. Of these studies, one study also included a recovered AN group, two included an ASD group, and one included a group with BPD. Two studies compared those with binge eating disorder (BED) to HC, and one study compared participants with BN to HC.

In total, 6 different self-report measures were used across studies, with the Interpersonal Reactivity Index [IRI; (62)] being used most often (9 studies). The IRI comprises of four subscales: perspective taking (PT; the tendency to spontaneously adopt the psychological viewpoint of others), fantasy (FS; the tendency to identify oneself with fictional characters in books, plays and movies), empathic concern (EC; assesses "other-oriented" feelings of sympathy and concern for others), and personal distress (PD; assesses "self-oriented" feelings of anxiety and unease in tense interpersonal settings). Cognitive and affective empathy scores can be calculated by taking the sum of PT and FS, and EC and PD respectively. The Empathy Quotient [EQ; (6)], and the EQ-short (63) were used in seven studies, and both have three subscales: cognitive empathy, affective empathy, and social skills. Other measures used were: the empathy subscale of the Impulsiveness, Venturesomeness, and Empathy questionnaire (I_7; (64) (2 studies), the empathy subscale of the Socio-Emotional Questionnaire [SEQ; (65)] (1 study), and the Basic Empathy Scale [BES; (66)] (1 study). One study used two different versions of the EQ depending on participants' age; the parent reported version for younger adolescents, and the self-report version for older adolescents (47). Only the self-report scores are included in the meta-analysis, as this was the focus of the present review.

Methodological quality of the studies varied considerably (range: 7–16). None of the studies reported a power calculation, and sample sizes were generally small (ranging from 11 to 66 in ED groups). All but one study (46) matched participants on at least one characteristic, most often sex. The mean age of participants ranged from 14.02 to 50.60 years, although three studies did not report the mean age of at least one participant group (51, 52, 61). Seven studies did not report mean BMI or percentage IBW in at least one participant group (47–49, 52, 54, 56, 61). Most studies used exclusively female samples, however three studies included male participants (46, 50, 56).

Synthesized Findings

Only studies comparing AN and HC could be included in meta-analyses, due to too few studies with other ED groups (2 BED, 1 BN). The number of studies in each meta-analysis is displayed in **Figure 2**.

Total Empathy

Fourteen studies were included in a meta-analysis comparing total empathy scores in AN and HCs. The random effects model with a total sample size of 2165 participants (AN = 379, HC =

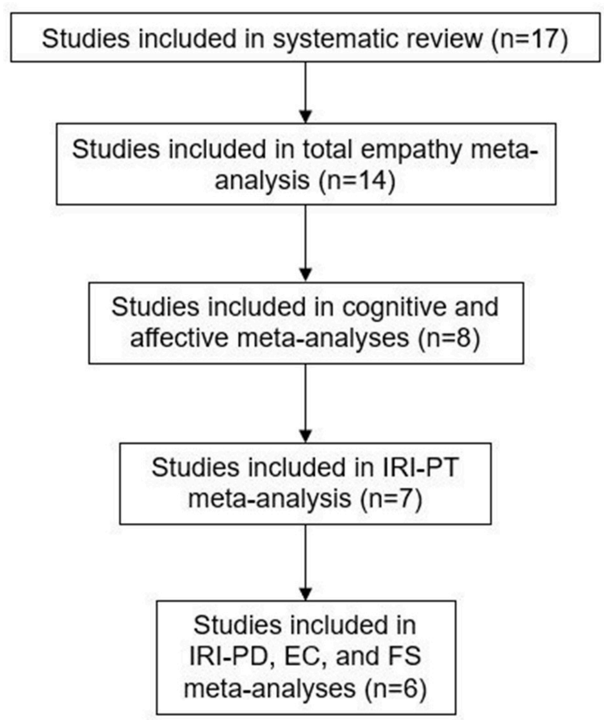

FIGURE 2 | Studies included in the review and meta-analyses.

1746) revealed that total empathy scores in AN did not differ from those of HCs [$d = -0.11$, (95% CI −0.36, 0.13) $z = -0.92$, $p = 0.36$] (**Figure 3**).

There was evidence of significant heterogeneity across studies [$Q_{(15)} = 79.61$, $p < 0.001$], therefore meta-regressions with age and empathy measure as moderator variables were performed. The moderators explained a significant amount of the variance [$QM_{(6)} = 27.88$, $p = < 0.001$], however no single factor had a significant influence on the size of the effect. The test for residual heterogeneity was significant [$QE_{(8)} = 65.08$, $p = < 0.001$].

Cognitive Empathy

Eight studies were included in a meta-analysis comparing cognitive empathy scores in AN and HC. The random effects model with at total sample size of 773 participants (AN = 227, HC = 546) revealed that cognitive empathy scores in AN were significantly lower than HCs [$d = -0.34$, (95% CI −0.58, −0.11) $z = -2.86$, $p = 0.004$] (**Figure 4**). There was no evidence of significant heterogeneity [$Q_{(7)} = 12.27$, $p = 0.09$].

Affective Empathy

Eight studies were included in a meta-analysis comparing affective empathy scores in AN and HC. The random effects model with a total sample size of 773 participants (AN = 227, HC = 546) revealed that affective empathy scores in AN did not differ from those of HCs [$d = 0.18$, (95% CI −0.17, 0.52) $z = 1.01$, $p = 0.31$] (**Figure 5**).

There was evidence of significant heterogeneity across studies [$Q_{(7)} = 26.99$, $p < 0.001$], therefore meta-regressions with age and empathy measure as moderator variables were performed. The moderators did not explain a significant amount of the variance [$QM_{(3)} = 0.64$, $p = 0.88$], and the test for residual heterogeneity was significant [$Q_{(4)} = 17.6$, $p = 0.002$].

Risk of Bias

The funnel plots for total empathy, cognitive empathy, and affective empathy scores are displayed in **Figures 6–8**. There was no evidence of publication bias in the total empathy meta-analysis (Begg's test $p = 0.45$), however there was evidence of publication bias in the studies included in the cognitive empathy meta-analysis (Begg's test $p = 0.03$, Rosenthal's fail safe $N = 38$). Studies included in the affective empathy meta-analysis did not show any evidence of publication bias (Begg's test $p = 0.40$).

Additional Analyses

Because several studies reported on the PT, FS, EC, and PD subscales of the IRI, additional meta-analyses were performed to test for differences between AN and HC. Six studies reported scores for all four subscales, while one additional study reported PT scores only. The results are shown in **Table 2**. AN had significantly lower FS scores compared to HC, however there were no significant differences in the other sub-scales. There was no evidence of significant heterogeneity in any of the subscale meta-analyses, nor was there significant evidence of publication bias (Begg's test all $p > 0.05$) (see **Supplementary Material** for subscale forest and funnel plots).

Qualitative Findings

Studies in AN

Studies using the EQ or the EQ-short reported very mixed findings. Adenzato et al. (45) found that those with AN had significantly lower total EQ scores compared to HCs. In adolescents, this was only found to be true for those aged 12–15years, using the parent report version of the EQ (47). The older AN group did not differ from age-matched HC on the self-report EQ. Redondo and Herrero-Fernández (61) found that while total EQ-short scores in those with AN and HCs did not differ, those with AN scored significantly lower than HCs on the social skills subscale. Three studies found no differences in EQ scores between AN and HC, however both groups scored significantly higher than those with ASD (50, 55, 56).

Results from studies using the IRI were similarly mixed. Only two studies tested for group differences in total IRI scores, with one reporting significantly lower scores in those with AN than HCs (56) and the other reporting no differences (57). Two studies tested for group differences in cognitive and affective empathy sub-scores of the IRI. Cognitive empathy scores are calculated by summing the F and PT subscale scores together, while the EC and PD subscale scores are summed to calculate affective empathy scores. Calderoni et al. (49) found that those with AN had significantly lower cognitive empathy scores, whereas Peres et al. (60) reported significantly higher emotional empathy scores in AN compared to HC.

Six studies reported on group differences between AN and HCs on IRI EC, PD, FS, and PT (with one additional study included the PT subscale only). Regarding EC, there were no significant differences between AN and HC across all six studies (49, 50, 53, 54, 56, 60). However, those with AN had significantly higher EC scores compared to those with ASD (50), and significantly lower scores than women with BPD (54). Two studies found that those with AN scored higher on PD than HC (53, 60), while one reported that AN and ASD groups had lower scores than HCs (56). Three studies reported no differences in PD scores between AN and HC, however those with BPD had higher scores than both AN and HC groups (49, 50, 54). Regarding the FS subscale, it was found that those with AN had significantly lower scores than HC, similar to those with ASD (49, 50). However, four studies did not find significant differences between groups (53, 54, 56, 60). Calderoni et al. (49) and Redondo and Herrero-Fernandez (61) reported that AN had significantly lower PT scores compared to HCs, however the remaining five studies found no significant differences (50, 53, 54, 56, 60).

The remaining AN studies used the I_7, the empathy subscale of the SEQ, and the BES. Morris et al. (58) found that AN scored significantly lower on the SEQ than HC. Scores in the recovered AN group did not differ from either group, lying between the two. The remaining two studies found no significant differences between AN and HCs (48, 59). However, both studies were limited in their sample sizes (15 and 23 participants in the clinical groups respectively), and therefore there may not be sufficient power to detect group differences.

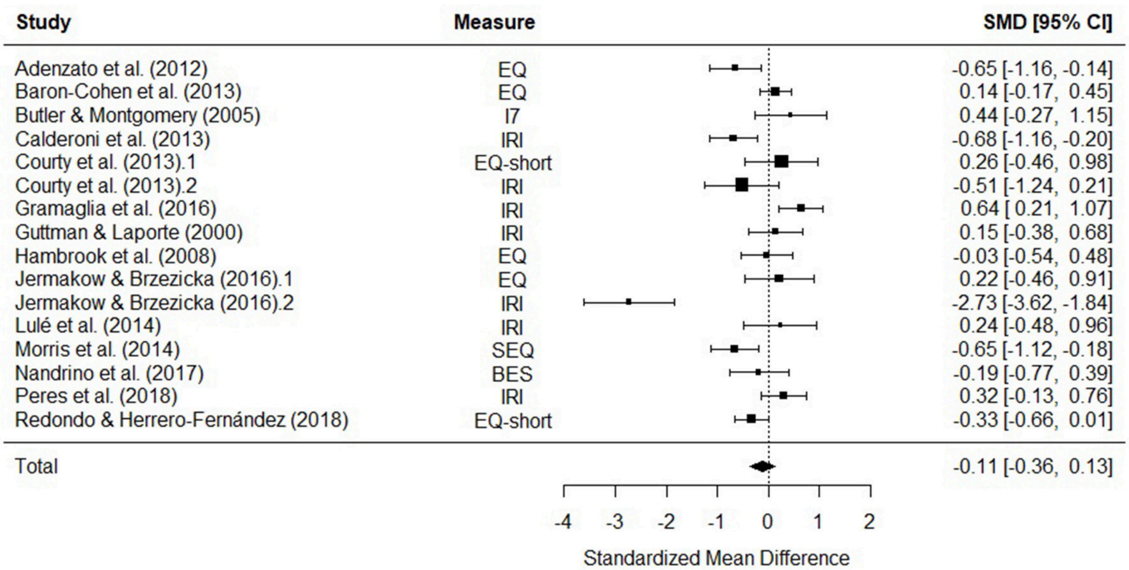

FIGURE 3 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on total empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; I_7, Impulsiveness, Venturesomeness, and Empathy questionnaire; IRI, interpersonal reactivity index; SEQ, Socio-Emotional Questionnaire.

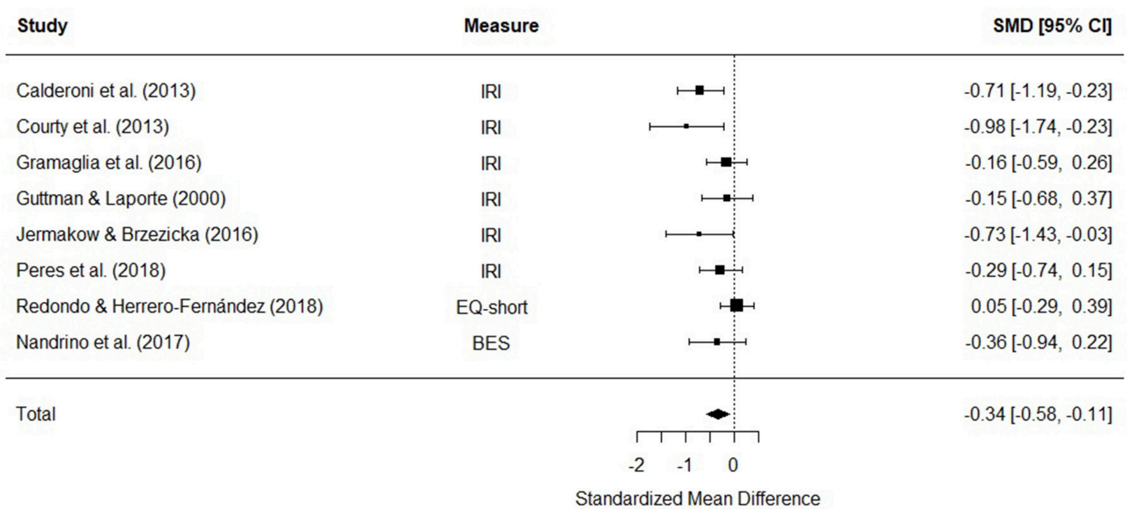

FIGURE 4 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on cognitive empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; IRI, interpersonal reactivity index.

Studies in Other EDs

Only three studies involved participants with BED or BN. Feldman and Eysenck (52) reported no differences in empathy scores between women with BN and HCs. However, this study had the poorest methodological quality rating of all studies include in the review, mainly because it included little information about the HC group, and did not control for any confounding variables. In BED, total empathy scores did not significantly differ across those with BED, subthreshold BED, and HCs (46). However, 51 reported that women with BED scored significantly higher than obese and HC women on the PD subscale of the IRI. Further, a logistic regression revealed that lower PT and higher PD scores were associated with BED. Unfortunately, this study did not control for confounding variables such as depression, which has been found to be associated with PD (9).

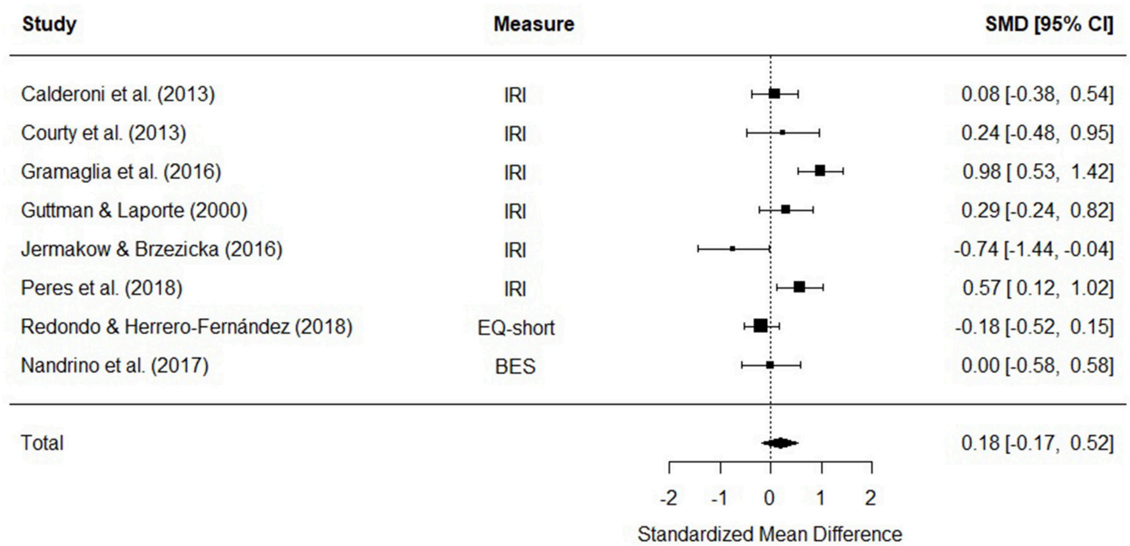

FIGURE 5 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on affective empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; IRI, interpersonal reactivity index.

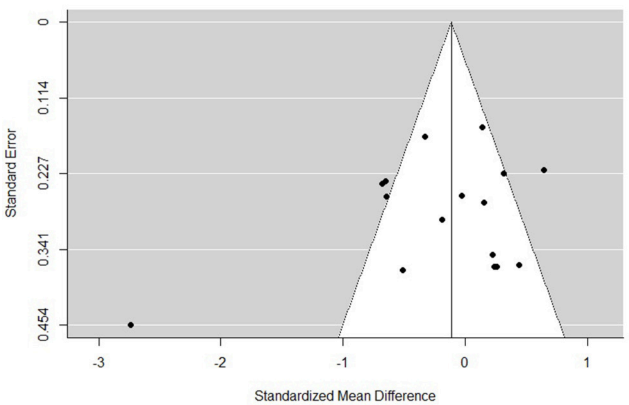

FIGURE 6 | Funnel plot of studies included in the total empathy meta-analysis.

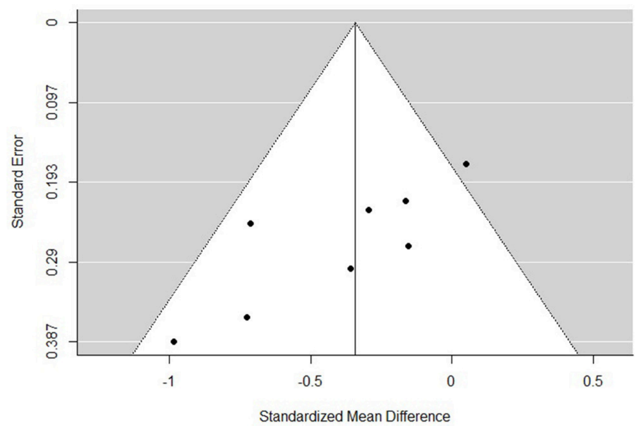

FIGURE 7 | Funnel plot of studies included in the cognitive empathy meta-analysis.

Associations With Psychopathology and Clinical Variables

Few studies examined associations between empathy and clinical variables or other measures of psychopathology. In BED and AN, negative correlations were found between EQ and alexithymia scores on the twenty-item Toronto Alexithymia Scale [TAS-20; (67)], such that lower levels of empathy were associated with higher alexithymia (45, 46). The latter study also found that higher EQ scores were associated with more social support in AN, as measured by the Multidimensional Scale of Perceived Social Support [MSPSS; (68)]. Only two studies examined whether empathy was associated with ED psychopathology and illness severity in AN. Baron-Cohen et al. (47) reported that EQ scores were not associated with scores on the Eating Disorder Examination Questionnaire [EDEQ; (69)], and Calderoni et al. (49) found that cognitive empathy scores were not associated with BMI, disease duration, or general psychopathology in AN. Finally, Peres et al. (60) reported that IRI, AE and PD subscale scores were positively associated with anxiety, but not depression, as measured by the Hospital Anxiety and Depression Scale [HADS; (70)]. However, linear regressions revealed that anxiety did not explain the differences in empathy between AN and HC better than group membership.

DISCUSSION

Summary of Main Findings

The aim of this review was to examine group differences in empathy in those with EDs compared to HC, and provide a

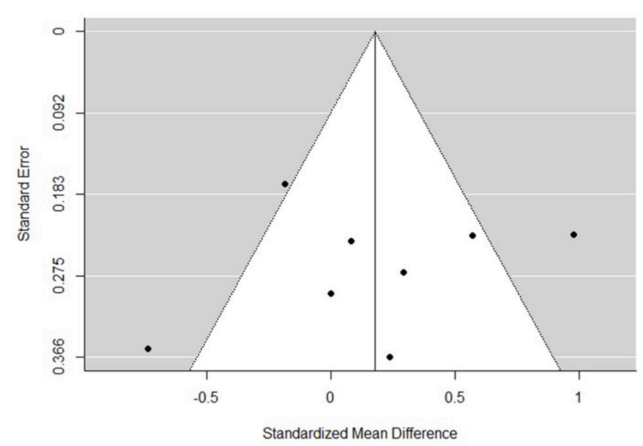

FIGURE 8 | Funnel plot of studies included in the total affective meta-analysis.

qualitative synthesis of the literature. Meta-analyses were run for total empathy, cognitive empathy, affective empathy, and four further sub-components of empathy: PT, FS, EC, and PD. There were no significant differences between those with AN and HC in overall empathy (14 studies) or affective empathy scores (8 studies). However, it was found that those with AN had significantly lower cognitive empathy scores compared to HC (8 studies), with a small effect size. Further, it those with AN had significantly lower FS scores than HC (6 studies), with a small effect size, but did not significantly differ from HC on any of the other IRI subscores.

The finding that AN have lower cognitive empathy abilities compared to HC is in accordance with studies examining related, performance-based measures of empathy, such as ToM (32), emotion recognition (31), and emotional intelligence (71). Affective empathy has been less well-studied in EDs, although it appears from this review, and a few experimental studies, that individuals with ED are not impaired in affective empathy. For example, one study found that those with BN reported higher levels of sadness than restrained eaters and HCs in response to video clip, during which they were asked to identify themselves with the protagonist whose boyfriend leaves them for an attractive woman (72). Another study examined individuals' own emotional reactions to video clips depicting an individual displaying emotion, finding that the intensity of the emotions experienced by those with EDs (AN and BN) did not differ from HC (73). However, those with EDs did show less facial expressivity while watching the clips—a component of empathy that has been termed "motor empathy" (74). Studies that utilize physiological measurements of empathy, such as facial electromyographic activity (EMG), skin conductance, and heart rate may be useful in further understanding affective empathy in EDs.

There are a number of possible explanations for the dissociation between cognitive and affective empathic abilities found here. Distinct brain systems for cognitive and affective empathy have been described: the ventromedial prefrontal cortex is involved in cognitive empathy, while the inferior frontal gyrus is involved in affective empathy (75). Neuroimaging studies have reported differences in the ventromedial prefrontal cortex in those with AN (76, 77), thus providing a possible explanation for lowered cognitive empathy abilities. fMRI studies utilizing performance-based measures of empathy could be useful in testing this hypothesis. Relatedly, difficulties in executive functioning are reported in those with AN and BN (78). Since executive functions contribute to the development of cognitive empathy (79), it would be of interest to determine whether there is a relation between empathy abilities and executive functioning in those with EDs. Relatedly, it might be that reduced attention to faces and eyes found in AN (28, 80, 81) leads to decreased cognitive empathy abilities.

There was evidence of significant heterogeneity in the overall empathy and affective empathy studies. While age and empathy measurement did explain some of the variance in total empathy scores, no single factor had a significant influence on the size of the effect. Due to a lack of studies reporting on factors such as BMI and illness duration, it was not possible to include these indicators of illness severity as moderators. The two studies that did examine potential associations between ED severity and empathy did not find any significant relationships (47, 49). Research examining the relationship between illness severity and constructs related to empathy such as mentalizing (the ability to understand the mental states of oneself or others, and how such states might influence behavior) have been mixed. While some have reported independence from BMI and illness length (82), a meta-analysis found that poorer performance on the RMET was associated with longer illness duration (83). Examining whether cognitive or affective empathy are state or trait variables will be important in characterizing the socio-emotional phenotype proposed for EDs (84).

Relatedly, it would be of interest to examine whether other psychopathological variables may have influenced the effect sizes reported in this review. One candidate is ASD symptoms. Support for this idea comes from a longitudinal population-based study which examined mentalizing abilities in those with AN and HCs (21), in which 29% of the AN group also met criteria for a diagnosis of ASD. They found that when mentalizing ability was compared between AN+ASD, AN only, and HCs, only the AN+ASD group had significantly lower scores than HC. Thus, it is possible that there is a sub-group of individuals with AN who display the most severe difficulties in socio-emotional measures, whose difficulties are missed when assessing group differences. While ASD symptoms could not be included as moderators in the meta-analyses presented here, it would be important to ascertain whether reduced empathy in AN is a characteristic of the ED, or some other comorbid psychopathology.

Alternatively, it could be the case that the heterogenous results in AN might be explained by alexithymia. Indeed, a few studies included in this review found that lower levels of empathy in AN and BED were associated with higher alexithymia (45, 46). Alexithymia is a subclinical phenomenon characterized by difficulties in describing and recognizing one's own emotions, and distinguishing feelings from bodily sensations of emotional arousal. "Shared network" models of empathy propose that the networks in the brain responsible for processing one's own

TABLE 2 | Statistical outcomes for meta-analyses of the four IRI subscales.

IRI subscale	N studies	Pooled AN sample N	Pooled HC sample N	Cohen's *d*	95% CI	*Z*	*p*
Perspective taking	7	204	523	−0.2	−0.44, 0.05	−1.59	0.11
Fantasy	6	166	202	**−0.41**	−0.62, −0.20	3.83	**>0.001**
Empathic concern	6	166	202	0.01	−0.20, 0.22	1.1	0.92
Personal distress	6	166	202	0.3	−0.13, 0.74	1.36	0.17

Significant differences between AN and HCs are indicated in bold. AN, anorexia nervosa; CI, confidence intervals; HC, healthy control; IRI, Interpersonal Reactivity Index.

emotions are the same networks used to represent the emotions of others (85–87). Thus, it is possible that the high levels of alexithymia experienced by those with AN might be responsible for lower levels of empathy compared to HCs. In support of this hypothesis, an fMRI study in ASD showed that the strength of empathic brain responses in the left anterior insula were predictive of degree of alexithymia in both ASD and HCs, but did not vary as a function of group (88). The potential contribution of alexithymia to reduced empathy, and indeed other aspects of socio-emotional functioning in EDs, should be explored.

Only two studies examined empathy in BED, finding no difference in total empathy scores, but significantly higher PD scores compared to HCs (46, 51). The finding that those with BED experience more stress and unease in tense social settings is consistent with literature documenting emotion regulation difficulties in those with BED, and it is hypothesized that binge eating may be a strategy to deal with increased negative emotions (89). It would therefore be of interest to examine whether higher PD scores in BED are associated with more severe ED psychopathology. The only study that measured empathy in BN found no significant differences in empathy compared to HCs (52). This study used the I_7 to measure empathy, and therefore no study has yet examined cognitive and affective components of empathy in BN. Clearly, the lack of studies in BN and BED prevent any conclusions being made regarding empathy in these groups. Given that problems with interpersonal functioning are a prominent feature in BN (18, 90), research using multidimensional measures of empathy in this population are needed.

The findings from the current review have implications for treatment of AN. Socio-communicative and interpersonal problems are associated with poorer outcomes (20, 21, 82, 91, 92) and more severe ED psychopathology (36, 37), therefore socio-emotional functioning may be a potential target for the development of new, more holistic treatment approaches. For example, group social skills interventions are effective in improving communication, social anxiety, and social functioning in those with ASD (93, 94). There is also evidence to suggest that Cognitive Remediation and Emotion Skills Training (CREST), an intervention designed to improve emotion processing, is effective in decreasing alexithymia and social anhedonia, while increasing motivation in those with AN (95, 96). Recently, there has also been interest in exploring the effect of oxytocin, a hormone implicated in prosocial behavior, on socio-emotional functioning (97, 98). In ASD, administration of intranasal oxytocin has been found to increase interactions with socially cooperative peers, and enhance feelings of trust (99). Oxytocin also increased participants' attention to the eyes of pictures of faces, avoidance of which is a core feature of ASD (100). A few studies have examined the effect of oxytocin on socio-emotional cognition in those with EDs. One study found intranasal oxytocin increased emotion recognition and decreased calorie consumption in those with BN, however no effects were seen in AN (101). Another found no effect of oxytocin on RMET performance in AN (102). However, whether oxytocin has an effect on real-life social behavior in those with EDs has yet to be examined.

Limitations

Several limitations of this review should be noted. Firstly, many studies did not report empathy subscale scores, and therefore could not be included in affective and cognitive empathy meta-analyses. Secondly, although this method has been employed in previous reviews of this type (103, 104), it could be questioned whether it is appropriate to compare different scales that purport to measure the same empathy constructs. For example, the affective subscales of the IRI have been criticized as more closely reflecting sympathy, as they focus on reactions to others, rather than emotion matching (105). However, studies in this review generally included the most widely used measures of empathy (e.g., the EQ and the IRI), and as previously noted, empathy measure did not significantly influence effect sizes in moderator analyses.

It is also important to note the limitations of self-report empathy measures generally. Socially desirable responding may be an issue with self-report measures, as they do not objectively measure empathic abilities, but rather how empathetic individuals perceive themselves to be. In other psychiatric disorders, a discrepancy between performance-based empathy tasks and self-report measures has been reported. For example, a meta-analysis found that people with schizophrenia display greater affective empathy deficits in performance-based tasks than on self-report measures (103). If affective empathy partly relies on one's ability to report on their own emotional reactions, this might be especially difficult in populations with high levels of alexithymia, such as AN (106).

The number of studies in other EDs, such as BN and BED, was greatly lacking. Therefore, meta-analyses for group differences between these groups and HCs could not be carried out. Furthermore, only three studies included males with EDs, thus the results from this review cannot be generalized to this population. Interestingly, it is reported that while males with EDs (AN, BN, or eating disorder not otherwise specified) show the same difficulties in cognitive flexibility and weak central coherence often found in women with EDs, they do not differ from HC men in terms of ToM performance or sensitivity to social threat (107). Future work should therefore examine performance in a broader range of socio-emotional tasks in order to understand possible similarities and differences in the male and female presentations of EDs.

Finally, there was evidence of publication bias in the cognitive empathy meta-analysis, indicating that studies with non-significant results may have been missing from analyses. However, the fact that the affective empathy meta-analysis, which included the same studies as the cognitive meta-analysis, did not show any evidence of publication bias and showed a non-significant result, perhaps lends support to the validity of our findings. Nonetheless, the results should be interpreted with caution.

CONCLUSIONS

Although there is an extensive literature documenting difficulties in ToM and emotion recognition in those with EDs, relatively little is known about empathic abilities in this population. This systematic review and meta-analysis aimed to examine whether those with EDs differed from HCs on several dimensions of self-reported empathy, and provide a qualitative synthesis of the literature. While those with AN did not differ from HCs in overall empathy, a meta-analysis of 8 studies found that AN had significantly lower levels of cognitive empathy compared to HC, with a small effect size. It was also found that AN had significantly lower levels of fantasy, a subdivision of cognitive empathy. AN did not differ from HC in affective empathy. This profile of intact affective empathy and lowered cognitive empathy mirrors that of those with ASD, a disorder that shares a number of neuropsychological and socio-cognitive traits with AN. Conclusions regarding the empathic profiles of those with other EDs are not possible, given the lack of studies in these groups. Future research should investigate empathic abilities in other EDs, and examine the influence of comorbid psychopathological traits.

AUTHOR CONTRIBUTIONS

JK-G performed the search, data extraction, and wrote the manuscript. KT leads the research group within which this work was conducted and is JK-G lead supervisor for Ph.D. KT and AH edited the manuscript before submission.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00102/full#supplementary-material

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Transcultural Adaptation of the Oldenburg Burnout Inventory (OLBI) for Brazil and Portugal

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During the last few years, burnout has gained more and more attention for its strong connection with job performance, absenteeism, and presenteeism. It is a psychological phenomenon that depends on occupation, also presenting differences between sexes. However, to properly compare the burnout levels of different groups, a psychometric instrument with adequate validity evidence should be selected (i.e., with measurement invariance). This paper aims to describe the psychometric properties of the Oldenburg Burnout Inventory (OLBI) version adapted for workers from Brazil and Portugal, and to compare burnout across countries and sexes. OLBI's validity evidence based on the internal structure (dimensionality, reliability, and measurement invariance), and validity evidence based on relationships with other variables (work engagement) are described. Additionally, it aims presents a revision of different OLBI's versions—since this is the first version of the instrument developed simultaneously for both countries—it is an important instrument for understanding burnout between sexes in organizations. Data were used from 1,172 employees across two independent samples, one from Portugal and the other from Brazil, 65 percent being female. Regarding the OLBI internal structure, a reduced version (15 items) was obtained. The high correlation between disengagement and exhaustion, suggested the existence of a second-order latent factor, burnout, which presented measurement invariance for country and sex. Confirmatory factor analysis of the Portuguese OLBI version presented good goodness-of-fit indices and good internal consistency values. No statistically significant differences were found in burnout between sexes or countries. OLBI also showed psychometric properties that make it a promising and freely available instrument to measure and compare burnout levels of Portuguese and Brazilian employees.

Keywords: Oldenburg Burnout Inventory (OLBI), burnout, measurement invariance, Brazil, Portugal, multi-occupational, validity evidence

INTRODUCTION

Work organizations and labor relations all over the world are undergoing significant changes, with an impact on workers' lives and health, since the demands of modern working life are increasing pressure to levels never seen before (International Labour Office, 2016). Thus, the workforce must deal with a new landscape where psychosocial risks at work must be addressed

(European Agency for Safety and Health at Work, 2018). Stress is a risk which, at extreme levels, can lead to burnout. Burnout has become a global concern, and work-related stress is a big challenge to organizations' performance and to their workers' health. Burnout levels vary depending on country, occupation, and individual characteristics, among which sex, is one of the most important factors (Purvanova and Muros, 2010). Burnout can affect any worker, with consequences not only in terms of health, safety, and well-being, but also for productivity, quality of service, and cost-effectiveness to the organization (Poghosyan et al., 2010; Carod-Artal and Vázquez-Cabrera, 2013). It is a severe reaction to occupational stress, having in its symptomatology changes to physical and psychological health and behavioral-motivational aspects, expressed through a reduction in job satisfaction or even a change of profession (Marques-Pinto et al., 2003). It is a syndrome (psychological in nature) that may occur when workers chronically face a stressful working environment and feel low resources to face high job demands (Maslach et al., 2001; Bakker and Demerouti, 2007; Maslach, 2015). The definition of Burnout has been expanded from a concept associated with human services professions to a concept related to all kinds of professions that can be affected (Lindblom et al., 2006).

From a historical perspective, burnout was initially considered as a psychological phenomenon in the USA, beginning with studies by the psychologist Freudenberger (1974) and the psychologist Maslach (1976). Despite some criticism (Bianchi et al., 2017) and the existence of several other related constructs, such as karōshi (過労死), meaning "death by overwork" (International Labour Organization, 2013) and karōjisatsu (過労自殺), meaning "suicide from overwork" (Amagasa et al., 2005), burnout became a popular topic in occupational health (Marques-Pinto et al., 2008; Schaufeli, 2017). There is some discussion about burnout (Bianchi, 2015; Bianchi et al., 2017; Epstein and Privitera, 2017; Mion et al., 2018) in terms of its dimensionality. The names attributed to the constructs can vary (Simbula and Guglielmi, 2010; Larsen et al., 2017). The most commonly suggested structure is a tri-factor one (Maslach et al., 2001, 2016), comprising emotional exhaustion (or simply exhaustion), depersonalization (also known as cynicism or disengagement), and reduced sense of personal accomplishment (or professional efficacy) (Halbesleben et al., 2004). It is expected that if a worker has high levels of the first two dimensions, there should be low levels of the third dimension since it is measured in the opposite direction to the other two. Carod-Artal and Vázquez-Cabrera (2013) state that emotional exhaustion is the most important dimension of burnout syndrome—being referred to as a state of having feelings of being emotionally overextended and depleted of one's emotional resources—representing the individual stress component (Bresó et al., 2007). Depersonalization refers to cynical or excessively detached responses to others in the work context; this is the interpersonal component of burnout (Maslach, 1998). Finally, diminished personal accomplishment refers to the decreased sense of competence and of productivity, representing the component of self-evaluation (Maslach, 1998).

There is also a two-dimensional approach to burnout (Demerouti et al., 2000). Based on empirical evidence, some authors consider that disengagement and exhaustion are the core dimensions of burnout, while reduced personal accomplishment plays a less important role (Maslach et al., 2001; Shirom, 2002). In fact, it has been shown that the relation of reduced personal accomplishment to burnout outcomes and antecedents is weaker than the other two dimensions (Lee and Ashforth, 1996). Moreover, while emotional exhaustion leads to disengagement, reduced personal accomplishment develops individually in relation to the other two dimensions (Leiter, 1993). Cordes and Dougherty (1993) suggest that it is an individual difference similar to self-efficacy.

Currently, burnout is becoming increasingly prominent in the literature (Leiter and Maslach, 2017); it has been associated with multiple occupational groups, beyond human services (Maslach and Leiter, 2017). In fact, burnout's prevalence has increased in some occupations, such as physicians in the USA (Shanafelt et al., 2015); it shows a high prevalence in various occupations, including radiology residents (Guenette and Smith, 2017), midwives in Australia (Creedy et al., 2017), nurses in various countries (Gómez-Urquiza et al., 2017). One reason why burnout is so common is due to the high levels of stress and emotional demands present in the job (Demerouti et al., 2001). Job stress can increase absenteeism, affect family roles, productivity, and mental and physical health, and decrease job satisfaction, which, in turn, can lead to reduced personal accomplishment, depersonalization, and emotional exhaustion (Carod-Artal and Vázquez-Cabrera, 2013).

Burnout Measurement With the Oldenburg Burnout Inventory

Despite the existence of several instruments to measure burnout, the Maslach Burnout Inventory (MBI; Maslach et al., 2016) is the most used (Ahola et al., 2017) and is commercially available. However, there are other options, some of them free, such as the Copenhagen Burnout Inventory (Kristensen et al., 2005); the Burnout Measure (Pines and Aronson, 1988; Malach-Pines, 2005); the Educator Burnout Inventory (Wang et al., 2003), the Oldenburg Burnout Inventory (OLBI; Bakker et al., 2004); the Shirom-Melamed Burnout Measure (Shirom and Melamed, 2006); the Bergen Burnout Indicator (Salmela-Aro et al., 2011); the Karolinska Exhaustion Scale (Saboonchi et al., 2013); and the Spanish Burnout Inventory (Gil-Monte et al., 2017).

OLBI seems to be the most prominent alternative to MBI (Demerouti et al., 2000). It was originally developed by Demerouti and Nachreiner (1998), who suggested two burnout dimensions, disengagement and exhaustion, applicable to professionals outside human services occupations. OLBI's versions vary across occupational groups and countries (see **Table 1**). In some countries—Brazil and Portugal (Campos et al., 2012), Sweden (Dahlin et al., 2007; Rudman et al., 2014), Slovenia (Kogoj et al., 2014), South Africa (Mokgele and Rothmann, 2014), Germany and Greece (Reis et al., 2015), and Malaysia (Mahadi et al., 2018)—OLBI has a version for students. OLBI does not contain any factor correspondent to what the MBI

TABLE 1 | OLBI's versions: validity evidence based on the internal structure.

Country (Authors)	Occupational group	*N*	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	*TLI/NNFI*	*GFI*	*CFI*	*RMSEA*	*SRMR*
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
Brazil Schuster and Dias, 2018	Multi-occupational	273	16 (two)	CFA	–	*CR* = 0.93	*CR* = 0.89	–	2.59	0.91	0.90	0.93	0.07	0.06
			13 (two)		–	*CR* = 0.88	*CR* = 0.92	–	2.41	0.93	0.92	0.94	0.07	0.05
Cameroon Mbanga et al., 2018	Nurses	143	16 (two)	–	–	–	–	–	–	–	–	–	–	–
England Delgadillo et al., 2018	Psychological well-being practitioners	13	16 (two)	–	–	–	–	–	–	–	–	–	–	–
	Mental health nurse practitioners	15		–	–	–	–	–	–	–	–	–	–	–
	Cognitive behavioral therapists	21		–	–	–	–	–	–	–	–	–	–	–
	(Total)	(49)		–	–	α = 0.87	α = 0.84	–	–	–	–	–	–	–
Iraq Al-Asadi et al., 2018	Primary school teachers	706	16 (two)	–	–	–	–	–	–	–	–	–	–	–
Ireland Chernoff et al., 2018	Administrators	8	16 (two)	–	–	–	–	–	–	–	–	–	–	–
	Care assistants	3		–	–	–	–	–	–	–	–	–	–	–
	Nurses	50		–	–	–	–	–	–	–	–	–	–	–
	Physicians	23		–	–	–	–	–	–	–	–	–	–	–
	Porters	3		–	–	–	–	–	–	–	–	–	–	–
	Radiographers	10		–	–	–	–	–	–	–	–	–	–	–
	(Total)	(97)		–	–	–	–	–	–	–	–	–	–	–
Italy Estévez-Mujica and Quintane, 2018	Research and development	57	13 (two)	EFA	–	α = 0.86	α = 0.85	–	–	–	–	–	–	–
Malaysia Mahadi et al., 2018*	Medical students	452	16 (one)	CFA	–	–	–	–	7.606	0.577	0.768	0.633	0.121	–
			16 (two)		–	–	–	–	7.551	0.580	0.768	0.640	0.121	–
			9 (two)		α = 0.80	α = 0.74 *CR* = 0.73	α = 0.70 *CR* = 0.71	–	3.585	0.905	0.958	0.934	0.076	–
England Westwood et al., 2017	Psychotherapists	210	16 (two)	–	–	α = 0.83	α = 0.86	–	–	–	–	–	–	–
India Ananthram et al., 2017	Call center representatives	250	16 (two)	–	–	α = 0.84	α = 0.85	–	–	–	–	–	–	–
Kosovo Turtulla, 2017	Teachers	531	16 (two)	–	–	α = 0.73	α = 0.71	–	–	–	–	–	–	–
Malaysia Rosnah et al., 2017	Multi-occupational	492	8 (one)[E]	CFA	–	–	α = 0.50	–	3.21	–	0.98	0.92	0.066	–
Russia Smirnova, 2017	Multi-occupational	392	16 (one)	CFA	–	–	–	–	10.97	0.550	0.746	0.610	0.160	–
			16 (two)		–	α = 0.84	α = 0.65	–	9.60	0.612	0.804	0.709	0.148	–

(Continued)

TABLE 1 | Continued

Country (Authors)	Occupational group	*N*	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	*TLI/NNFI*	*GFI*	*CFI*	*RMSEA*	*SRMR*
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
			15 (two)		–	$\alpha = 0.84$	$\alpha = 0.68$	–	9.85	0.631	0.803	0.702	0.150	–
			7 (one)		–	–	–	–	8.72	0.802	0.911	0.868	0.141	–
			7 (two)		–	$\alpha = 0.65$	$\alpha = 0.72$	–	9.34	0.786	0.911	0.868	0.146	–
Saudi Arabia Al-shuhail et al., 2017	Physicians	140	16 (two)	–	–	–	–	–	–	–	–	–	–	–
Serbia Petrović et al., 2017	Multi-occupational	860	16 (two)	–	$\alpha = 0.81$	–	–	–	–	–	–	–	–	–
Singapore Suyi et al., 2017	Health	37	16 (two)	–	–	$\alpha = 0.79$–88	$\alpha = 0.63$–89	–	–	–	–	–	–	–
Taiwan Ko, 2017	Hotel frontline employees	521	16 (two)	–	–	$\alpha = 0.75$	$\alpha = 0.78$	–	–	–	–	–	–	–
UK Halliday et al., 2017	Consultant	123	16 (two)	–	–	–	–	–	–	–	–	–	–	–
	General practitioner	93		–	–	–	–	–	–	–	–	–	–	–
	Higher specialist trainee	139		–	–	–	–	–	–	–	–	–	–	–
	Junior specialist trainee	153		–	–	–	–	–	–	–	–	–	–	–
	Foundation doctor	40		–	–	–	–	–	–	–	–	–	–	–
	(Total)	(548)		–	–	–	–	–	–	–	–	–	–	–
USA Olinske and Hellman, 2017	Executive directors	140	16 (two)	–	–	$\alpha = 0.78$	$\alpha = 0.88$	–	–	–	–	–	–	–
USA Yanos et al., 2017	Clinicians	472	16 (two)	–	$\alpha = 0.87$	$\alpha = 0.75$	$\alpha = 0.87$	–	–	–	–	–	–	–
England Sales et al., 2016	General practitioners trainees	48	16 (two)	–	–	–	–	–	–	–	–	–	–	–
India Subburaj and Vijayadurai, 2016	Police constables	492	16 (one)	CFA	$CR = 0.65$	–	–	–	9.14	0.802	0.738	0.828	0.129	–
			16 (two)		–	$CR = 0.91$	$CR = 0.90$	–	3.75	0.933	0.911	0.942	0.075	–
	Higher secondary teachers	385	16 (one)		$CR = 0.62$	–	–	–	8.65	0.760	0.697	0.792	0.141	–
			16 (two)		–	$CR = 0.90$	$CR = 0.90$	–	3.64	0.917	0.902	0.929	0.083	–
	(Total)	(877)	–		–	–	–	–	–	–	–	–	–	–
Norway Innstrand, 2016	Advertising	301	16 (two)	CFA	–	–	–	–	3.38	0.96	–	0.96	0.092	0.069
	Bus drivers	381			–	–	–	–	3.21	0.97	–	0.97	0.083	0.051
	Church ministers	500			–	–	–	–	3.58	0.96	–	0.97	0.075	0.055
	IT	358			–	–	–	–	4.10	0.95	–	0.96	0.097	0.074
	Lawyers	412			–	–	–	–	3.66	0.96	–	0.97	0.084	0.056
	Nurses	496			–	–	–	–	4.87	0.96	–	0.97	0.092	0.064
	Physicians	523			–	–	–	–	5.58	0.94	–	0.95	0.098	0.072
	Teachers	504			–	–	–	–	4.86	0.96	–	0.96	0.091	0.067
	(Total)	(3,475)		MGCFA	–	$\alpha = 0.86$–88	$\alpha = 0.87$–88	Partial scalar invariance among occupational groups.	4.47	0.95	–	0.95	0.094	0.067

(Continued)

TABLE 1 | Continued

Country (Authors)	Occupational group	*N*	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	*TLI/NNFI*	*GFI*	*CFI*	*RMSEA*	*SRMR*
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
Pakistan Khan et al., 2016	Female academicians	299	16 (two)	–	–	–	–	–	–	–	–	–	–	–
Pakistan Khan and Yusoff, 2016	Academic staff	450	16 (four)	EFA	α = 0.83	–	–	–	–	–	–	–	–	–
			16 (one)	CFA		–	–	–	0.60	–	0.87	1.00	0.014	–
			16 (two)			–	–	–	2.62	–	0.99	0.98	0.004	–
Poland Baka and Basinska, 2016	Teachers	545	–	–	–	–	–	–	–	–	–	–	–	–
	Medical staff	491	–	–	–	–	–	–	–	–	–	–	–	–
	Police officers	768	–	–	–	–	–	–	–	–	–	–	–	–
	(Total)	(1,804)	16 (two)	EFA	–	α = 0.73	α = 0.69	–	–	–	–	–	–	–
USA Rogala et al., 2016	Health care	135	16 (two)	–	–	α = 0.86	α = 0.81–86	–	–	–	–	–	–	–
Zimbabwe Buitendach et al., 2016	Bus drivers	283	16 (two)	–	α = 0.76	α = 0.73	α = 0.72	–	–	–	–	–	–	–
Brazil Schuster et al., 2015	Multi-occupational	273	16 (two)	–	α = 0.90	α = 0.86	α = 0.83	–	–	–	–	–	–	–
			9 (two)	EFA	α = 0.88	α = 0.87	α = 0.76	–	–	–	–	–	–	–
Germany Reis et al., 2015	Nurses	385	15 (one)	CFA	–	–	–	–	5.28	0.82	–	0.84	0.11	0.07
			15 (two)		–	–	–	Partial metric invariance with German students	3.59	0.89	–	0.91	0.08	0.06
			16 (one)		–	–	–	–	5.26	0.80	–	0.82	0.11	0.07
			16 (two)		–	α = 0.81	α = 0.87	–	3.78	0.87	–	0.89	0.09	0.07
India Rajeswari and Sreelekha, 2015	Nurses	200	16 (two)	–	–	–	–	–	–	–	–	–	–	–
Poland Staszczyk and Tokarz, 2015	White-collar	210	16 (two)	–	α = 0.83	α = 0.78	α = 0.74	–	–	–	–	–	–	–
Slovenia Sedlar et al., 2015	Multi-occupational	1,436	8 (two)	CFA	–	–	–	–	7.51	0.988	–	0.992	0.067	–
			16 (one)		α = 0.83	–	–	–	39.94	0.753	–	0.786	0.165	–
			16 (two)[W]			–	–	–	8.38	0.953	–	0.960	0.072	–
			16 (two)			α = 0.71	α = 0.73	–	40.09	0.752	–	0.787	0.165	–
			16 (four)[PN]			–	–	–	8.06	0.955	–	0.963	0.070	–
USA Foster, 2015	Multi-occupational	579	8 (one)[D]	CFA	–	α = 0.82	–	Full-uniqueness measurement invariance between sex.	11.68	–	–	0.88	–	0.064
			8 (one)[E]	CFA	–	–	α = 0.84	Full-uniqueness measurement invariance between sex.	–	–	–	–	–	–
			16 (two)	–	–	–	–	–	–	–	–	–	–	–

(Continued)

TABLE 1 | Continued

Country (Authors)	Occupational group	*N*	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	*TLI/NNFI*	*GFI*	*CFI*	*RMSEA*	*SRMR*
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
USA Shupe et al., 2015	Librarians	282	16 (two)	–	α = 0.87	–	–	–	–	–	–	–	–	–
Sweden Lundkvist et al., 2014	Coaches	277	8 (two)[N]	CFA	–	–	–	–	3.25	0.940	–	0.959	0.090	–
			16 (two)		–	–	–	–	2.82	0.879	–	0.897	0.081	–
Sweden Rudman et al., 2014	Nurses	1,178	10 (two)[T]	–	–	α = 0.75	α = 0.78	–	–	–	–	–	–	–
		1,086	8 (two)[T]	–	–	α = 0.75	α = 0.71	–	–	–	–	–	–	–
		1,135	8 (two)[T]	–	–	α = 0.77	α = 0.71	–	–	–	–	–	–	–
		908	10 (two)[T]	–	–	α = 0.78	α = 0.80	–	–	–	–	–	–	–
		811	10 (two)[T]	–	–	α = 0.80	α = 0.81	–	–	–	–	–	–	–
Australia Scanlan and Still, 2013	Occupational therapists	34	16 (two)	–	–	α = 0.79	α = 0.84	–	–	–	–	–	–	–
Brazil Schuster et al., 2013	Multi-occupational	273	9 (two)	EFA	α = 0.88	α = 0.86	α = 0.76	–	–	–	–	–	–	–
			9 (two)	CFA	*CR* = 0.95	*CR* = 0.85	*CR* = 0.93	–	2.36	0.956	0.954	0.968	0.071	–
Poland Rzeszutek, 2013	Psychotherapists	200	16 (two)	–	α = 0.88	α = 0.82	α = 0.79	–	–	–	–	–	–	–
USA Ford et al., 2013	Information technology	91	16 (two)	–	–	α = 0.82	α = 0.79	–	–	–	–	–	–	–
South Africa Lekutle and Nel, 2012	Cement factory	187	5 (two)	EFA	–	α = 0.68	α = 0.69	–	–	–	–	–	–	–
Norway Innstrand et al., 2012	Multi-occupational	3,475	16 (two)	MGCFA	–	α = 0.86–88	α = 0.87–88	Longitudinal metric invariance.	–	–	–	–	–	–
China Qiao and Schaufeli, 2011	Nurses	717	16 (one)	CFA	–	–	–	–	11.62	0.73	0.75	0.76	0.11	–
			16 (two)[W]			–	–	–	5.58	0.88	0.90	0.90	0.08	–
			16 (two)			–	–	–	11.25	0.74	0.78	0.77	0.12	–
			16 (four)[PN]			–	–	–	4.42	0.91	0.92	0.93	0.07	–
Poland Baka, 2011	Teachers	292	16 (two)	–	α = 0.88	–	–	–	–	–	–	–	–	–
Sweden Peterson et al., 2011	Multi-occupational	3,719	16 (two)	CFA	–	α = 0.83	α = 0.83	–	27.88	0.93	–	0.94	0.08	0.06
			16 (one)		–	–	–	–	47.24	0.92	–	0.93	0.12	0.09
Poland Baka and Cieślak, 2010	Teachers	236	16 (two)	–	α = 0.87	–	–	–	–	–	–	–	–	–
South Africa Demerouti et al., 2010	Construction	528	16 (two)	–	–	α = 0.79	α = 0.74	–	–	–	–	–	–	–

(Continued)

TABLE 1 | Continued

Country (Authors)	Occupational group	N	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	TLI/NNFI	GFI	CFI	RMSEA	SRMR
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
South Africa Tilakdharee et al., 2010	Training and development	80	16 (two)	–	α = 0.928	α = 0.80	α = 0.82	–	–	–	–	–	–	–
Belgium Barbier et al., 2009	Public sector	955	16 (two)	–	–	α = 0.79	α = 0.82	–	–	–	–	–	–	–
Canada Chevrier, 2009	Catering	84	16 (five)	PCA	α = 0.80	–	–	–	–	–	–	–	–	–
			16 (two)	PCA		α = 0.69	α = 0.81	–	–	–	–	–	–	–
Netherlands Demerouti and Bakker, 2008	Health care	979	16 (two)	EFA	–	–	–	–	–	–	–	–	–	–
	White collar	644	16 (two)	EFA	–	–	–	–	–	–	–	–	–	–
	(Total)	1,623	16 (two)	CFA[T]	–	–	–	–	8.08	–	0.88	0.86	0.07	–
			16 (two)[W]	CFA[M]	–	–	–	–	12.51	–	0.76	0.76	0.08	–
			16 (two)	CFA[MTMM]	–	α = 0.85	α = 0.85	Metric invariance for burnout factors between occupations.	4.25	–	0.95	0.95	0.05	–
Sweden Peterson et al., 2008	Health care	3,719	16 (two)	–	–	α > 0.70	α > 0.70	–	–	–	–	–	–	–
Australia Timms et al., 2007	Teachers	298	16 (two)	–	–	α = 0.79	α = 0.81	–	–	–	–	–	–	–
South Africa Bosman et al., 2005	Government	297	16 (two)	–	–	α = 0.71	α = 0.66	–	–	–	–	–	–	–
United States of America Halbesleben and Demerouti, 2005	Multi-occupational	2,431	16 (one)	CFA	–	–	–	–	2.26	0.62	0.72	0.68	0.14	–
			16 (two)[W]		–	–	–	–	1.90	0.75	0.81	0.79	0.09	–
			16 (two)		–	α = 0.76–0.83	α = 0.74–0.79	–	1.09	0.96	0.97	0.95	0.03	–
	Fire department	168	16 (one)		–	–	–	–	2.66	0.75	0.71	0.78	0.14	–
			16 (two)[W]		–	–	–	–	2.93	0.71	0.68	0.74	0.16	–
			16 (two)		–	α = 0.83	α = 0.87	–	1.18	0.95	0.96	0.95	0.04	–
	(Total)	2,599	–	–	–	–	–	–	–	–	–	–	–	–
South Africa le Roux, 2004	Earthmoving	326	15 (two)	PCA	–	α = 0.82	α = 0.71	–	–	–	–	–	–	–
			16 (two)		–	–	–	–	–	–	–	–	–	–
Greece Demerouti et al., 2003	Multi-occupational	232	13 (one)	CFA	–	–	–	–	5.04	–	0.79	0.71	0.13	–
			13 (two)[W]			α = 0.83	α = 0.73	–	5.06	–	0.79	0.72	0.13	–
			13 (two)					–	3.39	–	0.87	0.83	0.10	–
			13 (two)[M]					–	1.90	–	0.94	0.95	0.062	–

(Continued)

TABLE 1 | Continued

Country (Authors)	Occupational group	N	Dimensionality		Reliability: internal consistency			Measurement invariance	χ^2/df	*TLI/NNFI*	*GFI*	*CFI*	*RMSEA*	*SRMR*
			Items (factors)	Analysis	Total	Disengagement	Exhaustion							
Germany Demerouti et al., 2002	Human services	149	–	–	–	–	–	–	–	–	–	–	–	–
	Production employees	145	–	–	–	–	–	–	–	–	–	–	–	–
	(Total)	294	15 (one)	MGCFA	–	–	–	–	2.22	0.83	0.87	0.90	–	–
			15 (two)[U]			α = 0.84	α = 0.85	–	2.08	0.84	0.90	0.91	–	–
			15 (two)[W]					–	2.20	0.84	0.87	0.90	–	–
			15 (two)					–	1.26	0.91	0.93	0.99	–	–
German Demerouti et al., 2001	Human services	140	15 (one)	CFA	–	–	–	–	2.13	–	0.86	0.84	–	–
			15 (two) [W]		–	–	–	–	2.10	–	0.87	0.85	–	–
			15 (two)		–	–	–	–	1.45	–	0.91	0.94	–	–
	Production	93	15 (one)		–	–	–	–	1.86	–	0.86	0.91	–	–
			15 (two) [W]		–	–	–	–	1.73	–	0.87	0.92	–	–
			15 (two)		–	–	–	–	1.29	–	0.91	0.97	–	–
	Transport	119	15 (one)		–	–	–	–	1.52	–	0.86	0.86	–	–
			15 (two) [W]		–	–	–	–	1.35	–	0.87	0.91	–	–
			15 (two)		–	–	–	–	1.14	–	0.90	0.96	–	–
	(Total)	352	15 (one)		–	–	–	–	3.73	–	0.87	0.88	–	–
			15 (two) [W]		–	–	–	–	3.57	–	0.89	0.89	–	–
			15 (two)		–	α = 0.83	α = 0.82	–	1.50	–	0.96	0.98	–	–
			15 (one)	MGCFA	–	–	–	–	1.97	–	0.85	0.86	–	–
			15 (two) [W]		–	–	–	–	1.90	–	0.86	0.87	–	–
			15 (two)		–	–	–	Metric invariance between occupations.	1.38	–	0.90	0.95	–	–
Germany Demerouti et al., 2000	Nurses	109	15 (two)	–	–	α = 0.92	α = 0.84	–	–	–	–	–	–	–
Germany Demerouti and Nachreiner, 1998	Service-Professionals	145	–	–	–	–	–	–	–	–	–	–	–	–
	Production	134	–	–	–	–	–	–	–	–	–	–	–	–
	Air traffic controllers	95	–	–	–	–	–	–	–	–	–	–	–	–
	(total)	374	25 (two)	EFA	–	α = 0.93	α = 0.82	–	–	–	–	–	–	–

**Although a medical students sample was used, this version's items were adapted for workers; M, with modification indices applied; U, uncorrelated model; W, all positively phrased items of both burnout dimensions were specified to load on one factor and all negatively phrased items on a second factor; PN, two negatively worded scales (exhaustion items and disengagement items), and two positively worded scales (exhaustion items and disengagement items); D, disengagement subscale; E, exhaustion; N, only negatively worded items included, four each subscale; T, trait; M, method; MTMM, multitrait-multimethod.*

The extracted results for the goodness-of-fit indices are presented with two or three decimal places depending of the original authors report. CFA, confirmatory factor analysis; EFA, exploratory factor analysis; MGCFA, multi-group confirmatory factor analysis; PCA, principal component analysis; GFI, goodness-of-fit index; RMSEA, root mean square error of approximation; NNFI, non-normed fit index; TLI, Tucker Lewis index; CFI, comparative fit index; SRMR, standardized root mean square residual.

calls "professional efficacy"; this dimension received criticism in some studies (Bresó et al., 2007; Marôco et al., 2014), and, in the opinion of various authors, it is not a core burnout dimension (Bakker et al., 2004; Demerouti and Bakker, 2008) but can be interpreted as a possible burnout consequence (Koeske and Koeske, 1989) related to personality characteristics (Cordes and Dougherty, 1993).

The exhaustion subscale of OLBI has eight items which relate to feelings of emptiness, work overload, the need to rest, and physical, cognitive, and emotional exhaustion (Demerouti et al., 2003). Differently from the exhaustion concept presented in the MBI, the OLBI approach to exhaustion covers cognitive, physical, and affective aspects of exhaustion, which may facilitate the use of the instrument with workers of different kinds of activity (Demerouti et al., 2003; Bakker et al., 2004). The disengagement subscale has also eight items which refer to distancing oneself from the work, together with negative and cynical behaviors and attitudes in relation to one's job (Demerouti and Bakker, 2008). The OLBI's concept of disengagement differs from MBI's depersonalization in terms of the amplitude of the distancing, since OLBI's concept is broader: it may refer to distancing oneself from work in general or, more specifically, to distancing oneself from the content and object, along with experiencing negative attitudes (Demerouti et al., 2003). Thus, disengagement offers a less restricted view of the lack of interest in work. It is important to note that González-Romá et al. (2006) suggested that two of the three work engagement dimensions measured by the Utrecht Work Engagement Scale (UWES), vigor and dedication (the third dimension is absorption), can be paired with emotional exhaustion and cynicism (burnout dimensions). One dimension, named "identification," involved dedication and cynicism; the other, named "energy," comprised vigor and exhaustion factors, this indicates that OLBI's negatively- and positively-worded items can be markers for work engagement and burnout (Halbesleben and Demerouti, 2005).

Table 1 summarizes the different OLBI versions used with different samples found through a search of Embase, Scopus, PubMed, Web of Science, and Google Scholar using the terms: "OLBI," "Oldenburg Burnout Inventory," "adaptation," "version," "validity," and "psychometric properties." The OLBI's total number of items changed since its original structure of 25 items (Demerouti and Nachreiner, 1998) to 15 (Demerouti et al., 2001); today's English language version has 16 items (Bakker et al., 2004; Halbesleben and Demerouti, 2005). It has positively and negatively worded items—an equal number of each kind in the two dimensions—something that is considered an advantage (Price, 1997) since it can diminish acquiescence bias despite diminishing the internal consistency of the instruments (Salazar, 2015). OLBI has been translated into many languages, although not always evaluated in its psychometric properties (**Table 1**). Some studies use OLBI without taking into consideration the recommended steps to adapt an instrument for a country or culture different from the one for which it was originally developed (van de Vijver, 2016). There is a certain lack of use of adequate guidelines when translating and adapting the instrument for a new sample (International Test Commission, 2018). As can be observed in **Table 1**, the majority of the new OLBI versions have not evaluated their psychometric properties with the appropriate technique (confirmatory factor analysis [CFA]; Brown, 2015). In fact, some of them have avoided both exploratory and confirmatory factor analysis. Usually, the original two-factor structure is the one with better goodness-of-fit indices—even when compared with the other two-factor structures (e.g., with positive items in one group and negatively-worded items in the other), and with one- or four-factor structures (Demerouti et al., 2001). The measurement invariance/equivalence of the instrument across different groups is essential to properly establish comparisons (Davidov et al., 2014). OLBI invariance has been addressed by Demerouti et al. (2001) in its 15-items version for three different professions, they observed metric invariance (same factor's loadings). Demerouti and Nachreiner (1998) stated that three different groups of professionals obtained a similar OLBI (25-items) structure after a principal component analysis for each of the groups. Others researchers have obtained measurement invariance between countries (Demerouti et al., 2003) and between workers and students (Reis et al., 2015). These findings suggest that burnout is not exclusive to human services professions (Demerouti and Nachreiner, 1998; Demerouti et al., 2001) since various studies have tested burnout levels using OLBI in other occupations (e.g., executive directors, white-collar employees, construction workers). Altogether, few studies tested the measurement invariance of the groups with which they established comparisons. Finally, regarding the reliability of the scores, the internal consistency estimates were acceptable to good in most of the studies, while almost all studies reported only the Cronbach's α (see **Table 1**).

This study aims to describe the psychometric properties of an OLBI version developed simultaneously for workers from Brazil and Portugal, its validity evidence based on the internal structure (dimensionality, measurement invariance, reliability), and the validity evidence based on the relationship with other variables (work engagement); and to compare burnout across sexes and countries. Additionally, the study seeks to present a revision of OLBI's different versions since this is the first version of the instrument developed simultaneously for Portugal and Brazil, adapting an important instrument for understanding burnout in relation to sexes in the organizations. It will be structured by presenting some considerations about burnout among sexes, followed by burnout measured by OLBI.

Research Hypotheses

Following the recommendations of *The Standards for Educational and Psychological Testing* (American Educational Research Association, 2014), this paper aims to assess two types of validity evidence for the Portuguese version (PT-BR and PT-PT) of the OLBI (Bakker et al., 2004)—one related to the internal structure, the other based on the relations to other variables (work engagement). Since various studies have successfully confirmed the original two-factor structure of OLBI (Halbesleben and Demerouti, 2005; Peterson et al., 2011; Subburaj and Vijayadurai, 2016), it was hypothesized that the tested OLBI version would present a good fit confirming its original dimensionality of two factors (H1). Burnout has been hypothesized by some authors as a higher-order dimension (Taris et al., 1999; Shirom and Melamed, 2006; Marôco et al., 2008). Thus, a possible second-order latent factor, burnout, was tested for OLBI (H2). Through the review of the different versions (**Table 1**), the majority of the studies showed acceptable to very good reliability of the scores' evidence in terms of internal consistency (e.g., Demerouti and Bakker, 2008; Innstrand, 2016; Subburaj and Vijayadurai, 2016). Consequently, it was assumed that OLBI would present acceptable internal consistency reliability estimates (H3). Some studies found evidence of measurement invariance for OLBI between occupations (Demerouti et al., 2001; Demerouti and Bakker, 2008; Innstrand, 2016) and sex (Foster, 2015), but none investigated measurement invariance among workers of different countries. H4 hypothesized that OLBI will present evidence of measurement invariance between sexes and countries.

Research has found that burnout levels can vary among sexes, with females usually presenting slightly more exhaustion than males (Purvanova and Muros, 2010; Innstrand et al., 2011), females being more likely to experience burnout (Dimou et al., 2016). However, others suggest that research does not allow one to conclude any sex-specific risks (Seidler et al., 2014; Adriaenssens et al., 2015) considering that the burnout differences can be related with the levels of workload as well as care-load (Bekker et al., 2005; Langballe et al., 2011). Burnout can also vary among countries also (Poghosyan et al., 2010; Alexandrova-Karamanova et al., 2016; Jovanović et al., 2016). North American countries have a tendency to present higher exhaustion and disengagement levels than European countries—differences that can be related to cultural aspects (Maslach et al., 2001). However, regarding the Portugal-Brazil comparison, no differences were reported in a previous study (Dias et al., 2010). Occupations can play a substantial role in burnout levels (e.g., emotional challenges of working in the teaching or caregiving role) (Maslach et al., 2001). Altogether, it was hypothesized that burnout's latent means differ between sexes and countries (H5).

Work engagement is known to be a construct with strong correlations with burnout (Demerouti et al., 2010; Petrović et al., 2017), since both can be considered indicators of well-being (Bakker et al., 2014). Thus, the divergent validity evidence based on the relation to other variables, work engagement, was assessed (H6).

METHODS

Sample

A total sample composed of 1,172 participants was collected by combining two independent samples: one sample of Brazilian workers in various occupations ($n = 604$), and one of Portuguese workers in various occupations ($n = 568$). Both samples completed the OLBI and the Utrecht Work Engagement Scale (Schaufeli and Bakker, 2003). Participation was anonymous and voluntary. The average age of the total sample was 35.47 years ($SD = 9.95$), with 65% being female. Workers' occupations were according to the International Standard Classification of Occupations ISCO-08 (International Labour Office, 2012)—mainly professionals or administrative support—and 73% of the sample were, at least, college graduates (**Table 2**). Regarding children, 59% had none; 45% reported being married or cohabiting.

A non-probabilistic convenience sampling was used. The inclusion criteria were: (1) all participants were workers with a contract or formal ties with their employers, (2) had easy access to a PC, smartphone, or tablet to access the online platform where the instruments were deployed, and (3) were literate.

Measures

The OLBI was used to assess burnout, through the development of a version transculturally adapted both for Brazil and Portugal (**Table 3**). The OLBI is a self-report five-point rating scale (1 = "Strongly disagree"; to 5 = "Strongly agree") with eight questions within each of the two dimensions, disengagement and exhaustion (Demerouti et al., 2001). The disengagement factor refers to distancing from work in terms of both object and content, and to the development of cynical and negative attitudes and behaviors in relation to one's job (Bakker et al., 2004). Exhaustion refers to feelings of physical fatigue, the need to rest, and feelings of overtaxing and emptiness in relation to work (Demerouti and Bakker, 2008). To develop the Portuguese version (**Table 3**) the English version of the OLBI was used (Bakker et al., 2004) following *The ITC Guidelines for Translating and Adapting Tests* (International Test Commission, 2018), adapting the items to the Portuguese language according to the *Orthographic Agreement* signed by both Portugal and Brazil in 2009. The items were discussed with Portuguese and Brazilian psychologists and methodologists to create a version of the items that gathered the consensus of specialists regarding cultural, semantic, and idiomatic equivalence in the two countries. Finally, a small pilot test was done with 15 workers from each country; this did not suggest any modifications and the Portuguese adapted OLBI's 16 items were understood. The final single version (for both countries) had no other changes.

Work engagement refers to a positive motivational state and is composed of vigor, dedication, and absorption. This construct was measured with UWES-9 in its transculturally adapted version to both Brazil and Portugal (Sinval et al., 2018). It is a self-report instrument scored on a seven-point rating scale (0 = "Never"; 6 = "Always"), with three questions in each of its three dimensions. The UWES has shown good divergent validity evidence with the OLBI, since work engagement and burnout are moderately and negatively related (Goering et al., 2017). It was chosen not only for its good psychometric qualities for both countries, but also because it showed measurement invariance between both countries and it is a short instrument that allows for a robust work engagement measure with only a few items (Schaufeli and Bakker, 2003). It is a well-spread measure across many countries (Sinval et al., 2018) and is actually the most used instrument to measure work engagement. However, studies that investigated the relations between burnout and work engagement have mainly used the MBI for burnout and the UWES for work engagement (Schaufeli and de Witte, 2017). This study used OLBI together with UWES, trying to enrich the discussion about the two concepts, rather than just discussing instruments. The UWES dimensions are vigor, referring to the energy and resilience that one has in work; dedication, referring to being enthusiastic,

TABLE 2 | Sociodemographics, occupational group, and academic level for each country, and total.

	Brazil (*n* = 604) Multi-occupational	Portugal (*n* = 568) Multi-occupational	Total (*n* = 1,172)
SOCIODEMOGRAPHICS			
Age: *M* (*SD*)	35.11 (10.13)	35.83 (9.76)	35.47 (9.95)
Sex: Female %	67.23%	62.84%	65.07%
Children: Yes%	38.97%	42.61%	40.77%
OCCUPATIONAL GROUP			
Armed Forces Occupations	1.55	4.44	2.97
Managers	15.53	8.87	12.27
Professionals	36.12	53.63	44.70
Technicians and Associate Professionals	8.74	12.90	10.78
Clerical Support Workers	27.38	9.48	18.60
Services and Sales Workers	6.21	6.05	6.13
Skilled Agricultural, Forestry and Fishery Workers	–	–	–
Craft and Related Trades Workers	2.14	2.22	2.18
Plant and Machine Operators and Assemblers	0.78	0.60	0.69
Elementary Occupations	1.55	1.81	1.68
ACADEMIC LEVEL			
PhD	5.12	5.64	5.38
Master	9.49	38.52	23.82
Post-graduation (not master neither PhD)	25.62	9.34	17.58
Graduation	34.16	29.57	31.89
Unfinished graduation	13.09	4.67	8.93
High school, vocational education or less	12.52	12.26	12.40

TABLE 3 | OLBI original and Portuguese versions.

Item	Original OLBI (Bakker et al., 2004)	Portuguese (Brazil and Portugal) version of OLBI
	Strongly disagree 1; Disagree 2; Neutral 3; Agree 4; Strongly agree 5	Discordo totalmente 1; Discordo 2; Nem concordo, nem discordo 3; Concordo 4; Concordo totalmente 5
	DISENGAGEMENT	**DISTANCIAMENTO**
1[R]	I always find new and interesting aspects in my work	Encontro com frequência assuntos novos e interessantes no meu trabalho
3	It happens more and more often that I talk about my work in a negative way	Cada vez mais falo de forma negativa do meu trabalho
6	Lately, I tend to think less at work and do my job almost mechanically	Ultimamente tenho pensado menos no meu trabalho e faço as tarefas de forma quase mecânica
7[R]	I find my work to be a positive challenge	Considero que o meu trabalho é um desafio positivo
9	Over time, one can become disconnected from this type of work	Com o passar do tempo, sinto-me desligado do meu trabalho
11	Sometimes I feel sickened by my work tasks	Às vezes, sinto-me farto das minhas tarefas no trabalho
13[R]	This is only type of work that I can imagine myself doing	*Este é o único tipo de trabalho que me imagino a fazer
15[R]	I feel more and more engaged in my work	Sinto-me cada vez mais empenhado no meu trabalho
	EXAUSTÃO	**EXAUSTÃO**
2	There are days when I feel tired before I arrive at work	Há dias em que me sinto cansado antes mesmo de chegar ao trabalho
4	After work, I tend to need more time than in the past in order to relax and feel better	Depois do trabalho, preciso de mais tempo para relaxar e sentir-me melhor do que precisava antigamente
5[R]	I can tolerate the pressure of my work very well	Consigo aguentar bem a pressão do meu trabalho
8	During my work, I often feel emotionally drained	Durante o meu trabalho, muitas vezes sinto-me emocionalmente esgotado
10[R]	After working, I have enough energy for my leisure activities	Depois do trabalho, tenho energia suficiente para minhas atividades de lazer
12	After my work, I usually feel worn out and weary	Depois do trabalho sinto-me cansado e sem energia
14[R]	Usually, I can manage the amount of my work well	De uma forma geral, consigo administrar bem a quantidade de trabalho que tenho
16[R]	When I work, I usually feel energized	Quando trabalho, geralmente sinto-me com energia

*R, reversed; *Removed item for the proposed Portuguese (Brazil and Portugal) version.*

inspired, and proud of one's work; and absorption, referring to being immersed in one's work without the perception of time passing (Schaufeli et al., 2002). It is expected that high levels of work engagement correspond to highly energized workers (Schaufeli and Bakker, 2010).

Procedures

Data were gathered from 2015 to 2017, in both countries, in an effort to have a larger sample, since web surveys present low response rates (Massey and Tourangeau, 2013). Both samples completed the OLBI, a brief sociodemographic questionnaire, and the UWES-9. All the collected data were obtained online using *LimeSurvey* software (LimeSurvey GmbH, 2017) running on the website of two major universities in each country. Nearly 35 percent of the disseminated questionnaires were completed in both countries. Participants were both contacted individually and through companies which answered positively to the invitation to participate in the study. Before filling out the survey, participants were informed about the study, assuring them that the study was a research study and that the company would not access individual data and that companies simply helped the researchers disseminate the study. Informed consent was obtained online from all participants.

To allow comparative studies, the same procedures were used in both countries. The study was approved by the Ethics Committee of the University of Porto (on 03-18-2015), Portugal, and the University of São Paulo (on 01-09-2014; CAAE no. 33301214.2.0000.5407), Brazil, and followed the usual rules for online surveys, namely, no access of participants' companies to individual results and no direct contact between participants and researchers [A few used the email to clarify some details about access to individual data, but it is not possible to identify whether they participated in the study].

Data Analysis

A confirmatory factor analysis (CFA) was conducted to verify if the original two-factor structure proposed by Bakker et al. (2004), presented an adequate fit to the study sample. Only complete data cases were considered. As goodness-of-fit indices, SRMR (Standardized Root Mean Square Residual), RMSEA (root mean square error of approximation), NFI (Normed Fit Index), CFI (Comparative Fit Index), and the TLI (Tucker Lewis Index) were used. The fit of the model was considered good for TLI, CFI and TLI values above 0.95; SRMR below 0.08; and RMSEA values below 0.08 (Hoyle, 1995; Boomsma, 2000; McDonald and Ho, 2002; Byrne, 2010). All statistical analyses were performed with *R* (R Core Team, 2018) and *RStudio* (RStudio Team, 2018). The descriptive statistics were obtained with the *skimr* package (McNamara et al., 2018), the standard error of the mean (SEM) was calculated with the *plotrix* (Lemon, 2006) package and the coefficient of variation (CV) was estimated with the package *sjstats* (Lüdecke, 2019). To assess multivariate normality, Mardia's multivariate kurtosis (Mardia, 1970) was used; it was calculated using the *psych* package (Revelle, 2018). The *lavaan* package (Rosseel, 2012) was selected to conduct the CFA analyses using the Weighted Least Squares Means and Variances (WLSMV) estimation method (Muthén, 1983).

To test the proposed structure for OLBI, the cross-validity evidence was assessed to give information about how well the new structure will fit an independent sample of the same population (Cudeck and Browne, 1983). To do so, the sample was randomly split into two sub-samples through the package *minDiff* (Papenberg, 2018). The workers' age was used as criteria variable for which it was desired to minimize differences between subsamples (Papenberg, 2018). The subsamples were generated using 1,000 repetitions in order to minimize the differences, since the most equal group assignment was selected. Having two independent subsamples with similar properties, one subsample can be used as calibration subsample, and another as validation subsample (Chin and Todd, 1995).

The convergent validity evidence was analyzed using the average variance extracted (AVE) which was estimated as described in Marôco (2014) and Fornell and Larcker (1981). The constructs' convergent validity evidence was assumed for values of AVE $\geq$ 0.5 (Hair et al., 2009).

The discriminant validity evidence was checked (Fornell and Larcker, 1981; Marôco, 2014) to verify whether the items that represent a dimension were strongly correlated with other dimensions (Marôco, 2014): for two factors, x and y, if AVEx and AVE$y \geq \rho^2{}_{xy}$ (squared correlation between the factors x and y), there is discriminant validity evidence. The Heterotrait-monotrait (HTMT) criterion (Henseler et al., 2015) was also used. Values above 0.85 were considered indicative of satisfactory discriminant validity evidence (Kline, 2016). The HTMT ratios of correlations were calculated using the *semTools* package (Jorgensen et al., 2018).

The reliability of the scores was assessed with various estimates of internal consistency as recommended (Irwing and Hughes, 2018): $\alpha_{ordinal}$ (Zumbo et al., 2007), and $\omega_{ordinal}$ (Bollen, 1980; Raykov, 2001) using the *semTools* package (Jorgensen et al., 2018), higher values were indicative of better internal consistency results. Also, the McDonald's hierarchical omega (ω_H; Zinbarg et al., 2005) was estimated; a higher value of ω_H indicates a stronger influence of the latent variable common to all factors, and that the observed scale scores generalize to scores for the common latent variable (Zinbarg et al., 2007). The omega hierarchical subscale (ω_{HS}) was calculated for each specific factor, it reflects the reliability of each subscale after controlling for the variance due to the general factor (Reise et al., 2013). Both the ω_H and the ω_{HS} were used for calculating the internal consistency of the bi-factor model. There is some discussion about the use of $\alpha_{ordinal}$ (Revelle and Condon, 2018) as so we reported other estimates. The $\alpha_{ordinal}$ was calculated based on the polychoric correlations. However, the $\omega_{ordinal}$ and ω_H accounts for both item covariances and item thresholds (Green and Yang, 2009). The $\omega_{ordinal}$ and the ω_H are different in the denominator, the first assumes a congeneric factor model where measurement errors aren't correlated (Bollen, 1980), the second uses the observed covariance matrix instead of the model-implied covariance matrix (McDonald, 1999; Jorgensen et al., 2018). The CR was calculated by summing the z scores of the item scores. The second-order factor reliability was also calculated using the omega coefficient (Jorgensen et al., 2018). The proportion of observed variance explained by the second-order factor after controlling for the uniqueness of the first-order factor ($\omega_{partialL1}$); the proportion of the second-order factor explaining the variance of the first-order factor level (ω_{L2}); and the proportion of the second-order factor explaining the total score (ω_{L1}) were also calculated. The reliability estimates were calculated with the *semTools* package (Jorgensen et al., 2018).

The measurement invariance of the higher-order model was assessed using the *lavaan* package (Rosseel, 2012), the categorical items were considered into account through theta-parameterization (Millsap and Yun-Tein, 2004) to compare a group of seven different models based on the recommendations of Millsap and Yun-Tein (2004) and on the second-order models' invariance specificities (Chen et al., 2005): (a) configural invariance; (b) first-order factor loadings; (c) second-order structural loadings; (d) thresholds of measured variables; (e) intercepts of first-order factors; (f) disturbances of first-order factors; and (g) residual variances of observed variables. Mean scores for burnout latent variable were compared within the structural equation modeling framework; effect sizes (Cohen's *d*) were determined (Cohen, 1988). The raw means, SDs and score percentiles were calculated using the *doBy* package (Højsgaard and Halekoh, 2018).

RESULTS

The results related to psychometric properties of the OLBI in terms of internal structure are presented first, followed by the latent means comparisons, and finally by the validity evidence based on the relations to other variables.

Validity Evidence Based on Internal Structure

Dimensionality

Items' distributional properties

To judge distributional properties and psychometric sensitivity on the Portuguese and Brazilian samples, summary measures, skewness (Sk), kurtosis (Ku), and a histogram for each of the 16 items were used (**Table 4**). No strong deviations from the normal distribution (Finney and DiStefano, 2013) were considered for absolute values of Ku smaller than seven (7) and Sk smaller than three (3), assuring that they wouldn't compromise CFA results (Marôco, 2014). Mardia's multivariate kurtosis for the 16 items of OLBI was 48.88; $p < 0.001$. All possible Likert-scale answer values were observed on all items; no outliers were deleted. These items follow an approximately normal distribution in the normative population under study, since their distributional properties are indicative of appropriate psychometric sensitivity.

Factor-related validity evidence

To proceed with OLBI's transcultural adaptation to Brazil and Portugal, a cross-validity evidence approach was adopted. The sample was divided in two subsamples: calibration ($n = 586$) and validation subsamples ($n = 586$). The first was used to test which is OLBI's best solution in terms of fit to the data, and theoretical sense. The second subsample was used to assess cross-validity evidence of the proposed model. The two-factor OLBI fit to the data was mediocre ($\chi^2_{(103)} = 720.764$; $p < 0.001$; $n = 586$; $CFI = 0.980$; $CFI_{scaled} = 0.918$; $NFI = 0.977$; $TLI = 0.977$; $SRMR = 0.072$; $RMSEA = 0.101$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.094; 0.108[), since CFI, NFI, and TLI values were above 0.95 (good fit), SRMR values were bellow 0.08 (good fit), but RMSEA values were above 0.10 being indicative of poor fit (MacCallum et al., 1996). One item presented a very low loading ($\lambda_{\text{item13}} = 0.220$): and thus, this item was deleted. Also, based on the analysis of the modification indices, four correlations between items' residuals of the same factor were added, since it seems reasonable that indicators from the same factor explain shared error variance (Kline, 2016). The reduced model of 15 items showed better goodness-of-fit indices (**Figure 1**; $\chi^2_{(85)} = 514.098$; $p < 0.001$; $n = 586$; $CFI = 0.986$; $CFI_{scaled} = 0.937$; $NFI = 0.984$; $TLI = 0.983$; $SRMR = 0.064$; $RMSEA = 0.093$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.085; 0.101[), which indicated an acceptable fit, all items presented loadings above or equal to 0.47 ($p < 0.001$). The Cheung and Rensvold (2002) criterion ($\Delta CFI \leq 0.01$) supported the preference for the reduced model ($\Delta CFI_{scaled} = -0.019$). Thus, H1 was accepted.

Convergent validity evidence

To check if items contained within each factor are related to each other, the AVE was calculated for disengagement ($AVE = 0.57$), and for exhaustion ($AVE = 0.50$). These results suggest acceptable convergent validity evidence for the OLBI-15.

Discriminant validity evidence

The discriminant validity evidence between the two OLBI factors was unsatisfactory. These findings showed that the two factors are strongly related to each other, since $AVE_{disengagement} = 0.57$ and $AVE_{exhaustion} = 0.50$ were smaller than $r^2_{DE} = 0.69$. Regarding the HTMT ratio of correlations (Henseler et al., 2015) the obtained value (0.80) is below the satisfactory threshold. These findings point to the fact that the two factors' correlation might be explained by a second-order latent factor, by a bi-factor model or by a unidimensional model.

Unidimensional model

A unidimensional model where the factor burnout loads on all 15 items was tested. The four residuals' correlations were maintained. This model assumes that the only latent factor that explains the manifest variables is *burnout*. As so, it assumes that the other two latent variables (i.e., *disengagement* and *exhaustion*) aren't meaningful by themselves since the discriminant validity evidence wasn't satisfactory. The content explained by them is similar, the unidimensional model tests if it is plausible to specify a single latent variable.

The OLBI's unidimensional model presented an mediocre fit (**Figure 2**; $\chi^2_{(86)} = 737.139$; $p < 0.001$; $n = 586$; $CFI = 0.979$; $CFI_{scaled} = 0.913$; $NFI = 0.977$; $TLI = 0.975$; $SRMR = 0.077$; $RMSEA = 0.114$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90%

TABLE 4 | OLBI's items: descriptive statistics.

OLBI-16 items	Brazil										Portugal									
	M	*SD*	*SEM*	*Min*	*Max*	*Mode*	*CV*	*Sk*	*Ku*	Histogram	*M*	*SD*	*SEM*	*Min*	*Max*	*Mode*	*CV*	*Sk*	*Ku*	Histogram
OLBI1^{D}	2.42	1.13	0.05	1	5	2	0.47	0.64	−0.34		2.31	1.02	0.04	1	5	2	0.44	0.72	0.06	
OLBI2^{E}	3.38	1.26	0.05	1	5	4	0.37	−0.39	−0.96		3.33	1.24	0.05	1	5	4	0.37	−0.44	−0.90	
OLBI3^{D}	2.27	1.23	0.05	1	5	1	0.54	0.65	−0.68		2.58	1.25	0.05	1	5	2	0.49	0.38	−0.94	
OLBI4^{E}	3.11	1.34	0.05	1	5	4	0.43	−0.10	−1.19		3.34	1.19	0.05	1	5	4	0.36	−0.31	−0.89	
OLBI5^{E}	2.27	1.02	0.04	1	5	2	0.45	0.73	0.12		2.17	0.9	0.04	1	5	2	0.42	0.74	0.40	
OLBI6^{D}	2.50	1.23	0.05	1	5	2	0.49	0.48	−0.78		2.61	1.12	0.05	1	5	2	0.43	0.36	−0.73	
OLBI7^{D}	2.13	1.07	0.04	1	5	2	0.50	0.90	0.22		2.23	1.02	0.04	1	5	2	0.46	0.76	0.11	
OLBI8^{E}	3.13	1.31	0.05	1	5	4	0.42	−0.14	−1.14		3.09	1.21	0.05	1	5	4	0.39	−0.14	−1.01	
OLBI9^{D}	2.39	1.20	0.05	1	5	2	0.50	0.51	−0.76		2.43	1.16	0.05	1	5	2	0.48	0.44	−0.75	
OLBI10^{E}	2.93	1.24	0.05	1	5	2	0.43	0.07	−1.05		2.79	1.07	0.04	1	5	2	0.38	0.23	−0.73	
OLBI11^{D}	2.94	1.29	0.05	1	5	4	0.44	−0.01	−1.17		2.99	1.24	0.05	1	5	4	0.41	−0.07	−1.09	
OLBI12^{E}	3.00	1.29	0.05	1	5	4	0.43	−0.05	−1.11		3.02	1.13	0.05	1	5	4	0.38	−0.06	−0.91	
OLBI13^{D}	3.78	1.3	0.05	1	5	5	0.34	−0.80	−0.56		3.62	1.30	0.05	1	5	5	0.36	−0.58	−0.84	
OLBI14^{E}	2.24	0.98	0.04	1	5	2	0.44	0.72	0.14		2.15	0.87	0.04	1	5	2	0.40	0.98	1.25	
OLBI15^{D}	2.53	1.09	0.04	1	5	2	0.43	0.40	−0.48		2.76	1.04	0.04	1	5	3	0.38	0.28	−0.38	
OLBI16^{E}	2.58	1.14	0.05	1	5	2	0.44	0.39	−0.60		2.47	0.96	0.04	1	5	2	0.39	0.61	−0.05	

D, disengagement items; E, exhaustion items.

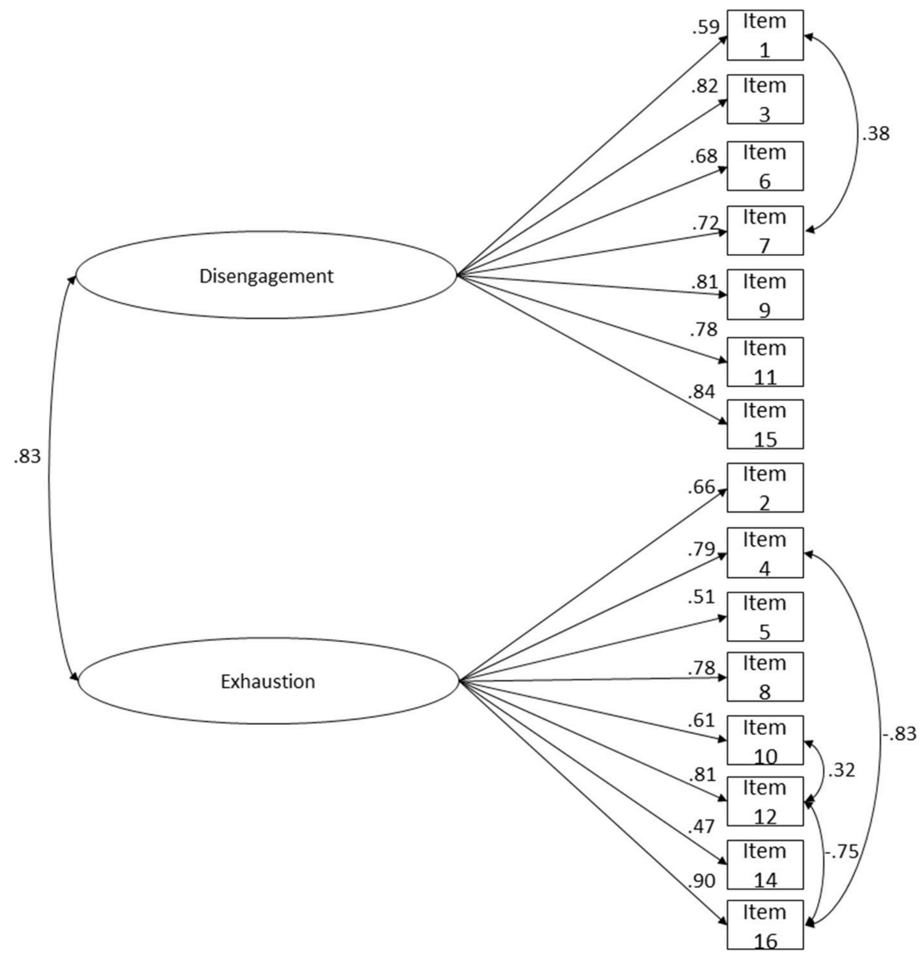

FIGURE 1 | OLBI's two-factor reduced version (15-item) structure fit. A combined sample of Portuguese ($n = 268$) and Brazilian ($n = 318$) workers. Correlations between latent variables, residuals' correlations and factor loadings for each item are shown. $\chi^2_{(85)} = 514.098$; $p < 0.001$; $n = 586$; $CFI = 0.986$; $CFI_{scaled} = 0.937$; $NFI = 0.984$; $TLI = 0.983$; $SRMR = 0.064$; $RMSEA = 0.093$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.085; 0.101[.

CI]0.106; 0.121[). Based on the Cheung and Rensvold (2002) criteria ($\Delta CFI \leq 0.01$) the two-factor reduced model was found to have a statistically better fit to these data than the unidimensional model ($\Delta CFI_{scaled} = -0.024$). All the factor loadings and residuals' correlations were statistically significant ($p < 0.001$). Item 14 had the lowest factor loading ($\lambda_{item14} = 0.450$).

Bi-factor[1] *model*

A bi-factor model (Holzinger and Swineford, 1937; Holzinger and Harman, 1938) is a *nested factor model* (Gustafsson and Balke, 1993) or *direct hierarchical model* (Gignac, 2008) that specifies a single *general* factor among each measured variable that accounts for commonality shared by the related domains; and multiple *specific* orthogonal factors each of which account for unique variance above and over the general factor (Rios and Wells, 2014; Mansolf and Reise, 2017; Chen and Zhang, 2018). The bi-factor model has advantages (Canivez, 2016; Chen and Zhang, 2018), but also some limitations (Mulaik and Quartetti, 1997; Reise et al., 2010; Murray and Johnson, 2013) in comparison with higher-order models (e.g., second-order models), as so, the choice between them should be carefully weighted.

The OLBI's bi-factor model presented an acceptable fit (**Figure 3**; $\chi^2_{(75)} = 392.202$; $p < 0.001$; $n = 586$; $CFI = 0.990$; $CFI_{scaled} = 0.937$; $NFI = 0.987$; $TLI = 0.986$; $SRMR = 0.056$; $RMSEA = 0.085$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.077; 0.093[). The $\Delta CFI \leq 0.010$ criterion (Cheung and Rensvold, 2002) didn't find *meaningful* differences between the two-factor reduced model and the bi-factor model ($\Delta CFI_{scaled} = 0.000$). All factor loading of the general factor (i.e., *burnout*) were statistically significant ($p < 0.001$), although the *specific* factors presented two non-significant loadings ($\alpha = 0.05$), one on the

[1]Bi-factor or bifactor model are both acceptable forms, we adopted the first one, originally used by Holzinger and Swineford (1937).

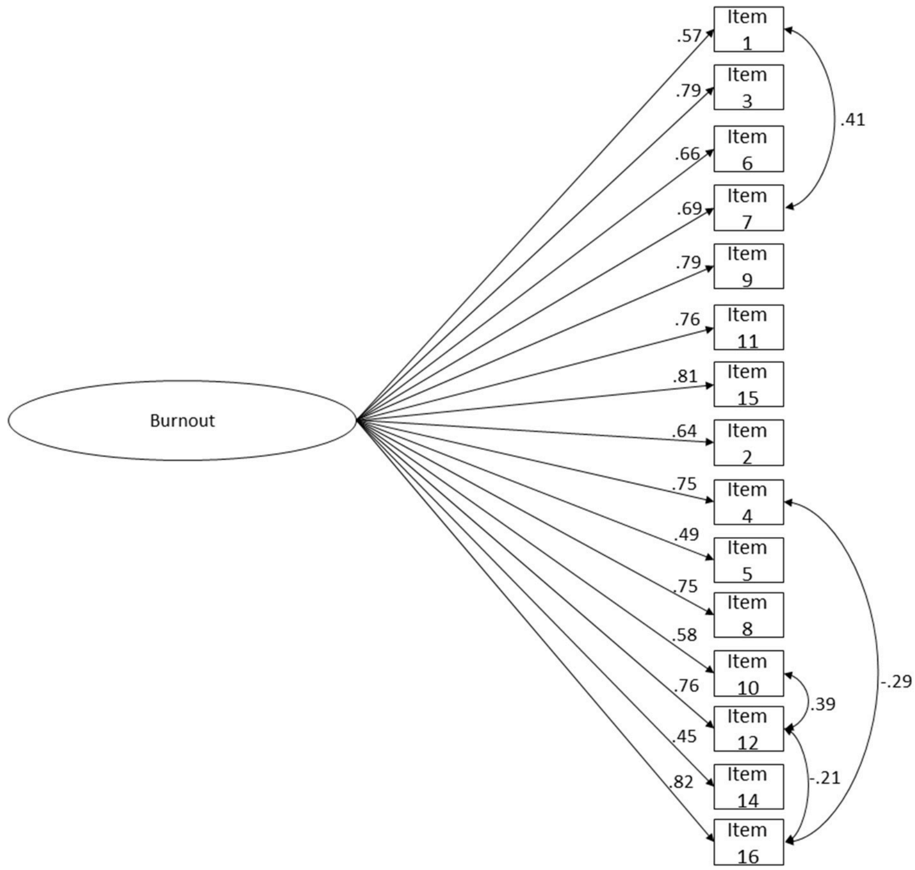

FIGURE 2 | OLBI's unidimensional reduced version (15 items) structure fit. A combined sample of Portuguese ($n = 268$) and Brazilian ($n = 318$) workers. Residuals' correlations and factor loadings for each item are shown. $\chi^2_{(86)} = 737.139$; $p < 0.001$; $n = 586$; $CFI = 0.979$; $CFI_{scaled} = 0.913$; $NFI = 0.977$; $TLI = 0.975$; $SRMR = 0.077$; $RMSEA = 0.114$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.106; 0.121[.

disengagement subscale ($\lambda_{item11} = -0.001$), and one on the *exhaustion* subscale ($\lambda_{item16} = 0.037$).

Second-order model

A second-order latent factor may be admissible when two factors have high correlations between them, or/and when exists a higher order construct which might explain the lower order factors (Chen et al., 2005; Marôco, 2014). Since the two OLBI factors did not present satisfactory discriminant validity evidence between them, a second-order model was tested. The higher-order construct was named as *burnout*. Having as a start point the reduced model, and since there were not enough degrees of freedom to test the second-order latent model, the two structural weights between the second-order factor and the first-order factors were constrained to be equal.

The OLBI's second-order latent factor model presented an acceptable fit (**Figure 4**; $\chi^2_{(85)} = 514.098$; $p < 0.001$; $n = 586$; $CFI = 0.986$; $CFI_{scaled} = 0.937$; $NFI = 0.984$; $TLI = 0.983$; $SRMR = 0.064$; $RMSEA = 0.093$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.085; 0.101[). The RMSEA value was mediocre, however its confidence interval was precise and point estimates for RMSEA have been shown to depend on sample size and model misspecification and model degrees of freedom (MacCallum et al., 1996; Chen et al., 2008). Nevertheless, other goodness-of-fit indices were used in conjunction to assess models' adequacy. SRMR values were acceptable, which seem to be generally accurate across all conditions (Maydeu-Olivares et al., 2018). The constrained structural weights from burnout to disengagement and exhaustion were high ($\gamma = 0.91$; $p < 0.001$). These results suggest that burnout is a higher order construct reflected on disengagement and exhaustion. The findings show that hypothesis 2 can be confirmed, since the paths from the second-order latent to the first-order ones were statistically significant ($p < 0.001$) and had high values.

The differences between the second-order model and the two-factor reduced model ($\Delta CFI_{scaled} = 0.000$) and the bi-factor model ($\Delta CFI_{scaled} = 0.000$) weren't *meaningful* based on the ΔCFI criteria (Cheung and Rensvold, 2002). After having in consideration all tested models (**Table 5**) the second-order model was selected, since it hadn't a worst fit than the bi-factor and the two-factor reduced model (based on the used criterion). This choice emerged as solution for the lack of evidence of

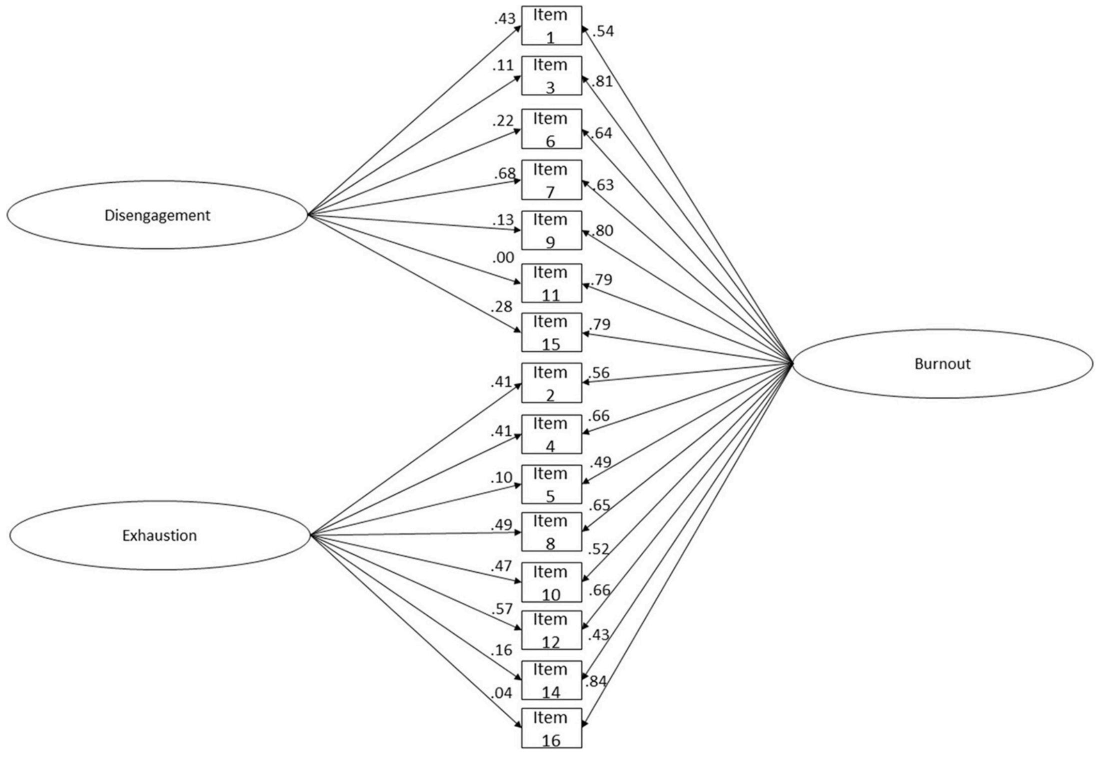

FIGURE 3 | OLBI's bi-factor reduced version (15 items) structure fit. A combined sample of Portuguese ($n = 268$) and Brazilian ($n = 318$) workers. Latent loadings for each factor; and factor loadings for each item are shown. $\chi^2_{(75)} = 392.202$; $p < 0.001$; $n = 586$; $CFI = 0.990$; $CFI_{scaled} = 0.937$; $NFI = 0.987$; $TLI = 0.986$; $SRMR = 0.056$; $RMSEA = 0.085$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.077; 0.093[.

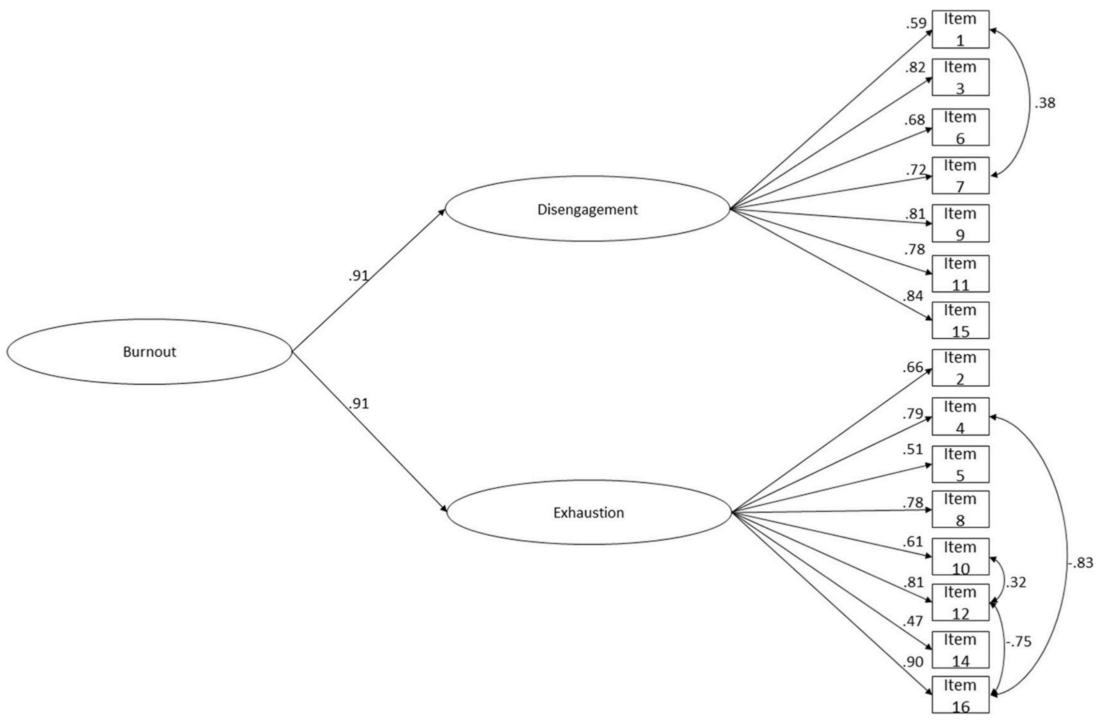

FIGURE 4 | OLBI's second-order factor reduced version (15 items) structure fit. A combined sample of Portuguese ($n = 268$) and Brazilian ($n = 318$) workers. Latent loadings for each factor; residuals' correlations and factor loadings for each item are shown. $\chi^2_{(85)} = 514.098$; $p < 0.001$; $n = 586$; $CFI = 0.986$; $CFI_{\text{scaled}} = 0.937$; $NFI = 0.984$; $TLI = 0.983$; $SRMR = 0.064$; $RMSEA = 0.093$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.085; 0.101[.

TABLE 5 | OLBI models' goodness-of-fit indices.

Model	χ^2	*df*	*CFI*	CFI_{scaled}	*NFI*	*TLI*	*SRMR*	*RMSEA*	*RMSEA 90% CI*
Two-factor^{C}	720.764	103	0.980	0.918	0.977	0.977	0.072	0.101	]0.094; 0.108[
Two-factor^{MI,C}	514.098	85	0.986	0.937	0.984	0.983	0.064	0.093	]0.085; 0.101[
Unidimensional^{MI,C}	748.051	86	0.979	0.913	0.976	0.974	0.079	0.115	]0.107; 0.122[
Bi-factor^{C}	392.202	75	0.990	0.937	0.987	0.986	0.056	0.085	]0.077; 0.093[
Second-order^{MI,C}	514.098	85	0.986	0.937	0.984	0.983	0.064	0.093	]0.085; 0.101[
Second-order^{MI,C}	591.172	85	0.985	0.934	0.983	0.982	0.068	0.101	]0.093; 0.109[

^{MI}Modification indices applied (four residuals' correlations); ^{C}Calibration sample; ^{V}Validation sample.

TABLE 6 | Internal consistency of OLBI dimensions (two-factor reduced version).

OLBI dimension	$\alpha_{ordinal\ total\ sample}$	$\omega_{ordinal\ total\ sample}$	$CR_{total\ sample}$
Disengagement	0.91	0.87	0.90
Exhaustion	0.87	0.87	0.88
Total	0.93	0.92	–

discriminant validity of the two-factor reduced model. And also as a plausible option in theoretical terms as also suggested by other authors who have proposed a burnout second-order factor using MBI, CBI and OLBI (Marôco et al., 2008, 2014; Marôco and Campos, 2012). The bi-factor model presents equivalent fit, and some authors also proposed it as an alternative structure using MBI and the Job Burnout Scale (Wang and Gao, 2010; Mészáros et al., 2014; Morgan et al., 2014) although with problems in some cases (i.e., non-convergence, unsatisfactory unique proportion of variance explained of the observed scores). The second-order factor had very high structural weights, while the bi-factor model had only one factor loading above 0.50 on each for the two *specific* factors, pointing for clear insufficient proportion of the variance explained on the *specific* factors. Altogether, the obtained results seem to present evidence that favors the second-order model.

This structure also showed cross-validity evidence, since it presented a good fit to the data also when using the validation sample ($\chi^2_{(85)} = 591.172$; $p < 0.001$; $n = 586$; $CFI = 0.985$; $CFI_{scaled} = 0.934$; $NFI = 0.983$; $TLI = 0.982$; $SRMR = 0.068$; $RMSEA = 0.101$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.093; 0.109[). The structural weights were high ($\gamma = 0.93$; $p < 0.001$).

Reliability of the Scores: Internal Consistency Evidence

To estimate the reliability of the scores on the various models, the complete sample was used. The internal consistency values of the two-factor first-order model reduced were high for the three coefficients (**Table 6**). They suggest very good validity evidence in terms of the reliability of the scores.

The same was observed on the unidimensional model internal consistency estimates ($CR_{burnout} = 0.93$; $\alpha_{ordinal} = 0.93$; $\omega_{ordinal} = 0.91$). Based on a bi-factor model, the hierarchical omega was high ($\omega_H = 0.85$) and omega hierarchical subscale (ω_{HS}; Reise, 2012; Reise et al., 2013; Rodriguez et al., 2016b) were low ($\omega_{HS\ disengagement} = 0.08$; $\omega_{HS\ exhaustion} = 0.20$). The *specific* factors reliability score after controlling for the variance due to the general factor was clearly unsatisfactory, reinforcing the evidence in favor of the second-order model. The ω_H value was high (Rodriguez et al., 2016a), suggesting a strong influence of the latent variable common to the two factors.

The proportion of observed variance explained by the second-order factor after controlling for the uniqueness of the first-order factor ($\omega_{partial\ L1}$) was 0.93. The proportion of the variance of the first-order factors explained by the second-order factor (ω_{L2}) was 0.91, and the proportion of the second-order factor explaining the total score (ω_{L1}) was 0.86. Thus, the internal consistency of the second-order construct was indicative of very good values.

Measurement Invariance

To verify if measurement invariance holds, the complete sample was used. The fit to the data of each individual group was globally acceptable. The Brazilian sample had an acceptable fit ($\chi^2_{(85)} = 687.077$; $p < 0.001$; $n = 604$; $CFI = 0.982$; $CFI_{scaled} = 0.922$; $NFI = 0.980$; $TLI = 0.978$; $SRMR = 0.073$; $RMSEA = 0.109$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.102; 0.117[) as so did the Portuguese sample ($\chi^2_{(85)} = 494.338$; $p < 0.001$; $n = 568$; $CFI = 0.988$; $CFI_{scaled} = 0.943$; $NFI = 0.985$; $TLI = 0.985$; $SRMR = 0.065$; $RMSEA = 0.092$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.084; 0.100[). The fit of the Females sample was slight better ($\chi^2_{(85)} = 537.474$; $p < 0.001$; $n = 678$; $CFI = 0.989$; $CFI_{scaled} = 0.944$; $NFI = 0.987$; $TLI = 0.986$; $SRMR = 0.059$; $RMSEA = 0.089$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.082; 0.096[) whereas the Males sample fit was marginally worse ($\chi^2_{(85)} = 492.213$; $p < 0.001$; $n = 364$; $CFI = 0.979$; $CFI_{scaled} = 0.922$; $NFI = 0.975$; $TLI = 0.974$; $SRMR = 0.081$; $RMSEA = 0.115$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.105; 0.125[).

To assess if the same second-order latent model holds in each sex and country, seven nested models with indications of equivalence were used (Marôco, 2014). Full uniqueness measurement invariance was supported for countries (**Table 7**) based on the Cheung and Rensvold (2002) criterion (absolute $\Delta CFI_{scaled} \leq 0.010$) and on the Chen (2007) criterion (absolute $\Delta RMSEA_{scaled} \leq 0.015$). The $\Delta\chi^2$ criterion (Satorra and Bentler, 2001) demonstrated the second-order metric invariance. Since

TABLE 7 | OLBI second-order latent model measurement invariance.

Model	χ^2	*df*	CFI_{scaled}	$RMSEA_{scaled}$	$\Delta\chi^2_{scaled}$	ΔCFI_{scaled}	$\Delta RMSEA_{scaled}$
COUNTRIES							
Configural (factor structure)	1,192.415	167	0.932	0.129	–	–	–
First-order loadings invariance	1,243.826	180	0.931	0.125	57.168***	0.001	0.004
Second-order loadings invariance	1,246.442	183	0.935	0.120	0.696[ns]	0.004	0.005
Thresholds of measured variables	1,365.285	224	0.932	0.111	139.591***	0.003	0.009
Intercepts of first-order factors invariance	1,402.498	225	0.931	0.112	12.342***	0.001	0.001
Disturbances of first-order factors invariance	1,431.365	227	0.933	0.110	6.352*	0.002	0.002
Residual variances of observed variables invariance	1,683.368	242	0.934	0.105	73.549***	0.001	0.005
SEX							
Configural (factor structure)	1,029.687	165	0.940	0.122	–	–	–
First-order loadings invariance	1,069.647	180	0.939	0.118	46.568***	0.001	0.004
Second-order loadings invariance	1,069.647	181	0.939	0.118	<0.001[ns]	0.000	0.000
Thresholds of measured variables	1,140.656	224	0.943	0.103	61.446*	0.004	0.015
Intercepts of first-order factors invariance	1,196.237	225	0.941	0.104	14.210***	0.002	0.001
Disturbances of first-order factors invariance	1,205.425	227	0.942	0.103	2.558[ns]	0.001	0.001
Residual variances of observed variables invariance	1,337.136	242	0.947	0.095	36.259**	0.005	0.008

[ns]*p > 0.05; *p < 0.05; **p < 0.01; ***p < 0.001.*

the $\Delta\chi^2$ criterion is too restrictive, we opted for the ΔCFI_{scaled} criterion. Results supported the structural invariance of the OLBI between Portugal and Brazil. The measurement invariance for OLBI among sexes (**Table 7**) was obtained, since full uniqueness measurement invariance was observed with the support of the Cheung and Rensvold (2002) criterion (absolute $\Delta CFI_{scaled} \leq 0.010$) and of the Chen (2007) criterion (absolute $\Delta RMSEA_{scaled} \leq 0.015$).

Sex's and Country's Burnout Latent Means Comparisons and Dimensions' Quartiles

Following the existence of full uniqueness measurement invariance, latent means can be compared. The results of the chi-square difference test suggest that weren't significant differences in burnout ($\Delta\chi^2_{scaled}$ (1) = 1.110; $p = 0.292$; $d = 0.067$) among countries. There weren't also statistically significant differences among countries in relation to the burnout dimension ($\Delta\chi^2_{scaled}$ (1) = 1.066; $p = 0.302$; $d = 0.066$). The quartiles, means, and SDs (raw values) for each sex within each country are presented in **Table 8**, these values are presented with the intent of providing population norms values.

Validity Evidence Based on the Relations to Other Variables

Burnout can be conceptualized as being the opposite of work engagement (Halbesleben and Demerouti, 2005). The UWES-9 second-order latent factor model presented a good fit ($\chi^2_{(24)} = 175.820$; $p < 0.001$; $n = 1,104$; $CFI = 0.999$; $CFI_{scaled} = 0.992$; $NFI = 0.999$; $TLI = 0.999$; $SRMR = 0.028$; $RMSEA = 0.076$; $P(\text{rmsea} \leq 0.05) < 0.001$; 90% CI]0.065; 0.086[). All factor loadings were statistically significant as also one added residuals' correlation from item 1 and 2 ($r = 0.76$). The internal consistency reliability estimates were good both for the first-order model ($\omega_{vigor} = 0.84$; $\omega_{dedication} = 0.92$; $\omega_{absorption} = 0.88$; $\omega_{total} = 0.96$) and for the second-order ($\omega_{partialL1} = 0.96$; $\omega_{L1} = 0.94$; $\omega_{L2} = 0.97$).

The first-order models of each instrument were used to establish correlations among the first-order latent variables (**Table 9**), and the second-order models of the instruments were used to analyze the correlation among the respective second-order latent variables ($r_{burnout*work\ engagement} = -0.85$). The obtained correlation between the latent OLBI and UWES dimensions was negative and moderate to high, demonstrating

TABLE 8 | Quartiles, means, and SDs for OLBI's dimensions (raw values) for countries and sexes.

OLBI dimension	Country									
	Brazil					Portugal				
	Multi-occupational (n = 604)					Multi-occupational (n = 568)				
	M	*SD*	25	50	75	*M*	*SD*	25	50	75
Disengagement	2.46	0.89	1.71	2.43	3.14	2.56	0.87	1.86	2.43	3.14
Exhaustion	2.83	0.84	2.25	2.88	3.50	2.80	0.75	2.25	2.75	3.25
Burnout	2.66	0.80	2.07	2.67	3.20	2.69	0.73	2.20	2.67	3.20

	Sex																			
	Brazil (n = 528)										Portugal (n = 514)									
	Female (n = 355)					Male (n = 173)					Female (n = 323)					Male (n = 191)				
	M	*SD*	25	50	75	*M*	*SD*	25	50	75	*M*	*SD*	25	50	75	*M*	*SD*	25	50	75
Disengagement	2.50	0.90	1.79	2.43	3.14	2.34	0.86	1.71	2.29	2.86	2.52	0.89	1.86	2.43	3.14	2.63	0.88	2.00	2.57	3.29
Exhaustion	2.88	0.85	2.25	3.00	3.50	2.66	0.80	2.13	2.63	3.25	2.87	0.76	2.38	2.88	3.38	2.64	0.72	2.19	2.75	3.13
Burnout	2.70	0.82	2.07	2.73	3.27	2.51	0.77	1.93	2.53	3.00	2.71	0.75	2.20	2.73	3.20	2.63	0.73	2.13	2.67	3.17

TABLE 9 | Correlations between OLBI's and UWES-9's latent variables.

	Vigor	Dedication	Absorption	Disengagement	Exhaustion
Vigor	1	–	–	–	–
Dedication	0.98	1	–	–	–
Absorption	0.88	0.92	1	–	–
Disengagement	−0.85	−0.87	−0.76	1	–
Exhaustion	−0.73	−0.63	−0.56	0.83	1

All correlations were statistically significant $p < 0.001$; df = 1,102.

the divergent validity of the measures obtained with OLBI (*burnout*) and the UWES-9 (*work engagement*).

DISCUSSION

Regarding the psychometric properties of the OLBI, results of this study provide evidence of the two-factor structure of the original instrument, having convergent validity evidence and good goodness-of-fit indices except for RMSEA value, which can be indicative of moderate errors of approximation in the population. Nevertheless, this value had a narrow confidence interval, that reflects a good precision of the model fit in the population (MacCallum et al., 1996). However, the discriminant validity evidence was not satisfactory (H1), which led us to test a possible second-order latent factor. Item 13 was removed from the tested version. Problems with item 13 also have been reported by Chevrier (2009). Item 13 has also been deleted from the OLBI-S proposal for Portuguese and Brazilian students (Campos et al., 2012) and OLBI's Malay version for students (Mahadi et al., 2018). In the Brazilian version for workers, that item was removed from the proposed reduced 13-item version (Schuster and Dias, 2018). Its removal was also suggested from the Italian version (Estévez-Mujica and Quintane, 2018). Other authors found that item 13's removal increased the disengagement internal consistency (Baka and Basinska, 2016). In the OLBI reduced Russian version (Smirnova, 2017), that item was the only one that lacked statistically significant loading, also being removed. In the Swedish version, it was the item with the lowest loading ($\lambda_{item\ 13} = 0.38$) (Peterson et al., 2011). Item 13's content, "*This is the only type of work that I can imagine myself doing*," did not seem to make sense within today's economic and professional context, where careers are so uncertain and the number of different employers across a career is increasing (Savickas, 2012). Furthermore, the sample is composed mainly of younger workers, most of whom have a higher education. This can contribute to a perception of more control over their career and desire for more professional experiences rather than maintaining the same employer for a long period. Additionally, four correlations within pairs of residuals' belonging to the same factor were added. Such modifications mean that some unwanted or unexplained source of variance exist outside of the original model, which can be due to various reasons (e.g., lack of comprehension of the items or an unwanted theoretical trait present in that factor) and as such is speculative (Cote et al., 2001). Nevertheless, it seems plausible that theory can be slightly imprecise, and since the model (second-order) passed through the cross-validation approach and reinforced the validity evidence obtained with the calibration subsample. The correlation between the two OLBI's dimensions was high; this finding is shared by other studies which found correlation values between OLBI's factors similar to ours (Khan et al., 2016). Those findings also pointed to unsatisfactory discriminant validity evidence between disengagement and exhaustion.

Our internal consistency estimates presented very good values supporting H2, in line with most of the studies which evaluated this kind of estimate (**Table 1**). Still, this study goes one step further, since it obtained estimates that gave evidence about the reliability of the second-order latent factor and the reliability of a potential bi-factor model (ω_H).

We admitted a possible second-order factor which was confirmed (H3) since the goodness-of-fit indices were not worse than the reduced version of the first-order model. The second-order model was also compared with a bi-factor model, which also didn't present *meaningful* better fit (i.e., $\Delta CFI_{scaled} <$ 0.01) to the data than the second-order model. The bi-factor model has various advantages (Reise et al., 2010), although—in this study- those potential advantages weren't confirmed by the obtained results. Since the unique variance explained by the *specific* factors of (after controlling for the variance due to the general factor) wasn't satisfactory (Rodriguez et al., 2016b). Additionally, empirical observations strongly suggest the second-order model presented high values of structural weights both on the calibration as on the validation subsamples. Regarding the existent theory, some authors proposed burnout as a second-order factor (Taris et al., 1999; Shirom and Melamed, 2006; Marôco et al., 2008) the same applies to the bi-factor model with some authors preferring it in relation to hierarchical model (Mészáros et al., 2014). However, if there wasn't prior knowledge from the field regarding burnout conceptualization, exploratory bi-factor analysis (Jennrich and Bentler, 2011) or bi-factor exploratory structural equation modeling (Morin et al., 2015) cloud be also suitable analyses. If one desires to analyze bi-factor models outside the standard CFA procedures (e.g., setting to zero paths from latent constructs to indicators that are not theoretically associated) can adopt the already referred bi-factor exploratory structural equation modeling or the bi-factor Bayesian structural equation modeling (Golay et al., 2013) analyses. Marôco and Campos (2012) have proposed the a second-order interpretation of burnout, although using a different instrument, the MBI. In other study, Marôco and Campos (2012) made the same suggestion using the MBI, CBI and OLBI. This suggests that, besides the two OLBI first-order factors, there is a higher-order more general burnout dimension. The obtained findings contribute to the study of OLBI and the burnout dimensionality, maintaining the two-order structure, but also suggesting a second-order latent, which brings a novelty to this study, since this was proposed for the first time for OLBI using a sample of workers.

The OLBI presented measurement invariance for sex and country supporting H4. To the best of our knowledge, this was the first time measurement invariance was assessed across sexes for the full OLBI instrument, since Foster (2015) only tested measurement invariance among sex on the separate factors. No study has found testing measurement invariance among countries, bringing a novelty to this study.

No statistically significant differences were found between sexes for burnout (H5), which shows that each sex experiences that dimension in the workplace similarly. Females are known for having higher levels of negative emotional states than males (Kessler et al., 2005); in consequence, females usually score higher than males on exhaustion (Purvanova and Muros, 2010; Kumar and Mellsop, 2013; Pu et al., 2017; Schadenhofer et al., 2018). However, a meta-analysis (Purvanova and Muros, 2010) found that males usually have higher depersonalization levels than females. Altogether, the differences reported on previous studies seem to be annulling each other in terms of the general second-order factor. The relationship between burnout dimensions and sex is not always clear. O'Connor et al. (2018) suggested in a meta-analysis on burnout in health professionals, that the burnout dimensions and sex have an inconsistent relationship. A similar finding was reported by Estévez-Mujica and Quintane (2018), which found no relationship between exhaustion, disengagement, and burnout and sex in a sample of research and development workers. A recent study with Portuguese health professionals at the national level, found no significant differences among sexes in terms of burnout (Marôco et al., 2016). For the country factor, no significant differences were observed for the burnout latent variable (H5). These results are in line with the findings of a comparative study among Portuguese and Brazilian health professionals using the MBI (Dias et al., 2010), no significant differences were found between the burnout dimensions. Western European countries seem to present lower average burnout scores than in other parts of the world (Golembiewski et al., 1996). These differences can be due to cultural differences (Golembiewski et al., 1993; Maslach et al., 2001), In some countries, as Brazil, such differences can also occur between regions of the same country as a result of being such a big and culturally-mixed country (Hofstede et al., 2010b). Differences between Portugal and Brazil seem to exist at the individualism level, with Portugal being more collectivist and with smaller power distance (Hofstede et al., 2010a). In Brazil, employers seem to be more risk-taking than their Portuguese counterparts (Silva et al., 2009). In other words, Portugal has larger avoidance to uncertainty values (Hofstede et al., 2010a). In Brazil, organizations operate through general rule as much as through personal relationships (Garibaldi de Hilal, 2009); whereas in Portugal, the work relations appear to be more impersonal and formal (Dias et al., 2010). Brazil presents larger indulgence values than Portugal (Hofstede et al., 2010a); the Brazilian culture also reflects ambiguity and double-edged ethics (Garibaldi de Hilal, 2006). Brazilian organizations seem to perceive responsibility toward employees as one of the less important business priorities (Hofstede et al., 2010a), which can lead to poorer attention to work conditions.

Regarding the last hypothesis, the validity evidence based on the relations with other variables was good (H6), since the presented correlations were moderate to high between OLBI and UWES factors. Other studies found Pearson's correlation value −0.55 between the work engagement (UWES) score and OLBI's disengagement factor, and −0.48 between work engagement (UWES) and OLBI's exhaustion (Bosman et al., 2005). In the present study, a higher work engagement correlation with disengagement than with exhaustion was also found. The produced results were in line with the findings of Petrović et al. (2017), who found similar correlation values between the instruments' dimensions and a higher correlation between the pairs of variables previously referred to González-Romá et al. (2006). In other words, the correlations between vigor and exhaustion were higher than with the other UWES variables, and the same for the disengagement-dedication pair. This study's results are in the same direction, reinforcing the higher association between disengagement and dedication than between disengagement and vigor or absorption, and a higher association between exhaustion and vigor than between exhaustion and dedication and absorption.

Our results confirmed the four of the five hypotheses and gave us, globally, good validity evidence regarding this OLBI version. However, since H1 had unsatisfactory validity evidence in terms of discriminant validity, this study brought a novelty (in terms of OLBI dimensionality studies); therefore, a second-order latent model was proposed, which is admissible from a theoretical and practical perspective. Thus, it is suggested that OLBI can be used to compare burnout levels among samples with different occupations and sexes from Portugal and Brazil. However, since the proposed version is a reduced version, it must be said that the reduced version must be tested in independent samples of the same populations (Marôco, 2014).

Theoretical Implications

Burnout seems to be a second-order factor that loads on two first-order factors, disengagement, and exhaustion—which are burnout's core dimensions. This underlines the expansion of the burnout domain beyond the exhaustion affective component (Halbesleben et al., 2004). Female and male workers experience similar levels of burnout, the same happens among Portuguese and Brazilian workers. The obtained results demonstrate that the absence of differences in burnout between sexes and countries suggest that the work experiences in terms of stress are similar in both samples. The observed differences between sexes reported on other studies are small (Purvanova and Muros, 2010) and might be related to other factors—namely family and workload (Bekker et al., 2005; Langballe et al., 2011).

Practical Implications

To have instruments with good validity evidence, it is mandatory to have confidence in the obtained measures. OLBI can help to establish comparisons between sexes, and countries. However, one should be aware of the different versions and of the quality of the evidence provided in each study. Also, OLBI can be useful and practical, since it is a freely available self-report psychometric instrument which can contribute to studies where the impact of companies' interventions are studied (Gíslason and Símonardóttir, 2018). In fact, there is evidence that occupational stress can be reduced with specific interventions (Ruotsalainen et al., 2015). The development of a family-friendly work environment should be approached, allowing one a focus on the importance of a balance between work and life (Lo, 2003; Rubino et al., 2013). Giving workers paid sick days, medical and family leave insurance programs, and greater control over their schedule (Appelbaum et al., 2014) are good suggestions to improve the balance between work and home activities. However, any change in organizational practices without a corresponding change in social attitudes will not be enough (Field and Bramwell, 1998). Prevention strategies should consider the social and individual level of those that will receive them (Maslach and Leiter, 2017).

Limitations

This study used two convenience samples. It had no other psychological measures besides burnout and work engagement, which would allow better assessment of the validity evidence based on the relationship between other variables—namely, predictive, concurrent, and discriminant evidence (American Educational Research Association, 2014). For example, a concurrent burnout measure which would allow verification of the concurrent validity evidence between different burnout instruments, as some studies have done (Demerouti et al., 2003; Marôco and Campos, 2012) would have been useful. Another limitation is that culture-specific aspects of stress were not assessed, which could explain some of the observed differences.

Future Research

Further studies using OLBI should test its concurrent validity evidence with other burnout instruments (American Educational Research Association, 2014), something that has been tested with success in the Portugal-Brazil version for students (Campos et al., 2012) and in the Greek version for workers (Demerouti et al., 2003). The Portugal-Brazil OLBI version should be tested in samples of specific occupational groups (e.g., Armed Forces Occupations, Craft and Related Trades Workers, Skilled Agricultural, Forestry and Fishery Workers, Plant and Machine Operators and Assemblers, and Elementary Occupations), of whom there was not a satisfactory number in the sample collected for this study. The same applies to lower academic levels, which showed unsatisfactory frequency in this study. Future research should also assess the family load together with the workload to understand the family-work interaction regarding burnout.

CONCLUSION

Initially, burnout research was linked to human services occupations: thus, sex was not a concern since most employees in this area were female. This study compared burnout levels between sexes in two different countries, and simultaneously adapting a specific instrument that allows establishing direct comparisons between countries.

OLBI offers various advantages over other instruments that can measure burnout, and the obtained findings focus on the utility of this inventory to compare burnout among sexes and countries using samples from Portugal and Brazil. The instrument showed validity evidence based on the internal structure and on the relation with other variables (work engagement and its first-order dimensions). Altogether, the proposed OLBI version appears to be a valid alternative to assess burnout and establish rigorous comparisons between Portuguese and Brazilian workers. The differences between sexes seem to non-existent. Burnout differences reported in other studies seem to be related to other factors, such as work and family load, as previous research suggested (Bekker et al., 2005; Langballe et al., 2011).

AUTHOR CONTRIBUTIONS

All authors of this research paper have directly participated in the planning, execution, or analysis of this study. More specifically, JS wrote the first draft, and with JM performed all statistical analysis and its discussion. JS and SP discussed cross-cultural topics, and JS and CQ discussed theoretical framework.

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Empathy at the Heart of Darkness: Empathy Deficits That Bind the Dark Triad and Those That Mediate Indirect Relational Aggression

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The dark triad (DT) traits–psychopathy, narcissism and Machiavellianism–have collectively been linked to reduced empathy and increased aggression; however, their association with distinct empathic subtypes remains unclear; and unique links to indirect relational aggression (IRA) have not been delineated. Moreover, whether dark traits should be conceptualized individually, as a dyad or as a triad with a dark core centered around the absence of empathy is debated. The current study examines (i) whether impaired empathy indeed represents a common "dark core" binding Machiavellianism, narcissism, and psychopathy, and (ii) this core explains associations between the dark traits and IRA. Participants ($N = 301$, 262 F/39 M) completed measures of the DT traits, cognitive and affective empathy components and IRA (Social Exclusion, Malicious Humor and Guilt Induction). The individual traits model without links between narcissism and IRA showed the best fit, suggesting that, at least in the context of IRA, the DT traits are best viewed as three independent personality traits. Distinct cognitive and affective empathy deficits and capacities are seen in the DT. Peripheral responsivity was the only type of empathy deficit associated with all dark traits, but unrelated to IRA. Psychopathy was the strongest indicator of impaired empathy and all IRAs; however, only online simulation, an affect-related cognitive empathy facet, partially mediated the relationships of psychopathy and Machiavellianism with IRA. Whilst the unique pathways for the dark triad traits suggest stronger alignment of psychopathy and Machiavellianism in their empathic deficits and indirect aggression; the data do not support the notion that an unempathic dark core underpinning all three traits drives indirect aggression. This is the first paper delineating the specific empathic deficits involved using a facet approach and their link to indirect forms of aggression. Results therefore inform theoretical models of aggression in the DT and offer some clarity on the debates surrounding the unempathic dark core in the DT.

Keywords: dark triad, cognitive empathy, affective empathy, online simulation, relational aggression

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INTRODUCTION

Empathy is central to prosocial interactions, understanding the suffering of others, and attenuates the propensity to maladaptive aggressive behavior (1). Reduced empathy, along with other traits, is proposed to represent a "core," interconnecting three maladaptive personality constructs–Machiavellianism, narcissism, and psychopathy—which have been conceptualized as the Dark Triad [DT; (2, 3)], and associated with aggression (4). Whether this is indeed the case is fuelled by a lack of empirical findings that delineate facets of empathy underpinning the core and those more uniquely linked to the individual dark traits [e.g., (5)]. According to the Violence Inhibition Mechanism model [VIM; (6)], a selective impairment in the emotional recognition and response to distress cues, such as fearful and sad expressions, exacerbates aggression in psychopathy (7). However, less is known about the empathy-aggression link in the context of the other two DT traits. If aggression is driven by the absence of those empathic traits that also form the dark core, the VIM model would theoretically also apply to Narcissism and Machiavellianism. Conceptualizations of the dark traits as separate traits without an unempathic core, currently debated in the field [e.g., (8) for review; (9–13)], might challenge this notion. Moreover, whilst direct forms of physical aggression have been typically studied in this context, less is known about these associations for more indirect forms of aggression. The current study seeks to close this gap by examining (i) whether impaired empathy indeed represents a common "dark core" binding Machiavellianism, narcissism, and psychopathy, and (ii) whether empathy deficits explain associations between the dark traits and indirect relational aggression [IRA; (10)].

In Search of the Core of Evil

Each DT trait has been described with unique characteristics: Machiavellianism describes an exploitative cynical nature, being a manipulator rather than manipulated (14, 15). Narcissism is characterized by an exaggerated sense of entitlement, superiority, and grandiose thinking (2). Psychopathy comprises a constellation of affective-interpersonal (superficial charm, callous affect) and behavioral (erratic lifestyle, antisocial behavior) deficits (16, 17). Nevertheless, the DT traits are significantly inter-correlated (18) with considerable convergent correlations between subscales (19).

Collectively, the DT traits share a propensity for a callous and manipulative interpersonal life-style, leading prior research to examine the empirical overlap between these subclinical personality traits, in order to designate the underlying core of "evil" personalities. The so-called "dark core" is proposed to comprise a set of traits and emotional deficits that is common across all three traits, explains their shared variance and promotes a selfish and antagonistic lifestyle (4). Most notably, callous-unemotional (CU) traits and empathic deficits have been proposed to constitute the shared dark core of all three dark traits (3), as well as low Agreeableness (2), low Honesty-Humility (13, 20, 21), and a behavioral overlap of an alternative fast and exploitative life history strategy (22).

Importantly, there are debates in the field as to how the DT should be best conceptualized–as individual traits or shared constructs with a joint dark core (8). For example, some authors propose that narcissism is less central to the dark core than psychopathy and Machiavellianism, and best viewed as a separate construct, leaving psychopathy and Machiavellianism as a dark dyad [e.g., (10, 23)]. Indeed, a factor analytic study showed a stronger clustering of psychopathy and Machiavellianism with other variables (e.g., moral disengagement, unethical attitudes, and disagreeableness) capturing antisocial variance, whereas narcissism was much stronger associated with a non-antisocial factor alongside traits such as extraversion and intellect (11). Psychopathy and Machiavellianism share more overlap than they do with narcissism, and greater similarity in their associations with other CU personality correlates [i.e., low Agreeableness and Conscientiousness; (12)]. Nevertheless, confirmatory factor analyses suggest that a two-factor model combining psychopathy and Machiavellianism, and keeping narcissism separate, has equivalent fit to the standard three factor model; as such, deciding between the optimal model may need to be based on theoretical grounds (12). However, a recent meta-analysis [102 studies, $N = 46{,}234$; (13)] suggests that the DT model inadequately captures the malevolent side of personality. Machiavellianism and psychopathy were more strongly linked to adverse psychosocial outcomes than Narcissism. Moreover, once psychopathy had been controlled, it alone remained significantly associated with all of the considered outcomes (including direct aggression). In comparison, the majority of the average effect sizes for both Machiavellianism and narcissism became considerably smaller and mostly non-significant (apart from interpersonal difficulties for both and antisocial tactics for Machiavellianism). These findings suggest the DT traits should be treated as independent constructs. Finally, examining the factorial structure of the DT traits, another recent study showed better model fit for a single latent dark core dimension compared to conceptualizing three independent traits (9), suggesting that the dark personalities are best represented through the single dark core and rendering the individual traits redundant. The mixed findings in the literature may partly be attributable to the measurement tools used, and their respective reliability and validity issues (8). Taken together, it is heavily debated whether the DT traits are best conceptualized as (i) three unique monads (single constructs), (ii) a Machiavellianism and psychopathy dark dyad, with narcissism as a separate construct, or (iii) a single joined dark triad core subsuming the three traits in predicting maladaptive behavior.

Dark Traits and Different Forms of Aggression

Each DT trait has been linked to different forms of aggressive behaviors. Psychopathy is the strongest predictor of physical and premeditated aggression (13, 24–26); however, under certain conditions of response provocation, narcissistic and

Machiavellian individuals are also likely to act aggressively. For example, narcissistic individuals are particularly responsive to ego-threat [i.e., any perceived attack on their self-image; (4)]. Whilst direct aggression has been extensively studied in the context of the DT, less is known about associations with indirect forms of aggression (i.e., those that are manipulative and more covert in nature). For example, whilst psychopathy has been linked to direct bullying behaviors in adults, narcissism and Machiavellianism have been linked to more indirect methods of intimidation (27). However, the association for narcissism was weak and potentially due to the shared variance with psychopathy (27), which would be in line with the findings of the recent meta-analysis (13).

Indirect relational aggression (IRA) reflects clandestine behaviors, aimed at damaging relationships and social status [e.g., peer group exclusion, rumor spreading, gossiping; (28)]. In this context, Machiavellianism has been linked to increased relational aggression in both adults and children, indicating that the cold, calculating nature suits a less direct and less physical use of force (29, 30). Similarly, whilst psychopathy and pathological vulnerable narcissism (more emotional, anxious and sensitive to criticism and rejection) have both been linked with increased reactive and proactive relational aggression in adults, grandiose narcissism (more akin to the DT-Narcissism) was linked to reduced relational aggression (31). Thus, in terms of both direct and indirect types of aggression more specific associations can be observed for the individual DT traits with different expressions of aggressive behavior.

Empathy Deficits at the Core of Aggressive Behavior: Which Ones?

If the dark core is proposed to be underpinned by a lack of empathy that drives increased aggression in the DT, we would expect to see similar patterns across the DT. However, the unique associations of each DT trait with different expressions of aggressive behaviors are likely driven by more distinct affective and cognitive empathic deficits. Empathy is a multidimensional construct [e.g., (32)]—constituting cognitive and affective components. Cognitive empathy has been defined as the capacity to recognize and understand another person's mental states—*knowing what someone thinks*. Such perspective taking is essential for predicting behavior of others and manipulating them (33). Affective empathy involves a vicarious response to the emotional display of others—*feeling what someone feels*. It is this type of empathy that is implicated in the functioning of the Violence Inhibition Mechanism model [VIM; (6)], and the selective impairment in this capacity is thought to underpin aggression at least in psychopathy (7, 34). In addition to deficits in affective empathy, impairment in *affect-related* cognitive empathy–defined as the inability to *know* (rather than feel) *the emotions of another*—were also found in institutionalized offenders with psychopathic tendencies (35). By extension, if driven by the unempathic dark core, these mechanisms would then also apply to the other two traits. Indeed, affective empathy deficits have been linked to all three dark traits (individually and within the context of the DT), indicating a mutual inability to share the emotional experience of others (15, 36). However, once shared variance was accounted for, these findings were driven by psychopathy (15). On the other hand, there is also some evidence that all three DT traits are associated with reduced cognitive empathy, though this was driven only by psychopathy once shared variance was accounted for (37). In other cases, cognitive empathy appeared to be spared, or even increased in the case of Narcissism, which would suggest normal or better understanding of others' thoughts and intentions (15). Thus, the links between the DT and cognitive empathy deficits are less consistent.

Mixed findings might be due to the jingle-jangle fallacy, whereby different definitional constructs of cognitive (or affective) empathy have been measured and conflated across different studies (38). Moreover, whilst most studies have focused on general or more basic assessments of affective or cognitive empathy, a more fine-tuned facet approach within those types of empathic deficits may be more useful in predicting more specific forms of aggression (39). Reniers et al. (40) devised a multidimensional model of empathy distinguishing between different aspects of cognitive and affective empathy. Firstly, in their working definition cognitive empathy is the attribution of emotion (rather than cognition) more akin to the affect-related cognitive empathy construct above. Affective empathy is defined as sensitivity to and experience of others' feelings (rather than sharing or being aware of others' feelings, and distinct from sympathy). Their resulting model (and measurement instrument) encompasses perspective taking–*understanding and seeing others' emotional perspective*–and online simulation–*understanding another's perspective by imagining what they are feeling* as cognitive empathy components, whereas affective empathy comprises emotional contagion–*automatic mirroring of another's emotions*, proximal responsivity–*affective response to emotional cues of others*, and peripheral responsivity–*affective response to emotional cues in detached contexts (e.g., immersive settings like TV).* With a few exceptions, (different factors of) psychopathy and Machiavellianism were associated with deficits across those scales and affective empathy was more strongly linked to expressive and instrumental forms of aggression; however, shared variance and mediation effects were not assessed in these analyses to derive a more informative distinct pattern of associations and predictions for the current study. Thus, the exact nature of such specific deficits in the DT traits remains unclear, as to the knowledge of the authors, prior research has not looked at these facets of cognitive and affective empathy in the context of the DT. Therefore, the current study examines these links controlling for the overlap of the DT traits to assess their unique and shared associations with those facets of affective and cognitive empathy in more detail. As such we want to examine which of these facets underpins the dark core (if supported) and which are more uniquely linked to individual traits.

Moreover, whilst direct forms of aggression have been examined within the VIM model, the extent to which this model applies to indirect aggression is less clear.

Cognitive empathy has been shown to mediate the link between callous-unemotional (CU) and reactive relational aggression in women, indicating that women with reduced perspective taking skills are more likely to engage in relational aggression (41). Thus, whilst affective empathy has been proposed to play a central role in direct physical aggression [*cf.* VIM model; (6)], indirect aggression may be driven by cognitive empathy components. Given that distinct brain systems underpin those processes (42), it is clear that distinguishing those systems is crucial to further our understanding of the distinct motivational and behavioral mechanisms and pathways involved. Moreover, delineating those associations is important in terms of their theoretical implications as to whether such deficits are driven by an unempathic dark core and as such are common across all DT traits. This extends further to a practical need to better understand which subtypes of empathy drive different forms of aggression in order to inform more targeted intervention strategies.

Summary and Hypotheses

There is a debate over the conceptualization of the DT traits as monad, dyad or triad, and whether the expression of distinct empathic deficits is linked to the unique or shared (aka dark CU core) variance of the three traits. Also little is known about the extent to which they subsequently promote similar or distinct patterns of indirect relational aggression. Few studies have taken a more fine-tuned facet approach to examine the unique and shared empathic deficits in the DT to examine whether they jointly or uniquely underpin aggressive behavior. Delineating these association will directly address one of the most prominent debates in the field and have strong theoretical implications in terms of the usefulness of the concept of the Dark Triad or indeed the individual dark triad traits.

The aim of this study was to examine which conceptualization of the DT best explains the relationships between the DT traits, empathy and indirect relational aggression: (1) an unique trait contribution of three *dark monads*, (2) a *dark dyad* (Machiavellianism and psychopathy) with a separate narcissism construct, or (3) a joint *dark triad* (Machiavellianism, psychopathy and narcissism). The study examined their unique and shared relations to distinct facets of cognitive and affective empathy, and different forms of IRA—social exclusion, malicious humor, and guilt induction. As with direct aggression, we hypothesized that, psychopathy will be the strongest predictor of all three IRA behaviors, whereas the manipulative and strategic nature of Machiavellianism will be linked to social exclusion and guilt induction. Both affective and cognitive empathy deficits were expected to be more (similar and) apparent in psychopathy and Machiavellianism. Specifically impairment in cognitive empathy components were expected to mediate the relationship of psychopathy and Machiavellianism with IRA. For narcissism, we did not expect empathy deficits or direct links to IRA after controlling for the other two traits.

METHODS

Participants and Procedures

Three-hundred and one participants [262 females;[1] age range 18–71 years, $M = 26.87$, $SD = 11.66$] were recruited from two UK University participant pools and via general online participation schemes. Ethical approval was obtained from the University Ethics Committees.

Measures

The Dark Triad

Machiavellianism, narcissism, and psychopathy were measured using the 27-item Dark Triad of Personality Scale [D3-Short; (17)], scored on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Mean scores are calculated for the three subscales (9 items each) with higher scores indicating higher level of DT traits. The SD3 is a reliable measure with Cronbach's alphas ranging from 0.77 to 0.80, and respective associations with standard measures of psychopathy, Machiavellianism, and narcissism (13).

Empathy

Empathy was measured using the Questionnaire of Cognitive and Affective Empathy [QCAE; (40)] comprising 31 items in total scored on a 4-point Likert scale (1 = strongly agree to 4 = strongly disagree). Cognitive empathy consists of two facets: (1) perspective taking (PT; 10 items)–understanding internal mental states of others; and (2) online simulation (OS; 9 items)–understanding another's perspective by imagining what they are feeling. Affective empathy splits into three facets: (1) emotional contagion (EC; 4 items)–automatic copying of another's emotions, (2) proximal responsivity (ProR; 4 items)–response to emotional cues of others, and (3) peripheral responsivity (PerR; 4 items)–response to emotional cues in immersive settings. Cronbach's alphas range from 0.65 to 0.85. Scale scores were calculated by summing respective items.

Indirect Relational Aggression

Indirect relational aggression was measured using the Indirect Aggression Scale – Aggressor version [IAS-A; (28)]. The 25-item IAS-A consists of three subscales: Social Exclusion (SE; 10 items); Malicious Humor (MH; 9 items) and Guilt Induction (GI; 6 items). Participants indicate to what extent they had behaved aggressively during the last 12 months on a 5-point Likert scale (1 = never to 5 = regularly). Mean scores were obtained for each subscale. Cronbach's alphas range from 0.81 to 0.84.

[1]Participants were asked to indicate their biological sex with males, females and other as response options (none indicated latter); hence, we use sex rather than gender when we refer directly to our study data. When we refer to the wider literature, we are either concordant with what the respective authors use in their terminology or use both "sex/gender" terms [see (43)] if used interchangeably within the respective literature. Some previous research suggests that relational aggression is more prominent in women; however, a large meta-analysis shows minimal gender differences (44). Nevertheless, we control for sex in our analyses to account for the overrepresentation of females in the sample.

Statistical Analyses

Preliminary analyses revealed that several variables were skewed[2]; however, maximum likelihood estimators can provide estimates that are robust to non-normality (45). To gain a clearer understanding of how empathy relates to indirect aggression, the first step of analysis regressed all three IRA outcome variables on the five empathy variables. Following this, three main path models were specified from zero-order correlations and estimated using maximum likelihood in order to assess the fit of the different DT conceptualizations, and examine the relationships between the DT traits, empathy and indirect aggression factors. The first model assessed the unique contribution of the DT traits as *monads*, whereby the DT traits (Machiavellianism [M], psychopathy [P] and narcissism [N]) were separate observed variables and specified as correlated in order to account for their shared variance. The other two models assessed shared dark core contributions. The *dark dyad* model tested a latent variable with Machiavellianism and psychopathy as indicators, and narcissism as separate observed variable[3], the *dark triad* model tested a latent variable with all three DT traits as indicator variables. Direct paths were specified from the DT traits compositions to IRA variables (with and without direct paths between Narcissism and IRA, and from the DT traits compositions to cognitive (PT and OS) and affective empathy variables (EC, ProR, PerR). Pathways were tested relating to the significant paths from the empathy variable/s (based on the regression results) to the IRA outcome variables (SE, MH, GI). Furthermore, empathy subscale scores were correlated with one another. Indirect effects were examined where applicable.

All analyses were undertaken in Muthén and Muthén (47) and if not stated otherwise, estimates reported are based on STDYX standardization. Model fit was deemed adequate with a non-significant chi-square value (taking sample size considerations into account), a root mean square error of approximation (RMSEA) below 0.05, a standardized root mean square residual (SRMR) below 1, and comparative fit (CFI) and Tucker-Lewis indices (TLI) above 0.90 (48).

RESULTS

Descriptive Statistics

Mean, standard deviations and Cronbach's alphas for the DT traits, cognitive and affective facets of empathy and IRA are displayed in **Table 1**. All variables show good reliability with alphas ranging between 0.74 and 0.92.

Relationship of Empathy to IRA

Regressing all empathy variables on the three IRA outcome variables while controlling for age and sex led to a significant prediction of variability in SE (12.4%), MH (15.3%) and GI (14.9%) (all $ps < 0.001$). Looking at the predictor variables, only OS significantly and negatively predicted SE (unstandardized $b = -0.042$), MH (unstandardized $b = -0.034$), and GI (unstandardized $b = -0.047$) (all $ps < 0.001$). The standardized beta values can be seen in **Table 2** (zero-order correlations can be found in the **Supplementary Material**). Consequently, the path model tests specified a path from the empathy variable OS only to all IRA variables.

TABLE 1 | Descriptive statistics for all variables.

Measures	Alpha	Mean	*SD*
DARK TRIAD			
Machiavellianism	0.80	2.87	0.66
Psychopathy	0.75	2.06	0.59
Narcissism	0.74	2.65	0.60
INDIRECT RELATIONAL AGGRESSION			
Social exclusion	0.89	1.50	0.60
Malicious humor	0.89	1.45	0.60
Guilt induction	0.90	1.50	0.74
EMPATHY			
Perspective taking	0.92	32.80	5.30
Online simulation	0.87	27.50	4.90
Emotional contagion	0.85	11.00	8.80
Proximal responsivity	0.74	12.00	2.40
Peripheral responsivity	0.74	11.70	2.87

TABLE 2 | Standardized betas from the regression results of empathy predicting IRA.

	SE	MH	GI
Perspective taking	0.08	0.01	0.11
Online simulation	−0.34***	−0.28***	−0.31***
Emotional contagion	−0.07	−0.05	0.02
Proximal responsivity	0.03	−0.04	−0.11
Peripheral responsivity	−0.05	−0.06	−0.10
Sex	0.02	−0.09	0.05
Age	−0.03	−0.13*	−0.01

****p* < 0.001; **p* < 0.05. SE, social exclusion; MH, malicious humor; GI, guilt induction.*

Specified Path Models Testing the Conceptualization of DT Traits

Model fit statistics are presented in **Table 3**. When direct paths from all DT traits to IRA were specified, Model 1 (*dark monads*) was not deemed a good fit: other than the SRMR, none of the indicators reached acceptable levels. Model 2 (*dark dyad*) also showed a poor fit, despite the SRMR and the CFI reaching acceptable limits. Model 3 (*dark triad*) showed a questionable fit: while CFI and SRMR reached acceptable thresholds, and TLI was only slightly below, RMSEA did not show adequate fit. These analyses confirmed that there were no significant paths between N and any of the IRA variables. Model 2a (*dark dyad* model without paths from N to IRA) did not reach acceptable

[2] Psychopathy was positively ($z = 5.67$), PT, OS, ProR, and PerR were negatively skewed (z scores between −3.59 and −5.93). The IRA subscales showed the greatest skew (all $z > 15$).

[3] Models with two indicators for a latent variable are deemed problematic as construct representation is less accurate; however, they are nevertheless often specified in empirical research as this bias can be reduced when there is high communality between the indicators (46).

model fit as both the RMSEA and the TLI missed specified cut-offs. However, Model 1a (*dark monads* model without paths between N and IRA) was deemed to fit as the Chi-square is non-significant, and all fit indices reach the cut-off values, even though the upper boundary of the 90% confidence interval of the RMSEA is not below 0.08 (49). This model also fit when age and sex were controlled for (model 1a_control), even though the upper boundary of the 90% confidence interval of the RMSEA was not below 0.08. A path model with standardized estimates and showing significant paths only is shown in **Figure 1**.

With regards to the empathy variables, only P was negatively related to all ($ps \leq 0.043$), whereas M was negatively related to OS and PeriR only ($ps \leq 0.011$). N was negatively related to PeriR ($p = 0.037$), as well as positively to PT ($p < 0.001$). In terms of the relationship with IRA, only P was positively related to all three outcomes ($p < 0.001$), M only significantly positively to GI ($p = 0.004$). Both M and P also negatively predicted OS ($ps \leq 0.001$), suggesting OS as partial mediator. Furthermore, M may have indirect effects on SE and MH through OS, as OS is negatively related to all IRA outcome variables ($ps \leq 0.001$). The analysis controlled for age and sex which were only significantly related to the ProR and EC empathy variables ($ps < 0.05$), and not significantly related to any of the IRA variables.

DISCUSSION

There has been considerable debate in the literature on the conceptualization of the dark traits as individual traits or sharing a dark core, with impaired empathy at the center [e.g., (9–13)]. In this study, we examined the different conceptualizations of the DT traits–as *dark monads* (three single units), a *dark dyad* of Machiavellianism and psychopathy (with narcissism kept separate), and a *dark triad* with a shared core as a latent variable–in their distinct and joint associations with cognitive and affective empathy facets and the link to indirect relational aggression. All three dark traits were associated with reduced peripheral responsivity, suggesting this facet of affective empathy may underpin the shared dark core; however, peripheral responsivity was unrelated to IRA, challenging the notion that the unempathic core of the DT drives relational aggression. Importantly, the monads model without links between narcissism and IRA showed the best fit, whereas the joint dark core models (with or without narcissism) showed unsatisfactory fits to our data. Our findings show that, individually, psychopathy is the most severe trait in terms of its global maladaptive relationships with empathy and IRA, and Machiavellianism produces weaker but more specific deficits, while narcissism is spared. This suggests that the DT traits are best viewed as three independent personality traits, rather than a joint (latent) dyad or triad core, at least in the prediction of these specific empathic deficits and indirect relational aggression.

The Distinct Profiles of the DT Traits

The current findings support distinct profiles of the individual DT traits due to their specific characteristics that drive distinct expressions of empathic deficits (and spared capacities) and indirect aggressive behavior. Psychopathy was compromised on all levels of cognitive and affective empathy, and all types of relational aggression. Thus, consistent with previous research on direct aggression (4, 13), psychopathy showed a more severe and global pattern of maladaptive outcomes. Machiavellianism and narcissism showed more specific links to empathy. Only a partial cognitive deficit–online simulation–was observed in Machiavellianism, whereas perspective taking appears intact; being able to predict another's intentions would facilitate their manipulation strategies (33). Machiavellianism predicted only guilt induction reflecting their use of manipulation (e.g., emotional blackmail) to influence others (28). Narcissism, on the other hand, was not related to any IRA, and indeed model fit was only achieved when the paths between narcissism and IRA were removed. This questions to what extent previously observed narcissism-aggression links [e.g., (27)] were driven by the shared variance with psychopathy and/or Machiavellianism. Moreover, narcissism was linked to increased perspective taking ability, perhaps enabling them to create a more favorable self-image through understanding and predicting others reactions. Thus, the spared and more adaptive associations of narcissism, once psychopathy and Machiavellianism are controlled for, emphasize the importance of teasing DT traits apart to examine their unique variance.

What Empathy Deficits Underpin the Dark Core and Which Drive Aggression in the DT: Implications for the VIM

This study examined whether by extension, the same mechanisms of the Violence Inhibition Mechanism model [VIM; (6, 34)] apply to (i) Machiavellianism and narcissism – if driven by the shared dark core, and/or (ii) other expressions of aggressive behavior such as relational aggression. Studying relational aggression in this context, means less observable, more indirect means of antagonistic behaviors in the Dark Triad traits can be explored, and allows us to test theoretical assumptions in different contexts. Our monad model conceptualizations of the dark traits as independent constructs and without an unempathic core that drives IRA challenge both assumptions.

Firstly, all three DT traits shared at least one affective empathy deficit—reduced peripheral responsivity, which arguably may underlie their shared dark core and reflect selfishness and tough-mindedness, and to care less about others in detached contexts. However, this shared deficit in peripheral responsivity did not drive indirect relational aggression. This does not necessarily contradict the extension of the VIM to the dark core as this shared deficit may still drive physical aggression; however, it does not apply to less direct means of aggression studied here.

Secondly, only the *affect-related cognitive* empathy facet online simulation was a partial mediator, driving indirect effects on IRA for Machiavellianism and psychopathy. Indeed, relational aggression has previously been associated with cognitive empathy deficits in women (41), and the current study supports this finding in a mixed sex sample. Though the current sample comprises an over-representation of the female sex, when controlled for, the main model fit was not affected and sex was not significantly related to any IRA variable suggesting that

TABLE 3 | Model fit statistics for all specified models.

Model	Chi-square (df, p)	RMSEA (90% CI)	SRMR	CFI	TLI
1. Monads (No-Core)	123.108 (4, $p < 0.001$)	0.315 (0.268–0.364)	0.076	0.879	−0.573
1a. Monads, no paths N to IRA	3.401 (3, $p = 0.334$)	0.021 (0.000–0.102) Probability RMSEA ≤ 0.05 0.616	0.014	1.000	0.993
1a_control. Monads, no paths N to IRA, age/sex controlled for	3.678 (3, $p = 0.2984$)	0.027 (0.000–0.105) Probability RMSEA <=0.05 0.582	0.013	0.999	0.985
2. Dyad (Partial Core)	83.716 (9, $p < 0.001$)	0.166 (0.135–0.200)	0.087	0.934	0.596
2a. Dyad, no paths N to IRA	86.068 (12, $p < 0.001$)	0.143 (0.116–0.172)	0.095	0.934	0.699
3. Triad (Full Core)	50.614 (16, $p < 0.001$)	0.085 (0.059–0.112)	0.037	0.969	0.895

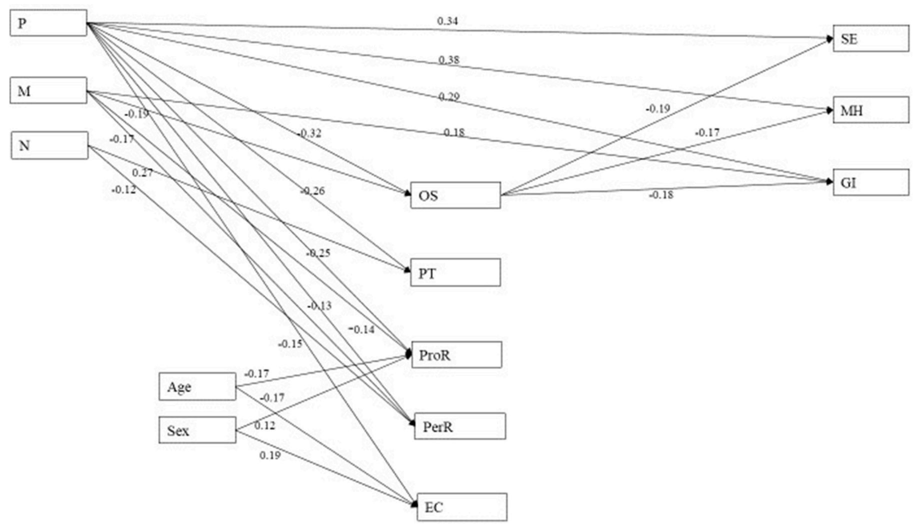

FIGURE 1 | Path model of significant paths between DT, empathy and IRA. Values shown are STDYX estimates; paths significant at $p < 0.05$. P, psychopathy; M, Machiavellianism; N, narcissism; OS, online simulation; PT, perspective taking; ProR, proximal responsivity; PerR, peripheral responsivity; EC, emotional contagion; SE, social exclusion; MH, malicious humor; GI, guilt induction.

these mechanisms hold for males also. However, replication in a (predominantly) male sample is needed before drawing any firm conclusions. Though traditionally a lack of a*ffective* empathy has been seen as the hallmark deficit of psychopathy [e.g., VIM model; (6)], similar *affect-related cognition* deficits as found in the current study have been previously reported in criminal male offenders with psychopathic tendencies (35). Our findings do not contradict the classic VIM notion, however, they do highlight an additional nuance of its functioning in driving this specific type of aggression. Whilst a cognitive component of understanding intentions and cognitions of others is essential for manipulating and deceiving (33), a lack of understanding what individuals feel in response to that may indeed facilitate such behavior, and hence, drive indirect relational aggression as measured in the current study.

Our interpretations and comparisons with findings across the literature must be taken with care. Firstly, they are based on self-report measures rather than psychophysiological indices of empathic responses or emotional reactivity and actual observed aggressive behavior (e.g., in the lab). For example, future research should examine empathic deficits underpinning direct and indirect behavioral aggression using carefully designed behavioral and/or psychophysiological experimental paradigms that tap into these specific aspect. From a psychometric perspective, previous studies have used different measures of empathy, and none used the facet approach distinguishing between different aspects of affective and cognitive empathy in the context of the whole DT. As such, the jingle-jangle fallacy posed within empathy research (38) needs to be considered here. For example, both of Renier's et al (40) cognitive empathy scales, online simulation and perspective taking, are defined by the capacity to make attributions about affect–akin to *affect-related* cognitive empathy (35). As such, Renier's et al. (40) and Davis' (32) perspective taking scales present us with a jingle issue (inference that two measures with the same labels measure the same things). Whilst former is proposed to measures attributions about affective processing (e.g., *I can tell when someone is masking their true emotions; good at predicting how someone will feel*), latter is defined as the tendency to spontaneously adopt the psychological point of view of others and appears to take a more traditional conceptualization of perspective taking as attributions about others cognitions and mental states for most items [e.g., *see things from the "other guy's" point of view; look at everybody's side of a disagreement; imagining how things look from their perspective;* (32)]. Thus, they are not likely measuring the same type of empathic attributions. To complicate matters more, Reniers et al.' online simulation scale presents us with a jangle problem (inference that two measures with different labels measure different things) as the majority of its items (five out of nine) are actually from Davis' perspective taking scale. On face validity, four items clearly concern attributions of cognitions (as mentioned above), two tap into attributions of affect (e.g., *I try to imagine how I would feel if I was in their place*) and the rest could be interpreted as both (e.g., *I find it easy to put myself in somebody else's shoes*). Thus, this scale appears to not just encompass "an effortful attempt to put oneself in another person's position by imagining what that person is feeling" [(40); p. 90] but also how they may think and react (i.e., mental states). In other words, it is the capacity to simulate another's thoughts *and* emotions. Subsequently, the current findings suggest that indirect relational aggression in psychopathy and Machiavellianism is in fact underpinned by the impairment in the capacity to simulate both, other's cognitions and emotions.

One Good, One Bad, One Ugly–Narcissism as the Odd One Out?

As IRA is more proactive—premeditated and instrumental—in nature, it would appeal more to strategic, pragmatic and manipulative individuals akin to Machiavellianism and psychopathy, rather than narcissism. In contrast, narcissism has been more associated with reactive aggression in response to perceived provocation [e.g., ego-threat; (17)]. Thus, our findings do not mean that narcissistic individuals are not aggressive *per se*, but suggest that IRA is a type of aggression they are unlikely to engage in—perhaps because it would not provide them with admiration and positive social standing they desire. Moreover, when studied independently, narcissism is split into two subtypes, grandiose and vulnerable (50), which manifest differently on general personality measures [e.g., the Big Five; (10)] and show diverging associations with hostility [e.g., vulnerable narcissism is linked to hostile behaviors once grandiosity and attention-seeking are controlled for; (51)]. However, DT measures such as the SD3 focus on grandiose narcissism at the expense of vulnerable narcissism. To thoroughly understand the relationship between narcissism and aggression, we need to consider the conceptualization of narcissism as utilized by various psychometric measures.

Moreover, research has considered Machiavellianism simply a less severe expression of clinical psychopathy (52). However, an overlap between constructs also reflects limited theoretical distinction, and suggests a need to refine measures of Machiavellianism, free from psychopathic traits (12). A recent meta-analysis revealed different degrees of overlaps for different DT measures: the SD3 incorporates more components of psychopathy, whereas the Dirty Dozen (53) shows more overlap with Machiavellianism and narcissism (13). Therefore, current findings need to be replicated with other measures of the DT traits as well as more comprehensive measures of each individual traits before drawing firm conclusions.

Though there appear adaptive qualities in narcissism, including self-confidence (54), their desire for social desirability leads to a tendency to exaggerate their abilities and reflect themselves in a positive light. This is a limitation when using self-reported measures to study individuals prone to dishonesty and may have affected our results. However, recent research suggests that even in large groups of psychopathic offenders response distortion was not a concern (55). Nevertheless, future studies may consider including measures of social desirability or lie-scales to control for such unwanted effects.

Finally, whilst our monads model without links between narcissism and IRA showed the best fit, recent bi-factorial modeling approaches suggest that the common core of dark traits might not depend on the individual DT traits but can be seen as a separate global construct (56, 57). Due to sample size restrictions we could not evaluate such models in the current study. It is important to note for the interpretation of our current best-fitting monad model, that we have partialled out the overlap between the DT traits to look at their unique impact. However, this can come under scrutiny because there is an interpretative difference between the concept of narcissism (measured as a whole) and the statistical variance that is left once the other traits have been accounted for (58). Thus, further research needs to focus on specifying what the differentiation of the whole and the partialled construct of Narcissism actually is (same applies for the other two traits).

Conclusion

The current paper addressed one of the most debated questions as to whether the dark traits are best conceptualized as individual traits (monads) or shared constructs (dyad or triad)–with a joint dark core. In addition, we examined whether the joint dark core is underpinned by empathy, and whether this drives their aggression—a debate fuelled by a lack of empirical findings that distinguish facets of empathy underpinning the core and those more uniquely linked to the individual dark traits. Our findings suggest the DT traits are best conceptualized as distinct monads with unique pathways in terms of affective and cognitive empathy deficits and capacities, and their role in relational aggression. Narcissism showed the greatest differentiation from the other two, and a more adaptive nature with increased empathic capacities (perspective taking) and lack of association with IRA. This supports the notion that the DT traits are not equal members of the DT, and as such highlight the important distinction between them. Machiavellianism demonstrates more similar, though less global empathic deficits and relational aggression as psychopathy—as such adding further weight to research indicating greater overlap amongst these two traits. Importantly, in contrast to theoretical models focusing on affective empathy deficits in direct physical aggression, cognitive empathy deficits related to affect (and cognition) inference drive indirect relational aggression in psychopathy and Machiavellianism. Thus, our results highlight the importance of assessing empathy as a multidimensional construct in relation to DT traits and maladaptive outcomes, such as different forms of aggression.

Few studies have taken a more fine-tuned facet approach to examine the unique and shared empathic deficits in the DT and their link to aggressive behavior. Delineating the specific aspects involved is crucial to further our understanding of the distinct motivational and behavioral mechanisms involved, inform theoretical models of aggression in the DT such as the VIM, and more targeted intervention strategies for different expressions of aggressive behavior in the dark traits. However, in taking this approach studies need to carefully take the empathy jingle-jangle fallacy into account whereby inconsistent findings may be based on conceptual misconceptions about what is being measured, and therefore, care needs to be taken in the interpretation of findings and comparison across studies. Finally, the current findings only suggest that indirect relational aggression in non-clinical populations is partially mediated by reduced online simulation—whether this extends to direct physical aggression and forensic populations remains to be tested. Nevertheless, they are the first to show these unique pathways for the dark trait traits their links to specific empathic deficits and indirect relational aggression.

AUTHOR CONTRIBUTIONS

NH, AS, and CB conceptualized the initial project idea and designed the study with further contributions from VE. JF contributed to the implementation and acquisition of the data. NH, FK, and JF contributed to the data analyses and all authors to the interpretation of findings. NH and JF wrote the initial draft of the paper and subsequent revisions. All authors were involved in editing the individual drafts. NH revised the final draft for submission to the special issue with final editing support by AS. All authors approve publication of the content and agree to be accountable for all aspects of the work.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00095/full#supplementary-material

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Dissociating Empathy From Perspective-Taking: Evidence From Intra- and Inter-Individual Differences Research

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Humans have the capacity to share others' emotions, be they positive or negative. Elicited by the observed or imagined emotion of another person, an observer develops a similar emotional state herself. This capacity, empathy, is one of the pillars of social understanding and interaction as it creates a representation of another's inner, mental state. Empathy needs to be dissociated from other social emotions and, crucially, also from cognitive mechanisms of understanding others, the ability to take others' perspective. Here, we describe the conceptual distinctions of these constructs and review behavioral and neural evidence that dissociates them. The main focus of the present review lies on the intraindividual changes in empathy and perspective-taking across the lifespan and on interindividual differences on subclinical and clinical levels. The data show that empathy and perspective-taking recruit distinct neural circuits and can be discerned already during early and throughout adult development. Both capacities also vary substantially between situations and people. Differences can be systematically related to situational characteristics as well as personality traits and mental disorders. The clear distinction of affect sharing from other social emotions like compassion and from cognitive perspective-taking, argues for a clear-cut terminology to describe these constructs. In our view, this speaks against using empathy as an umbrella term encompassing all affective and cognitive routes to understanding others. Unifying the way we speak about these phenomena will help to further research on their underlying mechanisms, psychopathological alterations, and plasticity in training and therapy.

Keywords: empathy, perspective-taking, theory of mind, lifespan development, personality, mental disorders

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EMPATHY AND PERSPECTIVE-TAKING

When confronted with someone else's emotions, people often spontaneously share that affective state–your grief can become my grief, your joy, my joy. Such a vicarious, isomorphic emotion in an observer of another person's emotions has been referred to as *empathy*, a term introduced by Vischer and Lipps as "Einfühlung" (German for "feeling into," derived from the Greek empatheia) (1). In humans, empathy may even arise, when the other is not present, but thought of or imagined. Critically, however, it has been proposed to involve self-other distinction, that is, the awareness that another is the source of one's emotions, differentiating it from emotional contagion, where such an awareness is not present (2).

Of course, empathic affect sharing is only one possible response to another person's emotion. Complementary affective states such as schadenfreude, envy or compassion occur as well, but the peculiarity of empathy is that it enables access to another's internal state by re-creating a representation of that state in the observer (3–6). Correspondingly, neuroscience research on empathy has not identified one single neural network associated with empathy, but rather the brain regions found to be active depend on what affective state is shared. While empathy for others' pain and negative affect activate the anterior insula and anterior midcingulate cortex (core nodes of the salience network), sharing others' joy and positive emotion yields activity in the ventral striatum and medial orbitofrontal cortex (**Figure 1**) (8–10). These activations seem to be relatively high-level, affective representations, as the specific patterns associated with one negative state, for instance, empathic pain, enable predictions of other negative states such as empathic disgust or unfairness (11). Furthermore, first-hand and empathic emotion experience—being stimulated painfully or watching someone else in pain—also lead to mutually predictive activation patterns in anterior insula and anterior cingulate cortex (12, 13). The observation of such "shared neural networks" has been interpreted as agreeing with simulation theory's account of how we understand others—we impersonate them and imitate their mental states (14).

Empathy, then, needs to be differentiated from an alternative route to understanding others. Theory theory, assumes abstract, propositional knowledge about others' behavior to underlie the understanding of the motives that drive others' behavior (15). This conceptualization corresponds to psychological and neuroscience research on *perspective-taking* or *Theory of Mind (ToM)*, the capacity to make inferences about and represent others' intentions, goals and motives (other terms include mentalizing and cognitive empathy) (16, 17). A classic test of ToM is false-belief understanding. If I can apprehend your incorrect view on a matter, while knowing the actual truth, the information conflicts and I must represent it in an abstract manner (18). Neuroscientific investigations of false-belief understanding have identified a network of brain regions to be involved, including the temporoparietal junction, precuneus/posterior cingulate cortex, medial prefrontal regions as well as the temporal poles and superior temporal sulcus (partially overlapping with the default mode network; **Figure 1**) (19, 20). While the main nodes of this network are also involved in other experimental paradigms assessing ToM, some regions within the overall network seem to be specific for particular ToM tasks (21, 22). Assuming a "constructivist view" on ToM (23), this may be due to different tasks drawing different component processes of ToM (24). Ecologically complex ToM tasks, in contrast, activate the entire network, possibly because all component processes are required (25, 26).

Thus, the abilities to empathically share others' affect and take their perspective can be well-differentiated conceptually and have more recently also been directly dissociated on a neural network level (for a summary see **Table 1**) (25). However, they may also interact and facilitate or impair one another in complex situations that require both functions simultaneously. For instance, Lamm et al. (8) meta-analytically contrasted cue-based and picture-based empathy for pain studies. When only presented with abstract cues of how painfully another person is stimulated, regions in the ToM-related neural network are activated, possibly reflecting the reasoning about the other's state, which then facilitates or enables empathic sharing of that state. In contrast, when the painful stimulation is directly displayed, ToM is not required to empathize and ToM-related neural activity is absent. Similarly, brain regions in inferior parietal and frontal cortex that have been associated with motor simulation ["mirror neuron system; "(27)] can also trigger empathic responding, if an action needs to be understood for the affective consequences to become clear (28). Empathy and ToM can also show a different interactive pattern in highly emotional situations. Here, ToM performance has been found to be impaired, which is associated with an inhibitory influence of empathy-related anterior insula activation on ToM-related temporoparietal junction activation (29). This may reflect an adaptive response to highly salient situations requiring immediate action, but could also turn maladaptive as has been hypothesized with a stress-related mentalizing deficit in borderline personality disorder (30).

Given the distinguishable neural networks enabling empathy and ToM, it is interesting to ask, if they share interdependent or distinct developmental trajectories over the lifespan, which we will discuss in the next section.

INTRAINDIVIDUAL DIFFERENCES

Lifespan Development

Speaking with the words of Hutman and Dapretto (31): "Determining the age at which infants display empathy depends in large part upon the way the construct is defined." Defining empathy as above—as sharing others' emotions while being able to differentiate between oneself and the other—it could be argued that empathy emerges very early in life. Precursors of affect sharing, like emotional contagion, and indirect self-other distinction can already be observed in newborns, well before the emergence of verbal abilities (31–33). For instance, infants display greater and longer distress when confronted with the cry of another newborn compared to their own (34). During childhood, these capacities refine and become more explicit—they can be named and regulated (35–37). Thus, there is no clear age cut-off at which empathy is fully developed or not. Determining the age at which infants display empathy depends on the methods used to capture it—observational and physiological measures, adult-reports or self-reports—which vary highly in their validity and outcomes throughout development (38). With incremental development of its subcomponents and language abilities empathy becomes more apparent and easier to quantify in preschool children. It further develops during adolescence with increases from age 12 to 16 years (39). In sum, the emergence and development of empathy depends strongly on the definitions and methods used, but first signs of affect sharing are already present in newborns.

For ToM, numerous studies show that classical tests of false-belief understanding are not passed before the age of 4–5 years (40). However, when tested with non-traditional tasks, early preverbal ToM abilities such as mental state attribution and

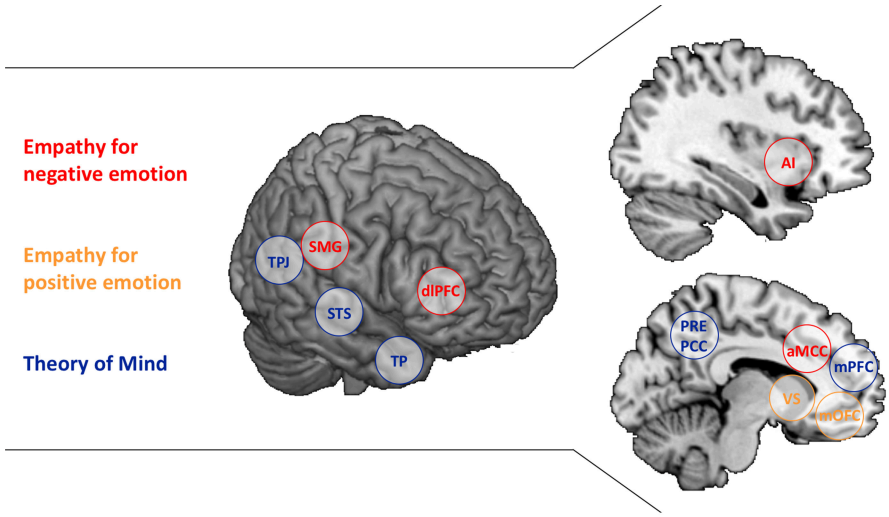

FIGURE 1 | Brain regions associated with Empathy and Theory of Mind. The separable brain regions associated with Empathy for negative emotion (red), Empathy for positive emotion (yellow), and Theory of Mind (blue) are presented. AI, anterior insula; aMCC, anterior middle cingulate cortex; dlPFC, dorsolateral prefrontal cortex; mOFC, medial orbitofrontal cortex; mPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; PCUN, Precuneus; SMG, supramarginal gyrus; STS, superior temporal sulcus; TP, temporal poles; TPJ, temporoparietal junction; VS, ventral striatum. SMG and dlPFC are listed as well as they have been associated with regulating empathic emotion (7).

TABLE 1 | Summary of the conceptual and empirical dissociation of empathy and perspective-taking.

Empathy	Perspective-taking
• Affective process	• Cognitive process
• Sharing another's emotional state	• Taking another's perspective
• Awareness that other is source of emotion	• Abstract representation of others' mental state
• Involved brain regions depend on emotional valence, largely overlaps with salience network	• Widespread network for information processing, core nodes overlap with default mode network
• Develops ontogenetically early, does not decline in old age	• Later ontogenetic development, declines in old age
• State/trait reductions mainly for motivational/habitual reasons	• State/trait reductions for motivational/habitual and cognitive reasons

intentional communication seem to emerge already in infancy at 6–9 months of age, gradually developing further throughout the first years of life (18, 41–44). Setoh et al. (45) could further demonstrate that 2.5-year-olds are able to succeed in classic false belief tasks if overall processing demands are reduced by lowering inhibitory control and response-generation demands. This supports the view that ToM also develops incrementally, starting before the age of 4–5 years.

Taken together, empathy and ToM become well-measurable in preschool aged children with increasing abilities in language and executive function. Nevertheless, non-verbal precursors of both capacities are already observable in infancy, in newborns for empathy and from about 6 months on for ToM. Longitudinal studies testing both empathy and ToM jointly, which could yield the most profound evidence for independent trajectories throughout childhood, are still missing. Recently, a cross-sectional study examined empathy and ToM within a single group of children ranging from 3 to 5 years of age (46). Children had to pass a certain number of subtasks for empathy and ToM to be classified as having developed either ability. ToM seemed to emerge at 4 years and empathy at 5 years of age. Interestingly, a subgroup of kids, including 4-and 5-year olds, displayed empathy but not ToM. These results cannot yet answer if the development of empathy follows ToM or vice versa, but they hint at some independence in their developmental trajectories.

While numerous studies addressed the emergence of empathy and ToM in childhood, growing evidence also sheds light on their development in old age. In a recent cross-sectional study (47) younger and older adults performed a newly developed naturalistic task which measures both empathy and ToM within the same individuals [EmpaToM; (25)]. Older adults performed significantly worse than younger participants on the ToM questions whereas empathy was still preserved in older adults. These findings are in line with previous studies in younger and older adults, separately testing their abilities to empathize (48–50) and to take others' perspectives (51). The decline of ToM in older adults is a consistent finding across various ToM tasks regardless of stimulus modality or the specific form of ToM that is measured (52). For empathy, in contrast, no age-related changes or even increases with age have been reported (53–55). These findings depict independent developmental paths for empathy and ToM in old age.

Taken together, empathy and ToM evolve and decline independently during lifespan development. A number of factors have been found to influence this development, particularly in childhood, including preterm birth (56), child to parent attachment (37), language use of the parents (57, 58), mental disorders of the parents (59), the presence of older siblings (60, 61) and the specific culture a child grows up in (62, 63). Such influencing factors cause interindividual differences in empathy and ToM that could even reach into psychopathology and might be greatly informative regarding the relation of the capacities—a question we discuss in the following section.

State Variability

While typically developed adults possess the capacity to empathize and take others' perspectives, there is still variation in the propensity to translate this capacity into actual behavior. Whether and to what extent we empathize with others or take their perspectives may depend on situational and relational variables as well as motivational factors (2). Empathic processes are generally more salient in situations in which we are confronted with negative rather than positive emotions [e.g., (64)]. We display stronger empathic reactions when interacting with those we are closely affiliated with (65), which points to a central role of empathy in human and non-human evolution (66, 67). This is supported by recent advances in understanding the role of oxytocin in both, empathy and attachment (68). Similarly, we tend to experience higher empathy toward ingroup others, and lower empathy toward outgroup others (69), even when group membership is experimentally varied (70). We typically experience low empathy in states of personal distress or depression (71), particularly due to an incapacity to inhibit own emotional states (72).

ToM is high in states in which we are motivated to understand others' mental states and intentions, which allows making predictions about their actions, and also to influence these actions (16). This can happen for altruistic or also egoistic motives. For instance, one might take another's perspective to be better able to help them, or also to effectively manipulate them. ToM can be low in states which may block the cognitive route to understanding others, such as alcohol intoxication (73), or also depression (74). Though reduced ToM in depression is frequently hypothesized to emerge from heightened egocentric focus, it is not fully understood whether alterations of ToM in depression, for example, are specific to social cognition, or might also be attributed to deficits in executive functioning (75). This highlights the necessity of controlling for general processing capacity in studies investigating individual differences in ToM.

Taken together, contextual factors substantially determine the extent to which we engage in empathy and ToM. Contextual factors may also guide whether we engage affective or cognitive routes to understanding others, which reflects in the respective neural activation (76).

INTERINDIVIDUAL DIFFERENCES

Beyond transient variations in empathy and ToM, there are also interindividual difference variables that are reliably associated with dispositional variation.

At a most basic level, women score higher on self-report measures of empathy than men, which may be due to gender-role stereotypes (77) as gender differences are not clearly present in neural empathy responses [but seem to depend largely on context effects, (78)]. Among the Big Five personality traits, agreeableness is most consistently and strongly linked to variation in empathy [e.g., (79)], which has recently been substantiated by neuroimaging research (80). Agreeable individuals have a higher propensity to display empathic reactions, or conversely, empathy can be thought of as a low-level function that serves higher-order facets of agreeableness, such as altruism. Regarding lowered empathic responses, the "dark" personality traits narcissism, Machiavellianism and psychopathy (81) are commonly associated with reduced empathy [e.g., (82)]. These are tied together by interpersonal antagonism—the opposite of agreeableness—in terms of a self-focused and callous interpersonal style (83). Emotional contagion and empathy are typically lower in narcissism (82, 84, 85) and psychopathy (86, 87). Interestingly, empathic alterations in narcissism and psychopathy are not due to an incapacity to empathize, but rather due to motivational factors. Experimental evidence shows that narcissistic individuals experience regular levels of empathy when being instructed to put themselves into the perspective of a suffering person (88). Similarly, psychopathic individuals—viewed as similar, yet more severely disordered (89)—can indeed experience empathy. Psychopathic individuals show similar brain activation as controls in the anterior insula and anterior cingulate cortex, but only deliberately, not spontaneously (90). This confirms the notion of reduced propensity for empathic reactions, not reduced capacity in terms of general inability to share others' affect, in psychopathic individuals.

While the majority of individual differences research on empathy focuses on variables that are accompanied by lowered empathy, there are also examples in which empathy is hypothesized to be higher. For instance, clinical observations suggest the existence of "borderline empathy" in terms of surprisingly accurate emotional resonance in individuals with borderline personality disorder (91). The overall evidence on borderline empathy, however, is mixed (92), and some research indicates that the phenomenon might be conceptualized in terms of increased emotion recognition ability [e.g., (93)], which does not necessarily involve affective sharing.

Unlike empathy, variation in ToM is less clearly associated with sex [e.g., (94)], but similarly associated with the Big Five dimension of agreeableness; particularly when complex ToM measures are used (95). ToM is also not uniformly lowered in the Dark Triad traits [e.g., (96)]. A recent study found that only automatic ToM is lowered in psychopathy, whereas controlled ToM does not differ from controls (97). This points to a diminished propensity rather than capacity to take others' perspective, which highlights the motivational role of personality characteristics in ToM. Taking this idea one step further, there is even evidence for increased social cognition in individuals high on "dark" personality traits, which could enable antagonistic individuals to effectively deceive and manipulate others (98, 99).

Taken together, research on intra- and interindividual differences shows that there is substantial variation in affective and cognitive interpersonal functioning. Both can be selectively heightened or lowered, depending on state and trait characteristics. This corresponds to behavioral and neuroscience evidence showing that strong empathizers are not necessarily better mentalizers, and vice versa (29). Whether and to what extent we empathize and take others' perspectives depends substantially on situational and motivational variables, the latter of which reflect in personality traits. Altered social affect and cognition related to personality traits and disorders are likely more a matter of reduced propensity than capacity.

CONCLUSION AND OUTLOOK

While the phenomena of affect sharing and perspective-taking may be relatively well-understood, there is considerable variation in the terminology used to describe them. The definition of empathy ranges from confining it to affect sharing [applied in the current review; (2)] to a very broad usage as an umbrella term. The latter view would merge (i) affect sharing, personal distress and emotional empathy as an emotional and (ii) mentalizing, perspective-taking and ToM as a cognitive component of empathy (100, 101). Here, we reviewed evidence that dissociates these functions, with differential neural networks related to empathy and ToM (**Figure 1**). Lifespan developmental research further indicates independent trajectories—the affective route seems to develop earlier and remains unaffected by aging compared to the cognitive route. Moreover, state variables like the shared emotions' valence, the experienced affiliation with others or the motivation to take someone's perspective and personality traits like agreeableness selectively affect the intra- and interindividual capacity to empathize or to engage in ToM (see **Table 1** for a summary).

Given this separability of the phenomena of affect sharing and perspective-taking, we argue for clear-cut terminology that differentiates among them. An argument for restraining the term empathy to affect sharing, as is being done in a large portion of the current literature (2, 3, 46, 47, 102, 103), is that it makes usage of the term unmistakable and distinctive. The umbrella usage, in contrast, requires specification as to which component is actually referred to in order to avoid misunderstanding. While a few studies also dissociate affective and cognitive components of ToM (104), the term ToM is used much more consistently already for what the umbrella usage would describe as cognitive empathy. Thus, there is no need for or reason to expand the term empathy to account for the phenomenon of perspective-taking. We believe clear-cut terminology is best suited to further research in the field (105, 106).

Foci of future research should be on (i) longitudinal developmental investigations, (ii) comprehensive assessments of empathy and ToM in psychopathology and subclinical variability as well as (iii) probing the differential plasticity of these social affective and cognitive capacities. Longitudinal studies could give in-depth understanding of the bases and influencing factors that affect the emergence and decline in empathy and perspective-taking. Differential development of the underlying brain structures could be informative regarding the differentiation of developmental empathy and ToM trajectories (107). Further research on situational, personality, and psychopathology factors related to empathy and ToM is needed to understand whether differences reflect alterations in the propensity or the capacity to mobilize these functions. Lastly, first evidence on the differential plasticity of social affect and cognition (108, 109) should be followed up with studies in clinical groups that show social interaction deficits.

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All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Effects of Childhood Maltreatment on Social Cognition and Brain Functional Connectivity in Borderline Personality Disorder Patients

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Borderline personality disorder (BPD) is a chronic condition characterized by high levels of impulsivity, affective instability, and difficulty to establish and manage interpersonal relationships. However, little is known about its etiology and neurobiological substrates. In our study, we wanted to investigate the influence of child abuse in the psychopathology of BPD by means of social cognitive paradigms [the Movie for the Assessment of Social Cognition (MASC) and the reading the mind in the eyes test (RMET)], and resting state functional magnetic resonance imaging (rs-fMRI). For this, we recruited 33 participants, 18 BPD patients, and 15 controls. High levels of self-reported childhood maltreatment were reported by BPD patients. For the sexual abuse subdimension, there were no differences between the BPD and the control groups, but there was a negative correlation between MASC scores and total childhood maltreatment levels, as well as between physical abuse, physical negligence, and MASC. Both groups showed that the higher the level of childhood maltreatment, the lower the performance on the MASC social cognitive test. Further, in the BPD group, there was hypoconnectivity between the structures responsible for emotion regulation and social cognitive responses that have been described as part of the frontolimbic circuitry (i.e., amygdala). Differential levels of connectivity, associated with different types and levels of abuse were also observed.

Keywords: borderline personality disorder, social cognition, functional connectivity, brain remodeling, childhood maltreatment

INTRODUCTION

Borderline personality disorder (BPD) is a chronic psychiatric condition characterized by high levels of impulsivity and affective instability, as well as a marked difficulty to establish and manage interpersonal relationships (1, 2). In patients with this multifactorial disorder, a genetic vulnerability has been identified (1, 2). This vulnerability may interact with environmental factors such as lower quality parental care (3, 4) and a history of child abuse, which is present in a large number of research subjects with BPD and has been proposed to be a contributing factor of the disorder (5).

Chronic difficulties in interpersonal relationships are a BPD characteristic and have been studied within the social cognition construct (6–8). With regard to performance in recognizing the emotions of others, some studies have found higher levels of performance on tests among BPD patients, including the reading the mind in the eyes test (RMET) (9, 10), while other studies have not reported any differences in the ability to infer the mental states of self and others, compared to controls (11–13). Similar results have been found in studies using a more ecological paradigm called the Movie for the Assessment of Social Cognition (MASC). It consists of a film that shows the social interaction of different characters and has been successfully used to evaluate social cognition in pathologies such as autism (14) and schizophrenia (7, 15) and correlates well with other tasks that measure theory of mind (16). In a number of studies the BPD patients showed deficits in the performance of the test compared to healthy participants, while other studies did not find this difference (15). It has been proposed that the possible deficit found in BPD is observed at the expense of a pattern of hypermentalization (17).

The neurobiological substrate of social cognition in BPD has been studied by task-related neuroimaging studies such as the RMET paradigm and stimuli adaptations that test Theory of Mind (ToM). These studies showed BPD patients have lower activation in areas within the temporal lobe, the superior and medial frontal regions, the cingulate cortex, parietal cortex, hippocampus, and the insula, as well as higher activation in bilateral amygdala, left temporal pole, medial frontal gyrus, right middle and superior temporal gyrus, left precuneus, left middle occipital gyrus, and right insula compared to controls (10, 18, 19). In addition, a lower brain response has been reported in the BPD group in the left superior temporal sulcus and gyrus in response to the modified version of the Multifaceted Empathy Test (MET) (20). Functional connectivity is described as the BOLD signal correlation between different brain regions when measured with fMRI. Most studies describe correlations observed between low-frequency fluctuations (<0.1 Hz) at resting state, which are organized in intrinsic neural networks which are the same previously described in task-related research (21–23). One of these networks is the default mode network (DMN), which shows a decreased connectivity in the precuneus (18), and the right posterior cingulate (24), as well as hyperconnectivity in the medial prefrontal cortex, the anterior cingulate cortex, and the posterior precuneus/cingulate in BPD compared to healthy subjects (25).

Most regions where differences were found in the brain function in BPD form part of the frontolimbic circuit. Dysfunction of frontolimbic circuitry is one of the most accepted models to explain the BPD symptoms, including emotional dysregulation and social cognition deficits (26). This same circuit has been related to morphologic and functional brain changes associated with a history of child abuse (27). For example, studies show a decrease in gray matter volume on the orbitofrontal cortex and temporal regions (28–30), as well as greater functional brain activation in amygdala (31) and basal ganglia in response to paradigms of emotional identification (32). Resting-state fMRI studies have shown both increased (33) and decreased (34) in functional connectivity in the fronto-amygdala circuit in samples of adolescents exposed to trauma. Another study reported a decrease in connectivity in the amygdala with the dorsal anterior cingulate cortex, precuneus, and frontal regions in adults with a history of emotional abuse (35). Overall, it may seem that the brain structures reported in BPD and child abuse are similar to those related to social cognition, which it is clinically relevant, as studies have shown that children with abuse presents deficits in social cognition (36). Due to the high prevalence of child abuse in BPD and the presence of social cognition problems in both, it seems plausible that this is an important aspect to study.

Even though brain activation has been studied regarding social cognition tasks in BPD, the relationship between functional connectivity at resting state and its association with the performance in such tasks has not been explored. The inclusion of the childhood maltreatment variable may offer information that could contribute to understanding the heterogeneity of clinical and neuroimaging results in BPD studies (37). The primary goal of this study was to assess differences compared to healthy controls in the clinical performance of social cognitive paradigms and functional connectivity in resting state and how it related to child maltreatment levels.

MATERIALS AND METHODS

For our study, we included 18 patients diagnosed with BPD and 15 controls without any psychiatric diagnosis (CN) in a cross-sectional design. Both groups were matched by age and education. Due to the higher prevalence of the psychiatric diagnosis among women, all study participants were women (38) and right-handed. Participants were recruited from the outpatient clinic of the Institute for Social Security and Services for State Workers (ISSSTE). We also recruited four participants from Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz" from an ongoing study (39). The protocol was approved by the Ethics Committee of the ISSSTE (317.2017_P_2017) and the Ethics Committee of the Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz." All the participants signed an informed consent form, and the study followed the guidelines in the Declaration of Helsinki.

Patients diagnosed with BPD between 18 and 45 years old were included. The BPD diagnosis was established by the attending psychiatrist and corroborated by a psychiatrist with experience in BPD, who used the Diagnostic Interview for Borderline Revised (cut-off of 6) (40). To determine comorbidity, we used the Spanish version of the Mini International Neuropsychiatric Interview (MINI) (41). To obtain a representative sample of the clinical population, the study included patients with Major depressive disorder (MDD), posttraumatic stress disorder comorbidity (PTSD), and the use of medication. Exclusion criteria were disorder caused by use of addictive substances in the last 6 months, bipolar disorder diagnosis, schizophrenia, obsessive-compulsive disorder, eating disorders, and mental disability as described by the attending physician. For the control group, psychopathologies were ruled out with the MINI.

Diagnosis of Axis II disorders was ruled out by means of SCID-II screening, and positive results were evaluated by the psychiatrist.

We measured the social cognition construct using the Spanish version (14) of Movie for the Assessment of Social Cognition (MASC) (42). This version is a 16-min video depicting social situations where the protagonists' emotions, thoughts, and social intentions are assessed through 46 multiple-choice questions. For each question, there is only one right answer. Mistakes were classified as hyper-, hypo-, and lack of mentalization. The test has high inter-rater (ICC = 0.99) and test-retest reliability ($r = 0.97$) and is highly consistent among observers (Cronbach's $\alpha = 0.86$) (42). The video was provided by the author of the Spanish version (Guillermo Lahera; Universidad de Alcalá, Madrid, Spain) and professionally dubbed into Mexican Spanish with an adaptation to the Mexican accent and words. In addition, the study used the Reading the Mind in the Eyes test (RMET) to assess the ability to infer mental states with information from the eye gaze in pictures (43). Each participant was asked to choose one of four descriptions of mental states for each picture. To determine whether there was a history of childhood trauma, the Spanish version of the Childhood Trauma (self-administered) Questionnaire (CTQ) (44) was used.

Magnetic Resonance Imaging

Imaging data were obtained using a Philips Ingenia 3 Tesla with a 32-channel phased-array head coil. We acquired structural and resting state functional (fMRI) sequences. The use of substances was ruled out during clinical interview. For the resting-state fMRI (rsfMRI), participants were instructed to remain quiet, keep their eyes open, without thinking of anything in particular and were presented with a white cross on a black background. T2*-weighted echo planar images were acquired with the following parameters: 36 axial slices, repetition time = 2000 ms, echo time = 30 ms, flip angle = 75°, field of view = 240 mm, slice thickness = 3.0 mm, acquisition matrix = 80 × 80, and voxel size = 3.0 × 3.0 × 3.0 mm^3. Structural T1-weighted images were acquired with a repetition time = 7 ms, echo time = 3.5 ms, flip angle = 8°, field of view = 240 mm, slice thickness = 1.0 mm, acquisition matrix = 240 × 240, and voxel size = 1.0 × 1.0 × 1.0 mm^3.

Statistical Analysis of Clinical Measures

The statistical software SPSS-X version 22.0 for Windows, PC, was used for the analyses. We visually inspected the clinical data and used the Shapiro-Wilks test to assess for normality. We first compared the scores from the social cognition variables (MASC and RMET) and CTQ between the BPD and CN groups using a paired t-test (Mann-Whitney U-test for non-normal variables) with alpha of 0.05. We then performed Pearson's correlation between the MASC and RMET and CTQ scores to search for a possible relationship between childhood maltreatment and social cognition. Because patients with BPD often present depressive symptoms (45), we created a new nominal categorical variable using the MINI with the following factors: BPD with depression ($n = 11$), BPD without depression ($n = 7$), and CN. Then we used a one-way ANOVA to find differences in social cognition variables between the groups.

Resting State Functional Connectivity Preprocessing and Analysis

Data were preprocessed and analyzed using the CONN-fMRI Functional Connectivity toolbox (46). The preprocessing pipeline prior to the analysis included: functional realignment and unwrap (subject motion estimation and correction, functional center to (0,0,0) coordinates (translation), slice-timing correction, detection of motion artifact sources with ART (Artifact Detection Tools; developed by Stanford Medicine, Center for Interdisciplinary Brain Sciences Research) (Time points exceeding the movement threshold of 2 mm or a global signal Z-value of nine were defined as outliners), direct segmentation and normalization (simultaneous Gray/White/CSF segmentation and normalization to MNI space), and smoothing (5 mm FWHM Gaussian filter). With a general linear model, nuisance variables were regressed out. The nuisance variables included were: subject motion parameters, raw white matter, and cerebrospinal fluid signals. To correct for physiological noise, we used the CompCor method (47). Signal time series were band-pass filtered between 0.008 and 0.09 Hz.

To assess baseline functional connectivity (rs-FC), we carried out a seed-based correlation analysis. The seed regions were defined in CONN using an 8 mm kernel sphere (**Figure 1**). The definition of the seeds was based on previous BPD results and regions associated with mentalization, especially those in the DMN (10, 18, 19, 25, 48, 49) (For details see **Table S1**). The whole-brain individual correlation maps were computed with the average value of the BOLD signal time course in resting state in each seed region, and correlation coefficients were estimated with the BOLD signal time course for each voxel. A normal distribution of the resulting coefficients was obtained with the Fisher transformation, and correlation maps (functional connectivity) were obtained for each seed region and subject. The correlation maps for each seed were used to carry out a second-level between-groups contrast GLM using age as a covariate. All contrasts were corrected for multiple comparisons with the false discovery rate, with a p-threshold of 0.05 for each test and cluster. Finally, we extracted the Z-maps (Fisher-transformed connectivity values) for each significant cluster in each subject to perform Pearson correlation between functional connectivity and clinical measures. Previous research indicated a higher likelihood of false positives resulting from multiple comparisons. This was particularly the case of studies that correlated brain activation with behavioral variable results, thus, we corrected for multiple comparisons (50, 51). Since depression is associated with altered functional connectivity (52) and patients with BPD often present depressive symptoms, we used a one-way ANOVA to evaluate the difference in connectivity levels associated with this variable.

RESULTS

Clinical Measures

The psychiatric comorbidity and medications of the BPD group are summarized in **Table S2**. Compared to the controls, BPD patients showed higher scores on the CTQ. Regarding abuse

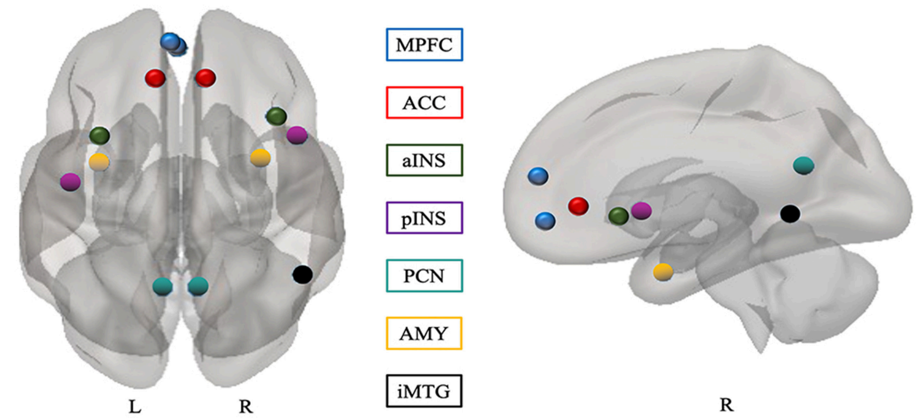

FIGURE 1 | Seeds for functional connectivity. All seeds were defined based on previous studies (see **Table S1** in the Supplementary Materials). MPFC, medial prefrontal cortex; ACC, anterior cingulate cortex; PCN, precuneus; iMTG, inferior middle temporal gyrus; AMY, amygdala; INS, insular cortex; L, left; R, right; a, anterior; p, posterior.

TABLE 1 | Demographic and clinical characteristics of BPD patients and healthy participants groups.

	BPD (*n* = 18)		HC (*n* = 15)		*p*-value
Age in years	31.17	± 9.5	32.80	±8.6	$p = 0.613^a$
Years in education	15.06	±2.2	15.22	±2.5	$p = 0.790^a$
CTQ TOTAL	59.06	±18.6	38.13	±7.9	$p = 0.001^a$
Emotional abuse	16.56	±5.3	9.53	±2.4	$p = 0.000^a$
Emotional neglect	11.44	±3.6	7.87	±3.1	$p = 0.006^a$
Physical neglect	9.11	±3.6	6.20	±1.3	$p = 0.006^b$
Physical abuse	11.11	±5.8	7.13	±2.2	$p = 0.059^b$
Sexual abuse	10.83	±6.1	7.67	±4.0	$p = 0.137^b$
MASC total correct	30.00	±5.3	31.03	±2.5	$p = 0.449^a$
Overmentalizing errors	6.00	±2.8	5.27	±2.6	$p = 0.538^a$
"reduced ToM" errors	5.83	±4.2	6.13	±2.7	$p = 0.686^b$
"no ToM" errors	3.28	±2.19	3.53	±3.1	$p = 0.714^b$
RMET	25.06	±3.26	25.73	±4.3	$p = 0.614^a$

Data are presented in means ± standard deviation unless otherwise specified. BPD, borderline personality disorder; HC, healthy controls; CTQ, Childhood Trauma Questionnaire; MASC, Movie for the Assessment of Social Cognition; ToM, theory of mind; RMET, Reading the mind in the eyes; [a]Two-sample two-tailed t-test; [b]Mann–Whitney U-test.

subdimensions, there were no significant differences in sexual abuse between the groups (**Table 1**). There was a negative correlation between MASC scores and total CTQ score; for the subdimensions, there was a negative correlation between physical abuse, physical negligence, and total MASC, as shown in **Table 2**. In the BPD group, depression manifested in different ways. Depressed BPD subjects had lower performance on the MASC (M = 27.73, SD = 5.350) and a decrease in the mean of −5.84, 95% CI [−11.02, −0.67]($p = 0.026$), compared to non-depressed BPD subjects (M = 33.57, SD = 3.15), who even performed better than the controls on the MASC (M = 31, 17, SD = 2.57); the difference was, however, not statistically significant ($p = 0.53$), as determined by one-way ANOVA for the three groups, $F_{(2, 14.041)} = 4.09$, $p < 0.040$. No significant differences in RMET scoring were found between the groups, $F_{(2, 30)} = 0.479$, $p = 0.305$.

Functional Connectivity

Hypoconnectivity was found between limbic regions that play a role in emotional and affective regulation and social responses in BPD patients. A hyperconnectivity was observed between the medial prefrontal cortex and the left superior parietal lobe (**Table 3**; **Figure 2**). There were no statistically significant differences in the connectivity values between non-depressed and depressed BPD subjects (**Table S3**).

Correlation Between Clinical and Functional Connectivity

We used Fisher-transformed connectivity values of the seven clusters identified with the comparative analysis of the groups and correlated with the Movie for the Assessment of Social Cognition (MASC), Reading the Mind in the Eyes (RMET) and Childhood Trauma Questionnaire (CTQ) scores. When analyzing both groups as a homogenous group, we found that for the greater number of regions studied, a negative correlation was found between functional connectivity and the total levels of child maltreatment, as well as some subdivisions of abuse as shown in **Table S4**. That is, higher levels of child abuse were related to less connectivity in these regions (**Figure S1**). However, the above was reversed when correlation analysis was performed per group, between the CTQ and the connectivity values. In the BPD group, a negative correlation was found between the sub-dimension of emotional abuse and connectivity values in middle temporal gyrus with primary motor cortex, supplementary motor, and anterior area cingulate cortex (Cluster + 00, - 16, + 62: $r = -0.475$, $p = 0.046$; cluster +04, −04, +46: $r = -0.496$, $p = 0.036$) and positive correlation between sexual abuse score and connectivity of the left MPFC with nucleus accumbens, caudate, putamen,

TABLE 2 | Table of correlations between variables of social cognition and CTQ scores.

		1	2	3	4	5	6	7	8	9	10	11
1	MASC total correct	1										
2	MASC overmentalizing errors	−0.02	1									
3	MASC "reduced ToM" errors	−0.77**/++	−0.43*/++	1								
4	MASC "no ToM" errors	−0.50**/++	−0.40*/+	0.48**/++	1							
5	RMET	0.35*/+	0.37*/+	−0.42*/++	−0.20	1						
6	CTQ_Total	−0.38*/+	−0.04	0.34*/+	0.09	−0.15	1					
7	Physical neglect	−0.38*/+	−0.05	0.42*/++	0.03	−0.23	0.75**/++	1				
8	Emotional abuse	−0.30	0.13	0.18	−0.04	−0.15	0.86**/++	0.59**/++	1			
9	Emotional neglect	−0.24	−0.34*/+	0.36*/+	0.19	−0.29	0.69**/++	0.62**/++	0.56**/++	1		
10	Physical abuse	−0.40*/+	−0.06	0.37*/+	0.16	−0.04	0.88**/++	0.59**/++	0.74**/++	0.47**/++	1	
11	Sexual abuse	−0.18	0.04	0.12	0.05	0.02	0.69**/++	0.31	0.40**/+	0.22	0.57**/++	1
	Mean	30.53	5.67	5.97	3.39	25.73	49.55	7.79	13.24	9.82	9.30	9.39
	Standard Deviation (SD)	4.31	2.74	3.59	2.63	3.38	17.99	3.18	5.56	3.81	4.92	5.49

*n = 33; **: p < 0.01 (bilateral); *: p < 0.05 (bilateral); +: FDR < 0.1; ++: FDR < 0.05; MASC, Movie for the Assessment of Social Cognition; ToM, theory of mind; RMET, Reading the mind in the eyes; CTQ, Childhood Trauma Questionnaire.*

TABLE 3 | Seeds showing significant functional connectivity differences between groups (BPD> HC) with age as covariate.

Seed	Regions	Peak voxel coordinate			Cluster size	β	*t*-scores	Cluster significance (FDR-corrected, threshold of $p = 0.05$)	Connectivity
		x	y	z					
MPFC_L	SPL_R	+26	−48	+40	61	0.21	6.05	0.0383	higher
	NaC.L, SubCalC, P_L, Cd_L, OFC.L	−06	+10	−10	80	−0.17	−5.82	0.0213	lower
	OFC.R, SubCalC	+14	+16	−24	76	−0.19	−7.34	0.0213	lower
ACC_R	SFG_L, SFG_R	+10	+10	+66	110	−0.18	−5.42	0.0059	lower
AMYG-R	SI_L, aSMG_L, SPG_L pSMG_L	−46	−40	+52	154	−0.16	−5.72	0.0010	lower
iMTG-R	M1_R, M1_L, SMA_R, SMA_L	+00	−16	+62	180	−0.23	−4.62	0.0008	lower
	SMA_R, M1_L, M1_L, M1_R, ACC	+04	−04	+46	131	−0.23	−4.66	0.0034	lower

*β, effect size (positive effects represent higher connectivity; negative effects represent lower connectivity); T, T-value; p-FDR, p corrected false discovery rate; L, left; R, right; a, anterior; p, posterior; i, inferior, s; superior; **Seeds**: MPFC, medial pre-frontal cortex; ACC, anterior cingulate cortex; AMYG, amygdala; MTG middle temporal gyrus. **Correlated areas**: Cd, caudate; M1, precentral gyrus (primary motor cortex); NaC, accumbens; OFC, orbitofrontal cortex; P, putamen; SI, post-central gyrus (primary somatosensory cortex); SFG, superior frontal gyrus; SubCalC, subcallosal cortex; SMG, supramarginal gyrus; SPL, superior parietal lobe; SMA, supplementary motor area. All analyzed contrasts where corrected by multiple comparisons using the false discovery rate (FDR) at 0.05. BPD, borderline personality disorder; HC, Healthy control.*

subcallosal cortex, and orbitofrontal cortex (cluster −06, + 10, −10: $r = 0.660$, p. 002) (**Table 4**; **Figure 3**). However, only the latter remained significant after the correction for multiple comparisons (**Table S5**).

DISCUSSION

We found that as the level of childhood maltreatment increased, the performance on the MASC social cognitive test decreased in both the BPD and the control groups. In addition, we observed hypoconnectivity between structures associated with emotion regulation and structures associated with social cognitive responses in the BPD group.

Our findings are consistent with those of another study, where they showed that child abuse impacts the skills that are necessary for the development of stable and long-lasting interpersonal relationships (36). It has been well-established that the development of social cognition is linked to that of emotional and affective communication through primary caregivers, and an environment that is safe and free from excessive stress-conditions that do not exist in the case of child abuse (53). Several studies have demonstrated that either disruptions in the relationships between children and primary figures or extremely stressful environments can activate the hypothalamic-hypophyseal axis, releasing, and activating several mechanisms that have an effect on the brain (54, 55). Environments characterized by extreme stress cause physiological changes that interfere with the integration of mental representations during development, thus disrupting the concepts of self and other and producing an unrealistic, unstable, and disproportionate representation of the affection perceived and expressed (3). These circumstances arise in relational contexts, a fact that accounts for BPD patients' clinical characteristics. These traits include aggression, impulsivity, and dissociative symptoms that are observed in BPD patients.

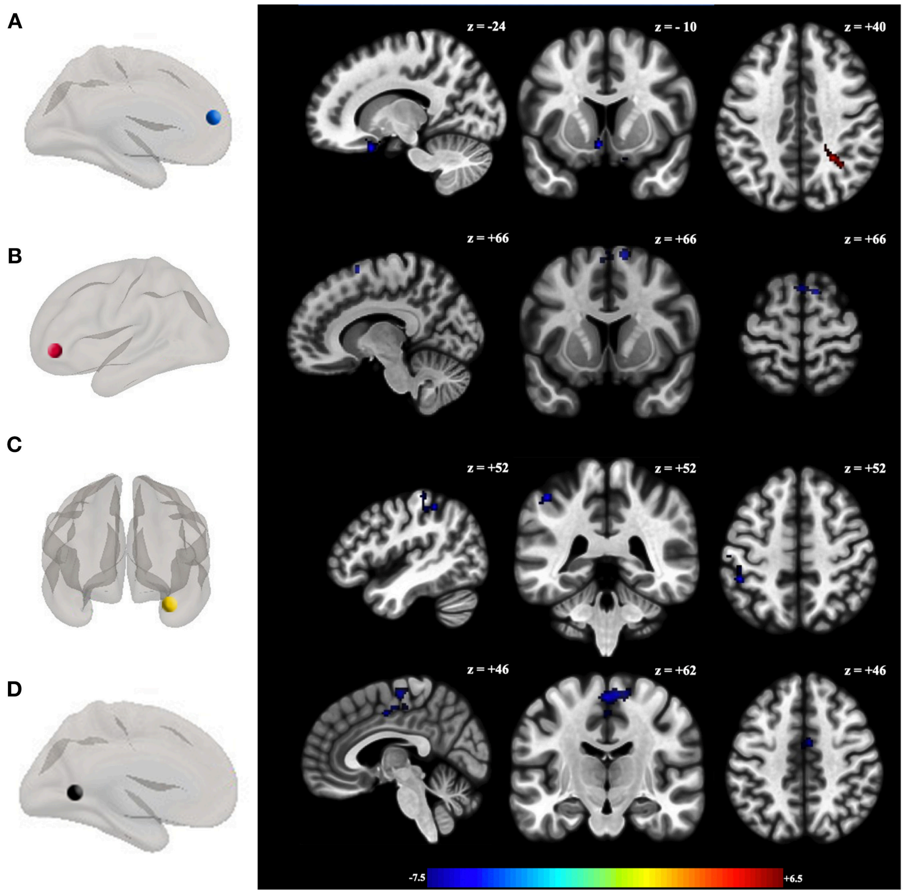

FIGURE 2 | Functional connectivity differences between groups (HC > BPD). Seeds showing significant functional connectivity differences between groups with the **(A)** left medial prefrontal cortex, **(B)** anterior cingulate cortex right; **(C)** right amygdala; and **(D)** inferior middle temporal gyrus between BPD patients and healthy controls with age as covariate. All analyzed contrasts where corrected by multiple comparisons using the false discovery rate (FDR) at 0.05. Blue and orange/hot represent decreased and increased functional connectivity, respectively. The color bar indicates the *t*-value. Details of the clusters are shown in **Table 3**.

We did not find differences between social cognitive tasks for both paradigms, which contrast with the ongoing controversy regarding a BPD patient's ability to read mental states. Data collected with the MASC goes beyond the underlying process of recognizing emotions during social interactions by collecting data from the eye gaze, as evaluated by RMET (43). It also includes an assessment of the content of the mental state of the "other," based on contextual information and elements that are not physically evident (16). This suggests that the instrument is ideal as it reflects real-life situations. Nevertheless, the two paradigms evaluate the cognitive dimension of the social cognitive process, and it is impossible to rule out the limitations of the affective dimension that are associated with emotional regulation and the difficulties in distinguishing between self and the other in BPD subjects (56). Our study showed that depression is associated with decreased social cognitive performance. Although other research has found similar results (57), not all studies have found differences between BPD and control groups, and other researchers have surmised that social cognition performance is a trait rather than a state of mind (58).

Functional Connectivity Results

Our results identified differences in the organization of brain connectivity patterns between the groups, primarily finding hypoconnectivity between the regions explored. It noteworthy that these regions are components of the fronto-limbic circuit and are related to a broad range of cognitive and emotional processes, which have been described as being altered in BPD. These processes have been studied as dysfunctional traits in this disorder and include emotional dysregulation, impulsiveness, aggressive behavior, suicidal tendencies, and self-destructive behavior (59). Some of these regions are a part the default mode network, which is usually related to processes that involve thought formation by self as autobiographical memory, future planning, and inferring one's mental states and those of others (60), which are all processes involved in social cognition (61). The MPFC is involved in the detection of emotions and the process of self-other differentiation (62, 63), while the ACC regulates the monitoring of behavior, the detection and prediction of error, decision making, and processes related to self-evaluation in social contexts (64, 65). On the other hand, the temporal lobe

TABLE 4 | Correlations between functional connectivity and clinical measures in BPD patients.

Cluster MNI	MPFC_L	MPFC_L	MPFC_L	ACC_R	AMYG-R	iMTG-R	iMTG-R
Clinical Measures	*+26 −48, +40* r (*p*-value)	*−06+10 −10* r (*p*-value)	*+14+16 −24* r (*p*-value)	*+10 +10 +66* r (*p*-value)	*−46 −40 +52* r (*p*-value)	*+00 −16 +62* r (*p*-value)	*+04 −04 +46* r (*p*-value)
CTQ TOTAL	−0.003 (0.991)	0.338 (0.171)	0.149 (0.554)	−0.065 (0.797)	0.200 (0.427)	−0.107 (0.674)	−0.017 (0.946)
Emotional abuse	0.088 (0.729)	0.275 (0.269)	0.176 (0.485)	−0.094 (0.710)	0.186 (0.461)	−0.261(0.296)	−0.169 (0.502)
Emotional neglect	−0.168 (0.505)	−0.164 (0.516)	−0.405 (0.096)	0.121 (0.633)	0.227 (0.364)	**−0.475 (0.046)**	**−0.496 (0.036)**
Physical neglect	0.250 (0.317)	−0.057 (0.823)	−0.129 (0.610)	−0.034 (0.893)	0.177 (0.483)	0.015 (0.954)	0.103 (0.684)
Physical abuse	−0.112 (0.659)	0.255 (0.307)	0.226 (0.368)	−0.085 (0.737)	0.282 (0.257)	0.018 (0.945)	−0.036 (0.885)
Sexual abuse	−0.027 (0.914)	**0.669 (0.002)**$^{+}$	0.400 (0.100)	−0.087 (0.733)	−0.061 (0.809)	0.156 (0.536)	0.358 (0.144)

MPFC, medial prefrontal cortex; ACC, anterior cingulate cortex; AMYG, amygdala; MTG middle temporal gyrus; L, left; R, right: Numbers represents: Pearson coefficient, (p-values); Bold indicates P < 0.05 (unadjusted for multiple comparisons); MASC, Movie for the Assessment of Social Cognition; ToM, theory of mind; RMET, Reading the mind in the eyes; CTQ, Childhood Trauma Questionnaire. +: FDR < 0.05.

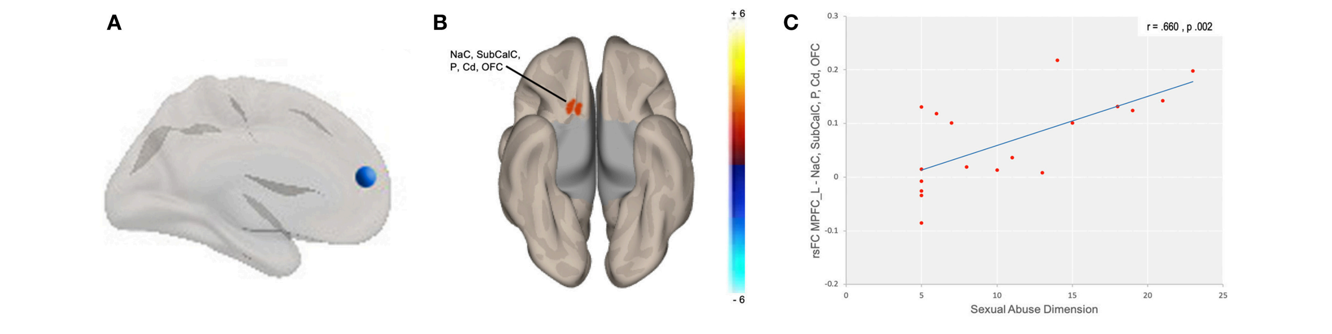

FIGURE 3 | Correlation between sexual abuse and functional connectivity. Correlation between subdimension of sexual abuse and functional connectivity in **(A)** left medial prefrontal seed in BPD patients with **(B)** NaC, accumbens; Cd, caudate; OFC, orbitofrontal cortex; P, putamen; SubCalC, subcallosal Cortex; cluster: x = −06, y = +10, z = −10; **(C)** Correlation between subdimension of sexual abuse and connectivity values.

participates in the processing of language and facial expressions, which are two essential elements in the theory of the mind and mentalization (66, 67). Finally, the amygdala has a critical role in the emotional aspect of the interactional experience (68).

Some of the results observed in our study coincide with those of multiple previous studies that examined the resting state connectivity, such as the findings for the temporal lobe, which represents one of the most commonly replicated results among this group of patients (25, 48, 69). However, with regards to the MPFC and the ACC, some studies have also found a decrease in connectivity (70, 71) while others have found increased connectivity (25, 72). The results observed in the amygdala are similar to certain regions of brain activation observed in response to emotional processing tasks (73), although the result we obtained as the opposite to what was observed in resting state, where an increase in connectivity has been reported (72). This may be explained by the effect of medication on the connectivity in this structure or by the different preprocessing methodologies between studies (74). The effect of medication should be investigated with treatment-naïve patients, while the latter is still an open debate on which is the appropriate preprocessing pipeline (75). Although differences in brain connectivity in regions that are considered to be strongly associated with social behavior were observed in this study, we did not observe any correlations between connectivity and the clinical variables of social cognition. Differences in the abilities of BPD patients to assess mental states have been observed previously, especially under conditions of emotional stress (76, 77). In that sense, we assume that the clinical performance in social cognition tasks related to brain organization at rest could vary under intense emotional states. Stress is associated with an abnormal pattern of deactivation of intrinsic neural networks (78, 79), which could be associated with variations in the performance of social skills. However, it was not possible to show the effects of stress on brain organization in this study.

When we studied both groups together, we observed an effect of child maltreatment on connectivity. Higher levels of child abuse were associated with reduced levels of brain connectivity. However, this result disappears when analyzing per group. The group analysis showed that different types of abuse had differential effects on the connectivity values in the BPD group. The experience of emotional neglect was associated with lower connectivity for the temporal lobe, although this result should be viewed with caution because it did not survive the multiple comparisons correction. In addition, a strong positive correlation was observed between the sub-dimension of sexual abuse and connectivity in the reward circuit (80). Studies have associated hyperconnectivity in this circuit with the presence of psychotic symptoms (81). This finding may explain the tendency toward excessive mental state attribution (over mentalizing) in BPD patients (82), although, in our study we did not find more overmentalizing errors in BPD patients than in controls.

It has been proposed that child maltreatment can be studied as an "ecophenotype," a phenotype modified by specific adaptive response to environmental factors, in order to disentangle heterogeneous diagnoses such as BPD (37). Our results strengthen this approach even though it seems necessary to take into account not only the levels of abuse, but also the type of abuse experienced. In addition, it would be important to study the presence of vulnerability factors associated with BPD, since in the case of the control group, no effect of abuse on connectivity was observed. Another explanation for our result may be an underpowered analysis.

Although the effect of child maltreatment on brain structures has been widely documented (32, 83, 84), the mechanism with which child abuse might have an impact on organization and functional connectivity is still unclear. A possible explanation may be that child abuse is a factor associated with brain remodeling rather than a harmful factor *per se* (37, 85), especially within corticolimbic structures, as shown by a preclinical study of adolescent rats (86). This "modeling" effect on brain organization is present especially during critical stages and processes, such as pruning, that is necessary for normal brain development (87). In the first 2 years of life, a synaptic overproduction occurs in the brain, followed by remodeling through pruning, and these processes continue into adolescence (88). Although remodeling occurs due to cellular programming, researchers have reported that pruning in this second phase is highly sensitive to experience (89), including stress, due to the effect of inflammation mechanisms on glial cells (90, 91). This seems consistent with the new paradigm that regards the brain as an active system that self-organizes dynamically, based on the information that it receives (92). This paradigm has been studied in schizophrenic and autistic patients, for whom dysfunctional pruning has been proposed (88, 93). In BPD patients, stressful childhood events or a lack of proper parenting, may be associated with remodeling and differential pruning. Such hypothesis needs to be tested, as it would enhance our understanding of BPD as a result of maladaptive brain remodeling, resulting from the effects of traumatic experiences on brain development.

Finally, there are some limitations in our study as the lack of differences in the MASC and RMET scores between groups, and significant differences in childhood maltreatment levels. Nevertheless, even with these similarities in the MASC and RMET scores, we found differences in brain connectivity suggesting a dysfunctional resting state that should be explored further.

CONCLUSION

BPD patients endured more child abuse than controls, which correlated with poorer performance on the MASC social cognitive test. We showed that BPD was associated with altered functional connectivity between structures involved in emotion regulation and social cognitive responses that are part of the frontolimbic circuitry. The rsfMRI results provide information about resting state networks that seem altered in BPD patients, and that were associated with different types and levels of abuse. Further investigation of these results is necessary to determine whether the introduction of safeguards to avoid abuse and stress during critical periods, such as childhood and adolescence, would be beneficial, and whether patients can recover from these harmful effects.

DATA AVAILABILITY

The datasets generated for this study are available on request to the corresponding author.

AUTHOR CONTRIBUTIONS

XD-A, FP, EG-V, and JG-O were involved in the design of the research protocol. XD-A, RA-L, and EG-V contributed to acquisition and analysis of data; XD-A, FP, and EG-V drafted the manuscript, and all authors contributed revising and approved it for publication.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00156/full#supplementary-material

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The Heterogeneity of Empathy: Possible Treatment for Anhedonia?

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Traditionally, empathy has been described as a process by which an individual "tries on" the negative emotion of others (i. e., empathic concern). A corpus of empirical work has been devoted to the study of this particular form of empathy. However, in this paper, the *heterogeneity model of empathy* is proposed as a method for counteracting the lack of attention paid to "positive-valence empathy"— our ability to respond to the negative and positive emotion of others with appropriate positive affect. Both empathic concern and positive-valence empathy are argued to have distinguishable behavioral manifestations and at least partially distinguishable neurobiological underpinnings. The potential value of positive-valence empathy induction for therapeutic purposes is also discussed.

Keywords: empathy, empathic concern, positive-valence empathy, prefrontal cortex, ventral striatum, reward

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Various researchers have defined the term empathy differently because psychologists and neuroscientists alike have had trouble coming to a consensus about the scientific meaning of the term. As a result, it has been difficult to formulate, and test theories of empathy in a rigorous fashion. The lack of a clear definition of empathy has made it particularly difficult to pair the behavioral manifestations of empathy with their neurophysiological correlates. Working from a phenomenological definition of empathy would be useful for generating specific, testable hypotheses—enabling researchers the opportunity to systematically determine how well each one aligns with known brain circuitry. This *Perspective* piece has the following structure:

- The concept of empathy as it is traditionally studied is presented.
- An alternative definition of empathy is presented that is more comprehensive (i.e., inclusive of positive-valence empathy).
- Predictions/premises of this reformulated definition/theory of empathy are proposed.
- Neurobiological evidence supporting the proposed reformulation/conceptualization of empathy is presented.
- Discussion of the treatment potential, or usefulness of empathy inductions for therapeutic change, is presented.
- Remaining empirical questions are presented.

THE "STANDARD" EMPATHY DEFINITION VS. A NON-CANONICAL APPROACH TO EMPATHY

Most often, the term *empathy* is used to refer to the vicarious sharing of another's pain or sorrow (1). This form of empathy has been described as *empathic concern* (2–4) because the empathizer "shares in" the negative emotional experience of the target. However, the main argument made here is that positive-valence forms of empathy exist and should be studied alongside empathic concern because they may be useful in clinical settings as a standalone or adjunctive tool to well-established forms of behavioral treatment (e.g., Cognitive Behavioral Therapy-CBT) for positive affect deficits that are commonly observed in individuals with various psychological (e.g., Major Depressive Disorder-MDD, schizophrenia) and/or neurological (e.g., Parkinson's disease) disorders.

There are at least two forms of positive-valence empathy. An individual may exude positive emotion while in the presence of someone who is experiencing a negative emotional state as a means to convey tenderness and comprehension of the person's physical or emotional pain or sadness; in order to catalyze a positive emotional state in the target (e.g., an observer says "cheer up" to someone who has done poorly on a test). In contrast, an individual may exude positive emotion as a means to induce a state of joy in another person who is in a neutral emotional state, for its own sake. These are examples of *empathic cheerfulness*. Similarly, an individual may vicariously experience pleasure in response to someone else's positive emotion (e.g., the observer "shares in" another's joy). This is *empathic happiness*. Collectively, *empathic happiness*, and *empathic cheerfulness* can be referred to as "positive-valence empathy" (5, 6). In general, the exchange of happiness may ultimately serve to amplify—or up-regulate—the experience of happiness for one or both of the individuals involved, increasing *hedonic impact* (7). In fact, during *positive-valence empathy*, the observer and the target stand to generate "new" and heightened positive emotion that they may not otherwise have experienced if it were not for their interaction.

These concepts stem from the ancient Buddhist ideas of "sympathetic joy" and "loving-kindness" (8). In this tradition, positive-valence empathy can be acquired through intense mental training via meditative practice. The concept of *positive-valence empathy* was also later discussed by historical figures such as Theodor Lipps (9) and Adam Smith. For example, in 1759 Adam Smith wrote in *The Theory of Moral Sentiments*:

When we have read a book or poem so often that we can no longer find any amusement in reading it by ourselves, we can still take pleasure in reading it to a companion. To him it has all the graces of novelty; we enter into the surprise and admiration which it naturally excites in him, but which it is no longer capable of exciting in us; we consider all the ideas which it presents rather in the light in which they appear to him, than in that in which they appear to ourselves, and we are amused by sympathy with his amusement which thus enlivens our own [excerpt taken from Goldman (10)].

Though Smith uses the word "sympathy" in this passage, an argument could be made that the description illustrates our present day definition of *positive-valence empathy*. Importantly, here empathic cheerfulness is conceptualized as being separate from prosocial behavior; at least based on the results of prior research. Namely, in previously unpublished aspects of the [Light et al. (6)] data set, the correlation between *trait* empathic cheerfulness (as measured by an independently validated self-report scale) and prosocial behavior (operationalized as selection of actual children's books for donation) was non-significant ($r = -0.009$, $p = 0.94$); and similarly, *task* empathic cheerfulness (measured via self-report as participants viewed a television program that tends to elicit empathy) did not predict subsequent prosocial behavior ($r = -0.036$, $p = 0.769$). This provides preliminary evidence in a healthy adult sample that empathic cheerfulness is distinct from prosocial behavior. Though *trait* empathic cheerfulness does correlate with *trait* empathic concern (as measured by the Interpersonal Reactivity Index-IRI) ($r = 0.574$), and *task* empathic cheerfulness correlates with *task* empathic concern ($r = 0.611$) (6).

Given the existence of positive-valence empathy, a reformulated model of empathy seems necessary [e.g., (11)]. The "standard" model of empathy, which generally equates empathy with affective sharing, is lacking primarily because it conflates emotion identification (i.e., the ability to correctly "read" or interpret the emotion of another) with affect sharing (the ability to feel *with* someone else) [see (11)]; and the entire model is generally based on the singular observation of empathy for *physical* pain. Our working model of empathy needs to evolve to reflect our expanding understanding of the above mentioned empathy subtypes and their underlying neurobiology. In other words, although the neurocircuitry that forms the basis for our ability to empathize with the *physical* pain of others has been well-elucidated to date, it alone fails to explain more recently evolved subtypes of empathy.

Our empathy ability for additional, more complex emotional states than physical pain likely evolved *after* the mechanism responsible for our ability to empathize with the physical pain of others (i.e., from an evolutionary perspective). Furthermore, the underlying neural mechanisms involved in these more complex, later evolving empathy subtypes likely relate to the functioning of neural circuitry that layered over—or emerged from—the basic building blocks of the pain circuit (12, 13). Thus, there is an evolutionary-based and neural-based cause for continuing to expand our conceptualization of empathy.

Just as basic principles of affective neuroscience (and even cognitive neuroscience) were initially formulated based on attributing psychological functions (e.g., "emotion," "memory," "language") to specific brain regions, these fields have evolved over time and now take much more of a systems approach to understanding psychological constructs. Similarly, given that the corpus of empathy research has focused on one subtype of empathy for a long time (i.e., empathy for physical pain), the resulting theories of empathy have generally been limited by this conceptual focus. Here, an attempt is made to promote an empathy model that is more comprehensive and can account for all known subtypes of empathy; with the idea that common and dissociable neural circuitry evolved from the pain circuit are involved in all empathy subtypes.

Therefore, the primary question is how best to (parsimoniously) account for/explain both empathic concern on the one hand, and positive empathy subtypes on the other hand. The fundamental threads of such an inclusive and refined model have already been articulated [e.g., (11, 12)]. Specifically, Coll et al. (11) suggest that empathy should refer to the degree to which the empathizer's emotional state matches that identified in the target, though this emotional response may deviate from the target's *actual* emotional state. Using this definition, empathy can be measured as a single process, rather than as affective identification + affect sharing. However, here it is argued—given the existence of empathic happiness and empathic cheerfulness—even this Coll et al. (11) model stops short. Specifically, we know that empathic cheerfulness occurs on a time-scale consistent with empathic concern (as does empathic happiness), but uniquely does not predict prosocial behavior (as noted above) in the same way that empathic concern or empathic happiness does. Given these facts, it seems likely that empathic cheerfulness does represent a "true" alternative response to the physical or emotional pain of someone else (e.g., other than empathic concern or personal distress), and thus should be included in any explanatory model of empathy. That said, the definition of empathy should make reference to the fact that the empathic response is an emotional reaction that is both relevant and other-oriented in relation to the emotional state of the target (and can be either positive or negative in valence). For example, I may perceive someone who has lost an adored pet, and thus infer that they are likely feeling sad. At this stage of the process, I may either show one of three potential empathy–related responses: (a) personal distress, (b) empathic concern, or (c) empathic cheerfulness. Important to note here, the experience of empathic cheerfulness can occur without a corresponding prosocial act (i.e., the experience of empathic cheerfulness need not involve an overt helpful act). For example, in the situation described above, where the empathizer encounters someone who they perceive to be feeling sad, the empathizer may smile and say "cheer up" without there being a subsequent overt helpful act (e.g., a pat on the back). Overall, the model proposed here deviates from Coll et al. (11) in that it is not required that the emotion "expressed" or consciously "felt" by the empathizer—on a time scale of seconds to minutes—has to even be particularly similar (e.g., in valence, intensity, or quality) to that which is perceived to be present in the target. The emotion need only be *other-oriented*, *relevant,* and clearly *reflective/resultant* from the empathizer's own apprehension/*comprehension/interpretation* of the target's emotional state.

Relatedly, in naturalistic settings, such as the psychotherapy room, researchers have already found that defining empathy narrowly as affective matching is not particularly explanatory or helpful. Specifically, Elliot et al. (14) found that when it comes to measuring the flow of empathy in a therapeutic relationship (i.e., between a client and their psychotherapist), empathic accuracy (i.e., my affect matches yours) does not significantly account for variance in treatment outcome. This provides further support for the idea that conceptualizing empathy as literally "accurate emotional state matching" is limiting, and we should move away from definitions of empathy that advocate this conceptualization.

The Coll et al. (11) model also stipulates that empathy has occurred only when the empathizer *consciously* identifies the emotional state of the target and has an affective sharing experience; whereas personal distress results when the emotion of the target is *unconsciously* identified and affect sharing ensues. The proposed model does not include this conscious/unconscious distinction because, again, empathic cheerfulness appears to be a valid empathic response, but it violates this tenet (at least in certain instances). For example, someone may unconsciously perceive the emotional state of a target who has lost their pet (e.g., sadness), but they actually may only (or predominantly) experience and exude positive emotion, as in empathic cheerfulness. Data pertaining to the minute timescale of emotional responsiveness, and the miniscule timescale with which the underlying neurobiology of emotion can unfold, supports this assertion (15–17).

Re-conceptualizing Empathy: The Heterogeneity Model of Empathy

Under the umbrella of the "*heterogeneity model of empathy*," the following general definition of empathy is offered**: empathy refers to a *change* in emotional state triggered by the formation of an internally generated replica of the emotional state of another.** The integration of information held in mind about the observer's own emotional state with information held in mind about the emotional state of the target provides the substrate for the onset of an entirely new emotional state in the observer. **In addition to the creation of this new vicarious-based emotional state, an other-oriented feeling of goodwill may also be generated in the observer, and this may include (or rise to the level of) feelings of enjoyment in certain instances.** Together, this package is empathy (18). There are several assumptions embedded in this definition.

First, for empathy to occur, the observer must hold at least two mental representations in mind simultaneously: one that contains information about their own emotional state and one that contains information about the emotional state of the target. Furthermore, this information needs to be kept in an online, highly accessible state for a brief period of time *while* the information is also being actively manipulated. Therefore, at certain times the observer must hold a mental image of what the target is feeling on the one hand, and hold a mental image of their own feelings on the other hand, while the situation is actively unfolding (19). This can be unconscious.

Second, it is proposed that the replica of the emotional state of the target that takes shape within the observer is built using several forms of information, including: (a) conscious or unconscious information taken in through the senses about the target's emotional state (e.g., facial expression, vocal tone, body posture), which is based on simulation theory (20), and (b) "as-if" information (e.g., this is self-generated information that the observer obtains by imaginatively placing him or herself in the target's shoes and "trying on" their emotional state; for example the observer may ask themselves "what would it actually feel like if x occurred?"), and (c) "if-then" information (e.g., applying tacit rules about the cause-and-effect relationship between events and emotional states; for example, a tacit rule may be "generally people feel happy [emotion] when they receive a gift [event]." This is consistent with the Theory of mental state attribution (21). For example, if I hear that my friend received a gift from her mother, I can apply this general rule and infer that my friend likely feels happy.

Third, similar to Coll et al.'s (11) and Stotland's (22) definition of empathy as "an observer's reacting emotionally because he perceives that another is experiencing or is about to experience an emotion" [pp. 272; (22)], this conceptualization of empathy does not assume that the observer's emotional experience will be an *exact* replica of the target's emotional state. In fact, the definition only asserts that the observer's emotional state *changes* from its original state as a result of the impact caused by internally representing the emotional state of someone else. In other words, the dual representation of emotional states (i.e., the observer's own and that of the target) can cause the observer's mental/emotional state to *change*.

Finally, this definition does not restrict the use of the term *empathy* to situations in which the observer shares in the negative emotion of another. Instead, the definition allows for the term *empathy* to be applied when an observer shares in the positive emotion experienced by a target. In fact, this definition allows for the term *empathy* to be applied even if the observer experiences an emotion that differs in valence from the emotional state of the target. Stotland (22) referred to this special case of empathy as *contrast empathy*.

Predictions of the Heterogeneity of Empathy Model

In general, the so-called "empathy circuit," which tends to include the anterior cingulate cortex and anterior insula most prominently, is often described in the literature regarding the experience of empathy for *physical* pain [e.g., (23)]. Although prefrontal cortex activation is also generally reported in these studies, it is not emphasized [e.g., (23–25)]. **The heterogeneity model asserts that although this prefrontal cortex (PFC) activation is often overlooked, it likely plays a more prominent role in empathy processes than currently thought, particularly in empathy for emotional states that do not involve physical pain (e.g., emotional pain, happiness, etc.).** This is hypothesized because, in general, the PFC organizes information from lower levels of processing (e.g., the limbic system, sensory systems) and uses that information to orchestrate thought, emotion, and motor actions in accordance with internal goals (26). Specifically, the prefrontal cortex plays a central role in both emotional processing and executive functioning, making this region particularly interesting to study in relation to empathy because the occurrence of empathy—as described above—likely increasingly depends upon (across the lifespan) the ability to hold emotional information in mind (i.e., a working memory function) and orchestrate, step-by-step, an appropriate emotional response.

Given the hypothesis about the role of dual representation of emotional states in the empathizer, a significant role of the dorsolateral prefrontal cortex (DLPFC), extending into the frontopolar prefrontal region, is suspected to occur in all forms of empathy (particularly those that do not involve physical pain), to some degree. A review of recent anatomical, neuroimaging, electrophysiological and developmental findings (presented below) support the existence of a rostro-caudal hierarchy in the prefrontal cortex, with the frontopolar cortex processing more abstract information than the dorsolateral region, and the two regions being heavily interconnected (27). Both regions show activation during empathy tasks. The dorsolateral prefrontal cortex may become activated when representing multiple emotional states, whereas the frontopolar region may be recruited to oversee the completion of higher order goals relevant to empathic interpretation and execution of empathic behavior. The following evidence exists to support the idea that the dorsolateral and frontopolar prefrontal cortex may collaboratively contribute to such empathic ability; across both empathic concern and positive empathy.

Evidence Supporting A Role for the PFC in Empathic Concern. Singer et al. (23) found that adult participants showed significant activation in the dorsolateral prefrontal cortex (BA 47) when viewing their romantic partner receive a painful stimulus. Interestingly, this pattern of prefrontal activity was not present when these participants received the painful stimulus themselves. In fact, participants did not show any significant prefrontal activity when they were the direct recipients of a painful stimulus. This result implicates the dorsolateral region of the prefrontal cortex in empathic processing. The dorsolateral activity observed in this study may be an indication that the observer registered the emotion of the other person. This view is supported by other data that suggests that the dorsolateral PFC region is involved in holding internal representations of external stimuli. The ability to form and hold an internal representation of someone else's emotional state may provide a means for the observer to experience some kernel of that same emotion (28, 29).

Activity in the frontopolar cortex has also been found to relate to negatively-valenced empathic emotion. For example, using a neuroimaging paradigm, Jackson et al. (30) found that there was a significant increase in frontopolar activity (BA 10) when adult participants thought about someone else's pain. Furthermore, Ruby and Decety (31) found that the frontopolar cortex became more active when adult participants had to respond to emotionally evocative situations from the perspective of another person compared to when participants had to take a first person perspective. Additionally, using a cross sectional design, Decety and Michalska (32) found that adults demonstrated greater dorsolateral and ventrolateral activity during an empathy induction task relative to children and adolescents, suggesting that adults rely more heavily on attention and cognitive control circuitry in empathic situations (33).

Similarly, across 4- to 8-year-olds, affective empathy (the ability to be emotionally reactive to the emotional displays of others) related positively with dorsolateral activation in older children relative to younger children (34). This set of findings suggests an increase in recruitment of dorsolateral prefrontal cortex with advancing empathy ability (34). Similarly, in a study with individuals with traumatic brain injury, damage to the dorsolateral prefrontal cortex was found to significantly diminish one's ability to perceive (via the human face) emotion and use emotional information to make interpretations (35).

Evidence Supporting A Role for the PFC in Positive-Valence Empathy. In a study of the neural correlates of charitable donation, fMRI was used to visualize brain activity while people played computer games by which they could earn money for real-life charities. The results indicate that the "joy of giving" has an anatomical basis in the brain—the same one that exists for other types of reward (e.g., food, sex, money)—and can be found in the ventral striatum (36). However, importantly, activity in the frontopolar cortex related participant's report of their feelings of joy and everyday charitable involvement (36).

Electrophysiological and neuroimaging data also suggest that increased activity in the dorsolateral [(37–40), orbitofrontal (41), ventrolateral (42), and frontopolar prefrontal cortex (43) relate to the subjective experience of basic positive emotions such as happiness and/or pleasure, which is linked to increased empathy behavior (44). Results from an electroencephalographic (EEG) study involving children aged 6–10 years old (5) suggest that children who tend to exhibit *empathic concern* vs. *positive empathy* have distinct neurophysiological profiles during the elicitation of pleasure (on a completely separate day). For example, children who demonstrated substantial behavioral *empathic happiness* exhibited relatively symmetrical co-activation of dorsolateral and frontopolar prefrontal activity via EEG when they were exposed to a positive stimulus on a separate day (5). The sustained maintenance of equal amounts of left and right lateral and anterior prefrontal cortex activity over the course of a positive stimulus may indicate that these children bring both lateral frontal hemispheres to bear on pleasure-inducing tasks. Children who demonstrated a high level of behavioral *empathic concern* exhibited right-sided *and* then left-sided prefrontal activity across the lateral and anterior-most regions of the prefrontal cortex during a positive affect inducing task (5). The ability to exhibit right and then left-sided prefrontal activation during a positive task might relate to an ability to flexibly experience (or shift between) positive and negative emotional states during a task, and may be facilitated by amygdala connectivity (15). If a child can flexibly experience negative and positive emotional states, this general ability may enhance their ability to internally represent the emotional states of others and respond to the negative emotion of others with a combination of negative emotion (e.g., sadness and concern) and/or positive emotion (e.g., positive empathy, goodwill). The results from a separate behavioral study involving children under the age of 2-years-old provide evidence that young children experience greater happiness when giving treats to others rather than receiving treats themselves (45), further supporting the role of positive emotion in empathy.

Finally, a neuroimaging study of vicarious reward revealed that adult participants who reported enjoying observing other people winning a game show exhibited greater bilateral frontal pole activation, in addition to ventral striatum activation (46). Ventral striatum activity also increased when the participants played the game themselves and won, but prefrontal activation was absent. Again, these results support the findings of Light et al. (5) because a dorsolateral-frontopolar prefrontal circuit was implicated in empathy; in this case, positive-valence empathy.

Empathy Circuits. It is important to note that the dorsolateral and anterior-most regions of the prefrontal cortex do not work in isolation to enact empathic feelings or behavior in adults (or children), and these different regions may be distinguishable in terms of what they *do* in the various empathy subtypes. For example, it is hypothesized that the dorsolateral prefrontal cortex facilitates the dual representation of the emotional state of the observer and the target. However, as the emotions that need to be represented become more abstract, it is likely that the frontopolar cortex becomes more active (36).

Both prefrontal regions are likely active in empathic concern and both forms of positive empathy. What may distinguish the different subtypes of empathy are the extent of prefrontal activation, different patterns of lateralization of prefrontal activity [see (5, 40)], and/or differential patterns of concomitant subcortical activation. Altogether, several primary brain structures are hypothesized to be involved in the various empathy subtypes, including: the amygdalae, the ventral striatum (e.g., nucleus accumbens and globus pallidus), anterior cingulate, insula, and the dorsolateral and frontopolar prefrontal cortex (see **Figure 1**). Bottom-up and top-down processing among these structures may contribute to our capacity to resonate with each other emotionally and experience the various empathy subtypes. Bottom-up processing allows for the rapid processing of an affective signal, such as someone in pain (39; 26); and top-down processing allows for the perceiver's intentions, motivations, and feelings to be attached to the comprehended feeling state initiated by the bottom-up process. In adults, signals sent from the amygdala and/or anterior cingulate/insula to the lateral and anterior-most prefrontal cortex are thought to form the basis of the bottom-up empathic processes, while activity originating in prefrontal regions is thought to play an important role in top-down empathic processing (47). There is likely a bi-directional route by which the lateral aspect of the prefrontal cortex not only is involved in processing the initial affective signal generated by the amygdala (i.e., which carries information about the emotional state of the target) as proposed by Decety (47), but also plays a role in generating the first kernels of the other-oriented feeling of goodwill in the empathizer, a form of positive affect, that may get elaborated by prefrontal cortex. It is hypothesized that the prefrontal cortex is largely responsible for the higher order feeling of goodwill that is central to the proposed model of empathy, though subcortical structures likely contribute too, such as the nucleus accumbens, which is involved in reward.

Treatment Potential

The proposed "heterogeneity of empathy" model is based on preliminary work that indicates that *increased* empathy (all types) predicts *increased* positive emotionality (5); and positive affect is associated with many desirable outcomes, such as problem solving, well-being, longevity, and reduced likelihood of dementia. Thus, understanding the idiosyncrasies between various empathy *subtypes* and the symptom of anhedonia (i.e., the reduced ability to experience pleasure) could perhaps inform new therapeutic approaches that make use of empathy induction paradigms as a means to reduce anhedonia; especially given the ethics of increasing positive affect—i.e., the need to increase positive affect without use of potentially addictive medication or unhealthy increases in risky behavior.

Although anhedonia is an elusive construct to study, most agree it is a symptom that everyone would like to decrease/eliminate. In its place, most would rather experience "happiness." Happiness can be defined as the frequent experience of positive emotions (48–50) and is trait-like (but is not as

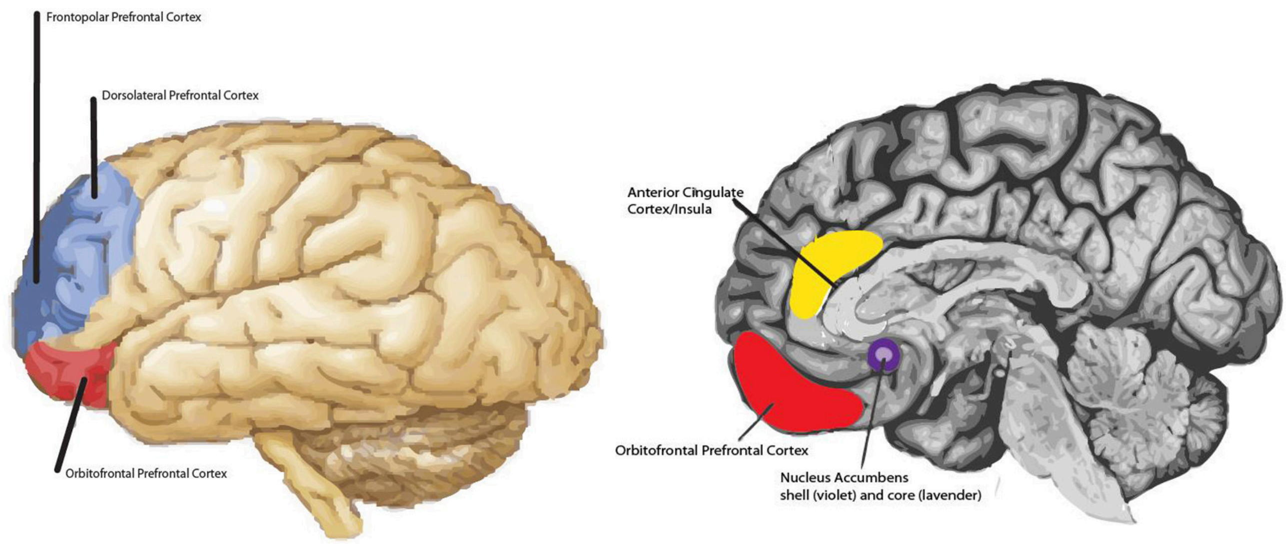

FIGURE 1 | Main regions hypothesized to be involved in non-physical pain empathy processes. For example, frontopolar prefrontal cortex is shaded in dark blue and the dorsolateral prefrontal cortex is shaded in light blue. Both regions may be involved in empathic concern and positive-valence empathy. The extent of prefrontal activation and lateralization effects may distinguish one form of empathy from another; in addition to differential patterns of subcortical activity (e.g., nucleus accumbens vs. amygdala). Note: Amygdala not highlighted.

stable across time as most would assume, with ∼33% of variance in happiness being accounted for by an unstable state/error variable) (51). Its neurobiological substrate is rooted in the functioning of frontostriatal circuitry; and subjective happiness has been linked to orbitofrontal and dorsolateral prefrontal cortex, and ventral striatum activity most commonly (52–55). It is still somewhat unclear whether happiness and anhedonia exist as opposite ends of a continuum or represent distinct constructs, each with their own continuum; however, longstanding research suggests that anhedonia is a viable candidate for an underlying endophenotype for psychiatric/neurological dysfunction, given that it appears across several psychiatric and neurological disorders, is trait-like itself, and also has neurobiological underpinnings focused in frontostriatal activation (56). In other words, it fits within the Research Domain Criteria (RDoC) framework put forth by the National Institute of Mental Health (NIMH) (57). "RDoC" is a research framework for new approaches to investigating mental disorders. It integrates many levels of information (from genomics and circuits to behavior and self-reports) in order to explore basic dimensions of functioning that span the full range of human behavior from normal to abnormal. One of the RDoC domains is "Positive Valence Systems," and part of the urgency in studying this domain is due to the fact that there is a strong need for novel/alternative methods of *inducing* positive affect (e.g., in various clinical populations) given the difficulty of safely and repeatedly increasing positive affect without the use of medication or other substances, or without having people engage in unhealthy, risky behavior.

For example, although treatments such as Behavioral Activation (BA) are effective in treating MDD—and despite its focus on scheduling pleasant events—anhedonia remains a residual symptom in a large subset of these patients, particularly once the treatment is stopped (56, 58). Attempting to directly increase positive emotion has proven difficult in clinical populations. This is also reflected in the research literature, which demonstrates the difficulty of inducing a robust positive affective response in laboratory settings. Given these limitations, and our own work suggesting that some MDD patients may have a tendency to unconsciously suppress positive emotion (42) (at least in certain situations), systematically inducing empathic happiness offers an alternative route to help people decrease anhedonia.

Inducing empathic happiness may have treatment potential most likely as an adjunctive treatment to Cognitive Behavioral Therapy (CBT) or Behavioral Activation (BA). Behavioral Activation (BA) is a treatment that has been shown to be effective in treating Major Depressive Episodes (59), and its mechanism of action is primarily thought to relate to the scheduling of pleasant events. This treatment is primarily based on addressing *anticipatory anhedonia*, or the reduced ability to experience pleasure in the pursuit of pleasurable activities. However, the treatment generally does not directly address *consummatory anhedonia* (i.e., the ability to enjoy rewards in-the-moment once obtained). Indeed, anhedonia remains a residual symptom at a rate that is similar to other behavioral treatments that do not necessarily focus of positive affect at all. Therefore, attempting to directly increase/train the subjective experience of, and sustenance of, positive emotion via positive-valence empathy induction specifically in response to the *attainment of a reward* (i.e., consummatory pleasure) may be a useful adjunct to lower the rate of persisting anhedonia in this clinical population.

Through the induction of empathic happiness (and possibly empathic cheerfulness), "new" positive emotion may be produced in the empathizer; and given the route of induction, it may be more sustainable than any positive emotion invoked by medication use or engagement in currently available behavioral remedies. This is primarily because the positive emotion produced through empathy induction will likely both quantitatively (a) increase subjective positive emotion (i.e., increase *hedonic impact*) and (b) increase the execution of prosocial behaviors in the community at large (increasing social connectedness more broadly). This is predicted because the underlying biological mechanism/route to increased positive emotion is likely different; with empathic happiness induction being more focused on the experience of pleasure vs. just increasing the *number of* pleasant activities. Teaching individuals to enjoy *obtained* rewards (i.e., consummatory pleasure) in a new way is in contrast to Behavioral Activation's focus on the *pursuit/scheduling* of pleasurable activities (i.e., anticipatory pleasure). The proposed empathy induction process likely maps onto a separable fronto-striatal circuitry (possibly mediated by broader prefrontal involvement) and neurotransmitter system functioning than BA alone; given animal models showing that consummatory and anticipatory positive affect are mediated by separable neurotransmitter systems (i.e., dopamine vs. opioids) and neural circuits. Opioids relate to consummatory pleasure, which is likely emergent from its role in the pain analgesia system.

Thus, the proposal here is that a brief intervention designed to teach individuals to engage in empathic happiness represents a novel technique for treating anhedonia in-the-moment, and is based on a literature that suggests that the hedonic treadmill hypothesis is not entirely accurate as originally conceptualized (54) in that the generation of prosocially-mediated positive affect may be quantitatively greater (i.e., increased hedonic impact) and more resistant to tolerance effects across time because it may tap a slightly different, broader fronto-striatal circuitry than self-focused "discrete" joy or anticipatory pleasure does. The proposed intervention relies on the popular and well replicated finding in the literature that most people feel quantitatively *more* happiness when they engage in other-oriented, prosocial activities (60) opposed to self-focused activities. Capitalizing on this phenomenon, tailor-designed empathy inductions could be carried out with patients to maximize hedonic impact. Learning to effortfully evoke/increase empathic happiness using behavioral techniques such as "savoring" (i.e., relishing in one's positive experiences) and "capitalization" (telling someone/sharing the good things that happen in life) may serve to ultimately diminish anhedonia (60)—via novel activation of previously dysregulated neurotransmitter systems and dysregulated nodes of fronto-striatal circuitry—and promote longer-term/sustainable happiness.

The hypothesis that empathic happiness may be harnessed as a treatment—or adjunct to established treatments such as Behavioral Activation—fundamentally stems from the belief that empathy is mutable, and anhedonia may be altered via targeted modification of aspects of fronto-striatal activation by behavioral means, such as a successful empathy induction. The idea that empathy is mutable stems from a small but growing empirical base. Research findings suggest that interventions derived from ancient contemplative practices that focus on increasing traits such as compassion (e.g., through the practice of "loving-kindness meditation")–a construct related to empathy–can induce plasticity-related alterations in the brain, and these alterations support a range of positive behavioral outcomes such as improved immune function, increased prosocial behavior, and enhanced problem solving ability (61). Thus, the experience of "empathic happiness"—under normal circumstances and by definition—should increase the experience of positive emotion in vulnerable individuals (i.e., particularly in anhedonic individuals). It is important to note that positive empathy is not expected to be a panacea of any sort. It is only expected that certain patients in particular, i.e., patients that suffer with anhedonia and other residual symptoms following "successful" treatment of MDD (either pharmacological and/or behavioral), may be more impacted by this type of training vs. individuals who demonstrate a different symptom pattern. However, this technique could be useful for several disorders characterized by anhedonia; not just MDD.

Empathic happiness and empathic cheerfulness may also be beneficial to professional providers of care. This idea stems from results from a recent neuroimaging study. Engen and Singer (62) found that individuals trained in compassion-based emotion regulation vs. cognitive reappraisal demonstrated increased positive affect (vs. dampened negative affect in the cognitive reappraisal condition) and this subjective experience was reflected by increased activity in ventral striatum and medial orbitofrontal prefrontal cortex in the compassion-based emotion regulation group. Compassion relates to empathy and can be defined as a feeling of concern for the suffering of others that is associated with the motivation to help (63). Essentially, these results suggest that the elicitation of compassion-based emotion regulation circumvented the experience of personal distress. This finding has implications for how to reduce caregiver burnout. However, it would also be interesting to determine whether training caregivers to engage in empathic happiness and empathic cheerfulness in relation to their clients—and then training clients to engage in empathic happiness in their everyday lives—may also be an effective and alternative route for reducing caregiver burnout, but may also directly facilitate therapeutic change in the client.

The primary techniques that clinicians (and clients) can be taught to use include basic theory-of-mind/emotion decoding, "emotion regulation/cognitive reappraisal" (64) and "capitalization/savoring" (60). For example, in order to practice "capitalization/savoring," empathizers can go through training in which they learn how to better concentrate on the positive characteristics of others (14), including their clients. An example of how they can be trained to use the "theory of mind/emotion decoding" technique would look like this: "Focus on instances when you noticed an individual smiling. Try to notice whenever the individual smiles, and try to imagine how good the person may feel at those moments; and inquire about their emotional state at those moments." As an example of an "emotion regulation/cognitive reappraisal"-based strategy, empathizers can be trained to: think about what past happy memories may mean for that person, with particular emphasis on how they can manifest similar experiences in their current and future life. Overall, training empathizers to focus on thinking about people of interest in the most positive light possible could be effective for inducing more empathic happiness. Another example of "savoring:" prompt trainees (i.e., empathizers) to incorporate how they are feeling in the moment in reaction to their current experience, later in their day, or a week from now. Empathizers undergoing this type of "training" could be given an opportunity to practice these techniques as they view selected video clips from movies or television shows that tend to evoke positive empathy. For example, our prior work (6) indicates that reality television can be a useful elicitor of positive empathy, and could be used in a training context to "teach" positive empathy skills.

Concluding Remarks and Future Directions

Using the lens of the *heterogeneity of empathy model*, it is suggested that frontostriatal reward circuitry plays a special role in empathy processing. Extending from this, several general statements can be made about the nature of empathy based on the empirical data currently available. First, the successful execution of empathic processes (both *positive-valence empathy* and *empathic concern* processes) likely involve activity in the prefrontal cortex; the lateral and anterior-most regions of the PFC seem particularly relevant given their particularly strong roles in working memory, abstract thought, and positive affect (5, 40).

According to ancient Buddhist teachings, "sympathetic joy"—the earliest known reference to positive-valence empathy—can be achieved through meditative practice (8). Similarly, according to Lipps (9), empathy is the result of a contemplative state that can result in enjoyment/pleasure; and as Adam Smith eloquently stated in *Theory of Moral Sentiments*: "How selfish soever man may be supposed, there are evidently some principles in his nature, which interest him in the fortune of others, and render their happiness necessary to him, though he derives nothing from it except the pleasure of seeing it (pp. 585)." In sum, evidence abounds that human beings have a capacity to relate to the emotions of others, including the positive emotions of others. Importantly, this process may be rewarding, just as food, money, and artwork are (65). In fact, there is some evidence to suggest that, at least in children, *greater* happiness can be derived from cultivating happiness in others rather than experiencing personal happiness (45). This leads to the final premise of the heterogeneity model: empathy may indeed be a rewarding process, and likely contributes to eudaimonia (i.e., well-being). Well-being, or the "good life," can be conceptualized as having at least two dimensions: hedonic (e.g., the experience of moment-to-moment pleasure) vs. eudaimonic (e.g., the experience of positive meaning and/or sustained, long-term positive affect). We are only beginning to tease these constructs apart; but basic neuroscience research in hedonic processing suggests that heightened "liking" (i.e., pleasure derived from the *attainment* of a reward) is mediated by a relatively small set of brain structures that includes the nucleus accumbens shell and orbitofrontal prefrontal cortex, whereas subjective well-being or eudiamonia likely involves the prefrontal cortex more widely (7). Therefore, the intersection of prefrontal cortex activity, subcortical activity, short and long-term positive affect, and empathy may be an important cornerstone of prosocial behavior and heightened well-being.

"Positive-valence empathy," if it can be taught, a currently hotly debated question in the empathic concern literature, stands as a potentially relevant clinical tool (66). Anhedonia, the reduced ability to experience pleasure, is a common symptom across various disorders including Major Depressive Disorder (MDD) and Parkinson's disease. Thus, training people to increase their "positive-valence empathy" skills may be an efficacious treatment technique against anhedonia, in addition to more traditional techniques for increasing "personal" positive affect (e.g., Behavioral Activation).

The future of the field of positive affect and empathy research will benefit from mainstreaming the concept of "positive-valence empathy" alongside "empathic concern." Any comprehensive theory of empathy needs to account for the existence of "positive-valence empathy." Work to date provides good evidence for a role of fronto-subcortical reward circuitry in complex empathy. However, future work will need to address the potential neurobiological link between empathy and well-being, and focus on elucidating the unique neurobiological contributions of "empathic concern" vs. "positive-valence empathy" subtypes to differential prosocial behaviors.

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The author confirms being the sole contributor of this work and has approved it for publication.

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Shared Environment Effects on Children's Emotion Recognition

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Empathy is relevant to many psychiatric conditions. Empathy involves the natural ability to perceive and be sensitive to the emotional states of others. Thus, emotion recognition (ER) abilities are key to understanding empathy. Despite the importance of ER to normal and abnormal social interactions, little is known about how it develops throughout childhood. We examined genetic and environmental influences on children's ER *via* facial and vocal cues in 344 7-year-old twin children [59 monozygotic (MZ) and 113 same-sex dizygotic (DZ) pairs], who were part of the Longitudinal Israeli Study of Twins. ER was assessed with the child version of the Diagnostic Assessment of Nonverbal Accuracy. For both facial and vocal cues of emotion, twin correlations were not higher for MZ twins than for DZ twins, suggesting no heritability for ER in this population. In contrast, correlations were positive for both types of twins, indicating a shared environmental effect. This was supported by a bivariate genetic analysis. This pattern was robust to controlling for twins being of the same sex and age. Effects remained after controlling for background variables such as family income and number of additional siblings. The analysis found a shared environmental correlation between facial and vocal ER (r_c = .63), indicating that the shared environmental factors contributed to the overlap between vocal and facial ER. The study highlights the importance of the shared environment to children's ER.

Keywords: empathy, emotion recognition, shared environment effect, individual differences, childhood

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INTRODUCTION

Empathy, the ability to perceive and be sensitive to others' emotional states (1), is relevant to many psychiatric conditions (2). Emotion recognition (ER) abilities are relevant to feeling empathy for others (3), specifically cognitive empathy (4), the ability to recognize and understand the emotions of others (5). Despite the importance of ER for social interaction and functioning (6–8), individuals vary markedly in ER ability (9, 10). Our research addresses the origin of these individual differences. Specifically, we investigated genetic and environmental effects on children's recognition of emotion from facial and vocal cues using data from seven-year-old twins.

Childhood may be a unique developmental period for ER, with important developmental advances such as the ability to take others' perspective, which contribute to better understanding of emotions and social interactions (11–13). Nevertheless, little is known about how ER develops throughout childhood [e.g., Ref. (12)]. Most of the studies on the contribution of the family context to children's emotional development did not directly address ER but focused on related skills, such as children's emotion understanding (14). Many environmental factors may influence social development, including parental socialization, peer influence, teachers, school, and culture (15–17). Much research has also addressed the roles of socioeconomic status (SES) and sex on ER development (18). There is evidence that children with low SES show difficulties in terms of their overall emotional development (19) and, particularly, in ER (20), and in a meta-analysis of 215 studies (21), females had a small but reliable advantage in ER tasks.

Although theoretical and empirical research suggests that individual differences in empathy are affected by both genetic and environmental factors (22), only little research has examined genetic and environmental effects on ER. Studies estimating genetic and environmental influences on empathy have typically relied on the classic twin design, which compares monozygotic (MZ) and dizygotic (DZ) twins (23). Higher similarity between MZ than DZ twins indicates genetic influence (*heritability*), while twin similarity that is not higher for MZ twins cannot be accounted for by their genetic relatedness and is attributed to the *shared environment.* Finally, dissimilarity between family members despite their genetic and environmental relatedness indicates the influence of the *nonshared* environment and measurement error.

We found only two past studies of genetic effects on ER. Studying 10-year-old twins (N = 250 pairs), Lau and colleagues (24) found modest and largely nonsignificant genetic effects on recognition of specific emotions from facial expressions, and a strong (75% of the variance) genetic effect on a global factor estimated across emotions. The second study (25) also examined facial emotion recognition in a larger sample of twins (N = 957 individuals) in a wide range of ages, 9 to 17. The findings show a significant genetic effect (34%–57%) for the recognition of six basic emotions. Only modest evidence was found for shared environment effects (1%–12%), controlling for age and sex. Nonshared environmental effects accounted for the remaining variance in both studies.

Substantial changes occur in ER during middle childhood (11, 12). For example, age plays an important role in the emotion comprehension process, and cognitive nonverbal factors are predictors of 3- to 10-year-olds' emotion comprehension (26). Moreover, past work has shown that the relative importance of genetic and environmental effects changes with age [for a meta-analysis on empathy, see Ref. (22)]. It is therefore important to extend the results to younger samples. Based on past work, we expected to find a genetic effect and nonshared environmental influence on children's ER in our 7-year-old sample. Additionally, based on the above evidence, we examined the role of SES and sex in ER.

Past work (24) focused on facial expressions. Importantly, recent studies have shown the importance of vocal cues to accurate ER (27). Vocal cues improve nonverbal communication and ER in social situations [e.g., Refs. (28, 29)]. While preschool children tend to rely more on facial expressions during social interaction, school-aged children (ages 7–12) rely on both facial expression and tone of voice (30). The importance of vocal cues to emotion, then, calls for studying them in addition to facial cues. Our study, therefore, expands the scope of ER by testing both facial expressions and vocal tone. In addition, studying both kinds of cues in the same design enables an investigation of the origin of the association between understanding vocal and facial cues to emotion. Overlapping genetic effects on facial and vocal ER would indicate a global cross-modality genetic tendency. In contrast, overlapping environmental effects will indicate that similar environmental forces promote (or hinder) development of ER across modalities.

METHODS

Participants

A total of 344 Jewish Israeli children (52% male, 59 MZ pairs and 114 same-sex DZ pairs) participated in the Longitudinal Israeli Study of Twins (LIST) (31) at the age of 7 years (90.05 ± 3.87 months). Children were observed performing a variety of tasks in the lab. Each child was tested separately by a different experimenter from his or her twin to avoid any bias effects. Written informed consent was obtained from the participants' parents.

Measures

Emotion Recognition Measure

We used the child version of the Diagnostic Assessment of Nonverbal Accuracy Scale-2 (DANVA-2) (7, 32, 33). Children watched 24 different pictures of children's faces one at a time and classified each as angry, happy, fearful, or sad. Similarly, they are required to identify the different emotions in 24 recordings of oral speech, where the words themselves are emotionally neutral (the same sentence is used: "I am going out of the room now but I will be back later"). The DANVA has been extensively used and well validated in child samples [e.g., Refs. (34–36)]. Inter-item reliability of the items yielded Cronbach's α = .70. Facial and vocal cues correlated positively (r = .30, p < .001) and were analyzed separately as well as summed into an overall ER score.

Demographic Data

Mothers reported demographic data, including number of additional siblings and SES. SES was indexed by family income, asking parents to rate their income relative to the given national average using a scale ranging from 1 "a lot below" to 5 "a lot above" the average (M = 3.26, SD = 1.26).

Analyses

We performed descriptive analyses with SPSS (version 25). Genetic analyses were performed using the Mx structural equation modeling software (37). Mx was specifically designed to analyze twin data, estimating the relative contribution of additive genetic (A), shared environment (C), and nonshared environment and error (E) effects on individual differences. We also used a bivariate extension of the twin design using the correlated factors model (38), which estimated the ACE components for each modality separately, as well as the associations between the genetic and environmental components contributing to each modality.

RESULTS

Table 1 presents descriptive statistics and correlations between MZ and DZ twins for overall ER and for facial and vocal cues separately. Results showed positive correlations in both MZ and DZ twin pairs. Correlations were not higher for MZ twins, indicating no heritability for ER in this population. Instead, positive correlations for both DZ and MZ twins indicate that at least part of the individual differences in these measures is associated with shared environmental factors. Although the DZ correlation was somewhat higher than the MZ correlation, this difference was not significant (Fisher's test of independent correlations, $z = -1.85$). Similar correlation patterns were found for both facial and vocal cues of emotion.

Our first genetic analysis fitted a univariate genetic model to the overall ER scores. As the genetic effects were estimated at zero, they were dropped from the model without affecting model fit [$\Delta\chi^2$ (df = 1) = 0.00]. Thus, the model without a genetic effect (CE) was preferred over the less parsimonious full model (ACE). The shared environment effect accounted for 44% of the variance, and the remaining variance was accounted for by the nonshared environment effect and error (**Table 1**). We estimated genetic and environmental contributions to facial and vocal ER, as well as the association between these two variables. We fitted a bivariate genetic model to the data. Again, genetic effects were estimated at 0 and could be dropped from the model without worsening fit [$\Delta\chi^2$ (df = 3) = 0.00], and the more parsimonious CE model was preferred. The shared environment component accounted for 32% and 38% of the variance in facial and vocal ER, respectively. The bivariate genetic analysis indicated that the correlation between facial and vocal ER reflected a shared environmental correlation between these variables [r_c = .63, 95% confidence interval (CI) = .34–.94], with little correlation between the nonshared environment components (r_e = .09, 95% CI = −.05 to .25) (**Figure 1**). The shared environment effect accounted for 73% of the correlation between facial and vocal ER (based on the product of r_c and the nonsquared standardized shared environment path coefficients) with the rest of the association accounted for by the nonshared environment effect.

Table 1 presents fit indices for the univariate and bivariate CE models. These model fit indices reflected the pattern in which similarity between the DZ twins is greater than the MZ twins, which is not expected in the CE model given that the shared environment is estimated as affecting siblings growing up together similarly regardless of genetic similarity.

Age variation in months within our sample correlated with facial ER (r = .23, p < .01) and vocal ER (r = .22, p < .01). In addition, girls performed better than boys in facial [t (376) = −4.43, p < .004, D = .46] and vocal ER [t (375) = −1.72, p < .001, D = .18], in line with previous work (21, 30). It was therefore important to account for age and sex differences among twin pairs and to verify that the shared environment effects found in the study go beyond the effects of twins sharing their sex and age. We thus calculated a new ER variable, partialing out the effects of sex and age in a regression analysis. Controlling for sex and age, the results still held (rMZ = .23, rDZ = .46), showing no genetic effect. That is, age and sex did not inflate twin correlations and could not account for the shared environment effects estimated.

ER correlated modestly with demographic variables such as greater SES (r = .14, p < .05) and fewer additional siblings (r = −.16, p < .001). However, as was the case with age and sex, follow-up analyses showed that the presence of the shared environment effects was beyond twins' sharing these variables. Specifically, analysis of scores residualized for number of siblings, SES, sex, and age did not substantially change the results, including the lack of genetic effect. The shared environment component was estimated at 23% (CI = .07–.38) and 38% (CI = .23–.51) of the variance in facial and vocal ER, respectively, and a shared environmental correlation accounted for the association between these variables (r_c = .46, CI = .06–.88).

DISCUSSION

This study examined genetic and environmental influences on children's ER, for the first time adding vocal to facial cues of

TABLE 1 | Twin correlations and genetic/environmental influences on ER.

	Correlations		Variance component estimates proportion (95% CIs)			Model fit indices	
	MZ twins	DZ twins	Genetics	Shared environment	Nonshared environment	AIC	BIC
Total ER	.35**	.49**	.00 (.00–.24)	.44(.24–.56)	.55 (.44–.68)	263.99	−396.18
			–	[.44(.32–.56)]	[.56 (.44–.68)]	261.99	−398.76
M (SD)	24.32 (6.12)	25.48 (5.85)					
Facial	.29**	.35**	.00 (.00–.38)	.32 (.03–.45)	.68 (.52–.82)	540.72	−781.26
			–	[.32 (.18–.45)]	[.68 (.55–.82)]	534.72	−788.99
M (SD)	15.48 (4.40)	16.41 (4.11)					
Vocal	.21	.47**	.00 (.00–.19)	.38 (.19–.50)	.63 (.50–.76)	540.72	−781.26
			–	[.38 (.24–.50)]	[.63 (.50–.76)]	534.72	−788.99
M (SD)	8.84 (3.37)	9.03 (3.02)					

*The second line for each variable represents the best-fitting model after dropping the genetic effect estimated at 0.00. The parentheses portray the estimates from the full ACE model including the genetics, whereas the brackets contain the estimates from the model without the genetics. AIC, Akaike information criterion, calculated in comparison to the full ACE model. BIC, Bayesian information criterion. CI, confidence intervals. MZ, monozygotic, DZ, dizygotic, same-sex twins. *p < .05, **p < .001*

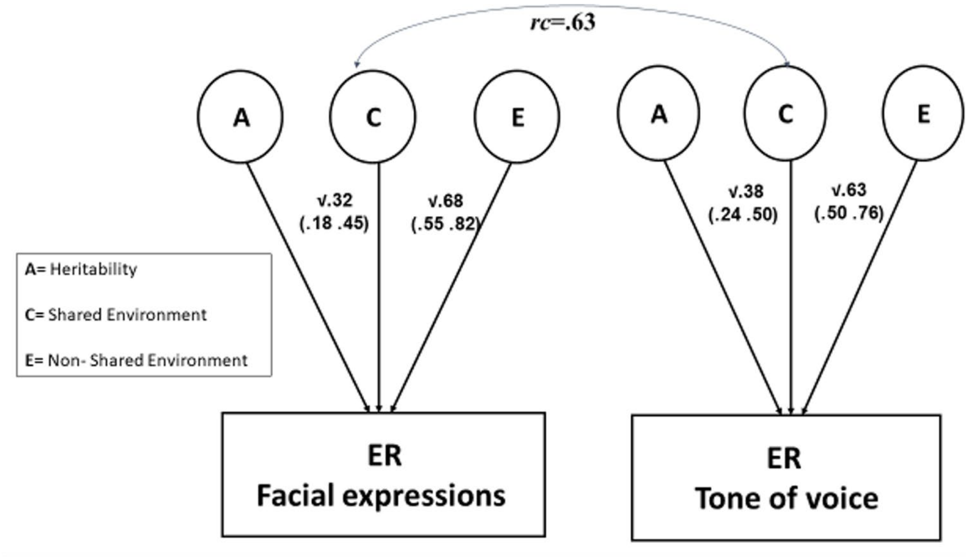

FIGURE 1 | The bivariate model: genetic and environmental influences on ER.

emotion. Our results indicate that individual differences in ER by 7-year-old children are accounted for by shared and nonshared environmental variables. Moreover, the association between facial and vocal cues reflected mainly overlapping shared environmental effects. This study highlights the importance of the environment to children's ER.

Shared environment effects suggest that the family milieu plays an important role in the development of children's ER (16), although the exact process needs further research. Moreover, the bivariate analysis indicated that shared environmental factors largely account for the association between vocal and facial ER. Across species, the social environment provides a place for training and learning about the emotional world, helped by social factors such as contact and familiarity (39). Research has shown that it is easier for individuals to identify others' emotion expressions from their own cultural in-group (40, 41). In addition, culture may be influential through stereotypical displays found in various media (42). These archetypes provide an opportunity to gain exposure and learn about the emotional social world. Going to the family level, it is possible that differences among families in the expression of emotions affect children. These shared experiences may affect the ability to understand emotions in a stereotypical and nonexhaustive way, increasing similarity between siblings being exposed to similar events in their family.

A large portion of the individual differences in ER in this study were attributed to nonshared environment effects (43). Nonshared effects are child specific and can include life events such as illness and relationships with family and peers. The study focused on 7-year-olds who, in the Israeli context, are already attending school. School may serve as an important source of nonshared environmental influences, as twins are exposed to a variety of different peers and often different classrooms. Communicating with diverse children exposes children to others' varied emotional states. This can then enable further peer experience and expertise in ER, which may contribute to the nonshared environment effects on ER.

We did not find any genetic effects, while most past twin studies on empathy and related variables found meaningful genetic effects and little evidence for shared environmental effects (22, 36, 44, 45). One possibility is that our use of a test method vs. the more commonly used questionnaire methods led to lower heritability estimates, as was found for other variables (e.g., parenting) (46). However, past work on facial expressions did find genetic effects (25). Another possibility is that the lack of genetic effects reflects the younger age of our sample as compared to past studies (5, 24). Indeed, heritability increases with age for several traits (47, 48), including empathy (22), in longitudinal studies using the same method across ages (49).

Thus, further longitudinal research might support the increase in heritability with age. One way in which heritability might increase with age is through evocative gene–environment correlation processes, in which the child's genetically influenced traits increasingly affect the environment, which in turn influences the developing person, leading to an increase in heritability with age (50–52). In addition, the absence of heritability should be interpreted in light of the possibility that genetic effects are moderated or influenced by environmental factors, known as gene–environment interactions.

The consistency of results for facial and vocal cues strengthens our findings. Similarly, controlling for the effects of sex and age, the results still held and showed no genetic effect while highlighting the importance of the shared environment. We note that the sample is not large and focused only on 7-year-olds. Future studies should increase the sample size and examine different ages and development over time.

We tested children's ER directly using the DANVA (29, 53). As the two were examined in separate rooms, they could not affect one another during testing. At the same time, the DANVA emphasizes very specific facial expressions that could be influenced by family background. Future work should also use subtler cues to express emotion in a more complex and less stereotypical way. In addition, in real life, emotion is perceived through an integration of visual and auditory cues (27), and thus, a pathway for future work is to study vocal and facial cues jointly in the same stimulus.

Our findings contribute to understanding the development of emotion recognition, a core aspect of empathy. They call for in-depth investigation of environmental factors involved in psychiatric disorders characterized by difficulties in emotional recognition.

ETHICS STATEMENT

The study was approved by the Ethics Committee of the Hebrew University of Jerusalem, Israel.

AUTHOR CONTRIBUTIONS

RS, AK-N, HA, and CZ-W contributed to the conception and design of the study. RS organized the database. AK-N performed the statistical analysis. RS wrote the first draft of the manuscript. AK-N, HA, MA-S, and CZ-W wrote sections of the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

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The Measurement of Positive Valence Forms of Empathy and Their Relation to Anhedonia and Other Depressive Symptomatology

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Construct validity of a brief self-report measure of "positive-valence empathy" (the tendency to exude positive emotion as a means to stimulate positive affect in others, and/or to vicariously share in another's positive emotion; Light et al., 2009) was attained utilizing a sample of 282 healthy adults. Positive-valence empathy may have unique predictive ability for differentiating depression versus depression with anhedonia. Confirmatory factor analyses revealed a two-factor structure for the final 15-item Light-Moran Positive Empathy Scale (PES), with an 8-item "Empathic Happiness" subscale (e.g., "I find that other people's happiness easily rubs off on me") and a 7-item "Empathic Cheerfulness" subscale (e.g., "I enjoy making others feel good"). "Empathic Happiness" was a significantly better predictor of overall depressive symptomatology (Beck et al., 1996) than anhedonia (Snaith et al., 1995). The Light-Moran PES-15 may have real-world impact and predictive utility for well-being.

Keywords: positive-valence empathy, anhedonia, hedonic capacity, Beck Depression Inventory-II, empathic concern

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INTRODUCTION

Anhedonia – the reduced ability to experience positive emotions – is a key feature of Major Depressive Disorder (MDD) (Heller et al., 2009, 2012; Light et al., 2011). To date, the relative lack of attention to the varieties of positive affect and how they may be impaired in MDD may in part be responsible for the difficulty in developing treatments that are universally effective at targeting MDD and other disorders in which positive affect deficits are prominent. Although anhedonia is one of two possible primary diagnostic criteria (the other is sad mood) that must be present for the diagnosis of MDD to be made, most of the pharmacological treatments currently available do not address this symptom; failing in approximately 30% of patients with MDD (Rush et al., 2006).

Anhedonia is a significant problem, yet we do not have sufficient means to measure all of the facets of this symptom (Ho and Sommers, 2013). The lifetime prevalence of anhedonia in MDD is 5.2% (First et al., 1990), and recent reports estimate that approximately 37% of individuals diagnosed with MDD experience clinically significant anhedonia (Pelizza and Ferrari, 2009). We are only beginning to understand the nuances of anhedonia. The DSM-V states that individuals meeting criteria for anhedonia may report feeling "less interested in hobbies, 'not caring anymore,' or not feeling any enjoyment in activities that were previously considered pleasurable," and "family members often notice social withdrawal or neglect of pleasurable avocations" (American Psychiatric Association [APA], 2013) (p. 163).

Anhedonia is important to recognize and diagnose because it has troubling prognostic value (Spijker et al., 2001), with most research suggesting that anhedonia persists beyond resolution of negative affect in depression – and importantly for our overarching aim to increase our ability to match individuals to targeted treatments based on an accurate assessment of their particular symptom profile – is the fact that anhedonia is a significant prodromal symptom, and a predictor of relapse in adult (Iacoviello et al., 2010) and adolescent samples (McMakin et al., 2013; Rubin, 2013).

The present work specifically addresses "positive-valence empathy" (i.e., the tendency to exude positive emotion as a means to stimulate positive emotion in another person, and/or to share in another's positive emotion) (Light et al., 2009) as a novel and useful construct to measure as an adjunct to measures that tap anhedonia proper. We focus on "positive-valence empathy" to facilitate the development of better behavioral and pharmacological treatments for anhedonic patients, with the present research project designed to formally assess the putative link between positive-valence empathy and anhedonia in a healthy sample with intent to apply it to clinical samples in the future. Specifically, we hypothesize that positive-valence empathy may have treatment potential; i.e., when evoked, positive-valence empathy may actually antagonize the experience of anhedonia.

Some may question the use of a healthy sample in the present work. However, examining anhedonia and other depressive symptoms that do not reach diagnostic significance represents a more stringent test of our hypotheses about the relationship between positive-valence empathy and anhedonia given that any significant effects would be more difficult to achieve given the fairly restricted range and variability inherent in a non-clinical sample. More importantly, however, given that anhedonia represents a putative endophenotype (i.e., a trait that is associated with the expression of an illness and represents the genetic liability of a disorder in non-affected individuals), there is reason to suggest that even healthy individuals vary in their level of anhedonia along a continuum (Harvey et al., 2007). Overall then, this study is best thought of as capturing "everyday" anhedonia symptoms as they occur in the general population (Harvey et al., 2007).

The National Institute of Mental Health's (NIMH) Research Domain Criteria (RDoC) has provided a compelling framework for conceptualizing symptomatology such as anhedonia that cuts across DSM diagnoses (Cuthbert, 2014). Here we focus in on the RDoC "Positive Valence Systems" aspect of RDoC because we believe that, as mentioned previously, anhedonia is a viable candidate for an underlying endophenotype for neuropsychiatric dysfunction, as it appears across several psychiatric and neurological disorders (e.g., MDD, Parkinson's disease, schizophrenia, dementia, and TBI). Thus, anhedonia is transdiagnostic though it is perhaps a cardinal symptom of MDD, and therefore its relationship to depression was chosen as the focus here.

To facilitate the empirical measurement of positive-valence empathy in relation to anhedonia, the development of an accurate, simple to administer, and psychometrically sound means for detecting *variability* in positive-valence empathy at pre-treatment may be a very important strategy for characterizing the need for treatment, and tracking an individual's treatment response, and may ultimately spur the development of new behavioral treatments and/or antidepressants; if this construct proves to be mutable pre- to post-treatment. Therefore, our overarching aim was to provide initial validation of the construct of positive-valence empathy in a healthy sample. A self-report measure of the construct should show:

(1) Convergent validity with a well-validated hedonic capacity measure, given the putative relationship between one's ability to experience joy first hand/first-person (i.e., first-person joy/happiness refers to an individual's ability to enjoy a rewarding stimulus primarily directed toward oneself, or joy experienced individually; for example, the enjoyment derived from reading a good book, eating a delicious meal, watching a sunset, or watching a pleasant video clip) as a potential correlate for the ability to relish in the joy of someone else. For example, a deficit in positive empathy may or may not also signal a deficit in first-person joy/happiness, and having an understanding of the possibility of such a dissociation could be useful clinically; i.e., a patient may need to focus on making gains in the experience of first-person joy *and* positive empathy (e.g., the patient may struggle with deriving pleasure from basic self-focused rewards and empathic situations), or may only need to make gains in positive empathy skills (if their basic first-person positive emotional skills are relatively intact). Therefore, it would be important to measure both aspects of hedonic responsivity (i.e., first-person hedonic capacity and positive empathic hedonic capacity) in order to better characterize the patient's individual treatment needs.
(2) Convergent validity with other empathy measures (e.g., that tap empathic concern – the tendency to experience sadness or tender feelings for others who are suffering).
(3) The existence of two distinct, yet positively correlated, *subtypes* of positive-valence empathy (described in detail in the next section) – empathic cheerfulness and empathic happiness – using principal components analysis (PCA).
(4) Discriminant validity; the construct of positive-valence empathy should be distinct from depression proper.

Two Subtypes of Positive-Valence Empathy

An individual may express positive emotion while in the presence of someone who is experiencing a negative emotional state as a means to alleviate the negative emotion that person is feeling by catalyzing a positive emotional state in that person (e.g., the observer tries to "cheer" the target up). Similarly, an individual may express positive emotion as a means to induce a state of joy in another person who is in a neutral or content emotional state for its own sake. This subtype of positive-valence empathy can be referred to as *empathic cheerfulness*. Furthermore, an individual may vicariously experience pleasure in response to someone else's positive emotion (e.g., an observer feels vicarious joy at a wedding or birthday party). This subtype of positive-valence empathy can be referred to as *empathic happiness*.

Positive-Valence Empathy and Anhedonia

It is proposed here that positive-valence empathy and anhedonia are antithetical constructs, and in fact, positive-valence empathy may be a useful means by which to work with patients who are anhedonic (i.e., learning to experience positive affect vicariously may be one route toward relieving anhedonia). Positive-valence empathy, as a scientific construct, is based on the idea that humans have the capacity (and perhaps the propensity) to share in the positive affect of other people, and the intact presence of this ability may be protective psychologically. Furthermore, deficits in this ability may be reversible, and gains made in positive-valence empathy may contribute to reduction in overall anhedonia. As the parsing of emotional processes becomes ever more refined, an investigation of the processes by which positive affect can be transmitted between people (i.e., how positive affect gets under the skin) could prove to be a useful endeavor for the purposes of developing *treatments* for various mood disorders – particularly Major Depressive Disorder and Persistent Depressive Disorder (i.e., dysthymia) – and other conditions that affect a person's basic interest in life and/or their subjective experience of positive emotional states.

The Light-Moran Positive Empathy Scale (PES)

The present work was designed to create a paper-and-pencil analog for the positive-valence empathy construct which can be used in conjunction with functional magnetic resonance imaging in the future to interrogate the neural correlates of positive empathy in healthy and clinical samples. Though previous measures have been established for the quantification of empathic concern, such as the "Interpersonal Reactivity Index (IRI)" (Davis, 1996) and the "Empathy Quotient (Baron-Cohen and Wheelwright, 2004; Lawrence et al., 2004)" (but note: this measure contains items pertinent to social aptitude, perspective-taking, and empathic concern), we sought to develop a brief self-report measure of *positive-valence empathy*. The scale developed differs from the "Empathy Quotient" and the "Interpersonal Reactivity Index" because all of the items relate to positive emotional responses to others emotional displays, and we only attempt to measure the *emotional* component of empathy whereas the EQ and IRI measure the cognitive and emotional components of empathy.

When developing the original (pre-factor analysis) 41-items for the scale, we hypothesized that positive-valence empathy would be observable via two underlying behaviors: (1) *empathic happiness*, or cases in which someone tends to respond with positive affect, evincing pleasure, in response to another's positive experience (e.g., "I feel pleasure in watching other people open gifts"), and (2) *empathic cheerfulness*, or cases in which someone exhibits positive affect as a means to catalyze a positive mood state in another who is dysphoric or neutral (e.g., "I get a lot of pleasure from making other people feel good").

Hypotheses

We were particularly interested in investigating the relation between positive-valence empathy and anhedonia given the putative relationship between capacity to experience personal pleasure as an important correlate to any such experience vicariously. We predicted a positive correlation between positive-valence empathy and pleasure capacity as measured by the Snaith-Hamilton Pleasure Scale (Snaith et al., 1995) (i.e., convergent validity).

As an additional validity measurement (i.e., discriminant validity), we chose to investigate the relation between negative affect and positive-valence empathy by examining the relationship between scores on our measure and scores on the Beck Depression Inventory-II (Beck et al., 1996; Steer et al., 1999) – a scale that assesses overall severity of depressive symptoms.

However, first, we sought to validate our measure of positive-valence empathy via principal component analysis (PCA). We expected the scale to have two factors. Indeed, the *Light-Moran Positive Empathy Scale* (PES) is composed of items designed to tap empathic happiness and empathic cheerfulness. Planned confirmatory factor analyses utilizing PCA extraction and oblique rotation were performed. Then the scale was examined in relation to other constructs of interest, namely hedonic capacity/anhedonia and depressive symptomatology.

In sum, a consideration of a wider variety of positive affective states, e.g., empathic happiness, and empathic cheerfulness – beyond the study of "happiness" *per se* – is warranted. Our hypotheses center on the idea that positive-valence empathy should relate to anhedonia, and individuals who are anhedonic and/or demonstrate heightened depressed symptoms will score lower on both aspects of positive-valence empathy.

MATERIALS AND METHODS

Participants

Two-hundred and twenty-six participants responded to either email advertisements or flyers posted throughout the general University of Wisconsin–Madison area in 2007–2008. In either scenario, individuals completed an online survey in exchange for being entered into a raffle for a chance to win a free digital music player. We retained data from a total of 214 participants after excluding 12 people who aborted the survey without answering all items. Of these, 67 were male (31.3%), 147 were female, and all were aged between 18 and 56 years (M = 22.45, SD = 6.25). The majority of these participants were students (80.89%). The sample consisted of individuals of Caucasian (84.44%), Asian (9.78%), Hispanic/Latino (1.78%), and African (1.33%)

descent, with 2.67% of our participants reporting a mixed racial heritage.

An additional 68 participants contributed data in 2011–2012. Of these, 23 were male (34%), and all were age 18–63 (M = 25.68, SD = 10.64). Half of our participants were undergraduate students (51.47%). 20.59% of participants were college graduates, 17.65% were high school graduates or had obtained their GED, and 10.30% had obtained a graduate degree (e.g., masters, PhD, MD, JD, etc.). Around 74% of participants were white, 8.82% of participants were Asian, 8.82% of participants were African-American, 7.4% of participants were Hispanic, and 1.4% of participants were of Native American descent.

In total, 282 adults contributed data. All participants provided informed consent (written) and all aspects of this study were approved by the University of Wisconsin–Madison Institutional Review Board (IRB) and were in compliance with the Declaration of Helsinki.

Measures

Positive-Valence Empathy

The *Light-Moran PES* utilizes a Likert scale, i.e., extremely untrue (=1), quite untrue (=2), slightly untrue (=3), neither true nor false (=4), slightly true (=5), quite true (=6), extremely true (=7). Item examples include: "I very much enjoy and feel uplifted by happy endings" (i.e., Empathic Happiness) and "I enjoy helping people to see that they can turn "lemons into lemonade" (i.e., Empathic Cheerfulness). The total score on the PES is calculated by summing all items. Subscale scores were computed by summing items 1, 3, 5, 6, 7, 8, 14, and 15 (Empathic Happiness); or summing items 2, 4, 9, 10, 11, 12, and 13 (Empathic Cheerfulness) (see **Appendixes A**,**B**). Higher scores indicate greater empathic ability.

The original items for the scale were generated based on the following criteria: A panel composed of two researchers independently rated – on a Likert scale from 0 to 2, with 2 representing full agreement, 1 representing partial agreement, and 0 representing a lack of agreement – each of the following: (1) is this item tapping an essential feature of the construct? (2) is it useful, but not essential?, or (3) is it not necessary in assessing the relevant trait? Items that were not agreed upon (i.e., scored a "0") were eliminated.

Validation

Participants also completed the *Empathy Quotient* (EQ) (Baron-Cohen and Wheelwright, 2004; Lawrence et al., 2004), which constituted the primary means by which construct validity of the PES was assessed. The EQ is composed of 28-items. Each participant had to indicate their agreement with statements pertaining to their general tendency toward social interaction, perspective taking, and empathic concern. An example of an item on the EQ is: "I get upset if I see people suffering on news programs." Higher scores indicate greater empathic ability.

As an additional validation check, a subset of the sample (68 participants) also completed the "Empathic Concern" subscale from the *Interpersonal Reactivity Index* (Davis, 1996). Higher scores on this measure indicate greater empathic concern.

Social Desirability

The Marlowe-Crowne Social Desirability Scale (SDS) (Crowne and Marlowe, 1960) is a self-report measure designed to quantify the tendency of individuals to project a favorable image of themselves during social interaction. The scale contains 33 true-false items that describe both acceptable but improbable behaviors, as well as unacceptable but probable behaviors. Higher scores indicate a greater propensity for responding in a socially desirable manner.

Hedonic Capacity

The Snaith-Hamilton Pleasure Scale (SHAPS) (Snaith et al., 1995) is a 14-item scale used to measure levels of anhedonia present over the "last few days" and is listed as a measure of "sustained/longer-term responsiveness to reward attainment" by the RDoC website. Participants choose one of four responses for each item, i.e., Definitely Agree (=4), Agree (=3), Disagree (=2), and Definitely Disagree (=1). Higher scores reflect greater pleasure capacity (i.e., lower anhedonia). Originally, the authors of the scale recommended a scoring system whereby the four response categories are recoded dichotomously into agree (=0) or disagree (=1). However, following the advice of Franken et al. (2007), we opted to calculate a total score by using the above mentioned 4-point scale for each item. In doing so, we allowed for a greater dispersion of the data given the relatively few number of items. Item examples include: "I would enjoy a cup of tea or coffee or my favorite drink" and "I would find pleasure in small things, e.g., a bright sunny day, a telephone call from a friend." Scores can range from 14 to 56.

Depressive Symptoms

The Beck Depression Inventory-II (BDI-II) (Beck et al., 1996) is a 21 item multiple choice self-report measure that is based on Beck's "triad of negative cognitions" pertaining to the world, the future, and the self. Thus, the development of the BDI-II reflects that in its structure, with items such as "I have lost all of my interest in other people" to reflect the world, "I feel discouraged about the future" to reflect the future, and "I blame myself for everything bad that happens" to reflect the self. The structure of the BDI-II is also based on the idea that depression is composed of two components: an affective component (e.g., mood) and a physical or "somatic" component (e.g., loss of appetite). The items that pertain to the affective component include the following eight items: pessimism, past failures, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts or wishes, and worthlessness. The items that pertain to the somatic component are the remaining thirteen items, including: sadness, loss of pleasure, crying, agitation, loss of interest, indecisiveness, loss of energy, change in sleep patterns, irritability, change in appetite, concentration difficulties, tiredness and/or fatigue, and loss of interest in sex.

We were primarily interested in the BDI to assess *severity* of symptoms rather than particular symptom clusters. Indeed, recent research suggests that the BDI-II cannot be reliably broken into subdomains (McElroy et al., 2018); and these and other researchers (e.g., Reise et al., 2010, 2013) recommend using the total score in research and clinical practice. Higher scores indicate more severe depression; a total score of 0–13 is considered minimal, 14–19 is mild, 20–28 is moderate, and 29–63 is severe.

Procedure

The 226 participants recruited in 2007–2008 completed the scales online. Upon beginning the survey, all respondents electronically gave their informed consent for participation. No participant was granted access to the remainder of the survey unless s/he did so. Average response time was approximately 30 min. An additional 68 participants completed the 15-item Light-Moran PES (amongst other measures) via computer in the laboratory as part of a comprehensive study not reported on here. All respondents gave their written informed consent for participation.

Factor Analysis

Principal components analysis yields one or more composite variables that capture much of the information originally contained in a larger set of items. The components are weighted sums of the original items. Components account for a portion of the total variance among the original variables. Oblique rotation is useful when the underlying latent variables are believed to correlate somewhat with each other.

RESULTS

Cohort Effects

An ANOVA was run to investigate cohort effects. Gender, and both positive-valence empathy subtypes, i.e., empathic happiness and empathic cheerfulness, did not differ statistically between the two cohorts (all *p*'s > 0.852). However, the groups did differ in terms of SHAPS score and age (but not gender) such that the larger group of 214 was more anhedonic, and the smaller group of 68 was significantly older. The minimum SHAPS score in the larger sample was 27, whereas the minimum score in the smaller sample was 30. This adds important variability to the data set; thus, we elected to keep the groups combined in analyses to maximize generalizability to a broader swathe of the hedonic capacity continuum.

Concerning age, given the significant difference between groups, we ran regression analyses with age as a covariate where appropriate (i.e., **Figures 1A,B**), and the results and our interpretation remained the same when looking at the groups separately versus combined.

Positive Empathy Scale – 41-Item Version

Data Screening

The mean score on the 41-item PES was 243 (*SD* = 31.71). The distribution was leptokurtic (*Kurtosis statistic* = 1.62, *SE* = 0.33), and negatively skewed (*skewness statistic* = −0.83, *SE* = 0.17).

Validity/Reliability

Reliability was very high (Cronbach's $\alpha = 0.96$). Initially, we sought to establish factor validity of the PES in terms of a two-factor model, with one factor corresponding to *empathic happiness* and the other factor corresponding to *empathic cheerfulness*. In order to test this hypothesis, we implemented a PCA using oblique rotation and extracted two factors; one accounted for 18.18% and the other accounted for 24.49% of the total variance, for a total of 42.67% of the variance explained. Thus, the analysis supported the existence of a two-factor model, as items that loaded highly on each factor generally discriminated between *empathic happiness* and *empathic cheerfulness*. Next we sought to shorten the questionnaire.

Light-Moran Positive Empathy Scale – 15-Item Version

In re-reviewing the items, we attempted to reduce the questionnaire based upon three criteria: (1) clarity of expression – i.e., whether the item explicitly and unambiguously expressed the emotions that were being held by both the subject and target of empathy; (2) clarity of the divide between our two *a priori* factors, i.e., which items best capture *empathic happiness* and which items best capture *empathic cheerfulness*?, and (3) items that correlated less than 0.30 with the scale, were eliminated from the scale.

The end result was a shorter PES containing 15 of the original 41-items (see **Appendix A** for the 15-item Light-Moran PES). The mean score on the 15-item PES was 88 (*SD* = 10.94), with a median of 89. The distribution was leptokurtic (*Kurtosis statistic* = 2.00, *SE* = 0.33), and negatively skewed (*skewness statistic* = −0.98, *SE* = 0.17). When 1 outlier with a PES score of 35 was removed, the mean PES score remained 88 (*SD* = 10.35), the median remained 89; the distribution was more mesokurtic (*Kurtosis statistic* = 0.11, *SE* = 0.33); yet still negatively skewed (*skewness statistic* = −0.61, *SE* = 0.17).

Using all 282 participants, the 15-item PES maintained a very high inter-item reliability (Cronbach's $\alpha = 0.92$). Furthermore, the PCA with oblique rotation performed on the 15-item PES once again confirmed a two-factor structure, with excellent discrimination between *empathic happiness* and *empathic cheerfulness*. Cronbach's alpha for each subscale was as follows: 0.84 for *empathic cheerfulness* and 0.87 for *empathic happiness*. The factor analysis of the 15-item PES was more successful in explaining variance in the underlying construct of interest (56.23%), relative to the 41-item PES. Additionally, each of the 15 items produced significant factor loadings (factor loadings ranged from −0.42 to 0.96; **Table 1**). Kaiser-Myer-Olkin Measure of Sampling Accuracy was above 0.50 (*KMO* = 0.941), and Bartlett's Test of Sphericity was significant ($p < 0.001$); confirming sampling adequacy and good fit to the data, respectively.

Convergent Validity

Higher scores on the Light-Moran PES-15 were associated with higher scores on the *Empathy Quotient*, even with *Social Desirability* score entered as a covariate [$F(2,212) = 42.95$; $R^2 = 29\%$, $p < 0.001$], which suggests that the PES-15 is a valid measure of empathy, and also provides evidence that positive empathy relates positively to general empathy.

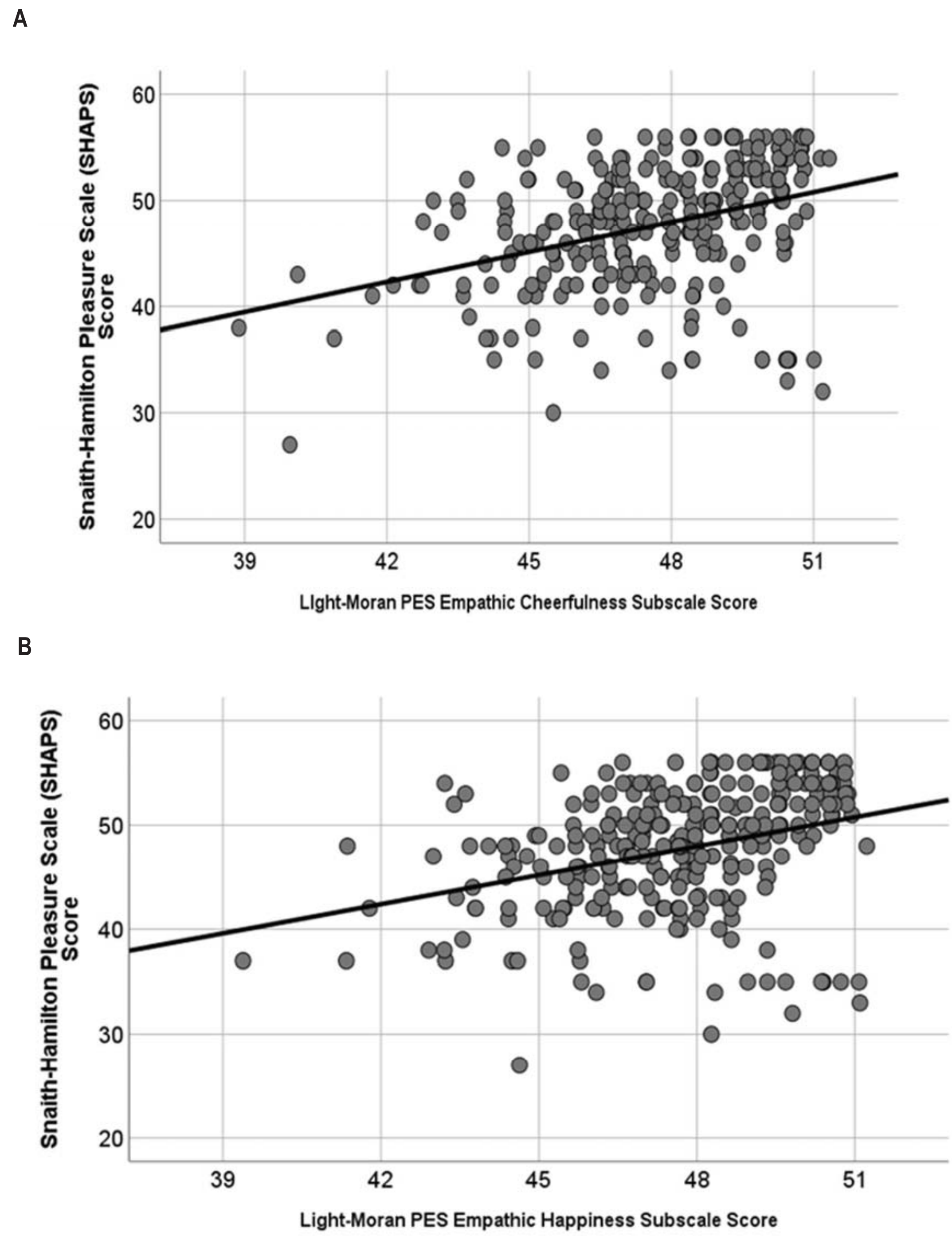

FIGURE 1 | (A) Empathic cheerfulness [R^2 = 15%, $F(2,279) = 24.28$, $p < 0.001$] and **(B)** empathic happiness [R^2 = 12%, $F(2,279) = 19.59$, $p < 0.001$] were about equally predictive of anhedonia score (measured via the SHAPS).

In addition, when looking at the data from the 68 participants who completed the *Interpersonal Reactivity Index-Empathic Concern* subscale and the PES-15, empathic *concern* correlated positively with *positive empathy* even with *Social Desirability* entered as a covariate [$F(2,67) = 9.03$; R^2 = 22%, $p < 0.001$].

Demographic Analyses

Gender

A multivariate ANOVA revealed that women (*M* = 89.63, *SD* = 9.74) scored higher than men (*M* = 83.95, *SD* = 10.68) on the PES-15.

Ethnicity

A multivariate ANOVA revealed similar scores across ethnicity groups for the PES-15 [$F(8,416) = 1.4$, $p = 0.18$].

Age

There was no correlation between age and PES-15 score ($r = -0.07$, $p = 0.34$).

TABLE 1 | Factor matrix.

Factor matrix for 15-item Positive Empathy Scale (PES-15) N = 282		
PES Item #	**Factor 1 (empathic happiness)**	**Factor 2 (empathic cheerfulness)**
14 "I easily get excited when those around me are lively and happy"	0.711	0.050
11 "I enjoy making others feel good"	0.096	−0.767
5 "I also feel good when someone I know feels good"	0.60	−0.197
7 "It often makes me feel good to see the people around me smiling"	0.609	−0.268
15 "I can't help but smile when my friends smile at me"	0.719	−0.043
10 "I feel good when I know I have pleased someone"	−0.133	−0.922
1 "I very much enjoy and feel uplifted by happy endings"	0.462	−0.155
2 "I like to tell people nice things to make them feel good"	0.209	−0.608
4 "I feel great when I find out that I have made someone else happy"	0.026	−0.822
5 "I enjoy hearing about my friends' good days"	0.670	−0.128
12 I enjoy helping a person change their bad mood into a good mood	0.350	−0.415
9 "I enjoy helping people to see that they can turn 'lemons into lemonade"'	0.50	−0.223
3 "I can't stop myself from laughing when others are doing so"	0.759	0.123
13 "I enjoy making others laugh"	0.266	−0.469
8 "I find that other people's happiness easily rubs off on me"	0.958	0.193

Occupation

A multivariate ANOVA revealed similar scores on the PES-15 across participants who were students and participants who were not [$F(2,210) = 0.09$, $p = 0.92$].

The Relationship Between Empathy and Anhedonia

A greater *general* pleasure capacity (i.e., the ability to enjoy a wide range of positive stimuli; i.e., less anhedonia) – as reflected by a greater Snaith-Hamilton Pleasure Scale score – predicted greater total *positive-valence empathy* across the sample as a whole even with *Social Desirability* entered as a covariate [total sample: $R^2 = 13\%$; $F(2, 212) = 15.03$; $p < 0.001$; Men: $r = 0.38$, $p < 0.001$; Women: $r = 0.31$, $p < 0.001$], and to a much lesser extent, greater general empathy (as measured by the EQ) with *Social Desirability* entered as a covariate [total sample: $R^2 = 3\%$, $F(2,213) = 3.3$; $p = 0.04$].

Both *Empathic Cheerfulness* [$R^2 = 15\%$, $F(2,279) = 24.28$, $p < 0.001$; **Figure 1A**] and *Empathic Happiness* [$R^2 = 12\%$, $F(2,279) = 19.59$, $p < 0.001$; **Figure 1B**] were about equally predictive of anhedonia score, even with age entered as a covariate.

The Relationship Between Empathy and General Depressive Symptoms

Greater capacity for *positive-valence empathy* relates to lower overall depression ($r = -0.33$, $p < 0.001$, **Table 2**), as does *empathic concern* as measured by the *Empathy Quotient* ($r = -0.27$, $p < 0.001$). When we looked at the relation between *BDI-II score* and the *positive-valence empathy* subscales – with age included as a covariate – we discovered that *Empathic Happiness* ($\beta = -0.51$, $p < 0.001$) was a better predictor of BDI-II score relative to *Empathic Cheerfulness* ($\beta = -0.20$, $p < 0.001$). Furthermore, using a stepwise regression, we were able to determine that the *Empathic Happiness* subscale score was also a significantly better predictor of BDI-II score [$R^2 = 16\%$, $F(2,212) = 19.51$; $p < 0.001$; **Figure 2**] than hedonic capacity/anhedonia as measured by the SHAPS when both predictors were entered into the same regression model, even with *Marlowe-Crowne Social Desirability* score included as

TABLE 2 | Correlations.

	Positive Empathy Scale-PES-15 item total (N = 282)	**Positive Empathy Scale-PES-15 item Empathic Happiness subscale (N = 282)**	**Positive Empathy Scale-PES-15 item Empathic Cheerfulness subscale (N = 282)**
Marlowe-Crowne Social Desirability Scale (SDS)	0.20	0.188	0.184
M = 14.09 (*SD* = 2.15) Range = 10–20	($p < 0.01$)**	($p < 0.01$)**	($p < 0.01$)**
Empathy Quotient (EQ)	0.53	0.451	0.551
M = 32.29 (*SD* = 8.88) Range = 6–53	($p < 0.001$)***	($p < 0.001$)***	($p < 0.001$)***
Snaith-Hamilton Pleasure Scale (SHAPS)	0.35	0.312	0.33
M = 46.95 (*SD* = 6.04) Range = 27–56	($p < 0.001$)***	($p < 0.001$)***	($p < 0.001$)***
Beck Depression Inventory-II (BDI-II)	−0.33	−0.394	−0.196
M = 8.26 (*SD* = 7.77) Range = 0–42	($p < 0.001$)***	($p < 0.003$)**	($p < 0.01$)**

***p < 0.01; ***p < 0.001.*

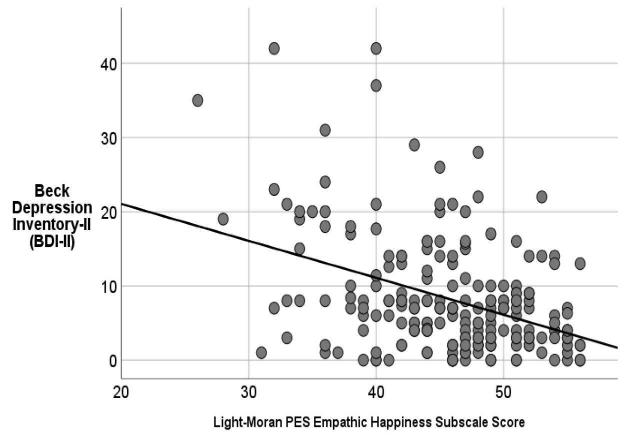

FIGURE 2 | Greater *empathic happiness* score uniquely predicts lower depression (as measured by the BDI-II) better than anhedonia (as measured by the *SHAPS*) or *empathic cheerfulness* even with Social Desirability included in the model as a covariate (R^2 = 16%, $p < 0.001$).

a covariate (combined model: R^2 change when SHAPS score added = 0.02, ns).

Post hoc Tests: Evidence for Dissociation Between Empathic Happiness and Anhedonia

When viewing **Figure 1B**, it becomes clear that there are a group of individuals high in empathic happiness and also high in anhedonia. Inspection of the frequency plot for the SHAPS revealed a multi-modal distribution, whereas empathic happiness was more normally distributed. The dissociation between SHAPS score and Positive empathy delivers the point that empathic happiness is at least partially dissociable from self-focused pleasure capacity. *Post hoc* analyses comparing the subgroup in **Figure 1B** to the rest of the sample were completed to better characterize these individuals who are anhedonic but also report feeling a lot of empathic happiness. This subset of 14 participants (who had a PES score of >45 and a SHAPS score equal to or less than 40), were derived and entered into analyses. This subgroup, relative to the remainder of the sample, had higher (1) *Empathy Quotient-Cognitive* scores [$F(1,212) = 5.01$, $p = 0.02$], and (2) empathic cheerfulness subscale scores [F(1,281) = 10, $p = 0.002$]; but did not differ in terms of BDI-II score [$F(1,212) = 1.76$, $p = 0.186$], age [$F(1,212) = 1.57$, $p = 0.21$], or gender. These findings suggest that these individuals are good at taking the perspective of, and reading the mental states of others. It is possible that this type of individual might also have better executive function (e.g., Light et al., 2017), which can be compromised in individuals who are clinically depressed. However, it is really unknown how these individuals function in their day-to-day lives, and these results raise important questions about the role of positive empathy in overall well-being. If personal pleasure capacity is lacking, but they are able to derive pleasure from seeing others happy, does this relate to a particular pattern of symptomatology? Can these individuals be trained to indulge their personal hedonic capacity system as a means to reduce risk of developing depression or some other psychopathology later?

In sum, these *post hoc* results suggest that anhedonia can be multi-modal in distribution across the general population, and can appear independent of frank depression and positive empathy capacity, and supports findings in the literature that suggest that anhedonia exists on a continuum even in the general population (Harvey et al., 2007), and dissociations are possible.

DISCUSSION

These results provide preliminary support for the validity of the Light-Moran PES-15 with a Cronbach's alpha value of 0.92 and 56.23% explained variance. Furthermore, our results indicate that people who tend to exhibit *positive empathy* also tend to experience *empathic concern*, consistent with data from a child sample (Light et al., 2009).

The Relationship Between Empathy and Anhedonia

The Light-Moran PES-15 provides a novel means to assess the functioning of the positive affect system. Particularly, the PES-15 offers researchers and clinicians a way to measure an as yet-untapped component of the positive affect system which, upon examination, could allow for better assessment and intervention of dysfunction (or skill) most relevant to subjective happiness.

Our data provide evidence that hedonic capacity/anhedonia does relate to one's ability to vicariously experience the positive affect of another individual; and also relates to empathic concern. Based on the data collected for this study, we can say that individuals who show empathic happiness also tend to score higher on empathic concern, but these variables were not highly correlated, suggesting that there are some people who are high on one form of empathy, but not necessarily both.

Our results also indicate that positive-valence empathy deficiencies may better predict depressive symptomatology than total anhedonia. Consistent with models of depression which posit the centrality of interpersonal deficits in maintenance of the disorder (e.g., McCullough, 2000), this finding highlights the interpersonal dimension of low positive affect. This may be useful for clinicians wishing to assess this facet of low positive affect.

Application: Positive-Valence Empathy as a Potential Treatment for Anhedonia

Although happiness is an elusive construct, most agree that it is a quality that everyone would like to increase, and certainly there are several mental disorders that feature lack of happiness or positive affect as a central feature (e.g., Major Depressive Disorder). Happiness can be defined as the frequent experience of positive emotions (Lyubomirsky et al., 2005). The repeated experience of "empathic happiness" over time may increase happiness. Overall, we believe happiness is a skill that may be harnessed/developed via the induction of empathic happiness, possibly utilizing emotion regulation techniques from the extant neuroscience literature. We believe this is a viable and meaningful paradigm because there is a growing corpus of evidence to suggest that interventions based on emotion regulation and positive psychology theory, ranging from "cognitive reappraisal" to "counting one's blessings" to interventions derived from ancient contemplative practices (e.g., "loving-kindness meditation") induce plasticity related alterations in the brain (e.g., Ochsner et al., 2012; Klimecki et al., 2013; Weng et al., 2013; Engen and Singer, 2015) and support a range of positive behavioral outcomes, such as immune function, prosocial behavior, and problem solving (Davidson and McEwen, 2012). Prior research has established that primary positive emotion (e.g., joy) can be up-regulated on a moment-to-moment basis utilizing reappraisal strategies borne from the extensive emotion regulation research literature (e.g., for a review of positive emotion regulation see Carl et al., 2013). For example, Heller et al. (2013) found that individuals with MDD that responded to pharmacological treatment showed an increase in ventral striatal activity – and fronto-striatal connectivity – from baseline to 8-weeks of antidepressant treatment in response to positively valenced visual stimuli; suggesting that changes in positive emotionality relate to neuroplastic changes in brain circuitry related to emotion regulation and positive affect. We extrapolate this idea by suggesting that the induction of empathic happiness, via emotion regulation strategies, may also lead to neuroplastic changes in the brain, and ultimately such brain changes may promote increases in subjective happiness.

In addition, research to date also provides preliminary evidence that qualities such as empathy and compassion, in addition to primary positive emotions such as joy, can be cultivated or otherwise increased; much like other skills are learned through sustained repetitive practice that over time leads to automatized habits (Davidson and McEwen, 2012). For example, the results of a recent study suggest that, compared with a control group, compassion training elicits activity in a neural network including the medial orbitofrontal cortex, putamen, pallidum, and ventral tegmental area – brain regions previously associated with positive affect (Klimecki et al., 2013). Thus, we argue that there is reason to believe that complex positive emotions, such as compassion and (positive) empathy, can be up-regulated just as basic positive emotions such as joy can be. Overall, we believe inducing empathic happiness via cognitive means (i.e., via routinized instruction) will ultimately increase the amount of, and/or sustenance of, positive emotion generated and experienced, and may thus have utility in addressing the symptom of anhedonia.

CONCLUSION

The Light-Moran Positive Empathy Scale (PES-15) offers a novel means to measure positive-valence empathy. Importantly, our results suggest that positive affect is a heterogeneous construct and the various known forms of positive affect (e.g., joy versus *positive-valence empathy*) are likely not synonymous. Use of more than one scale to measure these various facets of positive affect is needed and may be important to implement in clinical practice so that a fuller picture of the functioning of the positive emotional system can be gleaned. Such an approach may prove useful for choosing treatment strategies that fit an individual's unique positive affectivity profile. Essentially, ascertaining the level of functioning of one's positive affectivity system can be helpful for determining areas of positive affect weakness, which once identified may potentially be effortfully strengthened (Heller et al., 2009; Light et al., 2011).

The two subsets of items that make up the PES-15 likely do entail different psychological processes: in one case, the observer is identifying with the negative emotion of someone else (i.e., Empathic Cheerfulness) versus identifying with the positive emotional state of someone else (i.e., Empathic Happiness). However, importantly, both psychological processes entail relating to the emotional state of someone else; and we believe this is what unifies these constructs. However, empathic cheerfulness has more of an "active" component than empathic happiness. Indeed, the results from a recent fMRI study with adults (Mirabito et al., 2019) revealed that empathic happiness relates more so to nucleus accumbens shell activity, whereas empathic cheerfulness correlated with globus pallidus activation. Together, this suggests that there are separable behavioral and neurobiological aspects to empathic cheerfulness versus empathic happiness. Therefore, depending on the level of analysis, and whether the researcher is interested in understanding more comprehensively the correlates of identifying with the emotional state of someone else regardless of valence, then the total PES-15 score may be of more interest, whereas a researcher particularly interested in the relationship between vicarious positive affect versus empathic cheerfulness (or empathic concern) may be more interested in looking at the subscale scores of the PES-15 separately. Along the same line, it should be noted that the two factor solution accounts for a moderate proportion of total variance. This suggests to us that we are indeed only measuring a *subcomponent* of hedonic capacity, and this result should be viewed as evidence that our scale is a specialized measurement of an aspect of hedonic capacity; and it does not represent hedonic capacity in its entirety. Positive-valence empathy may nevertheless represent a particularly important facet of hedonic capacity that as yet has not been extensively investigated.

Limitations of the current study include the fact that only healthy adults were utilized. Furthermore, our sample was homogeneous and had limited ethnic minority representation. Therefore, future work is needed to provide normative data for various sub-group/patient populations. Also, the sample was mostly composed of college-aged individuals, thus further investigation is warranted to determine the relationship between positive-valence empathy and anhedonia in child and elderly samples as well. Age was used as a covariate in certain analyses to control for an age difference between the large and small subsamples used in the present investigation. Importantly, the results did not change when age was included versus excluded.

Directions for future research might examine the predictive utility of positive-valence empathy. For example, longitudinal changes in empathic happiness may be hypothesized to predict changes in depression scores over the course of treatment. In conclusion, the PES-15 assesses an aspect of functioning of the positive affect system in healthy adults that is not typically addressed, and may have diagnostic value in detecting difficulties in the experience of positive emotions. Positive-valence empathy may represent a higher order positive affective state that relates to a basic ability to experience positive emotions such as joy and contentment.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the University of Wisconsin–Madison Institutional Review Board, with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the University of Wisconsin–Madison Institutional Review Board.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

APPENDIX A: 15-ITEM POSITIVE EMPATHY SCALE (POST-FACTOR ANALYSIS)

Positive Empathy Scale

Instructions:

- There is a list of statements below.
- Please read each statement *carefully*.
- Rate how strongly you agree or disagree with the statement.
- Check *one* of the boxes [x] to indicate your answer.
- There are no right or wrong answers, or trick questions.

1. I very much enjoy and feel uplifted by happy endings.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
2. I like to tell people nice things to make them feel good.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
3. I can't stop myself from laughing when others are doing so.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
4. I feel great when I find out that I have made someone else happy.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
5. I also feel good when someone I know feels good.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
6. I enjoy hearing about my friends' good days.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
7. It often makes me feel good to see the people around me smiling.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
8. I find that other people's happiness easily "rubs off" on me.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
9. I enjoy helping people to see that they can turn "lemons into lemonade."
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
10. I feel good when I know I have pleased someone.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
11. I enjoy making others feel good.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue
12. I enjoy helping a person change their bad mood into a good mood.
   [ ] Extremely true
   [ ] Quite true
   [ ] Slightly true
   [ ] Neither true nor false
   [ ] Slightly untrue
   [ ] Quite untrue
   [ ] Extremely untrue

13. I enjoy making others laugh.
    [ ] Extremely true
    [ ] Quite true
    [ ] Slightly true
    [ ] Neither true nor false
    [ ] Slightly untrue
    [ ] Quite untrue
    [ ] Extremely untrue
14. I easily get excited when those around me are lively and happy.
    [ ] Extremely true
    [ ] Quite true
    [ ] Slightly true
    [ ] Neither true nor false
    [ ] Slightly untrue
    [ ] Quite untrue
    [ ] Extremely untrue
15. I can't help but smile when my friends smile at me.
    [ ] Extremely true
    [ ] Quite true
    [ ] Slightly true
    [ ] Neither true nor false
    [ ] Slightly untrue
    [ ] Quite untrue
    [ ] Extremely untrue

APPENDIX B: PES-15 SCORING INSTRUCTIONS

7	Extremely true
6	Quite true
5	Slightly true
4	Neither true nor false
3	Slightly untrue
2	Quite untrue
1	Extremely untrue

"Empathic Happiness" subscale: Sum items 1, 3, 5, 6, 7, 8, 14, and 15. Empathic happiness is a vicarious emotional response that involves happiness (or a similar positive affect) and an other-oriented feeling of goodwill toward the other person (Light et al., 2009).

"Empathic Cheerfulness" subscale: Sum items 2, 4, 9, 10, 11, 12, and 13. Empathic cheerfulness is an emotional response that involves the display of positive affect in response to someone in distress as a means to cheer the victim up, and involves a feeling of goodwill (Light et al., 2009).

Total Score: Sum all items, score range is 15–105. The mean score for healthy women is $M = 89.63$, $SD = 9.74$; and the mean score for healthy men is ($M = 83.95$, $SD = 10.68$).

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ORIGINAL RESEARCH
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Empathy, Autistic Tendencies, and Systemizing Tendencies—Relationships Between Standard Self-Report Measures

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The aim of the present study was to investigate associations between four highly used self-report measures assessing empathy (measured as both a unidimensional and multidimensional construct), autistic tendencies, and systemizing tendencies. Participants in this study completed the following self-report measures: The Interpersonal Reactivity Index (IRI) and the Empathy Quotient (EQ) to measure empathy, and the Autism Spectrum Quotient (AQ) and the Systemizing Quotient–Revised (SQ-R) to assess autistic and systemizing tendencies, respectively. The final sample consisted of N = 1,098 participants (304 males) without a diagnosed autism spectrum disorder, most of whom were university students. The IRI scale "Perspective Taking" and the EQ were negatively related to the AQ in male and female participants, while the IRI scale "Empathic Concern" was negatively related to the AQ in females only. Moreover, the AQ was positively related to the SQ-R in females only. Lastly, the SQ-R and a number of the empathy scales were significantly associated: For example and surprisingly, the EQ correlated weakly and positively with the SQ-R in both male and female participants. The results from this study illustrate how standard self-report measures of empathy, autistic tendencies, and systemizing tendencies are associated with each other in a large sample not diagnosed with an autism spectrum disorder. Additionally, some potential gender-specific effects are revealed.

Keywords: empathy, autism, systemizing, Interpersonal Reactivity Index, Empathy Quotient, Autism Spectrum Quotient, Systemizing Quotient–Revised

INTRODUCTION

Empathy can be understood as an important concept contributing greatly toward successful human social interaction (1–3). However, despite empathy being a widely used term in science, as well as in everyday life, a consensus definition of the concept remains somewhat elusive [see, for example, the review and discussion of this topic in Refs. (4, 5)]. Nevertheless, there is some agreement that empathy comprises both affective (i.e., feeling similar emotions to another person) and cognitive components (i.e., understanding the feelings of another person) [for a summary covering many definitions of empathy, please see Ref. (4), and for examples, please see Refs. (6, 7)].

In line with the various definitions of empathy, a range of self-report measures assessing individual differences in empathy exist [e.g., Refs. (6–9)]. These questionnaires assess the degree of empathy on a continuum from low to high empathy. Two widely used measures in this area of research are the Interpersonal Reactivity Index (IRI) and the Empathy Quotient (EQ) (6, 8). The IRI assesses empathy using four distinct scales/dimensions of empathy labeled "Perspective Taking" (PeT), "Empathic Concern" (EmC), "Personal Distress" (PeD), and "Fantasy" (Fan). The PeT scale assesses the ability/tendency to take another's perspective. The EmC scale assesses the extent to which someone feels warmth, but also concern for others. The PeD scale assesses self-oriented feelings of tension and worry in difficult social situations, or when someone else is hurt or in danger. Lastly, the Fan scale asks participants about their tendency to relate to fictional characters (8, 10). In most studies, it is claimed that the PeT and Fan scales measure cognitive aspects of empathy, whereas the EmC and PeD scales assess affective aspects of empathy. However, there is some controversy about this putative structure. For example, not all researchers agree that the Fan scale actually measures a facet of empathy (2, 3, 11–15). Moreover, there has been a suggestion that the PeD scale strongly overlaps with facets of the personality dimension Neuroticism (3). In contrast to the IRI, the EQ was originally developed to measure empathy as a unidimensional construct. The authors justify this decision by arguing that cognitive and affective components of empathy cannot be easily separated (6). Studies across various countries that have examined the associations between the scores of both self-report measures show that the EQ has the strongest and most consistent positive associations with the PeT and EmC scales of the IRI (2, 14, 16, 17).

Different versions of the EQ are often used in studies investigating empathy in the context of the neurodevelopmental condition of an autism spectrum disorder (ASD; see results reported below). ASD is/will be classified (including diagnostic criteria) and divided into various subtypes in the *International Classification of Diseases 11th Revision* (ICD-11) and the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). It is—among other things—characterized by deficits in social functioning and communication (18, 19). According to the previous literature, samples of people diagnosed with an ASD show lower scores in empathy, as measured using different versions of the EQ, compared to control samples (20–24). However, autistic tendencies can also be studied on a continuum in the normal population. One instrument that assesses autistic tendencies using a dimensional approach is the Autism Spectrum Quotient (AQ) (21, 25, 26). As such, the AQ has been correlated with the EQ in previous studies (using a range of slightly different versions of the measures). Studies consistently report a negative association between the two measures in both control samples and samples of participants diagnosed with an ASD (6, 20, 21, 24, 27). To the best of our knowledge, however, there is only one study that has previously reported associations between the AQ and IRI scores. In this study, negative correlations between the AQ and the IRI scales PeT and EmC, and to a lesser extent Fan, were found. On the other hand, positive associations between the AQ score and the PeD scale were reported in these largely student samples from Germany and China (28).

Aside from reporting lower levels of empathy, samples of participants diagnosed with an ASD also show higher systemizing tendencies compared to control samples (20, 21, 24). These tendencies describe "the drive to analyze, understand, predict, control and construct rule-based systems" (p. 48) (21). Additionally, these tendencies might explain some of the characteristic symptoms of an ASD, such as repetitive behavioral patterns and problems with change (19, 29). A widely used self-report measure that assesses individual systemizing tendencies in the general population, as well as in people diagnosed with an ASD, is the systemizing quotient (SQ), and its revised version (SQ-R) (20, 21). Again, using a dimensional approach to measurement of this construct, correlations between autistic and systemizing tendencies have been shown to be positive for both control samples and those diagnosed with an ASD (20, 21, 24). This supports the idea that the key characteristics of an ASD can be observed in mild forms in participants sampled from the general population.

Although higher autistic tendencies are robustly associated with both lower empathy and higher systemizing tendencies, empathy and systemizing tendencies are not robustly correlated with each other. Correlations between scores in different EQ and SQ(-R) versions have been reported to lie between −0.06 and −0.21 in general population samples, and at around −0.29 in a sample of people diagnosed with an ASD (20, 21, 24, 30, 31). No study so far, however, seems to have reported associations between the IRI and the SQ-R.

Taken together, the aim of the present study was to investigate the relationships between empathy, autistic tendencies, and systemizing tendencies. Previous studies investigating these relationships typically used versions of the EQ, AQ, and SQ(-R). The findings previously shown with these scales should be replicated. In addition to this, the present study also sought to examine these relationships using the IRI, which, contrary to the EQ (which assesses empathy as unidimensional construct), assesses empathy as a multidimensional construct. In line with results from previous studies, we expected the following associations:

1. Positive correlations between the EQ and the IRI scales PeT and EmC
2. Negative correlations between the AQ and both the EQ and the IRI scales PeT and EmC
3. Positive correlations between the AQ and the SQ-R
4. Positive correlations between the AQ and the IRI PeD scale
5. No significant correlations between both the EQ and the IRI scales with the SQ-R[1]

MATERIALS AND METHODS

Registration

This study is registered at https://osf.io/q2arp/. Data will be made available upon reasonable request.

[1]No significant associations were expected, because especially in control samples (not diagnosed with an ASD) the associations found in previous literature were of rather low effect size.

Participants

Participants took part in an online study including various self-report questionnaire measures presented using the SurveyCoder-Tool (https://www.ckannen.com/). The data collection took place at Ulm University, Ulm, Germany. Therefore, most participants tended to be younger and were students. More specifically, 1,249 participants took part online in the present study, which is part of the Ulm Gene Brain Behavior Project (UGBBP). However, 11 participants were excluded due to missing data. Hence, 1,238 participants (373 males) were retained for subsequent analyses. One participant reported suffering from Asperger syndrome. This participant was excluded from further analyses, as he/she was identified as an outlier in terms of the AQ score.

More specifically, after calculating scores of all scales under investigation (see the paragraphs on Self-Report Measures), 140 participants were excluded due to their categorization as an outlier on at least one of the scales under investigation, or because of their reported age. All participants who scored lower than [25th-Quantil – (1.5x(75th-Quantil – 25th-Quantil))] or higher than [75th-Quantil + (1.5x(75th-Quantil – 25th-Quantil))] on at least one of the scales under investigation, or for age, were treated as outliers and excluded from further analyses (32). This is also the formula used in the Statistical Package for the Social Sciences (SPSS) statistics software of the International Business Machines Corporation (IBM) to detect outliers (unidimensionally) by means of the boxplot method. Results from the total sample, including those participants identified as outliers, are presented in the **Supplementary Material**. As can be seen there, the results of the analyses are similar whether the participants classified as outliers are included or not.

The mean age of the final sample of N = 1,098 participants (304 males) was 21.94 years (SD = 2.72 years; median = 21 years). The age range was 18–30 years.

All subjects gave electronic informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the local ethics committee of Ulm University, Ulm, Germany.

It should be noted that as all participants are members of the UGBBP, the sample reported in this study partly overlaps with other samples derived from this project. For example, a previous study investigated a smaller subsample in relation to associations between oxytocin receptor genetics and the IRI and the AQ (28). Moreover, the IRI was also investigated in a recent experimental study on music perception in n = 160 participants from the UGBBP (33).

Self-Report Measures

Interpersonal Reactivity Index

A German version of the Interpersonal Reactivity Index (IRI) was administered to measure empathy multidimensionally (8, 10). It consists of 28 items split into four scales. These are named "Perspective Taking" (PeT), "Empathic Concern" (EmC), "Personal Distress" (PeD), and "Fantasy" (Fan). Each scale consists of seven items. No total score across all items is calculated. All items are answered on a five-point Likert scale from "0" to "4". The internal consistencies (using Cronbach's alpha) of the four scales in the present sample were as follows: PeT: .78, EmC: .82, PeD: .76, Fan: .81.

Empathy Quotient

A German version of the 60-item Empathy Quotient (EQ) was used in the study to measure empathy unidimensionally (6). The items of this questionnaire are answered on a four-point Likert scale. The answer to each item is transformed into either "0" (for two of the four responses indicating nonempathic tendencies), "1," or "2," with higher values indicating higher empathy. The scores for 40 of the items are then summed to create a total scale score. It should be noted that it is also possible to calculate several subscales from the EQ. However, such subscales were not originally intended by the authors (6). Additionally, details about such subscales remain debatable (16, 17, 34–36). The present study therefore focused on the total scale. Its internal consistency (using Cronbach's alpha) in the present sample was .88.

Autism Spectrum Quotient

A German version of the Autism Spectrum Quotient (AQ) was used to measure autistic tendencies in the current study (25, 26). It consists of 50 items answered on a four-point Likert scale. The answer to each item is transformed into a "1" for more autistic-type responses, and a "0" for nonautistic-type responses. From this, a total score, as well as scores for several subscales, can be calculated [see Refs. (26, 37) for different approaches to splitting the AQ into subscales]. The current study focused only on the total scale score. Its internal consistency (using Cronbach's alpha) was .73 in the present sample.

Systemizing Quotient–Revised

The German version of the Systemizing Quotient–Revised (SQ-R) was used to measure systemizing tendencies (21) (German version available from: http://docs.autismresearchcentre.com/tests/SQ_German.pdf). It consists of 75 items, which are answered on a four-point Likert scale. The answer to each item is transformed into either "0" (for two of the four answer options indicating nonsystemizing tendencies), "1," or "2," with higher scores indicating stronger systemizing tendencies. From this, a total score is calculated by summing across the items. The internal consistency (using Cronbach's alpha) of this scale was .85 in the present sample.

Statistical Analyses

All analyses were implemented using SPSS statistics version 24.

First, the distributions of the scales under investigation were checked for a normal distribution. The statistical tests (Kolmogorov–Smirnov and Shapiro–Wilk) indicated significant deviations from the normal distribution for all scales. This is most likely due to the large number of participants in the present study. Therefore, the skewness and kurtosis of all distributions were additionally checked. For all of the scales under investigation, as well as age, the skewness and kurtosis were smaller than +/−1. Hence, in line with the rules of thumb suggested by Miles and Shevlin, normality could be assumed (38). Inspecting the histograms of all scales also led to the conclusion that an approximate normal distribution could be assumed.

Following this, the associations between the scales of all of the self-report measures included in the study, along with age, were calculated using Pearson correlations. Next, differences across gender were investigated using t-tests (if necessary, Welch's t-tests were used and reported).

Finally, associations between the scales were calculated using partial Pearson correlations, controlling for age (see significant associations with age). These analyses were implemented in the total sample (N = 1,098), as well as split by gender. This procedure was chosen given the unequal gender distribution and the differences in the mean scores of the self-report measures across males and females. The correlations were compared across males and females using Fisher's z-tests (http://www.markenkunde.de/korrleation_tool/markenkunde_corrcomparer1_0.xls).

We present correlational analyses between the self-report measures instead of, for example, regression analyses in the main manuscript in order to report "unbiased" associations (i.e., not controlling for potential overlaps between the self-report measures). However, as an additional and exploratory analysis, a regression model to predict the AQ score is also presented in the **Supplementary Material**.

All results were evaluated for significance using two-tailed tests.

RESULTS

Associations With Age and Gender

Age correlated significantly with the IRI scales EmC (r = −0.10, p < 0.001), PeD (r = −0.12, p < 0.001), and Fan (r = −0.17, p < 0.001), and with the EQ (r = −0.11, p < 0.001). The p-values for all other correlations with age were >0.247. Age was therefore controlled for in further analyses.

Significant differences across gender were found for all of the scales under investigation. For descriptive statistics and results of the t-tests, please see **Table 1**. Females scored higher on all empathy-related scales, whereas males scored higher on the AQ and SQ-R.

Correlations Between the Self-Report Measures

Correlations between the self-report measures in the total sample are presented in **Table 2** (without any correction for multiple testing). After manually applying a Bonferroni correction for multiple testing (alpha = 0.05/21 = 0.0024; divided by 21 because 21 correlations were calculated), the following results with regard to the hypotheses remained significant: Partly in line with the first hypothesis, the EQ correlated significantly and positively with the IRI scales PeT, EmC, but also Fan. The EQ and the IRI scales PeT and EmC correlated significantly and negatively with the AQ. This is in line with the second hypothesis. The AQ correlated significantly and positively with the SQ-R and with the IRI scale PeD, which supports the third and fourth hypotheses. In relation to the fifth hypothesis, the SQ-R showed (mostly) weak correlations with the empathy measures. Only its negative correlation with PeD remained significant.

The correlations between the self-report measures for males and females separately are presented in **Table 3** (without any correction for multiple testing). After manually applying a Bonferroni correction for multiple testing (alpha = 0.05/21 = 0.0024), the following significant correlations with regard to the hypotheses

TABLE 1 | Descriptive statistics for all scales under investigation and t-tests for gender differences.

	Total sample (N = 1,098)		Males (n = 304)		Females (n = 794)		t-test		Hedge's g
	M	SD	M	SD	M	SD	t(df)	p	
IRI PeT	17.29	4.29	16.55	4.38	17.57	4.23	t(1096) = −3.53	<0.001	−0.238
IRI EmC	19.07	4.51	16.38	4.47	20.09	4.09	t(507.47) = −12.61	<0.001	−0.886
IRI PeD	13.50	4.29	11.24	3.78	14.37	4.16	t(599.19) = −11.93	<0.001	−0.772
IRI Fan	18.67	5.04	16.38	5.04	19.55	4.76	t(1096) = −9.74	<0.001	−0.657
EQ	42.18	10.60	36.34	9.75	44.42	10.06	t(1096) = −12.01	<0.001	−0.810
AQ	16.47	5.66	18.01	5.54	15.89	5.59	t(1096) = 5.65	<0.001	0.381
SQ-R	51.20	14.80	56.59	14.64	49.13	14.35	t(1096) = 7.66	<0.001	0.517

TABLE 2 | Partial correlations between all scales under investigation in the full sample.

	IRI PeT	IRI EmC	IRI PeD	IRI Fan	EQ	AQ	SQ-R
IRI PeT							
IRI EmC	0.40***						
IRI PeD	−0.03	0.30***					
IRI Fan	0.20***	0.39***	0.22***				
EQ	0.47***	0.61***	0.04	0.33***			
AQ	−0.23***	−0.22***	0.26***	−0.08**	−0.43***		
SQ-R	0.09**	−0.01	−0.18***	0.09**	0.07*	0.18***	

*N = 1,098. All correlations are corrected for age. ***p < 0.001, **p < 0.01, *p < 0.05 (two-tailed). Of the significant (*p < 0.05) correlations reported in this table, those between IRI PeT and SQ-R (p = 0.003), between IRI Fan and AQ (p = 0.005), between IRI Fan and SQ-R (p = 0.003), and between EQ and SQ-R (p = 0.028) would not remain significant after manually applying a Bonferroni correction for multiple testing (alpha = 0.05/21 = 0.0024).*

TABLE 3 | Partial correlations between all scales under investigation for males and females separately.

	IRI PeT	IRI EmC	IRI PeD	IRI Fan	EQ	AQ	SQ-R
IRI PeT		0.41***	0.04	0.25***	0.51***	−0.20***	0.15**
IRI EmC	0.39***		0.32***	0.35***	0.55***	−0.07	0.14*
IRI PeD	−0.10**	0.17***		0.22***	−0.03	0.32***	−0.20***
IRI Fan	0.15***	0.32***	0.12***		0.30***	−0.02	0.09
EQ	0.45***	0.57***	−0.09*	0.26***		−0.39***	0.23***
AQ	−0.22***	−0.22***	0.33***	−0.05	−0.41***		0.07
SQ-R	0.10**	0.05	−0.09*	0.19***	0.12***	0.18***	

*Results for the male participants (n = 304) are presented above the diagonal. Results for the female participants (n = 794) are presented below the diagonal. All correlations are corrected for age. ***p < 0.001, **p < 0.01, *p < 0.05 (two-tailed). Of the significant (*p < 0.05) correlations, the correlations between IRI PeT and SQ-R (p = 0.008) and between IRI EmC and SQ-R (p = 0.017) for males, and between IRI PeT and SQ-R (p = 0.004), between IRI PeD and SQ-R (p = 0.012), between IRI PeD and EQ (p = 0.013), and between IRI PeT and PeD (p = 0.004) for females would not remain significant after manually applying a Bonferroni correction for multiple testing (alpha = 0.05/21 = 0.0024).*

remained significant: Within the male and female sample, the EQ was significantly and positively related to the PeT and the EmC scales of the IRI. This supports the first hypothesis. The EQ was also significantly and positively related to the Fan scale of the IRI in both samples. The AQ was significantly and negatively related to the EQ and the IRI scales PeT and EmC for females, but for males, only the negative relationships between the AQ and both the EQ and the IRI scale PeT were significant. Hence, the second hypothesis is only fully supported for females. Regarding the third hypothesis, the AQ was significantly and positively related to the SQ-R in the female sample only. Moreover, the AQ was significantly and positively related to the IRI scale PeD for both males and females, which supports the fourth hypothesis. Contrary to the fifth hypothesis, in the male and female samples, the SQ-R correlated weakly but significantly with the EQ (positively) and some of the IRI scales (negatively with the IRI scale PeD for males; positively with the IRI scale Fan for females).

Of note, only a few of the correlations between males and females differed significantly. These were the correlations between the AQ and the IRI scale EmC ($z = 2.18$, sigma = 0.068, $p = 0.029$; higher negative correlation in the female sample as compared to the male sample), between the IRI scales PeT and PeD ($z = 2.07$, sigma = 0.068, $p = 0.038$; negative correlation in the female sample and weakly positive correlation in the male sample), and between the IRI scales EmC and PeD ($z = 2.31$, sigma = 0.068, $p = 0.021$; higher positive correlation in the male sample as compared to the female sample).

Lastly, to further elucidate the correlations between the AQ and the SQ-R, especially the nonsignificant result found for males, the relationships between the AQ subscales and the SQ-R were also examined for males and females separately. These results are presented in the **Supplementary Material** as additional *post hoc* analyses.

DISCUSSION

The present study sought to investigate the relationships between standard self-report measures assessing empathy, autistic tendencies, and systemizing tendencies in a large sample of participants not diagnosed with an ASD. More specifically, the current study sought to extend the existing literature that has examined these links by considering the relationships between autistic and systemizing tendencies and a unidimensional measure of empathy, the EQ, as well as a multidimensional measure of empathy, the IRI.

Firstly, gender differences typically found in healthy/control samples for empathy (i.e., females > males) and for autistic and systemizing tendencies (i.e., males > females) were also found in the present study [e.g., Refs (6, 8, 20, 21, 24, 26, 30)].

Consistent with most of the literature, the EQ correlated most strongly with the IRI scales PeT and EmC for both males and females (2, 14, 16, 17). With a correlation of around .50, these associations can be considered a large effect size (39). However, it should be noted that the Fan scale of the IRI was also significantly and positively related to the EQ, albeit more weakly, in males and females. This is also in line with earlier studies (2, 16). These effect sizes can be considered medium in magnitude (39), and they might indicate that the Fan scale of the IRI is indeed associated with empathic processes [see also Ref. (2)].

The AQ was significantly and negatively related to the EQ and the IRI scale PeT for both males and females with medium effect sizes (39). Additionally, the AQ was negatively related to the IRI scale EmC in the female sample only. Hence, for the female participants, the results of the present study are similar to the results from the study by Montag and colleagues on which the second hypothesis in the present study was partly based (28). It should be noted, though, that the samples for these studies overlap, as described in the "Participants" section above. The results from the present study also suggest that, for males, lower cognitive empathy (IRI scale PeT), but not affective empathy (IRI scale EmC), might be associated with higher autistic tendencies, and ultimately an ASD. In line with this, results from earlier studies also indicate that specifically cognitive empathy (using the IRI, among other instruments) is lower for those with an ASD. On the other hand, the scores for affective empathy in groups diagnosed with an ASD are typically similar to the scores in the respective control group [e.g., Refs. (40, 41)]. It should be noted that the samples from these studies consisted mostly of males, underlining the idea that these differential associations are relatively specific to males. However, for the females in the present study, no conclusions can be drawn regarding differential associations of autistic tendencies with affective (IRI scales EmC and PeD) and cognitive (IRI scales PeT and Fan) aspects of empathy.

The AQ was significantly and positively related to the SQ-R for females, but not for males; for females, the effect size of the correlation between these variables (r = 0.18) could only be considered small to medium (39). Investigating the scatterplots of the associations between the AQ and the SQ-R for males revealed that the nonsignificant findings in this sample could not be explained by potential outliers or limited variance. Nonetheless, the nonsignificant, near-zero correlation for males can potentially be explained by the different correlations between the SQ-R and the AQ subscales (see **Supplementary Material**). More specifically, after implementing a correction for multiple testing, in males, the SQ-R was only significantly and positively related to the AQ subscale "Attention to Detail". When only considering the total AQ score, this effect appears to have been obscured by the nonsignificant, sometimes negative, associations of the SQ-R with other subscales of the AQ in the male participants. It should be noted, however, that the "Attention to Detail" subscale of the AQ and systemizing tendencies, as measured by the SQ-R, overlap in their content (21, 25, 26). Moreover, the applicability of the AQ subscales to neurotypical samples remains questionable (see, for example, low internal consistencies and test–retest reliabilities, as well as the finding that neurotypical participants score higher on "Attention Switching" and "Attention to Detail" compared to the other scales, which is not necessarily the case for patients) (25, 26, 42). In sum, the associations between the AQ and SQ-R in male-only samples not diagnosed with an ASD should be investigated in more detail in future studies.

The AQ was significantly and positively related to the IRI scale PeD in males and females. Hence, higher autistic tendencies seem to be associated with higher feelings of anxiety and tension in interpersonal situations (10). This linear association fits with the social and communicative problems often observed in an ASD according to the diagnostic criteria (18, 19).

Lastly, the SQ-R was significantly and positively related to the EQ in both males and females. In the female sample, the effect size was small; however, in the male sample, the effect size was small to medium (39). Moreover, in the male sample, this correlation was even higher than the correlation between the SQ-R and the AQ, but the difference was not significant (t = 1.80, p = .073). Some of the IRI scales were also significantly related to the SQ-R depending on the sample (males versus females). This is in contrast to previous results and assumptions indicating that empathy and systemizing tendencies are (weakly) negatively related and therefore potentially distinct and independent phenomena (21, 24, 30). Given these previous results, it is difficult to explain the positive correlations found in the current study. It may be possible that the positive correlations reflect a common cognitive component shared by the empathy measures and the SQ-R, as mostly the IRI scales assessing cognitive empathy were more strongly positively correlated with the SQ-R, as compared to the scales assessing affective empathy. Nevertheless, we do not want to overinterpret these findings, as the effect sizes were not particularly high.

Some limitations of the present study should be mentioned. Firstly, the sample consisted of participants not diagnosed with an ASD, limiting the generalizability of the results from the study. Moreover, other demographic variables, and clinical symptom severity for other disorders, such as depression or anxiety, might also be worth considering in relation to ASD.

In regard to the latter point, participants also completed the BDI-II (Beck Depression Inventory-II; assessing depression symptoms) and the Affective Neuroscience Personality Scales (ANPS), including its FEAR scale (assessing facets of anxiety using a trait approach) (43–45). The results presented in **Tables 2** and **3** did not, however, change substantially if the BDI-II score or the FEAR scale was included as a control variable alongside age. Further information on these analyses is given in the **Supplementary Material**.

Next, the sole use of self-report questionnaires as measures for the constructs could be criticized. Clearly, this methodology has several disadvantages (46). The specific questionnaires used in the study might be criticized too. For example, the AQ (including all 50 items) was found to show high sensitivity, but low specificity, with clinical ASD diagnosis as a criterion, and overall did not predict clinical ASD diagnosis very well in a sample of participants suspected of a potential ASD diagnosis. Also, the correlations between the AQ score, and current ASD behaviors and reported early-life ASD symptoms, were weak in this sample (47). Moreover, in this paper, it is also hypothesized that the AQ score might be positively influenced by anxiety (hence, not only explicit ASD symptoms), again pointing toward the importance of assessing markers of other psychiatric disorders. In the current study, we can only provide information about the FEAR score, which is assessing trait anxiety, but not anxiety disorder symptoms (as noted above). Another study found that items of the AQ often correlated more strongly with scales assessing constructs such as psychological distress, sleepiness, quality of life, psychoticism, or alcoholism than with their own AQ scale. It was also found that the total AQ score correlated positively with psychological distress and psychoticism in controls and patients (48). However, criticizing the self-report measures was not within the scope of the present study; rather, the aim of the present study was to investigate relationships between these self-report measures. This is clearly important given their widespread use in research and applied contexts. Moreover, self-report measures also have several advantages. They are easy to use and cheap, especially if large sample sizes are required, and the interpretation of the results is straightforward. Most importantly, to assess subjective experiences in relation to latent traits, such as empathy, autistic tendencies, or systemizing tendencies, we need to ask the individuals themselves. Additionally, we aimed to provide further insights into associations between self-reported empathy (using unidimensional and multidimensional measures), autistic tendencies, and systemizing tendencies using a dimensional approach to measurement. Newer measures also exist that assess empathy in relation to specific emotions (49). These measures should also be investigated in relation to the widely used measures covered in the present study.

In conclusion, the results from this study provide insights into the relationship between empathy, autistic tendencies, and systemizing tendencies in a large, mostly student, sample not diagnosed with an ASD. The results generally support the notion that autistic tendencies are negatively related to empathy, but positively related to systemizing tendencies, although in males the association between autistic and systemizing tendencies was weak and nonsignificant. Therefore, the results suggest that future studies should report findings with these measures separately for males and females, and also support the notion that future studies should focus on facets of autistic tendencies and empathy to examine these relations in more fine-grained detail.

ETHICS STATEMENT

All subjects gave electronic informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the local ethics committee of Ulm University, Ulm, Germany.

AUTHOR CONTRIBUTIONS

CS and CM planned and implemented the study and collected the data. CS implemented the statistical analyses and wrote the manuscript. CM worked over the manuscript to improve it. AC gave helpful advice and also worked over the manuscript to improve it.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00307/full#supplementary-material

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Atypical Reward-Driven Modulation of Mimicry-Related Neural Activity in Autism

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Autism spectrum disorder (ASD) is characterized by deficits in social functioning and difficulties in forming social bonds. According to the social motivation theory of ASD, people with ASD fail to attend social stimuli because they do not experience them as rewarding, resulting in deficits in social cognition. In neurotypical (NT) individuals, more rewarding faces have been shown to elicit greater spontaneous facial mimicry. This association between reward and mimicry is reduced in people with high autistic traits, suggesting that altered reward processing might explain the deficits in spontaneous facial mimicry observed in individuals with ASD. In a previous study, we observed that learned reward value of a face modulates mimicry-related neural response to it and that this modulation is reduced in people with high autistic traits. Using an identical evaluative conditioning paradigm where neutral faces were conditioned with high and low rewards, we tested the modulating effect of reward value on mimicry-related brain activity in a group of adults with and without ASD. We focused on the activity in a cluster within the inferior frontal gyrus (IFG) identified through an independent meta-analysis of 139 neuroimaging studies of mimicry, in response to passively viewing videos of the conditioned faces. The blood oxygen level dependent (BOLD) response contrast of high- vs. low-reward faces was reduced in participants with ASD compared to NT controls. The extent of reward-driven modulation was negatively correlated with autistic traits across the whole sample. Our results indicate that the mimicry-related brain response is less modulated by learned reward value in individuals with ASD when compared to NT controls. In previous studies, we found in a similar sample that being mimicked by faces was associated with less reward-related brain response in individuals ASD compared to an NT sample, suggesting that the link between reward and mimicry is affected in both directions in ASD. Together, this reduced bidirectional link between reward and mimicry can point to a potential mechanism underlying some of the social cognitive features of ASD.

Keywords: autism, reward, mimicry, mirror system, fMRI, inferior frontal gyrus, social, conditioning

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INTRODUCTION

Humans mimic each other automatically and unconsciously (1, 2). Mimicry leads to an increased feeling of closeness (1, 3), liking (4, 5) and more trust toward the mimicker (6, 7), as well as increased prosocial behavior (8–10). Hence, mimicry is believed to be crucial for forming social bonds (3, 11). Not only does mimicry increase liking but also vice versa, i.e., we mimic others more if we like them (12–14), suggesting a bidirectional link between mimicry and liking.

Mimicry of facial expressions and gestures can be overt or covert, i.e., characterized by small, invisible muscle contractions that can be measured with electromyography (EMG). The activation of motor-related brain regions while passively viewing others in action is often seen as a neural signature of mimicry (15). Using electroencephalography (EEG), the "mirroring" of others' facial actions leads to an increase in mu suppression (16, 17). Functional neuroimaging techniques including positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been used to record mimicry-related neural activity. A meta-analysis of functional neuroimaging studies on action observation and imitation experiments in humans, involving both hand movements and facial expressions, revealed a largely bilateral network of premotor, primary somatosensory, parietal, and temporo-occipital areas (15). Especially, the caudo-dorsal part of brodmann area (BA) within the inferior frontal gyrus (IFG) was consistently activated during both processes, suggesting this region as a core region for the overlap between action and action observation. This region is a key component of the putative "mirror system," and is homologous to the macaque ventral premotor area F5, where mirror neurons were discovered originally (18–20). Mirror neuron response in F5 in monkeys is modulated by the reward value associated with the observed action (21). Similarly, reward value has been shown to modulate mimicry-related brain response in humans as indexed by mu suppression (22).

Lab-based experiments indicate that people who spontaneously mimic more tend to be better in recognizing emotions (23, 24) and that hindering people from mimicking spontaneously can impair their emotion recognition ability (25). Further, explicitly instructing people to mimic can enhance their ability to identify emotional facial expressions, especially among neurotypical (NT) participants who have high autistic traits (26), but can impair the differentiation between true and faked emotions (27).

People with autism spectrum disorder (ASD) typically mimic less spontaneously (28–31), which might contribute to their deficits in social cognition and social interaction. Interestingly, voluntary mimicry or inhibition of mimicry responses seems to be intact in people with ASD (30, 32). The social top–down response modulation (STORM) model proposed that rather than being impaired in mimicry per se, people with ASD, in contrast to controls, fail to modulate their mimicry according to the social context information (33). In line with this view, deficits in gaze-dependent (direct vs. averted gaze of the other) modulation of mimicry have been shown in people with ASD (34) and high autistic traits (35). The mechanism underlying such a reduced use of context is unknown, and it is not clear under which conditions spontaneous facial mimicry is reduced or intact. However, it has been suggested that attention to social input plays a major role (31). Consistent with this view, the social motivation account of ASD proposes that a diminished motivation to attend social stimuli might be causal to the social processing deficits characterizing ASD (36). This reduced social motivation might thereby result from a reduced subjective reward value of social stimuli. Evidence for this view comes from findings that infants from 6 months and young children who later develop ASD show a reduced preference for social over non-social stimuli compared to NT controls (37, 38), and similar alterations were found in adolescence (39). Further, altered brain activation in response to reward has been found in people with ASD, with some studies suggesting these alterations to be specific to (40) or stronger for social rewards (41), while others propose that monetary reward processing is affected as strongly or more strongly than social reward processing (42, 43).

Studies systematically manipulating the reward value of faces have shown that face identities paired with positive rewards are subsequently liked more and looked at longer (44) as well as remembered better (45) than those paired with negative or neural outcomes. Further, pairing faces with electrical shocks leads to conditioned responses in NT participants that are transferred within the dimension of face identity and stronger if the conditioned valence was congruent to the target face's expression during the test phase, e.g., a negatively conditioned face with an angry expression (46). In our lab, we specifically assessed the effect of learned reward value on measures of mimicry. Participants underwent an evaluative conditioning experiment where the presence of certain face identities during a card game was associated with winning (**high reward, 'hi'**), while other faces were associated with losing money (**low reward, 'lo'**). When subsequently presented with the same face identities smiling at them, participants spontaneously mimicked high-reward faces more than low-reward faces as indicated by increased mu suppression (22) and facial EMG response (47). This modulating effect was negatively correlated with autistic traits (47). Using an identical paradigm on a different sample of NT participants, autistic traits were found to be negatively correlated with the reward-driven modulation of mimicry-related neural response assessed using fMRI (48). We therefore proposed that a failure to modulate mimicry levels based on reward value of a face might be a crucial piece of the puzzle in understanding atypical spontaneous facial mimicry in people with ASD, which in turn can contribute to difficulties in social bonding (47, 48).

In this study, we used the same reward-conditioning paradigm that successfully demonstrated correlated spontaneous facial mimicry (facial EMG and mu suppression) with conditioned reward values of faces (22, 47–49) to investigate whether reward value modulates mimicry-related brain activity in the IFG (50). For the first time, we compared a group of clinically diagnosed adults with ASD to a group of matched NT controls.

METHODS

Participants

Thirty-six adults with ASD and 35 adults without any self-reported neurological or psychiatric disorder were recruited within and around the University of Reading from a database of research volunteers or advertisements. All ASD participants had a confirmed ASD diagnosis based on *Diagnostic and Statistical*

Manual of Mental Disorders, *Fourth Edition* (DSM-IV) criteria from a registered clinic and were additionally assessed with the Autism Diagnostic Observation Schedule (ADOS) Module 4 (consensus of two researchers certified for reliability). All participants had normal or corrected-to-normal vision and completed a nonverbal IQ test (Raven's Matrices). The study conforms to the norms laid out in the Declaration of Helsinki and was approved by the University Research Ethics Committee of the University of Reading, UK. All participants provided written informed consent and received either a small compensation or credit points for their participation. Ten ASD and nine NT participants were excluded, leading to a total sample of 52 participants (see **Supplementary Material** for details). Participants were matched for age, gender, handedness, and IQ between the two groups (see **Table 1**). Prior to participating in the experiment, participants (except one from the NT group) completed an online survey, including the Autism-Spectrum Quotient (51) and the Empathy Quotient (52).

Procedure

The procedure closely resembled that which was described previously in Sims et al. (48). Prior to scanning, participants underwent a conditioning phase outside the scanner where they completed an evaluative conditioning task (47). In this computerized card guessing game, a target face appeared alongside with one faceup and one facedown standard playing card, and participants guessed whether the second card would be of greater or lesser value than the first card. In the presence of one of the faces, participants won 25p to 25 pence in 90% of the trials (**hi**), while they lost 20p to 20 pence in 90% of the trials with another face (**lo**). In order to disguise the underlying structure of the game, half of the trials were paired with two further faces, where participants won and lost 60% of trials, respectively. All remaining trials were "tie" trials, i.e., the participant neither won nor lost money. Immediately after the conditioning phase, participants were positioned in a 3T Siemens Trio MRI scanner, where they completed the test phase. The test phase was designed in an event-related fashion where participants were presented with 4,000 ms video clips of the four conditioned faces making happy facial expressions. Each of the two target faces (**hi** and **lo**) was presented 30 times and each of the two additional faces 15 times. The conditioned faces were intermixed with nine unfamiliar ("oddball") faces, and participants were asked to press a button each time an oddball face was presented in order to ensure that they were paying attention to the task. Each clip was preceded by a fixation cross, the duration of which was jittered. The stimulus order and duration of the jitter were designed to maximize power for estimating the contrast of interest, i.e., **hi** vs. **lo** (https://surfer.nmr.mgh.harvard.edu/optseq/).

During both parts of the experiment, stimuli were presented using E-Prime 2.0 (Psychology Software Tools, PA, USA). Participants took part in a different experiment reported elsewhere (53) before they were debriefed and dismissed.

Stimuli

All stimuli were selected from the Mind Reading set (54), available at www.jkp.com/mindreading. During the conditioning phase, stimuli consisted of static images of four faces (two male and two female) with neutral facial expressions. In the test phase, stimuli consisted of four 4,000 ms video clips showing dynamic happy facial expressions made by the same four target identities. The faces were assigned to the four conditions so that they were counterbalanced between participants.

Regions of Interest

Regions of interest (ROIs) within the left and right inferior frontal gyrus (IFG) were identified using coordinates reported in a published meta-analysis of 139 neuroimaging studies of action observation and imitation as peak activations from the conjunction analysis between observation and imitation of face, hand, finger, leg, and foot movements in humans (15). The Wake Forest University (WFU) Pickatlas tool (55) was used to draw spheres with a 10 mm radius around the center coordinates [left IFG (LIFG) = (−56 12 10); right IFG (RIFG) = (58 15 10)] of the selected ROIs (**Figure 1**).

FMRI Data Acquisition and Preprocessing

Participants were scanned in a 3T Siemens TIM Trio MRI scanner with a 32-channel head coil. 32 slices, 3-mm-thick axial slices were acquired in descending sequential order. A multi-echo sequence with three different echo times [Repetition time (TR) = 2,400 ms; Echo time (TE) (1; 2; 3) = 20; 36; 52 ms] was used in order to increase the signal-to-noise ratio (56–58). Preprocessing and multi-echo independent component analysis (ICA) (58) were performed in analysis of functional neuroImages (AFNI) (59). The first four volumes were discarded to allow for the stabilization of the magnetization. The data were further preprocessed using slice-timing correction, motion correction, and the functional-to-structural coregistration. Subsequently, the multi-echo ICA was performed in order to enable separating blood oxygen level dependent (BOLD) from non-BOLD components. The non-BOLD

TABLE 1 | Sample characteristics.

Measure	NT (*n* = 26)		ASD (*n* = 26)		Statistics	*p*-value
	Mean (SE)	Range	Mean (SE)	Range		
Age	32.31 (1.90)	18–57	34.35 (2.59)	18–60	*t*-test	0.63
Gender (M:F)	17:9	–	16:10	–	Chi-square	0.77
Handedness (R:L:Amb)	21:5:0	–	19:6:1	–	Chi-square	0.45
IQ (Raven's percentile)	46.46 (5.41)	6–90	55.96 (5.59)	2–96	*t*-test	0.23
AQ	16.48 (1.01)	6–25	37.19 (1.57)	22–49	*t*-test	<.0001

NT, neurotypical; ASD, autism spectrum disorder; SE, standard error of the mean; M, male; F, female; R, right-handed; L, left-handed; Amb, ambidextrous; AQ, autism spectrum quotient.

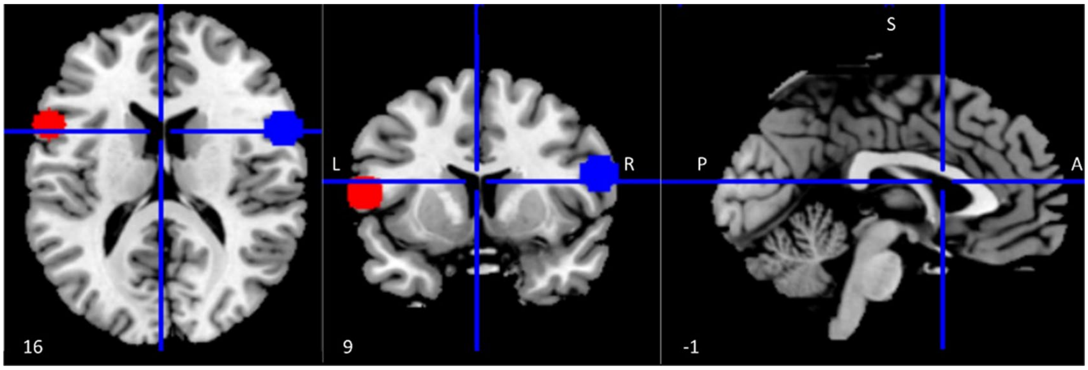

FIGURE 1 | Regions of interest (ROIs) within the mirror network. ROI (10 mm radius) placement in left (red) and right (blue) inferior frontal gyrus (IFG). Coordinates were derived from a meta-analysis on action observation and imitation, corresponding to a peak of activation consistently associated during both observation and imitation of facial expressions as well as movements of other body parts (15).

components were used as nuisance regressors to denoise the functional data, which were then converted to 3-D images with dcm2nii, normalized to Montreal Neurological Institute (MNI) space, and spatially smoothed with a Gaussian kernel of full width at half maximum (FWHM) 5 mm using statistical parametric mapping version 8 revision 6313 (SPM8) (www.fil.ion.ucl.ac.uk/spm).

FMRI Data Analysis

Statistical parametric maps were calculated using SPM8 with multiple regressions of the data onto a model of the hemodynamic response (60). The first-level general linear model analyses contained five regressors of 4,000 ms duration for the five conditions, i.e., **hi**, **lo**, the two distractor faces (60% win and loss, respectively), and the oddball faces. Regressors were convolved with the canonical hemodynamic response function. Mean *t*-statistics of the contrast [**hi** > **lo** faces] for each participant was extracted for the left and right IFG ROIs with MarsBaR (version 0.44) and used as dependent variables for the group-level analysis.

To test both categorical as well as dimensional approaches, two models of ordinary least-squares regression were computed. The first model tested the effect of group, while the second model tested the effect of autistic traits autism spectrum quotient (AQ). Mean ± 3SD was used as the criterion to filter outliers, and none were identified. Due to the directional nature of the hypothesis (i.e., IFG activation for **hi** vs. **lo** faces would be reduced in participants with ASD as compared to controls), one-tailed *p*-values are reported.

RESULTS

Behavioral Outcomes

We evaluated the task performance during the test phase to verify that participants attended to the task. None of participants had more than two misses in the test phase, indicating that they attended the stimuli. Two participants from the ASD group and two from the control group had more than two false alarms. These participants were included in the analyses reported below. To guard against the possibility of the data from these participants having an undue influence on the reported results, all analyses were rerun after excluding them, which confirmed that the results remained the same (see **Supplementary Material**). For the remaining participants, the low number of false alarms (accuracy above 97%) indicates that they recognized the conditioned faces.

fMRI Results

There was a significant interaction between group and condition within the LIFG ($\beta = -.287$, $p = .033$), but this interaction fell below the standard threshold of significance for RIFG ($\beta = -.250$, $p = .069$). Planned *post hoc* analyses revealed that the direction of the **hi>lo** contrast was inverse between the ASD and NT groups in the LIFG (see **Figure 2A**). When each group was considered separately, the difference between conditions was not significant (ASD: $t = -1.193$, df = 25, $p = .878$; NT: $t = 1.312$, df = 25, $p = .101$). In the RIFG (see **Figure 2B**), neural response was significantly stronger for **hi** compared to **lo** faces in NT controls ($t = 2.092$, df = 25, $p = .023$), while no significant difference was observed in the ASD group ($t = .112$, df = 25, $p = .456$).

Similar to the effect of group within the categorical model, autistic traits (**Figure 3**) were negatively correlated with the **hi>lo** contrast within the LIFG ($r = -.303$, $t = -2.224$, df = 49, $p = .0154$) but fell short of the $p < 0.05$ threshold in the RIFG ($r = -.198$, $t = -1.414$, df = 49, $p = .082$).

There was no difference between the NT and ASD groups in head motion as indicated by the euclidean distance between head position parameters [mean(TD) = 0.078; mean(ASD) = 0.083; $t = -0.435$, df = 48.466, p(2-sided) = 0.665].

DISCUSSION

Spontaneous facial mimicry is atypical in people with ASD, but the underlying mechanism is unclear. By using an evaluative conditioning paradigm for associating different reward values with different faces, we found that reward value modulated mimicry-related brain activity in the IFG (50) differentially in individuals with ASD vs. NTs. Specifically, NT individuals showed greater IFG

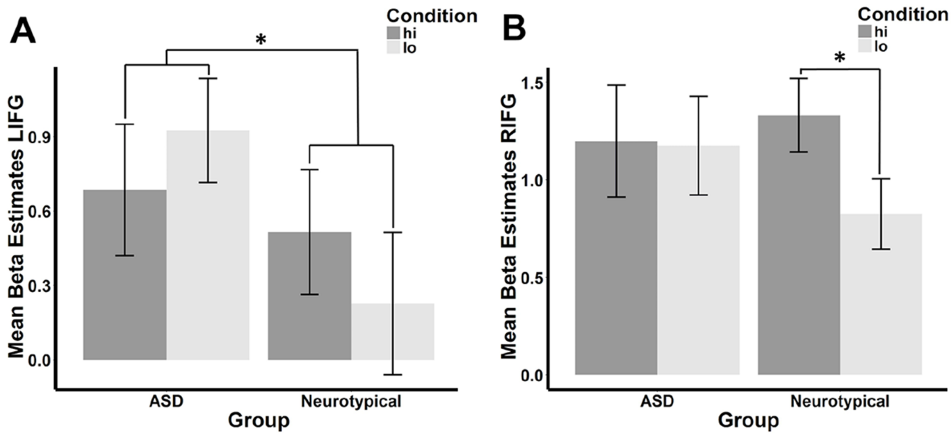

FIGURE 2 | Mean beta estimates per group (ASD vs. neurotypical) and condition in the **(A)** left and **(B)** right IFG. Mean beta estimates in response to faces conditioned with high reward (**hi**) are marked in dark gray, while those in response to faces associated with low reward (**lo**) are marked in light gray. Asterisks indicate significant differences, a group-by-condition interaction in the LIFG, and an effect of condition in the neurotypical group in the RIFG.

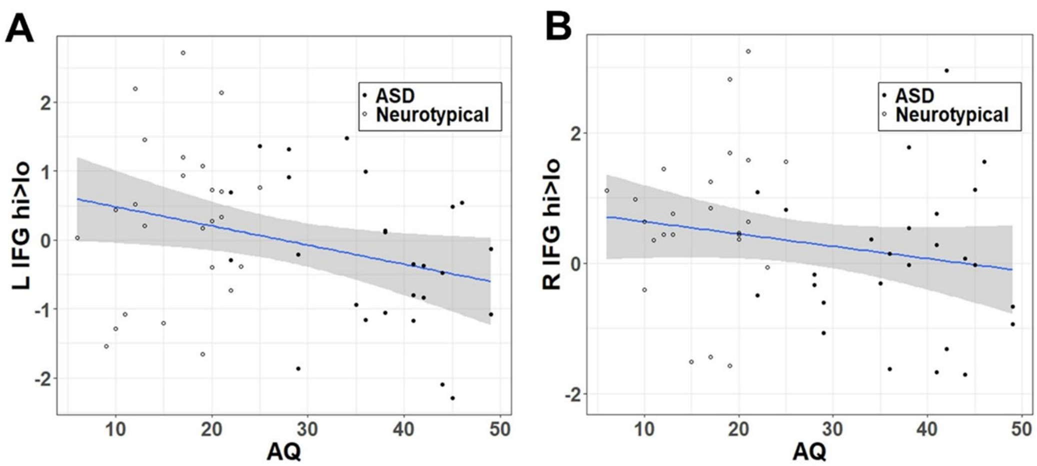

FIGURE 3 | Correlation between **hi>lo** beta contrast within the IFG ROI and autistic traits (AQ) in **(A)** left and **(B)** right hemisphere.

response to faces that were associated with high vs. low reward than those with ASD. Additionally, NT but not ASD participants had significantly more RIFG activation for the **hi** faces as compared to the **lo** faces. The results support the notion that the effect of learned reward value on spontaneous facial mimicry is altered in ASD.

Reward Modulates Mimicry-Related Brain Response in Neurotypicals

The stronger activation of the IFG as a core component of the human mirror system (15) when passively viewing smiling faces associated with high vs. low reward value observed in NT participants is in line with previous findings that more rewarding faces are mimicked more (47). It also corresponds to findings indicating that humans typically mimic whom they like better more (12–14). Similarly, we found in a previous study that NTs had increased functional connectivity between the IFG and the right ventral striatum, a core region for reward processing, for high- vs. low-reward faces (48).

Atypical Reward-Dependent Modulation of Mimicry-Related Brain Response in Autism Spectrum Disorder

In our ASD participants, there was no increased IFG response to faces associated with high vs. low reward in either hemisphere, suggesting that reward conditioning did not modulate mimicry-related brain activity in the same way in these individuals. It is unlikely that the lack of a difference between high- and low-reward faces in IFG activation results from a failure to learn to associate the conditioned reward value with the faces in ASD participants. First, participants from both groups rated the high-reward faces as more likeable than the low-reward faces after conditioning, and this effect showed no interaction with group (see **Supplementary Material**). Second, one of our previous studies demonstrated that people learn to implicitly associate reward with faces, irrespective of their autistic traits (49). In accordance with these previous results and the hypothesis of a weaker link between reward and mimicry in ASD (44, 45, 48), we propose that rather than failing to learn to adjust the reward value of faces in the current study, participants with ASD did not use the learned reward value for adjusting their spontaneous facial mimicry to the same extent as NT participants did. Similarly, it has been proposed that people with ASD make less use of social context information (such as direct vs. averted gaze) than controls in order to modulate their mimicry (33). Hence, rather than being impaired in mimicry per se, people with ASD might typically modulate their mimicry response less, due to atypical reward-driven modulation. This observation can provide a parsimonious explanation for the atypical contextual modulation of mimicry effects reported in ASD. It might also explain why some studies report reduced spontaneous mimicry (28–31) in ASD, while studies of deliberate mimicry or those involving inhibition of a preplanned movement (often used as a marker of automatic mimicry) do not observe group differences (30, 32, 61–63). Previous observations of altered social and nonsocial reward processing in ASD (40, 42, 64–67) lead to the question of whether these atypical reward-modulation effects detected here are specific for social stimuli. The current study does not answer this question, since there is no control condition with nonsocial stimuli. However, in a previous study, we have shown that the impact of autistic traits on reward modulation of automatic mimicry was seen for social but not nonsocial stimuli (68). Future studies should explicitly test this possibility using the current paradigm.

In studying adults cross-sectionally, it remains unclear whether the deficient reward–mimicry link is a cause or consequence of altered trajectory in brain development. Future studies should investigate this link longitudinally in young children. Additionally, since only high-functioning ASD individuals were included in the current study, our results do not necessarily generalize to the entire autism spectrum. Future studies should test this question in the more severe end of the spectrum (69). Additionally, the variability of mean beta estimates was higher in our ASD than in our NT sample, as indicated by higher standard errors. This suggests that the modulating effect of reward on mimicry might not be reduced in all ASD participants and correspond to previous findings of more variability in behavioral and neural response outcomes in ASD vs. NT samples (70).

Categorical vs. Dimensional Accounts of Autism Spectrum Disorder

To account for the view of ASD as the extreme end of a spectrum of continuously distributed traits (71), we further conducted dimensional analyses where we tested the relationship between the IFG response to high- vs. low-reward faces and autistic traits. Similar to the categorical account, we observed a negative association between autistic traits and the high- vs. low-reward contrast within the LIFG. This result corresponds to previous findings from our group in a different sample, indicating that autistic traits predict the extent of reward-driven modulation of spontaneous facial mimicry (47, 48). Together with these previous findings, the results therefore confirm a similar effect of both categorical and dimensional accounts of ASD on the modulating effect of reward on mimicry. While this relationship was significant across the whole sample, it was driven by the greater range of AQ scores in the ASD group.

A Bidirectional, Weakened Link Between Mimicry and Reward in Autism

Just as reward modulates mimicry, being mimicked by others is also perceived as rewarding (72). NT females show an immediate reward-related brain response while observing others being mimicked (73), and emotional synchrony between primed and presented emotion leads to reward response regardless of the emotional valence (74). We have previously demonstrated that faces that consistently mimic the participant are liked more and looked at longer compared to faces that consistently perform the facial expression opposite to that of the participant (44). In another study in our lab, we used the same mimicry conditioning to demonstrate that mimicking as compared to anti-mimicking faces evoked stronger reward-related activation of the ventral striatum in NT but not ASD participants (53). Together with these previous findings, the current study contributes to the evidence for a weakened link between reward and mimicry people with in ASD in both directions. Given the potential role of mimicry in both social cognition (*via* embodied cognition) and building rapport, a weakened bidirectional link between reward and mimicry could be a key mechanism underlying difficulties in social interaction in ASD.

ETHICS STATEMENT

The study conforms to the norms laid out in the Declaration of Helsinki and was approved by the University Research Ethics Committee of the University of Reading, UK. All participants provided informed consent.

AUTHOR CONTRIBUTIONS

BC developed the study concept. BC and JN contributed to the study design. Data collection was done by JN. C-TH and JN contributed to the analysis. The draft of manuscript was written by JN, while both other authors contributed to critical editing of the draft. All authors approved the final version of the manuscript for submission.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00327/full#supplementary-material

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Enhanced Processing of Painful Emotions in Patients With Borderline Personality Disorder: A Functional Magnetic Resonance Imaging Study

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Previous research has demonstrated that patients with borderline personality disorder (BPD) are more sensitive to negative emotions and often show poor cognitive empathy, yet preserved or even superior emotional empathy. However, little is known about the neural correlates of empathy. Here, we examined empathy for pain in 20 patients with BPD and 19 healthy controls (HC) in a functional magnetic resonance imaging (fMRI) study, which comprised an empathy for pain paradigm showing facial emotions prior to hands exposed to painful stimuli. We found a selectively enhanced activation of the right supramarginal gyrus for painful hand pictures following painful facial expressions in BPD patients, and lower activation to nonpainful pictures following angry expressions. Patients with BPD showed less activation in the left supramarginal gyrus when viewing angry facial expressions compared to HC, independent of the pain condition. Moreover, we found differential activation of the left anterior insula, depending on the preceding facial expression exclusively in patients. The findings suggest that empathy for pain becomes selectively enhanced, depending on the emotional context information in patients with BPD. Another preliminary finding was an attenuated response to emotions in patients receiving psychotropic medication compared to unmedicated patients. These effects need to be replicated in larger samples. Together, increased activation during the observation of painful facial expressions seems to reflect emotional hypersensitivity in BPD.

Keywords: empathy for pain, borderline personality disorder, functional magnetic resonance imaging, anterior insula, supramarginal gyrus

INTRODUCTION

Borderline personality disorder (BPD) is a severe psychiatric disorder that occurs in 1% to 6% of the general population (1). The disorder is characterized by fragile self-images, poor impulse control, emotional instability, and self-injurious behavior (2–4). Moreover, BPD is often accompanied by comorbid depression, posttraumatic stress disorder, eating disorders, and addiction (5).

With regard to social cognition, a growing body of literature suggests that patients with BPD experience difficulties in "mentalizing" (or "cognitive empathy"), which refers to the ability to reflect upon one's own and others' mental states in terms of intentions, beliefs, desires, or feelings (6, 7). In contrast, emotional empathy describes the representation of own and others' emotions (8, 9) [for reviews, see Refs. (10, 11)]. Studies in BPD have shown that patients are unimpaired or even better than controls in emotional empathy, but perform more poorly in cognitive empathy tasks (12–14). Related to this, other research focusing on emotion recognition reported no general difference between BPD patients and healthy control (HC) participants, whereas other studies reported a hypersensitivity toward negative emotions and a tendency to ascribe negative emotions to even neutral facial expressions (15–20).

As regard the neuronal correlates of these processes in BPD, Dziobek and colleagues examined empathy by using the multifaceted empathy test (MET) in a neuroimaging paradigm. They described decreased activation of the left superior temporal sulcus and gyrus (STS/STG) in BPD associated with cognitive empathy and increased activation of the right middle insular cortex during emotional empathy (21). Moreover, consistent with the above mentioned behavioral studies, other work reported hyperactivation of the amygdala during the processing of social stimuli or emotional facial expressions implying threat (22–24).

A novel approach to the study of empathic processes has introduced tasks in which participants are asked to put themselves into the shoes of another individual who experiences somatic pain. Research has shown that psychologically healthy participants activate a neural network comprising brain regions that strongly overlap with those areas that are involved in first-person pain processing. The core areas of this "pain matrix" include the bilateral anterior insular cortex and medial/anterior cingulate cortex, and these regions are also activated when observing someone else in a painful situation (25, 26). However, empathy for pain and the activation of the pain matrix depend on several state- and trait-dependent factors that facilitate the strength of empathy, as for example the psychological stress level of the participant, the level of familiarity of the person exposed to the painful stimulus, and the level of habituation or suppression to the presented stimuli. For example, one study showed that clinicians may express attenuated empathic responses to pictures of syringes (10, 27–29). Thus, the magnitude of one's empathy for pain seems to crucially depend on the social and individual context.

In a recent study, our group aimed to investigate whether the presentation of facial emotions prior to the observed bodily pain affected the activation of the pain matrix (30). Since the presentation of a facial expression prior to the pain stimulus creates a particular emotional context in which the pain occurs, the activation of the pain matrix may therefore vary due to the divergent processing of empathy for the contextual painful situation. Aside from an activation of the pain matrix, we found an increased response to pain in the left dorsolateral prefrontal cortex after the presentation of angry facial expressions, a region that is supposedly involved in top-down control of emotional responses to negatively valenced stimuli (30).

In the present study, we sought to examine the neuronal correlates of empathy for pain in patients with BPD. Specifically, we were interested in the question whether the presentation of facial expressions of emotions prior to the painful stimulus would alter the empathic response in participants with BPD. Aside from altered general emotional and empathic processing found in patients with BPD (31), previous research reported elevated thresholds for somatic pain in BPD (32–34). Two other studies reported that firsthand experience of somatic (heat) pain was also shown to be altered in patients with BPD, as shown by decreased activation in the amygdala and the anterior cingulate cortex during painful stimulation and increased response in the dorsolateral prefrontal cortex (35, 36). Thus, patients with BPD seem to show attenuated responses to the firsthand experience of pain, whereas there are no findings that point toward decreased empathy for pain processing. In our study, we hypothesized that patients with BPD would show a stronger activation of the "pain matrix" compared with controls, particularly when the painful image followed the observation of negative facial emotions. We were also interested in how activation patterns would correlate with subjective empathy ratings.

MATERIALS AND METHODS

Participants

For the present study, 20 female in-patients diagnosed with BPD according to a structured interview [Strukturierte Klinische Interview für DSM-IV (SKID-II) for personality disorders] according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria [German version by Ref. (37)] were recruited from the LWL University Hospital in Bochum, Germany. Nineteen female HC participants were recruited *via* advertisement. HC were free of present or past psychiatric disorders as well as their first-degree relatives. Participants in both groups were Caucasians and needed to be free of neurological and severe physical illness (including pain-related illnesses). Patients with BPD were excluded if they suffered from psychotic or bipolar disorder or current substance abuse. Comorbid disorders and medication within the patients group are shown in **Table 1**. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008. All participants gave their written informed consent after the nature of the procedures had been fully explained. The study was approved by the Ethics Committee of the Medical Faculty of the Ruhr-University Bochum.

TABLE 1 | Comorbid disorders and medication of patients with borderline personality disorder (BPD) in absolute (*N*) and relative (%) quantity.

	N	%
Comorbid disorders of BPD patients		
Depressive episode	9	45
Posttraumatic stress disorder	4	20
Phobic disorder	1	5
Eating disorder	1	5
Cannabis misuse	3	15
Alcohol misuse	2	10
Other substance misuse	1	5
Medication		
Without regular medication	10	50
Antidepressant	6	30
Antipsychotic	2	10
Antidepressant and antipsychotic drugs	2	10

Questionnaires and Behavioral Data

The Interpersonal Reactivity Index (IRI) (8) was used to assess self-reported empathic abilities that are suggested to reflect trait empathy. The questionnaire consist of 28 questions from which four subscales, namely, "perspective taking" (PT), "fantasy" (FS), "empathic concern" (EC), and "personal distress" (PD) are calculated. Here, it is important to note that high PT, FS, and EC reflect high trait empathy, whereas a high PD score indicates a high stress level that impairs empathy behavior. The Mehrfachwahl–Wortschatz–Intelligenztest Test (MWT-A) (38), a task that is similar to the "Spot-the Word-Task" developed by Baddeley (39), was used to examine verbal intelligence. For validation of the emotional pictures used in the functional magnetic resonance imaging (fMRI) paradigm, participants rated each picture regarding its emotional content ("angry," "happy," "neutral," or "painful") on a visual analog scale ranging between 10 and 90. As an additional question, participants were asked to indicate the gender of the depicted face. However, since we did not focus on a gender effect in the present study, the results obtained are not reported. The validation task took place after the fMRI scanning.

Empathy for Pain Functional Magnetic Resonance Imaging Paradigm

The paradigm used in the present study was similar to an empathy-for-pain task developed by Lamm and colleagues (40) and was used in a similar way in our previous study (30). Briefly, a picture showing an emotional face (depicting an angry, happy, neutral, or painful facial expression) was presented to the participants for 3 s, followed directly by a hand exposed to a painful (needle penetrating the hand) or a nonpainful stimulus (Q-tip touching hand) for another 3 s. The trial ended with a jittered intertrial interval for 3–6 s and 10 occasional short breaks (4–6 s; **Figure 1**). The face and hand images were taken from Caucasian males or females (two different faces per gender); as a control condition, a black square was shown instead of faces preceding male hands. Participants were asked to empathize with the presented scenarios. In summary, each combination of facial emotion, gender, and pain condition was presented three times (control conditions six times), resulting in 60 trial presentations per run (30 painful and 30 nonpainful conditions), which together took approximately 11 min, with 4 runs leading to a total sum of 240 trials and 45 min. The inter-run-interval between run 1 and run 2 was in average 77.2 s (*SD* = 22.5 s; range 55.2–143.7 s), between run 2 and run 3 106.75 s (*SD* = 1; range 59.8–573.2 s), and between run 3 and run 4 82.7 s (*SD* = 19.1 s; range 61.9–137.8 s). After each run, participants were asked how well they could empathize by using a visual analog scale. More detailed, participants were asked to rate their success in feeling with the presented character ("empathy character") and with the presented painful situation ("empathy pain"). Finally, they were asked to rate their current subjective well-being ("well-being"). The paradigm was presented using the

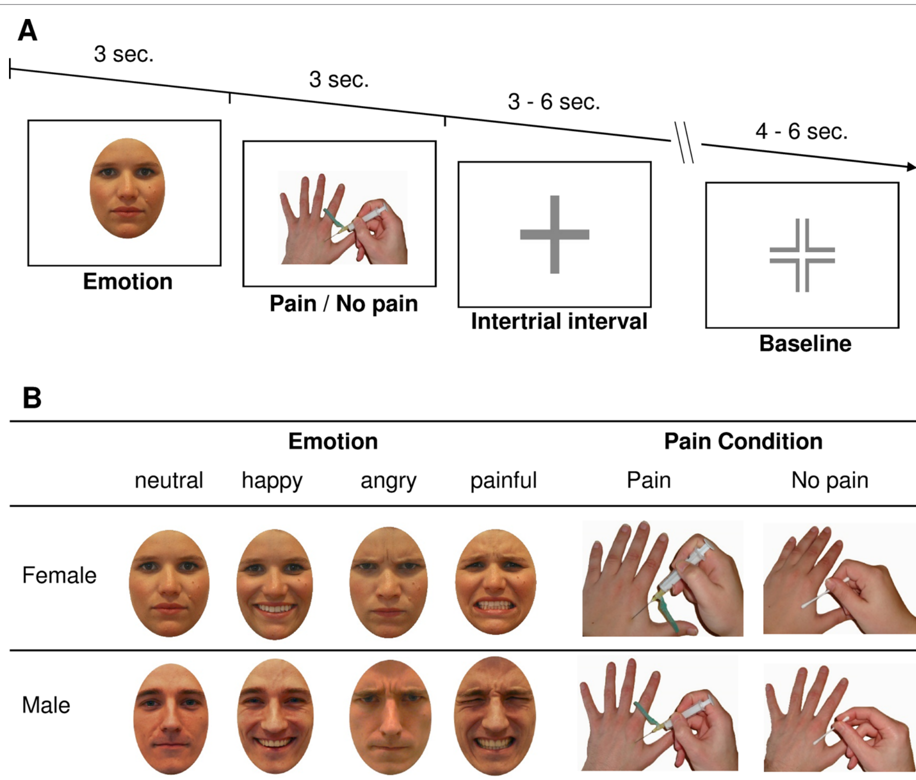

FIGURE 1 | Description of the functional magnetic resonance imaging (fMRI) paradigm. Panel **(A)** shows the timing of one single trial of the empathy for pain paradigm, and Panel **(B)** shows exemplary pictures used in the paradigm showing the emotions "neutral," "happy," "angry," and "painful" and the painful conditions "pain" and "no pain" for females and males, respectively.

"Presentation" software (Neurobehavioral Systems Inc., Albany, CA) *via* MRI-compatible liquid crystal display (LCD) goggles (Resonance Technology Inc., Los Angeles, CA).

Functional Magnetic Resonance Imaging Acquisition and Data Analysis

The fMRI data were recorded using a 3-tesla whole-body MRI system (Philips Achieva 3.0T TX) and a 32-channel SENSE head coil. The MRI scan started with a high-resolution T1-weighted anatomical gradient echo scan (3D TFE: matrix 300 × 235 mm^2, reconstructed to 320 × 320 mm^2, field-of-view 240 × 188.8 × 192 mm^3, in-plane resolution 0.8 × 0.8 mm^2, slice thickness 0.8 mm, reconstructed to a final voxel size of 0.75 × 0.75 × 0.8 mm^3). In total, 240 slices in transverse orientation were acquired (TR = 10 ms, TE = 4.6 ms, flip angle α = 8°, SENSE factor RRL = 2.5 and RFH = 2.0). Functional data during the empathy for pain paradigm were collected using T2*-weighted echo-planar imaging (EPI) sequences. Thirty-two slices were acquired in interleaved order parallel to the bicommissural plane. To obtain blood-oxygen level-dependent (BOLD) contrasts, we used a sensitivity encoded single-shot echo-planar imaging protocol (SENSE-sshEPI: number of slices 32, matrix 80 × 80 mm^2, reconstructed to 112 × 112 mm^2, field-of-view 220 × 220 mm^2, in-plane resolution 2.75 × 2.75 mm^2, slice thickness 3 mm with 1 mm gap, reconstructed to a final voxel size of 1.96 × 1.96 × 3 mm^3, TR = 2,000 ms, TE = 30 ms, flip angle α = 90°, SENSE factor RAP = 2.0). The EPI sequence started with five scans that were discarded due to saturation effects. Every run contained 335 volumes and takes approximately 11 min. In total, participants completed four scanning runs.

The collected fMRI data were preprocessed and analyzed statistically using SPM12 (Wellcome Trust Center for Neuroimaging, Institute of Neurology, University College London, UK; http://www.fil.ion.ucl.ac.uk) and MATLAB 7.11 (The MathWorks Inc, Natick, MA). Preprocessing of the data implies slice timing correction, realignment, coregistration, and normalization with a T1 template provided by Statistical Parametric Mapping (SPM). The images were smoothed with an isotropic 8-mm full-width half-maximum Gaussian kernel, and the final voxel size of resampled images was 2 × 2 × 2 mm^3. We applied a high-pass filter (cutoff, 100 s) to eliminate low-frequency signal drifts. Based on our previous study (30), we focused the analyses on the phase of pain/no pain perception according to the preceding emotional facial expression [e.g., (angry face+pain), (happy face+no pain), etc]. Thus, at the single subject level, regressors were combinations of pain condition, emotion, and gender. The realignment parameters were entered as regressors of no interest in the design matrix. A statistical model for each participant was calculated by convolving a hemodynamic response function with the abovementioned design (41). Subsequent statistical analysis followed the general model approach (42). As proposed by Poldrack and colleagues (43), and already used in social cognition research (44), we focused our analysis on hypothesis-driven regions of interest (ROIs) known to be involved in empathy for pain. To this end, we designed a mask containing the ROIs by using the WFU PickAtlas (45). All ROIs were chosen in accordance with a recent meta-analysis by Lamm and colleagues (26). The following ROIs were included: the anterior bilateral insula, the left medial cingulate cortex, the bilateral supramarginal gyri, the bilateral pallidum, the bilateral inferior temporal gyri, the bilateral amygdala, the left precentral gyrus, the right frontal inferior gyrus (pars opercularis), and the left thalamus. To visualize the brain areas involved in pain processing, the so-called pain matrix, we examined the T-contrast "effect of pain," that is, [pain > no pain] collapsed over all emotions and gender using the "full factorial" option in SPM. This options shows activations with p[uncorrected] <0.001 for an extent k > 10 voxel. To deal with the still existing multiple testing problem and in accordance with the developers of the WFU PickAtlas software, peak voxel FWE correction was applied and only activation surviving a threshold of $p[FWE] < 0.05$ was considered significant. All activations were labeled according to the anatomical automatic labeling (AAL) atlas (46) implemented in the WFU PickAtlas (45). Afterward, percent signal changes from the abovementioned ROIs that showed activations were extracted using the "MarsBar" toolbox (http://marsbar.sourceforge.net/) for SPM12 (47). In a more fine-grained analysis, percent signal changes were further analyzed regarding the facial expression using SPSS 25.0. By using this localizer-based approach, we aimed to avoid the problem of "double dipping" (48). In the **Supplemental Material**, we show additional alternative analyses for further confirmation of the findings.

Statistical Analysis

Further statistical analyses were performed using "IBM SPSS Statistics for Windows," version 25 (IBM Corp., Armonk, NY). The differences between groups in questionnaires were examined by independent sample t-tests. For comparison of the frequency of distribution regarding the participant's handedness, we calculated Fisher's exact test (two-sided). Behavioral data were investigated using mixed-model ANOVA with the factors presented "facial expression" (i.e., angry, happy, neutral, or painful pictures) and identification of the emotion (angry, happy, neutral, or painful), that is, the response of participants and the between subject factor group (BPD, control). One-sample t-tests were used to assess whether category ratings differed significantly from the value 50, which was the center of the visual scale and therefore 50 indicates inconclusiveness in attribution of picture descriptions. To investigate whether habituation occurred, we calculated mixed-model ANOVAs with the within-subject factor "run" (runs 1–4) and the between-subject factor group (BPD, control). The ANOVA was calculated for each question separately ("empathy character," "empathy pain," and "well-being") and for the reaction time, which was defined as the initial reaction on the first question at the end of each block.

The fMRI data were analyzed by mixed-model ANOVAs with the factors, pain condition (pain/no pain), facial emotion (angry, happy, neutral, and painful, no emotion), and group (BPD/HC), for each region separately. We calculated an additional mixed-model ANOVA including only patients with BPD and the within-subject factors pain condition (pain/no pain) and facial emotion (angry, happy, neutral, and painful, no emotion) and the between-subject factor medication (patients with BPD receiving medication and patients free of medication), for each region separately. Dependent and independent *t*-tests were used for *post hoc* comparisons. All ANOVA results reported were Greenhouse–Geisser corrected. According to the work of Costantini et al., we calculated correlations between IRI scores and brain activity during painful conditions only for the supramarginal gyri (49). In detail, we calculated Pearson correlation coefficients for each IRI subscale and activation during "pain" conditions pooled for emotional faces. We further corrected for multiple testing with results considered significant only if $p < 0.05/4 = 0.0125$.

RESULTS

Participant Characteristics

We found significant differences between groups for IRI PT and PD scores (see **Table 2**), but not for age and IQ and handedness.

Behavioral Data

The mixed-model ANOVA with the factors "facial expression" and "identification" and group revealed a significant main effect of facial expression ($F(2.3, 73.7) = 9.11$, $p < 0.001$) and identification ($F(2.6, 88.1) = 15.81$, $p < 0.001$) and the interaction facial expression–identification ($F(3.3, 106.3) = 391.40$, $p < 0.001$), indicating selective rating depending on facial expression and identification. Importantly, no main effect or interaction with group appeared, showing that both patients and controls recognized the emotional content equally well. In addition, participants recognized the emotions correctly as indicated by significantly higher ratings than the "inconclusive value" of 50 (angry expressions rated as angry: $t(33) = 17.49$, $p < 0.001$; happy expressions rated as happy $t(33) = 37.65$, $p < 0.001$; neutral facial expressions rated as neutral $t(33) = 7.05$, $p < 0.001$; painful facial expressions rated as painful $t(33) = 19.78$, $p < 0.001$). All other comparisons (e.g., angry faces described as neutral) reached significance with values lower than 50, which stands for rebuttal of the suggested emotion category. In other words, participants did not mistake any emotion for another. For the behavioral results, ratings of one patient and four controls are missing due to timing/technical problems (BPD, $n = 19$; HC, $n = 15$).

The analyses of behavioral data during the fMRI task aimed to check whether participants habituated to the task over the four runs and whether a difference in subjective empathy occurred between patients with BPD and controls. First, the mixed-model ANOVA with the factors "run" and "group" did not show any main effects or interactions ("empathy character": main effect "run": $F(2.0, 59.2) = 0.22$, $p = 0.804$; interaction run–group $F(1.97) = 1.92$, $p = 0.156$; "empathy pain": main effect "run": $F(2.2, 67.4) = 0.88$, $p = 0.432$; interaction run–group $F(2.25) = 1.73$, $p = 0.181$; and "well-being": main effect "run": $F(2.5, 75.0) = 1.52$, $p = 0.221$; interaction run–group $F(2.50) = 1.25$, $p = 0.295$). Thus, rating did not change over time and did not differ between groups.

We further compared the reaction time of the initial reaction on the first response screen to check whether participants attended constantly to the task. Here, the ANOVA did not show any main effects or interactions (main effect "run": $F(2.1, 64.3) = 1.65$, $p = 0.199$; interaction run–group $F(2.14) = 0.15$, $p = 0.875$), which indicates that participants attended constantly to the task with no difference between groups.

Functional Imaging Data

Investigation of the contrast "effect of pain versus no pain" showed activation of the left thalamus, the left anterior insula, and bilateral supramarginal gyri (**Table 3**). For these regions, statistical analysis by mixed-model ANOVA were performed with the factors condition (pain, no pain), facial emotion (angry, painful, happy, neutral, no emotion) and group (BPD and HC). Accordingly, we found a significant main effect of "condition" for the left insula ($F(1, 37) = 5.92$, $p = 0.020$), the left thalamus ($F(1, 37) = 7.53$, $p = 0.030$), left supramarginal gyrus ($F(1, 37) = 29.08$, $p < 0.001$), and right supramarginal gyrus ($F(1, 37) = 10.84$, $p = 0.002$) (**Figure 2A–C**). Further *post hoc* comparisons showed that activation during "pain" trials differed in all regions from activation during "no pain" trials (left insula $t(38) = 2.08$, $p = 0.045$, left thalamus $t(38) = 2.909$, $p = 0.006$, left supramarginal gyrus $t(38) = 4.86$, $p < 0.001$, and right supramarginal gyrus $t(38) = 3.93$, $p < 0.001$).

Moreover, we discovered a "condition–emotion–group" interaction for the left insula ($F(3.18) = 3.01$, $p = 0.030$) and the right supramarginal gyrus ($F(3.63) = 4.71$, $p = 0.002$). Independent *t*-test showed differences between groups for responses to painful pictures following the presentation of painful faces [painful face+pain] ($t(37) = 2.56$, $p = 0.015$) and to nonpainful pictures after angry faces [angry face+no pain]

TABLE 2 | Participant characteristics and results of comparisons of Interpersonal Reactivity Index (IRI) results (M = mean and range, SD = standard deviation) between patients with BPD and healthy controls (HC). *T*-test statistics (*t, p,* and Cohen's *d*) are reported. For the comparison of handedness, Fisher's exact test was calculated and the *p*-value (two-sided exact test value) is reported.

	BPD		HC		Test statistics		
	M (range)	*SD*	*M* (range)	*SD*	*t*	*p*	Cohen's *d*
Age	26.1 (18–39)	6.4	23.4 (18–48)	6.2	1.28	0.207	0.41
IQ	106.6	19.6	108.6	15.5	–0.36	0.722	0.11
Handedness (right/left/ambidextrous)	17/2/1		18/1/0			1.000	
IRI perspective taking	15.2	5.6	18.7	4.5	–2.12	0.041	0.69
IRI fantasy	20.4	5.6	19.1	4.5	0.77	0.446	0.25
IRI empathic concern	20.3	4.1	18.9	4.6	0.92	0.362	0.30
IRI personal distress	21.0	5.4	10.6	3.8	6.80	0.001	2.25

TABLE 3 | Activated brain regions for the contrast [positive effect of pain] collapsed over gender and emotions.

Region name	Hemisphere (left/right)	Coordinates (MNI)	*t* value	*z* value	$p_{FWE\text{-}corr}$
***T* Contrast: [pain > no pain] collapsed over all emotions and groups**					
Anterior insula	Left	−34 14 0	3.90	3.78	0.039
Thalamus	Left	−10 −22 8	5.18	5.08	<0.001
Supramarginal gyrus	Left	−56 −28 36	4.82	4.75	0.001
Supramarginal gyrus	Right	58 −24 34	3.98	3.94	0.034

Initial threshold p[uncorr]. < 0.001 for k > 10 voxel.
FWE correction with p < 0.05 on voxel level.
MNI, Montreal Neuroimaging Institute.

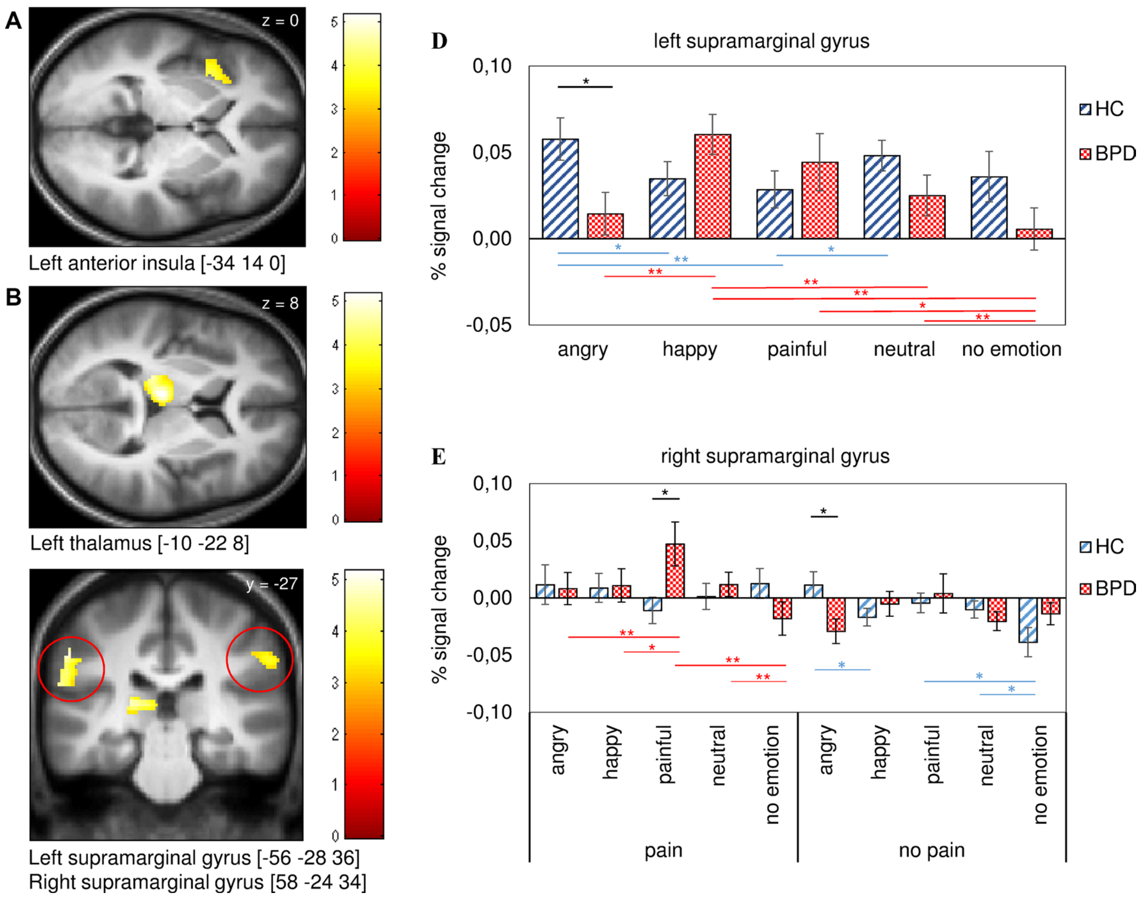

FIGURE 2 | Activation and signal change in percent for regions of interest (ROIs) derived from the contrast (positive effect of pain) for patients with BPD and healthy controls (HC). Regions shown are the left anterior insula **(A)**, the left thalamus **(B)**, and the left and right supramarginal gyri **(C)**. The statistical parametric maps show a threshold of *p* [uncorr]. < 0.001 for *k* > 10. The diagram in Panel **(D)** shows differences between groups for the facial expressions in the left supramarginal gyrus and the diagram in Panel E contains pain and no pain conditions with preceding facial emotions in the right supramarginal gyrus. Note that differences between groups are marked in black, differences within the BPD group are marked in red, and within the control group in blue. We decided to exclude differences between condition (e.g., [angry face+no pain] vs. [angry face+pain] from diagrams to reduce confusing labeling. Error bars represent standard error of the mean (SEM) and **p* < 0.05, ***p* < 0.010, ****p* < 0.001.

($t(37) = -2.60$, $p = 0.013$) for the right supramarginal gyrus (**Figure 2E**). We further observed differences within groups for painful emotional conditions compared with the same emotional but nonpainful condition (see **Supplemental Table S2**).

In the BPD group, we found differences for [angry face+pain] versus [neutral face+pain] in the left insula $t(19) = -2.16$, $p = 0.044$), [painful face+pain] versus [no emotion+pain] (left insula $t(19) = 3.05$, $p = 0.007$; right supramarginal gyrus $t(19) = 3.29$, $p = 0.004$), and for [neutral face+pain] versus [no emotion+pain] (left insula $t(19) = 4.04$, $p = 0.001$; right supramarginal gyrus $t(19) = 2.96$, $p = 0.008$). Further differences were found in the right supramarginal gyrus for [angry face+pain] versus [painful face+pain] ($t(19) = -3.22$, $p = 0.005$) and for [painful face+pain] versus [happy face+pain] ($t(19) = 2.33$, $p = 0.031$)

Figure 2E shows comparisons in the right supramarginal gyrus; comparisons in the anterior insula are not shown.

Significant differences, though to a lesser degree, were also found in the control group, showing differences only within the nonpainful conditions for [neutral face+no pain] versus [no emotion+no pain] ($t(18) = 2.18$, $p = 0.043$), [angry face+no pain] versus [happy face+no pain] ($t(18) = 2.57$, $p = 0.019$), and [painful face+no pain] versus [no emotion+no pain] ($t(18) = 2.38$, $p = 0.028$) in the right supramarginal gyrus.

Finally, the ANOVA revealed a significant interaction of emotion-with group for the left ($F(3.24) = 6.07$, $p < 0.001$) and the right supramarginal gyrus ($F(2.89) = 3.13$, $p = 0.030$). Here, independent *t*-tests between groups showed a significant difference for angry faces for the left supramarginal gyrus ($t(37) = -2.48$, $p = 0.018$; see **Figure 2D**). Further *post hoc* comparisons within groups showed differences in activation between the emotions. These differences were apparent in both groups but showed a tendency toward more significant differences between emotions in patients with BPD (see **Figure 2D** and **Supplemental Table S1**).

An additional explorative mixed-model ANOVA with the within subject factors pain condition (pain/no pain), facial emotion (angry, happy, neutral, and painful, no emotion), and medication (BPD with medication/BPD without medication) revealed a significant interaction of emotion–medication for the right supramarginal gyrus ($F(2.13 = 5.90, p = 0.005)$). Independent *t*-test of medicated vs. unmedicated patients with BPD further revealed a difference in response to angry, happy, and painful faces (angry $t(18) = 4.16$, $p = 0.001$; happy $t(18) = 2.47$, $p = 0.024$; painful $t(18) = 2.63$, $p = 0.017$; **Figure 3**).

These results indicate that patients with BPD showed lower activation regarding angry, painful, and happy facial expressions under medication when compared with unmedicated patients. The other main effects and interactions detected by the ANOVA are listed in **Supplementary Table S3**.

Regarding subjective reports, we found a significant correlation between the IRI subscale "perspective taking" and brain activation during "pain" trials (r_s $(37) = 0.409$, $p = 0.012$).

DISCUSSION

The present study aimed to investigate the neural correlates of empathy for pain combined with emotional facial expressions in patients with BPD using fMRI. Behaviorally, patients scored significantly higher on the alexithymia questionnaire and reported higher PD and lower PT on the IRI questionnaire. However, ratings of facial emotions used in the fMRI paradigm did not differ between groups, indicating that both patients and HC recognized the emotional expressions equally well. In our fMRI analysis, we focused on the contrast "effect pain" [pain > no pain] for hypothesis-driven ROIs derived from previous neuroimaging work on empathy for pain (26). Most importantly, we found significant interactions of condition–emotion–group and emotion–group for the left and right supramarginal gyri. *Post hoc* test revealed that patients showed significantly higher activations to painful pictures following the presentation of painful faces in the right supramarginal gyrus. Lower activation was discovered for nonpainful pictures following angry faces in the right supramarginal gyrus. In addition, patients with BPD generally showed lower activation in the left supramarginal gyrus when viewing angry facial expressions compared to HC.

This finding is consistent with Van der Heiden et al.'s study who found enhanced activation in the left supramarginal gyrus in an empathy-for-pain task in which psychologically healthy participants were asked to adopt the "Self"-perspective compared to the "Other"-perspective (35). Moreover, Costantini and colleagues reported activations in the left and right supramarginal gyri during an empathy-for-pain task. They further found significant correlations between these activations and the PT subscale of the IRI (49), which

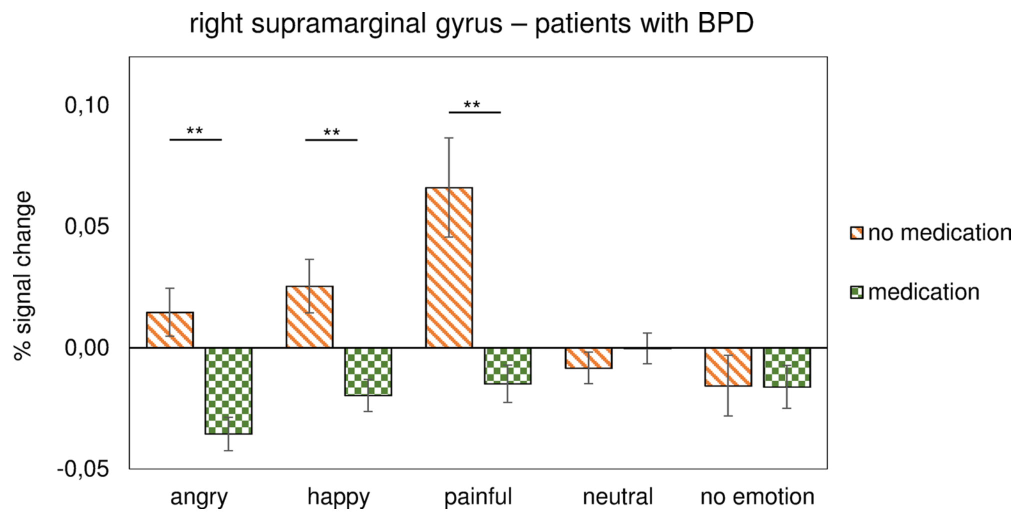

FIGURE 3 | Activation during emotional face processing in percent signal change for the right supramarginal gyrus in patients with BPD. The diagram compares patients under medication with unmedicated patients. Error bars represent SEM and *$p < 0.05$, **$p < 0.010$, ***$p < 0.001$.

was replicated in our present study for the left supramarginal gyrus. Our findings are also in line with those of previous studies in healthy participants, suggesting that increased activation within the insula may correspond to the subjective experience of negative emotions, including disgust, fear, and anger (50–52), and enhanced activity in the same region in patients with BPD (53–55). Consistent with this idea, comparisons between conditions and emotions revealed several significant differences within the patient group in terms of insula activation, but no such differences in the control group. These findings may reflect differences in emotion processing, with more pronounced activations in response to painful faces and an attenuated response to angry faces in BPD relative to controls. Another possible reason for the weaker response to angry faces could be that anger usually does not fit into the context of pain (especially nonpainful conditions) and thus does not lead to activation of the empathy for pain network.

In the present study, we did not observe between-group differences in general processing of empathy for pain. Previous research reported increased thresholds for somatic pain in BPD and altered neuronal processing during painful stimulation (32–34, 36, 53). However, reduced sensitivity to physical pain in BPD does not automatically translate into attenuated empathetic responsivity. Instead, we contend that patients with BPD are overly responsive to another's bodily pain, specifically, when the painful situation is cast in a social cognitive context, such as facial emotions suggestive of how the person experiencing the pain responds to it emotionally. Put another way, we do not conclude from our data that patients with BPD are impaired in their ability to empathize with another person exposed to somatic pain—rather, their "smoke detector" is more sensitive to potentially threatening or otherwise aversive situations (56).

Another important result that should be considered as preliminary is the impact of medication in empathy for pain. In the present study, medication seems to decrease the patients' neural response to emotional faces (angry, happy, and painful faces) in the right supramarginal gyrus. Due to the small sample size and the uncontrolled nature of the comparisons regarding medication, we caution that these results need to be replicated in larger samples.

The current study has several limitations. First, since we recruited only female participants, the results are not generalizable for both genders. Second, we did not include a clinical control group, so, it is unclear whether our findings are specific to BPD. Third, patients with BPD were in an inpatient psychotherapy setting, and we were unable to control for potential therapeutic effects. Fourth, the comorbidity pattern, especially the presence of comorbid depression or posttraumatic stress disorder, may have influenced our findings. Fifth, since we performed the diagnostic interview only with patients, the control group was less carefully examined for potential psychological problems. Finally, the small and heterogeneous sample (e.g., with regard to eligibility criteria or medication as mentioned above) may have lowered statistical power. In summary, our study suggests that patients with BPD display heightened sensitivity to another's somatic pain, especially when the observed pain stimulus is preceded by a painful facial expression. Future research may utilize these insights including the study of longitudinal effects of psychotherapeutic treatment on empathy for physical pain.

ETHICS STATEMENT

The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008. All participants gave their written informed consent after the nature of the procedures had been fully explained. The study was approved by the Ethics Committee of the Medical Faculty of the Ruhr-University Bochum.

AUTHOR CONTRIBUTIONS

VF: Study design, fMRI scanning, data analysis, manuscript writing. BE: Study design, fMRI scanning, data analysis, manuscript writing. MB: Study design, manuscript writing, and editing. All authors have approved the final article.

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SUPPLEMENTARY MATERIAL

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Do Individuals With Autism Spectrum Disorders Help Other People With Autism Spectrum Disorders? An Investigation of Empathy and Helping Motivation in Adults With Autism Spectrum Disorder

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Individuals with autism spectrum disorder (ASD) often lack cognitive empathy, so they experience difficulty in empathizing with others. Although deficits in social abilities, such as empathy, have been demonstrated in previous studies, most stimuli used in previous studies were developed for typically developing (TD) individuals. Previous studies have demonstrated that adults with and without ASD display empathetic responses toward similar others. Adults with ASD (n = 22, 7 women and 15 men, mean age = 26.8 years) and intelligence- and age-matched TD adults (n = 20, 8 women and 12 men, mean age = 24.0 years) participated in the study. They were instructed to read 24 stories (12 stories featured protagonists with characteristics of ASD, and the other 12 featured TD protagonists) and respond to the following questions: “How did the protagonist feel?” and “Would you help if the protagonist were in trouble?” After controlling for alexithymia and AQ based on multiple regression analyses, individuals with ASD empathize with other people who have ASD and are motivated to help other people with ASD. Additionally, social skills and attention to detail were associated with decreased helping motivation for story characters with ASD. Social skills among AQ subscales (social skills, attention switching, attention to detail, communication, and imagination) were the most potent predictor of decreased helping motivation. These findings suggest that the reason why individuals with ASD are considered to have limited cognitive empathy and helping motivation could be related to alexithymia and the lack of social skills and attention to detail, which are related to atypical perception.

Keywords: empathy, helping, autism spectrum disorders, social cognition, alexithymia, social skill

INTRODUCTION

Autism spectrum disorder (ASD) is characterized by difficulties with reciprocal social interaction, atypical communication, repetitive behaviors, and narrow interests (1). Empathy plays a crucial role in communication because it enables individuals to understand another's feelings and to use judgment to assess others' actions (2, 3). It is known that empathy does not always lead to helping behaviors (4, 5). Moreover, empathy can be divided into two types: cognitive empathy, which is to identify the emotions of others, and affective empathy, which is to share or match one's emotions with another's (5). Furthermore, the degree of an empathetic response seemingly depends on different variables, including the similarity between people, and traits such as alexithymia.

Empathy is more likely to occur when there is a similarity between the participant and the target (6). For example, we are often more satisfied with interactions involving individuals similar to ourselves (7). People generally prefer individuals with personalities similar to their own (8, 9). People also show in-group biases toward their in-group and feel more similar to them than to members of out-groups, even when the composition of those groups is based on random assignment (10).

Individuals with ASD often lack cognitive empathy, which is the ability to attribute mental states to oneself and others and to understand that others have beliefs different from their own (11). Although deficits in social abilities, such as empathy, have been demonstrated in previous studies (12, 13), most target stimuli used in previous studies were developed for typically developing (TD) individuals. TD individuals tend to empathize with other people who are similar to themselves (14). Other studies have demonstrated that adults with and without ASD display empathetic responses toward similar others (6, 15). Using functional magnetic resonance imaging, Komeda et al. (15) examined whether individuals with ASD experience empathy toward other people with ASD. The ventromedial prefrontal cortex (vmPFC) was significantly activated in individuals with ASD in response to characters with ASD and in TD individuals in response to characters without ASD. Additionally, higher Autism-Spectrum Quotient (AQ) scores (16) in individuals with ASD were significantly correlated with greater activation in the vmPFC while reading about characters with ASD. Thus, individuals with ASD tend to empathize with others with ASD, at least on an explicit social judgment task (15). Although individuals with ASD have affective empathy toward other individuals with ASD, it is still unclear if they have cognitive empathy toward other individuals with ASD.

If an individual with ASD experiences alexithymia, it is unlikely that helping motivation will occur. This is due to dysfunction in emotional awareness, social attachment, and interpersonal relating (17). Additionally, alterations in perception may play a role in explaining deficits of social interaction in individuals with ASD. For example, higher sensory reactiveness is associated with lower social functioning (18). Alexithymia and certain aspects of sensory alterations are based on atypical interoception (19, 20). The prevalence of alexithymia in the general population is 10% (21, 22), and it is known that alexithymia frequently co-occurs in individuals with ASD (50%; 23). Given the occurrence of alexithymia in individuals with ASD, alexithymia was measured in the current study.

Previous studies that used verbal stimuli and declarative knowledge demonstrated that individuals with ASD have a preference for other individuals with ASD (24, 25). However, it remains unclear whether adults with ASD also show the motivation to help similar others as a consequence of empathetic responses. It is hypothesized that individuals with ASD are more likely to empathize with others with ASD and show a motivation to help other people with ASD, compared to TD individuals. In order to test our hypothesis, we examined cognitive empathy and helping motivation in ASD by considering the alexithymia and autistic traits.

METHOD

Participants

Japanese adults with ASD (n = 22, 7 women and 15 men, mean age = 26.8 years) and intelligence- and age-matched TD adults (n = 20, 8 women and 12 men, mean age = 24.0 years) were recruited at the Department of Neuropsychiatry at the University of Fukui Hospital, Japan. At the time of this study, the second author confirmed that none of the participants had other psychiatric disorders according to *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*) diagnostic criteria, including depression or anxiety disorder. We followed recommended guidelines (26) and calculated our target sample size using an estimated effect size, d, of 0.45 (27), which would require a sample size of approximately 42 participants for the study to have 80% power. The effect size of a previous study (28) was used in the current study.

The second author diagnosed the participants based on the classifications in the *DSM-5* (1) and standardized criteria using the Diagnostic Interview for Social and Communication Disorders (DISCO) (29). The second author was trained in the diagnosis of ASD and certified to use the DISCO (30). He is a licensed psychiatrist and has over 20 years of clinical and research experience with individuals with ASD. The DISCO has adequate psychometric properties (31). Further, it contains items on early development and a section on activities of daily life, thereby giving the interviewer an idea of the level of functioning in several different areas, besides social functioning and communication (29).

The Autism-Spectrum Quotient (AQ) (16) was used to assess ASD symptoms in all participants (**Table 1**). AQ scores were significantly higher in the ASD (M = 32.8, SD = 6.4) than the TD group (M = 17.8, SD = 7.3). Alexithymia was measured by the Toronto Alexithymia Scale (TAS-20) (32, 33). The TAS-20 is a 20-item self-report scale that includes statements like "I have feelings that I cannot quite identify" (Difficulty Identifying Feelings), "I find it hard to describe how I feel about people" (Difficulty Describing Feelings), and "I prefer to analyze problems rather than just describe them" (Externally Oriented Thinking). Items are rated on a scale from 1 (does not describe me) to 5 (describes me very well), with scores ranging between 20 and 100, higher scores indicating more alexithymic traits.

TABLE 1 | Mean chronological age, full-scale intelligence quotient (IQ), verbal IQ, performance IQ, total TAS-20, Difficulty Identifying Feelings, Difficulty Describing Feelings, Externally Oriented Thinking, total Bermond–Vorst Alexithymia Questionnaire (BVAQ), cognitive alexithymia, emotional alexithymia, total Autism-Spectrum Quotient (AQ) scores, social skill, attention switching, attention to detail, communication, and imagination in individuals with autism spectrum disorder (ASD) and typically developing (TD) adults.

	ASD group (*n* = 22)	TD group (*n* = 20)		*p*	
Gender			Chi square		
Female	7	8	0.3	*p* > .05	
Male	15	12			
			t		*Cohen's d*
Age in years	26.8 (7.3)	24.0 (4.2)	1.5	*p* > .05	0.5
Full-scale IQ	108.0 (12.4)	114.4 (8.8)	–1.9	*p* > .05	0.6
Verbal IQ	111.1 (14.3)	115.7 (9.5)	–1.2	*p* > .05	0.4
Performance IQ	105.0 (13.2)	110.0 (11.7)	–1.3	*p* > .05	0.4
Total TAS-20	50.5 (23.1)	39.3 (12.3)	1.9	*p* > .05	0.6
Difficulty Identifying Feelings	31.2 (17.9)	23.9 (18.1)	1.4	*p* > .05	0.4
Difficulty Describing Feelings	19.0 (4.9)	14.4 (3.6)	3.4*	*p* < .05	1.1
Externally Oriented Thinking	21.4 (3.3)	18.1 (3.1)	3.3*	*p* < .05	1.0
Total BVAQ	90.6 (45.9)	85.6 (37.1)	0.4	*p* > .05	0.1
Cognitive alexithymia	73.6 (12.3)	64.8 (8.8)	2.7*	*p* < .05	0.8
Emotional alexithymia	58.8 (32.0)	63.6 (41.0)	–0.4	*p* > .05	0.1
Total AQ	32.8 (6.4)	17.8 (7.3)	6.8*	*p* < .05	2.2
Social skill	8.4 (1.7)	3.5 (2.7)	6.8*	*p* < .05	2.2
Attention switching	7.1 (1.9)	4.2 (2.2)	4.3*	*p* < .05	1.4
Attention to detail	5.3 (2.5)	4.3 (2.3)	1.3	*p* > .05	0.4
Communication	6.5 (2.2)	3.0 (2.2)	5.0*	*p* < .05	1.6
Imagination	5.6 (1.9)	2.9 (1.6)	4.8*	*p* < .05	1.5

Means (SDs) are presented.
$^*p < .05$. Results based on two-sample t-tests.
Cognitive alexithymia consists of identifying, analyzing, and verbalizing, while emotional alexithymia consists of emotionalizing and fantasizing, based on Vorst and Bermond (35).

The Bermond–Vorst Alexithymia Questionnaire (BVAQ) was also used to measure the cognitive and emotional components of alexithymia (34, 35). Cognitive alexithymia consists of identifying (e.g., "When I am tense, it remains unclear from which of my feelings this comes"), analyzing (e.g., "I hardly ever consider my feelings"), and verbalizing (e.g., "I find it difficult to express my feelings verbally"), while emotional alexithymia consists of emotionalizing (e.g., "When something unexpected happens, I remain calm and unmoved") and fantasizing (e.g., "I have few daydreams and fantasies") (34).

Table 1 shows the mean chronological age; full-scale intelligence quotient (IQ); verbal IQ; performance IQ; total TAS-20; means of the TAS-20 Difficulty Identifying Feelings items, TAS-20 Difficulty Describing Feelings items, and TAS-20 Externally Oriented Thinking items; total BVAQ; means of the BVAQ cognitive alexithymia items and BVAQ emotional alexithymia items; total Autism-Spectrum Quotient (AQ) scores; and means of the AQ social skills items, AQ attention switching items, attention to detail items, communication items, and imagination items in adult individuals with ASD and TD.

Procedure

All participants completed the Wechsler Adult Intelligence Scale—Third Edition (WAIS-III) (36). Previously developed materials by the authors (14) were revised and used in the study to investigate cognitive empathy and helping motivation in ASD, and the materials were revised to include situations that required help. These materials consisted of 24 stories with 6 sentences in each narrative, such that 12 stories featured protagonists with ASD characteristics and the other 12 featured TD protagonists. Our project team, which included a certified psychiatrist, conducted a thorough analysis of the confirmation of ASD or TD in each context and each outcome. The participants of the study were not instructed to report each story character as ASD or TD, because we were only interested in investigating the implicit similarity between the participants and the story characters. Each story contained five sentences about the context (story setting and the protagonist's characteristics) and a sixth sentence about the story outcome (**Table 2**). To avoid any confusion, we analyzed 1) the ASD context and ASD outcome stories as ASD stories and 2) TD context and TD outcome stories as TD stories[1].

The stories were presented on PC laptops with the software SuperLab 5.0 (Cedrus Corporation). Participants read two stories to familiarize themselves with the reading procedure before the test session. Then, participants were instructed to read each of the stories (after reading each target sentence), which were presented one sentence at a time on a computer screen, and respond to the following questions: "How did the protagonist feel?" and "Would you help if the protagonist were in trouble?"[2] They responded by using a seven-point scale (1: least empathy, 4: neutral, 7: greater

[1] It is often the case in real life that ASD people behave like TD individuals when interacting with TD people (37). We therefore conducted a 2 (ASD participants/TD participants) × 2 (ASD outcomes/TD outcomes) × 2 (ASD contexts/TD contexts) ANOVA (see **Supplementary Results**).

[2] The name of the protagonist was mentioned when rating empathy and helping motivation.

TABLE 2 | Sample story involving ASD context.

Mai's best friend deeply trusted Mai, and she was open with Mai about her important secrets. Mai told her roommate the secrets that her best friend had told Mai. Mai's best friend got angry and asked Mai, "Why did you tell my secrets to everybody?" Mai replied, "You didn't tell me that it was a secret or not to tell anyone." Mai's best friend cried and said, "Mai betrayed me."	
ASD outcome (target sentence)	TD outcome (target sentence)
Mai did not understand why her best friend got angry.	Mai decided to apologize to her best friend after she realized how sad she was.

empathy, and 1: least motivation for helping, 4: neutral, 7: greater motivation for helping). Each sentence remained on the screen until the participant pressed the space bar, which caused the next sentence to appear. The time it took for the participants to read each sentence was recorded. Participants read 26 stories including 2 practice stories, and 24 stories (experimental stories) were analyzed.

In the hierarchical multiple regression analyses, the ASD group was coded as 1, and the TD group was coded as 2 (**Tables 3** and **4**). Gender was the dummy variable (female was 0, and male was 1). The regression models included the participants' age in years and verbal and performance IQ scores. While the gender, age, and verbal and performance IQ scores were covariates, the group (ASD or TD), alexithymia scales (TAS-20 subscales Difficulty Identifying Feelings, Difficulty Describing Feelings, and Externally Oriented Thinking, and BVAQ cognitive and emotional alexithymia scores), and AQ subscales (social skills, attention switching, attention to detail, communication, and imagination) were experimental variables. Because alexithymia is based on atypical interoception (20) and lack of emotional recognition (19), these variables were put in the second regression model. The AQ subscales were calculated as a continuous value on a spectrum of typical development to atypical development. Thus, they were put in the third regression models.

Data Analysis

R package anovakun_480 (anovakun version 4.8.0) (http://riseki.php.xdomain.jp/index.php?ANOVA%E5%90%9B) was used in the analysis of variance (ANOVA). IBM SPSS Statistics version 21 was used in the hierarchical multiple regression analyses.

TABLE 3 | Standardized regression coefficients (*beta* weights) and R^2 from the hierarchical regression analyses based on empathy and helping values for ASD stories.

Individual scores	Empathy		Helping motivation	
First step	*Beta*	*t*	*Beta*	*t*
Group (1: ASD, 2:TD)	−.33	−1.8	−.05	−0.2
Gender (0: female, 1: male)	.04	0.2	.10	0.6
Age in years	−.06	−0.3	−.12	−0.6
Verbal IQ	.08	0.4	.01	0.1
Performance IQ	−.26	−1.5	−.05	−0.2
F	1.62		0.20	
Adjusted R^2	.08		−.12	
Second step	*Beta*	*t*	*Beta*	*t*
Group (1: ASD, 2:TD)	−.36	−1.9	−.27	−1.4
Gender (0: female, 1: male)	.11	0.7	.16	1.0
Age in years	−.02	−.14	−.02	−0.1
Verbal IQ	−.02	−.10	−.09	−0.5
Performance IQ	−.37	−2.0	−.36	−1.8
Difficulty Identifying Feelings	.02	0.0	−.38	−0.9
Difficulty Describing Feelings	−.10	−0.5	−.07	−0.3
Externally Oriented Thinking	−.54	−2.6*	−.55	−2.5*
Cognitive alexithymia	.36	1.9	−.10	−0.5
Emotional alexithymia	−.38	−1.0	.00	0.0
F	2.27*		1.84	
Adjusted R^2	.26		.19	
Third step	*Beta*	*t*	*Beta*	*t*
Group (1: ASD, 2:TD)	−.57	−2.6*	−.68	−3.0*
Gender (0: female, 1: male)	.31	2.1	.37	2.4*
Age in years	.05	0.3	.07	0.4
Verbal IQ	.06	0.4	−.07	−0.5
Performance IQ	−.35	−2.1*	−.36	−2.0
Difficulty Identifying Feelings	−.21	−0.6	−.58	−1.5
Difficulty Describing Feelings	.01	0.1	.11	0.5
Externally Oriented Thinking	−.62	−3.3*	−.73	−3.7*
Cognitive alexithymia	.51	2.7*	.05	0.2
Emotional alexithymia	−.20	−0.6	.15	0.4
Social skill	−.65	−2.5*	−.92	−3.5*
Attention switching	.28	1.2	.20	0.8
Attention to detail	−.33	−2.3*	−.10	−0.7
Communication	.31	1.3	.22	0.9
Imagination	−.10	−0.5	−.10	−0.3
F	2.86*		2.53*	
Adjusted R^2	.43		.38	

**p < .05, two-tailed.*
Three individuals with ASD did not answer AQs. Thus, the hierarchical regression analyses were conducted for 19 individuals with ASD and 20 TD individuals.
Because VIFs (variance inflation factors) of all variables were under 9.4, multicollinearity issues were not necessary to consider.

RESULTS

Reading times more than 2 standard deviations above the mean of each participant were excluded from the analysis. We conducted a 2 (ASD participants/TD participants) × 2 (ASD stories/TD stories) ANOVA on reading times. Results indicated that the interaction between participants and stories was significant [$F(1, 40) = 4.39$, $p < .05$, $\eta_p^2 = .10$]. TD participants read TD stories faster (2,356.1 ms) than ASD stories (2619.0 ms), which was significant [$F(1, 19) = 6.28$, $p < .05$, $\eta_p^2 = .25$]. However, the ASD participants did not read ASD stories (2,516.8 ms) faster than TD (2,512.9 ms) stories [$F(1, 21) = 0.00$, $p > .05$, $\eta_p^2 = .00$]. Moreover, the reading times of TD participants were shorter for similar stories than for dissimilar stories (38).

We also conducted a 2 × 2 ANOVA on empathetic response ratings (**Figure 1**). Results indicated that the interaction between participants and stories was significant [$F(1, 40) = 14.57$, $p < .05$, $\eta_p^2 = .27$]. ASD participants showed greater empathetic responses in ASD stories than TD participants [$F(1, 40) = 6.17$, $p < .05$, $\eta_p^2 = .13$], whereas TD participants showed greater empathetic responses in TD stories than ASD participants [$F(1, 40) = 12.27$, $p < .05$, $\eta_p^2 = .23$]. Both ASD and TD participants showed greater empathetic responses in TD stories than ASD stories [$F(1, 21) = 9.11$, $p < .05$,

TABLE 4 | Standardized regression coefficients (beta weights) and R^2 from the hierarchical regression analyses based on empathy and helping values for TD stories.

Individual scores	Empathy		Helping motivation	
First step	*Beta*	*t*	*Beta*	*t*
Group (1: ASD, 2:TD)	.46	2.7*	.46	2.8*
Gender (0: female, 1: male)	−.06	−0.4	.04	0.3
Age in years	−.05	−0.3	−.10	−0.6
Verbal IQ	.18	1.1	.15	1.0
Performance IQ	−.19	−1.1	−.03	−0.2
F	2.53*		2.86*	
Adjusted R^2	.17		.20	
Second step	*Beta*	*t*	*Beta*	*t*
Group (1: ASD, 2:TD)	.47	2.3*	.37	2.0
Gender (0: female, 1: male)	−.07	−0.4	.01	0.1
Age in years	.00	0.0	−.04	−0.2
Verbal IQ	.14	0.8	.07	0.5
Performance IQ	−.30	−1.4	−.24	−1.2
Difficulty Identifying Feelings	.28	0.6	.38	0.9
Difficulty Describing Feelings	−.14	−0.6	−.43	−2.0
Externally Oriented Thinking	−.21	−0.9	−.21	−1.0
Cognitive alexithymia	.08	0.4	.03	0.1
Emotional alexithymia	−.16	−0.4	−.24	−0.6
F	1.30		2.14	
Adjusted R^2	.07		.24	
Third step	*Beta*	*t*	*Beta*	*T*
Group (1: ASD, 2:TD)	.45	1.6	.28	1.0
Gender (0: female, 1: male)	−.14	−0.7	.00	0.0
Age in years	−.02	−0.1	.02	0.1
Verbal IQ	.08	0.4	.02	0.1
Performance IQ	−.32	−1.4	−.27	−1.3
Difficulty Identifying Feelings	.38	0.7	.52	1.1
Difficulty Describing Feelings	−.13	−0.5	−.47	−1.9
Externally Oriented Thinking	−.24	−1.0	−.24	−1.0
Cognitive alexithymia	.02	0.1	.03	0.1
Emotional alexithymia	−.22	−0.5	−.36	−0.8
Social skill	.05	0.2	.14	0.5
Attention switching	−.25	−0.8	−.22	−0.8
Attention to detail	.29	1.5	.16	0.9
Communication	−.01	−0.0	−.09	−0.3
Imagination	.06	0.2	−.15	−0.6
F	1.01		1.41	
Adjusted R^2	.00		.14	

*$p < .05$, two-tailed.
Three individuals with ASD did not answer AQs. Thus, the hierarchical regression analyses were conducted for 19 individuals with ASD and 20 TD individuals. Because VIFs of all variables were under 9.4, multicollinearity issues were not necessary to consider.

$\eta_p^2 = .30$ for ASD group; $F(1, 19) = 63.68$, $p < .05$, $\eta_p^2 = .77$ for TD group].

A 2 × 2 ANOVA on motivation-for-helping ratings was also conducted, which indicated that the interaction between participants and stories was significant [$F(1, 40) = 8.40$, $p < .05$, $\eta_p^2 = .17$]. **Figure 2** shows that TD participants had greater motivation for helping in TD stories than ASD participants [$F(1, 40) = 15.79$, $p < .05$, $\eta_p^2 = .28$], whereas ASD participants did not show increased motivation for helping in ASD stories than TD participants [$F(1, 40) = 0.00$, $p > .05$, $\eta_p^2 = .00$]. However, both ASD and TD participants showed increased motivation for helping in TD stories than ASD stories [$F(1, 21) = 8.76$, $p < .05$, $\eta_p^2 = .29$ for ASD group; $F(1, 19) = 42.14$, $p < .05$, $\eta_p^2 = .69$ for TD group].

Hierarchical multiple regression analyses were conducted for empathetic responses and motivation-for-helping ratings to control for alexithymia characteristics (39) and AQ (16).[3]

The variables included empathic responses and helping motivation responses toward story characters in ASD stories (**Table 3**). The first regression models were not significant (F = 1.62 for empathy rating, F = 0.20 for helping rating). Although the empathy rating of the second regression model was significant (F = 2.27), the group variable was not significant (beta = −.36 for empathy rating). The third regression model was significant (F = 2.86 for empathy rating, F = 2.53 for helping rating). In the third model, the group (ASD: 1, TD: 2) was negatively correlated with empathy for story characters in ASD stories. Thus, the ASD group was associated with increased empathy for story characters in ASD stories. In motivation for helping, the group (ASD: 1, TD: 2) was negatively correlated with helping motivation for story characters in ASD stories. Thus, the ASD group was associated with increased helping motivation for story characters in ASD stories. In addition, cognitive alexithymia was associated with increased empathy for story characters in ASD stories. The Externally Oriented Thinking, social skills, and attention to detail variables decreased helping motivation for story characters in ASD stories.

We also analyzed the TD stories using the variables of empathic responses and helping motivation responses toward story characters in TD stories (**Table 4**). The first regression model was significant (F = 2.53 for empathy rating, F = 2.86 for helping rating). In summary, the TD group was associated with increased empathy for story characters in TD stories, and the TD group was associated with increased helping motivation for story characters in TD stories. The second and the third regression models were not significant.

DISCUSSION

ASD participants showed greater empathetic responses in ASD stories than TD participants, whereas TD participants showed greater empathetic responses in TD stories than ASD participants. These results suggested that the empathy for ASD story characters was higher in participants with ASD than in TD participants, whereas the empathy for TD story characters was higher in TD participants than in participants with ASD. TD participants showed greater motivation for helping in TD stories than ASD participants, whereas ASD participants did not show a greater motivation for helping in ASD stories than TD participants. These results suggested that the motivation for helping ASD story characters was similar for participants with ASD and TD participants, whereas the motivation for helping TD story characters was higher in TD than in participants with ASD. A previous study using fMRI has suggested that participants with ASD show affective empathy toward other people with ASD (15). If participants with ASD have cognitive empathy toward other people with ASD, they would

[3] Three individuals with ASD chose not to complete questions on the AQ scale. Thus, total AQ, social skill, attention switching, attention to detail, communication, and imagination subscales were collected for the remaining 19 individuals with ASD.

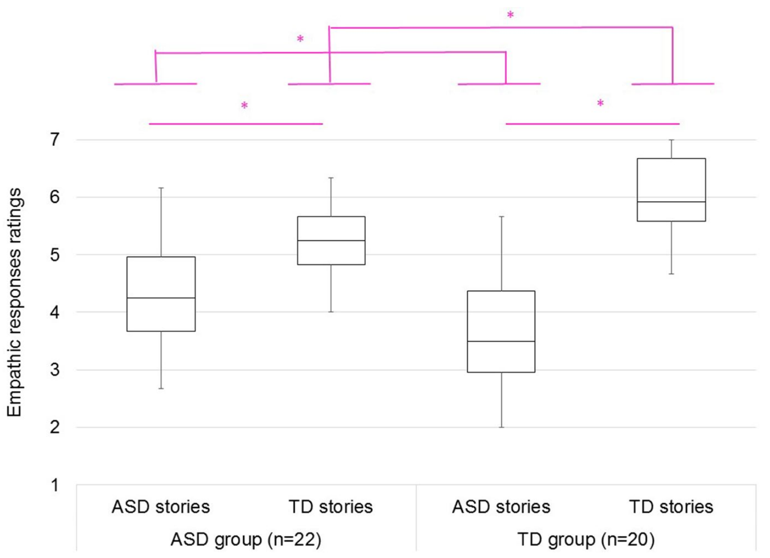

FIGURE 1 | The empathic response ratings for autism spectrum disorder (ASD) and typically developing (TD) stories of ASD (left) and TD (right) groups. 1: least empathy; 4: neutral; 7: greatest empathy.

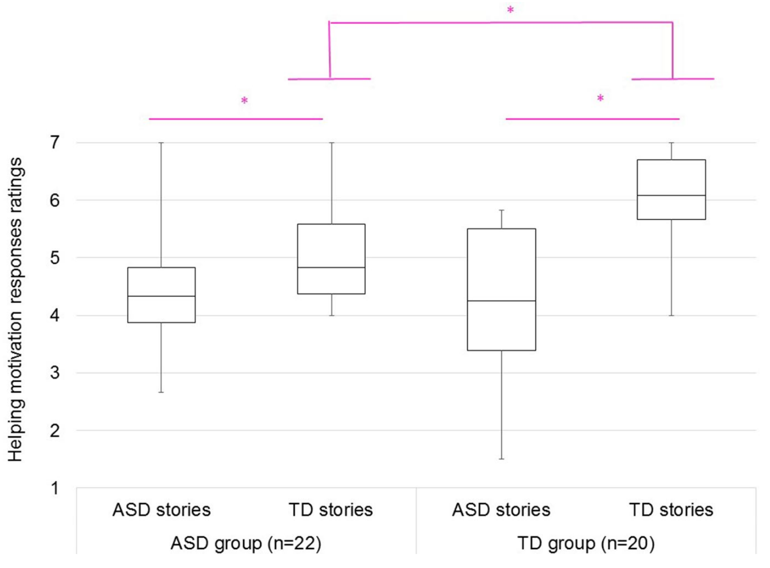

FIGURE 2 | The helping motivation ratings for ASD and TD stories of ASD (left) and TD (right) groups. 1: least motivation; 4: neutral; 7: greatest motivation.

show helping motivation for others with ASD. Cognitive empathy is an ability to intentionally understand other people's emotions, while affective empathy is unintentionally sharing in other people's emotions (40). Based on affective empathy, observing other people's deep sadness and feeling similar sadness disturb observers' minds. Consequently, it becomes difficult to help other people (41). On the other hand, cognitive empathy gives priority to understanding other peoples' situation, and consequently, enables helping other people who are sad.

In the present study, participants with ASD did not show greater helping motivation for others with ASD compared to others with TD. Thus, participants with ASD did not show greater cognitive empathy even if the targets had ASD characteristics. However, individuals with ASD showed helping motivation when alexithymia and AQs were controlled. These findings suggest the possibility that adults with ASD might not notice the necessity to help people if they are not explicitly asked to assist. There is another possibility that lies in differences between ASD and TD regarding social contacts. The possibility could be that individuals with ASD feel good if people leave them alone when they are sad, while TD individuals feel better when they have social contacts, such as words of encouragement or hugs (42). Of course, there could be individual differences in this effect, such that some individuals with ASD need words of encouragement or want to be hugged and some TD individuals want to be left alone. It is suggested that these issues of individual differences in ASD and TD groups be examined in future research.

Cognitive alexithymia was associated with increased empathy for story characters with ASD. It is possible that individuals with ASD share similar difficulties regarding cognitive alexithymia with story characters with ASD, and as a result, they empathize with others similar to themselves (15, 43). Additionally, it was demonstrated that Externally Oriented Thinking was associated with decreased empathy and helping motivation for story characters with ASD. Externally oriented thinking is a cognitive style that shows preference for external behavioral information instead of internal emotional information (44). Thus, individuals with high Externally Oriented Thinking focused on behavioral information of story characters (story characters did not mention help explicitly), and they did not infer story characters' implicit needs.

Finally, social skills were associated with decreased empathy and helping motivation for story characters with ASD, and attention to detail was associated with decreased empathy for story characters with ASD. Because higher sensory reactiveness is associated with lower social functioning (18), lower social skills due to atypical sensory input would predict limited cognitive empathy and helping motivation in ASD. The characteristic of lack of attention to detail in ASD was also caused by atypical sensory perception in ASD (45). These findings suggest that the reason why individuals with ASD are considered to have limited cognitive empathy and helping motivation could be related to alexithymia and the lack of social skills and attention to detail, which are related to atypical perception.

GENERAL DISCUSSION

ASD and TD groups showed greater empathetic responses and greater motivation for helping in TD stories than ASD stories. These results can be interpreted in the context of in-group/out-group biases. An in-group is a social group of which a person psychologically identifies as being a member; by contrast, an out-group is a social group with which an individual does not identify very much (46, 47). Both ASD and TD groups could interact and communicate more easily with in-group members than with out-group members (42). However, both TD individuals and individuals with ASD use the majority, or "non-autistic people," as the implied context (with whom) and the reference group (according to whom) in the assessment of autistic traits (37). Therefore, although individuals with ASD might have an in-group/out-group bias, they use the perspective of TD people when judging empathy and helping motivation in stories. In other words, whereas TD people consider majority rules by TD people (but consider minority rules by people with ASD to a lesser extent), people with ASD try to accept majority rules by TD people, even if the rules are not rules for ASD.

The findings in the present study indicate that adults with ASD empathize with other people who have ASD and show motivation to help other people with ASD if cognitive and emotional alexithymia and AQ measures (social skill, attention switching, attention to detail, communication, and imagination) are eliminated. High AQ scores are associated with higher functioning, as it is a self-rating questionnaire and a strong sense of self is required. When participants with ASD completed assessments of autistic traits, they used the perspective of TD people (37). If alexithymia and AQ are statistically controlled, individuals with ASD may help other individuals with ASD. However, in reality, many individuals with ASD have high alexithymia and AQ scores. Thus, individuals with ASD do not often show voluntary motivation to help others.

Helping motivation can originate from other motivations besides empathy and shared affect, such as targeted helping (assistance based on a cognitive understanding of the other's specific need) or altruistic helping (5). While altruistic helping by adults with ASD is not demonstrated in this study, they may have in fact demonstrated targeted helping toward others. Future studies should examine what kinds of helping motivation are demonstrated by adults with ASD.

Finally, it is important to consider the limitations of the present study. Firstly, the study could not recruit 21 people of the same gender per group with complete data sets, which resulted in group sizes of at least 39, to reach 78% power. Secondly, we did not ask the participants if the character/context was TD or ASD related after reading the stories. Rating of ASD stories by ASD people would be an important manipulation check, which would enhance the validity of the present study. Thirdly, because we used explicit tasks to ask for cognitive empathy and helping motivation, it is difficult to discuss the effects of social contacts and social desirability. Appropriate implicit tasks should be considered for future projects. Additionally, because participants had to interact with other people during the laboratory testing in our task, testing without further social interaction would be useful for reducing stress in ASD as well as social desirability in both groups.

SUPPLEMENTARY RESULTS

Reading times more than 2 standard deviations above the mean for each participant were excluded from the analysis. A 2 (ASD participants/TD participants) × 2 (ASD outcomes/TD outcomes) × 2 (ASD contexts/TD contexts) ANOVA on reading times was conducted. Results indicated that the interaction between participants and outcomes was significant [$F(1, 40) = 6.45$, $p < .05$, $\eta_p^2 = .14$]. TD participants read TD outcomes (2,468.9 ms) faster than ASD (2,852.1 ms) outcomes [$F(1, 19) = 13.41$, $p < .05$, $\eta_p^2 = .41$]. However, the ASD participants did not read ASD outcomes (2,679.6 ms) faster than TD (2,592.2 ms) outcomes [$F(1, 19) = 2.31$, $p > .05$, $\eta_p^2 = .10$]. The interaction between the outcomes and the contexts was significant [$F(1, 40) = 22.57$, $p < .05$, $\eta_p^2 = .99$]. These results were consistent with previous studies. Reading times for TD participants were shorter for stories about TD outcomes than stories about ASD outcomes (38). The interaction between participants and contexts was not significant [$F(1, 40) = 0.17$, $p > .05$, $\eta_p^2 = .00$], and the participants × outcomes × contexts interaction was not significant [$F(1, 40) = 0.41$, $p > .05$, $\eta_p^2 = .02$].

A 2 × 2 × 2 ANOVA on empathetic response ratings (**Supplementary Figure 1**) was also conducted. Results indicated that the interaction between participants and outcomes was significant [$F(1, 40) = 8.88$, $p < .05$, $\eta_p^2 = .18$]. ASD participants showed greater empathetic responses toward ASD outcomes than TD participants [$F(1, 40) = 4.06$, $p < .05$, $\eta_p^2 = .09$], whereas TD participants showed greater empathetic responses toward TD outcomes than ASD participants [$F(1, 40) = 5.83$, $p < .05$, $\eta_p^2 = .13$]. Moreover, TD participants showed greater empathetic responses toward TD outcomes than ASD outcomes [$F(1, 40) = 5.83$, $p < .05$, $\eta_p^2 = .13$]. ASD participants did not show greater empathetic responses toward ASD outcomes than TD outcomes [$F(1, 40) = 4.06$, $p > .05$, $\eta_p^2 = .09$]. The interaction between participants and context was significant [$F(1, 40) = 7.18$, $p < .05$, $\eta_p^2 = .15$]. TD participants showed greater empathetic responses toward the TD contexts than ASD contexts [$F(1, 40) = 26.36$, $p < .001$, $\eta_p^2 = .58$].

A 2 × 2 × 2 ANOVA on motivation for helping ratings was also conducted, which indicated that the interaction between participants and outcomes was significant [$F(1, 40) = 7.92$, $p < .05$, $\eta_p^2 = .17$]. **Supplementary Figure 2** shows that TD participants showed greater motivation for helping toward TD outcomes than ASD participants [$F(1, 40) = 13.94$, $p < .05$, $\eta_p^2 = .26$], whereas ASD participants did not show greater motivation for helping toward ASD outcomes than TD participants [$F(1, 40) = 0.06$, $p > .05$, $\eta_p^2 = .00$]. Additionally, while TD participants showed greater motivation for helping toward TD outcomes than ASD outcomes [$F(1, 40) = 13.86$, $p < .05$, $\eta_p^2 = .26$], ASD participants did not show greater motivation for helping toward ASD outcomes than TD outcomes [$F(1, 40) = 0.06$, $p > .05$, $\eta_p^2 = .00$]. These results indicated that the helping motivation of individuals with ASD was similar for ASD and TD targets, whereas the helping motivation in TD individuals was higher for TD than for ASD targets.

ETHICS STATEMENT

Our protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the University of Fukui (Japan). Before participation, written informed consent was obtained from each participant. All methods were carried out in accordance with the approved protocol.

AUTHOR CONTRIBUTIONS

HKom, HKos, and HO developed the concept of the study. All authors contributed to the study design of the study. TF and MJ performed the data analysis and interpretation under the supervision of HKos and HO. HKom and HKos drafted the manuscript. TF, MJ, and HO provided critical revisions. All authors approved the final version of the manuscript for submission.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00376/full#supplementary-material

SUPPLEMENTARY FIGURE 1 | The empathic responses ratings for each story of ASD (left) and TD (right) groups. 1: Least empathy - 4: Neutral- 7: Greatest empathy.

SUPPLEMENTARY FIGURE 2 | The helping motivation ratings for each story of ASD (left) and TD (right) groups. 1: Least motivation - 4: Neutral- 7: Greatest motivation.

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REVIEW
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Impact of Aging on Empathy: Review of Psychological and Neural Mechanisms

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Empathy in aging is a key capacity because it affects the quality of older adults' relationships and reduced levels are associated with greater loneliness. Many older adults also find themselves in the role of a caregiver to a loved one, and thus empathy is critical for the success of the caregiver–patient relationship. Furthermore, older adults are motivated to make strong emotional connections with others, as highlighted in the socioemotional selectivity theory. Consequently, reductions in empathy could negatively impact their goals. However, there is growing evidence that older adults experience at least some changes in empathy, depending on the domain. Specifically, the state of the research is that older adults have lower cognitive empathy (i.e., the ability to understand others' thoughts and feelings) than younger adults, but similar and in some cases even higher levels of emotional empathy (i.e., the ability to feel emotions that are similar to others' or feel compassion for them). A small number of studies have examined the neural mechanisms for age-related differences in empathy and have found reduced activity in a key brain area associated with cognitive empathy. However, more research is needed to further characterize how brain changes impact empathy with age, especially in the emotional domain of empathy. In this review, we discuss the current state of the research on age-related differences in the psychological and neural bases of empathy, with a specific comparison of the cognitive versus emotional components. Finally, we highlight new directions for research in this area and examine the implications of age-related differences in empathy for older adults.

Keywords: empathy, aging, neuroimaging, theory of mind, prosocial behavior

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DEFINING EMPATHY

Empathy is thought to be made up of two primary components, which include 1) emotional empathy—the capacity to feel either compassion or similar emotions to what another person is experiencing—and 2) cognitive empathy—the capacity to take the mental perspective of others and understand their thoughts and feelings (1, 2). Within each component of empathy, there are subdomains that are purported to have different influences on emotion, well-being, and prosocial behaviors towards others, such as donation and volunteerism (1, 3–5). Empathy can be measured as a general tendency (i.e., trait), a momentary emotional response (i.e., state), or as a behavioral response (1, 2, 4).

Empathy tends to occur when we observe others' physical and/or emotional suffering (1). Emotional empathy is the affective reaction to others' pain that entails feeling emotions that are the same or similar to that of the person who is suffering, feeling sympathy, or experiencing feelings of distress (4). An individual may experience compassion or sympathy in response to another person's suffering, which is a subdomain of emotional empathy called "empathic concern" (1, 2). This is thought to be the result of engaging one's emotion regulation capacities in order to reduce the levels of negative emotions one might experience when viewing another's pain. In contrast, if an individual is not able to regulate their negative vicarious emotions due to observing others' pain, they may experience the subdomain of empathic, or personal distress, which is a feeling of being overwhelmed with anxiety, distress, and negative emotions due to experiencing others' pain (1, 2). In addition to emotion regulation, other psychological interventions may be useful in increasing levels of empathic concern and reducing personal distress, such as engaging in loving kindness meditation (4).

The cognitive component of empathy includes one's capacity to understand the thoughts and feelings of others who are suffering (6, 7). One subdomain of cognitive empathy is perspective taking, which involves mentally putting oneself in another person's shoes in order to understand their thoughts and feelings. Perspective taking may engage such processes as imagination, autobiographical memory, and future thinking as an individual attempts to determine another person's thoughts and feelings. There is also evidence that actively attempting to engage in perspective taking can result in an increase in momentary levels of emotional empathy (1). Another subdomain of cognitive empathy is theory of mind, which involves accurately detecting others' mental states and allows us to understand that others may have different perspectives from our own. Empathic accuracy is the capacity to detect fine-grained changes in the thoughts and emotions of others that may rely on capacities such as emotion recognition and social knowledge. These subdomains may interact so that individuals can accurately detect the thoughts, emotions, and intentions of others. In the following sections, we will discuss age-related differences in the psychological and neural mechanisms of emotional and cognitive empathy.

IMPORTANCE OF EMPATHY IN AGING

Currently, adults 65 years and older make up 15% of the United States population, and by 2060, this percentage is expected to nearly double to 24% (8). Therefore, an understanding of how healthy aging affects the brain and cognitive and emotional processing is critical for older adults' well-being. Of particular importance, there is growing evidence that older adults experience at least some adverse changes in empathy (3, 9, 10), although the nature of the effect appears to differ based on the subtype of empathy. Briefly, in the field of empathy research, an important distinction has been made between the cognitive subtype (i.e., the capacity to understand others' feelings) and the emotional subtype (i.e., the capacity to experience similar emotions to others or to feel compassion), as these components have been shown to involve distinct neural and psychological processes (1, 11–14).

Clarifying how aging affects the biological and psychological processes underlying the subtypes of empathy is a serious public health concern, as reduced empathy in general has been associated with greater risk for loneliness and depression, and poorer personal life satisfaction (15–17), which are all major concerns that have been tied to increased morbidity in older adults (18). Furthermore, loss of emotional and/or cognitive empathy has emerged as a key symptom in patients with Alzheimer's disease and frontotemporal dementia, and some have suggested that these measures may even help to distinguish between the two conditions (19–24). There is evidence that as individuals age, they may experience higher levels of well-being (25), and that lower well-being is closely tied with increased mortality risk. In particular, a Gallup World Poll showed that the relationship between evaluative well-being (or life satisfaction) can be described as a U-shaped curve, reflecting greater life satisfaction with age; however, there are geographical differences (25).

Changes in empathy with age could have significant ramifications for older adults involved in helping roles, such as physicians or family caregivers. Many older adults find themselves to be in the role of a family caregiver to a spouse or parent with dementia, or another chronic disease (26). Both physician and caregiver burnout and compassion fatigue are already significant and pervasive issues (27, 28), and thus empathy changes as a function of aging could critically affect these professions, in addition to reducing quality care for patients. Taken together, it is clear that developing a greater understanding of how aging affects the neural and psychological factors subserving each subtype of empathy is a critical step in moving the field forward, especially with our increasing older population.

AGING AND EMPATHY: PSYCHOLOGICAL MECHANISMS

Aging and Emotional Empathy

There is growing evidence that the emotional domain of empathy is not lower in older than in younger adults (3, 5, 9, 10) (see **Table 1**). However, there is mixed evidence about whether older adults have similar levels of emotional empathy to younger adults (i.e., preservation) or experience higher levels (3, 5, 10). In the next section, we will review studies examining the degree to which there are age-related differences in emotional empathy between older adults and younger adults. In particular, we will clarify whether there are age-related differences in older adults' emotional empathy among the various subdomains, including the capacity to experience the same or similar emotions to others who are suffering (emotional resonance), feelings of compassion for others (empathic concern), and distressing feelings (personal distress). We will also compare the results of studies that have assessed emotional empathy as a general tendency (or trait) versus those that have measured it as a momentary response (state) to environmental stimuli that are likely to evoke an empathic state. Finally, we will also discuss the effects of demographic factors (e.g., gender, culture) and contextual factors (e.g., age relevance of stimuli).

Emotional Empathy—Trait

Trait emotional empathy can be measured through self-report questionnaires in which an individual is asked to rate the degree to which they agree with a series of statements reflecting actions and

TABLE 1 | Emotional empathy and aging: Review of findings.

Authors	Age group	Measurement	Difference	Findings
Bailey et al. (9)	YA, OA	EQ emotional empathy	OA vs YA: n.d.	OA vs YA: n.d. on self-report emotional empathy
Bailey et al. (29)	YA, OA	IRI PD, EC, ERS	OA vs YA: n.d.	OA vs YA: n.d. on emotional empathy; state PD: OA > YA; helping effort: OA > YA
Beadle et al. (10)	YA, OA	IRI EC	OA vs YA: n.d.	IRI-OA vs YA: n.d. on self-report empathic concern
Beadle et al. (3)	YA, OA	IRI EC, ERS, DG	OA vs YA IRI EC: n.d., OA vs YA ERS: n.d., OA > YA DG – empathy condition	OA vs YA self report empathic concern: n.d., OA vs YA state empathy: n.d., OA > YA prosocial behavior – empathy condition
Chen et al. (30)	YA, MA, OA	IRI, fMRI	OA < YA IRI EC and PD; OA < MA/YA brain activity in right insula to empathy condition	IRI-OA ↓ self-report on emotional empathy (EC and PD); OA ↓ brain activity in right insula to empathy for physical pain
Khanjani et al. (31)	AD, YA, MA, OA	EQ emotional empathy	OA > AD	OA > AD on EQ emotional empathy
Sze et al. (5)	YA, MA, OA	ERS, donation	OA > MA > YA ERS OA > MA > YA donation	ERS-OA ↑ than MA and YA on state empathy, OA ↑ on donation behavior
Moore et al. (32)	OA	MET, AFM, GNG, N-back, fMRI	OA with higher emotional empathy < bilateral amygdala and R insula during N-back	OA with higher emotional empathy outside scanner < bilateral amygdala and R insula during N-back task
Riva et al. (33)	AD, YA, OA		OA < YA R insula in empathy conditions	OA < YA R insula in pleasant and unpleasant touch empathy conditions

Age groups: AD, adolescents; YA, young adults; MA, middle age adults, OA, older adults; EQ, Empathy Quotient; IRI, Interpersonal Reactivity Index; EC, empathic concern; PD, personal distress; MRI, magnetic resonance imaging; fMRI, functional magnetic resonance imaging; ERS, emotional response scale (measures state emotional empathy); DG, dictator game (measure of prosocial behavior); MET, Multifaceted Empathy Test; AFM, Affective Facial Matching Test; GNG, Go/no-go Test; N-back, N-back test; R, right side; n.d., groups were not statistically different.

thoughts about individuals who are suffering or in need (2). One of the mostly widely used assessments of trait emotional empathy in aging is the well-validated and reliable Interpersonal Reactivity Index (IRI) (2), which has sufficient test/retest reliability (range: r = .61 to .81) and internal consistency (range Cronbach's alpha: .68 to .79). Although the IRI measures multiple components of empathy, here we focus on the subscales most relevant to emotional empathy, which include the Empathic Concern subscale, and the Personal Distress subscale. Each subscale ranges from 0 to 28 points, with higher scores indicating greater empathy. Another frequently used measure of trait empathy is the Empathy Quotient, which is a self-report measure that assesses cognitive and emotional empathy, in addition to social skills (34). Most relevant to this section is the affective empathy subscale. An example item from this subscale is, "Seeing people cry doesn't really upset me," which would be reversed scored. Higher scores on this measure indicate greater affective empathy.

Overall, most studies have not found lower trait emotional empathy in older adults than younger adults, and the majority of studies have found no age-related differences. Across two studies, Bailey and colleagues found no age-related differences in trait emotional empathy, which included two samples of participants from Australia (9, 29). In the first study by Bailey and colleagues (35), trait emotional empathy was measured by the affective empathy subscale of the Empathy Quotient and assessed age-related differences between younger (N = 80; 19–25 years; 29% male) and older adults (N = 49; 65–87 years; 33% male). They found no significant age-related differences on this measure (9). The second study by Bailey and colleagues used the IRI to measure age-related differences between younger (N = 40; 17–29 years; 30% male) and older adults (N = 39; 61–82 years; 36% male) in trait empathic concern and personal distress (29); no age-related differences in trait emotional empathy were found. Consistent with the Bailey and colleagues studies, our group found no age-related differences in trait empathic concern across two different studies with participant samples from the United States (3, 10). We used the IRI Empathic Concern subscale to assess empathic concern, and in both samples approximately 60% were women (3, 10).

A study by Chen and colleagues examined trait empathic concern and personal distress in a sample of ethnic Chinese participants including three groups: younger (N = 22; 20–35 years; 50% male), middle-aged (N = 22; 40–55 years; 50% male), and older participants (N = 21; 65–80 years; 52% male). In contrast to the other studies, Chen and colleagues found that older adults reported lower trait empathic concern and personal distress than the younger group (30). There are several possibilites as to why the Chen and colleagues study is not consistent with the other studies. For instance, the Chen and colleagues study included a sample of ethnic Chinese participants, whereas the other studies on this topic had samples based in Australia or the United States. Thus, there is a possibility that cultural differences in perceptions about empathy may interact with age-related differences. Another possibility is that differences in sample size across the studies could have impacted the results. The Chen and colleagues study included a smaller sample in each group (~22 participants) than most previous studies. Consequently, this smaller sample size may have impacted the results. More research is needed to clarify the effects of these methodological differences on the measurement of age-related differences in empathy.

In summary, the studies on trait emotional empathy in general show no age-related differences between younger and older adults, with the exception of the Chen and colleagues study. Most studies focus on trait empathic concern using the IRI and show no age-related differences. However, one study also reported the results of the Personal Distress subscale of the IRI and found no age-related differences (29). Typically, sample sizes range from 40 to 80 per age group. In order to further characterize age-related differences in trait emotional empathy, more consistency is needed in terms of the sample size per age group, equivalent numbers of males and females, questionnaire type, and reporting of both empathic concern and personal distress. Furthermore, future research is needed to examine the role of culture for age-related differences in trait emotional empathy, as there is a paucity of research in this area.

Emotional Empathy—State

Emotional empathy can also be assessed as a state, or a momentary emotional reaction to observing the suffering of others (1). Experimentally, state emotional empathy is measured in response to an empathy induction designed to elicit a temporary state of emotional empathy. Two subdomains of emotional empathy are typically measured, which include empathic concern, often measured through items, such as "compassion and sympathy," and personal distress, assessed through items, such as "distressed or upset." Some studies also assess emotional empathy at baseline prior to the induction because of significant individual variability in emotional empathy reported at baseline. By assessing baseline emotional empathy, researchers can examine the specificity of the emotional empathy response to the empathy induction. It is also common practice to compare the results of the empathy induction to some form of control condition, for example, a video of an individual engaging in neutral, unemotional activities, in order to account for social context.

Overall, researchers have found that older adults do not have lower state emotional empathy than younger adults (3, 5, 29, 36). However, the evidence is mixed in terms of whether older adults experience similar or higher state emotional empathy than younger adults in response to empathy inductions (3, 5, 29, 36). To further elucidate why the results have been mixed, key methodological differences will be highlighted.

In a study by Sze and colleagues (5), state emotional empathy was measured in response to a series of empathy inductions in three different age groups: 71 younger (age: M = 23.07), 72 middle-aged (age: M = 44.58), and 70 older (age: M = 66.43). Approximately 67% of participants were female and 33% were male, and these proportions were evenly distributed across the three groups. Emotional empathy was elicited using a series of two videos. One condition included an "Uplifting Film," which included photos of children with autism enjoying their time participating in a surf camp, and the second condition included a "Distressing Film," which showed depictions of the Darfur crisis through photos of children, women, and men experiencing inhumane conditions and suffering. Participants rated their state emotional empathy at baseline (at the beginning of the study), and then again immediately after they watched each video. The items used to assess empathic concern were "sympathetic, moved, and compassionate." Participants also rated their personal distress, and some basic emotions (e.g., anger, fear, and disgust). The scale ranged from, "1 = not at all; 5 = extremely." For their analyses of empathic concern, baseline ratings of empathic concern were used as a covariate in the model. Researchers also assessed participants' autonomic nervous system reactivity through measures of heart rate reactivity (interbeat interval), finger pulse amplitude, pulse transmission time to the finger, pulse transmission time to the ear, systolic blood pressure, diastolic blood pressure, and skin conductance.

In response to the videos designed to induce empathy, they found that older adults reported higher state empathic concern than middle-aged or younger adults, with the distressing video evoking higher empathic concern ratings than the uplifting video. Furthermore, they found that older adults reported higher personal distress in response to the distressing video than middle-aged and younger adults. There was a linear increase as a function of age in terms of autonomic activation. In particular, heart rate reactivity in the interbeat interval increased as a function of age, with older adults showing higher levels than younger adults. They also found that older adults showed the greatest prosocial behavior in the form of donating to charities associated with each video, with the greatest donations in response to the distressing film. Using a regression model, the authors determined that empathic concern ratings to the distressing film, interbeat interval reactivity to the uplifting film, and age were significant predictors of prosocial behavior, even when controlling for trait empathic concern and past donation behavior.

Our group compared state emotional empathy in 24 younger (age: M = 19.8 years) and 24 older adults (age: M = 77.9 years), and 63% of the sample was female. The premise of this study was that participants would be playing an economic game against two real participants, each of whom were in separate testing rooms. During the course of the study, the participants played the Dictator Game against the two "real" participants, which involved deciding how to split $10 with each participant (and the participant had to accept any offer they gave them). The Dictator Game offers served as the measure of prosocial behavior in this study. Participants were told that some of the study participants would be asked to write a note about an event that occurred during their weekend. The participants were asked to pick out of a hat to determine who would be a "Receiver" (i.e., person who reads the note) or a "Sender" (i.e., person who writes the note). Unknown to the participants, this was actually rigged, such that participants were always in the role of the "Receiver." These notes were created and piloted beforehand in the lab. One note was designed to evoke an empathic state, whereas the other note served as the control (neutral) condition and was designed to elicit an unemotional state. Specifically, the empathy note described the participant's experience finding out that they have a serious form of skin cancer. In the neutral note, the participant discussed their mundane errands and was unemotional in content. Participants read one note before each round of the Dictator Game; the order of the emotion inductions was counterbalanced across participants.

Similar to the Sze and colleagues study (5), participants rated their empathic concern, personal distress, and other basic emotions before and after each induction. Participants responded to the prompt, "Indicate to what extent you feel this way right now, that is, at the present moment," which was adapted from the Positive and Negative Affect Schedule (PANAS) questionnaire (37). State emotional empathy was measured through the items ("sympathetic"; "compassionate") and personal distress was measured through the items ("upset"; "distressed") that were drawn from the Emotional Response Scale, a well-validated measure of state emotional empathy and personal distress (1, 38). The rating scale ranged from "1 (very slightly or not at all) to

5 (extremely)." We examined age-related differences in empathic concern ratings. For this analysis, we used a ratio score such that, "participants' average rating after the empathy induction was divided by their average rating immediately prior to the empathy induction" (empathic concern ratio score: empathy induction/baseline score). We compared age-related differences in multiple emotions in the model: empathic concern, personal distress, sadness, hostility, and joviality.

We found no age-related differences for empathic concern, personal distress, or any other state emotion in response to the empathy induction. However, we did find that older adults showed greater prosocial behavior than younger adults in response to the empathy induction, but not the neutral induction. Specifically, older adults gave more money to their opponent who they thought had cancer than younger adults did. Furthermore, in the older group state, ratings of empathic concern were positively correlated with prosocial behavior. In summary, we found no age-related differences in state emotional empathy, but did find greater prosocial behavior in an empathic context in older versus younger adults.

A study by Bailey and colleagues examined age-related differences in emotional empathy for the physical pain of others in a sample of 40 younger and 40 older adults (29). Participants viewed video clips of arms engaged in painful versus nonpainful movements while undergoing electromyography and rating their emotions. State emotional empathy was measured in the same way as the Beadle and colleagues (3) study, by having individuals perform ratings before and after each video, which measured state empathic concern and personal distress, in addition to other basic emotions. Furthermore, they also calculated ratio scores of state emotion in a similar manner to Beadle and colleagues (3), by calculating the average ratings in each category divided by the prestimulus baseline for that category. In addition, they measured prosocial behavior by giving the participants the option to help the people in the videos by volunteering to prepare packets for mailing that would go out to the group "Pain Australia." Helping effort was measured as the number of pamphlets participants were able to compile divided by the digit symbol substitution test score, in order to control for age-related differences in processing speed. In terms of state emotional empathy, older adults reported greater personal distress than younger adults. However, they did not find any age-related difference in state empathic concern. Other age-related differences in ratings of state emotion included older adults reporting greater happiness, hostility, and sadness. In terms of physiological responses, older adults showed greater corrugator activity than younger adults in response to the pain videos, and older adults showed greater corrugator activity to pain versus non-pain videos. The authors did not find significant age-related differences in prosocial behavior.

A study by Wieck and Kunzmann (36), compared state empathic concern in a sample of women consisting of 101 younger (age: M = 24 years) and 101 older (age: M = 69 years) participants. The rationale for the authors' focus on women in this paper is that there is evidence for gender differences in self-reported empathy (women > men; 2), and by focusing on women, some variability in empathy would be reduced. Participants watched a neutral video and six different empathy induction videos. The neutral video depicted a woman sharing her thoughts on her way to work, whereas the empathy videos depicted a variety of different emotions (e.g., anger, sadness, or happiness). The videos included protagonists from the community reliving specific emotional experiences. They were asked to select age-relevant experiences, such as the "death of a long-term friend" for older adults and the "end of one's first love" for younger adults. After viewing each clip, participants were asked to rate their current emotions based on a list of emotion adjectives on a scale ranging from "0 (not at all) to 6 (extremely)" (36). For the emotion adjectives, participants rated their empathic concern through the item "sympathetic," in addition to rating other basic emotions related to happiness, sadness, and anger. Of note, they did not assess state emotions at baseline in this study, but emotions were assessed in response to the neutral video, which served as the control condition.

Across the various types of empathy inductions, older women reported greater empathic concern (or sympathy) than younger women. However, there were slight differences in the magnitude of the response, with older women showing higher ratings of sympathy for the happiness videos versus the sadness and anger. The age relevance of the videos did not significantly impact ratings of sympathy. In terms of emotion congruence, there were few age differences. Overall, participants rated higher emotion congruence for videos depicting older topics and for happiness and anger videos. For sadness films, both younger and older participants reported greater emotional congruence with those that depicted older protagonists. In the domain of anger, older women reported greater emotion congruence with videos depicting older topics. In summary, whereas older females reported greater sympathy, there were fewer differences in emotion congruence.

Overall, no studies have reported lower state emotional empathy in older adults than younger adults in response to an empathy induction. Yet, there is still little consensus on whether older adults' state emotional empathy is higher than or similar to that of younger adults. We have reviewed two studies that have shown no age-related differences in state empathic concern in older than in younger adults (3, 29) and two that have shown higher levels in older adults (5, 36). In terms of state personal distress, two out of three studies showed increased levels of personal distress in older adults in response to empathy inductions (5, 29), whereas the third study found no difference (3). Some researchers have measured older adults' physiological and facial mimicry responses to empathy induction and found that older adults show greater heart rate reactivity (5) and facial corrugator activity (29). In the domain of prosocial behavior, two out of three studies found greater prosocial behavior in response to empathy inductions in the older group than the younger group (3, 5, 29). However, the study that did not show age-related differences in prosocial behavior (29) measured behavior in terms of time spent helping rather than monetary donation, which was the method used in previous studies. Previous studies vary in terms of the type of empathy induction used (e.g., note versus video induction) and the content within the induction (e.g., uplifting versus distressing; emotional versus physical pain). Furthermore, only some studies include an equal number of males and females in their sample. While prosocial behavior is most often measured through monetary donation, more research is needed to assess whether age-related differences in empathy also affect other types of helping behavior. In conclusion, future research is needed to characterize the degree to which state emotional empathy is increased in older adults, whether there are gender differences, and the degree to which increased emotional empathy affects different types of helping behavior (e.g., monetary donation versus spending time helping others).

Conclusions about Aging and Emotional Empathy

Across studies, there is little evidence that emotional empathy is lower in older than younger adults. However, it is still not clear whether emotional empathy is similar to or higher than in younger adults, in particular in the empathic concern domain. There is growing evidence that in the personal distress domain, older adults may experience higher levels than in younger adults. Yet, this area is still in its infancy and more research is needed to assess all subdomains of emotional empathy, including empathic concern, personal distress, and emotional resonance through both trait and state measures. For future studies that measure age-related differences in trait empathy, more consistency is needed in the questionnaires used to measure empathy, as different questionnaires may assess empathy differently. In studies that focus on state emotional empathy, in order to reach a consensus, more research is needed that characterizes empathy through the use of multiple different types of induction techniques (e.g., video, photos, and notes) and that uses both negative and positive content, as well as emotional and physical pain. In order to assess the relationship between age-related differences in empathy and prosocial behavior, more research is needed to measure different types of prosocial behavior (e.g., donation, and volunteerism). Overall, there is a need to assess the role of gender and culture for age-related differences in empathy and prosocial behavior.

Much of the research on age-related differences in emotional empathy has focused on self-report measures. Yet, self-report measures of empathy are not without their limitations. For instance, these measures may be influenced by demand characteristics, as individuals may want to appear empathetic because it is thought to be a desirable trait. Furthermore, socioemotional selectivity theory suggests that older adults may be motivated by activities that enhance emotional meaning, such as spending time with close friends and family (39). Thus, for older adults, perceiving themselves to be compassionate may be particularly relevant to their personal goals. Studies that use more objective physiological measures provide some support for increased emotional empathy in aging. In particular, older adults show greater heart rate reactivity (5) and facial corrugator activity (29) in response to empathy inductions, which is consistent with higher levels of personal distress ratings. Moving forward, it is important that studies use converging methods to assess age-related differences in empathy, such as self-report, behavioral, physiological, and neuroimaging measures.

Aging and Cognitive Empathy

The cognitive component of empathy is thought to be made up of multiple subdomains that include theory of mind, empathic accuracy, and perspective taking (6, 7). Theory of mind is our capacity to detect the mental states and intentions of others (40–42), whereas perspective taking is the capacity to adopt the mental states of others, typically through imagining their point of view (30, 43, 44). A related construct, empathic accuracy, is our capacity to accurately discern the emotions, thoughts, and feelings of another person (30, 45–47). These three subdomains interact to enable individuals to understand the thoughts, feelings, and intentions of others. Below, we will describe age-related differences in cognitive empathy across the various subdomains of theory of mind, perspective taking, and empathic accuracy (see **Table 2**).

Theory of Mind

Theory of mind is described as a person's capacity to understand the mental states of others and can include both cognitive and affective content (53–55). People may use relevant personal experiences in order to comprehend others' cognitive and emotional states and predict social behavior (41). Theory of mind is important for social relationships and interactions because it can help us to connect with others in meaningful ways (42, 53, 56). Research on theory of mind has generally shown that older adults perform more poorly than younger adults (33, 48–53). One way to measure theory of mind is through the Faux Pas Test (57). In this task, participants are presented with short stories in which they answer questions about whether someone behaved inappropriately (i.e., committed a social faux pas) (57). Studies using this task have typically shown poorer performance in older than younger adults (48, 58).

Another way to assess theory of mind is through the False Belief Task, which is a widely used and well-validated task that involves mental state detection (59). In this task, participants read stories during two different conditions: 1) mental trials—stories about an individual who has a mistaken (or false) belief, and 2) physical trials—a physical image that is no longer accurate. The first condition will require theory of mind in order to infer the character's mental state, whereas the physical trial will serve as the control condition. Studies using this task have shown poorer performance in older than younger adults (53, 60).

Age-related differences in theory of mind have also been assessed through the Revised Reading the Mind in the Eyes Test (54). In this task, participants are shown a series of 36 pictures, including the eye region of the face only, and each photo depicts a different social emotion. Participants determine the emotion expressed in each photo by selecting from four different emotion response options, such as "jealous" or "embarrassed" (54). In general, studies have found that older adults perform more poorly than younger adults on this task (9, 31, 61). There is some evidence that individuals with better performance on the Reading the Mind in the Eyes task have higher levels of verbal intelligence and comprehension (62). Furthermore, individual differences in verbal comprehension have been shown to mediate performance on the Eyes Task (63), and this could potentially interact with age-related differences.

In summary, across multiple different theory of mind tasks, older adults typically show poorer performance than younger adults. While there is some evidence that their decreased performance may be due to declines in certain cognitive domains (e.g., working memory or executive function), studies

TABLE 2 | Cognitive empathy and aging: Review of findings.

Authors	Age group	Measurement	Difference	Findings
Bailey et al. (9)	YA, OA	EQ, RET	OA < YA	EQ-OA ↓ self-report on cognitive empathy, RET-OA ↓ on RET
Beadle et al. (10)	YA, OA	IRI	OA < YA	IRI-OA ↓self-report on cognitive empathy
Bottiroli et al. (48)	YA, OA (O-O, Y-O)	FPT, WMU	OA < YA	FPT-OA ↓ on cognitive ToM but not affective ToM; working memory updating mediated effect of age on cognitive ToM
Chen et al. (30)	YA, MA, OA	IRI, fMRI, FPS, CASI	OA vs YA/MA IRI PT: n.d.	No difference on IRI PT between OA/MA/YA
Duval et al. (49)	YA, MA, OA	RET, ToMS		ToMS - OA ↓, RET-OA ↓ on complex emotions
German & Hehman (50)	YA, OA	ToMS	OA < YA	OA with ↓ cognitive performance ↓ on ToMS with more executive functioning demands
Jarvis & Miller (51)	YA, OA	ToMS	OA < YA	OA ↓ on ToMS, episodic memory, and prospection; lowest score on cognitive ToMS
Khanjani et al. (31)	AD, YA, MA, OA	EQ, RET	OA > AD EQ cognitive empathy; OA < AD/YA/MA RET	OA > AD on self-report cognitive empathy; OA < AD/YA/MA on theory of mind task
Maylor et al. (52)	YA, OA (Y-O, O-O)	ToMS, WCST	O-O < YA/Y-O	ToMs-O-O/Y-O ↓ YA with memory load; O-O ↓ YA/Y-O without memory load
Moran et al. (53)	YA, OA	fMRI, FBT, MJT	OA < YA	OA ↓ on all tasks; OA ↓ dmPFC activity
Richter & Kunzmann (47)	YA, OA	EF	OA n.d. or < YA depending on context	OA ↓ on EA unless the task was motivationally relevant
Rosi et al. (41)	OA (Y-O, O-O)	ToMS (pre-test, training, post-test)	O-O < Y-O pre-tests	ToMS-O-O ↓ pre-test, both groups performed similar following training
Moore et al. (32)	OA	MET, AFM, GNG, N-back, fMRI	OA with higher cognitive empathy > insula during GNG task	OA with higher cognitive empathy > insula during GNG response inhibition task

Age groups: AD, adolescents; YA, young adults; MA, middle-aged adults; OA, older adults; Indicates older group split into a young–old and an old–old group; Y-O, young–old group; O-O, old–old group; EQ, Empathy Quotient; RET, Revised Eyes test; IRI, Interpersonal Reactivity Index; MRI, magnetic resonance imaging; fMRI, functional magnetic resonance imaging; FPT, Faux Pas test; PANAS, Positive and Negative Affect Schedule; CASI, cognitive abilities screening instrument; FPS, Facial Pain Scale; PT, perspective-taking; EA, empathic accuracy; GMV, gray matter volume; ToMS, theory of mind stories; FBT, false belief task; MJT, moral judgment task; EF, empathy films; WMU, Working Memory Updating Task; WCST, Wisconsin Card Sorting Task; MET, Multifaceted Empathy Test; AFM, Affective Facial Matching Test; GNG, Go/no-go Test; N-back, N-back test; R, right side; n.d., groups were not statistically different; ToM, theory of mind.

have shown that theory of mind is distinct from other measures of cognition. More research is needed to clarify the exact contribution of age-related changes in cognition to theory of mind performance in aging.

Perspective Taking

In general, older adults report lower perspective taking than younger adults, but there is still a lack of consensus in this area (3, 30, 31). Perspective taking is typically measured through the IRI (2) or the EQ (32), which are two self-report questionnaire measures of trait empathy that we have discussed in the sections on emotional empathy. The IRI has a perspective taking subscale and the EQ has a cognitive empathy subscale that measure an individual's general tendency to adopt the thoughts and feelings of others, in order to understand their emotions.

Four studies using the IRI, EQ, or other similar measures of trait empathy have shown that older adults report lower cognitive empathy than younger adults (3, 9, 10, 64), whereas one study found no difference (30), and another study showed higher levels in older adults (65). A task-based study measuring cognitive empathy through perspective taking in the context of stories included 20 younger adults (18–29 years) and 20 older adults (64–88 years; 66). The authors found that the older adult group used more positive words for perspective-taking than the younger adult group (66). In summary, there is growing evidence that older adults have lower cognitive empathy than younger adults, but not all studies show consistent results. Thus, more research is needed to assess cognitive empathy using both self-report and task-based measures. Furthermore, there is a need to conduct longitudinal studies examining cognitive empathy to disentangle generational from age-related effects.

Empathic Accuracy

Several studies have examined age-related differences in empathic accuracy (30, 46, 47, 67). One study utilized the FACES task (68) which included photos depicting facial expressions from which participants (younger and older couples) were asked to identify the emotion in the photo (46). On the FACES task, older adults performed more poorly than younger adults. They were also asked to identify the emotions of their partner (in addition to their own emotions) (46) and were asked to indicate whether their partner was in view (visible to them) when they were making their emotional judgments. The visibility of their partner did not impact the older adults' results, but for younger adults, they showed greater accuracy in predicting their partners' emotions when they were in view of them (46).

In another study of age-related differences in empathic accuracy, older adults showed greater performance on tasks that were relevant to them (47). This finding is supported by the socioemotional selectivity theory (39), which suggests that older adults prioritize situations that are emotionally meaningful to them. The authors concluded that the older adults' empathic accuracy performance in this situation may have less to do with their emotion recognition capacities, but instead relate to their prioritization of emotionally meaningful situations (47). In sum, this research suggests that, in general, older adults perform more poorly than younger adults on tests of empathic accuracy, except in cases where the information is emotionally relevant to them.

Conclusions about Aging and Cognitive Empathy

Overall, older adults tend to show reduced performance and report lower levels of cognitive empathy. In the theory of mind domain, older adults consistently show lower performance on most tasks assessing theory of mind across verbal and nonverbal measures. In terms of self-reported cognitive empathy, most studies show that older adults report lower levels than younger adults, but there a few exceptions. In the domain of empathic accuracy, there is evidence that older adults perform more poorly, except in cases where the information is highly age-relevant. In summary, the current consensus is that older adults have lower cognitive empathy than younger adults. However, future research is needed to clarify the role of other cognitive factors such as memory, attention, executive function, and verbal comprehension in age-related differences in cognitive empathy. Finally, more research is needed to elucidate the degree to which age-related differences in cognitive empathy can be consistently measured in the same individuals through behavioral versus self-report measures.

AGING AND EMPATHY: NEURAL MECHANISMS

Overview of Brain Networks Involved in Empathy

The emotional and cognitive components of empathy are thought to recruit largely distinct brain networks in younger adults (11–14). Studies examining the neural bases of empathy have used methods such as neuroimaging and lesion studies of patients with brain damage (13, 53, 69, 70). Key brain regions thought to be involved in emotional empathy include the anterior cingulate and insula, ventromedial prefrontal cortex, and amygdala (13, 69, 70). In contrast, cognitive empathy involves neural systems supporting self-projection into another person's mind, future thinking, and episodic memory. The key brain structures involved in cognitive empathy are thought to include medial prefrontal cortex, temporal pole, posterior superior temporal sulcus, and hippocampus (53).

Aging and Neural Correlates of Emotional Empathy

Little is known about the neural mechanisms supporting emotional empathy in aging. Three studies have investigated this question using fMRI (30, 32, 33). Moore and colleagues (33) conducted an exploratory study on the neural bases of empathy in 30 older adults (age: M = 79 years), but did not include a younger group comparison. For the purposes of this section, we focus on their investigation of emotional empathy, but they also assessed cognitive empathy in this study. In order to compare individuals with very high and very low empathy, they recruited from a previous registry based on empathy scores in the top decile and bottom decile of a self-report empathy questionnaire. Participants completed three tasks measuring cognitive and emotional processing including 1) affective facial matching task, 2) the Go/No-go task, and 3) the N-back Working Memory Task.

The empathy task was completed outside of the scanner and included the Multifaceted Empathy Test (71). In this empathy task, participants viewed photographs of people containing emotional content. Emotional empathy in response to these photos was measured by having participants rate their emotional response to each of the photos. Specifically, they responded to two questions: "How calm/aroused does this picture make you feel?" and "How concerned are you for this person?" and completed a rating scale that included "1 = calm/no concern to 9 = highly aroused/highly concerned." The first prompt was thought to assess arousal level, whereas the second prompt was thought to measure empathic concern. For the purposes of analysis, the authors chose to combine the arousal variable and the empathic concern variable in order to form a composite variable thought to be representative of emotional empathy (average of the z-scores).

The researchers had an *a priori* hypothesis that there would be involvement of the amygdala and insula for empathy. Thus, they used a region of interest (ROI) analysis for the bilateral amygdala and insula. The authors found that older adults with higher levels of emotional empathy outside the scanner on the Multifaceted Empathy Test showed greater deactivation in both the bilateral amygdala and the right insula while completing the N-back task (the measure of working memory). This suggests that older adults with higher emotional empathy in response to others may show decreased activation in regions relevant to emotional empathy (amygdala and insula) when experiencing greater working memory load. The authors suggest that, in this case, the amygdala may be playing a role in working memory and cognitive control and that individuals who experience high empathy may potentially experience more efficient emotion regulation in the same brain regions as those that are important for working memory.

There are some key methodological differences between the Moore and colleagues study (32) and other studies examining the neural bases of emotional empathy in aging. Specifically, because the empathy task was not conducted in the scanner, direct conclusions about the relationship between neural activations and empathic processes cannot be made. Furthermore, this study only includes an older group, and thus conclusions about age-related differences cannot be determined. In addition, this study employs a region of interest approach, and therefore the specificity of these brain regions for empathy cannot be determined. Finally, the completion of different cognitive and emotional tasks in the scanner adds further complexity to the interpretation of the findings. In this context, the finding is that older adults with higher emotional empathy on the task outside the scanner show decreased activation in empathy areas when experiencing greater working memory load. This would suggest that during a cognitive task targeted to engage brain networks associated with working memory, individuals who have higher empathy may be less likely to recruit brain regions typically implicated in emotion and empathy, such as the amygdala and insula. However, because the empathy task did not occur in the scanner, we cannot make specific conclusions about the role of these regions for empathy or comment on age-related differences.

In another study by Riva and colleagues, the researchers investigated female participants of three different age groups. The age groups included 28 adolescents (age: M = 15.7), 32 young adults (age: M = 24.5), and 28 older adults (age: M = 63). The study focused on the neural bases of age-related differences for empathy for physical touch. There were two main conditions in the fMRI task: 1) self: individual experienced stroking by an object that felt either unpleasant, pleasant, or neutral; and 2) other: this process occurred to another individual (actually a confederate), rather than to them. They were instructed to "empathize with the other participant by vividly imagining her feelings" (33). After each condition, the participants rated their own feelings (self condition) and that of the other person (other condition) on a scale ranging from "−10 (very unpleasant) to +10 (very pleasant)." They also assessed theory of mind using the Frith-Happé animation task (72).

For the fMRI results, they found differences in the empathy condition between older and younger adults. They conducted a categorical analysis using ANOVAs that compared the three groups and the brain activity in response to unpleasant touch versus neutral (self), unpleasant touch versus neutral (other), pleasant touch versus neutral (self), and pleasant touch versus neutral (other). Specifically, they found that older adults showed lower activity in the right anterior insula (AI) than younger adults for the empathy for unpleasant and pleasant touch. The researchers then investigated the degree to which performance on the theory of mind task explained variance in the neuroimaging results. To assess this, they included theory of mind performance as a covariate in their ANOVA analyses and found that the results did not significantly change. It could be that theory of mind is not required for processing less complex levels of emotional empathy related to touch, but may be required for more complex interpretations of others' emotional pain as found using empathy inductions that involve stories.

Only one neuroimaging study has used a standard empathy neuroimaging task to compare older to younger adults and has included both males and females (30). This study included three participant groups: 1) 22 younger (age: M = 23.4), 2) 22 middle-aged (age: M = 43.7), and 3) 21 older adults (age: M = 69.4). Participants were asked to passively view images of hands and feet either in pain or not in pain, but the rest of the body, including the face, was not shown). There were four conditions: 1) Solo pain (SP): one person is present in the image and the pain is caused by accident (e.g., slamming one's finger in a car door), 2) Solo no pain (SN): one person is present in a situation that does not cause pain (e.g., opening a door); 3) Dyad pain (DP): one person is in pain that was caused by another person (e.g., one person slamming the door on another person's finger); 4) Dyad no pain (DN): two individuals interact but neither individual experiences pain (e.g., opening a door near another person's arm). Emotional empathy was computed by comparing "[(SP + DP) − (SN + DN)]." This task is a well-established measure to assess emotional empathy for pain, and the stimuli have been used in previous studies (73–75).

Consistent with the Riva and colleagues study (33), Chen and colleagues found that older adults showed less activity than younger adults in the right AI in response to empathizing with others' physical pain and that greater averseness to others' pain was positively associated with activity in the anterior mid-cingulate cortex. These findings are consistent with two brain regions that have been implicated in the experience of empathy towards the pain of others in studies of younger adults, the AI and anterior cingulate (12, 76–79).

Overall, these studies have shown that in response to emotional empathy, older adults show reduced activity in regions typically associated with emotional empathy in younger adults (e.g., anterior cingulate and insula), despite behavioral reports of either intact or higher emotional empathy in older adults. More research is needed to characterize the mechanisms by which intact or greater emotional empathy in older than younger adults is linked to reduced activity in key emotional empathy regions. Furthermore, the methods used to assess the neural bases of emotional empathy in aging vary widely between the three studies. For instance, one study focused on older adults (with no younger group comparison), and one study included only females. Recommendations for future research include assessment of the neural bases of emotional empathy in aging through multiple, standard tests of emotional empathy, a larger sample of both women and men, and a comparison to a younger sample.

Aging and Neural Correlates of Cognitive Empathy

There are a growing number of studies on the neural bases of age-related differences in cognitive empathy, and in general, these studies find reduced brain activity in older adults versus younger adults in key regions implicated in cognitive empathy processes in younger adults (53); however, there are some exceptions. A study by Moran and colleagues examined age-related neural differences in cognitive empathy across three tasks in younger and older adults (53). These tasks fall under the theory of mind subdomain of cognitive empathy and included an "animate movement" task, a "moral judgment" task, and a "false belief task" (53). In the animate movement task, individuals were asked to infer mental states by viewing shapes interacting in either a social or nonsocial manner (80). In the second task (the moral judgment task), participants inferred the thoughts and feelings of others in stories where the target individual behaved in ways that could be considered moral or immoral (81). Finally, the third task was the false belief task (59) that we described in the psychological mechanisms of cognitive empathy section. Briefly, in the false belief task, participants read stories about others who have a false mental belief (false belief condition) or read about a physical image that is no longer accurate (physical condition). The primary findings of this study were that across the three tasks, older adults had reduced brain activity compared to younger adults in the dorsomedial prefrontal cortex (dmPFC), which is thought to be a key region in the cognitive empathy network in younger adults (53).

Moore and colleagues (32) also measured the neural bases of cognitive empathy in aging. (This study was described in detail in the neural bases of aging-related changes in the emotional empathy section). As a reminder, participants completed a response inhibition task (Go/No-go task) while undergoing fMRI, in addition to other tasks measuring cognitive and emotional function. Cognitive empathy was assessed outside the scanner using the Multifaceted Empathy Test (71), and measures were correlated with brain activity in response to the cognitive/emotional tasks conducted in the scanner. Specifically, cognitive empathy was measured by having participants make mental state judgements about each individual they viewed in the photos. They chose between four different emotions for each photo and they were provided with feedback as to the accuracy of their response immediately after they selected their response. The authors found a relationship between brain activity in response to the Go/No-go task and levels of cognitive empathy measured outside the scanner. Specifically, older adults with higher cognitive empathy (as measured by the Multifaceted Empathy Test) had greater insula activation than older adults with lower cognitive empathy. The findings from this study suggest that within the older adult group, there may be variation in levels of cognitive empathy and those with higher cognitive empathy may show greater activity in brain regions associated with empathy. However, further research may investigate whether a similar response will be found if the empathy task is conducted inside the scanner.

In summary, a small number of studies have investigated age-related differences in the neural bases of cognitive empathy (32, 53). The study by Moran and colleagues demonstrated reduced brain activity in the dorsomedial prefrontal cortex in older than in younger adults across three tasks measuring theory of mind. The Moore and colleagues study found that higher cognitive empathy performance outside the scanner was associated with greater activity in the insula than younger adults in response to a Go/No-go task. Because cognitive empathy also involves the domains of perspective taking and empathic accuracy, more research is needed to determine whether age-related differences in neural activity extend to these domains. Furthermore, more studies are needed to confirm these findings in larger samples and with a variety of cognitive empathy measures. Finally, additional research is needed on both task-based studies of the neural bases of empathy, in addition to studies assessing resting state functional connectivity and structural differences.

Summary of Imaging Findings and Future Research

The study of the neural bases of empathy in aging is still in its infancy. While there are a growing number of studies on this topic, more research is needed before there is conclusive evidence for age-related neural differences in the cognitive or emotional components of empathy. For the emotional component of empathy, the small number of studies on this topic point to a decrease in brain activity in older adults in key regions typically involved in emotional empathy. This is surprising given that behaviorally older adults consistently show similar or higher levels of emotional empathy than younger adults. Furthermore, more research is needed that uses gold standard tasks designed to specifically assess empathy that have also been measured in younger adults. Brain imaging studies examining cognitive empathy point to decreased activity in the dorsomedial prefrontal cortex in older adults versus younger adults during theory of mind tasks. Yet, little is known about whether this extends to other domains of cognitive empathy, such as perspective taking or empathic accuracy. Across both cognitive and emotional empathy, studies using standard empathy tasks are needed that assess the multiple subdomains of empathy. Finally, to further elucidate both functional and structural age-related differences in empathy, more research is needed using multi-modal imaging techniques, with larger, more generalizable samples including men and women, and younger and older adults.

PRELIMINARY CONCLUSIONS: STATE OF THE RESEARCH ON EMPATHY IN AGING

The question of how aging impacts empathy has important implications for public health because reduced empathy has been associated with greater loneliness, depression, and poorer relationship satisfaction. Socioemotional selectivity theory (39) highlights the importance of emotional meaning for older adults, and this typically takes the form of spending time with close others. Thus, if older adults experience decreases in empathy, this could have a significant, negative impact on their well-being.

Research studies focused on age-related psychological differences in empathy suggest that older adults have lower cognitive empathy and preserved or increased emotional empathy; however, there are exceptions. There is growing evidence that older adults show increased prosocial behavior towards others in the form of monetary donation in response to an empathic context. Overall, the lack of consistent results in the behavioral literature may be due to the large variation in methods used to measure empathy, inconsistent sample sizes, unequal numbers of men and women, and reduced capacity to generalize across cultures.

Only a small number of studies have examined the neural bases of empathy in aging. Across both the cognitive and emotional components of empathy, older adults show decreases in key regions thought to be involved in empathy relative to younger adults. In the cognitive component, older adults show reduced activity in the dmPFC relative to younger adults. For emotional empathy, older adults show reduced activity in the anterior cingulate and insula. The findings for emotional empathy are counterintuitive because, behaviorally, older adults show similar or higher levels of emotional empathy to younger adults. More research is needed with standard empathy tasks to further characterize the neural bases of empathy in aging.

The mixed findings in the literature on empathy and aging may be partially explained by the large variation in behavioral and neuroimaging methods used to study empathy. There are a few key areas where more research is needed. One, greater consistency is needed across studies to employ gold standard tasks assessing cognitive and emotional empathy to allow for direct comparisons across studies. Two, there is significant variability in how the age groups are defined, and thus consistent age ranges across studies are needed. Three, studies should be powered to compare sex differences in addition to age differences, as key sex differences in empathy have been reported in studies of younger adults. Four, both structural and functional neuroimaging techniques are needed to further characterize the neural bases of empathy. Five, more research is needed to better understand how culture may impact age-related differences in empathy. Finally, more research is needed to investigate this question longitudinally, in particular in task-based studies of empathy to tease apart cohort effects versus actual age-related differences. Taken together, the study of age-related differences in empathy is a growing area of research that has important implications for older adult well-being and health.

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JB contributed to the conceptualization and theoretical discussion within the paper and wrote and edited the paper. CV provided feedback on the conceptualization of the paper and wrote and edited the paper.

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Empathy in Females With Autism Spectrum Disorder

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Objective: Despite the fact that autism spectrum disorder (ASD) is a common psychiatric diagnosis, knowledge about the special behavioral and neurobiological female phenotype is still scarce. The present study aimed to investigate neural correlates of empathy for physical and social pain and to assess the impact of egocentric perspective taking on social pain empathy in complex social situations in women and girls with ASD.

Methods: Nine female individuals with high functioning ASD were compared to nine matched peers without ASD during two functional magnetic resonance imaging (fMRI) experiments, examining empathy for physical and social pain using well-established paradigms. Participants viewed multiple pictorial stimuli depicting a social target in either physically painful or socially unpleasant situations. In the social situations, the participant either shared the social target's knowledge about the inappropriateness of the situation (observed social target is aware about the embarrassment of the situation; e.g., tripping in public) or not (observed social target is unaware about the embarrassment of the situation; e.g., open zipper).

Results: Females with ASD did not rate the physical pain stimuli differently from non-clinical controls. Social pain situations, however, posed a greater challenge to females with ASD: For non-shared knowledge situations, females with ASD rated the social target's embarrassment as more intense. Thus, compared to non-clinical controls, females with ASD had a stronger egocentric perspective of the situation rather than sharing the social target's perspective. On the neural systems level, both groups showed activation of areas of the so-called empathy network that was attenuated in females with ASD during empathy for physical and social pain with a particular reduction in insula activation.

Conclusion: Females with high functioning ASD are able to share another person's physical or social pain on the neural systems level. However, hypoactivation of the anterior insula in contrast to individuals without ASD suggests that they are less able to rely on their shared representations of emotions along with difficulties to take over a person's perspective and to make a clear distinction between their own and someone else's experience of embarrassment.

Keywords: female ASD, empathy, social pain, vicarious embarrassment, fMRI

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INTRODUCTION

Autism spectrum disorder (ASD) is a pervasive neurodevelopmental disorder involving impairments in two core domains: social interaction, including verbal as well as non-verbal communication, and stereotyped, repetitive behaviors and interests (1). Despite the fact that ASD is a common psychiatric diagnosis, with an onset within the first years of life and very early impairments of social attention and reciprocity (2), knowledge about the special behavioral and neurobiological female phenotype of ASD is still scarce. One of the reasons for this imbalance in the literature is the predominance of male ASD cases which is a consistent epidemiological finding. The male-to-female ratio averages at 4–5:1 but increases to about 10:1 in cases of high functioning ASD and decreases to 2:1 in affected individuals with moderate-to-severe intellectual disability (3, 4). Current estimates range from 3:1 to 4:1 across the autism spectrum, but the reason for the consistently observed discrepancy in the sex ratio remains unclear (5). Although neuroanatomical and neurofunctional differences between sexes/genders have been described (6), research on the female peculiarities is still insufficient and results are often inconsistent. One reason for this lack of knowledge about the female ASD phenotype is the striking underrepresentation of females with ASD in neuroimaging research in general with an overall sex ratio of 8:1 (male:female). A recent meta-analysis of 329 articles revealed that only 1 out of 15 functional MRI studies actually included females with ASD (7). Knowledge about relations between biological as well as anatomical factors and the psychosocial impairments in ASD is therefore mainly based on the high functioning male phenotype of ASD. It has been hypothesized that specific aspects of the neuroanatomy underlying ASD may represent phenotypic diversity in brain structure that is specific for males, which could make females more resilient to autism-related social deficits (8). A recent study, however, could not find support for this claim (9), and at present, there might just not be sufficient data available to obtain robust evidence in support of this model. Further, research in mouse models for neurodevelopmental disorders suggests specific impairments in reward-directed learning only in male mice but not in females (10). The relevance of such efforts and generalizability to human social cognition and the ASD phenotype, however, remains unclear. We believe that further research is definitely needed to specify sex/gender differences related to ASD and social cognition. The lack of research on the female phenotype challenges the generalizability of the notion that alterations of processes in the domain of social cognition, such as emotion recognition, empathy, and theory of mind, could explain the observed peculiarities in social interactions in ASD. Here, we take a closer look at the empathic response of girls and young women with ASD to physically (painful) and socially (embarrassing) threatening situations of others. Thereby, we aim to broaden our perspective on the ASD phenotypes and to test specific assumptions about how the complexity of the social situation modulates the empathic response in females with ASD.

One core domain of difficulties in individuals affected by ASD is the domain of social cognition. Processes such as emotion recognition, empathy, and theory of mind (ToM) have been found to be severely disturbed (7). Impairments in these domains impede individuals with ASD to engage in social interaction (11). Many behavioral and neurofunctional studies (with mostly male participants) have demonstrated deviant patterns of empathy-related information processing in individuals with ASD along with diminished activation of brain areas involved in ToM and empathy, namely, inferior frontal gyrus, medial prefrontal cortex, and anterior insula (12–14). It has been argued that individuals with ASD show deficits in sharing another person's affective state (15, 16). However, such deficits might primarily surface in more complex social situations, in which contextual demands such as knowledge about social norms, expectations of the social environment, and appraisals of the social target need to be dynamically integrated (13, 17, 18).

Sharing another person's physical pain or empathizing with another person in a socially unpleasant situation (e.g., social exclusion or embarrassment; experiences also referred to as social pain[1]) increases activations in brain regions that are also recruited during the first-hand experience of the same affective state (19, 23, 24). This observation leads to the assumption that we are able to understand others' emotions based on our own shared affective experiences. For example, when making sense of rather complex social faux pas situations that typically elicit a shared experience of embarrassment with another person, brain areas of the so-called mentalizing network ([medial prefrontal cortex (mPFC) temporal pole, and superior temporal sulcus (STS)]) as well as the anterior insula (AI) and the anterior cingulate cortex (ACC) are recruited (17, 23). A previous study of ours contrasting male participants with ASD to non-clinical controls found the AI, a part of the so-called empathy network typically recruited when sharing another's physical or social pain (17, 19, 24, 25), to be hypoactivated when experiencing embarrassment on behalf of others (13). However, when sharing another person's physical pain, male participants with ASD did not reveal diminished neural activation of the empathy network (13). One explanation for these findings is that faux pas tasks are more demanding and require the observer to integrate contextual information, as well as to take into account the social target's perspective. Specifically, when one's own knowledge about a situation fundamentally deviates from the social target's knowledge, adjusting the own view in order to make sense of the other person's thoughts and feelings is inherently challenging. Since people tend to use their own subjective perspective as an anchor, perspective taking is described as a time consuming and effortful process of adjusting one's initial view that often results in subjectively biased assumptions and subjectively imbued representations on the neural systems level (26, 27). The more complex a situation gets, the more likely the

[1] Negative affective experiences in response to socially unpleasant situations like social exclusion or embarrassment are considered a form of social pain (17, 19–22). The term of social pain has been established to emphasize the conceptual overlap of the distress and affective arousal of social rejection or embarrassment with physical pain. While physical pain is thought to signal a threat for the bodily integrity of the individual, the affective experiences in the domain of social pain are thought to serve a similar function, signaling threats to the social integrity of individuals that are being excluded from or judged negatively by their social group (17, 20).

own perspective remains egocentrically biased. While egocentric anchoring is thought to be a typical process when making sense of another person's thoughts and feelings, individuals with ASD have been described to show a particular and exaggerated form of egocentrism with clear difficulties to make use of embodied simulation strategies (28) and to overcome their egocentric perspective (29, 30). These difficulties are of specific relevance when people navigate complex social situations and make sense of others' mental and affective states—that might be distinct from the own experience—in order to adequately engage in social interactions. However, to date there is little knowledge on how females with ASD can adopt another person's perspective in socially complex situations eliciting empathy for social and physical pain.

With the current work, we therefore aimed to shed light on the peculiarities in empathy-related processes in females with ASD. In line with our previous findings in male adolescents with ASD, we hypothesized that females diagnosed with ASD would also show hypoactivations in brain areas involved in empathic processes in response to complex social situations associated with embarrassment on behalf of others (AI, ACC). Similarly, we did not expect females with ASD to differ from non-clinical controls when empathizing with another person's physical pain (13). Specifically, when the task requires inferring another person's affective state, whose knowledge about the situation is different from one's own knowledge, we expected to see pronounced egocentric biases in females diagnosed with ASD.

METHODS

Participants

The study was conducted in the specialized outpatient clinic for ASD at the University Hospital for Child and Adolescent Psychiatry, Psychotherapy and Psychosomatic Medicine in Marburg, Germany. The study was approved by the local ethics committee (Az 197/12). Written informed consent was obtained from all participants and parents in case the participants were underage. Female participants with ASD (F-ASD; $N = 9$) were recruited from our outpatient clinic as well as other clinics, and the age span within the F-ASD group ranged from 12.5 to 24.5 years (mean age of 18.7 years). All patients matched the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM IV) criteria for ASD, had a confirmed International Classification of Diseases, 10th Revision (ICD-10)diagnosis of Asperger syndrome ($n = 5$; F84.5, ICD-10) and/or atypical autism ($n = 4$; F84.1, ICD-10), and had undergone standardized diagnostic procedures with either Module 3 or Module 4 of the Autism Diagnostic Observation Schedule (ADOS) (31). If parental informants were available, the Autism Diagnostic Interview-Revised (ADI-R) (32) was administered. The mean verbal IQ was 112 as confirmed with the Wechsler Intelligence Scale for either adults (WAIS-IV) (33) or children (WISC-IV) (34). The age- and IQ-matched non-clinical control group (F-CG; $N = 9$) had a mean age of 19.9 (range, 13.9–25 years) and a mean verbal IQ of 113 (for additional information, see **Table 1**). Due to technical problems with the response box, behavioral ratings of one control participant had to be excluded from further analyses. All participants had normal or corrected-to-normal vision. F-CG and F-ASD differed significantly ($p = .015$) concerning the self-report evaluation of autistic symptoms as conducted with the Autism Spectrum-Quotient questionnaire (AQ) (35).

fMRI Paradigm and Stimuli

In two consecutive functional magnetic resonance imaging (fMRI) experiments, we induced empathy for physical pain (EPP) and empathy for social pain (ESP) with stimuli and paradigms that have been previously described and similarly implemented in a study with male participants with a confirmed ASD diagnosis (13, 17). To investigate the neural correlates of EPP, participants viewed 28 color photographs depicting another person's left or right hand or foot from a first-person perspective in either painful [e.g., foot on a log with an axe landing on top of the big toe; physical pain (PP); 14 stimuli] or non-painful, neutral control situations [e.g., foot on a log with the axe hitting

TABLE 1 | Sample characteristics.

	F-ASD (*N* = 9)		F-CG (*N* = 9)		p	z
	Mean	SD	Mean	SD	(Mann-Whitney *U* test)	
Age	18;7	4;9	19;9	3;6	.667	0.486
Verbal-IQ	112.0	15.0	113.0	9.0	.797	0.265
AQ	22.6	10.1	9.8	2.5	.015	2.368
EQ	111.7	14.8	118.4	6.5	.277	1.157
ADOS-SA	7.7	3.1				
ADOS-RRB	1.0	0.9				
ADOS Comparison Score	4.9	2.1				
ADI-R Com	6.5	2.7				
ADI-R Soc	7.3	4.5				
ADI-R Stereo	2.7	2.0				

AQ, Autism Spectrum Quotient; EQ, Empathy Quotient; ADOS, Autism Diagnostic Observation Schedule; ADOS-SA, ADOS Social Affect Score; ADOS-RRB, ADOS Repetitive and Restricted Behavior Score; ADOS Comparison, ADOS Comparison Score; ADI-R, Autism Diagnostic Interview-Revised; ADI-R Com, ADI-R Communication Score; ADI-R Soc, ADI-R Social Interaction Score; ADI-R Stereo, ADI-R Stereotyped Behavior Score. F-ASD, female autism spectrum disorder group; F-CG, female non-clinical control group; SD, standard deviation; p-values and z-values refer to the Mann-Whitney U test comparing the two groups against each other.

next to it in the wood; no pain (NP); 14 stimuli; see **Figure 1**]. The photographs were chosen from a pool of 56 validated stimuli (13, 36). Stimuli were presented for 4.5 s. Subsequently, a fixation cross on a blank screen was presented for 1.5 s. Participants were then asked to respond within 3 s to the question "How strong is the pain of the observed person in this moment?" and rate the intensity of the depicted person's pain experience (from 1 "not at all" to 5 "very strong") on a five-point scale. Following the rating phase, a fixation cross was presented for an average of 6.1 s. Stimuli were presented in a fix pseudo-randomized order with no more than two stimuli from the same condition following each other. In total, the experiment lasted approximately 7 min.

To induce ESP, participants were confronted with 30 validated hand-drawn sketches of social situations displaying a protagonist in either socially undesirable (20 sketches) or neutral public scenarios (10 sketches). Each sketch was explained with a written caption, which introduced the context (e.g., "You are at the theatre") and the state of the person serving as the social target (e.g., "The actor forgets his lines during the play…"). Ten of the 20 social pain sketches illustrated scenarios in which the social target was aware of the predicament and thus could be perceived to be emotionally engaged and embarrassed in the situation. Here, participants shared the knowledge of the faux pas and the experience of embarrassment with the social target

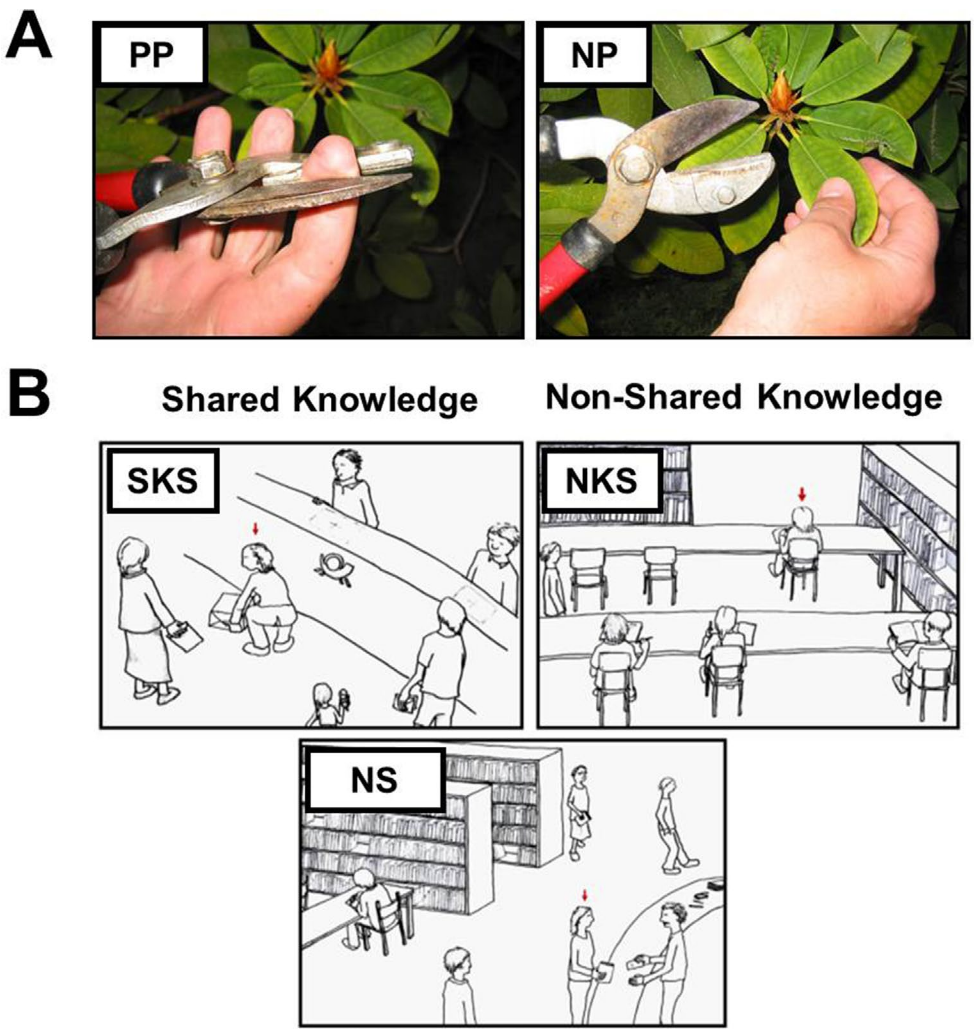

FIGURE 1 | Stimuli used in the functional magnetic resonance imaging (fMRI)experiments. **(A)** Depiction of one example stimulus of the experimental paradigm to induce empathy for physical pain. The physical pain situation (PP) is presented on the left and the neutral, no-pain control situation on the right side [NP; stimuli were taken from Jackson et al. (36)]. **(B)** The situations eliciting empathy for social pain varied concerning the social target's awareness about the inappropriateness of the situation and thus regarding the shared knowledge and affective experience of the observer and the social target. Ten situations depicted situations with shared knowledge about the inappropriateness of the situation (SKS) eliciting shared affect with the social target, e.g., sharing embarrassment with a person who's pants rip while she bends down to lift a package, and 10 situations depicted a social target unaware about the faux pas, thus not sharing the same knowledge with the observer [non-shared knowledge situation (NKS)], e.g., a person whose pants unknowingly slipped down while she is sitting on a chair. Ten sketches displayed non-norm-violating control situations [neutral control situations (NS)]. Stimuli were presented together with two sentences describing the situation below the sketches (e.g., You are at a library: you observe a women giving back a book she borrowed).

[shared knowledge situation (SKS); e.g., "You are at the grocery store. A person at the cashier realizes that she cannot pay for her purchase"]. The other 10 social pain sketches depicted situations in which the social target was unaware of the social norm violation and therefore would not notice that his or her social integrity was at stake. However, participants would notice the faux pas from an observer's perspective [non-shared knowledge situation (NKS); e.g., "You are on a train. A passenger walks by with an open pants zipper"]. Thus, the observer would be aware that the social target him- or herself does not experience the unpleasantness of the situation, but could nevertheless experience strong states of embarrassment on behalf of the social target (23). Importantly, these two conditions differently vary the impact of egocentricity in the judgement of the situation; when sharing the knowledge in the SKS condition, there is no need to distinguish the other's perspective from one's own, while in the NKS condition, the observer's knowledge could impact the evaluation of the affective experience in the other, if it is egocentrically biased. This notion originates from classic developmental psychological research claiming that young children are egocentric to the degree that they are only capable of contemplating the world from their egocentric perspective (37–39). It is the NKS condition which requires participants to abstract from their egocentric viewpoint (i.e., an open zipper is always embarrassing) but take the perspective of the target person (i.e., being unaware of the open zipper and thus not feeling embarrassed). Finally, 10 neutral control situations depicted comparable social scenarios lacking the faux pas component [neutral control situations (NS); e.g., "You are at a post office. At the neighboring counter you observe a man who is posting a package"]. The social targets were described as male (i.e., a man) in half of the situations or female (i.e., a woman) in the other half in the sentences below the picture. Participants were instructed to attend to each sketch for 12 s. Stimulus presentation was followed by a blank screen for 1 s and a 3-s rating period during which participants were asked to indicate the social target's embarrassment on a five-point scale (from 1 "not at all" to 5 "very strong") in response to the question: "How embarrassing is the situation for the observed person in this moment?". The stimuli were presented with an inter-trial interval of 8 s in a pseudo-randomized order, which was the same for every participant, with no more than two stimuli from the same condition in a row. The total duration of the experiment was approximately 12 min.

Before entering the MRI, participants received careful instructions about the experimental procedure using two example situations that were not displayed again during the MRI session. In the scanner, a response box was attached to the right leg and the participants' fingers were placed in the correct position. Stimuli were presented on an LCD screen with Presentation 12.1 software package (Neurobehavioral Systems, Albany, CA, USA).

Data Acquisition and Analysis

All participants were scanned at 3T (Siemens Trio, Erlangen, Germany) with 36 near-axial slices and a distance factor of 10% providing whole-brain coverage. An echo planar imaging (EPI) sequence was used for acquisition of functional volumes [repetition time (TR) = 2.2s, echo time (TE) = 30 ms, flip angle = 90°, slice thickness = 3 mm, field of view (FoV) = 192, matrix 64 × 64 voxels, voxel size 3 × 3 × 3 mm]. Overall, we obtained 204 volumes for EPP and 340 volumes for ESP. The first seven (EPP) and four (ESP) volumes of each session were discarded from further analyses. To rule out potential anatomical abnormalities, we acquired high-resolution images with a T1-weighed scan comprising the whole brain, employing a magnetization-prepared rapid gradient-echo sequence (3d MP-RAGE) in sagittal plane (176 slices, TR = 1.9 s, TE = 2.52 ms, flip angle = 9°, ascending slices, slice thickness = 1 mm, FoV = 256 mm, 50% gap, matrix 256 × 256 voxels, voxel size 1 × 1 × 1 mm).

Data were analyzed using SPM8 (www.fil.ion.ucl.ac.uk/spm). For each session, brain volumes were corrected for slice timing and head motion and spatially normalized to the standard EPI template of the Montreal Neurological Institute (MNI) using linear and nonlinear transformations of the mean EPI images of each time session. The normalized volumes were resliced with a voxel size of 2 × 2 × 2 mm, smoothed with an 8-mm full-width half-maximum isotropic Gaussian kernel, and high-pass filtered at 1/192 Hz for the EPP and 1/256 for the ESP task.

Analysis of Empathy for Physical Pain Data

All behavioral data were analyzed with PASW Statistics for Windows, Version 18.0 (SPSS Inc. Released 2009). Ratings of the social targets' pain in the EPP paradigm were analyzed using repeated-measures analyses of variance (ANOVAs). For the analysis of pain ratings, a 2 × 2 ANOVA was implemented with Condition (PP, NP) as within-subject factor and Group (F-CG and F-ASD) as between-subject factor.

On the neural systems level a fixed-effects general linear model (GLM) was calculated at the within-subject level for EPP in order to test for activation differences. The model for EPP included three regressors modeling the hemodynamic responses to the PP, the NP condition, and the rating period with the aforementioned stimulus durations. The PP events were additionally weighted with the corresponding rating response to align our analyses to previous experiments (13, 17). Six regressors modeling head movement parameters were introduced to account for noise. At the group level a flexible factorial design was implemented with condition as a repeated-measures factor (included β-maps for the PP and NP condition) and group as a between-subject factor (F-CG and F-ASD group). Previous results specifically stress areas of the so-called empathy network, the AI and the ACC, as key regions in processing EPP and ESP. Functional regions of interest (ROIs) were defined by deriving activation maps from previous studies using the same stimuli in samples of non-clinical control subjects. The physical pain ROIs were defined according to a previous study of our group assessing EPP contrasting PP-NP (13): ACC, left AI, right AI, and the somatosensory cortex. All ROI analyses were conducted using the small-volume correction as implemented in SPM8, applying voxel based family-wise-error (FWE) correction. Additionally, whole-brain analyses were conducted to assess activations outside of our ROIs, FWE corrected for the whole brain.

Analysis of Empathy for Social Pain Data

On the behavioral level, ratings of the social targets' embarrassment in the ESP paradigms were analyzed using a repeated 2 × 3 ANOVA the Condition (SKS, NKS, NS) as within-subject factor and Group (F-CG, F-ASD) as between-subject factor.

On the neural systems level, as for the EPP task, a fixed-effects GLM was calculated at the within-subject level. For the ESP, the first-level model included one regressor for the SKS, one for the NKS, one for the NS, and another regressor for the rating period. The trials in the SKS and NKS condition were additionally weighted with the corresponding rating response similar to previous approaches (see above), and six additional regressors modeling head movement parameters were included to account for noise. Beta-maps for the SKS, NKS, and NS condition for the F-CG and F-ASD group were analyzed at the group level using a flexible factorial design with condition as a repeated-measures factor and group as a between-subject factor. Functional ROIs for ESP were also defined according to activation maps of a previous study of our group assessing embarrassment on behalf of others with the respective contrast social pain vs. NS in a sample of subjects without ASD (23): ACC, left AI, and thalamus. Corrections for multiple comparisons and whole-brain analyses were conducted as described above for the EPP task. All anatomical coordinates are reported in MNI standard space.

RESULTS

Empathy for Physical Pain

On the behavioral level, participants in both groups rated that the social target experienced more pain in the PP situations as compared the NP situations as indicated by the main effect of Condition ($F_{(1,16)}$ = 513.08, p < .001). F-CG and F-ASD both rated the protagonist's physical pain as more intense for PP compared to NP (see **Table 2** for comparisons), and the general intensity level of pain ratings as well as the responsiveness to PP vs. NP did not differ between groups (main effect of Group: $F_{(1,16)}$ = 0.18, p = .679; Group × Condition interaction: $F_{(1,16)}$ = 1.43, p = .249).

On the neural systems level, participants of both groups showed increased activations of the ACC during PP compared to NP (F-CG at −2, 26, 46, $t_{(32)}$ = 6.44, p < .001, k = 587; F-ASD at −6, 18, 36, $t_{(32)}$ = 5.12, p = .002, k = 407; see **Figure 2A** and **Table 3**). The F-CG group additionally showed increased activations in the left AI (−36, 18, 0, $t_{(32)}$ = 5.91, p < .001, k = 156), right AI (42, 18, −4, $t_{(32)}$ = 4.59, p = .001, k = 110), and left somatosensory cortex (−58, −28, 36, $t_{(32)}$ = 3.77, p = .013, k = 42). Whole-brain analysis revealed an additional activation of the middle frontal gyrus in response to PP vs. NP of the F-CG group (see **Supplementary Table S1**). Comparing the F-ASD group to the F-CG group, the F-ASD showed significantly lower activation of the left AI (−34, 20, 4, $t_{(32)}$ = 3.28, p = .024, k = 16) and right AI (34, 24, 0, $t_{(32)}$ = 3.12, p = .033, k = 1) during PP vs. NP (see **Figure 2B**).

Empathy for Social Pain

Behavioral results showed a significant main effect of Condition for the ratings of the social targets' embarrassment ($F_{(2,30)}$ = 128.36, p < .001). The social targets' embarrassment was rated stronger during SKS and NKS compared to NS (see **Figure 3A** and **Table 2** for detailed comparisons). However, as expected, ratings of the social targets' experience of embarrassment were decreased for NKS, during which the social target was unaware of the ongoing norm violation, and thus not experiencing embarrassment as compared to SKS. Separate t-tests for both groups showed that F-CG and F-ASD rated the social target's embarrassment lower in NKS vs. SKS situations indicating an adjustment of their egocentric perspective towards the social target's affective state. There was a main effect of Group ($F_{(1,15)}$ = 21.32, p < .001) and a significant interaction of Group and Condition ($F_{(1,15)}$ = 9.32, p = .001). This indicates that F-ASD rated the social target's embarrassment higher than F-CG, particularly in the NKS compared to the SKS condition ($F_{(1,15)}$ = 7.41, p = .016; F-ASD (SKS vs. NKS) vs. F-CG (SKS vs. NKS); significant for Bonferroni corrected p-level: p = .05/3 = .017) pointing towards a stronger egocentric bias in F-ASD as compared to F-CG.

On the neural level, embarrassment situations compared to NS were associated with increased activations within the ACC and AI network. Contrasting SKS and NKS vs. NS [(SKS − NS) + (NKS − NS)] resulted in increased activations of the left ACC in both groups (F-CG at −6, 28, 42, $t_{(48)}$ = 5.76, p < .001, k = 222; F-ASD at −8, 18, 40, $t_{(48)}$ = 4.11, p = .005, k = 25; see also **Table 3**). The left AI (−28, 24, 0, $t_{(48)}$ = 5.49, p < .001, k = 33) and thalamus (−2, −6, 8, $t_{(48)}$ = 4.32, p < .001, k = 18) showed increased activation in the F-CG group (see **Figure 2C**). For the same

TABLE 2 | Behavioral results.

Contrast	Overall (N = 17)		F-CG (N = 8)		F-ASD (N = 9)	
	F	p	$t(7)$	p	$t(8)$	p
Empathy for physical pain						
PP vs. NP	513.08	<.001	23.07	<.001	12.53	<.001
Empathy for social pain						
NS vs. SKS	648.30	<.001	20.17	<.001	17.08	<.001
NS vs. NKS	44.83	<.001	2.59	.036	5.63	<.001
SKS vs. NKS	53.33	<.001	7.93	<.001	3.03	.016

Results of the contrasts between conditions following the overall ANOVAs across groups and separate t-tests within each of the experimental groups for the empathy for physical pain task and empathy for social pain task. F-CG, non-clinical control group; F-ASD, autism spectrum disorder group; PP, physical pain situations; NP, no-pain, neutral control stimuli; NS, neutral control situations; SKS, shared knowledge situations (see Methods for description); NKS, non-shared knowledge situations; EPP degrees of freedom: $F_{(1,16)}$*; ESP degrees of freedom:* $F_{(1,15)}$*.*

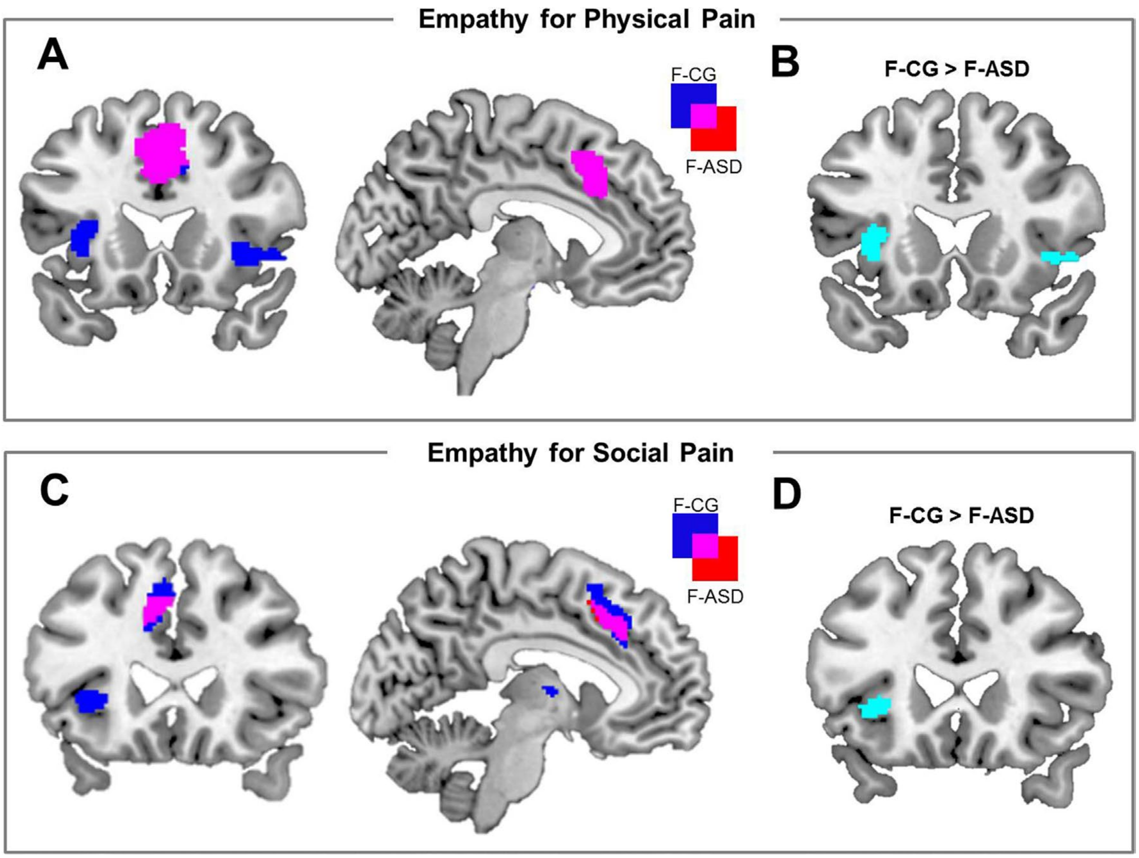

FIGURE 2 | Neural activation associated with empathy for physical pain and empathy for social pain and activation differences between groups. **(A)** Brain activation for the main effect of physical pain empathy [physical pain (PP) – no-pain (NP)] for females with autism spectrum disorders (F-ASD) and non-clinical controls (F-CG). **(B)** Reduced activation of the bilateral anterior insula in response to PP vs. NP in the F-ASD group as compared to F-CG. **(C)** Neural activation for the main effect of social pain empathy {[shared knowledge situations (SKS) – neutral control situations (NS)] + (non-shared knowledge situations (NKS) – NS)} for F-ASD and F-CG. **(D)** Reduced activation of the left anterior insula in response to social pain empathy [(SKS – NS) + (NKS – NS)] in the F-ASD group as compared to F-CG; all statistics are FWE-corrected within ROIs as described in the Methods section; results are presented uncorrected ($p < .05$; $T > 1.69$ for EPP and $T > 1.69$ for ESP) for displaying purposes within ROIs.

contrast, whole-brain analysis revealed additional activation of the left posterior medial frontal cortex in the F-CG group (see **Supplementary Table S1**). For both groups, the activation of the AI was decreased during NKS compared to SKS (F-CG at −28, 24, 2, $t_{(48)} = 2.83$, $p = .030$, $k = 3$; F-ASD at −40, 24, 4, $t_{(48)} = 2.72$, $p = .039$, $k = 2$; see **Figure 3B**), as well as activation of the thalamus (F-CG at −4, −6, 6, $t_{(48)} = 3.76$, $p = .002$, $k = 23$; F-ASD at −6, −8, 8, $t_{(48)} = 3.25$, $p = .006$, $k = 16$). Whole-brain analysis also revealed decreased activation of the ACC during NKS compared to SKS in the F-ASD group (see **Supplementary Table S1**).

When comparing the F-ASD group to the F-CG group, activation of the left AI was significantly lower when contrasting SKS and NKS vs. NS (−28, 24, 0, $t_{(48)} = 3.73$, $p = .003$, $k = 22$; see **Figure 2D**). This effect was present for SKS vs. NS (−28, 24, 0, $t_{(48)} = 3.23$, $p = .012$, $k = 9$) and also NKS vs. NS (−28, 24, 0, $t_{(48)} = 3.30$, $p = .010$, $k = 23$), replicating previous findings of decreased responses during embarrassment on behalf of others in ASD. Unlike the behavioural data, fMRI data showed no significant difference between groups when contrasting SKS vs. NKS within the regions of interest or in the whole-brain analysis (even with more lenient threshold of $p = .001$, uncorrected).

DISCUSSION

The current study targeted the female variant of ASD: by using ecologically valid and emotionally complex social scenes, we aimed to characterize behavioral and neurobiological markers of empathy for physical and social pain in nine females with ASD compared to a carefully matched control group. To our knowledge, this is the first study investigating empathy for physical and social pain in this way in a group of female participants affected by ASD. A general lack of research on the female phenotype poses a challenge to the generalizability of the notion that alterations of processes in the domain of social cognition, such as emotion recognition, empathy, and theory of mind, could explain the observed peculiarities in social interactions in ASD. With the current study, we aimed to broaden our perspective on the ASD

TABLE 3 | Regions of interest (ROIs) analyses.

Brain region		Side	Cluster size	MNI coordinates			*T*	*p*	*p*FWE
				x	y	z			
Empathy for physical pain									
PP > NP									
F-CG									
	Anterior cingulate		587	−2	26	46	6.44	<.001	<.001
	Anterior insula	L	156	−36	18	0	5.91	<.001	<.001
	Anterior insula	R	110	42	18	−4	4.59	<.001	.001
	Somatosensory cortex	L	42	−58	−28	36	3.77	<.001	.013
F-ASD									
	Anterior cingulate		407	−6	18	36	5.12	<.001	.002
F-CG (PP > NP) > F-ASD (PP > NP)									
	Anterior insula	L	16	−34	20	4	3.28	<.001	.024
	Anterior insula	R	1	34	24	0	3.12	<.001	.033
Empathy for social pain									
(SKS+NKS) > NS									
F-CG									
	Anterior cingulate		222	−6	28	42	5.76	<.001	<.001
	Anterior insula	L	33	−28	24	0	5.49	<.001	<.001
	Thalamus		18	−2	−6	8	4.32	<.001	<.001
F-ASD									
	Anterior cingulate		25	−8	18	40	4.11	<.001	.005
SKS > NKS									
F-CG									
	Anterior insula	L	3	−28	24	2	2.83	<.001	.030
	Thalamus		23	−4	−6	6	3.76	<.001	.002
F-ASD									
	Anterior insula	L	2	−40	24	4	2.72	<.001	.039
	Thalamus		16	−6	−8	8	3.25	<.001	.006
F-CG [(SKS+NKS) > NS] > F-ASD [(SKS+NKS) > NS]									
	Anterior insula	L	22	−28	24	0	3.73	<.001	.003

All statistics for the contrasts reported in the table are thresholded at p < .05, family-wise-error corrected (FWE), within regions of interest (ROIs). PP, physical pain condition; NP, no pain condition; SKS, shared knowledge social pain situations; NKS, non-shared knowledge social pain situations; NS, neutral social control situations; F-CG, non-clinical control group; F-ASD, autism spectrum disorder group.

phenotype by testing deficits in empathic responding as well as egocentric biases in a female sample in correspondence to what has already been discussed for males with ASD. We found that females with ASD were able to correctly detect another person's physical pain but were significantly less likely to accurately consider the protagonist's perspective in case of social pain. In contrast to non-clinical control participants, they attributed relatively strong embarrassment to the social target even in a situation the person was unaware about the ongoing threat to his or her social integrity. In addition, fMRI results indicated an attenuated activation of areas of the empathy network, specifically the AI, in females with ASD, which persisted regardless of the complexity of the social situation. In both the empathy for physical pain and the more complex empathy for social pain condition, the AI did not show elevated activity in response to the depicted integrity threat.

The anterior insula cortex is typically associated with social-emotional processing, such as interoceptive processes (40–42), and empathizing with others conditions (43–46). In light of this popular notion of the AI's functioning in social-affective processes, attenuated activity in the AI in females with ASD in response to another person's physical and social pain might reflect deficits in sharing another's perspective. Here, individuals with ASD might lack the intuitive access to another person's mind through automatically sharing their affective states on the neural systems level. Thus, they might be less able to rely on their "gut feelings" in situations involving empathic abilities. Nevertheless, the females with ASD did actively try to "walk in the protagonists shoes" and were able to cognitively grasp and understand the other person's situation (if they shared the same knowledge about the situation) as indicated by the ratings that were in a similar range as the non-clinical controls'. This notion

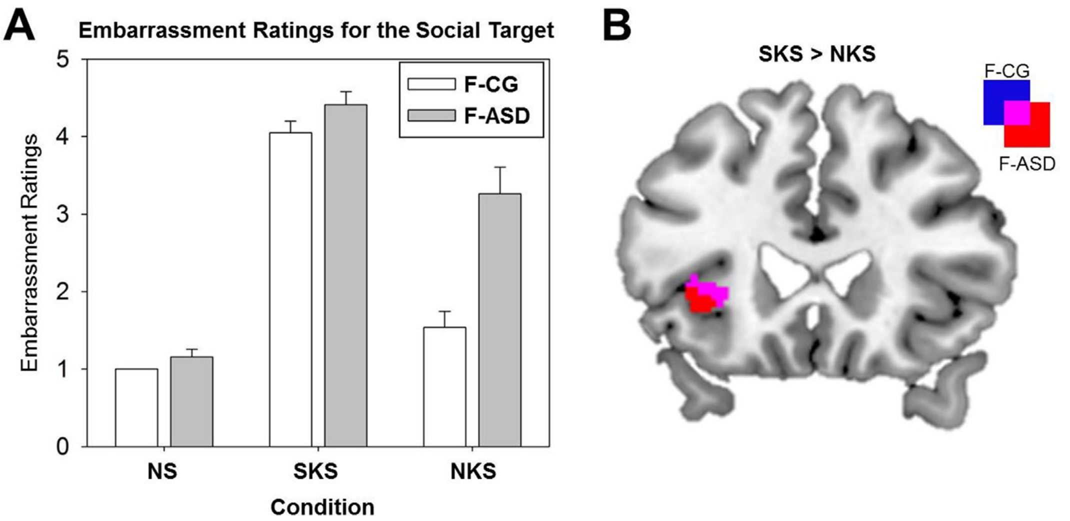

FIGURE 3 | Ratings of the social targets' experience of embarrassment and neural activation differences between shared and non-shared knowledge situations. **(A)** Mean subjective ratings of the social targets' embarrassment (bars indicate standard errors) for the neutral control situations (NS), the shared knowledge situations (SKS), and the non-shared knowledge situations (NKS) for the control group (F-CG) and the female autism spectrum disorder group (F-ASD). **(B)** Increased activation of the left anterior insula during SKS in contrast to NKS in the F-CG and F-ASD group; all statistics are FWE-corrected within ROIs as described in the Methods section; all results are presented uncorrected ($p < .05$; $T > 1.68$) for displaying purposes within ROIs.

is in line with previous studies suggesting that male patients with ASD might be able to make up for their lack of intuitive access to the shared representation of affect by adhering to learned social rules and conventions—however, often in an inflexible or stereotyped manner (13, 47).

This seemingly straightforward interpretation of altered AI responses in females with ASD, however, needs to be carefully considered, since the AI is well established in various other processes that are relevant for social behavior, most prominently salience (48). Reduced AI activation could refer to a qualitatively different level of social processes such as a reduced distribution of attention to social events in the environment in females with ASD. Reduced salience of social norm violations in the environment or threats to the physical integrity of another's body could very well explain different behavioral responses in the absence of any alterations in shared representation of affect (49). Females with ASD, however, did notice the violation of social norms in the observed situation and rated the protagonist's embarrassment just as high as the control participants—even higher in the non-shared knowledge condition—which points to the idea that the depicted norm violations are comparably salient to the females with ASD in this study. This is also supported by clinical observations and the importance of behavioral rules (47) and capabilities in understanding and realizing social norm transgressions in the high-functioning phenotype (50), particularly when these are very simple and do not rely on understanding another's intentions (18). The activation differences in the AI as observed here might therefore rather unlikely reflect alterations in the ascription of saliency to the social scenarios.

In contrast to our expectations derived from previous findings in male subjects, in the current female sample, deficits in sharing another person's state have surfaced even when participants were confronted with rather simple physical pain scenarios that did not require complex integrations of social context information with different social perspectives. Rather than indicating specific deficits in the female ASD phenotype, these more pronounced deficits in shared representation might be due to the younger age and thus earlier stage of maturation of the females in our sample compared to previous male samples (13). A previous study even pointed towards female superiority with respect to developmental aspects in younger individuals (non-clinical controls and individuals with ASD) when detecting faux pas in a theory of mind task (51). In this study, boys and girls aged 4–6 and 7–11 years were asked to detect a faux pas from a story. Besides a general effect of age (older children detected a faux pas better than younger children), girls outperformed boys in both age groups. The authors find faux pas detection performance to be at a lower level in children with high functioning autism compared to non-clinical controls. However, the group of female participants with autism was too small (N = 2) to statistically test for sex effects (51). Since the present study included only female participants with ASD precluding direct comparison to males, future research needs to include both male and female individuals with ASD and directly assess behavioral and neural aberrations associated with the disorder.

While females with ASD did not show any different behavior in the physical pain condition, complex social scenarios posed a greater challenge. Specifically, when the situations required to leave the own perspective and to accurately consider the social target's perspective, females with ASD exhibited increased egocentric biases. Interestingly, both groups of participants showed enhanced activation of brain regions of the empathy network when viewing situations depicting a social target being unaware of the faux pas in contrast to neutral situations and females with ASD also showed the same increase in activation in the ACC when the knowledge on the norm-transgression and affective experience was shared compared to when it was not. This might reflect the vicarious embarrassment that participants experienced on behalf of the observed person as indicated by previous studies and might not be fundamentally different also in females with ASD (17, 23). However, the activation in the non-shared condition was particularly diminished in both groups in contrast to shared knowledge situations in which participants could feel the same affect as the social target. This indicates that the representation of non-shared, vicariously experienced embarrassment is less prominent when participants are explicitly asked to focus on the other's mental states rather than their own affect on behalf of the other person. In this context, activations of the anterior insula might in part also reflect one's own experience of distress when observing another person in an uncomfortable social situation (52). Such vicarious and subjectively imbued neural representations have been found in previous studies confronting individuals with a person that was "not like them" (27), supporting the view that perspective taking requires the effortful regulation of one's egocentrically anchored experiences when another person feels different than oneself (26). While subjectively biased representations of another person's state are thought be a typical phenomenon (30, 53), in the current study, individuals without ASD were fully able to cognitively understand the social target's situation and make a clear distinction between the self and the other. Even though on the neural systems level participants without ASD represented the social pain on behalf of another to a stronger degree than females with ASD, they were also able to withdraw from this experience and to distinguish their own from the social target's feeling state. Thus, non-clinical control participants did not confuse self- and other-related emotional responses. In contrast, when confronted with such complex social scenarios, it seemed to be difficult for subjects with ASD to take a step back from their own judgment of a situation and create a valid evaluation of someone else's internal affective state. This finding is in line with clinical observations describing individuals with ASD as constantly observing themselves, directing their attention towards the own person, which results in an extreme form of egocentrism (29, 30). Naturally, such deficits in perspective taking in a social context may make it harder for individuals with ASD to react in a socially acceptable or culturally expected manner.

However, females with high functioning ASD did show activation of the same empathy networks as typically developed individuals, indicating that their ability to share another's affect is not fundamentally compromised (54, 55). Behavioral deficits in understanding another person's affective state only surfaced in more complex social settings that require disentangling different social perspectives. Thus, training of cognitive strategies, such as consultation of learned and memorized social relations, with an emphasis on perspective taking skills, might enable individuals with ASD to compensate some of these disadvantages and help them to get along in a social environment, even though they might not be able to intuitively feel it or "naturally" fit in.

Limitations

In the present study, we did not assess alexithymia, i.e., the inability to describe one's own affective states. In recent years, it has been observed that many individuals with ASD also suffer from alexithymia, leading to the assumption that emotional problems in ASD may rather be a symptom of (co-occurring) alexithymia than a core feature of the disorder itself (56). For example, it was suggested that processing of physical pain, sensitivity to subjective experiences of physical pain, or the report thereof may be affected in ASD (57). According to this reasoning, the attenuated AI activation in ASD in the present study may emerge because of deficits in processing pain per se, but not attributed to deficits in perspective-taking (58). This is in line with other studies in ASD demonstrating that insular activity varied over time during pain stimulation, with unobtrusive early but diminished late responses to physical pain (57). In sum, although there are studies showing no contribution of alexithymia to impairment in emotion processing (59), others highlight a mediating role of alexithymia on empathic processes in ASD (60). These conflicting findings call for more careful investigations of specific subgroups of individuals with co-occurring ASD and alexithymia. Regarding the interpretation of our results, the lack of information on alexithymia in the present sample thus needs to be considered.

Future research should take into account potential influences of age, sex/gender, and hormone status, e.g., female cycle, intake of oral contraceptives, oxytocin and vasopressin levels, and stress hormone levels, as studies show connections between these factors and social behavior, including empathic abilities, in humans (61, 62). Within this line, particularly the large age range within this study (12–24 years) needs to be discussed, as particularly within this period of development, substantial changes in biology and cognition may take place. Interpretation of the present results is further limited by the small sample size.

CONCLUSION

Our findings point towards a tendency of reduced shared representations of affect in empathic situations in females with high functioning ASD. While females with ASD do experience shared affect, they tend to differentiate less between the own and another person's perspective. The overreliance on their own perspective confirms the notion that deficits in understanding another's feelings might only surface in more complex social settings that require disentangling the own from another person's view of the situation. These findings fit very well into previous literature on the male ASD phenotype and suggest that the peculiarities in the domain of social cognition also generalize to the female phenotype (13). The here presented evidence yet relies on a small sample of high functioning females with ASD and should thus be treated with caution. Considering the strong asymmetry of males and females in high functioning ASD, however, we strongly believe that these efforts are inevitable and a valuable addition to the literature to obtain a more comprehensive understanding of the generalizability of altered social cognition in the heterogeneous ASD phenotype.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the ethics committee of the Medical

Department of the University of Marburg with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the ethics committee of the Medical Department of the University of Marburg (Az 197/12).

AUTHOR CONTRIBUTIONS

LP, IK-B, FMP, SK, and LM-P acquired the data. SS, LP, and LM-P analyzed the data. SS, LP, IK-B, A-KW, FMP, SK, and LM-P prepared, reviewed, and edited the manuscript.

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The Neural Basis of Empathy and Empathic Behavior in the Context of Chronic Trauma

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Background: Accumulating evidence in social neuroscience suggests that mature human empathy relies on the integration of two types of processes: a lower-order process mainly tapping into automatic and sensory mechanisms and a higher-order process involving affect and cognition and modulated by top-down control. Studies have also indicated that neural measures of empathy often correlate with behavioral measures of empathy. Yet, little is known on the effects of chronic trauma on the neural and behavioral indices of empathy and the associations among them.

Methods: Mothers exposed to chronic war-related trauma and nonexposed controls (N = 88, N = 41 war-exposed) underwent magnetoencephalography (MEG) while watching stimuli depicting vicarious emotional distress. Maternal empathic behavior was assessed during mother–child interaction involving a joint task.

Results: Empathy-evoking vignettes elicited response in alpha rhythms in a network involving both sensorimotor and viceromotor (anterior insula) regions, suggesting integration of the sensory and affective components of empathy. Whereas exposure to chronic stress did not affect the level of neural activations in this network, it reduced maternal empathic behavior. Furthermore, trauma exposure impaired the coherence of brain and behavior; only among controls, but not among trauma-exposed mothers, the neural basis of empathy was predicted by maternal empathic behavior.

Conclusions: Chronic stress takes a toll on the mother's empathic ability and indirectly impacts the neural basis of empathy by disrupting the coherence of brain and behavior.

Keywords: social brain, parent-child relationship, early trauma, magnetoencephalography, empathy

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INTRODUCTION

Empathy is a multifaceted psychological construct that plays a key role in social life and enables humans to feel and understand each other and form social groups and cultural communities. The neuroscience of empathy, an emerging field of research, has been informative in defining the multiple facets of empathy and the associations between its neural and behavioral manifestations (1). One aspect which has been repeatedly observed in various neuroimaging studies is that human empathy relies on the integration of two types of processes; a lower-order process mainly tapping into automatic and sensory mechanisms and a higher-order process involving affect and cognition and top-down control.

Importantly, both the automatic and higher-order mechanisms are needed for the expression of mature, full-blown empathy (2, 3). Functional neuroimaging studies have shown that mature human empathy integrates these two neural components and relies on the involvement of both sensorimotor (SM) and frontal viceromotor regions, mainly the anterior insula (AI). Such dual-system activations have been interpreted to reflect the integration of the lower-order, automatic, and sensory aspect of empathy with the higher-order, cognitive, and top-down aspect (2, 4–6). In parallel, EEG and magnetoencephalography (MEG) studies showed that the alpha, or *Mu* rhythm (alpha rhythms in sensory–motor areas) conveys a reliable marker of empathy (7–11). Consistent with these findings, we have shown in a large-scale MEG study of children, adolescents, and adults that whereas children and adolescents' response to others' pain implicated alpha rhythms in sensory-motor regions, only in adulthood did participants exhibit both sensory–motor and higher-order activations in viceromotor areas that support interoceptive sensitivity of one's own bodily milieu in the service of other-focused empathy (12). Taken together, these findings suggest that mature human empathy is underpinned by the SM-AI network that sustains full-blown adult empathy *via* the alpha rhythm.

Studies on the brain basis of empathy typically examine associations between neural activations in paradigms that call for empathic response and behavioral or self-reported indices of empathy (2, 13–16). Several studies revealed a robust link between measures of empathy in the brain and measures of observed social behavior, including empathy and synchrony or negative correlations between the neural empathic response and hostile behavior (11, 17). Yet, other studies failed to report such links and found no associations between the neural basis of empathy and empathic behavior. One explanation for such lack of correlations may relate to the heterogeneity of participants: it is possible that brain–behavior links exist only for certain groups of individuals but not for others. While this hypothesis has not been studied in depth, prior evidence lends support to this assumption. For instance, in a study on the neural basis of attachment, we found that among synchronous mothers, associations emerged between neural activations in key nodes of the maternal brain, oxytocin levels, and the mother's attuned parenting behavior; however, such links were not found for intrusive mothers, indicating that coherence among the neural and behavioral indices of social functions may index greater maturity and more optimal functioning (18). Similarly, children who experienced more empathic and synchronous parenting showed a greater coherence of theta, alpha, beta, and gamma rhythms across the social brain, including the superior temporal sulcus (STS)/superior temporal gyrus (STG) and AI and greater correlations of brain and behavior (19).

These findings raise the interesting assumption that coherence between activations in the social brain and observed social behavior may serve as a marker of greater maturity and functionality (20). This novel assumption is supported by several lines of evidence from various methods and samples. First, a previous functional magnetic resonance imaging (fMRI) study suggested that mothers tune their child's brain *via* behavior-based processes (21), while another fMRI study demonstrated that the integrity of empathic networks in the parental brain shape children's long-term behavior (22). A MEG study found that when mothers and children engaged in synchronous interactions, they also exhibited brain-to-brain synchrony which was tightly connected to their behavior, particularly to mothers' empathic behavior (23). A recent transcranial magnetic stimulation (TMS) study demonstrated a causal relationship between empathic neural response and prosocial behavior (24). Finally, animal studies also conveyed a clear coordination of mother and offspring's physiological systems with bottom-up behavioral processes (25, 26). Among the conditions that may disrupt the expression of brain–behavior correlations, particularly in the social brain, are chronic stress and prolonged trauma. Prolonged exposure to trauma has long been known to increase psychopathology and suicidal behavior (27), reduce social adaptation, and impair brain functioning (28). Prolonged exposure to trauma, particularly during early development, has long been known to increase psychopathology, and early life stress was found to explain nearly 32% of psychiatric disorders (29). In an earlier study of the current research cohort, over 80% of children exposed to early and chronic trauma displayed a full-blown Axis I disorder at some point in their childhood (30), and exposed mothers were found to have higher depression, anxiety, and posttraumatic stress disorder (PTSD) symptoms compared with controls (31). In addition to such deficits, studies have repeatedly shown that individuals exposed to early trauma exhibit impaired empathy (32–34) and abnormal neural functioning of social functions including response to negative emotional stimuli (35, 36). Chronic stress and trauma also impair the neural basis of empathy. For instance, a MEG study showed that veterans exposed to wartime trauma exhibited disrupted neural empathic response to others' pain as expressed by the alpha rhythm (37). In the context of parenting, another MEG study similarly showed disruptions in the neural basis of empathy among adolescents exposed to maternal depression throughout their first years of life and these disruptions were again found in the alpha rhythm (17). Thus, while no prior study examined the effects of chronic trauma on brain–behavior coherence in relation to the empathic brain, the aforementioned standard error (SEM) studies suggest that diminished coherence may be one result of chronic trauma exposure.

In light of the above, the current study examined whether prolonged exposure to trauma may either directly impact the empathic brain, or alternatively, indirectly affect the associations between the neural and behavioral markers of empathy. Previous research has shown that exposure to chronic stress impairs the neural foundation of empathy and its behavioral manifestations (35, 36, 38–40), but the association between the two has not been tested thus far. Further, we were interested to test whether empathic behavior in the context of parenting could predict neural empathic response based on our previous studies which indicated that empathic parenting, particularly affectively synchronized behavior that is tuned to the child's state and communications, is an individually stable maternal orientation when measured repeatedly from infancy and through adolescence and, moreover, such synchronized maternal behavior predicts the neural empathic response (17, 23, 41, 42). To probe the impact of chronic stress on the neural basis of empathy, we used an empathy paradigm which simulates

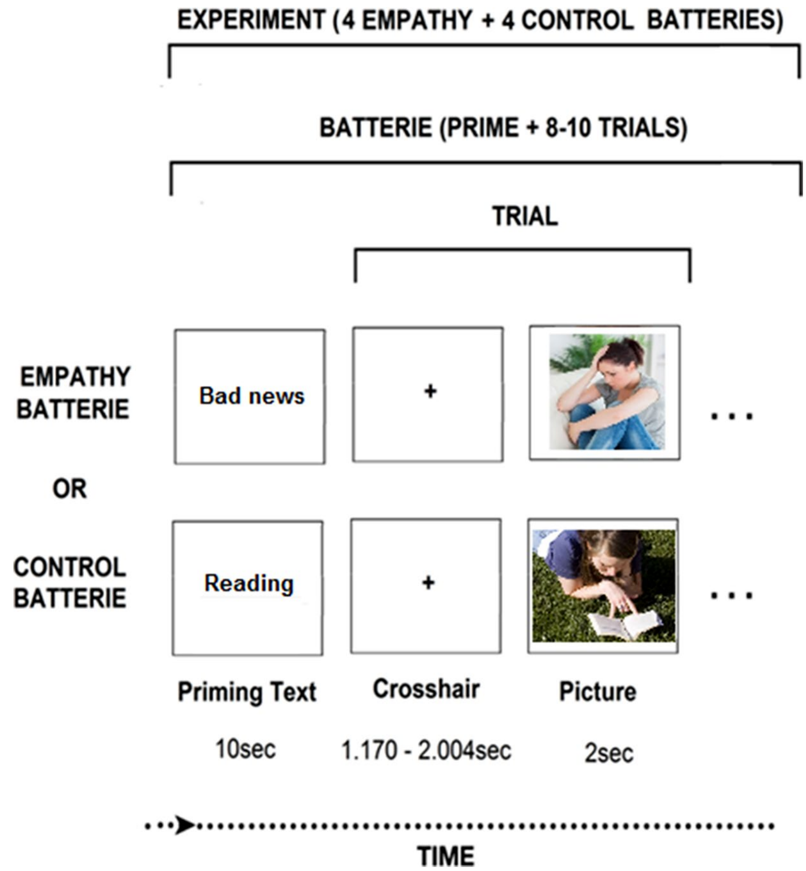

FIGURE 1 | Neuroimaging experimental design. The "bad news" photo: Wavebreak Media Ltd © 123RF.com. The "reading" picture: FreeImages.com/Ryan Day.

empathy to vicarious affective stress (**Figure 1**). This paradigm has shown to yield activations containing both the SM and AI components of empathy (13).

We utilized a sample of mothers who were exposed to chronic war-related trauma as representing a condition of mass trauma. Such trauma is defined by the exposure of large populations to the same natural disaster or war/violence condition at the same time point (43). One of the main characteristic of such trauma is that typically the whole family is exposed to the trauma together. As a result, mothers experience both the stress of being exposed to chronic war themselves, as well as raising their children in an atmosphere of constant fear and handing their children's worries and stress responses. Children depend on their cargivers to supply protection, security, and emotional regulation, especialy following trauma exposure (44). It is thus of imprtance to investigate the foundations of maternal sensitivity, support, and empathic behavior in the context of chronic stress. Three hypotheses were proposed. First, we expected trauma-exposed mothers to show lower behavioral empathy during interaction with their children. Second, we expected to see alterations in the neural basis of empathy in mothers living in a context of chronic trauma. Finally, we expected to see group differences in the connection of brain and behavior, such that only among the nonexposed mothers there will be correlations between greater neural activations to others' emotional distress and more empathic parenting, whereas in mothers exposed to chronic stress there will be a disconnect between brain and behavior.

METHODS AND MATERIALS

Participants

Participants were mothers of children who were part of a longitudinal study on the effects of war exposure on mothers and children. Between the years 2004 and 2005, we recruited 232 mothers (M ± SD 31.27 ± 5.55 years) and young children (M ± SD 2.76 ± 0.91years) in two groups; trauma exposed and controls. The trauma-exposed group included 148 families (148 mothers and 148 infants) from Sderot, a town in the south of Israel located 10 km from the Gaza border. This area has suffered for the past 20 years from chronic rockets and missiles attacks, a few wars, and military operations. The second group included 84 nonexposed control families from other areas in the center of Israel. The two groups were matched demographically in terms of age, gender, birth order, parental age and education, maternal employment, and marital status and screened for other trauma, and we included participants who were not physically or mentally handicapped (e.g., severe autism, mental retardation) [for more details, see (45)].

The current study presents data from the fourth stage of this longitudinal study, when children were at preadolescence (11–13 years). At that longitudinal stage, compatibility with MEG scanning was added to the inclusion criteria: this mainly required that participants were metal free (e.g., free of tooth-bracelets, metallic implants) and were not pregnant. Eighty-eight mothers[1] participated in MEG scanning (M ± SD 40.37 ± 5.26 years) and their children were now in preadolescence (M ± SD 11.65 ± 1.25); 41 of mothers were war exposed. Of 107 mothers participating in T4, 19 did not complete the MEG experiment: 8 were MEG incompatible, 5 declined the MEG part, 4 had poor MEG signal, and 2 were pregnant. The study was approved by the Ethics Committee at Bar Ilan University. Written informed consent was obtained from all participants. Experiments were performed in accordance with ethical guidelines.

Procedure and Measures

MEG Paradigm. During MEG scanning, we employed an empathy task contrasting situations where same-age targets were in distress (DS) versus non-distress(no-DS) and mothers were asked to take the targets' perspective and put themselves in "the other person's shoes" (13). This experimental contrast involves sensitivity to vicarious DS and activates both sensory and affective components of empathy (13). We created pool of 128 stimuli (photos in uniform size: 300 × 225 pixels) half depicting DS/anxiety situations and half neutral. Distress situations described typical anxiety-promoting (social exclusion, exam stress) versus nondistressing (shoe-lacing, reading) events in preadolescents' lives. Stimuli were piloted until the final 128 stimuli were each validated by independent raters (n = 21). Stimuli's affective valence (1-very negative, 2-negative, 3-neutral, 4-positive, 5-very positive) was rated as neutral (M ± SD 3.04 ± 0.25) and negative (M ± SD 1.95 ± .28) for the no-DS and DS stimuli, respectively, with a statistically significant difference ($P = 6.21 * 10^{-47}$) between categories. Stimuli's affective arousal (1-very low to 5-very high) was rated as low (M ± SD 2.05 ± 0.33) and high (M ± SD 3.83 ± .42) for the no-DS and DS stimuli, respectively, with a statistically significant difference ($P = 2.37 * 10^{-53}$) between categories. Finally, stimuli were matched for physical parameters, including complexity, contrast, and luminance, resulting in no statistically significant difference ($P > .35$) on any of these parameters. Photos were presented in blocks preceded by a contextual sentence, generically describing the situation in the ensuing photo (e.g., "this person heard that his friends plan to exclude him", "this person reads about the history of Sweden"). Sentences were designed to consist of M ± SD 9.07 ± 1.14 words and M ± SD 43.64 ± 5.10 characters long, with no statistically significant difference ($P > .3$) in length between categories. Paradigm was programmed and operated using E-Prime® 2 software (Psychology Software Tools Incorporated).

Imaging Session. Participants laid in supine position inside the MEG system while facing a screen projecting the stimuli in the center of gray background of 20-inch monitor at distance of 50 cm. Participants were told to take the targets' perspective and to imagine how he/she felt in that situation. Fourteen blocks consisted each of a contextual sentence describing the situation followed by 8–10 photos depicting different individuals in that situation. Sentences and photos were presented for 10 s and 2 s respectively. The interstimulus interval was jittered for 1.170–2.004 s and the interblock interval was jittered for 4.170 s–5.004 s. Participants were trained by watching two exemplar blocks and instructed to remain relaxed and not move their head or body and to pay attention to the events depicted in the photos. Movements were visually monitored by the experimenter *via* a camera, and by five coils attached to the participants' scalp to record head position relative to the sensor array.

MEG Recordings and Data Preprocessing. We recorded ongoing brain activity (sampling rate, 1,017 Hz, online 1–400 Hz band-pass filter) using a whole-head 248-channel magnetometer array (4-D Neuroimaging, Magnes® 3600 WH) inside magnetically shielded room. Reference coils located approximately 30 cm above the head, oriented by *x*, *y*, and *z* axes enabled removal of environmental noise. Head shape underwent manual digitization (Polhemus FASTRAK® digitizer). External noise (e.g., power-line, mechanical vibrations) and heartbeat artifacts were removed from the data using a predesigned algorithm for that purpose (46) and trials containing muscle artifacts and signal jumps were rejected from further analysis by visual inspection. We analyzed data of 2,000 ms epochs including baseline period of 700 ms filtered in the 1–200 Hz range with 10 sec padding and then resampled to 400 Hz.

Maternal Behavior. *Maternal empathic behavior* was observed during a mother–child interaction, which took place about 20 min prior to the MEG paradigm, and included a joint task. The interaction was videotaped and coded offline using the Coding Interactive Behavior Manual (CIB) (47). The CIB is a well-validated system for coding social behavior, extensively used across cultures and psychiatric conditions from infancy to adulthood (48). The CIB includes multiple scales coded from 1 (low) to 5 (high), which are averaged into theoretically determined constructs. Coding was conducted by trained coders who were blind to any other information, and reliability on 20% of the interactions exceeded 90% on all codes (k = 0.82, range = 0.78–0.95). *The maternal empathic behavior* construct included the following scales: emotional empathy, cognitive empathy, behavioral empathy, acknowledgement/recognition of the child affect and communication, expansion of the child's statements, and containment of the child's DS and high arousal (Cronbach's α = .92). From the 88 mothers who participated in the current study, eight dyads did not have a filmed interaction due to technical issues.

MEG Analyses. We analyzed data in alignment to stimulus onset and then averaged the power estimates across tapers. We performed analyses using MATLAB 11 (MathWorks®, Natick, MA, USA) and the FieldTrip software toolbox (49). To calculate induced oscillatory activity in the alpha band, a Hanning taper, applied to each epoch of the 248-sensor data yielded the FFT for short sliding time windows of 0.5 sec in the 6–15 Hz frequency range, resulting in spectral resolution of 2 Hz. For source localization, we built a single shell brain model based on MNI post-puberty template brain (50), modified to fit each subject's digitized head shape using SPM8 (51). The subject's brain volume was then divided into a regular grid. The grid positions were obtained by a linear transformation of the grid positions in a canonical 1-cm grid. This procedure facilitates the group analysis because no spatial interpolation of the volumes

[1]Children's brain was also imaged and results will be presented elsewhere.

of reconstructed activity is required. For each grid position, spatial filters were reconstructed in the aim of optimally passing activity from the location of interest, while suppressing activity which was not of interest. The spatial filter which we applied relies on partial canonical correlations (49, 52) and its cross-spectral density (CSD) matrix was computed between all MEG sensor pairs from the Fourier transforms of the tapered data epochs at the statistically significant time–frequency sensor pattern (**Figure 3**, left upper panel).

Behavioral Analyses. T-tests were used to compare brain and behavior variables between exposed and controls. Next, Pearson correlations assessed relationships between maternal brain and behavioral variables. In order to test our hypothesis regarding the different association between behavior and brain in the two groups, contemporary practices of simple linear moderation model by Hayes (53) was adopted. To estimate the conditional effect of the independent variable maternal behavior (X), on the outcome variable SM-AI (Y), with chronic stress exposure included as a moderator (M), the PROCESS macro for SPSS (v. 2.1.3.2) Model 1 was used (54). Exposure was dummy coded, with the control group given a value of "0" and the exposed group a value of "1". Maternal behavior and exposure were mean centered to facilitate the interpretation of the simple and interaction effects (54, 55). Following, the maternal behavior, exposure, and maternal brain activity variables were standardized in order to compute the standardized effects. The product term between mean centered maternal behavior scores and the exposure group was computed to test for the maternal behavior-by-group interaction. The group, maternal behavior, and group-by-maternal behavior interaction, were entered in the analyses described below.

RESULTS

Neuroimaging Results. We first contrasted stimuli involving DS versus no-DS. The statistical time–frequency contrast (0–2 sec; 6–14 Hz) of all MEG sensor-array yielded alpha suppression peaking between 7–11–Hz and 300–850–ms ($P_{\text{cluster-corrected}} <$ 0.001). Source localization revealed that this activation pattern peaked in the SM-AI, that is, the bilateral SM and the right AI ($P_{\text{cluster- corrected}} < 0.001$); the network is simulated in **Figure 2**. This confirms with our expectation that the paradigm used here will trigger both sensory and affective components of empathy. One mother scored more than 3SD above the SM-IA mean, and was considered an outlier and therefore was removed from the ensuing analyses. To explore whether trauma may directly impact this neural response, we compared between the two groups; however, no statistically significant difference emerged ($t_{(85)} = 1.37$, P = .17).

Behavioral Results. Maternal behavioral empathy showed a significant group effect ($t_{(77)} = 2.09$, P = .04), with war-exposed mothers displaying less empathy toward their child during the joint task compared to controls (**Figure 3**). There was no significant correlation between maternal empathic behavior and maternal brain activity (r = −.05, P = .66). Results from the PROCESS moderation analyses are displayed in **Table 1** and goodness of fit measures indicated 11% explained variance ($R^2 = .11$, $F_{(3,75)} = 3.03$, P = .02). Furthermore, the interaction term added unique explained variance in the model: the change between the model without the interaction effect to the model with the interaction effect was significant ($\Delta R^2 = .09$, $F_{(1,75)} = 8.22$, P < .01). No significant main effect of group or maternal behavior emerged for SM-AI. There was, however, a significant group-by-maternal behavior interaction predicting SM-AI brain activity (**Table 1**). For a significant interaction, PROCESS provides the conditional effects of the independent variable at each value of the moderator (i.e., "simple slopes"). As displayed in **Table 1**, tests of simple slopes (54, 55) showed that for control mothers the relationship between maternal empathic behavior and neural empathy (SM-AI) was significant, indicating a negative association between empathic behavior and brain activity (b = −.03, *se* = .01, P = .03, β = −.32, *95% CI*: (−.05, −.002)). Taking into consideration that alpha suppression indexes the degree of neural activity, the findings point to a positive association between greater maternal empathic behavior and increased neural activations. In contrast, no significant brain–behavior associations emerged for the trauma-exposed group [b = .03, *se* = .01,

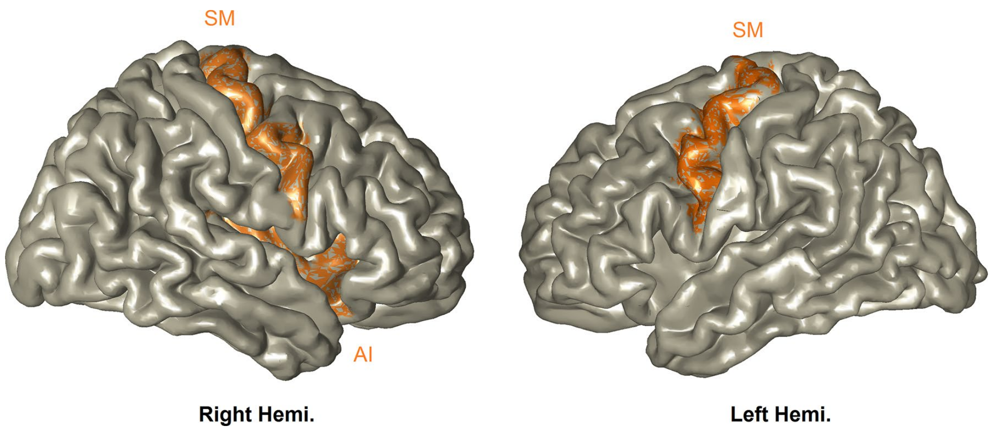

FIGURE 2 | Perception of vicarious distress. All participants activated the bilateral SM and right-AI ($P_{\text{cluster- corrected}} < 0.001$), and this activation was expressed as alpha-band suppression.

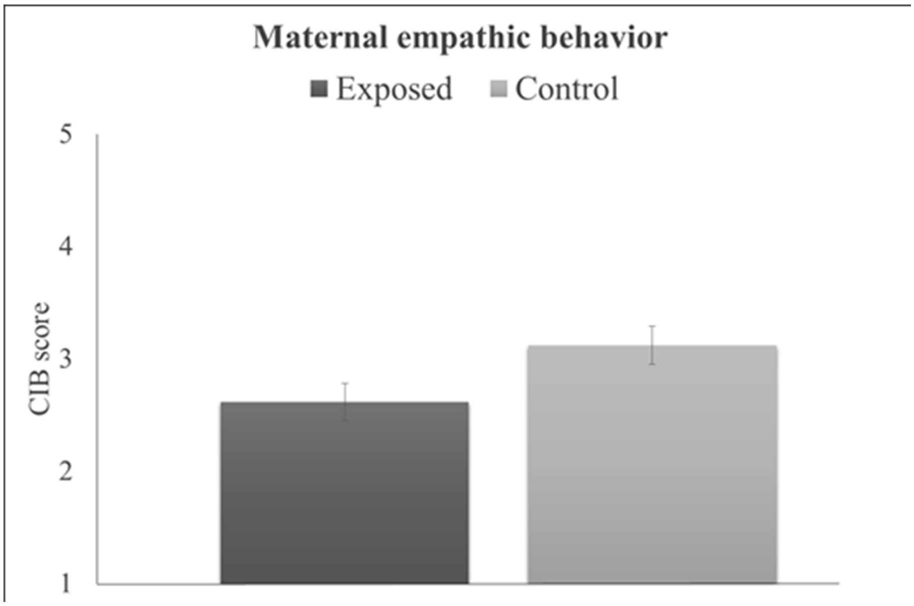

FIGURE 3 | Differences between groups in maternal empathic behavior. Error bars represent ±1 SEM.

TABLE 1 | The moderation effect of exposure and maternal empathic behavior on maternal SM-AI.

Predictor	b(se)	β	t	P	95%CI
Exposure	−.02(.02)	−.11	−.93	.36	(−.06,.02)
Maternal behavior	−.003(.009)	−.02	−.28	.78	(−.02,.02)
Exposure maternal behavior	.05(.02)**	.32	2.87	.005	(.02,.09)
Constant	.000(.01)		.04	.97	(−.02,.02)

*** P < 0.05.*

β = .31, P = .06, *95%CI* (–.001,.05)]. This finding suggests that chronic trauma decouples the links between the neural basis of empathy and empathic parenting behavior in mothers who are raising their children in the context of chronic stress and trauma.

DISCUSSION

Previous studies showed that chronic adversity carries dire consequences for the individual's mental and physical health (27). In the present study, we examined the effects of repeated trauma on the neural and behavioral aspects of empathic abilities. Several important findings emerged from our study, which targeted mothers who are raising their children in the context of chronic trauma exposure. As expected, we found that the neural basis of empathy to the emotional DS of others integrates both sensory and affective processes, as can be inferred by the robust recruitment of both the SM and AI substrates. We have previously shown that the integration of this network is a sign of developmental maturity and is only observed in adulthood, not during childhood or adolescence (12). Yet, contrary to our expectation, we found that chronic trauma did not impair the mothers' neural empathic response or dampened the integration of the sensorimotor with the interoceptive networks in the maternal brain. However, consistent with our hypotheses, results indicate that exposure to chronic war-related stress decreased the mother's empathic behavior during interaction with her child and decoupled the empathic brain from the mother's empathic behavior. Whereas among controls, the mother's neural empathic response to others' affective DS was linked to her cognitive, affective, and behavioral empathic response to her child, no such brain-behavior link was found for the trauma-exposed group. As millions of mothers must raise children in conditions of war, terror, and violence, while many others live in dangerous neighborhoods, poverty, and food insecurity, our findings highlight the effects of such contexts on mothers, including the dampening of the mother's empathic parenting and the diminished coherence between the mother's social brain and expressed social behavior.

The network of activation found here in response to the emotional DS of others, which includes the SM and AI, was similar to the network of activation we found in a previous study in response to others' physical pain (12). This implies that empathic neural response to salient bottom-up stimuli describing physical pain is similar to the empathic activations to cognitive and affective top-down stimuli that index emotional pain. An fMRI study that addressed the comparison in the brain response to physical and emotional pain showed similar activations; yet whereas pain empathy activated more sensory and embodied simulation regions including mainly the somatosensory and motor cortices, affective empathy additionally activated higher-order regions, particularly the viceromotor cortex (13). Previous studies provided sound evidence for the role that experimental paradigms of empathy have in the neural activations that they induce. For instance, empathy for pain relies on SM cortices when it is probed by provoking visual stimuli, whereas it relies on higher-order cortices when it is probed by abstract stimuli

(5, 6). The present study is in line with this view as it provides empathy which relies on both SM and AI and is probed by both visual and abstract cues.

We used MEG to assess the neural basis of empathy to others' emotional DS, which uniquely taps the complexity of rhythmic neural activity involved in social and affective experiences in combination with its underlying cortical generators (56) and can therefore provide a different look on the empathic brain as compared to the BOLD (blood-oxygen-level-dependent) signal. Much research has shown that the mu rhythm, the suppression of alpha oscillations above central sensors, provides a good index of the brain's empathic response (7, 10). Consistent with these studies, the current study, alongside our previous study (12), demonstrate in a combined large sample, perhaps the largest sample in MEG research on the neural basis of empathy, that alpha rhythms are implicated in the two types of empathy; the more automatic empathy to the physical pain of others and the more cognitive and affective empathy to the emotional DS of others. Thus, alpha over central areas participates in the two aspects of empathy, namely, the bottom-up sensory and top-down cognitive/viceromotor processes. Much further research is needed to determine whether the difference between those two components of empathy is expressed by other aspects of neural activity, for instance, neural communication or other neural rhythms in addition to the alpha rhythm.

Viceromotor regions, including the AI, anterior cingulate cortex, and orbitofrontal cortex, are crucial for the perception and understanding of vicarious affect and higher-order empathic representations (2). The mechanisms which are proposed to sustain the viceromotor recruitment suggests that interoception of one's own body milieu is crucial for empathizing with others (57). We previously showed that viceromotor recruitment is a sign of neural developmental maturity of empathy (12). Likewise, interoception is disrupted in various psychiatric conditions (58); for instance, interoceptive failure is associated with autism spectrum disorder (59) and heightened interoception may be related to anxiety disorders (60), which often result from exposure to trauma (61). These lines of research may be taken as an indication that empathic viceromotor function is a sign of healthy empathic behavior. In the present study we found that exposure to chronic stress does not directly affect the extent of viceromotor activations, but instead, indirectly impairs the correspondence between the empathic expressions of brain and behavior. This is an interesting and innovative finding which deserves further investigation in future research that addresses the links of brain to behavior in health and in cases of various psychopathologies.

The present study replicates prior studies on the neuroscience of empathy but at the same time adds to the emerging literature on the effects of trauma on empathy. One important aspect that the present study raises is the correspondence between the neural and behavioral manifestations of empathy, and the findings that chronic trauma and stress may impair this association. Yet, we recognize one limitation of the present study—it does not provide empirical evidence which could attempt to explain what exactly impairs the correspondence between brain and behavior. One possible explanation pertains to the impairment in emotion regulation which occurs at the neural circuitry and behavioral levels following trauma (28). Given that emotion regulation bridges between targeted neural activity (i.e., sustaining emotions) and its downstream implications (i.e., behavior) (62), it could be that the effects observed here stem from impaired emotion regulation. It would be informative in the future to explore this or other hypotheses to potentially reveal convincing mechanisms responsible for the impaired association observed here. Another shortcoming regards the heterogeneous exposure to trauma across participants, a limitation which is a downside of studying adversity under natural and ecological settings. Although all exposed participants lived in the same frontline neighbourhoods, it is impossible to rule out subtle differences in exposure (e.g., proximity to disaster), which may have resulted in altered neural impact, as previously reported (63).

Although the present study did not directly test for clinical interventions, we propose that the current study can be channeled toward translational venues in future research. The results of the present study demonstrate that stress-exposed mothers do not display the normal association between empathic brain activity and behavior, although their brain activity in of itself does not differ from that of controls, suggesting that exposure to chronic stress impairs empathic abilities mainly in the context of parenting. Based on these findings we suggest that in order to strengthen parenting-related emphatic abilities, a mother–youth brief intervention would be beneficial, and that the effects of such intervention can be measured by the restoration of the association between the mother's empathic brain activity and her behavior. Previous research assessed the ability of a short-term caregiver–child intervention to prevent the development of PTSD following exposure to a potentially traumatic event (64). However, the effects of such an intervention were studied in a relatively short period following the discrete traumatic event and focused only on the risk of PTSD in the child. We suggest that in situations of chronic exposure to stressful environments, an intervention comprising several sessions which highlight the importance of the maternal acknowledgement of the child's expressions and needs and DS and sensitive responsivity may improve the mother's emphatic behavior toward her child. The intervention may involve the mother–child dyad, only the mother, or a combination of these settings, while emphasizing the importance of the mother–child relationship and the well-being of the family in stressful situations. Furthermore, an interesting follow-up study would be to evaluate the brain response and behavior before and after such intervention, assessing whether the association between the mother's brain activity and empathic behavior increases following the interventions. We recently showed that targeted psychological interventions have the potential to impact empathy at the biological and behavioral levels (65). Thus, a possible take-home recommendation from the present study is that interventions targeting chronic exposure to trauma directly probe the various aspects of empathy: affect, cognition, and behavior.

Finally, our findings are not only relevant to the literature on stress, trauma, and empathy, but tap a more global question: Do brain and behavior always correspond with each other? The brain–behavior correspondence problem stems from the fact that the two operate in different dimensions and are not perfectly matched (66). To the best of our knowledge, this question has rarely been raised before in a systematic empirical program, yet it is important to test whether under certain contexts, including psychopathy or trauma, a dissociation between brain and behavior are more likely to occur.

As such, the associations among trauma, brain, and behavior are not only important and uninvestigated topics for future research, but may open new directions to understand the effects of psychiatric conditions on the human social brain.

AUTHOR CONTRIBUTIONS

JL, AG and RF designed the study, JL conducted MEG research and analyzed the neural data. KY conducted behavioral assessment and coding and analyzed the data. RF, JL, and KY wrote the manuscript.

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The Feasibility and Efficacy of Social Cognition and Interaction Training for Outpatients With Schizophrenia in Japan: A Multicenter Randomized Clinical Trial

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Background: Schizophrenia is a disabling illness. Social cognition and interaction training (SCIT) seeks to improve patients' social functioning by alleviating deficits in social cognition. SCIT has shown promise in improving social cognition in patients with schizophrenia, but has not yet been studied in Japan.

Design: An assessor-masked, randomized, parallel-group clinical trial was conducted to compare the feasibility and efficacy of SCIT with treatment as usual (TAU).

Setting: Participants were recruited from outpatient clinics at the National Center of Neurology and Psychiatry and four other hospitals in Japan.

Participants: Seventy-two patients diagnosed with schizophrenia or schizoaffective disorder consented to participate in the trial.

Procedure: Participants were randomly allocated to either a SCIT subgroup or a TAU subgroup. SCIT is a manual-based group intervention that is delivered in 20–24-h-long weekly sessions. Groups include two to three clinicians and four to eight patients.

Hypotheses: We hypothesized that SCIT would be found to be feasible and that patients who were randomized to receive SCIT would exhibit improvements in social cognition.

Results: Data from 32 participants in each subgroup were entered into analyses. The persistence rate in the SCIT subgroup was 88.9%, and the average attendance rate was 87.0%. Intrinsic motivation was significantly higher in the SCIT subgroup than the TAU group during the first half of the program. Mixed effects modeling of various outcome measures revealed no significant interaction between measurement timepoint and group in any measures, including social cognition, neurocognition, symptom severity, and social functioning. In the case of the social cognition measure, significant change was observed only in the SCIT subgroup; however, the interaction between timepoint and group failed to reach significance. In an exploratory subgroup analysis, a shorter duration of illness was found to be associated with significantly better improvement on the social cognition measure in the SCIT subgroup compared with the TAU subgroup.

Conclusions: In terms of the primary objective, the relatively low dropout rate observed in the present study suggests that SCIT is feasible and well tolerated by patients with schizophrenia in Japan. This view is also supported by participants' relatively high attendance and intrinsic motivation.

Keywords: social cognition and interaction training, social cognition, schizophrenia, theory of mind, randomized clinical trial

INTRODUCTION

Schizophrenia is a chronic, severe, and disabling illness that affects approximately 1% of individuals in the population, with onset usually during late adolescence or early adulthood (1). It is characterized by a combination of positive, negative, and affective symptoms, but cognitive deficits, including impairment of neuro- and social cognitions, are the core symptoms that affect patients' everyday lives. It has been pointed out that the variance in patients' social and community functional outcomes can be explained by composite measures of neurocognition (2). Pharmacological interventions have shown some ability to improve neurocognition, but their capacity to improve patients' social and community functional outcomes is extremely limited (3).

It has been reported that at most 20% to 40% of the variance in functional outcomes can be explained by composite measures of neurocognition (4). More recently, there is a growing body of evidence that social cognition may serve as a mediator between neurocognition and functional outcome (5–9). *Social cognition* refers to the cognitive and emotional functions required to understand and predict other people's mental states and behaviors (10). Patients with schizophrenia experience substantial deficits in social cognition across multiple domains. The most commonly studied domains include emotion perception, social perception, attributional bias, jumping to conclusions, metacognition, and theory of mind (ToM) (11). Therefore, improving social cognition may well lead to improvement in social functioning.

Social cognition and interaction training (SCIT), which was developed by Penn and colleagues, is a program for social cognitive rehabilitation in schizophrenia (12). Compared to other psychosocial interventions that have been designed to target specific social cognitive impairments to the exclusion of other domains (13, 14), SCIT targets a broader range of social cognition. SCIT includes training sessions focusing on emotion perception, distinguishing facts from guesses, generating alternative interpretations of social situations, and avoiding jumping to conclusions, which are designed to increase flexibility in attributional style and improve metacognition. SCIT is theorized to improve social cognition through a combination of rehearsal-based "bottom-up" learning and acquisition of social cognitive strategies that are consciously deployed by patients in social situations.

SCIT has shown promise in improving social cognition in patients with schizophrenia in various regions of the world. However, this research has consisted largely of studies with small samples, and no study has yet been carried out in Japan. Across a series of small trials conducted by its developers, SCIT has shown evidence of feasibility and tolerability in community settings (15), efficacy in improving social cognition and social functioning (16, 17), and some evidence that treatment gains persist over a 6-month follow-up period (18). SCIT has also yielded promising findings when implemented by independent research groups in Australia, Hong Kong, mainland China, Turkey, Spain, Israel, and Finland (19–25).

The main aims of the present study were to examine the feasibility of SCIT, whether patients would exhibit intrinsic motivation for the program, its efficacy in improving social cognition deficits, and possible predictors of improvements in social cognition in Japanese patients in a real-world outpatient setting. Specifically, we hypothesized that the social cognition measures, including facial emotion identification, theory of mind, attributional style, including hostile bias, and metacognition, would be improved since these domains are targeted in SCIT. We also explored the effects of SCIT on social functioning, positive and negative symptoms, and neurocognition. As already noted, since impairment in social cognition has been shown to have a significant impact on functional outcome in patients with schizophrenia, (4) we expected that social functioning may be improved along with improvement in social cognition. Moreover, theoretically, patients with enhanced social cognitive skills may show better coping strategies and be better able to gain social support to decrease their level of stress, and consequently, may be less likely to show positive and negative symptoms. Finally, as SCIT requires the patients to focus attention on facial expression and the social interaction vignettes, and also to remember what they learned in each session, treatment effects may well generalize from social cognitive to neurocognitive domains. However, we would expect this effect to be small because the program was not any more specific to neurocognition than other treatment programs. Although improvements in social functioning, positive and negative symptoms and neurocognition would be consistent with the SCIT intervention approach; these are not the primary treatment targets of SCIT, and so, we did not formally hypothesize change in these domains in this initial trial.

MATERIALS AND METHODS

Participants

Participants were 73 patients treated between August 2013 and July 2017. Sample characteristics are presented in **Table 1**. Inclusion in the trial required that the patient be at least 20 years old and no more than 65 years old, and that they meet the diagnostic criteria for schizophrenia or schizoaffective disorder specified in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revised (26). Participants were recruited from outpatient clinics at the National Center of Neurology and Psychiatry (NCNP), Sawa Hospital, Toho University Hospital, Inuyama Hospital, and Nara Medical University Hospital in Japan. All patients were attending psychosocial treatment at least once a week at the time of the study and had the capacity to give written informed consent.

Patients were excluded from participation in the study if they presented at screening with serious suicidal ideation or life-threatening, severe, or unstable physical disorders; had a history of substance or alcohol use disorder within 3 months prior to screening; or had an estimated IQ lower than 70, as assessed by the Japanese Adult Reading Test (JART) (27). Patients for whom participation in the study was deemed to be inappropriate by the doctor in charge and/or the investigator for any other reason were also excluded.

TABLE 1 | Participants' sociodemographic and clinical profiles. Continuous variables are presented in the form *M* ± *SD.*

Variables	SCIT subgroup (*n* = 32)	TAU subgroup (*n* = 32)
Sex (*n* male)	20	17
Age (years)	35.5 ± 10.1.5	37.5 ± 9.6
Duration of illness (months)	174.7 ± 118.4	161.4 ± 124.2
Daily dosage level (CPZ equiv.)	705.9 ± 506.3	559.0 ± 450.4
Years of education	13.1 ± 1.7	13.9 ± 2.1
Daily activities (*n*)		
Competitive work	17	14
Non-competitive work	4	5
Homemaker	1	2
Student	2	2
Community workshop	1	1
Day care center	2	2
Social withdrawal	5	2
Other	0	4
PANSS score		
Total	64.8 ± 18.2	63.8 ± 19.0
Positive	15.4 ± 5.1	15.4 ± 5.9
Negative	16.2 ± 5.4	16.7 ± 5.9
General	33.2 ± 9.8	31.7 ± 9.7
GAF score	51.6 ± 8.8	53.4 ± 9.5
JART score	100.5 ± 10.9	102.3 ± 12.2
IMI score		
BL–3M	104.7 ± 21.6**	89.3 ± 23.1
3M–6M	100.1 ± 24.3	91.2 ± 20.0
Attendance rate (%)		
BL–3M	87.4 ± 15.9	N/A
3M–6M	86.4 ± 18.7	N/A
BL–6M	87.0 ± 14.8	N/A

***P < 0.01 in student's t–test, SCIT subgroup vs. TAU subgroup, P < 0.01.PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of Function; JART, Japanese Adult Reading Test; IMI, Intrinsic Motivation Inventory; BL, baseline; 3M, 3-month timepoint; 6M, 6-month timepoint; SCIT, Social Cognition and Interaction Training; TAU, treatment as usual.*

Study Setting

The SCIT-J study was conducted at multiple sites: the NCNP, a general hospital specializing in psychiatry and neurology located in the suburbs of Tokyo; Sawa Hospital, a psychiatry hospital located in Osaka; Toho University School of Medicine, a university hospital located in Tokyo; Inuyama Hospital, a psychiatry hospital located in Aichi; and Nara Medical University, a university hospital located in Nara.

Procedure

Seventy-three potential participants were referred to the SCIT-J trial. Seventy-two patients consented to participate in the trial and met the enrolment criteria. Participants were randomly allocated to either a SCIT subgroup or a treatment as usual (TAU) subgroup in a 1:1 ratio using a computer-generated sequence obtained online. Restricted and adapted randomization (i.e., minimization) was used to minimize imbalances in age (30 or older *vs*. under 30). Throughout the whole process, no rater was able to access information that could possibly reveal a participant's subgroup allocation.

In order to adapt the SCIT program to the Japanese culture and people, the SCIT manual was translated into Japanese with the help of one of the authors (DR), who is one of the developers of SCIT (28). Additionally, social interaction scenarios used in the program were recreated using Japanese actors, following the original scripts. Although we did not follow the translation-back translation methodology, we received a training and were given supervision from the developers of SCIT and also had multiple sessions of interactive discussion in adapting the program to Japanese culture.

SCIT is a manual-based group intervention that is delivered in 20–24 h-long weekly sessions. Groups consist of two to three clinicians (psychiatrists, clinical psychologists, and/or occupational therapists) and four to eight patients. In the present study, treatment sessions were conducted by clinicians (psychiatrists, clinical psychologists, and/or occupational therapists) who were all trained extensively in a two-day hands-on training session and received ongoing supervision. Treatment fidelity was monitored using the Therapist Adherence Rating Scale for SCIT (28). SCIT is made up of three modules, targeting 1) emotion perception training, which consists of defining emotions, emotion mimicry training, and understanding paranoia (seven sessions); 2) figuring out situations, which consists of distinguishing facts from guesses and avoiding jumping to conclusions (eight sessions); and 3) integration (five to nine sessions).

During the study period, the TAU subgroup attended other psychosocial treatment programs other than SCIT and cognitive remediation therapy at least once a week. For all participants, the use of psychotropic medication was not necessarily fixed; rather, it was flexible according to their clinical state. Participants' antipsychotic medications at baseline are presented in **Table 2**; mean daily dosage levels (CPZ equiv.) did not differ significantly between the two subgroups. We compensated each participant for their time with a payment of 5,000 JPY (approximately 38.8 EUR) at each assessment.

Trial Design

The study consisted of an assessor-masked, randomized, parallel-group clinical trial that compared the feasibility and efficacy of SCIT in conjunction with TAU to TAU alone. Assessment measures were administered to all patients at baseline (between 4 and 1 weeks prior to the start of the SCIT treatment program), at a 3-month interim assessment (after 12 ± 2 weeks), and at a 6-month endpoint assessment (after 24 ± 2 weeks; **Table 3**).

Ethical approval was obtained for the study (Ethical Committee of the National Centre of Neurology and Psychiatry), and the trial was registered with the University Hospital Medical Information Network (UMIN000011240; URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000013171)

Measures

Feasibility

One of the primary outcome measures was feasibility, which was estimated by a) persistence rate at the 6-month endpoint, b) treatment adherence rate (attendance rate), and c) intrinsic motivation for SCIT (at the interim timepoint and endpoint), as assessed by the intrinsic motivation inventory (IMI) (29). The IMI (29) is a 21-item self-report measure assessing participants' subjective experiences in relation to a target program that they are engaging with. Subscales are interest/enjoyment, choice, and value/usefulness (range: 21–144, higher scores indicate stronger intrinsic motivation level).

TABLE 2 | Number of patients prescribed each antipsychotic medication at baseline.

Antipsychotic drug	SCIT subgroup (*n* = 32)	TAU subgroup (*n* = 32)
Olanzapine	11	10
Aripiprazole	10	12
Risperidone	7	8
Blonanserin	5	1
Paliperidone	4	4
Levomepromazine	4	2
Quetiapine	3	2
Risperidone LAI	3	0
Zotepine	2	3
Perospirone	2	1
Haloperidol	1	0
Chlorpromazine	1	2
Bromperidol	0	1
Sultopride	0	1
Mean daily dosage (CPZ equiv.)	705.9 ± 506.3	559.0 ± 450.4

TABLE 3 | Trial design, showing when each measure was administered.

Measure	Screening	Baseline	3-month interim timepoint	6-month endpoint
Sociodemographic and clinical profile	•			
Diagnosis (DSM-IV-TR)	•			
Japanese Adult Reading Test	•			
Positive and Negative Syndrome Scale		•	•	•
Brief Assessment of Cognition Schizophrenia		•	•	•
Face Emotion Selection Test		•	•	•
Hinting Task		•	•	•
Social Cognition Screening Questionnaire		•	•	•
Social Functioning Scale		•	•	•
Global Assessment of Functioning		•	•	•
Intrinsic Motivation Inventory			•	•

Social Cognition

The Social Cognition Screening Questionnaire

Another primary outcome measure was change in social cognition, as assessed by total scores on the Social Cognition Screening Questionnaire (SCSQ) (30). The SCSQ is a measure consisting of five subscales assessing verbal memory, schematic inference, ToM, metacognition, and hostility bias. The task comprises 10 short vignettes presenting an interaction between a fictional character and the study participant. Each vignette was read aloud by the tester. The tester then asked the participant to answer "yes" or "no" to three questions about the vignette, addressing verbal memory, schematic inference, and ToM. ToM items were designed to assess both ToM and hostile attributional bias. Scores for the verbal memory, schematic inference, and ToM subscales were computed by counting the number of correct answers to corresponding items (range: 0–10; higher scores indicate better performance). Scores on the hostility bias subscale were calculated by counting the number of instances in which the participant erroneously inferred that the character in the vignette had negative thoughts or feelings towards the participant (range: 0–5; higher scores indicate stronger bias). With regard to metacognition scores, if the subject answered correctly on the corresponding "yes" or "no" question, a score of

1 was given. If the subject answered incorrectly on the question, a score of 0 was given if he/she answered that he/she was "very sure," 0.33 for "pretty sure," 0.66 for "a little unsure," and 1 for "not sure at all." The total metacognition score was obtained by summing the scores for the 10 vignettes (range 0–10; higher scores indicate better metacognitive ability). The total SCSQ score was calculated by summing all subscale scores, except the hostility bias subscale, because the items used for calculating this score overlapped with those used to calculate ToM score (range 0–40; higher scores indicate better social cognition). We used the Japanese version of SCSQ, which was translated and adapted to Japanese language and culture and validated in our previous study (31).

The SCSQ addresses multiple subdomains of social cognition including theory of mind, hostile attributional bias, and metacognition within a reasonable time period of about 15 min. In our previous validation study (31), it was demonstrated that the SCSQ showed more robust discrimination between patients with schizophrenia and healthy controls than other measures of social cognition. Moreover, the SCSQ subscales showed both fair convergent and discriminant validity as indicated by its significant relationship with measures which are thought to address the same subdomains of social cognition and not with those that are thought to measure other domains. Finally, the SCSQ theory of mind subscale scores in particular was significantly correlated with the scores of four domains of the Social Functioning Scale (SFS) (32), which supports the ecological validity of the SCSQ. Based on these findings, we decided to use the SCSQ as a primary measure but also to use the conventional Hinting task (33) as a secondary measure.

The Face Emotion Selection Test

The Face Emotion Selection Test (FEST) (34) is a measure used to assess emotion perception, consisting of 21 photographs of human faces depicting seven different emotions (happiness, sadness, anger, disgust, surprise, fear, and a neutral expression), with three images for each emotion. The photographs of Japanese actors were presented in a random order to the participant, and in each case, the participant selected one of the seven emotions; these were listed below the stimulus photograph and printed in Japanese. The score for each emotion was the number of correct responses (range: 0–3) to faces depicting that emotion. The total score was the sum of all scores for individual emotions (range: 0–21, higher scores indicate better face emotion perception).

In our previous study (34), it was demonstrated that the patients with schizophrenia performed significantly worse on the FEST compared to healthy control subjects. The FEST total score was significantly positively correlated with scores of the Brief Assessment of Cognition in Schizophrenia (35) attention subscale, Hinting Task, SCSQ verbal memory, and metacognition subscales.

The Hinting Task

The Hinting Task (33) is a measure assessing ToM and requires participants to infer the real intentions behind indirect speech. The task comprised 10 short passages presenting an interaction between two characters in which dialogue produced by one of the characters provided a hint at an underlying message. The participant was then asked what the character really meant when s/he uttered the hint. If the participant failed to give the correct response, an additional hint was given, and the question was asked again. Therefore, a correct response scored either 2 or 1, depending on whether the extra hint was given. The total score was obtained by summing the participant's scores for each passage (range: 0–20, higher scores indicate better theory of mind capacity).

We used the Japanese version of the Hinting task, which was translated and adapted to Japanese language and culture, and its psychometric properties were verified by showing a significant relationship with the SCSQ ToM subscale and also a significant difference between the patients with schizophrenia and healthy controls in our previous study (31).

The Brief Assessment of Cognition in Schizophrenia

The BACS (35) is a measure assessing neurocognitive function in six cognitive domains: verbal memory, working memory, motor speed, verbal fluency, attention, and executive function. We used the Japanese version of the BACS (36). The primary BACS measure, namely, the total score, was standardized by computing *z*-scores with reference to a distribution in which the mean score of Japanese healthy controls was set at 0 and the standard deviation set at 1.

In a validation study of the Japanese version of the BACS, internal consistency was acceptable with Cronbach's alpha of 0.77 and showed a good construct validity with the composite score being significantly correlated with standard neurocognitive tests in general (36). Accordingly, the Japanese version of the BACS is widely accepted in Japan as a practical scale to evaluate cognitive function.

The Social Functioning Scale

The SFS (32) is a measure assessing social functioning across seven domains: social engagement, interpersonal communication, independence-performance, recreation, social activities, independence-competence, and occupation (with higher scores indicating a higher level of functioning); each domain is assessed either by the participant themselves or by an informant. In the present study, we used self-report rather than informant interview. The score for each domain was computed by summing the item scores in the corresponding domain; the total score was the sum of all seven domain scores (range: 0–222, higher scores indicate better social functioning level). We used the Japanese version of SFS, which was validated in a previous study (37).

In addition to the above measures, the PANSS (38) was used to assess symptom severity and the GAF to assess functioning (39).

Statistical Analysis

We used linear mixed effects modeling (conducted using SAS 9.4; SAS Institute Inc., Cary, NC, USA) to compare the SCIT and TAU subgroups over time on outcome variables reflecting their social cognition, neurocognitive functioning, symptom levels, and social functioning. The model included fixed main effects of treatment subgroup (TAU *vs*. SCIT) and timepoint (baseline *vs*. 3-month interim timepoint *vs*. 6-month endpoint), and a treatment subgroup × timepoint interaction. In addition, random effects for participants were included. A significant interaction term in such a model would imply a difference in the effect of the intervention between timepoints. It was hypothesized that the SCIT subgroup would show significant improvements over time on the SCSQ subscales relative to the TAU subgroup. Effect sizes are reported to supplement statistical tests, calculated using the following formula.

$$\frac{\left(SCIT_{6\text{ months}} - SCIT_{\text{baseline}}\right) - \left(TAU_{6\text{ months}} - TAU_{\text{baseline}}\right)}{\text{pooled SD of baseline scores}}$$

Next, in order to explore predictors of the effect of SCIT on SCSQ total scores, a stepwise multiple regression analysis was conducted. Improvement in total SCSQ score observed in the SCIT subgroup between the baseline, and 6-month endpoint assessments was entered into the analysis as a dependent variable, and sex, age, duration of illness, BACS score (baseline), SCSQ score (baseline), and IMI score (mean) were included as independent variables. When significant variables were identified in this analysis, the total sample was subdivided according to the median value of these variables, and a secondary analysis using linear mixed effects modeling was conducted for the subgroup that was likely to benefit from SCIT treatment.

The full analysis data set, including data from all participants who were assessed at least once after any kind of intervention, was submitted to data analyses.

RESULTS

Sociodemographic and Clinical Profiles of Participants

Seventy-three patients were referred as potential participants and 72 consented to participate in the trial. Thirty-six patients were allocated to the SCIT subgroup and 36 to the TAU subgroup. During the study, four patients in the SCIT subgroup dropped out before the 3-month interim assessment: one started a job after session 1, one shifted to a community workshop after session 5, one withdrew from participation after session 1, and one showed exacerbation of their symptoms after session 3. Four patients in the TAU subgroup also dropped out before the 3-month interim assessment: one started a job after the baseline test, one suddenly died, one withdrew from participation before the baseline test, and one withdrew from participation after the baseline test. In addition, three further patients in the TAU subgroup dropped out before the 6-month endpoint assessment: one began a university course, one showed exacerbation of their symptoms, and one withdrew from participation. Data from the eight patients who dropped out after randomization but before the 3-month interim assessment were omitted from the full analysis data set because they were not assessed after any intervention. Thus, the data from 32 SCIT subgroup and 32 TAU subgroup participants were submitted to statistical analyses (**Figure 1**).

The SCIT and the TAU subgroups did not differ significantly on any sociodemographic or clinical variables, such as sex, age, duration of illness, daily antipsychotic dosage level, years of education, daily activities, baseline level of symptoms, level of functioning, or IQ as estimated by the JART (**Table 1**). Average total PANSS scores showed that the patients were generally at a moderate level of symptom severity (40), and nearly half the patients were engaged in competitive work, suggesting that the participants in the present study were relatively high-functioning.

Feasibility of SCIT

We estimated the feasibility of SCIT by using a) persistence rate at the 6-month endpoint, b) attendance rate, and c) IMI at the interim timepoint and endpoint.

The persistence rate in the SCIT subgroup was 88.9% (32/36), as only four out of 36 participants dropped out, all during the first half of the program, i.e., before the 3-month interim timepoint.

The average attendance rate at SCIT was 87.4% (*SD* = 15.9) between the baseline assessment and the 3-month interim assessment, 86.4% (*SD* = 18.7) between the 3-month interim assessment and the 6-month endpoint assessment, and 87.0% (*SD* = 14.8) over the entire period.

In addition, IMI scores for the first half of the program (between the baseline and 3-month interim timepoints) were significantly higher in the SCIT subgroup than in the TAU subgroup ($P < 0.01$). However, the groups did not differ significantly at end-point analysis.

Change in the Total SCSQ Score

The results of the mixed effects modeling revealed no significant interaction between timepoint and group in the total SCSQ score (**Table 4**). However, significant change was observed between the baseline and 3-month interim assessments, and also between the baseline and 6-month endpoint assessments, only in the SCIT subgroup (**Figure 2**).

Change in Other Measures of Social Cognition, Symptom Severity, Neurocognition, and Social Functioning

The results of the mixed effects modeling revealed no significant interaction between timepoint and group in any of the outcome measures, including social cognition, symptom severity, neurocognition, and social functioning (**Table 4**).

Possible Predictors of Efficacy of SCIT for Social Cognition

Stepwise multiple regression analysis of the improvement in SCSQ total scores over the 6 months of treatment with SCIT, with sex, age, duration of illness, BACS score (baseline), SCSQ score (baseline), and IMI score (mean) as independent variables revealed that a low SCSQ (baseline) score and a short duration of illness significantly contributed to improvement in SCSQ total score (**Table 5**). Therefore, the full sample was subdivided according to the median value of the variables identified as

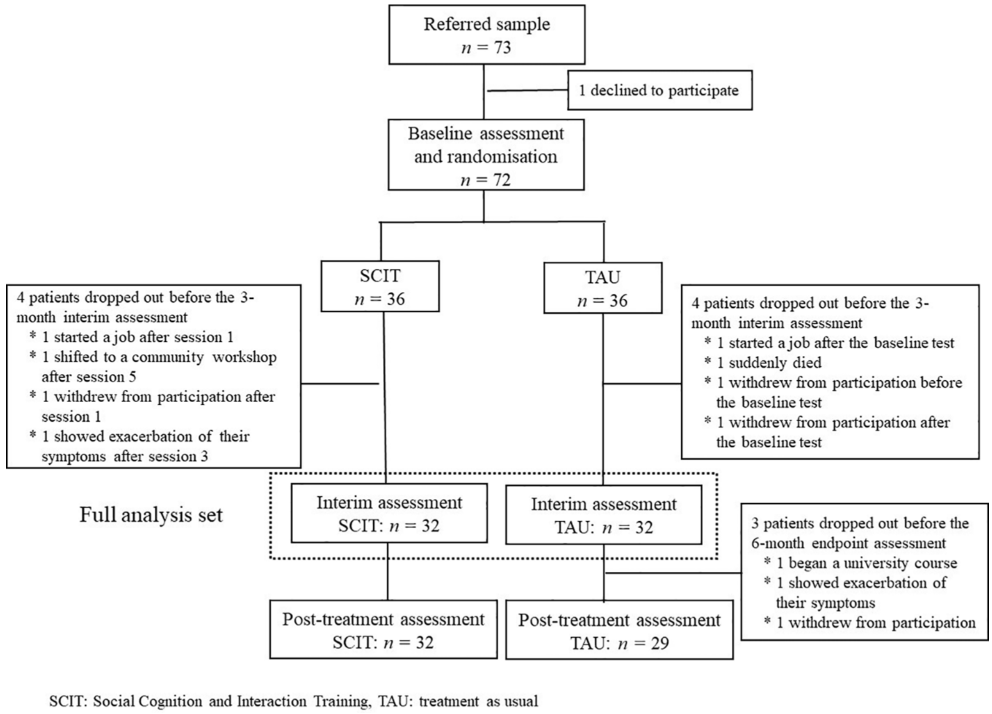

FIGURE 1 | Consort flow diagram. Seventy-three patients were referred to the trial, and 72 agreed to participate. Thirty-six patients were allocated to the SCIT subgroup and 36 to the TAU subgroup. During the study, four patients in the SCIT subgroup and four patients in the TAU subgroup dropped out before the 3-month interim assessment. In addition, three in the TAU subgroup left the study before the 6-month endpoint assessment. Thus, data from 32 SCIT subgroup and 32 TAU subgroup participants were submitted to statistical analyses.

predictors (median baseline SCSQ score: 32; median duration of illness: 149 months), and participants with total baseline SCSQ scores lower than or equal to 32 and those whose illness had a duration shorter than or equal to 149 months were submitted to secondary analyses using linear mixed effects modeling. Although there was no significant interaction between timepoint and group in the subgroup with low baseline SCSQ scores, a significant interaction was observed in the subgroup with a short duration of illness (**Table 6**). Specifically, this indicated that the change in total SCSQ scores between the baseline assessment and both the 3- and 6-month assessments was larger in the SCIT subgroup than in the TAU subgroup among participants with a relatively short duration of illness.

DISCUSSION

In this study, we translated, adapted, and evaluated SCIT for use with Japanese-speaking outpatients with schizophrenia. The persistence rate in the SCIT subgroup was relatively high, as only 4 out of 36 participants dropped out over the course of the whole program (persistence: 88.9%), and the average attendance rate for SCIT between the baseline and endpoint assessments was also high (87.0%, *SD* = 14.8). Both the persistence rate and the attendance rate in the present study were higher than those observed in previous community-based studies of SCIT (15, 41, 42). The relatively high IMI score in the SCIT subgroup compared with the TAU subgroup, especially in the first half of the program, indicates that the patients were well motivated. In fact, the IMI score observed in the SCIT subgroup (first half; 104.7 ± 21.6, second half; 100.1 ± 24.3) was much higher than that in Choi *et al.* (29), which presented a score of 61.14 ± 16.83 in the schizophrenia remediation sample. All in all, we found that SCIT appears to be feasible and well tolerated by patients with schizophrenia in Japan, as it has been when used with patients from other countries.

Regarding the social cognitive outcome measure (total SCSQ score), a significant change was observed between the baseline and 3-month interim assessments, and also between the baseline and 6-month endpoint assessments, only in the SCIT subgroup; however, the interaction between timepoint and group failed to reach significance, which suggests that the effect of SCIT was no different from that of TAU. These effectiveness results are not conclusive since the sample size may be too small, based on the meta-analytic study by Kurtz and Richardson (43). In their review of social cognitive interventions for schizophrenia, effect sizes varied from 0.07 to 1.01 across various subdomains of social cognition with a mean level of 0.40. If we used the effect size of 0.4, alpha set at 0.05, and power set at 0.8, the required sample size would be calculated to be 200. Again, as a first study in Japan, we decided the present study should be focused on feasibility and to generate effect size estimates for a future, more definitive study.

There was also no significant interaction between timepoint and group in their associations with any other measures of social

TABLE 4 | Results of mixed effects modeling of various outcomes.

Measure	Subgroup	BL	3M	6M	Main effect of time	Time × group interaction	Effect size (6M–BL)
SCSQ total	SCIT	31.04 (3.58)	32.94 (3.20)	32.79 (3.17)	$F(2,123) = 6.94$ $P = 0.0014$	$F(2,123) = 1.74$ $P = 0.18$	0.33
	TAU	32.83 (3.47)	33.45 (2.63)	33.40 (2.63)			
SCSQ ToM	SCIT	6.91 (1.20)	7.41 (1.54)	7.09 (1.38)	$F(2,123) = 2.22$ $P = 0.11$	$F(2,123) = 0.32$ $P = 0.73$	0.07
	TAU	7.22 (1.39)	7.47 (1.19)	7.31 (1.45)			
SCSQ HB	SCIT	1.66 (0.94)	1.28 (0.99)	1.08 (1.08)	$F(2,123) = 1.79$ $P = 0.17$	$F(2,123) = 0.80$ $P = 0.45$	–0.35
	TAU	1.59 (0.87)	1.50 (0.95)	1.75 (1.11)			
SCSQ MC	SCIT	9.04 (0.91)	9.41 (0.61)	9.35 (0.71)	$F(2,123) = 2.14$ $P = 0.12$	$F(2,123) = 1.31$ $P = 0.27$	0.33
	TAU	9.35 (0.70)	9.39 (0.64)	9.40 (0.61)			
Hinting Task	SCIT	12.69 (3.41)	14.09 (4.28)	14.88 (3.68)	$F(2,124) = 401.13$ $P < 0.0001$	$F(2,124) = 1.76$ $P = 0.18$	0.23
	TAU	14.28 (4.58)	15.16 (3.66)	15.53 (3.89)			
FEST	SCIT	66.01 (12.26)	73.15 (15.26)	68.73 (16.67)	$F(2,124) = 6.07$ $P = 0.0031$	$F(2,124) = 1.41$ $P = 0.25$	–0.05
	TAU	64.35 (13.50)	67.51 (12.97)	67.69 (15.33)			
BACS	SCIT	–1.64 (1.01)	–1.37 (1.09)	–1.13 (1.22)	$F(2,124) = 25.31$ $P < 0.0001$	$F(2,124) = 0.57$ $P = 0.57$	–0.05
	TAU	–1.33 (1.42)	–1.16 (1.36)	–0.77 (1.35)			
PANSS total	SCIT	64.78 (18.18)	61.34 (19.15)	60.03 (18.68)	$F(2,124) = 5.86$ $P = 0.0037$	$F(2,124) = 0.10$ $P = 0.91$	–0.04
	TAU	63.78 (18.98)	59.94 (18.02)	59.81 (17.32)			
PANSS P	SCIT	15.38 (5.13)	14.59 (5.58)	14.28 (4.79)	$F(2,124) = 6.99$ $P = 0.0013$	$F(2,124) = 0.71$ $P = 0.49$	0.18
	TAU	15.41 (5.87)	13.78 (5.19)	13.34 (5.00)			
PANSS N	SCIT	16.22 (5.38)	15.56 (5.09)	14.75 (5.27)	$F(2,124) = 3.06$ $P = 0.05$	$F(2,124) = 0.55$ $P = 0.58$	–0.10
	TAU	16.72 (5.86)	15.53 (6.21)	15.78 (5.36)			
PANSS G	SCIT	33.19 (9.82)	31.19 (10.07)	31.00 (10.18)	$F(2,124) = 2.87$ $P = 0.06$	$F(2,124) = 0.37$ $P = 0.69$	–0.13
	TAU	31.66 (9.70)	30.63 (9.03)	30.69 (8.83)			
GAF	SCIT	51.59 (8.81)	52.25 (13.63)	56.09 (15.33)	$F(2,124) = 2.71$ $P = 0.07$	$F(2,124) = 2.23$ $P = 0.11$	0.26
	TAU	53.44 (9.49)	58.06 (13.47)	55.59 (14.50)			
SFS	SCIT	116.06 (23.95)	118.44 (25.31)	117.45 (25.42)	$F(2,121) = 0.63$ $P = 0.53$	$F(2,121) = 0.30$ $P = 0.74$	–0.04
	TAU	106.53 (23.47)	107.41 (28.03)	108.91 (26.60)			
IMI	SCIT	N/A	104.68 (21.57)	100.10 (24.28)	$F(1,57) = 0.63$ $P = 0.53$	$F(1,57) = 0.30$ $P = 0.74$	–0.39
	TAU	N/A	89.30 (23.13)	93.97 (21.55)			

SCSQ, Social Cognition Screening Questionnaire; ToM, theory of mind; HB, hostility bias; MC, metacognition; FEST, Face Emotion Selection Test; BACS, Brief Assessment of Cognition in Schizophrenia; PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of Functioning; SFS, Social Functioning Scale; IMI, Intrinsic Motivation Inventory; BL, baseline; 3M, 3-month timepoint; 6M, 6-month timepoint; SCIT, Social Cognition and Interaction Training; TAU, treatment as usual.

cognition. Interestingly, most variables showed improvement between the baseline and 3-month interim timepoint, while changes between the 3-month interim timepoint and 6-month endpoint were small or absent. One possible explanation for this may be that a practice effect was more strongly in operation between the first two timepoints (baseline to 3-month interim timepoint) than between the second two timepoints (3-month interim timepoint to 6-month endpoint). A similar trend was observed in the TAU subgroup, which supports this view. Another possible explanation is that the treatment sessions in the latter half of the program were not as effective as expected, possibly because the tasks were too complex for some patients. In participants' subjective reports, they rather often complained of difficulty in generating alternative views and differentiating between inferences and facts, activities that are included in the sessions that form the second half of the program. The decrease in IMI scores in the SCIT subgroup in the latter half of the program compared to the former may support this view

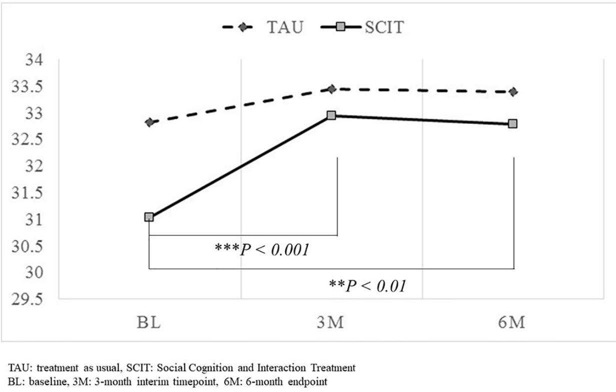

FIGURE 2 | Comparison of changes in total SCSQ score from baseline to the 3-month interim timepoint and the 6-month endpoint. Significant change in total SCSQ scores was observed between the baseline and 3-month interim assessments, and also between the baseline and 6-month endpoint assessments only in the SCIT subgroup. However, the interaction between timepoint and group failed to reach significance. ** P<0.01, *** P<0.001.

TABLE 5 | Summary of stepwise multiple regression analysis on improvement in SCSQ total scores during 6 months of treatment with SCIT (dependent variable: change in SCSQ score over this period). Sex, age, duration of illness, BACS (baseline), SCSQ (baseline), and IMI (mean) were entered into the analysis as independent variables.

Variable	Standardized beta	R^2	*P*
SCSQ (baseline)	–0.52	0.34	0.001
Duration of illness	–0.01	0.16	0.011

SCSQ, Social Cognition Screening Questionnaire; SCIT, Social Cognition and Interaction Training; TAU, treatment as usual; BACS, Brief Assessment of Cognition in Schizophrenia; IMI, Intrinsic Motivation Inventory.

at least in part. In addition, another possibility is that there was a ceiling effect on the SCSQ score. In fact, the mean level of the baseline SCSQ total score was 31.9 (SD = 3.6), which was slightly higher than the mean score obtained in our previous psychometric study (31.2, SD = 3.47) (31), and the distribution of the data was significantly skewed to the left (Shapiro-Wilk test, W = 0.96, P = 0.024).

The lack of effect on emotion perception, as measured by the FEST task, is inconsistent with previous research on SCIT (16, 17). Like the other measures of social cognition, participants' FEST scores increased steeply at the 3-month interim assessment, but decreased substantially thereafter. Perceiving and understanding emotions are the primary focus of the first half of the sessions, and although the skill is revisited throughout the program in the form of "checking in," the treatment is less intensive on this topic in the second half than in the first half. Thus, it may be beneficial to increase emotion perception training throughout the second half of the SCIT intervention program. In response to feedback and outcome data from previous studies, the developers of SCIT have revised several points in the treatment protocol manual (44). They have added partner exercises for practice and have also revised the SCIT content to make it easier for clients to digest and more flexible for clinicians to implement across a wide range of clinical settings in the current manual. These revisions were not present in the earlier version of the manual (28), which we followed in the present study. Further studies incorporating these new techniques are warranted in the future.

There was a significant interaction between timepoint and group when only patients with a relatively recent onset of illness were entered into the analysis, suggesting that SCIT may be more effective in patients with a shorter duration of illness. This finding needs to be interpreted with caution, since Kurtz and Richardson reported in a 2012 meta-analysis of interventions for social cognition that a longer duration of illness is associated with greater improvements in emotion perception and ToM (44). In the meta-analysis, participant samples were heterogeneous and included both inpatients and outpatients, which may explain this difference from the findings of the present study, in which only outpatients were recruited. A more recent systematic review suggests that studies highlighting the role of possible moderating factors, including areas such as illness chronicity, initial levels of functional or cognitive impairment, diagnosis, gender, and inpatient/outpatient status, would be important in developing a new generation of social cognition treatment programs (45). As some studies suggest that SCIT shows efficacy in patients with schizotypal personality and first-episode psychosis, early intervention for social cognition may well be effective in securing

TABLE 6 | Exploratory analysis in subgroups with low total SCSQ scores at baseline (≤32) and a short duration of illness (≤149 months). Both values represent the median in the full sample.

Median split subgroup	Subgroup	BL	3M	6M	Main effect of time	Time × group interaction	Effect size (6M–BL)
SCSQ total score ≤ 32 (*n* = 32)	SCIT (*n* = 19)	28.60 (2.29)	31.86 (3.10)	32.19 (3.35)	$F(2,60) = 21.32$ $P < 0.0001$	$F(2,60) = 1.16$ $P = 0.32$	0.57
	TAU (*n* = 13)	29.79 (3.24)	32.56 (2.56)	31.85 (4.43)			
Duration of illness ≤ 149 months (*n* = 32)	SCIT (*n* = 15)	31.20 (3.45)	33.56 (3.16)	34.04 (2.72)	$F(2,59) = 8.31$ $P = 0.0007$	$F(2,59) = 3.17$ $P = 0.049$	0.66
	TAU (*n* = 17)	33.02 (2.99)	33.53 (2.59)	33.71 (2.94)			

SCSQ, Social Cognition Screening Questionnaire; SCIT, Social Cognition and Interaction Training; TAU, treatment as usual; BL, baseline; 3M, 3-month timepoint; 6M, 6-month timepoint.

better outcomes in the future (19, 20). The period after recovery from a first episode of schizophrenia, extending over up to the subsequent 5 years, is known as the early course. If patients experience deterioration in symptoms and/or function, it is most likely to occur during this time, because by 5–10 years after onset, most patients experience a plateau in their level of illness and function, which is a so-called critical period (46, 47). It would be worthwhile to attempt to replicate our exploratory finding that patients with an onset of illness within the last 12 years, which overlaps with the critical period, may benefit from SCIT, because if this is the case, the program may well have the capacity to prevent functional deterioration.

The current study has a number of limitations. As noted above, the small sample size may have led to insufficient power to detect differences between the groups on outcome measures. Moreover, although as the first study to test the feasibility of SCIT in Japan we attempted to recruit the patients from a wide population, the patients who consented to participate in the study were relatively high functioning despite the moderate level of PANSS scores. Therefore, we could not conclude whether the program could be applied to lower functioning patients. Second, we did not account for changes to pharmacotherapy during the treatment period of this study. However, the potential effects of changes in pharmacotherapy on the efficacy assessment cannot be denied. Third, subjects' participation in psychosocial treatments other than SCIT was not controlled, which may have caused confounding effects. Finally, the therapeutic durability of training effects was not assessed. All these limitations should be taken into consideration in interpreting the efficacy analyses; however, none impacts conclusions regarding the feasibility and acceptability of SCIT.

In summary, although this study showed limited benefits for social cognition outcome measures associated with SCIT compared with TAU, SCIT is feasible for use with and well tolerated by Japanese patients with schizophrenia in real-world outpatient settings.

ETHICS STATEMENT

Ethical approval was obtained for the study (Ethical Committee of the National Centre of Neurology and Psychiatry) and the trial was registered with the University Hospital Medical Information Network (UMIN000011240; URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000013171)

AUTHOR CONTRIBUTIONS

AKa, KI, EI, TN, KN, and DR were involved in the conceptualization and planning of the study. AKi, DH, YT, YY, AI, YM, TM, TF, ST, KH, and SO were involved in the implementation of the trial. AKa, AKi, KH, SO, and KN developed the Japanese version of the treatment intervention. AKa was responsible for management of the trial, including implementation of randomization procedures, data management, and drafting the manuscript. KN was responsible for the statistical analyses. All authors critically reviewed the manuscript and approved the final version.

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HYPOTHESIS AND THEORY
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The Relation Between Empathy and Insight in Psychiatric Disorders: Phenomenological, Etiological, and Neuro-Functional Mechanisms

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Lack of insight, i.e., unawareness of one's mental illness, is frequently encountered in psychiatric conditions. Insight is the capacity to recognize (psychical insight) and accept one's mental illness (emotional insight). Insight growth necessitates developing an objective perspective on one's subjective pathological experiences. Therefore, insight has been posited to require undamaged self-reflexion and cognitive perspective-taking capacities. These enable patients to look objectively at themselves from the imagined perspective of someone else. Preserved theory-of-mind performances have been reported to positively impact insight in psychosis. However, some patients with schizophrenia or obsessive-compulsive disorders, although recognizing their mental disease, are still not convinced of this and do not accept it. Hence, perspective-taking explains psychical insight (recognition) but not emotional insight (acceptance). Here, we propose a new conceptual model. We hypothesize that insight growth relies upon the association of intact self-reflexion and empathic capacities. Empathy (feeling into someone else) integrates heterocentered visuo-spatial perspective (feeling *into*), embodiment, affective (*feeling* into) and cognitive processes, leading to internally experience the other's thought. We posit that this subjective experience enables to better understand the other's thought about oneself and to affectively adhere to this. We propose that the process of objectification, resulting from empathic heterocentered, embodiment, and cognitive processes, generates an objective viewpoint on oneself. It enables to recognize one's mental illness and positively impacts psychical insight. The process of subjectification, resulting from empathic affective processes, enables to accept one's illness and positively impacts emotional insight. That is, affectively experiencing the thought of another person about oneself reinforces the adhesion of the emotional system to the objective recognition of the disease. Applying our model to different psychiatric disorders, we predict that the negative effect of impaired self-reflexion and empathic capacities on insight is a transnosographic state and that endophenotypical differences modulate this common state, determining a psychiatric disease as specific.

Keywords: insight, empathy, perspective-taking, self-reflexion, psychiatric disorders, process of objectification, process of subjectification

INTRODUCTION

Unawareness of illness is frequently encountered in neurological [e.g., stroke (1, 2), traumatic brain injury (3), fronto-temporal dementia, Alzheimer disease (4)] and psychiatric conditions [schizophrenia (5), bipolar disorder (BD) (6–8), obsessive-compulsive disorders (OCD) (9), substance use disorders (SUD), behavioral addiction (10, 11)].

It significantly correlates with poor recovery over time and moderate to low outcomes from therapies and rehabilitation programs (12–15). Conversely, awareness of illness is associated with a better compliance to treatment, a greater efficiency of the therapeutic strategies, positive effects on prognosis, and a global amelioration of the patient's quality of life (15–17).

The present contribution focuses on the psychiatric form of awareness of illness, which is termed "insight", and on its deficits (18–23) (**Box 1**). Lack of insight is defined as the incapability of psychiatric patients to recognize and accept that they are suffering from a mental illness. Patients are unable to relabel their own mental events as abnormal, to identify the consequences of the illness (at physical, cognitive, and social levels), and to consent to treatment and hospitalization (19, 23–25).

Firstly, this definition indicates that there are two main stages in insight: recognition (psychical insight) and acceptance of the mental illness (emotional insight). Secondly, it suggests that insight growth necessitates the patients' capability to develop an *objective* perspective on their *subjective* pathological experiences (**Box 1**). Insight has been, thus, posited to rely upon a combination of intact self-reflection and cognitive perspective-taking capacities (18–21, 26). These enable respectively to focus on oneself and to shift perspective. In other words, insight requires "the cognitive capacity to adopt the other's perspective which, if intact, contributes to the metacognitive capacity to reflect upon "one's own" mental health from the other's perspective" (26).

Empirical studies using theory-of-mind (ToM) tasks tend to validate this assumption (27–29) (**Box 2**). It has been shown that difficulties in first-person perspective (1PP-PT) ToM tasks (with instructions neither directly evoking mental state inferences nor prompting to recruit inferential processing) in patients with schizophrenia have a more negative impact on insight, in comparison to difficulties in third-person perspective (3PP-PT) ToM tasks (with instructions directly asking what *X* thinks) (26). Hence, insight is better predicted by performances to tasks in which a more spontaneous processing is calculated. Langdon and Ward (26) concluded that theoretically reasoning about the other's thought without simulating his/her perspective is not sufficient for insight growth.

However, it has been reported that certain patients with schizophrenia (30) or OCD (31) recognize their mental illness but are not convinced of this. These data suggest that 1PP-PT ToM capacities, even in association with undamaged self-reflexion abilities, are not sufficient for the acceptance of the mental illness. Accordingly, perspective-taking only partly explains insight: that is, psychical insight (recognition) but not emotional insight (30) (acceptance) (**Box 1**).

To overcome these limitations, we propose a new conceptual model. It aims to explain the dysfunctional mechanisms underpinning lack of insight in psychiatric disorders. On the basis of empirical data showing that empathizing with someone else at both the affective and cognitive levels increases insight in schizophrenic patients (32), we hypothesize that insight growth (**Box 1**) relies upon the relationship between intact self-reflexion and empathic capacities.

BOX 1 | Insight and related concepts.

Insight: Psychiatric form of awareness of illness. It refers to the capability of psychiatric patients to recognize and accept that they are suffering from a mental illness. Insight is composed of three main dimensions, i.e., psychical, somaesthetic, and emotional.

Psychical Insight: One of the three main dimensions of insight. The psychical insight is further composed of three sub-dimensions, i.e., clinical, cognitive, and metacognitive. The psychical insight is necessary for the recognition of the mental illness.

Clinical Insight: One of the three sub-dimensions of the psychical insight. It refers to the awareness of symptoms and their consequences, the capacity to relabel mental events as pathological, to attribute a cause to the symptoms, and to agree with others (physicians, family, or friends) on the reality of the disease.

Cognitive Insight: One of the three sub-dimensions of the psychical insight. It refers to the patient's capacity to recognize that his/her experienced cognitive deficits (e.g., attentional disorders in unipolar depression) are induced by the mental illness.

Metacognitive Insight: One of the three sub-dimensions of the psychical insight. It refers to the reflexive awareness of oneself as a "diseased subject". It relies upon the capacity to make "the self as a diseased subject" a consistent object of thought.

Somaesthetic Insight: One of the three main dimensions of insight. Based on the awareness and representation of the bodily state, it refers to the patient's capacity to understand that his/her physical deficits (motor, sensory, somatosensory, etc.) are an effect of the mental illness (e.g., motor slowdown in unipolar depression).

Emotional Insight: One of the three main dimensions of insight. It refers to the patient's capacity of being convinced that he/she is suffering from a mental illness. The emotional insight is necessary for the acceptance of the mental illness.

Insight growth: Refers to the development of insight. Insight growth is specifically needed when psychiatric patients lack insight. It necessitates intact self-reflexion and empathic capacities.

Self: Entity which immediately and indubitably feels and knows to be the same person (ipseity) across time (temporality) and space (spatiality), to be the author of one's own thoughts and actions (agency), and to be localized within one's bodily borders at a given position in space (self-location).

Self-reflexion: Cognitive process by which an individual reasons about him/herself and evaluates whether a given attribution pertains or not to the self. It results in representations of one's own traits, abilities, and attitudes.

BOX 2 | Empathy and related concepts.

Empathy: Critical social skill. It refers to the capacity to feel and understand the lived experiences of someone else while mentally adopting his/her visuo-spatial and psychological perspective and maintaining self-other distinction. It recruits embodiment, heterocentered visuo-spatial perspective-taking, emotional/affective, higher-order cognitive, and self-regulatory processes. Under specific conditions, empathy further motivates concern and helping behavior.

Embodiment: One of the core processes of empathy. This automatic process enables individuals to directly and internally reproduce what another person is currently experiencing, regardless of the experiential content (motor, somatosensory, emotional, intentional, etc.).

Spatial and temporal decentering: Mental process enabling individuals to disengage themselves from here and now, i.e. from their own lived experience. It is required for visuo-spatial perspective-taking in empathy.

Perspective-taking: General term referring to a process by which individuals mentally adopt the perspective of someone else. There are different levels of perspective-taking: visual, visuo-spatial, or cognitive.

Visual perspective-taking enables to understand what people can see from their visual perspective (simple visual perspective-taking) and how people can see things differently (complex visual perspective-taking).
Heterocentered visuo-spatial perspective-taking enables individuals to mentally locate themselves into the body of someone else and to experience the world from his/her body position in space (heterocentered). It relies upon specific body-related mental imagery and transformation. Heterocentered visuo-spatial perspective-taking is one of the core processes of empathy and is specific to empathy
Cognitive perspective-taking is used in ToM and enables to understand the psychological perspective and mental state of someone else. According to the theory-theory, complex and higher-order cognitive perspective-taking uses logical inferences and contextual information to understand the other's mental state, i.e., "from the outside looking in". It is termed "third-person perspective-taking" (3PP-PT) (26). According to the simulation theory, individuals mentally put themselves in the other's shoes and use simulation processes to understand the other's mental state, i.e., "from the inside looking out" (26). It is termed "first-person perspective-taking" (1PP-PT).

Theory-of-mind (ToM): Cognitive ability enabling to represent and understand the mental states of others, including their emotions. According to the *theory-theory* account of ToM, individuals develop already in their childhood a theory about the mind of others. It enables them to reason about the thoughts and mental states of someone else with the help of logical inferences and contextual information.
According to the *simulation theory* account of ToM, individuals adopt the psychological perspective of another person while mentally putting themselves in the other's shoes and using simulation processes.
Cognitive ToM-like processes are core processes of empathy. They enable individuals to understand the other's current mental state and representations and how these may be similar to or different from their own representations.

Self-regulation: One of the core processes of empathy. This inhibitory process plays an important role for self-other distinction. At the *emotional level*, it enables to inhibit negative emotions that are spontaneously triggered when individuals are confronted with the other's distress. At the *visuo-spatial level*, it enables to partially inhibit one's egocentered visuo-spatial perspective. It is central for a balanced ego-heterocentered referential coding. At the *cognitive level*, it enables to decouple representational mechanisms associated with one's and other's mental state. Self-regulation also monitors the tendency to project onto someone else what individuals have already felt in similar past situations or would have potentially felt.

Metacognition: Cognitive ability that refers to the knowledge that individuals have about (1) their own cognitive processes, constructs, and productions (the content of the mental act), (2) their own mental states, intentions, beliefs, emotions, etc. (the form of the mental act), and (3) their capacity to analyze, understand, and think about their thoughts.

Simulation: Automatic process based on imagination that enables to mentally experience the others' mental states, including their emotions. It is specifically used in first-person perspective-taking (1PP-PT). When simulating, individuals mentally use and project onto someone else their own perceptive, emotional, and cognitive schemas and patterns. It potentially leads to egocentric biases.

Emotional contagion: Automatic process by which an individual (*A*) attributes to himself/herself the emotion of another individual (*B*). It leads to a self-other confusion in which *A* is experiencing the same emotional state as *B* although this emotion originally stems from *B* and does not directly concern *A*. Emotional contagion is the hallmark of sympathy in contrast to empathy.

Empathy (feeling into someone else) integrates heterocentered visuo-spatial perspective-taking (feeling *into*), embodiment, emotional/affective processes (*feeling* into), and higher-order cognitive representations (33–36) (**Box 2**). It enables to internally and more efficiently experience the other's thoughts, beliefs, emotions, etc. We posit that this subjective experience (based on feelings) enables to better understand the other's thought about oneself and facilitates the affective adherence to this thought.

Firstly, we hypothesize that empathic heterocentered, embodiment and cognitive processes, in association with self-reflexion capacities, result in the "process of objectification" (37). Generating an objective viewpoint on oneself, it enables to recognize one's own illness. The process of objectification positively impacts psychical insight.

Secondly, we hypothesize that empathic affective processes, in association with self-reflexion capacities, result in the "process of subjectification". That is, affectively experiencing the thought of another person about oneself reinforces the adherence of the emotional system to the objective evaluation and recognition of the illness. The process of subjectification enables to accept one's mental illness and positively impacts emotional insight.

We further apply our conceptual model to different psychiatric disorders: schizophrenia, unipolar, and bipolar mood disorders and OCD. (1) We propose that the negative effect of impaired self-reflexion and empathic capacities on insight is a transnosographic state. (2) We predict how endophenotypical differences modulate this common state, determining a psychiatric disease as specific.

PHENOMENOLOGY OF INSIGHT

Assessment of insight is consensually admitted as standard to the examination of the patients' general mental state and fundamental for diagnosis in psychiatry (23). However, there are still important debated issues. What etiopathogenic model does at best explain lack of insight? What is the phenomenal nature of insight?

Different Etiopathogenic Models of Lack of Insight

Five etiopathogenic models may be distinguished [for a review, see (15); see also (22, 26, 27)]. Because our working hypotheses are based upon the continuous model, this one is described in more details in a separate subdivision.

The Clinical, Psychological, Neuropsychological, and Neuro-Anatomical Models

The Clinical Model

The clinical or categorical model assumes that lack of insight is an isolated and constitutive symptom of the disease [(38); see (27)]. Lack of insight is defined as a stable trait, i.e., as a symptom being either present or absent ["all-or-none approaches"; for a criticism, see (22)]. This model specifically aims to account for lack of insight in psychoses. It posits that psychotic patients are not able to recognize their own illness. Here, the process of recognition is first impaired and impacts, as a consequence, the process of acceptance. In clinical studies using categorical methodologies, 70% of patients with schizophrenia were found to have a low insight [for a criticism, see (39, 40)] whereas OCD, as an example, was associated with a good insight [for a criticism, see (41)]. However, experimental data only little endorse the clinical model. It is probably due to that this model hardly produces testable hypotheses (15).

The Psychological Model

According to the psychological model, lack of insight is caused by a psychological defense mechanism. This form of denial is a copying strategy enabling to face up to the experienced stressful events [i.e., the illness itself; (15)] and to avoid distress and the negative consequences of a diminished self-esteem [(42, 43); see (15, 26, 27)]. Here, patients recognize their own illness but do not accept it. For instance, in first-episode schizophrenia, non-stabilized compared to stabilized patients exhibited defense mechanism in a more pronounced way (N = 52). This defensive attitude was further associated with a more severe lack of insight (43) [see also (28, 44, 45)]. Although interesting, this model does not disentangle whether defense mechanism is the primary cause of lack of insight or a secondary effect of the stigmatization that is often associated with psychiatric diseases (26).

The Neuropsychological Model

The neuropsychological model assumes that lack of insight originates in neuro-functional abnormalities and associated impairments of neuropsychological functions (e.g., memory, executive functions, etc.). Experimental results are still contradictory. Some studies report that better insight positively correlates with higher levels of intelligence [e.g., (12, 46)], greater executive functions, and augmented frontal activity in schizophrenia [e.g., (43, 47–49) (meta-analysis on 35 studies)]. Other studies failed to find this association [(50, 51) (N = 75)]. According to Langdon and Ward (26), it means that the deficits measured by standardized neuropsychological tests are not sufficient to account for lack of insight in most of its phenomenal and clinical manifestations. Another possible explanation is that the findings are dependent upon the evaluation timing. First-episode onset, decompensation, stabilization, or remission phases may have an important impact on the association between insight and neuropsychological functions (15). This further tends to validate the continuous model.

The Neuro-Anatomical Model

According to the neuro-anatomical model, insight deficits correlate with reduced cerebral volume in the dorso-lateral prefontal cortex (dlPFC), medial PFC (mPFC), anterior and posterior cingulate cortex (ACC/PCC), insula, temporo-parietal junction (TPJ), and hippocampus [(52) (N = 15); (53, 54) (N = 35); (55) (N = 14); (56–60)]. Neuroimaging data do not reach consensus. Again, this is probably due to that sample sizes are often small, leading to biased statistical analyses (15).

Although importantly contributing to the exploration of lack of insight, these four models have not been validated by consistent empirical data so far. In addition to methodological shortcomings (sample size, statistical methods, standardized test batteries, testable hypotheses, etc.), these contradictory results could be further due to the timing of evaluation (acute episode, remission phase, etc.). If correct, it suggests that insight may be variable over time and in intensity, depending upon multiple factors. This observation is the starting point of the continuous model.

The Continuous Model

The continuous model evidenced the complexity of insight. It does not define insight as a stable symptom of the disease but "a continuum of thinking and feeling, affected by numerous internal and external variables" (22), in contrast to the clinical/categorical model. Hence, insight is here considered a dynamic mental state that varies over time and in intensity, depending upon internal [in the self (61)] and external (in the environment) changes (22, 40, 62). Accordingly, insight corresponds to the patient's awareness of changes in the self that relate to his/her own pathological state and how these changes affect his/her perceptions and interactions with the world (40). Consequently, the phenomenon of insight, observed for a patient p at time t of the clinical evaluation, only reflects a given aspect of the concept of insight (37, 62).

According to the continuous model, insight is composed of three main dimensions: (1) psychical insight, which entails three sub-dimensions, i.e., clinical, cognitive and metacognitive; (2) somaesthetic insight; and (3) emotional insight (24, 30, 37, 40, 62–65) (for definitions, see **Box 1**).

Each dimension can be specifically altered. It depends upon the clinical features intrinsic to each mental illness and upon the variations of the clinical state over the illness time course. For a good insight, all these dimensions need to be preserved. This positively impacts prognosis, adherence to treatment, acceptance of hospitalization, and risks of relapse.

Lack of Insight Relates to the Clinical State and Is Not Specific to Psychoses

The clinical model has prevailed in last decades. Consequently, lack of insight has long been considered a clinical marker distinguishing psychotic from neurotic disorders, namely, a stable and specific symptom of schizophrenia. However, the use of multidimensional evaluation scales based upon continuous methodologies has led to reconsider the clinical model. Three main observations may be retained. Firstly, insight is impaired in psychiatric disorders other than psychoses. Secondly, the dimensions of insight are differentially altered according to the diseases. Thirdly, insight varies over time and in intensity depending upon the clinical state. This is also observed in schizophrenia.

Deficits in Insight in Different Psychiatric Disorders

As an example, in a sample of 421 schizophrenic patients, 32.1% were found to have a low insight, 25.3% a fair insight, and 40.7% a good insight [(5); see also (66)]. In a sample of 431 patients with OCD, 25% had a low insight and 5% were unaware of the absurdity of their obsessions (9). These data invalidated the hypotheses of the clinical model that insight is constitutively impaired in schizophrenia but preserved in other psychiatric disorders. Lack of insight was also reported in patients with alcohol use disorders (AUD). In a sample of 452 AUD patients, nearly 75% had poor insight into their alcohol-related problems (67). This lack of cognitive insight was reflected in a significant contrast between the patients' evaluation of their own cognitive performance, which was under-estimated, and the standardized neuropsychological evaluation by clinicians [(68) (N = 86); (69) (N = 91); see also (70, 71)]. Similarly, AUD patients evaluated their apathy and executive functions deficits as significantly less severe (N = 38), compared to their family members' ratings (N = 38) (72). Yen et al. (67) further reported that a greater metacognitive insight is associated with a more accurate self-estimation of the addictive symptomatology, i.e., with a greater clinical insight (N = 425).

Collectively, these studies heightened the hypothesis by Lewis (18) that insight is not useful to distinguish psychosis from neurosis insofar as lack of insight and good insight may be equally observed in both kinds of disorders [see also (22)]. According to Marková and Berrios's criticism (23), the empirical investigation of insight has been mostly limited to psychosis for two main reasons. Firstly, it is due to that "loss [of insight] is so dramatically apparent" (23) in psychoses, compared to neuroses. Secondly, it is due to an insufficient analysis of the concept of insight. It has led to ignore the multidimensional nature of insight and its variations over the illness time course. In general, this suggested that the quantitative analysis of insight should not prevail over its qualitative analysis.

Insight Correlates With the Clinical State

In addition, insight has been reported to correlate with the clinical state. It is worth noting that this correlation size is often small [see (73)]. As an example, a meta-analysis on 30 studies showed that insight negatively correlates with the severity of symptoms (global, positive, negative) in schizophrenia (74). Lack of insight was found to predict rehospitalization after 18 months following schizophrenic decompensation [(75); (N = 33); see (73)]. The severity of insight deficits at admission is also a significant predictive marker of symptoms worsening after 12 months [(76); (N = 278); see (73)].

Importantly, insight changes over the illness time course. This is the case in OCD [(9); (N = 431)]. But also in AUD, in which insight depends upon abstinence span, probably reflecting a decrease of the neurotoxic effects of alcohol on the activity of the frontal and temporo-parietal cortices [(77); (N = 117)]. This was also reported in first-episode schizophrenia: the worsening of insight deficits over the first 6 months after the disease onset predicts later functional impairments or relapse [(78); (N = 131)]. Early improvement of insight is, thus, considered an important marker for positive clinical outcome. In a sample of 670 stabilized patients with schizophrenia or schizoaffective disorders, the improvement of insight over 1 year was associated with an amelioration of the symptoms severity (79). This was also observed in a cohort of 614 schizophrenic patients with long-acting risperidone (80).

To sum up, the status of insight, in psychiatric disorders including schizophrenia, is generally associated with the patient's clinical and symptoms-related state and varies over time and in intensity. Accordingly, insight resembles more a variable state than a stable trait.

The Contribution of the Default Mode Network to Insight

Lack of insight is likely associated with functional abnormalities in the default mode network (DMN) (81, 82). The DMN, which is a largely distributed brain network (**Box 3**), sustains thoughts, imagination, memory and cognitive processes that relate to the Self (81, 82). Accordingly, it is considered a system underpinning internal, self-referential, affective, and introspective processes. The DMN neuro-functional feature is that its activity increases during state of unconstrained cognition (at rest).

The DMN together works with the fronto-parietal network (FPN) (**Box 3**). In contrast to the DMN, the FPN is "task-positive". Its activity increases during externally-focused attention and cognition (94). At rest, the DMN activity increases whereas the FPN activity decreases. Conversely, during externally-focused cognition, the FPN top-down modulates the DMN activity, enabling to disengage from internal and self-referential processing (95, 96).

In addition to neurological diseases (e.g., epilepsy and dementia), DMN dysfunctions have been observed in psychiatric disorders, such as schizophrenia (83, 87, 90), autism (91, 92), deficit/hyperactivity disorder (84, 88), OCD (93, 94), anxiety (86), and depression (85). For instance, the DMN activity and DMN-FPN functional connectivity during external stimuli-based tasks and at rest are abnormal in OCD patients [(93); (N = 18)]. These brain data are coherent with the phenomenology of the disease. The disruption between the processing of ongoing

BOX 3 | Brain systems involved in insight and empathy.

Default Mode Network (DMN): The DMN is thought to sustain insight. It encompasses the posterior cingulate cortex, restrosplenial cortex, ventro- and dorsomedian prefrontal cortex, precuneus, inferior parietal lobule expanding to the temporo-parietal junction, and hippocampal formation.
References: (81, 83–94)

Fronto-Parietal Network (FPN): The FPN is anti-correlated with the DMN. It encompasses the lateral frontal and parietal regions, anterior insula, and medial frontal cortex.
References: (94–96)

Mirror Neuron System (MNS): The MNS is thought to sustain automatic embodiment.
Isomorphic activations have been found in the motor system—i.e., in the inferior frontal gyrus, inferior parietal lobule, premotor cortex and superior temporal sulcus when individuals empathize with the other's *motor action*. Similar functional isomorphism has been also reported in the anterior part of the bilateral insula, rostral part of the anterior cingulate cortex, cerebellum, and brainstem in *emotional empathy*. This holds also true for the secondary somatosensory cortex when people empathize with the *somatosensory experience* of someone else.
References: (36, 97–106)

Vestibular System: It plays an important role in balance, perceptions of one's own-body and motion, location of one's own-body in space, and, spatial navigation. It is also involved in empathy, enabling individuals to mentally locate themselves in the other's body position in space. It encompasses the temporo-parietal junction, superior temporal gyrus, inferior parietal lobule (angular/supramarginal gyrus), posterior insular cortex, hippocampal formation, somatosensory cortex, precuneus, cingulate gyrus, and frontal cortex (motor cortex and frontal eye fields).
References: (35, 36, 107–109)

Theory-of-Mind Network (ToM-Network): The higher-order cognitive processes of empathy generate activations in the ToM-Network. That is, in the ventro-dorsomedian prefrontal cortex, temporo-parietal junction, anterior part of the superior temporal sulcus, precuneus, and temporal poles. Especially, the ventromedian prefrontal cortex and left temporo-parietal junction respectively code for the other's psychological perspective and perspective ownership.
References: (36, 110–114)

Executive System: The right dorsolateral prefrontal cortex within the executive system sustains self-regulatory and inhibitory processes. These enable to decouple between self- and other-centered computational mechanisms in empathy..
References: (33, 36, 112, 113, 115, 116)

Limbic System: It plays an important role in emotional/affective and mnemonic processing when individuals are empathizing. It encompasses the thalamus, hypothalamus, basal ganglia, hippocampus and amygdala. The hippocampus and amygdala are specifically involved in empathy, respectively sustaining reactivations of information from one's own past and embodiment and affective processing.
References: (117–122)

internal thoughts and external information is considered to reflect a lack of clinical and cognitive insight in OCD [(94); N = 30]. In schizophrenia, ACC activations within the DMN negatively correlate with the severity of symptoms while lower metabolism in the PCC tends to negatively correlate with the severity of insight deficits [(123); (N = 20)].

The Complexity of Insight Growth: Developing an Objective Perspective on One's Subjective Pathological Experiences

The complexity of insight is observable at three levels. Firstly, insight is multidimensional. Secondly, it varies over time and correlates with the patients' clinical state. Thirdly, insight growth necessitates the patients' capacity to develop an *objective* perspective on their *subjective* pathological experiences (18, 124). That is, a process in which the Self is an object of reflexion (26)—or a "self-as-object" processing (125). David designated it as the ability "to see ourselves as the others see us" [(21); see also (19, 20)]. It refers to the ability "to reflect upon the self's inner world from the imagined perspective of the other" (26).

For that, insight growth (**Box 1**) has been posited to involve both self-reflexion (126) (i.e., metacognition) (127) and cognitive perspective-taking capacities (i.e., social cognition) (18–21, 26). These respectively enable to focus on oneself and to shift perspective (18–21, 26).

Insight Growth Combines Intact Self-Reflection and Cognitive Perspective-Taking Capacities

Self-Reflexion and Metacognition

Self-reflexion is considered a core feature of metacognition which is broadly defined as "cognition about cognition" (127) or "thinking about thinking" (128). Self-reflexion enables to reflect on thoughts, intentions, emotions, beliefs, etc. as these specifically depend upon oneself, i.e., as one's owns (129) [see also (45)]. It further enables to adopt a critical viewpoint on one's own opinions and interpretations and to reconsider them according to different potential perspectives on the same situation and event [(130); see (126)] (**Box 2**).

At the clinical level, self-reflexion reinforces "the patients' capacity and willingness to observe their mental productions and to consider alternative explanations" (30). Accordingly, self-reflexion capacities are thought to facilitate insight. Conversely, lack of insight is considered being partially due to impaired self-reflexion capacities (21, 130–132).

Cognitive Perspective-Taking and Social Cognition

Cognitive perspective-taking as used in ToM is a core feature of social cognition (133, 134). Enabling to shift perspective and understand the psychological perspective of other people (135–137), it is considered necessary for insight growth in addition to self-reflexion (18–21, 26) (**Box 2**). In 1PP perspective-taking, individuals understand the other's mental state on the basis of simulation processes (138) (**Box 2**) and "from the inside looking out" (26). In 3PP perspective-taking, individuals understand the other's mental state on the basis of logical inferences (135) and "from the outside looking in" (26). 1PP- and 3PP-PT are fundamental for appropriate social cognition and successful self-other interaction.

Only a few studies investigated the association between lack of insight and impaired cognitive perspective-taking. Moreover, these focused on schizophrenia. Drake and Lewis (47) failed to report a relationship between difficulties in 3PP-PT ToM tasks and lower insight (N = 33). In contrast, other studies showed that 3PP-PT ToM deficits negatively impact insight [(27) (N = 58); (26) (N = 30); (29) (N = 58)]. This effect was independent of neurocognitive impairments and symptoms severity (26, 29). In the study by Bora et al. (27), ~30% of the variance in patients' insight scores was explained by their performance to second-order ToM tests (assessing the capacity to understand what the protagonist of a story thinks about the thoughts of a second character) (26). Langdon and Ward (26) found that only deficits in ToM tasks with indirect instructions (neither directly evoking mental state inferences nor directly prompting to recruit inferential processing) correlated with lower insight. This was not the case in ToM tasks with direct instructions [directly asking what *X* thinks about (…)].

Summary and Questions

To sum up, theoretical hypotheses and empirical data (18–21, 26, 30, 37, 124, 130, 132) suggest that insight growth relies upon the relationship between intact self-reflexion and cognitive perspective-taking capacities.

As pointed out by Langdon and Ward (26), it is worth noting that there is lack of insight (1) when the patient's perspective on his/her subjective pathological experiences is inaccurate and not conformed to the reality and (2) when the patient is at the same time unable to adopt the objective perspective that other individuals have on him/herself. However, the patient does not need to adopt the perspective of others on him/herself when his/her own perspective on his/her pathological experiences is already accurate. It means that self-reflexion and cognitive perspective-taking capacities are needed to improve insight when it is altered, i.e., for insight growth. In this case, it is only the combination of these two capacities that enables the patients to objectively look at themselves and their pathology from the outside, as if from the others' viewpoint. It results in what we have lately termed the "process of objectification of oneself" (37). That is, a process in which the self and its pathological experiences—or "the self as a diseased subject"—is a consistent object of thought. That is, a process in which the patient is objectively observing himself/herself from the perspective of someone else.

However, there are still important issues that need to be overcome. Firstly, how can it be explained that indirect ToM tasks better predict insight in patients with schizophrenia, compared to direct ToM tasks (26)? Secondly, how can it be explained that certain psychiatric patients (including schizophrenics) recognize the symptoms of their disease in others (46), have ToM task performances than fall within the normal range, but are, at the very same time, unaware of their own symptoms (see 26)? Thirdly, how can be it explained that schizophrenic (30) and OCD patients (31) recognize their mental illness but do not accept it?

We here argue that the relationship between self-reflexion and cognitive perspective-taking capacities are not sufficient for insight growth. These are sufficient for the recognition of the illness but not for its acceptance. We hypothesize that insight growth rather relies upon the association of undamaged self-reflexion and empathic capacities.

Before describing our conceptual model in more details in the third section (see, *The Contribution of Self-Reflexion and Empathy to Insight Growth in Psychiatric Disorders: Proposal for a New Conceptual Framework*), we come back below to the phenomenological and neuro-functional features of empathy.

PHENOMENOLOGY OF EMPATHY

Empathy is the capacity to feel and understand the lived experiences of someone else while mentally adopting his/her visuo-spatial and psychological perspective and maintaining self-other distinction (34, 36, 116, 139, 140). Phenomenological analyses [e.g., (141–146)] and neuroimaging research [(e.g., 33, 34, 36, 120, 137, 147, 148)] importantly contributed to understand the complex and multifaceted nature of empathy.

The Multidimensional Approach of Empathy

Over the two last decades, behavioral and brain data evidenced that the association of perspective-taking and feeling is the hallmark of empathy. These have also shown that the empathic perspective-taking has specific features that are not encountered in other closely related but nevertheless distinct socio-cognitive functions, such as first- and third-person perspective-taking ToM (34–36, 149, 150). Indeed, empathy specifically relies upon body-related mental imagery and transformation.

Spatial Decentering in Empathy: The Role of Mental Body Transformations

The English neologism "empathy" has been coined by E. B. Titchener in 1909 as a translation of the German term "Einfühlung" that was introduced by R. Vischer in 1872[1]. "Einfühlung" means literally "to feel [*fühlen*] into [*ein*]"

[1] R.Vischer firstly introduced the term "Einfühlung" in his thesis manuscript *Über das optische Formgefühl* in 1872 and further developed the concept of "Einfühlung" in two later articles (*Der ästhetische Akt und die reine Form* in 1874 and *Über ästhetische Naturbetrachtung* in 1890 (151)). He used this term to refer to the human capacity to "feel [fühlen] into [ein]" in the field of aesthetics (arts and nature). In 1913, T.Lipps applied the term "Einfühlung" to the field of psychology (152). E.B. Titchener coined the english neologism "empathy" as a translation of "Einfühlung", on the basis of the Greek term "empatheia". The question whether "empathy" appropriately reflects the original meaning of "Einfühlung" is still a debated issue [see, (153, 154); for a detailed etymological analysis, see 145; see also (155)]. We here refer to empathy as "to feel into" on the basis of the German term as in 36, 116, 150 [for a comparable approach, see as (34, 156–158)].

someone else (36, 145, 156, 157). This "feeling" enables to accede to the embodied mind of others "in their bodily and behavioral expressions" (146). It corresponds to the experience of one's physiological, bodily, and affective states and changes (159) that are internally generated by the perception of another individual's lived experience (motor, somatosensory, emotional, intentional etc.). the prefix "ein" refers to a process of mental decentering of oneself into the other.

Heterocentered Visuo-Spatial Perspective-Taking in Empathy

The prerequisite for empathy is to be "[…] aware that you are outside and have to reach inside the other one" (156). Spatial decentering (**Box 2**) (160) is first required to mentally locate oneself into someone else (161). This mental location into the other corresponds to a visuo-spatial perspective-taking process (**Box 2**). It relies upon specific body-related mental imagery and transformations.

That is, individuals imagine their own-body to be located in the other's body position. They mentally experience the world from this heterocentered [centered on the other's body; (162)] reference frame (34, 116, 149). Hence, empathy modulates two key phenomenological components of so-called bodily self-consciousness (163): self-location [the experience of where I am in space; (164)], and egocentered perspective [the experience from where I perceive the world; (164)] (149).

Preservation of the Self-Other Distinction

However, self-other distinction needs to be maintained simultaneously when empathizing. It enables individuals to appropriately feel and understand that the observed experiences are originally not their own lived experiences but those of someone else. For that, the awareness of being located at a specific position in space within one's bodily borders (egocentered reference frame) is concurrently required although it is partially top-down controlled (33, 36). Accordingly, empathy relies upon a dynamic interplay between egocentered and heterocentered visuo-spatial mechanisms. That is: (1) a mental shift from an egocentered to a heterocentered reference frame, enabling to imagine oneself in the other's body position. And (2) a parallel although top-down regulated coding of one's body position in space, maintaining self-other distinction at a minimal level and ensuring a balanced self-other relation (36, 116). This dynamic interplay enables to feel what the other "as other" is feeling, i.e., as the other is precisely not me.

The Automatic Embodiment, Heterocentered Visuo-Spatial Perspective-Taking, Emotional/ Affective, Cognitive, and Self-Regulatory Processes of Empathy

In addition to heterocentered visuo-spatial perspective-taking, empathy encompasses automatic embodiment processes (enabling to internally reproduce what another person is experiencing) [e.g., (105, 159, 165)], emotional/affective processes (103), cognitive ToM-like processes (enabling to represent the other's mental state) [e.g., (113, 136, 137, 166, 167)], and self-regulation processes (maintaining self-other distinction at the emotional, visuo-spatial, and cognitive level) (33, 36, 112, 113, 115, 116, 168) (see **Box 2**).

The embodiment and emotional/affective processes correspond to the "feeling" features of empathy. The heterocentered coding and ToM-like processes correspond respectively to its spatial and cognitive components.

The Neuro-Functional Networks of Empathy

The complex and multifaceted nature of empathy is reflected at the neuro-functional level. This is observed in the integration of parallel but also competing activations in the Mirror Neuron System (MNS), Theory-of-Mind Network (ToM-Network), Executive, Limbic, and Vestibular Systems (**Box 3**).

Functional Integration of the Mirror Neuron System, Theory-of-Mind Network, Executive System, and Limbic System in Empathy

MNS and ToM-Network have long been considered mutually exclusive (169). However, functional magnetic resonance imaging (fMRI) studies lately demonstrated parallel activations and functional integration in the MNS, ToM-Network, executive system, and limbic system when empathizing (117–121). As an example, judging changes in the affective states of a cartoon protagonist who is suffering from ostracism triggers in the observers co-activations in the anterior part of the ToM-network (superior temporal sulcus (STS) and ventromedian prefrontal cortex (vmPFC)) and in the limbic regions (amygdala and hippocampus).

This co-recruitment of top-down neocortical and bottom-up limbic components suggests that empathizing with the affective states of someone else relies upon the use of cognitive representations related to the other's mental state (vmPFC), embodiment and affective processing (amygdala), and reactivation of information from one's own past experiences (hippocampus) (120). Moreover, empathizing with fictional characters who experience moral dilemma and difficult emotional decision-making generates a bidirectional functional connectivity between areas in the MNS, ToM-Network, and limbic system (122).

Contribution of the Vestibular System to Visuo-Spatial Perspective-Taking in Empathy

Recruitment of the Insula, Right, and Left Temporo-Parietal Junction in Empathy

Using electrical neuroimaging (EEG), we showed that the brain vestibular system (**Box 3**) significantly contributes to empathy (35). It was found to sustain the shift from the egocentered to heterocentered visuo-spatial perspective. This was reflected in activations in the left insula and right TPJ at ~60–330 ms post-stimulus onset (PSO) and in the bilateral TPJ but predominantly in the left hemisphere at ~520–630 ms PSO (35, 36).

The Temporo-Parietal Cortex and the Bodily Self-Consciousness

The right TPJ encodes self-location, egocentered perspective and bodily self-consciousness under normal conditions (170, 171). This is in line with data from neurological or psychiatric patients with anatomical lesions or dysfunctions in the TPJ and experiencing pathological forms of self-location (107, 108, 172–178). In out-body experience (OBE), patients experience to be located outside their own-body borders at an elevated position in space and see their physical body from this perspective (179). In heautoscopy (HAS), patients see a reduplication of their own-body in extracorporeal space, facing them, with a "preservation of the lateral asymmetries" (180). They have further difficulties in deciding whether they are located within their own-body borders (egocentered reference frame) or within the autoscopic body (heterocentered reference frame) (179). HAS is considered the pathological pendant of the interplay between egocentered and heterocentered visuo-spatial mechanisms in empathy (155, 180). Most often, OBE and HAS are respectively associated with abnormalities in the right and left TPJ (164, 181).

Accordingly, this sequence of activations in our data, i.e., firstly in the left insula and right TPJ and, secondly, in the bilateral TPJ, confirmed that individuals, when empathizing, shift from the egocentered to heterocentered visuo-spatial perspective. This supports the hypothesis that visuo-spatial perspective-taking based upon mental own-body transformations is a key empathic process. Moreover, the later co-activation of the right and left TPJ suggests that individuals computed *at minima* their own egocentered perspective in parallel with the coding of the other's visuo-spatial perspective. This co-activation enables to maintain a basal reference to oneself and, thus, self-other distinction (35).

Differential Modulation of the Mirror Neuron System, Vestibular System, Executive System, and Tom-Network in Empathy

Using cortical dynamics and neural generators analyses, we reported that empathy, in addition to the vestibular system, also generates parallel activations in the MNS, ToM-Network, and executive system. Moreover, these parallel activations were differentially modulated, depending upon the time course of mental processes, i.e., embodiment, visuo-spatial perspective-taking, self-regulation, and cognitive processing (36). Activations in the MNS progressed from the right STS to the right inferior frontal gyrus (IFG) *via* the middle temporal gyrus (MTG) and inferior parietal lobule (IPL) between ~60 and ~420 ms post-stimulus onset (PSO). The vestibular system was recruited at ~60–630 ms PSO. Here, activations progressed from the insula and right TPJ (~60–330 ms) to the bilateral TPJ (~520–630 ms). The right dlPFC was specifically activated at ~330–420 ms. Finally, activations within the ToM-Network were found in the STS, right TPJ, temporal poles (~60–330 ms), left TPJ, and precuneus (~520–630 ms) between ~60 and ~630 ms.

Hence, our data confirm that empathy relies upon the integration of parallel activations in cooperating and/or competing brain networks, reflecting the recruitment of distinct but related mental processes. These further suggest that embodiment processes (STS, MTG, IPL, IFG), occur in parallel with (1) shifting from the egocentered (insula, right TPJ) to heterocentered visuo-spatial perspective (left TPJ), (2) decoupling computational mechanisms between self- and other-centered processes (right dlPFC), and (3) higher-order cognitive representations (temporal poles, left TPJ, precuneus). We did not report activations in the vmPFC. This is probably due to that our experimental paradigm and tasks did not involve complex judgments about the others' mental states. Another possible explanation is that vmPFC activations occur later in the neural time course. We focused on a time window from 0 to 700 ms PSO as the quality of the EEG signal was poorer after this time period (due to stimulus-locked analyses). Thus, it is probable that vmPFC occurred after 700 ms. The precise time window of the vmPFC activation in empathy needs to be tested in future EEG study.

Concluding Remarks: The Subjective and Objective Dimensions of Empathy

Collectively, neuroimaging studies converge on the contribution of cooperating and/or competing parallel brain networks to empathy, confirming its multifaceted and complex nature. EEG studies further shed light on the activations time course within these brain networks. Importantly, this neural time course informs on how visuo-spatial perspective-taking operates in empathy. Indeed, it enables to disengage oneself from one's own present experience, thoughts, beliefs, feelings, and emotions, etc. that are early encoded in the egocentered reference frame (insula/right TPJ). It is done in order to mentally locate one's own-body into the body position of another individual and to internally experience his/her experiences, thoughts, beliefs, feelings, and emotions from his/her body position (heterocentered) (bilateral/left TPJ) (to feel *into*).

Embodiment (MNS) and emotional/affective processes (anterior part of the ACC, brainstem/dorsal pons, cerebellum) also occur simultaneously. These correspond to the physiological, bodily, and affective states and changes (159) that are triggered in individuals when they are internally experiencing the others' experience (*to feel* into). This feeling results from sharing and embodying the other's mental state. It corresponds to the subjective dimension of empathy.

Moreover, visuo-spatial perspective-taking with the help of cognitive ToM-like (temporal pole, precuneus, vmPFC) and self-regulatory (dlPFC) processes enables to comprehend as objectively as possible the others' experience. That is, what the other *as other* is experiencing. This corresponds to the objective dimension of empathy.

Finally, the parallel reference to oneself that is encoded in the right TPJ and insula enables to compare what the other is experiencing with one's own current experience. It enables to adapt one's own behaviors toward the other and to correct one's first assessments and predictions concerning the other's mental state. It further maintains self-other distinction[2].

THE CONTRIBUTION OF SELF-REFLEXION AND EMPATHY TO INSIGHT GROWTH IN PSYCHIATRIC DISORDERS: PROPOSAL FOR A NEW CONCEPTUAL MODEL

There are empirical and clinical arguments in favor of the contribution of self-reflexion and cognitive perspective-taking capacities to insight growth. However, two important issues need to be addressed.

Limitations and Theoretical Hypotheses

Two Related Issues

Firstly, as pointed out by Langdon and Ward (26), difficulties in indirect ToM tasks in patients with schizophrenia have a more negative impact on insight, compared to difficulties in direct ToM tasks. It suggests that performances to tasks in which patients compute more spontaneous, implicit, or automatic processing better predict insight than tasks in which a more explicit and controlled processing is calculated [for comparable results, see (150); for a criticism, see (182)]. These data are in line with the simulation theory account of ToM, positing that ToM relies upon 1PP-PT capacities. Therefore, Langdon and Ward (26) concluded that theoretically reasoning about the other's thought (3PP-PT) (which is tapped by direct ToM-tasks) without simulating his/her perspective (1PP-PT) (which is tapped by indirect ToM-tasks) would not be sufficient for insight growth.

Secondly, as above-mentioned, clinical studies reported that certain psychiatric patients with schizophrenia (30) and OCD (31) are able to recognize their mental illness but are not convinced of this. That is, patients do not accept their disease.

Is this latter observation inconsistent with the hypothesis that impaired 1PP-PT ToM capacities negatively impact insight? Does it suggest that these are only sufficient for the recognition of the mental illness but not for its acceptance? Accordingly, 1PP-PT ToM capacities would explain psychical insight (recognition) but not emotional insight (acceptance).

Hypotheses

To overcome these limitations, we propose a new conceptual model. It aims to explain the dysfunctional mechanisms underpinning lack of insight in psychiatric disorders. We here further deepen our first theoretical approach published elsewhere (37).

Main Working Hypothesis

Our main working hypothesis is that insight growth relies upon the relationship between intact self-reflexion and empathic capacities. Accordingly, we suggest that 1PP-PT ToM capacities, even associated with intact self-reflexion, are not sufficient for the development of insight. The starting point of our working hypothesis is the assumption by Langdon and Ward (26) that deficits in 1PP-PT but not 3PP-PT ToM have a negative impact on insight. This is a very important and suitable hypothesis. However, we here aim to partially modulate this approach and bring further precisions.

There is no doubt that 1PP simulation ToM and empathy are two close phenomena. However, they distinguish for two related reasons. Firstly, empathy entails embodiment and affective processes (*to feel* into) whereas 1PP simulation ToM does not. It means that empathy is not only a cognitive and mental simulation of the other's mental state. It is also a way to embody and to affectively process this mental state. In empathy, the feeling stems from both these embodiment and affective processing (159). Thus, empathy does not only consist in "imagining what it would be like to be in the "mental shoes" of another person" (26) as in 1PP simulation ToM but also in internally experiencing what he/she is experiencing.

Secondly, according to simulation theoreticians, individuals, when simulating, use and mentally project onto someone else their own perceptive, emotional, and cognitive schemas and patterns (183–185). This potentially leads to egocentric biases (186). In contrast, individuals, when empathizing, inhibit the tendency to project their own schemas and patterns onto the other. It enables to feel and to understand what the other *as other* is experiencing. That is, precisely as the other *is not me*. For instance, this inhibition of projective processes in association with a basal self-other distinction (see second section *Phenomenology of Empathy*) is fundamental to helping behaviors and medical care (116, 157, 158).

Thus, we argue that feeling into another individual enables to internally and more efficiently experience his/her mental state than do 1PP simulation ToM processes. As a consequence, this subjective experience (i.e., based on feelings), in association with basal self-other distinction and inhibition of projective processes, would enable to understand more objectively the other's mental state and to facilitate the affective adherence to the other's thoughts.

But how feeling into someone else may positively impact insight and its two stages, i.e., the recognition and the acceptance of the mental illness? Our main working hypothesis further divides into two sub-hypotheses.

First Sub-Hypothesis: The Process of Objectification

Firstly, we hypothesize that intact heterocentered perspective-taking, embodiment, and cognitive processes, in association with self-reflexion, are necessary and sufficient for the recognition of the mental illness. It is not the case for its acceptance. That is, (a) looking at oneself and one's pathological mental experiences from the visuo-spatial perspective of another individual (heterocentered), (b) embodying his/her current thought about oneself, and (c) understanding this thought as being specifically related to oneself result in what we have previously termed a "process of objectification of oneself" (37).

This process of objectification enables to recognize one's own illness ("I am suffering from *this* mental illness"). It generates an

[2] We here note that empathy distinguishes from sympathy in that it maintains self-other distinction whereas sympathy does not [see (36, 144)].

objective viewpoint on the self. This would, thus, selectively impact psychical insight, particularly metacognitive insight and clinical insight (**Box 1**).

Second Sub-Hypothesis: The Process of Subjectification

Secondly, individuals need to have recognized their mental illness before being able to accept it. However, if the process of objectification enables to recognize one's own mental illness, it is not sufficient to accept it. Additional mechanisms probably occur.

Indeed, "to have the capacity to adopt another's point of view as so to imagine what it would be like to think something different than one actually believes about self" is completely different from "to be able to accept that the other person's point of view provides the more accurate representation of the true state of affairs" (26). Accordingly, the other's point of view needs not only to be objectively understood but also incorporated into the subjective representation of the self. We hypothesize that, if the mental illness has been already recognized (process of objectification), then, the association of both intact self-reflexion and empathic affective capacities contribute to accept the illness ("This mental illness is *mine*"). It means that the affective experience of the other's thought about oneself enables to subjectively adhere to this thought. Hence, it facilitates acceptance.

It has been well-documented that higher-order cognitive processes, such as acceptance or decision-making for example, require computational processing by the cognitive system but also the adhesion of the emotional system to the cognitive evaluation (187). "Any behaviour is by definition both cognitive and affective" (188). Brain data confirmed that emotion and cognition are "non-modular" (188) as these are integrated in specific areas, such as the lateral PFC (189, 190), orbito-frontal cortex, vmPFC and ACC (188).

We argue that affectively experiencing the thought of another person about oneself reinforces the adherence of the emotional system to the objective evaluation and recognition of oneself "as a diseased subject" (process of objectification). It refers to what we here propose to label a "process of subjectification". This would, thus, selectively impact emotional insight (**Box 1**).

Summary

To sum up, we posit that the process of objectification positively impacts psychical insight, leading to recognize one's mental illness. The process of subjectification positively impacts emotional insight, leading to accept one's mental illness. The process of objectification needs to be intact in order that the process of subjectification occurs. That is, there is no emotional insight if the psychical insight is impaired. In other words, the mental illness must have been already recognized to be, then, accepted. Insight as a whole process is still impaired—although less severely—if the recognition of the illness is intact (psychical insight) but its acceptance is altered (emotional insight).

Applications and Predictions

What are the applications and predictions of our conceptual model? We insist on that our model does not only focus on schizophrenia but aims to apply to psychiatric diseases in general. Firstly, as evidenced by the continuous model and clinical data, insight is not a symptom of the disease but a mental state that varies over the illness time course and in intensity. Secondly, lack of insight has been reported in different psychiatric conditions. Hence, lack of insight is not specific to schizophrenia. Thirdly, deficits in empathic capacities are also observed in most psychiatric diseases [for a review, see (115)].

Therefore, there are solid clinical and empirical arguments to examine the relationship between lack of insight and deficits in empathy in psychiatric disorders. Moreover, and in accordance with our hypothesis, cognitive and affective empathy has been shown to enhance insight in schizophrenia (32). We posit that the negative effect of the association of impaired self-reflexion and empathic capacities on insight is a transnosographic state in psychiatric diseases. We further argue that endophenotypical differences modulate the expression of this common state, determining a given disease as specific.

Below, we focus on schizophrenia, OCD, and BD.

Transnosographic State and Endophenotypical Modulations

We here note that, on the basis of prior studies, the data from at least 100 patients for each clinical group are needed to verify our conceptual model (i.e., to get a sufficient statistical power).

Schizophrenia

Firstly, in accordance with prior studies (78, 79), we predict that during acute and decompensation episodes, there is a complete breakdown of both self-reflexion and empathic capacities, with a deleterious effect on insight. In stabilized patients, self-reflexion and empathic capacities may be differentially altered and, thus, the dimensions of insight differentially impaired. This would depend upon symptoms features.

Schizophrenic Patients With Preeminent Negative Symptoms. Patients with a prevailing negative symptomatology are more impaired in emotions recognition, general social abilities, ToM performance, and empathy (150, 191–193), especially when their symptoms resemble those of autism (194, 195), in comparison to patients with a prevailing positive symptomatology. In a previous work (150), we showed that patients with negative symptoms were unable to spontaneously empathize with others. That is, they were impaired in inhibiting their egocentered visuo-spatial perspective and disengaging from themselves. We here predict that patients with a predominant negative symptomatology lack psychical insight because of deficits in heterocentered visuo-spatial perspective-taking capacities (hypo-functionality). Thus, the process of objectification is here impaired. Consequently, patients do not recognize their own illness.

Schizophrenic Patients With Preeminent Positive Symptoms. In contrast, we found that patients with prevailing positive symptoms have augmented facilities in using heterocentered visuo-spatial coding and imagining themselves in the body position of others (150). This is line with a study by Thakkar and Park (196), reporting that facilities in inhibiting one's egocentered perspective positively correlate with increased positive syndrome schizoptypy. This is further concordant with the hypothesis by Abu-Akel (197, 198) that patients with a predominant positive symptomatology have exaggerated ToM competences. These aberrant capacities would be responsible for the patients' tendency to overrate and over-attribute intentions, thoughts, emotions, etc. to other individuals, as in delusions (191, 197, 199).

We predict that patients with positive symptoms have normal empathic heterocentered visuo-spatial perspective-taking capacities. They are able to imagine themselves in the others' body position. However, they fail to appropriately feel, i.e., embody, what others are feeling. This yields to misinterpretations and misattributions at a higher-order cognitive level. Accordingly, we anticipate that deficits in empathic embodiment processes (hypo-functionality) trigger compensatory exaggerated empathic higher-order cognitive processes (hyper-functionality). The process of objectification is altered, negatively impacting psychical insight. There is no recognition of the mental illness.

In both clinical groups, lack of insight and associated alteration of empathic processes would vary over the illness time course and in intensity, depending upon the severity of symptoms and clinical state.

Intact Recognition but Altered Acceptance of the Mental Illness in Schizophrenic Patients With Either Negative or Positive Symptoms. Certain schizophrenic patients with a relative good insight recognize "the logical assertion that they are suffering from a mental illness" (15) but they are still not convinced of this (30). We posit that the process of recognition is here intact due to the preservation of the heterocentered, embodiment, and cognitive processes of empathy. This positively impacts the psychical insight. In contrast, the affective process of empathy is altered. It means that patients are unable to affectively experience the other's thought about themselves and, thus, to subjectively adhere to this thought. This negatively impacts emotional insight. We predict that this insight status is observed in patients with either positive or negative preeminent symptoms when the clinical state is significantly improved.

Bipolar Disorder

Manic episodes are well-documented to be associated with lower insight (200, 201). Recent data demonstrated that depressive episodes also correlate with deficits in insight, although the correlation size was smaller than for manic episodes (202). Deficits in insight during depressive episodes were especially associated with higher rates of suicide ideation. Moreover, empirical studies using the Interpersonal Reactive Index [IRI; (139)], i.e., a self-report questionnaire evaluating empathy, or the Multifaceted Empathy Test [MET; (203)] reported that manic and depressive episodes are associated with deficits in the cognitive processes of empathy (204–206). In contrast, manic BD patients had higher affective empathy than depressives and controls (204–206). This effect was interpreted as reflecting excessive affective empathic reactions due to disturbances in emotion inhibition and persistence of positive emotions (207). This way of perceiving social stimuli as more positive than these really are leads patients to the conviction to fully understand other individuals (206).

BD Patients in Manic Episodes. We predict that BD patients in manic episodes have intact empathic heterocentered visuo-spatial perspective-taking and are, thus, able to imagine themselves in the body position of others. However, they have altered empathic cognitive processes (hypo-functionality) and exaggerated embodiment and affective processes (hyper-functionality). There is a parallel alteration of the process of objectification and process of subjectification, negatively impacting psychical and emotional insight. That is, patients feel positively the negative content of the other's thought about themselves (e.g., the clinical evaluation of their physician), leading to misinterpretations.

BD Patients in Depressive Episode. In contrast, we predict that BD patients in depressive episodes have difficulties in inhibiting their own egocentered visuo-spatial perspective and using a heterocentered visuo-spatial coding (hypo-functionality). They are, thus, unable to disengage from themselves. In this case, the process of objectification is altered, leading to deficits in metacognitive and clinical insight. This triggers an augmentation of negative thoughts related to oneself and ruminations, potentially leading to suicide. We hypothesize that a comparable process may be also observed in unipolar depression.

Obsessive-Compulsive Disorders

Foa et al. (9) reported that, 70% of a sample of 431 OCD patients had a good insight, 25% a low insight, and 5% were unaware of the absurdity of their obsessions (see section *Phenomenology of Insight*).

OCD Patients With No Insight. We here predict that OCD patients with no insight have high difficulties in disengaging from themselves and using a heterocentered visuo-spatial perspective (hypo-functionality). This negatively impacts psychical insight, and, thus, the recognition of the mental illness. This would be more associated with egocentered OCD, i.e., a sub-clinical group in which patients suffer from obsessional fears concerning themselves (e.g., "I will contract a fatal illness, if I do not clean the house"), or OCD with impulsion phobia.

OCD Patients With Low Insight. In contrast, we predict that OCD patients with a low insight have preserved empathic heterocentered, embodiment, and cognitive processes (208). The process of objectification is here intact. However, the affective process of empathy is altered (hypo-functionality). Patients are unable to affectively experience the other's thought about themselves and, as a consequence, to subjectively adhere to this thought. This would lead to an alteration of the process of subjectification, impacting emotional insight and acceptance of the illness. That is, patients recognize the absurdity of their obsessions but are not convinced of this. Here, this would be encountered in patients whose "(…) affective states thus seem to take precedence over their rational thoughts" (31).

Model Limitations and Future Research Protocols

Limitations

There are potential limitations to our conceptual model. Clinical and neuro-functional hypotheses posit that psychiatric disorders may be explained by dysfunctional cognitive flexibility, associated with functional abnormalities in the prefrontal and frontal cortices (209–211). If correct, this would suggest that difficulties in developing an objective viewpoint on one's subjective pathological experiences are not triggered by impaired self-reflexion and empathic capacities but by control and executive dysfunctions. A recent meta-analysis based on brain data from 5,728 controls and 5,493 psychiatric patients with schizophrenia, bipolar or unipolar depression, anxiety and SUDs reported transdiagnostically abnormal activations in the left PFC, anterior insula, left vmPFC, right intraparietal sulcus, and mid-cingulate/pre-supplementary motor area (212). This suggests that psychiatric disorders rely upon a common pattern of cognitive disruption. These brain areas further overlap with the DMN, likely sustaining insight, and empathic brain networks. Hence, the precise contribution of cognitive flexibility to insight needs to be further examined.

As described in the first section, the clinical model considers insight a symptom of the disease whereas the continuous model considers insight a variable mental state. Clinical and empirical data seem to validate the continuous model. The same question needs to be addressed to lack of empathy. As an example, diminished empathic capacities seem to pertain to the symptom structure in OCD with impulsion phobia. Conversely, exaggerated empathic capacities seem to be a symptom of hetero-centered OCD, i.e., which is characterized by obsessional and inappropriate fears concerning other individuals and associated rituals and compulsions. Hence, our model should disentangle whether deficits in empathy are a symptom of the disease or a variable mental state, depending upon the symptoms severity and clinical state.

Our model also needs to take into account the negative effect of insight on depressive comorbidity. For instance, it is well-documented that insight improves in schizophrenic patients when these are stabilized. However, this improvement of insight is associated with an increase of the comorbid depressive symptoms. It is probably due to that patients become aware of the gravity of their disease. Hence, the effect of a good—or better—insight on depressive comorbid symptoms must be explored. Another issue is also to understand how depressive comorbidity may negatively impact, in turn, empathic capacities.

Research Protocols

Only a very few studies investigated the relationship between lack of insight and deficits in empathy. It means that our model is rather speculative and needs to be further tested in clinical, empirical, and neuroimaging studies. For that, it is necessary to develop extensive research protocols with different psychiatric groups and at different phases of the clinical state (first-episode onset, decompensation, stabilization, or remission). These protocols should entail: (1) clinical evaluation targeting symptoms severity [as an example in case of OCD: The Yale-Brown Obsessive-Compulsive Scale (Y-BOC); (213)] and insight status [Brow Assessment of Beliefs Scale (BABS); (214)]; (2) self-evaluation of symptoms severity [Obsessive Compulsive Inventory (OCIR), (215)], insight [Birchwood Insight Scale (IS); (216)], and empathy (IRI); (3) standardized neuropsychological test batteries; (4) measure of brain activity at rest (using fMRI or EEG); and (5) batteries of behavioral paradigms that evaluate insight [e.g., adaptation of the Insight Task by (217)] and empathic processes (hetero-centered visuo-spatial perspective-taking capacities (E.S.T; 149); ToM-processes ["Joke Appreciation Task"; (218)]; emotional processing ["Reading the Mind in the Eyes Test; (219); MET] using fMRI or EEG. Clinical, behavioral, and neuroimaging studies based on extensive research protocols with different psychiatric populations (schizophrenia, OCD, and AU) are in progress in our laboratory.

CONCLUSION

In the present contribution, we proposed a new conceptual model aiming to explain the dysfunctional mechanisms underpinning lack of insight in psychiatric disorders. We posited that the association between impaired self-reflexion and empathic capacities negatively impact insight. Moreover, we distinguished between two new concepts: the process of objectification and the process of subjectification. We showed that the process of objectification results from empathic heterocentered, embodiment, and cognitive processes. Generating an objective viewpoint on oneself, it enables to recognize one's own mental illness and, thus, positively impacts psychical insight. We further showed that the process of subjectification results from empathic affective processes. We argued that affectively experiencing the thought of another person about oneself reinforces the adhesion of the emotional system to the objective evaluation and recognition of the illness. Hence, the process of subjectification enables to accept one's mental illness and positively impacts emotional insight.

Furthermore, applying our conceptual model to different psychiatric conditions, we predicted that the negative effect of impaired self-reflexion and empathic capacities on insight is a transnosographic state. Moreover, we predicted that endophenotypical differences modulate this common state. Hyper vs. hypo-functional empathic processes (heterocentered visuo-spatial perspective, embodiment process, or affective processing, etc.) would impact differently psychical or emotional insight depending upon symptoms features and clinical state in each psychiatric disease.

Although based upon prior clinical, behavioral, and neuroimaging studies, our model is rather speculative. If validated by empirical data, our model would be helpful to develop new cognitive-behavioral therapies and neuro-stimulation protocols adapted to each psychiatric disease in each clinical phase (first onset, acute episode, stabilization, remission). This would be fundamental to ameliorate the quality of care.

AUTHOR CONTRIBUTIONS

BT and NJ theorized the link between lack of insight and deficits in empathy in psychiatric disorders. BT theorized the process of objectification, process of subjectification and predictions of the conceptual model. GH-G and NL respectively helped with the elaboration of the clinical and neuro-functional hypotheses. BT wrote the manuscript.

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Neural Correlates of Empathy in Boys With Early Onset Conduct Disorder

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Background: A deficit in empathy has repeatedly been described in individuals with conduct disorder (CD), and in particular in those with callous unemotional traits. Until now, little is known about the neural basis of empathy in children and adolescents with early onset conduct disorder. The aim of this study was to examine neural responses during empathizing in children and adolescents with CD with a task that allowed to differentiate between the judgment of the emotional states of other people and the own emotional response to other people's emotional state. Moreover, we investigated associations of callous-unemotional traits and neural activations during empathizing.

Methods: Using functional magnetic resonance imaging (fMRI) we investigated 14 boys with early onset CD and 15 typically developing (TDC) age matched controls between 8 and 16 years of age. Happy and sad faces were presented, and participants were asked to either infer the emotional state from the face (other-task) or to judge their own emotional response (self-task). A perceptual decision on faces was used as a control task. Individual empathic abilities and callous unemotional traits were assessed.

Results: During the other task, TDC boys showed significantly larger right amygdala responses than CD boys. Higher empathic abilities (as assessed with the Bryant Index of Empathy) were associated with higher responses in the right amygdala within the CD boys and across the entire sample. Moreover, across the entire sample, callous-unemotional traits were negatively related to the BOLD-response in the right amygdala. CD boys showed larger responses in the dorsal and ventral medial prefrontal cortex across tasks and increased activation in dorsal medial prefrontal cortex specifically during the self-conditions, which were also related to empathic abilities within the CD boys.

Conclusions: The data emphasize the important role of the amygdala in empathy related emotional processing. Diminished amygdala responses and their association with low empathy suggest a pivotal influence of impaired amygdala processing in early-onset

CD, in particular for deficits in empathic behavior and related callous-unemotional-traits. Elevated response in the medial prefrontal cortex in boys with CD point toward increased involvement of brain areas related to self-referential processing and cognitive empathy during empathizing.

Keywords: affective empathy, cognitive empathy, amygdala, medial prefrontal cortex, callous-unemotional traits, psychopathy

INTRODUCTION

Conduct disorder (CD) is a serious neurodevelopmental disorder characterized by a repetitive and persistent pattern of disruptive behavior that violates the basic rights of others and major age-appropriate social norms or rules (1). It is one of the most frequent psychiatric disorders in childhood and adolescence resulting in referral to mental health services (2). CD is accompanied by mental and physical health problems and negative psychosocial outcomes with an increased risk for lifelong antisocial behavior, resulting in considerable healthcare, and societal costs (3). However, children with CD are a strikingly heterogeneous group with respect to clinical presentation and outcome (4). Children and adolescents with an early onset CD (before age 10) show a particularly poor prognosis with frequent development of subsequent criminality, substance abuse and antisocial personality disorder (5, 6). A second criterion to differentiate CD—callous unemotional (CU) traits—was added to the Diagnostic and Statistical Manual of Mental Disorders [DSM-5, (1)]: the lack of empathy and guilt, callousness, and uncaring attitudes. CU-traits are associated with an early-starting and chronic trajectory of disruptive behavior with especially unfavorable developmental consequences (7). While CD without CU traits appears to be more strongly related to environmental risk factors, CD with high CU traits seems to have a greater biological foundation (8, 9) and high CU traits are associated with an early onset of the disorder (10).

Accordingly, theoretical models of CD etiology have proposed that dysfunction in different neurocognitive systems may be associated with different types of CD-related symptom sets (11), including CU traits [for a recent review, see (12)]. Accumulating evidence indicates that children with CD but low levels of CU traits typically show a heightened affective reactivity to perceived negative emotional stimuli, such as angry or ambiguous neutral facial expressions, which may be regarded as social threat or provocation, resulting in reactive aggressive acts (13). In stark contrast, a reduced affective responsiveness to others' distress signals, such as fearful or sad facial expressions, appears to be a characteristic dysfunction of CD individuals with high levels of CU traits. Such a profile is thought to contribute to a repertoire of rather proactive aggressive behavior that harm other people (e.g., violence) (14, 15). Thus, the latter form of CD is assumed to constitute a group of individuals with decreased emotional empathy, which involves a marked difficulty in decoding and representing the emotional states of other people.

Converging lines of research using functional magnetic resonance imaging (fMRI) have consistently demonstrated that higher CU traits among individuals with CD problems are particularly associated with reduced amygdala activation in response to distress cues, including fearful and sad facial expressions as well as witnessing other persons in pain (11, 16–20). While the vast majority of relevant fMRI studies has investigated rather basic affective responsiveness in youth with CD (i.e., recognizing simple emotion expressions), a minimal amount of work has more directly investigated higher-level empathic functioning (i.e., inferring the emotional state of others or one's own emotional response). Importantly, reduced empathy is a key criterion for identifying high CU traits and both traits are inversely related. Sebastian et al. (21) were the first to demonstrate amygdala hypoactivation (accompanied by reduced anterior insula cortex activation) in children with CD problems in the context of an empathy paradigm that required participants to infer how a story character would react to their companion's affective state through a series of pictorial story vignettes. Importantly, the authors found suppressor effects such that amygdala reactivity decreased as a function of CU traits but increased as a function of conduct problems. However, this study investigated a community sample with conduct problems but not a clinical sample with a diagnosis of CD. Other fMRI-studies of explicit empathizing in participants with psychopathic traits likewise point toward diminished neural responses in comparison to healthy participants (22–24). Moreover, these studies suggest that patients with psychopathic traits may have the ability to empathize with other people but are less inclined to use this ability during social interaction (23). Youth with CD and particularly those with high CU-traits appear to have deficits concerning affective responses relevant for empathy (13), but do not show impairments in cognitive aspects of empathy such as mentalizing or theory of mind (21, 25). Thus, a possible pathway to understand the ability to empathize in individuals with high CU-traits could be an increased use of strategies related to cognitive empathy.

Cognitive empathy involves the representation of thoughts and intentions of other individuals and the process of mentalizing (26). Mentalizing and theory of mind has typically been associated with activation of the medial prefrontal cortex (MPFC), also in the context of empathizing (26). While studies on explicit empathy tasks focusing on cognitive aspects (21) have not found dysfunctions in the MPFC in CD, other studies using resting state fMRI suggests functional alterations in this brain region in individuals affected by the disorder (27, 28), which the authors interpreted as reflecting deficient introspective processing, emotion processing and reduced empathy. Therefore, the authors recommended investigating correlates of cognitive empathy and deficient introspective processing in more detail.

In summary, while previous research has established a blunted amygdala reactivity, this has rarely been investigated using higher-level empathy tasks in youth with CD. Second, while CD individuals are able to empathize in order to achieve goals or when explicitly instructed (22), they still show deficits in processing sad and fearful faces, show little compassion, a shallow affect and lack of guilt, in particular with high CU traits (29). A detailed knowledge about neural mechanisms related to empathizing in CD, including cognitive and affective aspects, is lacking. This is of particular interest in early-onset CD, as this subtype is thought to be characterized by marked neurodevelopmental disturbances and a higher risk to develop CU-traits (10). Given the poor prognosis and very limited treatment options of early-onset CD particularly with high CU-traits (30), it is of great scientific and clinical interest to understand neural mechanisms of empathy in this cohort but has not been studied to date. Due to the relevance of reduced empathy for the concept of psychopathy and CU traits (31), and strong evidence for negative associations between individual empathy and CU-traits (32), we aimed for a combined investigation of neural substrates of empathy, individual empathy measures and CU-traits. We employed an established explicit empathy tasks, which involved a face-to-face situation and draws on both cognitive and affective aspects of empathy. This task requires participants to empathize with emotional faces by (a) inferring the emotional state of others as expressed by their facial expression (other-task) and (b) judging the own emotional state in response to the depicted facial expression (self-task). Thus, this task draws on evaluating someone's emotion, taking the self-perspective, and focusing on own evoked emotions. We investigated a clinical sample of early-onset conduct disorder (i.e., presence of at least one characteristic CD behavior prior to age 10, according to DSM-5), known to show severe antisocial behavior and high levels of callous-unemotional traits (33). We were particularly interested in neural activation of the amygdala, given its pivotal role in affective empathy processing and the history of studies indicating dysfunction in CD. In line with earlier research, we hypothesize a blunted amygdala response also during explicit empathize tasks. We also focused on neural activation within the MPFC in line with its pivotal role for cognitive aspects of empathy. Moreover, we expected a positive relationship between individual empathic abilities and brain activation in brain areas related to empathizing, and, accordingly, an inverse relationship with CU traits (32).

MATERIALS AND METHODS

Participants and Diagnostic Assessment

The final sample for the fMRI analysis comprised 14 boys with early onset CD between 8 and 16 years of age, and 15 TDC boys (see below for excluded participants after fMRI data analysis). Only subjects with an IQ $\geq$ 80 based on the Wechsler Intelligence Scale for Children-IV (WISC-IV, German version by (34) were included. Both groups were age-matched, however TDC showed slightly higher IQ (see **Table 1**). Participants of the CD group showed significantly higher CD traits and lower empathy abilities.

TABLE 1 | Sample description.

	TDC (*n* = 15)	CD (*n* = 14)
Age	12.7 (2.5)	12.2 (1.9)
Age range	8.5–16.8	8.1–14.6
Full-scale IQ (WISC-IV)	112.8 (10.5)	99.8 (14.2)*
IQ range	80–133	80–119
BIE (max. 88)	19.4 (16.2)	–0.3 (14.4)**
Callous-unemotional (APSD, T-score)	46.4 (7.9)	64.1 (7.6)**

*Means and standard deviations given if not noted otherwise. CD, Conduct disorder; TDC, typically developing controls; BIE, Bryant Index of Empathy; APSD, Antisocial process screening device; *p < 0.05; **p < 0.01.*

Participants with CD were recruited from the Department of Child and Adolescent Psychiatry of the RWTH Aachen University. Participants in the healthy control group were recruited by announcements in local schools. All participants were informed in detail about the experimental procedures and the aims of the study and provided written informed assent. Written informed consent was obtained by parents/legal custodian, after the parent(s)/legal custodian(s) had been informed about all aspects of the study. The study was approved by the local ethics committee in accordance with the Declaration of Helsinki and in compliance with national legislation.

Participants were included, if they did not have evidence for a neurological disorder, or a history or current diagnosis of psychosis, trauma, bipolar disorder, substance abuse, or pervasive developmental disorder based on a standardized semi-structured interview (K-SADS-PL) (35). Further exclusion criteria were any chronic physical illness and the use of any medication at the time of fMRI measurements. Medication with methylphenidate ($n = 8$) was stopped 48 h prior to the fMRI assessment.

Using the standardized semi-structured interview (K-SADS-PL) (35) with participants and caregivers, all participants were assessed for current and past CD, oppositional defiant disorder, ADHD, major depressive disorder, anxiety disorders, obsessive-compulsive disorder, tic disorder, elimination disorder, and posttraumatic stress disorder. The K-SADS-PL was also applied in TDC participants to rule out any current and past psychiatric condition.

Participants were included in the patient group if the diagnostic criteria of CD, early-onset subtype according to DSM-5 were fulfilled, i.e., if at least one symptom had started before the age of 10. Psychiatric comorbidity in the CD group was as follows: 10 participants (71%) were diagnosed with comorbid ADHD, two participants with comorbid enuresis, and one participant with comorbid chronic motor tic disorder. Cognitive testing (IQ) was performed in all participants using the WISC-IV, German version by (34).

Instruments Assessing Behavioral Characteristics

Psychopathic traits in the CD and TDC groups were measured by the Antisocial Personality Screening Device [APSD (36)], a 20-item rating scale that assesses callous-unemotional (CU) traits, narcissism and impulsivity. All parents completed a German version of the APSD, and the CU traits subscale was evaluated. Standardized values (T-Scores) were used, provided in the manual (36).

Empathic abilities: All children completed the German version of the Bryant Index of Empathy (BIE); (37, 38), an adaptation of the Emotional Empathic Tendency Scale (39) assessing predominantly affective aspects of empathy. Higher scores on the BIE reflect greater empathic ability. Items are rated on a 9-point Likert scale (−4 to +4); the maximum total sum score is 88.

ADHD symptoms: Parents completed the German Parental Report on ADHD symptoms, which is part of the Diagnostic System of Mental Disorders in Children and Adolescents (40) reflecting DSM-IV criteria. Sum scores are provided.

Stimuli

The facial stimuli were taken from an earlier study of our group, published in (41–43). In brief, happy, sad and neutral faces ($n = 72$, each) were used as stimuli. Happy and sad expressions were chosen since they have been shown to evoke congruent empathic reactions (e.g., feelings of sadness when viewing a sad face) (44). Since empathic feelings are more easily evoked when the counterpart is similar to oneself (e.g., in age and gender) (45), a set of face stimuli was constructed and morphed to the age of the participant groups. Furthermore, the stimuli were morphed to neutral and emotional faces according to established conventions (Facial Action Coding System) (46) using FaceGen 3.1 (Singular Inversions, Vancouver, Canada). Weak emotional expressions were used along with more obvious ones to provide sufficient variability with regard to emotional intensity (see **Figure 1**).

fMRI Paradigm

Three tasks alternated blockwise in a pseudo-randomized, counterbalanced order (see **Figure 1** for details). In the other-task, participants were instructed to empathize with a person whose face appeared on the screen and to infer the emotional state from that face. In the self-task, participants were again instructed to empathize with the depicted person. However, they were asked to *judge their own emotional response* to the face. In both tasks, happy and sad faces were mixed within blocks to prevent habituation effects. Half of the blocks contained high-intensity emotional stimuli, and the other half contained low intensity emotional stimuli. Response options were "sad," "neutral" or "happy". In the high-level baseline task, perceptual decisions on the width of neutral faces as "thin," "average," or "wide" were included. Participants responded with their right index, middle, and ring fingers using a three-button response device. Each block (19.2 s) was preceded by an instruction cue (3 s) and comprised six face trials (each 2.47 s), separated by a fixation cross (0.45–0.95 s). 10 blocks of each task were presented, resulting in 30 blocks.

To familiarize participants with task requirements, participants first practiced the task outside the scanner. To reduce potential bias in the self-report of own emotions (self-task), we explicitly instructed the participants that there was no "wrong" answer and they should respond according to their actual feelings. Faces shown during the practice session were not included into the fMRI stimulus set. After the fMRI experiment, participants were asked standardized open questions on how they resolved the tasks. All participants were able to recall and describe how they resolved the tasks. Participants who did not follow the task instructions correctly (e.g., stated that they

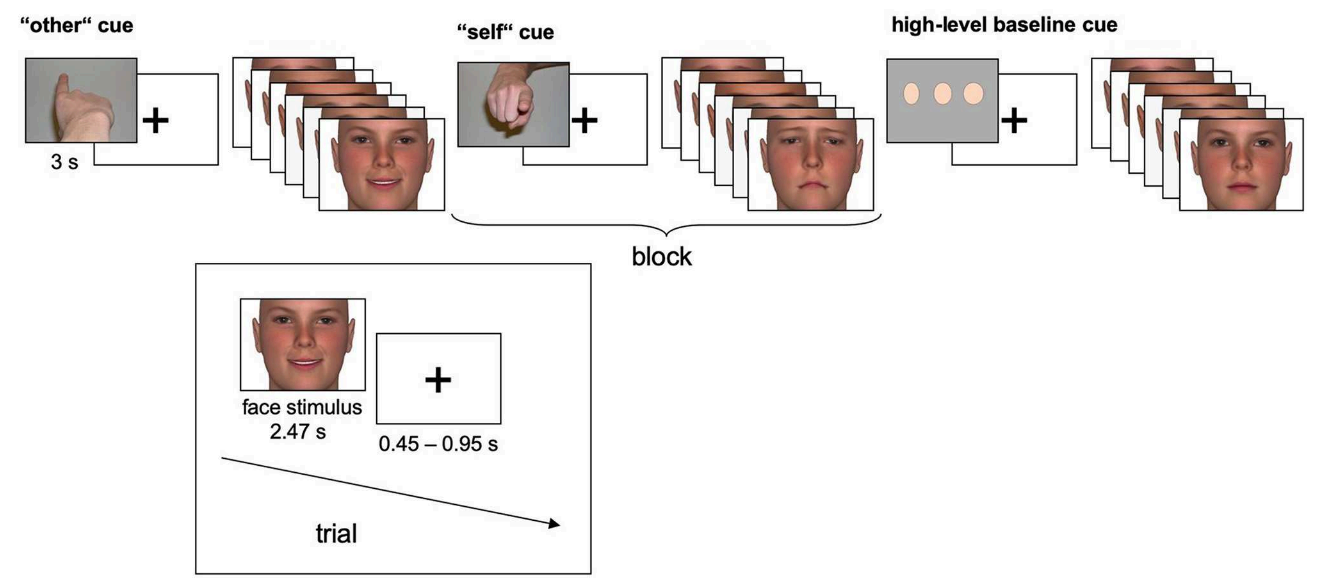

FIGURE 1 | Experimental time course. In the self- and other-task, happy and sad faces were presented, and participants assessed which emotional state (sad, neutral, or happy) best described the emotional state of the other person (other-task) or their own emotional response to the face (self-task). In the high-level baseline, subjects judged the width of neutral faces (thin, average, or wide). Each of $n = 72$ individual faces was presented once displaying a happy expression, once displaying a sad expression and once displaying a neutral expression.

judged the emotional state of the person whose face appeared on the screen during the self-task instead of judging their own emotional response to the face) were excluded from the sample; this applied to one TDC participant.

Seventeen boys with early onset CD and 18 typically developing controls (TDC) boys were investigated. After exclusion of six participants (3 CD, 3 TDC) due to excessive movement (see below for details), 14 CD and 15 TDC boys remained for the final analysis. Response collection and stimulus presentation were performed employing the software Presentation 9.9 (Neurobehavioral Systems, Albany, CA, USA). Visual stimuli were presented using a head mounted display.

MRI Acquisition

Scanning was performed on a 3.0-Tesla Trio-Tim system (Siemens, Erlangen, Germany) using a standard CP head coil. During the experimental task (11.8 min), whole brain echoplanar T2-weighted images (EPIs) were acquired (TE = 28 ms, TR = 2,230 ms, FlipAngle = 77°, FOV = 192 mm, matrix size = 64 × 64, 38 slices, slice thickness = 3 mm, voxel size = 3 × 3 × 3.45 mm^3). High-resolution T1-weighed anatomical images were collected using a rapid acquisition gradient-echo (MP-RAGE) pulse sequence (TE = 2.520 ms, TR = 1.900 ms, FlipAngle 9°, FOV = 256 mm, matrix size = 256 × 256, 176 slices, slice thickness = 1 mm, voxel size = 0.98 × 0.98 × 1 mm^3).

Data Analysis

Imaging data was analyzed using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK, http://www.fil.ion.ucl.ac.uk/spm/) implemented in MATLAB 8.4 (The Mathworks, Inc., Natick, MA, USA). The first four functional images of each participant were discarded. The remaining 312 volumes were realigned, spatially normalized to standard stereotactic Montreal Neurological Institute (MNI) coordinates and spatially smoothed with an 8-mm full-width half-maximum Gaussian kernel. Participants with excessive movement (i.e., >3 mm translation, > 4° rotation) were excluded from further analysis resulting in the final sample size described in the participants section. Additionally, we checked that the overall amount of movement was not significantly different between groups by comparing respective max translation and rotation parameters across groups (multiple t-tests, *all* $t < 0.84$, all $p > 0.41$). Model parameters were estimated for each voxel according to the General Linear Model. To account for individual residual movement-related variance, realignment parameters were included into the model as regressors. For group analyses, a second-level random-effects model was implemented. Individual contrast images coding for each experimental condition were analyzed using a flexible ANOVA model with group as a between subject factor, and condition as within subject factors. Anatomical images were coregistered to the mean EPI image and normalized into MNI space. Boxcar functions (19.2 s, corresponding to the experimental conditions) were convolved with a model of the hemodynamic response and its first-order temporal derivative. Violations of sphericity assumptions were accounted for by applying the non-sphericity corrections in SPM12 (estimation of covariance components). As initial analyses did not reveal differential significant group effects for the comparison of high- vs. low intensity conditions (or vice versa), we focused on tasks and task x group interactions for the following analyses. For between-group comparisons (CD vs. TDC), we compared other- and self-blocks (containing both high and low intensity stimuli), with the high-level baseline, respectively (other > high-level baseline; self > high-level baseline) and performed the direct comparison between self- and other-tasks (self > other, other > self).

Results are reported that met the statistical threshold of $p<$ 0.05 family-wise error (FWE) at the voxel level. For a-priori specified regions, we performed additional region of interest (ROI) analyses, i.e., the amygdala, and the medial PFC using a threshold of $p < 0.05$ (FWE corrected across each particular region). ROIs were constructed using standard neuroanatomical toolboxes implemented in SPM12 [Anatomy Toolbox (47), WFU PickAtlas (48)]. In detail, the ROIs for the left and right MPFC were constructed with regions of the aal-atlas including the cortices frontal superior medial, frontal medial orbital, gyrus rectus and frontal superior orbital.

Moreover, to assess whether brain activity was related to measures of empathy and callous-unemotional traits, linear regression analyses were performed with empathy scores (BIE/CU-traits respectively) for those regions and contrasts which yielded group differences between tasks. For regression analyses across and within groups, anatomical ROIs were used (amygdala, MPFC, thresholded at $p < 0.05$, FWE corrected for respective ROI). Additionally, we used a 15 mm sphere around coordinates with a significant group difference to further explore correlations within the CD group.

RESULTS

Behavioral Results

Reaction times (RT) were analyzed by a 2 × 2 × 2 mixed-model ANOVA with the factors task, emotion, and group. This analysis did not yield significant main effect of task, emotion or group (all *ps* > 0.25). Moreover, interactions involving the factor group were all non-significant (all *ps* > 0.28).

Correct identification of displayed emotions during empathizing was assessed using correct responses during the other-task and analyzed by a 2 (emotion) × 2 (group) mixed effects ANOVA. We found a significant main effect of emotion $F_{(1, 27)}$ =12.06, $p < 0.01$ due to a higher accuracy for sad (M = 82.5%; SD = 19.2) compared to happy faces (M = 71.0%; SD = 16.5; $p = 0.002$). The interaction of emotion x group was not significant [$F_{(1, 27)} = 1.14$] and there was no main effect of group [$F_{(1, 27)} = 0.211$].

Congruence of evoked emotions was assessed using congruent responses during the self-task (i.e., happy responses to happy faces and sad responses to sad faces) and analyzed by a 2 (emotion) × 2 (group) mixed effects ANOVA. We found a significant interaction of emotion × group [$F_{(1, 27)} = 6.88$, $p < 0.05$], but no main effect of emotion or group (all *ps* > 0.63). Post-hoc comparisons indicated a significantly higher congruency for sad (M = 64.3%; SD = 32.4) compared to happy faces (M = 51.4%; SD = 27.4; $p < 0.05$) in TDC but not in

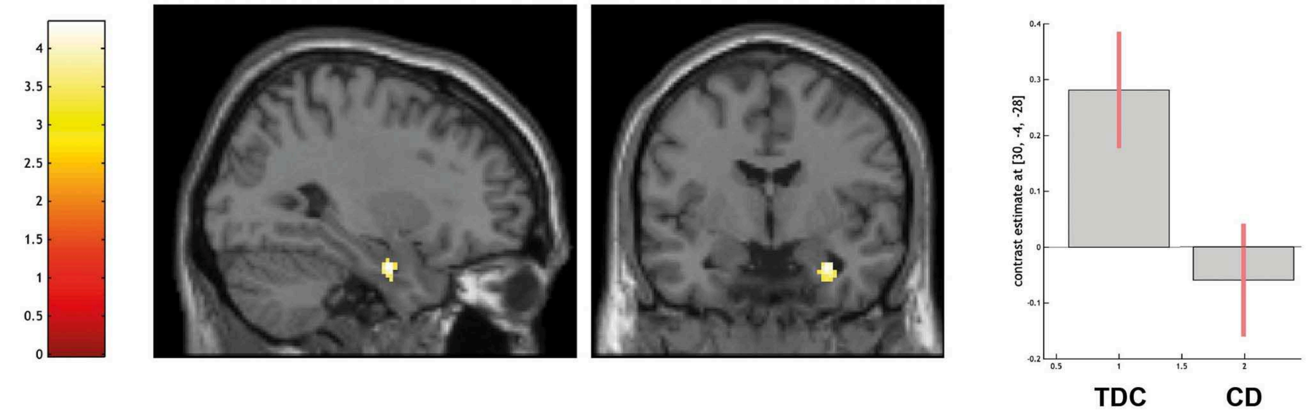

FIGURE 2 | Differential activation of typically developing controls (TDC) and youth with conduct disorder (CD) for the contrast other > high level baseline, SPM(T) overlaid on single subject T1 template, threshold for illustrative purposes $p_{uncorr.} < 0.001$. Increased activation in the right amygdala (peak coordinate 30, −4, −28) in TDC > CD (family-wise error corrected at $p < 0.05$ for ROI). Contrast estimates and 90% confidence intervals of contrast other > control in peak coordinate displayed. The color bar chart represents *T*-values.

CD. On a descriptive level, this pattern was reversed in CD (sad: $M = 44.2\%$; $SD = 38.2$; happy: $M = 60.8\%$; $SD = 29.2$). Additionally, we performed the same analyses including intensity as a factor in the ANOVA-models (2 × 2 × 2 mixed-model ANOVAS for the factors intensity, emotion and group). In these analyses, no additional significant effects of group or interactions with group were observed, but all effects mentioned in the main manuscript remained stable (see **Supplementary Material** for further details). CD-Patients had significantly higher CU-traits ($t = -5.9$, $p < 0.001$) and significantly lower BIE-scores than TDC ($t = 3.5$, $p = 0.001$). Both measures were inversely related across groups ($r = -0.5$, p = 0.007).

fMRI Results

Comparisons related to the main effect of task (i.e., self/other vs. control condition) yielded widespread activation in brain areas previously associated with empathic processing (41, 43, 49, 50) across both groups, including the amygdala, MPFC, middle temporal gyrus, temporal gyrus, inferior frontal gyrus, cingulum, and precuneus. For details see **Supplement 1**.

Whole brain comparisons or any contrast associated with group comparisons or interactions with the factor group did not yield significant activation peaks (FWE corrected threshold) for any task. Inference with respect to the factor group is drawn based on ROI analysis as outlined in the introduction and methods section.

Other vs. High-Level Baseline

ROI-based analyses of the amygdala confirmed that TDC yielded greater activation than CD in the right amygdala (peak voxel coordinates = 30, −4, −28; $t = 4.02$; $P < 0.05$ FWE-SVC; see **Figure 2**).

Across the entire sample, greater activation in the amygdala was associated with a higher degree of empathy (as indicated by higher BIE-scores, peak voxel coordinates = 30, −4, −26; $t = 4.33$; $P < 0.01$ FWE-SVC) and with a lower degree of CU traits (as indicated by CU scores, peak voxel coordinates = 26, −2, −28; $t = 3.65$; $P < 0.05$ FWE-SVC).

Within the CD group, higher BIE-scores were associated with greater BOLD-response in the amygdala (peak voxel coordinates = 30, 0, −24; $t = 6.85$; $P < 0.01$ FWE-SVC), however no significant association emerged with respect to CU traits. No group differences occurred in the ROI-based analysis of the MPFC.

Self vs. High-Level Baseline

ROI-based analyses of the left MPFC indicated a higher activation in CD over TDC in the left ventromedial prefrontal cortex (peak voxel coordinates = −8, 50, −24; $t = 3.95$; $P < 0.05$ FWE-SVC; see **Figure 3**). No difference in amygdala activation was detected.

Self vs. Other Task

ROI-based analyses for the comparison CD > TDC indicated no differences in the amygdala and larger activation in the right dorsal PFC (peak voxel coordinates = 12, 50, 20; $t = 4.19$; $P < 0.05$ FWE-SVC; see **Figure 4**).

Using ROI-based analysis with a sphere of 15 mm around the coordinates 12, 50, 20 a positive linear association with BIE-scores was detected in the CD group (peak voxel coordinates = 12, 52, 34; $t = 5.37$; $P < 0.05$ FWE-SVC). No difference in amygdala activation was detected.

Across all above-mentioned coordinates and contrasts no associations with IQ or ADHD-symptoms scores were detected.

DISCUSSION

The aim of this study was to examine neural correlates in an explicit empathizing task in early onset CD as compared to TDC. Key findings of this study include the hypoactivation of the amygdala during the other-task in CD participants. Amygdala activation was positively associated with measures of empathy in

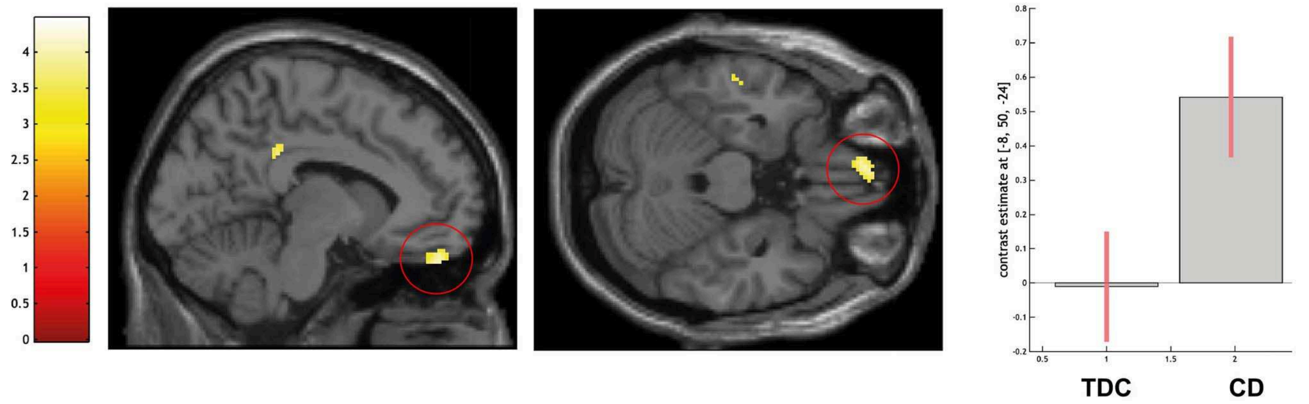

FIGURE 3 | Differential activation of typically developing controls (TDC) and youth with conduct disorder (CD) for the contrast self > high level baseline, SPM(T) overlaid on single subject T1 template, threshold for illustrative purposes $p_{uncorr.} < 0.001$. Increased activation in the left ventromedial prefrontal cortex (peak coordinate −8, 50, −24) in CD > TDC (family-wise error corrected at $p < 0.05$ for ROI). Contrast estimates and 90% confidence intervals of contrast self > control in peak coordinate displayed. The color bar chart represents T-values.

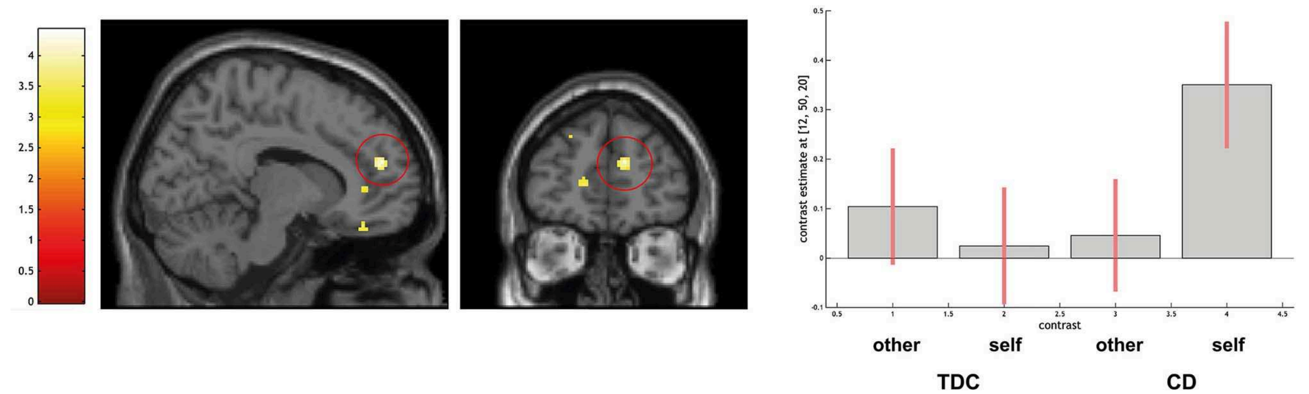

FIGURE 4 | Differential activation of typically developing controls (TDC) and youth with conduct disorder (CD) for the contrast self > other, SPM(T) overlaid on single subject T1 template. Threshold for illustrative purposes $p_{uncorr.} < 0.001$. Increased activation in the right dorsomedial prefrontal cortex (peak coordinate 12, 50, 20) in CD > TDC (family-wise error corrected at $p < 0.05$ for ROI). Contrast estimates and 90% confidence intervals of contrasts other > control and self > control in peak coordinate displayed. The color bar chart represents T-values.

the whole sample and in the CD group alone. Moreover, during the self-conditions, CD showed larger activation specifically in the ventral and dorsal MPFC pointing toward increased activation in areas relevant for cognitive empathy and self-referential processing (51).

With respect to behavioral performance, there were no significant differences in RTs between CD participants and control participants for any experimental condition. It is thus unlikely that differences in neural activations are related to domain-general performance deficits (such as differences in perceptual processing speed).

Moreover, consistent with other reports using a similar paradigm (24), our behavioral findings (i.e., task-performance) do not indicate deficits in CD for the identification of other people's emotional state (other task) during empathizing. While other studies have reported deficits for emotion recognition in CD (18, 52, 53), this does not appear to be the case in the context of empathizing with clearly identifiable facial expressions. However, despite comparable emotion *identification*, we could demonstrate atypical emotional *resonance* (self-task) in CD participants, revealing that CD participants do not show the same increased resonance with sad emotions as evident for TDC. Such a specificity for the displayed emotion is consistent with other reports of sad-specific impairments in antisocial individuals (18) for emotion processing. Furthermore, this pattern of results resonates well with the clinical characteristics of early-onset CD and in particular high CU traits. As outlined in the DSM-5, individuals with limited prosocial emotions show lack of remorse e.g., "after hurting someone" (1), and are less concerned about the feelings of others, or disregard others feelings. This aberrant pattern may be connected with a less empathic reaction to others' emotions and in particular to sad faces. A limited resonance with sad expressions as an example for a distress cue has been associated with the theory of reduced cognitive violence inhibition (13, 54). This theory suggests that a victim's distress cues can inhibit the attacks of an aggressor. In line with a limited responsiveness to distress cues or reduced violence inhibition, children with early onset CD often show an early onset of severe aggression (55).

The amygdala plays an important role for emotional processing, including empathy [see (56, 57) for recent meta-analyses]. Robust involvement of the amygdala across participants confirms this also in the context of the empathy task that we used (41, 58). Furthermore, we could demonstrate a correlation of individual empathic abilities and brain activation with the amygdala, underlining the importance of the amygdala integrity for empathic responses. Blunted amygdala activity has repeatedly been reported in the context of psychopathic traits and antisocial behavior in response to fearful faces (16, 21, 59, 60). Our finding of a hypoactivation of the right amygdala in early-onset CD is consistent with previous reports on reduced amygdala reactivity specifically for sad vs. neutral faces (20). Of note, the study of Passamonti et al. (20) revealed that this amygdala hypoactivation was more pronounced in early onset than adolescent onset CD. Our study is the first to reveal hypoactivation in the context of empathizing in early onset CD, and associations with CU traits and empathic abilities. Moreover, several studies point toward amygdala hypoactivation as an important neurobiological marker of reduced pain-related empathy and responses to distress in psychopathy in adolescents and adults (59, 61). While earlier studies on emotional processing in CD have demonstrated links between amygdala activation and callousness (16, 17), our study is the first to report an association between amygdala activity and empathy even within a CD group using a measure of individual empathic abilities (i.e., the BIE). This finding highlights that despite overall impairment, there is considerable variability of empathic abilities in CD participants which is associated with amygdala responsivity during empathizing. Although we found an inverse association between amygdala activity and CU-traits and, accordingly, an inverse relationship between empathy and CU traits across the whole sample, we could not demonstrate an association of amygdala activity and CU-traits within the CD group. This was likely due to the fact that the CD participants in our study had relatively high CU values with low variance. Further studies with larger sample sizes are needed to address the complex relationship between empathy, CU-traits and brain activation patterns.

With respect to (frequently) comorbid ADHD diagnoses in CD, our data did not point toward associations of amygdala activity and ADHD comorbidity in accordance with a recent meta-analysis (62). In summary, our finding of a blunted amygdala reaction in an empathy task in early onset CD adds to the body of literature which argues for a biological basis as an explanatory model for a high risk to show pervasive antisocial behavior (5).

During the self-task, as well as for the direct comparison of self vs. other task, we observed higher activation in the MPFC for the CD group (as compared to TDC). Brain activation in the MPFC has consistently been reported for diverse social tasks, including mentalizing and cognitive as well as affective empathy (49, 50, 56, 57, 63). A bulk of evidence converges on the finding of a gradual ventral-dorsal distinction within the MPFC with more dorsal aspects implicated for goal-directed behavior, cognitive control, and social-cognitive judgments, whereas ventral aspects are more associated with self-relevance in emotional contexts (such as autonomic responses and monitoring the evaluation of future outcomes) (64). Similarly, dorsal and ventral MPFC can be conceived as representing a functional gradient from more involvement for other-related judgments (dosal) to self-related judgments (ventral) (51). Accordingly, vMPFC has also been implicated in self-referential emotional cognition [e.g., (65)]. The anterior rostral part of the MPFC (arMPFC, in between the most dorsal and ventral parts) has been conceptualized as the central hub for more abstract metacognitive representations which support self-reference and mentalizing (64). This area is consistently activated during perspective taking, empathy, and theory of mind tasks (49, 50, 57, 66, 67). Our data reveal a greater involvement of the arMPFC (BA 32/10) for CD participants during explicit empathizing, in particular when attending to the self-perspective. Others have suggested that areas such as the arMPFC are more related to cognitive aspects of empathy (66). Interestingly, increased brain activation in the arMPFC was also correlated with *better* empathic abilities in CD participants, suggesting that this area may, at least in part also be interpreted as serving a compensatory role (in the light of decreased emotional resonance paralleled by reduced amygdala activation). It might be speculated that compensatory MPFC activation could also play a role to enhance activation of the amygdala and enhance emotional resonance per se. However, this would need to be verified in future studies with larger samples to reveal a potential direct relationship between arMPFC, amygdala activation, and emotional resonance. Furthermore, we observed increased activation for the CD group (relative to TDC) of the vMPFC for self-related processing during empathy. This finding suggests a stronger reliance on self-referential processing during empathizing for CD, in concert with a less congruent emotional response. Taken together with the finding of reduced amygdala responses, this pattern of results resonates well with the clinical phenotype of callous-unemotional traits in patients with CD (i.e., self-centered, emotionally cold, and low empathic behavior toward other people).

Both arMPFC (BA 32/10) and vMPFC (BA 11) are part of the so-called default mode network (DMN), which is characterized by increased connectivity during periods of rest (68) and has been suggested to support emotional and self-referential processing (69). Two studies have reported reduced functional connectivity for CD patients in the DMN, and particular in MPFC (27, 28), also in the subgroup of early onset CD (27) which the authors interpreted as potentially reflecting dysfunctional introspective processing and hypothesized a relation to social-cognitive deficits in CD. Our data, however, suggest hyperactivation during an explicit self-task, in concert with a positive association with empathic abilities. Interestingly, a study investigating anatomical integrity of the DMN observed *increased* myelination in the DMN in adolescents with CD in comparison to TDC (70), which was also associated with CU traits. Clearly, future studies are needed to address these inconsistencies which combine resting state connectivity, anatomical connectivity and functional activation patterns and investigate the relation with CU traits and empathic abilities.

Implications

Our data point toward increased brain activation in MPFC areas in CD known to be strongly involved in cognitive empathy, self-referential processing, and reward. Thus, in line with prior research, CD may have the ability to empathize (22), but rely on different neural mechanisms. The involved neural mechanisms may be less associated with emotional contagion, but possibly promote a more self-centered behavior displaying a shallow affect during social interaction.

A possible approach to improve empathy skills is the use of empathy training programs. A meta-analytic review on empathy training regimes indicates overall medium effect sizes of these programs (71). A study by Dadds (72) indicates that particularly boys with high CU traits may benefit from these programs in showing improved empathic skills and subsequently lower conduct problems. Future research could more closely evaluate if a targeted training of empathic skills could result in e.g., improved amygdala reactivity or differential neuronal processes underlying improved empathy in CD. Subsequently, a targeted fMRI-neurofeedback training in youth with low empathy could help improve the outcome of empathy-related trainings. Given that our study points to a certain variability of neural responses in the amygdala and the MPFC that were associated with empathy measures, an early and targeted beginning of empathy skills training could possibly help improving the outcome of an individualized treatment.

Strengths and Limitations

Strengths of the study include the investigation of a well-characterized clinical sample with early-onset conduct disorder and the use of an established explicit empathy task that has been successfully used in prior research of our and other groups (24, 41–43, 49). In line with previous studies (42, 43, 49, 50) we interpret behavioral responses for the self-task as an index of emotional resonance. Although we cannot completely rule out the possibility that this self-report response could be biased (e.g., due to a tendency to respond in a socially acceptable way), our interpretation is in line with previous findings of reduced emotional contagion in CD (41–43, 49, 50). However future studies should consider using more objective measures of emotional resonance, e.g., skin conductance measures or video recordings of facial expression.

A limitation of the study is the limited sample size, which requires a replication of our results in larger studies. Furthermore, previous studies have also reported structural abnormalities in CD, also in similar regions where we found functional differences. In particular, early onset CD might be characterized by stronger neurodevelopmental disturbance, thus, structural and functional deficits may interact and both contribute to deficits in empathy processing and related brain areas. Future studies should systematically investigate structural and functional trajectories of brain areas related to empathy processing and CU traits across development in early onset CD.

CONCLUSION

The data emphasize the important role of the amygdala in empathy related emotional processing in early onset CD during an explicit empathy paradigm. Diminished amygdala responses and their association with low empathy suggest a pivotal influence of impaired amygdala processing in early-onset CD, in particular for deficits in empathic behavior. Elevated response in the MPFC in boys with CD point toward increased demands on self-referential processing to solve empathy tasks, thus potentially pointing at a more cognitive biased processing strategy in this patient group. Future research may focus in more detail on neural correlates of cognitive empathy processing in CD and a possible improvement using empathy related trainings.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The study was approved by the local ethics committee and carried out in accordance with the recommendations of good clinical practice. All participants were informed in detail about the experimental procedures and the aims of the study and provided written informed assent. Written informed consent was obtained by parents/legal custodian, after the parent(s)/legal custodian(s) had been informed about all aspects of the study in accordance with the Declaration of Helsinki and in compliance with national legislation.

AUTHOR CONTRIBUTIONS

KK, BH-D, EG, and MS-R designed the study. EG and GP collected the data. GP, MS-R, and NG performed statistical analysis. GP, MS-R, EG, GK, and TV wrote the manuscript. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2020.00178/full#supplementary-material

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