INSIGHTS IN SOCIAL COGNITION: 2021

EDITED BY: Sören Krach and Frieder Michel Paulus
PUBLISHED IN: Frontiers in Psychiatry

frontiers Research Topics

frontiers

ISSN 1664-8714
ISBN 978-2-88976-521-8
DOI 10.3389/978-2-88976-521-8

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INSIGHTS IN SOCIAL COGNITION: 2021

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Citation: Krach, S., Paulus, F. M., eds. (2022). Insights in Social Cognition: 2021. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-88976-521-8

Table of Contents

04 ***Callous-Unemotional Traits Moderate Anticipated Guilt and Wrongness Judgments to Everyday Moral Transgressions in Adolescents***
Margarida Vasconcelos, Essi Viding, Catherine L. Sebastian, Susana Faria, Pedro R. Almeida, Óscar F. Gonçalves, Rui A. Gonçalves, Adriana Sampaio and Ana Seara-Cardoso

15 ***Restricted Visual Scanpaths During Emotion Recognition in Childhood Social Anxiety Disorder***
Johan Lundin Kleberg, Emilie Bäcklin Löwenberg, Jennifer Y. F. Lau, Eva Serlachius and Jens Högström

26 ***Alexithymia Is Associated With Deficits in Visual Search for Emotional Faces in Clinical Depression***
Thomas Suslow, Vivien Günther, Tilman Hensch, Anette Kersting and Charlott Maria Bodenschatz

40 ***An Explanation for Repetitive Motor Behaviors in Autism: Facilitating Inventions via Trial-and-Error Discovery***
Catherine L. Caldwell-Harris

44 ***Validation of the Rage Attack Questionnaire-Revised (RAQ-R) in a Mixed Psychiatric Population***
Lisa Palm, Martina Haas, Anna Pisarenko, Ewgeni Jakubovski and Kirsten R. Müller-Vahl

55 ***High Schizotypy Predicts Emotion Recognition Independently of Negative Affect***
Christopher Dawes, Claudia Danielmeier, Mark Haselgrove and Paula M. Moran

66 ***How Social Experiences Affect Interpretation Bias Among Individuals With Non-clinical Depression: The Role of Ostracism***
Avigail Bar-Sella, Thalia Richter, Sigal Zilcha-Mano and Hadas Okon-Singer

74 ***The Transdiagnostic Relevance of Self-Other Distinction to Psychiatry Spans Emotional, Cognitive and Motor Domains***
Clare M. Eddy

92 ***The Social Connectome – Moving Toward Complexity in the Study of Brain Networks and Their Interactions in Social Cognitive and Affective Neuroscience***
Lara Maliske and Philipp Kanske

99 ***Characterization of the Core Determinants of Social Influence From a Computational and Cognitive Perspective***
Hyeji Lee and Dongil Chung

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 05 March 2021
doi: 10.3389/fpsyt.2021.625328

Callous-Unemotional Traits Moderate Anticipated Guilt and Wrongness Judgments to Everyday Moral Transgressions in Adolescents

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OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: 02 November 2020
Accepted: 09 February 2021
Published: 05 March 2021

Citation:
Vasconcelos M, Viding E, Sebastian CL, Faria S, Almeida PR, Gonçalves ÓF, Gonçalves RA, Sampaio A and Seara-Cardoso A (2021) Callous-Unemotional Traits Moderate Anticipated Guilt and Wrongness Judgments to Everyday Moral Transgressions in Adolescents. Front. Psychiatry 12:625328. doi: 10.3389/fpsyt.2021.625328

Callous-unemotional (CU) traits observed during childhood and adolescence are thought to be precursors of psychopathic traits in adulthood. Adults with high levels of psychopathic traits typically present antisocial behavior. Such behavior can be indicative of atypical moral processing. Evidence suggests that moral dysfunction in these individuals may stem from a disruption of affective components of moral processing rather than from an inability to compute moral judgments *per se*. No study to date has tested if the dissociation between affective and cognitive dimensions of moral processing linked to psychopathic traits in adulthood is also linked to CU traits during development. Here, 47 typically developing adolescents with varying levels of CU traits completed a novel, animated cartoon task depicting everyday moral transgressions and indicated how they would feel in such situations and how morally wrong the situations were. Adolescents with higher CU traits reported reduced anticipated guilt and wrongness appraisals of the transgressions. However, our key finding was a significant interaction between CU traits and anticipated guilt in predicting wrongness judgments. The strength of the association between anticipated guilt and wrongness judgement was significantly weaker for those with higher levels of CU traits. This evidence extends our knowledge on the cognitive-affective processing deficits that may underlie moral dysfunction in youth who are at heightened risk for antisocial behavior and psychopathy in adulthood. Future longitudinal research is required to elucidate whether there is an increased dissociation between different components of moral processing from adolescence to adulthood for those with high psychopathic traits.

Keywords: Callous-unemotional (CU) traits, psychopathy, adolescence, moral emotion, moral judgement

INTRODUCTION

The term callous-unemotional (CU) refers to a constellation of personality traits that include blunted affect, lack of empathy and remorse, uncaring behavior and disregard for others' feelings and well-being (1–4). CU traits have received increased attention in the last decades. Its presence seems to distinguish a cohort of youth who exhibit instrumental and planned violence, and who display a subtype of conduct disorder that is more severe, more stable and more resistant to treatment [e.g., (5–7)]. High levels of CU traits are thought to contribute to the development of a more persistent and aggressive type of antisocial behavior in youth, found across forensic [e.g., (8, 9), community [e.g., (1, 5)], and mental health samples [e.g., (10)]. Even in the absence of conduct disorder, high levels of CU traits have been associated with higher risk for disruptive behavior [e.g., (5, 11, 12)]. Indeed, longitudinal data indicate that CU traits add to the prediction of serious and persistent criminal behavior in boys, over and above the presence of conduct disorder symptoms and oppositional defiant problems (13).

Contemporary perspectives on human morality have emphasized the role of emotions on moral reasoning and behavior (14, 15). Moral emotions—i.e., "emotions that respond to moral violations or that motivate moral behavior" [(16), p. 853]—in particular seem to have a prominent role in moral judgment—i.e., our ability to tell right from wrong (15, 17–19). It has been hypothesized that the experience of moral emotions, such as guilt, may help people to identify the moral implications of their judgments and behaviors and that the anticipation of moral emotions may support regulation of appropriate social behavior [see (20) for a recent review]. Studies suggest that the lack of adherence to moral and social norms may be rooted in emotional processes rather than moral reasoning processes (21, 22). For example, guilt proneness, i.e., the predisposition to experience negative feelings about personal wrongdoings, consistently predicts appropriate moral behavior (23). Also, guilt aversion—i.e., guilt evoked when an agent believes he had failed/hurt others based on failing their expectations (24)—is suggested to strongly motivate people's choices during cooperative efforts such as games, plausibly playing a role in moral judgments (25–27). Feelings of guilt are thought to provide immediate and salient feedback on either executed or imagined behavior (21). Therefore, the anticipation of guilt about committing a wrongdoing can work as a "brake" that curbs antisocial behavior.

CU traits are thought to be the precursor of affective and interpersonal psychopathic traits in adulthood (28). Extant evidence suggests that moral dysfunction in adults with high levels of psychopathic traits may stem from a disruption of the affective and motivational components of moral processing rather than from an inability to compute moral judgments *per se* (29). For example, high levels of psychopathic traits seem to be associated with reduced propensity to feel moral emotions (i.e., guilt) and reduced difficulty in judging actions in moral dilemmas (30, 31), but not with endorsement of such actions [(30, 32) but see (33) for an exception]. Concomitantly, psychopathic traits are associated with reduced responses in affective brain regions during moral processing despite apparent intact moral judgment ability (34, 35). In parallel, a growing body of research has been showing a dissociation between affective and cognitive empathy impairments in individuals with high level of psychopathy (e.g., 30, 36–38). Individuals with high levels of psychopathy seem to have intact cognitive empathy, i.e., are able to infer and describe what others feel, but show impairments in affective empathy, i.e., fail to resonate with others' feelings (30, 36–38). The same pattern of dissociation between affective and cognitive empathic processes has been identified in children with high levels of CU traits (39–41).

Whilst accumulating evidence suggests a dissociation between affective and cognitive components of moral processing in adults with high levels of psychopathy, it is not clear whether this dissociation is already at play during development. A few studies have now inspected correlates of moral dysfunction associated with CU traits. For example, akin to adults with high psychopathic traits (18, 42), children and adolescents with high levels of CU traits present difficulties in distinguishing between moral and conventional transgressions (43, 44). They report that, if given permission from a figure of authority, it is as acceptable to break a conventional societal rule, such as leaving the classroom, as it is to break a moral rule such as not to hit someone. This failure to distinguish between the two types of transgressions is thought to reflect diminished emotional resonance to the harm caused to the victim. More recently, Fragkaki et al. (45) found that high levels of CU traits were associated with lower feelings of guilt when individuals were imagining themselves committing antisocial acts. Neuroimaging research suggests that the atypical moral behavior that children and youth with high CU traits display may stem from dysfunction in brain regions implicated in affective processing, namely the amygdala and the ventromedial prefrontal cortex [vmPFC; for a review see, (46)]. For example, adolescents with higher CU traits show a negative association between amygdala responses and ratings of moral violations severity (47) and reduced amygdala response during implicit moral judgement (48). Additionally, they show a reduced connectivity between amygdala and vmPFC during both explicit and implicit moral judgment (47, 48). Overall, the evidence suggests that youths with high CU and adults with high psychopathic traits seem to be remarkably similar in terms of their behavioral and neurobiological impairments associated with moral judgments [for a review see (49)].

No study to date has tested if the dissociation between affective (i.e., anticipated guilt) and cognitive (i.e., wrongness judgments) dimensions of moral behavior observed in adults with high levels of psychopathy is also linked to CU traits during development. This is important, as it will help us gain a more precise picture of the cognitive-affective processing deficits that may underlie atypical moral processing in youth who are at heightened risk for antisocial behavior and psychopathy in adulthood. Moreover, extant research has been mostly conducted in populations with disruptive behavior disorders. However, an increasing number of studies have advocated the importance of studying CU traits in community samples because these traits are almost

always accompanied with some conduct disturbance, predict poorer outcomes and also because many children with clinically significant needs do not receive treatment (50–53). In youth, CU traits are linked to a constellation of problems indicative of a subclinical variation of antisocial behavior, such as increased risk-taking behavior, hyperactivity, and poor peer relationships (13, 53–55). Akin to psychopathic traits in adulthood (56), evidence suggests CU traits to be continuously distributed in the general population (57). Research with non-forensic adult samples has revealed similar associations (comparatively with forensic samples) between psychopathic traits and abnormal moral behavior (30, 31, 58).

In the present study, we developed a novel animated cartoon task depicting first-person everyday harm-based moral transgressions and asked adolescents from the community to report: (1) how they would feel in such situations, and (2) how wrong such actions would be. Importantly, in this task, and contrary to most of the tasks used in morality research, we used everyday scenarios to assess moral decision making rather than life and death situations which are unlikely to be encountered in everyday life. All scenarios portrayed situations that involve harming others for personal gain. Scenarios were carefully designed to guarantee that they corresponded to moral transgressions but also that their content was developmentally appropriate. We predicted that CU traits would be negatively associated with variance in anticipated guilt to everyday moral transgressions but not with variance in moral wrongness judgments (both in terms of participants' ratings and response times [RTs]). Importantly, we predicted that CU traits would be linked with a higher dissociation between anticipated guilt and moral wrongness appraisals.

MATERIALS AND METHODS

Participants

Forty-seven typically-developing male adolescents with ages ranging from 15 to 18 years ($M_{age} = 16.19$ years; $SD = 0.89$) took part in this study. We focused on male adolescents for a number of reasons. Male adolescents present higher levels of CU traits, antisocial behavior, delinquency and commit more crimes than girls (59). Plus, the majority of research on moral processing in adults with high levels of psychopathy has focused on adult males. A male adolescent sample would allow us a direct comparison of results with the literature on adult populations whilst avoiding the need to include an extra gender variable which would require a much larger sample. Participants had no history of substance abuse, neurological/psychiatric disorders, or other clinically relevant diagnoses. Participants filled in questionnaires and performed a moral transgressions experimental task on a laptop computer in a single, individual session at their school. Participants and their parents provided written informed consent before taking part in the study. The study was approved and conducted in full accordance with the guidelines set by the Ethics Committee for Health and Life Sciences of University of Minho.

Materials

Inventory of Callous-Unemotional Traits—Self-Report [ICU; (1, 60)]

CU traits were measured using participants' ratings on the Portuguese version of the ICU scale [1; see the validation for the Portuguese population in (60)]. The self-report version of the ICU is a 24-item questionnaire designed to assess callous, unemotional and uncaring traits in children and youth; (Callousness: "I do not care who I hurt to get what I want"; Uncaring: "I feel bad or guilty when I do something wrong"; Unemotional: "I do not show my emotions to others"). The items are rated on a four-point scale ranging from 0 (*not true at all*) to 3 (*definitely true*). Each sub-factor score is computed by summing up its items (some items are reverse-scored) and the total score is obtained by summing up all sub-factors' scores.

Everyday Moral Transgressions Task

We developed a novel, animated cartoons task depicting everyday moral transgressions, based on Seara-Cardoso et al. (35). In these cartoons, an avatar (a male youth) harms another person in order to achieve a personal goal. Moral transgressions were made as unambiguous as possible by clearly indicating the intentions of the avatar and the consequences of his actions (61). Twenty-seven cartoons depicting everyday moral transgressions were created according to the following structure: (1) the avatar's personal goal/desire is established (4 s); and (2) the avatar harms another person to get his goal/desire (6 s; harm-to-other scenarios, HTO). To ensure that all scenarios were deemed moral transgressions and did elicit feelings of guilt, 27 alternative ending control scenarios were created where, instead of causing harm to another person, the avatar causes harm to himself to achieve the same goal/desire (harm-to-self scenarios, HTS). The task was divided in two blocks, counterbalanced across participants. In one block, participants rated all cartoons on anticipated feelings of guilt (i.e., "How much guilt would you feel?") on a sliding scale from "*None*" (0) to "*A lot*" (20) passing through a middle stance ("*Some*"). In the other block, participants rated all cartoons on moral wrongness (i.e. "How wrong would this be?") on a sliding scale from "*Not wrong*" (0) to "*Extremely wrong*" (20) going through a middle stance ("*Somewhat*") (**Figure 1**). After watching each cartoon, participants had up to 4 s to complete the rating. Cartoons within each block were randomized. Cronbach's α for guilt and wrongness judgments of moral transgression scenarios were 0.924 and 0.941, respectively. Cartoon video clips were created using GoAnimate (https://www.vyond.com/). The task was programmed in E-Prime (E-Prime 2.0 Build 2.0.10.242). Participants were seated in a comfortable chair at a distance of ∼50−100 cm from a computer monitor of 17" and 1,280 × 1,024 resolution (Scenicview A17-3, Fujitsu Siemens) in a quiet, well-illuminated room and used headphones to reduce auditory distraction. Videos were displayed in the upper two thirds of the monitor, and the question and corresponding sliding scale were displayed below. Participants used the computer mouse to provide their answers.

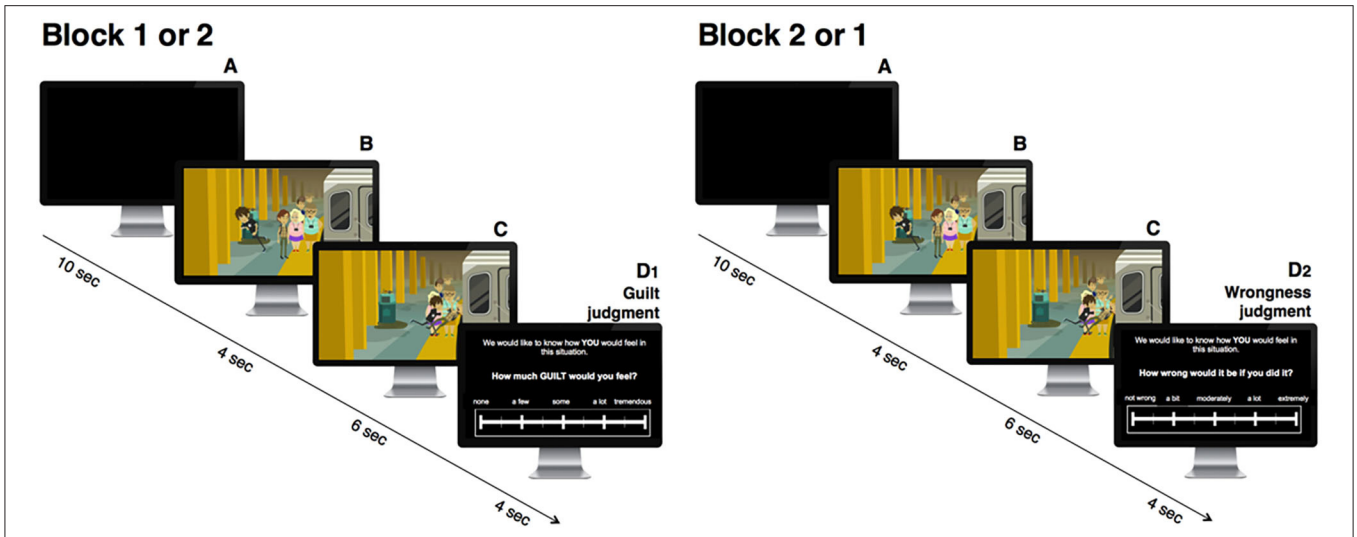

FIGURE 1 | Everyday Moral Transgressions task. Each trial was composed by A to D phases. (A) A black screen was displayed before the beginning of the cartoon. (B) During the first 4 s of the cartoon, the avatar's goal is established (e.g., running to get to the train on time). (C) In the following 6 s, to achieve his goal, the avatar inflicts harm to another person (e.g., pushes someone out of the way, throwing her to the ground). The cartoon is then followed by a question asking participants to anticipate guilt (D1) or perform a wrongness appraisal (D2), depending on the experimental block.

Statistical Analysis

Then, to check whether the moral transgression cartoons did portray a moral transgression and did elicit feelings of guilt, paired-*t*-tests were conducted to detect significant differences in wrongness and guilt judgments between all pairs of HTO and HTS scenarios. Missing values were excluded. All HTO scenarios, except one (scenario 16, see **Supplementary Table 1**), presented significantly higher ratings of anticipated guilt and moral wrongness than their alternative HTS scenario (all $t > 2.50$; $p < 0.01$). This scenario was excluded from further analyses to ensure that all the stimuli included portrayed guilt-eliciting moral transgressions.

To examine the relationship between appraisals (anticipated guilt and moral wrongness) of moral transgressions and CU traits (i.e., ICU total score) and between response times during appraisals and CU traits, linear mixed-*effects* models (LMMs) were estimated. LMMs are particularly appropriate for the analysis of nested structured data as is the case of this study. As the data were nested both within participants and within scenarios, participants and scenarios were treated as random effects. Additional LMMs were estimated to test whether CU traits moderated the relationship between feelings of guilt and wrongness ratings, i.e., to test whether levels of CU traits changed the strength of the association between these two variables; and whether CU traits moderated the relationship between RTs in ratings of anticipated guilt and wrongness judgments, which might be considered as a proxy of difficulty in making such judgments. The presence of univariate outliers was checked using the protocol described by Tabachnick and Fidell's (62). The highest RT in anticipated guilt (RT = 3891 ms) was identified as a potential outlier. Removal of this observation had a very small impact on the parameters estimates. We also ran additional models without the observation with the lowest RT in anticipated guilt (RT = 39 ms), given its extremely low value. Removal of both observations had a very small impact on the parameters estimates (see **Supplementary Materials** for these results). For completeness, we also computed additional models with age as a covariate. Our results indicate that age is positively associated with wrongness ratings and RTs but its inclusion does change the pattern of our results. It should be noted, though, that the limited age range in our sample precludes a definite interpretation of these findings (see **Supplementary Materials** for these results). Statistical analyses were carried out in R statistical software (63), using nlme package to perform linear mixed effects modeling, and ggplot2 package to construct the graphs. *P*-values lower than 0.05 were considered statistically significant. The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

RESULTS

The means, standard deviations and ranges for all variables are presented in **Table 1**. HTS scenarios were used only to confirm that all of HTO scenarios portrayed guilt-eliciting moral transgressions. All following analyses relate to moral transgressions (i.e., HTO) scenarios only.

Are CU Traits Associated With Anticipated Feelings of Guilt and Wrongness Judgments to Everyday Moral Transgressions?

We estimated LMMs with random intercepts for testing the association between anticipated guilt and ICU score, and between wrongness judgments and ICU score. Predictor variables were grand mean centered. Parameter estimates from each model

TABLE 1 | Characterization of the sample in terms of scores on the ICU, and ratings and response times to the everyday moral transgressions task.

	Adolescents ($N = 47$)		
	M	***SD***	**Range**
ICU score	**19.04**	**6.36**	**7 - 36**

	HTO scenarios			HTS Scenarios		
	M	***SD***	**Range**	***M***	***SD***	**Range**
Wrongness ratings	16.3	4.0	0-20	7.6	6.3	0–20
Guilt ratings	15.7	4.3	0-20	8.8	6.4	0–20
Wrongness RTs	1309.5	736.7	176-3989	1599.1	843.0	39–3955
Guilt RTs	1424.6	722.8	34-3891	1655.9	802.9	257–3993

ICU, Inventory of Callous-Unemotional traits; HTO, "Harm-To-Other" scenarios; HTS, "Harm-To-Self' scenarios; RTs, Response Times.

TABLE 2 | Linear mixed models of Anticipated Guilt and Moral Wrongness ratings including the effects of CU traits.

	Guilt ratings			Wrongness ratings		
Fixed effects	β	**SE**	***p-value***	β	**SE**	***p-value***
Intercept	15.81	0.30	< 0.001	16.44	0.29	< .001
ICU score	−0.18	0.02	< 0.001	−0.15	0.02	< .001
Random effects		***SD* (CI)**			***SD* (CI)**	
Scenario (intercept)		1.4 (1.03–1.96)			1.4 (1.03–1.94)	
Participant (intercept)		3.6 (2.52–5.07)			3.3 (2.45–4.52)	
Residual		1.4 (0.13–14.33)			1.3 (0.17–9.78)	
Marginal R^2		0.077			0.054	
AIC		6686.75			6517.14	

β, *unstandardized regression coefficient; SE, standard error; ICU, Inventory of Callous–Unemotional traits; CI, confidence interval; AIC, Akaike Information Criterion.*

are presented in **Table 2** and the relation between variables is illustrated in **Figure 2**. Higher CU traits were associated with less anticipated guilt ($\beta = -0.18$, $p < 0.001$) and less wrongfulness judgments ($\beta = -0.15$, $p < 0.001$). The variance in anticipated guilt explained by ICU score was 7.7% and in wrongness judgments was 5.4%, as indicated by the marginal R^2 statistic.

Two additional LMMs were estimated to test the associations between ICU score and response times in anticipated guilt and wrongness appraisals. Predictor variables were grand mean centered. Parameter estimates from each model are presented in **Table 3**. ICU scores were positively associated with response times in performing guilt and wrongness appraisals (Guilt: $\beta = 15.38$, $p < 0.001$; Wrongness: $\beta = 17.43$, $p < 0.001$). That is, those scoring higher on ICU took longer to provide ratings of guilt and wrongness (see **Table 3**).

Do Levels of CU Traits Moderate the Association Between Anticipated Guilt and Wrongness Judgments for Everyday Moral Transgressions?

To examine whether CU traits moderate the relation between anticipated guilt and wrongness judgments, a separate linear mixed model, adding an interaction term between anticipated guilt and CU traits, was fitted (see **Table 4**). All predictor variables were grand mean centered. ICU score moderated the relation between anticipated guilt and wrongness ratings ($\beta = -0.01$, $p < 0.001$) revealing a weaker association between those components of moral judgment in participants with higher CU levels. Adolescents with lower levels of CU traits showed a steep increase in the wrongfulness ratings as the ratings of anticipated guilt augmented, whilst this was not observed in those with high levels of CU traits (**Figure 3**).

Is the Strength of the Association Between Anticipated Guilt and Response Times to Wrongness Judgments Moderated by CU Traits?

Finally, and to inspect whether higher anticipated guilt has a facilitating effect on wrongness judgments and whether this is impacted by CU traits, we examined if CU traits moderate the relation between anticipated guilt ratings and wrongness judgments' RTs. A separate linear mixed model was fitted, adding an interaction term between anticipated guilt and CU traits (see **Table 5**). Higher levels of anticipated guilt were

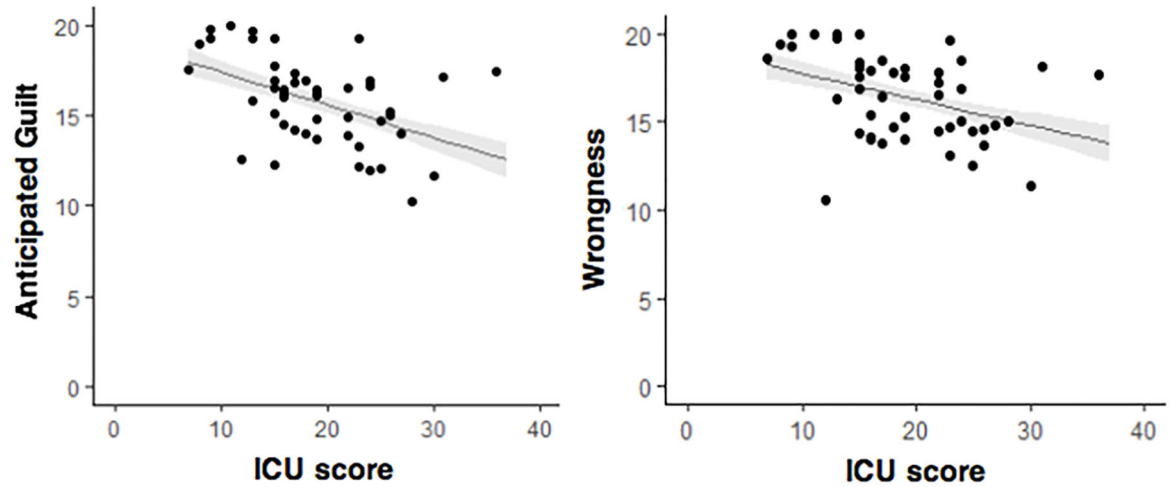

FIGURE 2 | Scatter plots depicting the associations between CU traits (X axes) and anticipated guilt (graph on the left) and wrongness (graph on the right) ratings to moral transgressions. The black lines at each graph illustrate linear effects of CU traits on guilt and wrongness ratings, respectively. The shaded area (in gray) represents the 95% confidence interval of the prediction.

TABLE 3 | Linear mixed models of Anticipated Guilt and Wrongness RTs including the effects of CU traits.

	Guilt RTs			Wrongness RTs		
Fixed effects	**β**	**SE**	***p-value***	**β**	**SE**	***p-value***
Intercept	1441.96	36.84	< 0.001	1310.18	37.45	< 0.001
ICU Total score	15.38	3.27	< 0.001	17.43	3.26	< 0.001
Random effects	***SD* (CI)**			***SD* (CI)**		
Scenario (intercept)	155.8 (104.86–231.39)			159.8 (107.42–237.58)		
Participant (intercept)	665.0 (34.87–12682.27)			664.4 (15.31–28838.92)		
Residual	251.8 (0.01–441062.82)			251.7 (0.01–649355.72)		
Marginal R^2	0.012			0.022		
AIC	19176.71			19173.87		

β, *unstandardized regression coefficient; SE, standard error; ICU, Inventory of Callous-Unemotional traits; CI, confidence interval; AIC, Akaike Information Criterion.*

associated with lower response times ($\beta = -35.05$, $p < 0.001$) to wrongness judgments. CU traits did not moderate the association between anticipated guilt and response time to wrongness judgements ($p = 0.71$).

DISCUSSION

The presence of high levels of CU traits, a constellation of personality traits marked by blunted affect, uncaring behavior and disregard for others [e.g., (3)], in youth is associated with increased antisocial behavior, even in the absence of a diagnosis of conduct disorder (5, 12). CU traits are considered to be developmental precursors of core affective-interpersonal aspects of psychopathy, a disorder marked by serious and persistent antisocial behavior (2, 4, 28, 64, 65). A growing body of research in adult samples suggests that moral dysfunction in psychopathy may stem from a disruption of the affective components of moral processing rather than from an inability to compute moral judgments *per se*. Here, we present data on a novel task of everyday moral processing and test if the dissociation between affective and cognitive dimensions of moral processing linked to psychopathic traits in adulthood is also observed in relation to CU traits in adolescence, in a typically-developing adolescent sample. In this task, adolescents were presented with personal everyday moral transgression scenarios and were asked to rate how much guilt they would feel and how wrong it would be if they performed such actions. We found that CU traits were negatively associated with both anticipated guilt and wrongness appraisals to the transgressions; adolescents with higher CU traits anticipated feeling less guilt and made less wrongfulness judgments. However, we also found that higher levels of CU traits were associated with increased dissociation between anticipated guilt and moral judgment. That is, in contrast to those with low

levels of CU traits, adolescents with high levels of CU traits did not show a steeper increase in wrongness ratings as the ratings of anticipated guilt augmented.

Our key finding relates to the moderating role of CU traits in the association between anticipated guilt and moral judgment. Contemporary perspectives of human morality emphasize the

TABLE 4 | Linear mixed model for the relation between anticipated guilt and wrongness judgments moderated by CU traits.

	Wrongness ratings		
Fixed effects	**β**	**SE**	***p-value***
Intercept	16.36	0.14	< 0.001
ICU score	−0.03	0.02	0.02
Guilt	0.6	0.02	< 0.001
Guilt*ICU score	−0.01	0.00	< 0.001
Random effects		***SD* (CI)**	
Scenario (intercept)		0.6 (0.34–0.87)	
Participant (intercept)		2.7 (2.27–3.10)	
Residual		1.0 (0.35–2.85)	
Marginal R^2		0.427	
AIC		5964.85	

β, unstandardized regression coefficient; SE, standard error; ICU, Inventory of Callous-Unemotional traits; CI, confidence interval; AIC, Akaike Information Criterion.

TABLE 5 | Linear mixed model for relations between anticipated guilt and wrongness judgments' RTs moderated by CU traits.

	Wrongness RTs		
Fixed effects	**β**	**SE**	***p-value***
Intercept	1307.64	32.75	< 0.001
ICU score	11.34	3.41	< 0.001
Guilt	−35.05	5.26	< 0.001
Guilt*ICU score	−0.30	0.82	0.709
Random effects		***SD* (CI)**	
Scenario (intercept)		127.9 (81.43–200.98)	
Participant (intercept)		653.8 (20.90–20450.47)	
Residual		246.5 (0.01–80769.77)	
Marginal R^2		0.061	
AIC		19145.91	

β, unstandardized regression coefficient; SE, standard error; ICU, Inventory of Callous-Unemotional traits; CI, confidence interval; AIC, Akaike Information Criterion.

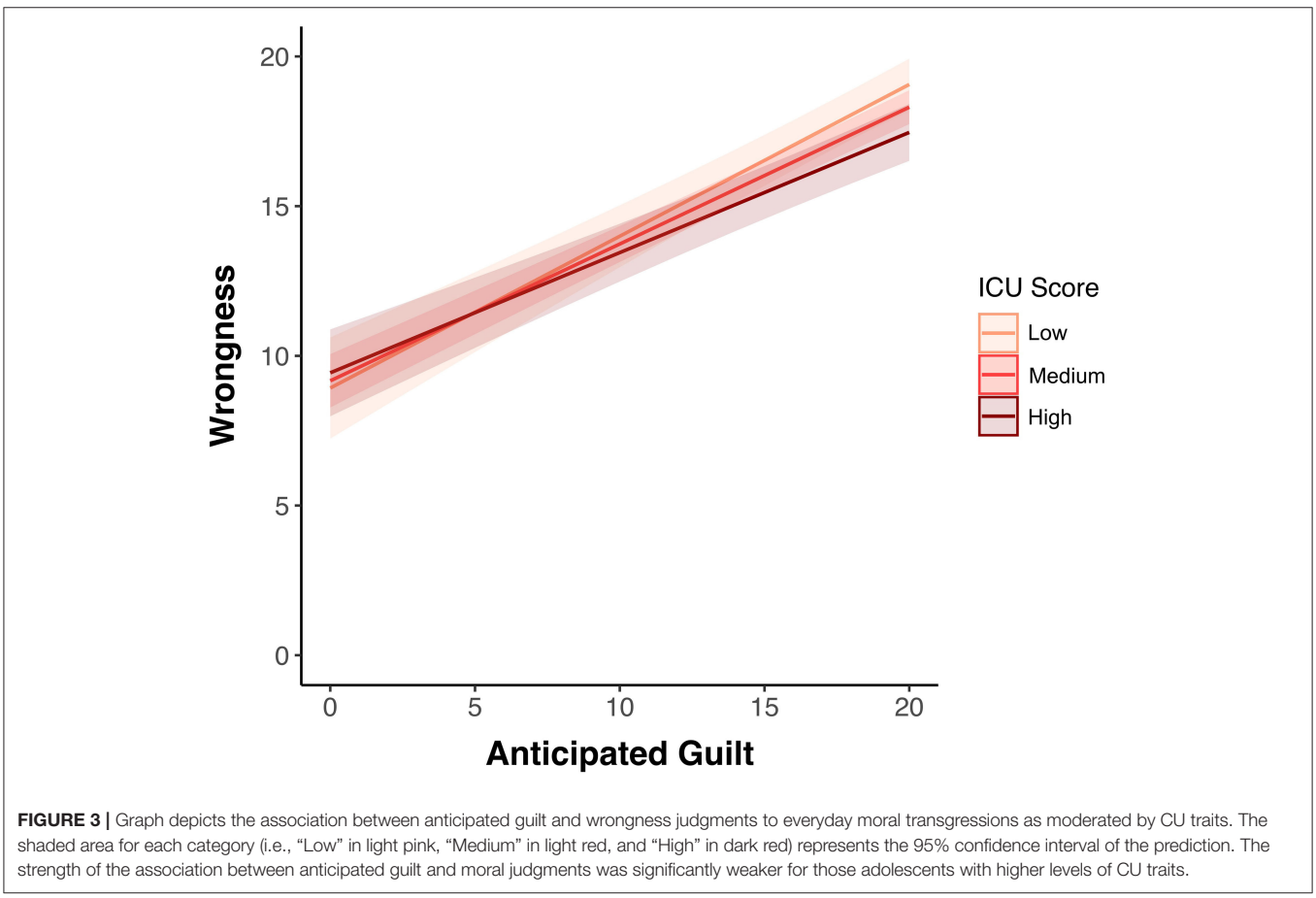

FIGURE 3 | Graph depicts the association between anticipated guilt and wrongness judgments to everyday moral transgressions as moderated by CU traits. The shaded area for each category (i.e., "Low" in light pink, "Medium" in light red, and "High" in dark red) represents the 95% confidence interval of the prediction. The strength of the association between anticipated guilt and moral judgments was significantly weaker for those adolescents with higher levels of CU traits.

role of moral emotions on moral judgement, in particular in care-based moral judgments (15, 18, 19). Moral emotions are thought to play a fundamental role on the development of judgments about moral situations (66, 67). In our sample, CU traits were negatively associated with the strength of the association between guilt and wrongness judgments. For adolescents with higher levels of these traits, moral emotions did not seem to play such an important role on moral appraisals. This is interesting, because it suggests that the dissociation between moral emotions and moral judgment linked to psychopathic traits may already be present during adolescence and evolve through adulthood. Findings from neuroimaging research on moral processing in adolescents with high CU traits, albeit sparse, are in-line with this idea. CU traits have been found to be associated with diminished amygdala response and connectivity with prefrontal regions during moral judgment (47, 48). The amygdala is a brain region critical for affective processing and this pattern of diminished response might reflect reduced affective input during moral judgement. It is possible that the moderating role of CU traits in the association between anticipated guilt and wrongness appraisals reflects a lack of "affective coloring" in moral judgment in adolescents with high levels of CU.

In line with findings from adult research [e.g., (30, 31, 35)] and a recent study with a youth community sample (45), we further found that adolescents with higher CU traits reported anticipating less guilt when imagining themselves performing everyday actions that cause harm to other people, and took longer to make these evaluations. This finding agrees with recent literature reporting emotional hypo-responsivity of children with high levels of CU traits, in particular to others' stress, manifested at behavioral, cognitive and neural levels (see 3, 49 for recent reviews). Our findings also revealed that adolescents with higher levels of CU traits judge everyday moral transgressions as less wrongful. This is in contrast to the majority of findings from adult studies indicating that individuals with high levels of psychopathic traits have apparently intact moral judgment abilities. For example, the endorsement of actions in moral dilemmas seems to be similar for adult psychopaths and controls (32, 68) and does not seem to vary with levels of psychopathic traits in community samples (30, 31). Additionally, psychopathic traits do not seem to be associated with moral wrongness judgments of aggressive behavior (69), nor of everyday moral situations (35). Findings from child and adolescent samples are sparser and less consistent. For example, Marsh et al. (48) did not find behavioral differences between youth with high levels of psychopathic traits and matched controls when making explicit moral judgments. Harenski et al. (47) found that psychopathic traits in a sample of incarcerated youth were negatively associated with ratings of violation severity of pictures with moral content. But, psychopathic traits were also negatively associated with ratings of non-moral but still unpleasant pictures, which might indicate a lack of specificity to moral content.

It has been proposed that, in the absence of an emotional response to moral transgressions, individuals with high levels of psychopathic traits use alternative cognitive strategies to process moral judgments (61). Individuals with high levels of psychopathy seem to know (and apply) the rules that are relevant to make moral judgements but do seem to do so without using "standard" affective routes that are taken by those with low levels of these traits (32, 68, 70). This point is supported by our last analysis. We found a negative association between guilt anticipation and response time to wrongness judgements. Participants took less time to provide their wrongness ratings when anticipated guilt was high. Hence, higher response time when making a moral appraisal in participants higher in CU may reflect the lack of emotional loading when judging the scenario and the reliance on other cues to provide a response. Our results thus suggest that differences in appraisals of wrongness are still present in adolescents with high CU, alongside difficulties in making these appraisals, but a weaker role of emotion on moral judgement is also already observed.

Additionally, it is possible that adults with high levels of psychopathic traits display typical moral judgment due to an intact ability to understand the thoughts of others (36, 44), as well as others' expectations (71). This would enable adults with high levels of psychopathic traits to respond to moral tasks and questionnaires in the same way they think other people would, thus engaging in successful impression management. Social cognition skills are not yet fully developed during adolescence [see (72) for a review]. The ability to understand the thoughts of others and flexibility in taking another's perspective into account seems to be still developing in late adolescence and early adulthood (73). Plus, recent evidence suggests that, although adolescents with higher levels of CU traits do not seem to be less able than their peers to infer the thoughts of others, they seem to be less prone to take others' thoughts into account, at least in a spontaneous and effortless manner (74). This could explain why more lenient moral appraisals are observed in adolescents with higher levels of CU but not in adults with higher levels of psychopathic traits. This could also explain why adolescents with higher levels of CU take longer to make such judgments.

The present work provides relevant evidence regarding early signs of a dissociation between affective (i.e., anticipated guilt) and cognitive (i.e., wrongness judgments) dimensions of moral behavior in adolescents with high levels of CU traits. However, it is important to bear in mind that the lack of a comparison group of adults precluded us from examining if and how the moderation of the association between guilt and moral judgments by psychopathy changes/increases with age. Future cross-sectional and, critically, longitudinal research is required to confirm an increased dissociation between different components of moral processing from adolescence to adulthood for those with high levels of psychopathic traits. A larger and mixed-gender sample would also allow us more power to detect possible smaller effects and also to test if the links found between moral processing components and CU traits are similar for boys and girls or whether there are gender-specific differences, in line with recent research examining gender differences in moral emotions (75). It should also be noted that cognitive ability was not controlled for in this study. Research findings on how intelligence interacts with psychopathy and antisocial behavior is diverse, with studies suggesting that IQ is likely a protective factor against antisocial behavior (76) whilst others indicate that enhanced verbal abilities potentiate the relation between

callous-unemotional traits and violent juvenile offending (77). We have not included a measure of cognitive ability in the current study for a number of reasons: there is limited evidence of the role of IQ on processing of everyday moral transgressions in adolescents (78); our sample was comprised of typically developing adolescents from a regular high school and we did not expect to find adolescents outside the typical range of IQ; and we had limited testing time imposed by the school. Future work should investigate whether IQ does play a role on the processing of both cognitive and emotional aspects of everyday transgressions in a large adolescent sample with varying levels of IQ, and also address whether and how cognitive abilities modify the effect we found in the present work.

Despite these limitations, this study presents important new evidence of how, in typically developing adolescents, the presence of CU traits moderates the association between affective and cognitive components of moral processing. Our findings are in line with the notion that evidence gathered from community studies often reflect the findings of forensic and clinical investigations (79) and support the dimensional approach to psychopathy suggesting that correlates of psychopathic traits in adults and CU traits in children and youth are present in a continuum in the population [see (80), for a review]. Plus, they add evidence to the view that CU traits are strongly linked to impairments in emotional functioning, and that these impairments may play an important role in explaining moral dysfunction in youth with high psychopathic traits (81). The present findings make important contributions to further characterize and comprehend the cognitive-affective processing deficits that may underlie atypical moral processing in youth who are at heightened risk for antisocial behavior and psychopathy in adulthood.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of University of Minho, Braga, Portugal (SECVS131/2016). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

AS-C, EV, CS, and AS: conceptualization. SF, MV, and AS-C: statistical analyses. AS-C, MV, EV, and CS: writing—original draft. AS-C: funding acquisition. All authors: writing—review & editing, contributed to the article, and approved the submitted version.

FUNDING

This study was supported by the Portuguese Foundation for Science and Technology (FCT) research grant awarded to AS-C (PTDC/MHC-PCN/2296/2014), co-financed by FEDER through COMPETE2020 under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-016747). The study was conducted at the Psychology Research Center (PSI/01662), School of Psychology, University of Minho, supported by FCT through the Portuguese State Budget (Ref.: UIDB/PSI/01662/2020).

ACKNOWLEDGMENTS

We would like to thank Ms. Andreia Queirós and Dr. Eugénia Fernandes for their assistance with data collection.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.625328/full#supplementary-material

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Conflict of Interest: 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.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 17 May 2021
doi: 10.3389/fpsyt.2021.658171

Restricted Visual Scanpaths During Emotion Recognition in Childhood Social Anxiety Disorder

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Background: Social anxiety disorder (SAD) has its typical onset in childhood and adolescence. Maladaptive processing of social information may contribute to the etiology and maintenance of SAD. During face perception, individuals execute a succession of visual fixations known as a scanpath which facilitates information processing. Atypically long scanpaths have been reported in adults with SAD, but no data exists from pediatric samples. SAD has also been linked to atypical arousal during face perception. Both metrics were examined in one of the largest eye-tracking studies of pediatric SAD to date.

Methods: Participants were children and adolescents with SAD ($n = 61$) and healthy controls ($n = 39$) with a mean age of 14 years (range 10–17) who completed an emotion recognition task. The visual scanpath and pupil dilation (an indirect index of arousal) were examined using eye tracking.

Results: Scanpaths of youth with SAD were shorter, less distributed, and consisted of a smaller number of fixations than those of healthy controls. These findings were supported by both frequentist and Bayesian statistics. Higher pupil dilation was also observed in the SAD group, but despite a statistically significant group difference, this result was not supported by the Bayesian analysis.

Conclusions: The results were contrary to findings from adult studies, but similar to what has been reported in neurodevelopmental conditions associated with social interaction impairments. Restricted scanpaths may disrupt holistic representation of faces known to favor adaptive social understanding.

Keywords: social anxiety disorder, eye tracking, visual scanpaths, social attention, child and adolescent, attention bias, emotion

OPEN ACCESS

Edited by:
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Reviewed by:
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Janna Marie Bas-Hoogendam, Leiden University, Netherlands

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Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: *25 January 2021*
Accepted: *07 April 2021*
Published: *17 May 2021*

Citation:
Kleberg JL, Löwenberg EB, Lau JYF, Serlachius E and Högström J (2021) Restricted Visual Scanpaths During Emotion Recognition in Childhood Social Anxiety Disorder. Front. Psychiatry 12:658171. doi: 10.3389/fpsyt.2021.658171

Social anxiety disorder (SAD) is a highly disabling mental health disorder characterized by intense fear of social evaluation, often leading to extreme distress and avoidance of social interaction (1). SAD has a typical onset in late childhood or adolescence, and if left untreated often takes a chronic course (2). Current theoretical models suggest that etiological factors for SAD include genetic predispositions, temperament, cognitive biases, negative life events, peer-relations and parent behavior, that interact to produce SAD (3). The influential model by Clark and Wells (1995) (4) proposes that when an individual with social anxiety enters a social situation, a set of assumptions and beliefs are activated concerning how they think they have to act and what

other people expect of them. A prediction of failure is made which causes the social situation to be perceived as dangerous and to protect the individual from harm, a number of behavioral, cognitive, attentional, affective and somatic processes are activated. These processes, however, are also involved in the long-term maintenance of social anxiety, which prevents habituation to social situations even as the individual engages in frequent interactions with others (5–7). Several models also implicate aberrant information processing in the maintenance or development of SAD (8).

So far, most studies of information processing in SAD have been conducted in adults (9–11). Adults with SAD tend to interpret social signals from others as indications of rejection or hostility (11), a bias that might be driven by disrupted allocation of attention, to socially threatening stimuli (9, 10). Individuals with SAD may also differ from healthy controls regarding the type of stimuli they perceive as threatening. According to the fear of positive evaluation hypothesis, individuals with SAD perceive social cues signaling both negative evaluation (such as an angry face) and positive evaluation (such as a smiling face) as threatening (12, 13).

Since an extensive literature has documented that the development of social attention and emotional brain mechanisms is protracted and often nonlinear, it is not clear whether these results generalize to the younger age range where SAD typically has its onset (14). For example, the period from late childhood to early adulthood is characterized by developmental changes in the relative balance between brain functions involved in automatic emotional reactivity such as the amygdala, and those involved in top-down control of attention and emotion regulation such as the anterior cingulate (ACC) and prefrontal cortex (14–16).

Late childhood and adolescence is a period of high plasticity and intense maturation of the social brain (17, 18). Therefore, aberrant information processing during this period is likely to have cascading developmental consequences (19). Conversely, late childhood and adolescence may be a period when interventions tailored to address disrupted information processing mechanisms are particularly likely to carry long-term benefits (14). To understand these mechanisms is therefore an important research priority.

There is some evidence that youth with SAD misinterpret signs of both negative and positive emotions in faces (20), and show atypical functioning of brain regions involved in face processing (21, 22). However, the patterns of visual attention linked to these observed SAD-linked anomalies are poorly understood.

Visual attention unfolds through a succession of fixations and saccades known as the *scanpath*. Fixated locations are highly prioritized for further cortical processing, and the scanpath is therefore a fundamental aspect of visual information processing. Cognitively demanding tasks typically lead to longer and more widely distributed scanpaths, reflecting a higher degree of mental effort and cognitive control of attention (23, 24). Stimuli signaling potential threats may also be viewed with longer scanpaths than neutral stimuli, possibly driven by increased allocation of attention (25). Some types of facial information can be identified with scanpaths consisting of as little as two fixations, including the identity of familiar individuals or emotional expressions which can be identified by a single feature (e.g., a furrowed eyebrow (26). More typically, novel faces are scanned with multiple fixations (27, 28). A spatially distributed scanpath is believed to facilitate encoding of the face into a holistic percept (26, 29), and improves face recognition (30). Holistic processing is a hallmark of face processing in healthy individuals (31), while individuals with impaired face processing abilities, including those with neurodevelopmental disorders, often use a piecemeal or detail focused strategy (32–34). Restricted scanpaths could be a marker of this detail-focused processing style (35).

So far, a small number of eye-tracking studies have been conducted in children and adolescents with SAD (36–42). These studies examined the relative distribution of attention between threat-related faces and other stimuli during free viewing tasks. Studies using free-viewing tasks are informative about how individuals with SAD spontaneously distribute their attention in the absence of an explicit task and are therefore likely reflecting multiple cognitive processes. However, results from free-viewing tasks are inconclusive, with reports of both avoidance (38, 39), prolonged monitoring of threat (41, 42), quicker orienting to angry faces (43) and equally quick orienting to and from emotional faces in youth with SAD and controls (36). Previous studies are limited by small sample sizes, typically ranging between 20 and 35 individuals [for reviews, see (9, 10)]. Studies in adults have suggested that individuals with SAD look less at the eyes of images of faces when accumulated looking time over several seconds is considered (9). Studies in children and adolescents have so far not reported reduced overall looking time at the eyes in SAD (38, 40). Looking time at the eyes or other regions of a face accumulated over several seconds is likely reflecting several attentional processes, and more temporally sensitive metrics may be needed to detect atypical social attention in child and adolescent SAD (41).

Scanpaths in SAD

Scanpath measures could provide important information about information processing strategies in SAD but have so far not been examined in pediatric samples. Previous studies in adults with SAD reported a pattern of atypical scanpaths during face perception termed hyperscanning [e.g., (44)]. Hyperscanning can be defined as atypically long and widely distributed scanpaths (42–44). Typically, scanpath length is positively correlated with the number of executed fixations in both healthy individuals and individuals with SAD (25, 44–46). However, one study in adults with SAD reported the opposite pattern – i.e., that individuals who made longer scanpaths also made a smaller number of fixations. One reason for this unusual pattern may be that short fixations with a duration of <200 ms which may be more frequent during hyperscanning were discarded from these analyses (47, 48).

Hyperscanning was initially reported during free viewing of static images of faces (47, 48), and later also for dynamic stimuli during a public speaking task (44). Wermes and colleagues (45) extended these findings and found hyperscanning in adults with SAD but only after an anxiety induction procedure. In contrast, the type of visual stimuli (search for threat or neutral stimulus)

did not modulate the results. Finally, Boll and colleagues (49) did not observe a group difference in scanpath length between adults with SAD and healthy controls during an emotion classification task.

Pupil Dilation in SAD

Theoretical models of SAD propose that enhanced perception of threat during social-evaluative situations affect not only allocation of attention, but also physiological arousal (3). Heightened arousal is a common aspect of anxiety, and social fear could therefore potentially lead to hyperarousal. Consistent with this, brain imaging studies have shown amygdala hyperreactivity during face processing in SAD (21, 22). So far, little is known about potential links between atypical scanpaths and arousal in SAD.

Pupil dilation is an index of arousal directly controlled by joint activity in the sympathetic and parasympathetic branches of the autonomic nervous system. At least two components of the pupil response can be distinguished during stimulus processing. The first is a rapid constriction and subsequent dilation caused by changes in in luminance called the pupillary light reflex (PLR). The second and slower component (the pupil dilation response, PDR) is characterized by a relative increase in pupil size during periods of attention, mental effort, and arousal. This later response is modulated by cholinergic and noradrenergic activity (50, 51). Traditionally, only the PDR has been linked to cognitive processing, but recent studies indicate that also the PLR is affected by such factors (52).

In light of previous studies, it could therefore be expected that SAD would be associated with enhanced pupil dilation to emotional faces. However, this has not been found in the two studies published so far (38, 40). Keil and colleagues examined pupil dilation in 10–13 year old children and controls during face processing (38). Groups did not differ in the amplitude of their pupil dilation response measured during the whole trial interval (10 s), but the SAD group had a larger PLR than controls, which may reflect blunted cognitive modulation of the PLR. A recent study from our group examined the time course of pupil dilation in a group of adolescents with SAD as well as the amplitude of the response (40). Although adolescents with SAD did not differ from healthy controls in pupil dilation amplitude, an atypical time course was found, characterized by a decrease in pupil dilation over the course of stimulus presentation. We sought to extend these results in a larger sample and in the current study we examined pupil dilation amplitude which is the most commonly studied measure in the literature on pupil dilation (53).

Analysis Plan

The analysis plan was pre-registered in the Open Science Framework after data collection but prior to analysis (link: https://osf.io/dytnf).

Hypotheses

The following hypotheses were tested:

Hypotheses 1: Youth with SAD will show longer scanpaths than healthy controls during face processing (longer total scanpath and more dispersion between fixations).

Hypothesis 2: Youth with SAD will show a blunted pupil dilation response during later stages of face processing (e.g., after initial adaptation to light).

We did not hypothesize group differences in accumulated looking time to the eyes or mouth but included exploratory analyses of these metrics.

METHODS

Participants With SAD

Participants aged 10–17 years with SAD were recruited from an ongoing clinical trial evaluating the efficacy of internet-delivered cognitive behavioral therapy (ICBT) for pediatric SAD. Initially, 107 individuals with SAD were invited and 64 of these accepted to participate in the study and completed the experiment. Three participants with SAD were excluded from all analyses because of invalid data (see *Recording and processing of eye tracking data and Statistical Analysis*), resulting in a sample size of 61. A principal diagnosis of SAD according to DSM-5 (1) criteria was confirmed by an experienced clinical psychologist interviewing the child and parents jointly with the Anxiety Disorders Interview Schedule [ADIS; (54)]. The ADIS interview is normally conducted with the child and parents separately, so to ensure that the child's account was given sufficient attention during the interview, parents were instructed to let the child respond first to all questions. Exclusion criteria were initiation or dose modification of psychotropic drug within the past 6 weeks, current psychosis, eating disorder, severe depression, suicidal behavior, or other current severe mental disorder including autism spectrum disorder, or substance or alcohol abuse. Comorbid diagnoses were specific phobia ($n = 5$), generalized anxiety disorder ($n = 8$), depression ($n = 4$), attention deficit/hyperactivity disorder ($n = 3$), separation anxiety ($n = 1$) and panic disorder ($n = 1$). Two individuals with SAD medicated with selective serotonin reuptake inhibitors (SSRIs), three with stimulants (lisdexamphetamine), and one with melatonin. All results remained when participants on medication were excluded.

Recruitment of the Healthy Control Group

We planned for a control group of $n = 40$. Participants were randomly selected from the Swedish tax registry and contacted by mail. Initially, addresses of 326 10–17 year old children living in the Stockholm area were randomly selected from the Swedish tax registry. Families were sent a letter describing the purpose of the study and were later contacted over telephone and asked to participate. Of the initial sample, 153 families did not respond to the telephone calls, and 107 declined to participate. The remaining 66 participants were asked screening questions before inclusion. Of these, 18 were excluded because of current or previous mental health diagnoses (SAD: $n = 4$, ADHD: $n = 10$, bipolar disorder: $n = 1$, chromosome abnormalities, $n = 1$, obsessive compulsive disorder, $n = 1$, autism, $n = 1$). Seven participants were initially included but did not complete the testing procedure because no suitable time was found. The remaining 41 individuals were included and completed the testing procedure.

Control participants were assessed by a clinical psychologist using the MINI-KID (55). No participant in the control group had a mental health disorder according to the clinical assessment. Two individuals were excluded from analysis because of invalid data, resulting in a sample size of 39. As expected, both youth- and parent reports indicated higher levels of social anxiety in the SAD group than in healthy controls (see **Table 1**). All participants in the control group scored within one standard deviation of the mean scores on the Liebowitz Social Anxiety Scale – child version (LSAS-C) previously reported in normative samples of youths (56), and could therefore be considered healthy and non-anxious. The LSAS is a self-report measure of fear and avoidance in 24 different social and performance situations, available for youth as well as parents. Groups were matched on age and gender (**Table 1**). The sample is partly overlapping with the second cohort in a previous study by (41), where data from another experiment are reported.

Ethical Considerations

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Stockholm regional research ethics committee (decision number 2017/1142-31/4).

Experimental Task

Images from a standardized database of actors displaying emotional expressions were used as stimuli (57). In total, 24 images were shown to each participant, evenly distributed between three emotional expressions (angry, happy, fearful)[1]. The same actors appeared once with each expression, meaning that the stimulus set contained eight unique actors (50% male, 50% female). Stimulus images were cropped to show only the inner regions of the face. Each trial began with a fixation cross on a uniform gray screen for 2 s, followed by an emotional face presented for 4 s. Immediately after stimulus offset, participants were asked to identify with a mouse click whether the depicted person felt angry, happy, or fearful. Participants were not asked to make a speeded response. We chose a presentation time of 4 s to give the participants enough time to identify the emotional expressions, and also execute enough eye movements to calculate scanpath metrics. Example of stimulus images are shown in **Figure 1**.

Recording and Processing of Eye Tracking Data

Data were recorded using a Tobii X-120 corneal reflection eye tracker (Tobii Inc, Danderyd, Sweden), which samples gaze at 120 Hz and pupil size at 40 Hz. Raw eye tracking data were processed using custom scripts written in MATLAB version 2019a (Mathworks, Inc). Fixations were identified using an I-VT filter (58) with parameters set according to recommendations by the manufacturer. Following linear interpolation of gaps in the data shorter than 100 ms, a moving average filter with a window size of 25 ms was applied to the x- and y-coordinates. Saccades were identified as periods with between-samples velocity exceeding 30°/s, and fixations were defined as periods between saccades. Subsequent fixations within 1° were merged. Fixations shorter than 50 ms were discarded.

Two pre-registered scanpath metrics were calculated: (1) The summed Euclidean distance between subsequent fixations (scanpath length); and (2) The root-mean-square (RMS) value of all fixations (scanpath dispersion). The RMS was calculated for each trial by (1) taking the average of the squared deviations from the mean of the x- and y-values of all fixations and (2) taking the square root of these values, and (3) averaging values for the x- and y-coordinates. Higher RMS values therefore reflect a higher degree of spatial dispersion of fixations, whereas scanpath length reflects the total distance that gaze travels during the entire stimulus presentations (see **Figure 2** for illustrations). The RMS of individual fixations should not be confused with the RMS of the unfiltered samples constituting a fixation, which is sometimes used as a quality metric in eye-tracking studies.

Scanpath length and dispersion are expressed in degrees of visual field. To account for the fact that more valid data from a trial would also result in longer scanpaths, we divided the scanpath measures by the total valid fixation time (defined as all successfully recorded samples identified as part of a fixation) in seconds. Previous studies of scanpaths in SAD have also analyzed the average number of fixations by trial [fixation count [e.g., 42–44]], a measure typically closely correlated with scanpath length. We included fixation count as an additional metric in the analyses to facilitate comparison with previous studies. Trials with <1,500 ms valid fixation time were discarded.

Pupil data were filtered according to procedures described in an earlier publication from our group (40). Gaps in the data shorter than 150 ms were replaced through linear interpolation and subsequently filtered by a moving median filter corresponding to 80 ms. A pupil dilation response was calculated for each trial and defined as the mean proportional change in pupil size during stimulus presentation relative to baseline pupil size. As in previous publications (40, 59), the initial increase in pupil size after stimulus onset that can largely be attributed to changes in screen luminance was discarded. Based on visual inspection of the data, pupil dilation response was defined as the mean pupil size during the 1,500–4,000 ms interval (see **Supplementary Figure 1**).

Baseline pupil size was measured during a 750 ms interval directly preceding the stimulus. An estimate of baseline pupil size was calculated for each participant by taking the mean pupil size during this interval from all valid trials. Values outside the +/− 3 SD range from the mean of each participant were considered outliers and were discarded.

Statistical Analyses

For each individual, a mean of all valid trials within each condition was computed. All data from an individual and condition were rejected if <4 trials were valid. Six participants (3 with SAD) were excluded from all analyses because they were

[1]The following images from the KDEF database were used as stimuli: ANSF07, ANSF09, ANSF33, ANSM07, ANSM08, ANSM09, ANSM32, HASF07, HASF09, HASF33, HASM07, HASM08, HASM08, HASM32, FESF07, FESF09, FESF33, FESM07, FESM08, FESM09, FESM32.

TABLE 1 | Demographics, clinical characteristics and number of valid trials.

	SAD ($n = 61$)		Healthy controls ($n = 39$)		
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**p**
Background					
Age	14.43 (2.19)	10–17.9	14.21 (2.21)	10.30–17.30	0.618
Gender (% Female)	77	–	68		0.355
LSAS (Child report)[1]	79.00 (27.78)	24–135	19.77 (12.25)	2–47	**<0.001*** **
LSAS (Parent report)[2]	87.62 (26.06)	34–130	13.63 (12.99)	0–58	**<0.001*** **
Mean nr of valid trials (max possible = 24)					
Scanpath analysis	21.45 (2.73)	13–24	20.79 (3.42)	13–24	0.311
Pupil dilation	22.92 (1.38)	18–24	22.62 (1.39)	19–24	0.285
%Correctly identified					
Angry	98 (4)	88–100	94 (9)	63–100	**0.009****
Fearful	95 (10)	63–100	95 (9)	63–100	>0.90
Happy	99 (4)	83–100	97 (7)	75–100	0.203

[1]*Based on n = 59 in the SAD group;* [2]*. Based on n = 58 in the SAD group; ***p < 0.001; *p < 0.01. SD, standard deviation. LSAS, Liebowitz Social Anxiety Scale.*

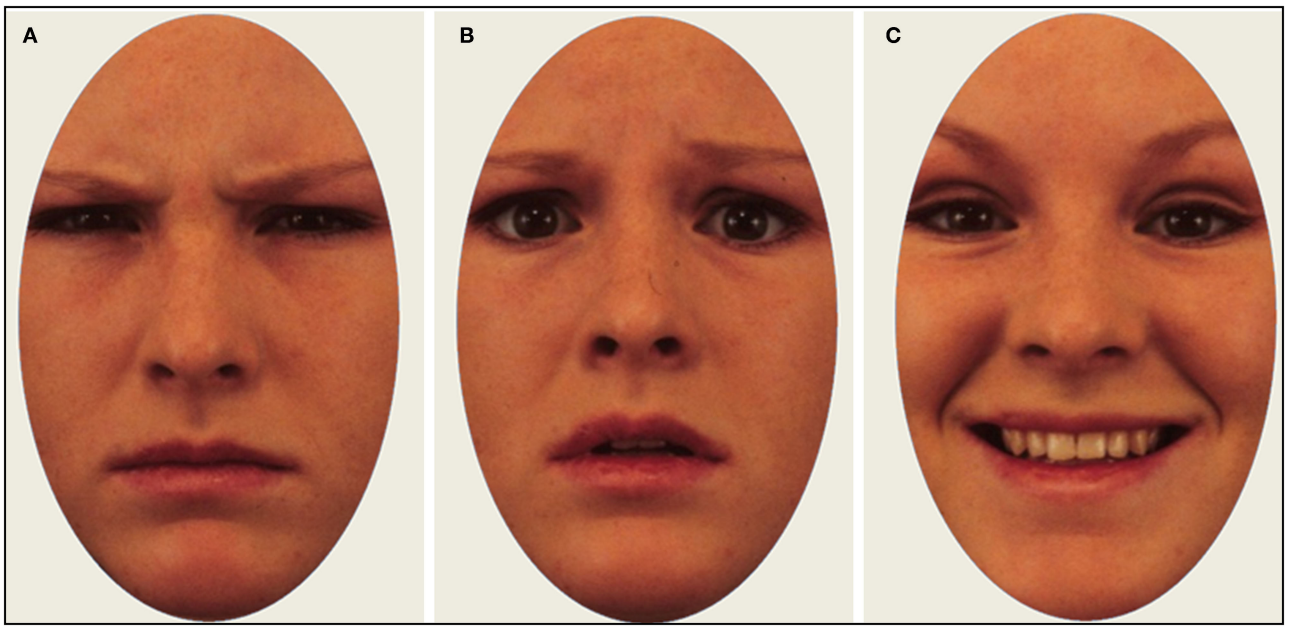

FIGURE 1 | Example of stimulus images with actors displaying an angry **(A)**, fearful **(B)**, and happy **(C)** expression.

lacking data from all conditions. Cohens' *d* is reported as a standardized effect size of group differences. Age and sex were added as covariates in all analyses. A power analysis indicated that the study had 80% power to detect small to medium effect sizes of $d = 0.2$ or higher.

Hypotheses were tested using generalized linear mixed effects models (GLMM) with random intercept for participant (i.e., treating multiple observations from the same individual as repeated measures). Statistical tests for an effect were performed by comparing a model including the effect to the most complex model without the effect in question (the *null model*). For example: a main effect of group can be tested by comparing the full model Y ∼ GROUP + (1|ID) to a null model including only the intercept: $Y \sim 1 + (1|\mathrm{ID})$, where Y is the response variable. Both frequentist statistics (i.e., *p*-values) and Bayesian analyses were conducted. Bayesian statistics have been proposed as an alternative to null hypothesis significance testing (NHST). In a Bayesian analysis, the relative evidence for a hypothesis and the null hypothesis given the observed data can be quantified in terms of a *Bayes factor*. Consequently, researchers may potentially not only conclude that the null hypothesis could not be rejected, but also that it may be supported. Bayesian statistics may be more robust to false positive results than NHST (60). Therefore, we interpreted our results based on

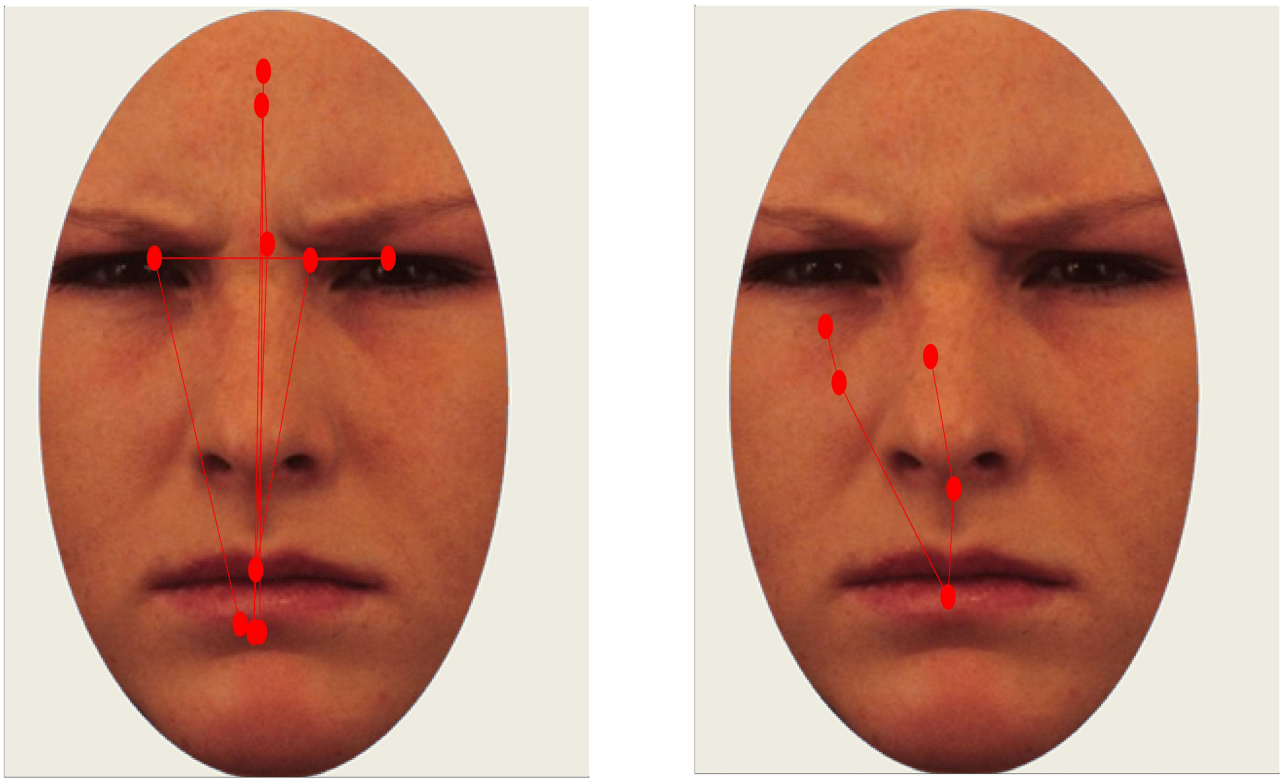

FIGURE 2 | Example of a long scanpath [**(A)**; scanpath length and RMS values above 75th percentile. Healthy participant] and restricted scanpath [**(B)**; scanpath length and RMS values below 25th percentile. Participant with SAD]. Red circles represent fixations.

the Bayesian statistics when results from the two statistical approaches were conflicting.

In a frequentist framework, the full- and null models were compared using χ^2-tests, yielding a *p*-value for the significance of the effect (61). The full- and null-models can also be compared using a Bayes factor (BF), expressing the relative likelihood of the two models. Following Wagenmakers (60), a BF is calculated from the Bayesian information criterion (BIC) values of the two models using the following equation:

$$BF_{10} = \exp^{(BIC\_H0 - BIC\_H1)/2}.$$

Where BF_{10} is the Bayes factor favoring H_1 over H_0, with higher numbers indicating more evidence supporting H_1. By reversing the terms, a BF_{01} can be calculated, with higher numbers indicating more support for H^0. By convention, a BF > 3 indicates positive evidence for the hypothesis, a BF > 20 indicates strong support, and a BF > 150 very strong support (60). *Post-hoc* analyses were conducted to examine whether the observed group differences in scanpath metrics would also be linked to symptom levels of SAD. These analyses were conducted with linear regression models with the mean of all valid trials across conditions as dependent variable. For each participant, the highest value of the child and parent version of the LSAS was used as a measure of SAD symptoms. Sex and age were added as covariates. Bayes factors were computed by comparing a model including SAD symptoms to the next most complex model (the null model). Additional analyses were also conducted to compare accumulated looking time at the eyes and mouth.

RESULTS

Preliminary Analyses

No group differences were found in the number of completed trials (see **Table 1**). As can be seen in **Table 1**, although correct identification of emotion was close to ceiling in all conditions, the SAD group was more accurate than the HC group in identifying expressions of anger, whereas no group differences were found for happy or fearful faces.

A main effect of emotion was found on scanpath length, so that scanpaths were shorter during processing of happy compared to fearful and angry expressions. No effects of emotion were found on scanpath dispersion. Expressions of anger and fear elicited higher pupil dilation than expressions of happiness. These results are shown in **Table 2**. Groups did not differ in overall looking time at the eyes ($\chi^2 = 0.12$, $p = 0.730$, $BF_{10} = 0.11$, $d = 0.07$) or mouth ($\chi^2 = 0.32$, $p = 0.575$, $BF_{10} = 0.12$, $d = 0.09$). There were also no interactions between group and emotion in looking time at either region (see **Supplementary Table 1**).

TABLE 2 | Main effects of emotion for the studied dependent variables.

	χ^2	p	b	SE	BF_{10}	BF_{01}	d
Scanpath Length							
Fearful > Angry	1.33	0.249	0.17	0.15	0.20	**5.16**	0.08
Angry > Happy	6.26	**0.012***	−0.34	0.14	2.30	0.44	0.15
Fearful > Happy	14.08	**<0.001*****	0.51	0.13	**114.91**	0.01	0.22
Scanpath Dispersion							
Fearful > Angry	1.04	0.307	−0.02	0.02	0.17	**5.91**	0.06
Angry > Happy	1.18	0.277	−0.03	0.02	0.18	**5.52**	0.07
Fearful > Happy	0.03	0.859	0.00	0.02	0.10	**9.80**	0.02
Pupil Dilation							
Fearful > Angry	4.85	**0.028***	−0.57	0.25	1.12	0.90	0.28
Angry > Happy	18.32	**<0.001*****	−1.22	0.27	**>500**	<0.01	0.57
Fearful > Happy	5.92	**0.015***	0.65	0.26	1.89	0.52	0.29

$^{***}p < 0.001$; $^{*}p < 0.05$. b, unstandardized beta coefficient; SE, standard error; BF_{10}, Bayes factor favoring the alternative hypothesis; BF_{10}, Bayes factor favoring the null hypothesis; d, Cohen's d.

Main Analysis (Registered Hypotheses)

Scanpath Length

Results are shown in **Table 3** and **Figure 3** and summarized here. Scanpaths were shorter in the SAD group than in healthy controls ($\chi^2 = 9.38$, $p = 0.002$, $BF_{10} = 10.94$, $d = 0.54$). This effect was not qualified by any interaction effect between group and emotion ($\chi^2 = 3.60$, $p = 0.167$, $BF_{10} = 0.06$).

Scanpath Dispersion

Scanpaths were also less dispersed in the SAD group compared to healthy controls ($\chi^2 = 7.68$, $p = 0.006$, $BF_{10} = 4.68$, $d = 0.51$; see **Table 3** and **Figure 2**). Again, no interaction between group and emotion was found ($\chi^2 = 0.43$, $p = 0.806$; $BF_{10} = 0.01$). To sum up, restricted scanpaths were observed in the SAD group, a conclusion supported by both Bayesian and frequentist statistics.

Fixation Count

As can be seen in **Table 3**, participants in the SAD group made a smaller number of fixations than healthy controls ($\chi^2 = 15.31$, $p < 0.001$, $BF_{10} = 211.90$, $d = 0.62$). No interaction between group and emotion was found ($\chi^2 = 0.27$, $p = 0.88$, $BF_{10} = 0.01$).

Relation Between Scanpaths and Symptoms of SAD

We conducted *post-hoc* analyses to examine whether symptom levels of SAD were linked to scanpath metrics. Higher levels of SAD symptoms were linked to shorter scanpath length ($\beta = 0.24$, $p = 0.015$, $BF_{10} = 2.29$) and smaller number of fixations ($\beta = 0.32$, $p = 0.001$, $BF_{10} = 24.70$). No relation was found between SAD symptoms and scanpath dispersion ($\beta = 0.04$, $p = 0.32$, $BF_{10} = 0.17$).

Pupil Dilation

The SAD group had higher pupil dilation than controls. The difference was statistically significant ($\chi^2 = 4.58$, $p = 0.032$, $d = 0.29$), but the Bayes factor indicated that the data were marginally more likely under the null hypothesis ($BF_{10} = 0.98$, equivalent to $BF_{01} = 1.03$), and that the data were therefore inconclusive (see **Figure 3** and **Table 3**). No interaction between group and emotion was found ($\chi^2 = 0.05$, $p = 0.792$, $BF_{10} = 0.01$).

Relation Between Pupil Dilation and Scanpaths

Exploratory *post-hoc* analyses were conducted to examine links between pupil dilation and scanpath measures. No relations were found between pupil dilation and scanpath length ($\beta = -0.11$, $p = 0.22$, $BF_{10} = 0.22$, $BF_{01} = 4.59$), between pupil dilation and scanpath dispersion ($\beta = -0.15$, $p = 0.10$, $BF_{10} = 0.40$, BF_{01} 2.50), or pupil dilation and number of fixations ($\beta = 0.04$, $p = 0.69$, $BF_{10} = 0.40$, $BF_{01} = 9.29$). The Bayes factors favored the null hypothesis.

DISCUSSION

Social anxiety disorder in children and adolescents is associated with cognitive biases that may maintain or exacerbate symptoms. One of the factors underlying these biases may be a pattern of disrupted allocation of attention during information processing. The current study examined visual scanpaths and pupil dilation during emotion recognition in children and adolescents with social anxiety disorder. Emotional faces are a social evaluative cue and are as such a disorder relevant stimulus in SAD. Compared to healthy controls, youth with SAD had shorter and less dispersed scanpaths, a finding supported by both frequentist and Bayesian statistics. Further analyses showed that higher levels of SAD symptoms were linked to shorter scanpaths and a smaller number of fixations, again suggesting restricted visual scanning in children with SAD.

These results were contrary to our registered hypothesis, and also contrary to what has been reported in adult studies (44, 47, 48) where it has been proposed that socially anxious individuals scan faces with prolonged scanpaths (10, 44). Our results suggest that this attention pattern is not present in pediatric populations. Instead, a pattern of restricted scanpaths was found. As noted in the introduction, under normal attentional circumstances, wider scanpaths are observed during periods of controlled attention and mental effort. The observed pattern of restricted scanpaths in the SAD group could therefore reflect difficulties with cognitive control and allocation of attention.

TABLE 3 | Group differences between youth with SAD and healthy controls in scanpath length, scanpath dispersion and pupil dilation response.

Measure	M (SD)		Group comparison					
	SAD	HC	χ^2	p	BF_{10}	BF_{01}	d	Direction
Scanpath length (° of visual field)	7.59 (2.02)	8.82 (2.44)	9.38	**0.002****	**10.94**	0.09	0.54	SAD < HC
Scanpath dispersion	1.36 (0.32)	1.56 (0.42)	7.68	**0.006****	**4.68**	0.21	0.51	SAD < HC
Fixation count	9.17 (1.53)	10.14 (1.50)	15.31	**<0.001*****	**211.90**	0.01	0.62	SAD < HC
Pupil dilation response	1.13 (2.08)	1.75 (2.18)	4.58	**0.032***	0.98	1.03	0.29	SAD > HC

$^{**}p < 0.01$; $^{*}p < 0.05$. b, unstandardized beta coefficient; SE, standard error; BF_{10}, Bayes factor favoring the alternative hypothesis; BF_{10}, Bayes factor favoring the null hypothesis; d, Cohen's d; HC, Healthy Control.

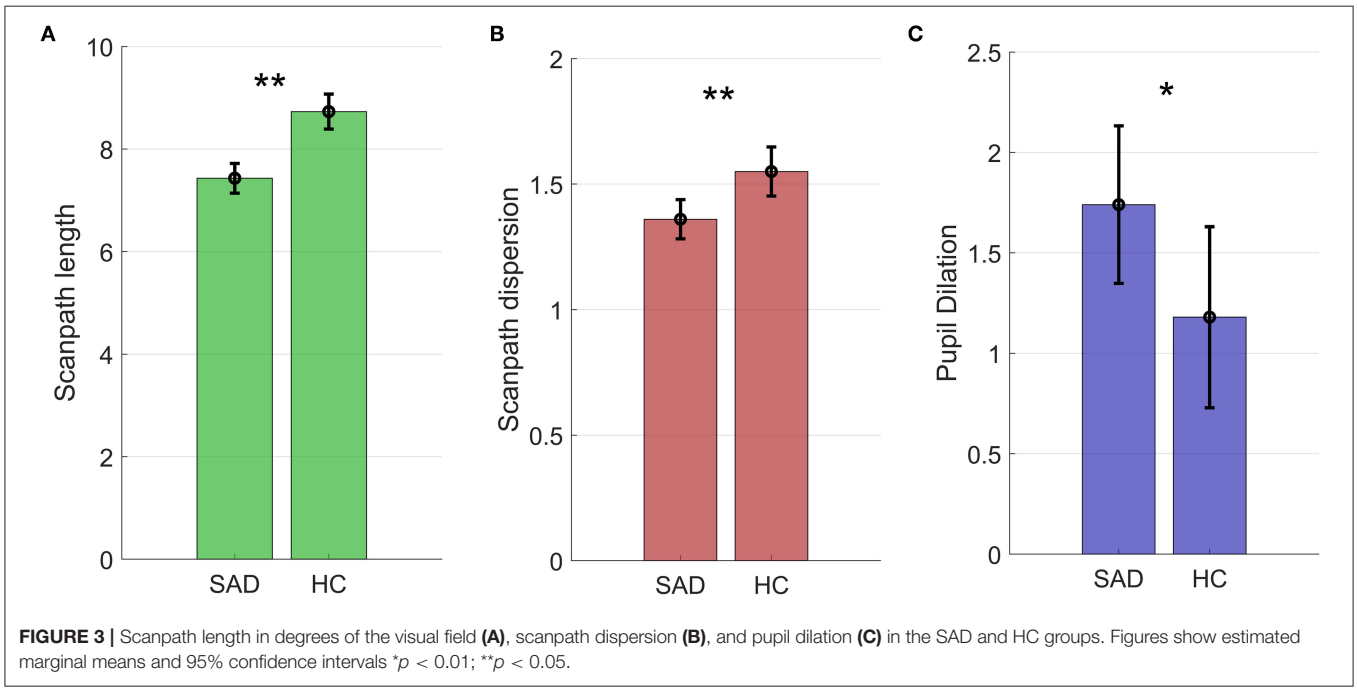

FIGURE 3 | Scanpath length in degrees of the visual field **(A)**, scanpath dispersion **(B)**, and pupil dilation **(C)** in the SAD and HC groups. Figures show estimated marginal means and 95% confidence intervals $^{*}p < 0.01$; $^{**}p < 0.05$.

Restricted scanpaths may lead to a face processing strategy based on attention to single features rather than global configurations (i.e., holistic face processing). Importantly, the observed pattern of restricted scanpaths in SAD was not modulated by the emotional expression of the facial images. In fact, longer scanpaths to negative emotions (anger and fear) compared to positive (happiness) were observed in both groups, replicating previous findings in healthy populations (25, 62). It is possible that smiling faces with direct gaze may be interpreted as threatening by individuals with SAD, since they signal possible social evaluation (12, 13, 63).

Holistic as compared to detail-focused processing is a hallmark of normal face perception. However, a piecemeal strategy can sometimes facilitate detection of negative emotional expressions such as anger or sadness (64), which can be detected based on single features (65). In the current study, patients with SAD were more accurate in identifying expressions of anger than controls but did not differ in accuracy for happiness or fear. Although this finding should be interpreted with caution due to potential ceiling effects, it suggests that youth with SAD may show superior detection of angry facial affect.

The relation between restricted scanpaths and social anxiety may be bidirectional. Previous studies in nonclinical samples have demonstrated that negative mood is associated with disrupted holistic face processing (64, 66). Similarly, social anxiety may therefore disrupt holistic face processing. It is also possible that disrupted holistic processing exacerbates or maintains social anxiety to the extent that it reduces the ability to interpret ambiguous or complex facial information.

The observed pattern of restricted scanpaths may also reflect patients with SAD needing less information than healthy individuals to identify facial expressions as emotional. Longer scanpaths are associated with task difficulty and complexity (24, 62). The fact that longer scanpaths were observed in the control group could therefore reflect task difficulty. In support of this interpretation, Melfsen and Florin (20) reported that children with SAD had lower perceptual thresholds for identifying facial expressions as emotional. Interestingly, restricted scanpaths to stimuli with social content have previously been reported in other conditions with known social interaction impairments, including autism (35), schizophrenia (32) and schizotypy (29), suggesting that it may be a transdiagnostic mechanism. Atypical scanpaths

were found in children with SAD despite the fact that they did not differ in overall looking time at the eyes or mouth.

Our finding of restricted scanpaths in the SAD group are opposite to what has been described in the adult studies (44, 48), pointing to a possible developmental difference between children and adults with SAD. It is possible that restricted scanning may have negative developmental consequences during this period, by restricting opportunities for learning. An interesting question for longitudinal studies is therefore whether restricted scanpaths predict worse social functioning or higher levels of SAD symptoms at later time points.

On the other hand, the transitional phase of adolescence may involve greater plasticity at the behavioral and neural level (14), thus interventions designed to alter these processing anomalies may yield greater and longer-lasting benefits. Interventions targeting SAD symptoms through attention training have been attempted, but evidence for their efficacy is so far limited (14). If these interventions are to be successful, a better understanding of the patterns of attention associated with SAD is needed. Our results suggest that restricted scanpaths may be a feasible target for interventions.

Our second aim was to examine pupil dilation during face processing. The SAD group had higher pupil dilation responses than healthy controls while viewing faces, regardless of their emotional expression. According to a conventional frequentist statistical analysis (i.e., inferential statistics based on *p*-values), this effect was statistically significant. However, the Bayesian analysis indicated that the hypothesis was marginally less likely than the null, rendering the result inconclusive. Bayesian statistics may be less vulnerable to false positives than frequentist statistics (60), and we believe that this result is therefore best interpreted as inconclusive. This means that we were not able to replicate previously reported findings of blunted pupillary reactivity during face perception in pediatric SAD, although it should be noted that these studies examined partly different pupil dilation metrics (38, 40). There was no relation between pupil dilation and any of the examined scanpath metrics, indicating no direct link between reduced scanpaths and hyperarousal.

Some limitations should be noted. Although the present study is one of the largest eye tracking studies of pediatric SAD to date, we were not able to compare individuals with SAD to groups with other mental health disorders. Future studies would also benefit from direct comparisons between child and adult populations with SAD. The generalizability of the findings may also be limited to treatment-seeking individuals with SAD, rather than to a broader population of youths with SAD. It should also be noted that the study did not include non-facial control stimuli. Therefore, it is not clear whether the findings are specific for faces or reflect a more general form of atypical attention. Future studies could benefit from the inclusion of additional experimental conditions, including nonsocial stimuli and more ambiguous and complex facial expressions. Finally, due to the limited sample rate of the equipment (40 Hz), we were not able to examine metrics which are sensitive to timing such as the time course of the pupil dilation response or the PLR amplitude, as was done in previous studies (38, 40). An interesting question for future studies is to examine whether scanpath lengths in children with SAD is related to other types of attention and perceptual judgement, including memory for faces. In a previous adult study (45), hyperscanning was found only after an anxiety induction procedure. An interesting question for future studies is whether scanpaths in youth with SAD are also affected by induction of state anxiety. Studies manipulating gaze behaviors (for example by instructing participants to scan either narrowly or broadly) could also examine whether scanpath length causally affects arousal.

Strengths of the study includes the use of a clinically well-characterized sample of treatment-seeking patients with SAD and a matched control group randomly selected from the general population.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Etikprövningsmyndigheten (Swedish Ethical Review Authority). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin and by participants aged 15 - 17. Participants aged 10 - 14 gave verbal ascent.

AUTHOR CONTRIBUTIONS

JK and JH designed the study. JK analyzed the data and drafted the manuscript. JL, EL, and ES contributed to the interpretation of the data. All authors contributed to the article and approved the submitted version.

FUNDING

This research was supported by Riksbankens jubileumsfond (grant numbers P18-0068), Claes Groschinskys minnesfond, Region Stockholm and the regional agreement on medical training and clinical research between Region Stockholm and the Karolinska Institutet (PPG 20150032, The Swedish Research Council for Health, Working Life and Welfare (Forte 2014-4052), the Strategic Research Area Neuroscience (StratNEURO) and the Center for Psychiatry Research, Stockholm, Sweden. ES was supported by Region Stockholm (clinical research appointment 20170605). JL is receiving research funding from the UK Economic and Social Research Council (ES/T00004X/1).

ACKNOWLEDGMENTS

A preprint version of this manuscript has been published on PsyArXiv (https://psyarxiv.com/m4d76/).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.658171/full#supplementary-material

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Conflict of Interest: 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.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 29 June 2021
doi: 10.3389/fpsyt.2021.668019

Alexithymia Is Associated With Deficits in Visual Search for Emotional Faces in Clinical Depression

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Background: The concept of alexithymia is characterized by difficulties identifying and describing one's emotions. Alexithymic individuals are impaired in the recognition of others' emotional facial expressions. Alexithymia is quite common in patients suffering from major depressive disorder. The face-in-the-crowd task is a visual search paradigm that assesses processing of multiple facial emotions. In the present eye-tracking study, the relationship between alexithymia and visual processing of facial emotions was examined in clinical depression.

Materials and Methods: Gaze behavior and manual response times of 20 alexithymic and 19 non-alexithymic depressed patients were compared in a face-in-the-crowd task. Alexithymia was empirically measured *via* the 20-item Toronto Alexithymia-Scale. Angry, happy, and neutral facial expressions of different individuals were shown as target and distractor stimuli. Our analyses of gaze behavior focused on latency to the target face, number of distractor faces fixated before fixating the target, number of target fixations, and number of distractor faces fixated after fixating the target.

Results: Alexithymic patients exhibited in general slower decision latencies compared to non-alexithymic patients in the face-in-the-crowd task. Patient groups did not differ in latency to target, number of target fixations, and number of distractors fixated prior to target fixation. However, after having looked at the target, alexithymic patients fixated more distractors than non-alexithymic patients, regardless of expression condition.

Discussion: According to our results, alexithymia goes along with impairments in visual processing of multiple facial emotions in clinical depression. Alexithymia appears to be associated with delayed manual reaction times and prolonged scanning after the first target fixation in depression, but it might have no impact on the early search phase. The observed deficits could indicate difficulties in target identification and/or decision-making when processing multiple emotional facial expressions. Impairments of alexithymic depressed patients in processing emotions in crowds of faces seem not

OPEN ACCESS

Edited by:
Peter Kirsch,
University of Heidelberg, Germany

Reviewed by:
Georg W. Alpers,
Universität Mannheim, Germany
Benjamin Becker,
University of Electronic Science and Technology of China, China

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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *02 March 2021*
Accepted: *03 June 2021*
Published: *29 June 2021*

Citation:
Suslow T, Günther V, Hensch T, Kersting A and Bodenschatz CM (2021) Alexithymia Is Associated With Deficits in Visual Search for Emotional Faces in Clinical Depression. Front. Psychiatry 12:668019. doi: 10.3389/fpsyt.2021.668019

limited to a specific affective valence. In group situations, alexithymic depressed patients might be slowed in processing interindividual differences in emotional expressions compared with non-alexithymic depressed patients. This could represent a disadvantage in understanding non-verbal communication in groups.

Keywords: alexithymia, major depressive disorder, face-in-the-crowd, emotional facial expressions, eye-tracking, visual search, anger, happiness

INTRODUCTION

The concept of alexithymia emerged to explain symptoms of psychosomatic patients (1). It comprises the facets difficulties in identifying and describing one's feelings, a restricted imagination, and a concrete, externally oriented style of thinking (2). In the majority of studies, the self-report questionnaire 20-item Toronto Alexithymia Scale (TAS-20 (3)) has been administered to empirically measure alexithymic features. There is evidence that alexithymia occurs more frequently in men, individuals with low educational level, low socioeconomic status, and advanced age (4). It is considered a transdiagnostic, non-specific feature in many mental disorders (5). Alexithymia has been discussed as a major personality risk factor for physical illness, psychological distress, and chronic psychopathology (6, 7).

An important ability for successful interpersonal communication is the identification of emotions from facial expressions (8). Emotional information from facial expressions is decoded rapidly indicating its high biological and social relevance (9). In a crowd or group of people, salience of emotional faces becomes especially useful. In these multiple stimulus conditions, cognitive mechanisms must be activated to locate the relevant faces against the competing distractors (10). In the last decades many studies using the face-in-the-crowd paradigm have been conducted to clarify the question whether angry or happy faces are, in general, detected more efficiently. To this aim, often one emotional face has been presented in a group of neutral faces (11, 12). Some studies provided evidence for anger superiority (i.e., more efficient search for angry faces) (13, 14) whereas, other studies have observed a happiness superiority effect (i.e., more efficient search for happy faces) (15, 16). Overall, it appears difficult to draw general conclusions on the detection superiority of a specific emotion since the pattern of results observed in visual search studies could largely depend on the specific stimulus materials applied (17).

The majority of visual search experiments has based their analyses on manual reaction time and accuracy of response. Reaction time provides only a single data point per trial with which it is difficult to make precise inferences about the component operations involved in searching for target objects (18). Eye-tracking can give more direct evidence, e.g., about which objects were attended, in what sequence, for how long. Analysis of gaze behavior based on eye-tracking allows to characterize the temporal evolution of search processes in more detail. Eye movements and fixations inform primarily about overt attention processes. Covert shifts of attention are not registered by eye-tracking. Covert attention in the visual domain refers to seeing something peripherally on which the gaze is not directly focused (which is not the object of foveal vision). However, covert shifts of spatial attention are known to be involved in saccade preparation and to precede overt shifts of gaze to the target location during visual search (19). Thus, there are close functional links between covert and overt attention processes. The visual system is capable of determining a face's emotion before the face becomes the focus of attention, and facial emotions can be used by the visual system to prepare subsequent overt attention allocation (20).

In many previous face-in-the-crowd experiments, no explicit labeling or identification of emotional expressions was required (13, 21). Typically, participants were asked to decide if all faces show the same expression or if one face has an expression differing from the others. In this way, multiple emotional expressions have to be compared and differences between them have to be detected. Findings in face-in-the-crowd studies suggest that detection responses occur generally after having fixated the target (22) and that response latencies are positively associated with the number of fixations until the target is fixated (23). This means that the detection of discrepant emotional expressions at least in larger groups of stimuli requires eye-movements (overt attentional orienting) and sequential processing of expressions. In some cases, target detection (and discrimination from the distractor faces) occurs after having fixated away from the target (22). It has been argued that fast detection responses could reflect efficient guidance of the target (i.e., features of the target are already processed covertly and guide overt attention to its position) and/or efficient distractor rejection (distractor faces are skipped more frequently and/or fixated more briefly) (14, 16). Measures of eye gaze that are often used to assess visual search efficiency in face-in-the-crowd tasks comprise the time from onset of matrix display to first fixation on the target (i.e., latency to first target fixation), the number of distractors fixated before first fixation on the target and the duration of fixation time per distractor viewed before the first fixation on the target (indices of distractor processing efficiency), and the number of on-target fixations (index of target processing efficiency or deficits in disengagement) (14, 16, 22).

The personality trait alexithymia is associated with deficits in identifying others' emotional facial expressions in healthy individuals (24). There is clear evidence that these identification deficits are more pronounced under suboptimal processing conditions (e.g., when faces are presented in degraded quality or with temporal constraints (25–27)). It has been argued that alexithymia could be characterized by less efficient reading out and use of emotional information in the evaluation of facial

expressions (28). According to a systematic review, alexithymic individuals' impairments in identifying emotions from facial expressions seem to be neither limited to a specific valence nor specific emotional qualities (29). That means that alexithymia has been found to be linked to deficits in identifying positive (i.e., happy) expressions as well as to deficits in identifying negative (i.e., angry, sad, and fearful) expressions. Findings from previous fMRI research with healthy individuals examining brain response to emotional faces suggest that alexithymic individuals may encode facial emotional information in general to a lesser degree at an automatic and controlled processing level (30, 31). So far, no studies have been conducted to investigate the relationship between alexithymia and visual search for emotional faces.

Alexithymic characteristics have been frequently observed in patients suffering from clinical depression (32). The prevalence of high levels of alexithymia (scoring above the upper cut-off score of the TAS-20 (33)) varies from 27% (5) to 50% (34) in depressed patients, whereas, in the general population the prevalence of high levels of alexithymia is only about 10% (35).

There exist different explanations why alexithymia goes along with increased depressive symptoms and is prevalent in depressed patients. It has been argued, e.g., that the limited ability of alexithymic individuals to regulate negative emotions may lead to chronic, undifferentiated dysphoria (36). Moreover, it has been suggested that the association between alexithymia and impaired interpersonal functioning could contribute to depression (37). Alexithymia scores in depressed patients show a relative stability over time. Several studies reported a decrease in alexithymia among depressed patients as depression severity diminishes (32, 38). However, patients' alexithymia scores in different treatment or illness phases were found to be strongly correlated, demonstrating relative stability (38, 39). The personality trait alexithymia influences course, symptoms, treatment choice, and outcome in depressed patients. It has been observed that alexithymia interferes with recovery from depression (40). Depressed patients with reduced interest in and insight into feelings are less likely to benefit from psychotherapy (41, 42). Depressed patients with high alexithymia experience a higher burden of disease and manifest higher antidepressant consumption compared with low-alexithymic patients (43).

Findings from studies in which alexithymia has not been assessed suggest that clinical depression is characterized by impairments in the identification of facial emotion across all basic emotions (e.g., fear, anger, and happiness) except sadness. However, the extent of these impairments seems to be rather small (44). Eye-tracking research has shown biased attentional preferences in the perception of emotional information in major depressive disorder under free-viewing conditions. Depressed patients allocate more attention to sad faces and less attention to happy faces compared to healthy individuals (45). Interestingly, in early studies based on the face-in-the-crowd task it was found that depressed individuals need more time to detect positive faces in crowds of neutral expressions compared to healthy controls (46, 47). Karparova et al. (48) found generally longer reaction times to positive but also to negative expressions in a face-in-the-crowd task for depressed patients. However, in three subsequent face-in-the-crowd studies, response times for happy and negative facial expressions did not vary between depressed patients and controls (49–51). In a recent fMRI study investigating cerebral reactivity to masked faces in clinically depressed patients an association between alexithymia and decreased neural response in striatal and frontal regions to negative and positive facial expressions was observed (52). Striatal and orbitofrontal areas are implicated in the detection of salient features of sensory inputs, including emotional value, and appear to contribute to automatic alerting and allocation of attention (53, 54). Thus, alexithymia seems to go along with deficits in facial emotion perception in depressed patients.

In our eye-tracking study, the relationship between alexithymia and visual processing of facial emotions in clinical depression was examined using reaction time and gaze behavior data. To our knowledge, this is the first study on attention to multiple emotional faces as a function of alexithymia using eye-tracking methodology. The analysis of patients' gaze behavior allows a rather detailed temporal exploration of attention orienting that accompanies visual search. Eye movements of alexithymic and non-alexithymic depressed patients were tracked during a face-in-the-crowd experiment in which photographs of facial expressions depicting happiness, anger, and neutral expressions were displayed. These emotional categories were examined, as previous alexithymia research has reported deficits in the identification of negative and positive facial expressions (29). To create realistic crowds of faces with some ecological validity, photographs of multiple individuals (i.e., different identities) were used in our experiment. A mixed design was implemented that included every combination of target and distractor with the three emotional expressions (angry, happy, and neutral). Angry and happy faces were examined in our investigation since previous research using the face-in-the-crowd task (in samples of healthy individuals) was focused on these two emotional expressions. Our visual search paradigm required processes of comparison and search for discrepancies between multiple facial stimuli: participants were instructed to indicate whether all stimuli are from the same category or if one (the "target" stimulus) is different from the others. Visual search efficiency differences can be explained by differential amounts of guidance provided by a target and by differences in attention allocation toward distractor stimuli (55, 56). Our depressed patients were classified as alexithymic or non-alexithymic on the basis of their TAS-20 scores (33).

We hypothesized that depressed patients with alexithymia would manifest a less efficient performance in the face-in-the-crowd task than depressed patients without alexithymia. Specifically, it was expected that alexithymic patients show slower response latencies than non-alexithymic patients in the visual search task. We focused on the analysis of four eye-gaze parameters: latency to target face (i.e., the time from onset of stimulus display to first fixation on the target), number of distractor faces fixated prior to fixating the target, number of fixations on the target, and number of distractor faces fixated after fixating the target. The last-mentioned parameter was included in our analyses because in a study like the present one on difficulties and potential delays in the perception of facial emotions it appears important to examine the processes of

attention allocation after target detection. It should be noted that the parameter number of distractor faces fixated after fixating the target has rarely been used in previous research on visual search efficiency in face-in-the-crowd tasks. We also conducted group comparisons on fixation times on distractors and targets that are reported as **Supplementary Material**.

Latency to target (entry time of gaze on target) and number of distractor faces fixated prior to target fixation can indicate processes of attention guidance to the target face (i.e., the discrepant facial expression) (16). When a target strongly guides attention, the entry time of gaze on target should be short, few distractors are fixated, and many distractors are skipped. When a target guides attention only weakly, visual search is time-consuming, many distractors in the crowd have to be checked before the target is located. A higher number of fixations on the target indicates more attention allocation, a need for more visual information to identify the target object (57). Finally, if many distractors are fixated after the target has been visited the search and decision strategy seems to lack efficiency.

The present investigation can help to clarify which attentional or cognitive processes during visual search are impaired due to alexithymia. Alexithymic patients may manifest already deficits in early phases of visual search and scanning and look at more distractors before target fixation. However, alexithymic patients could show processing impairments only during or after target fixation. That is, they might exhibit a higher number of fixations on target or a higher number of distractor fixations after target fixation than non-alexithymic patients. Post-target detection deficits in the face-in-the-crowd task could suggest difficulties in the processing of similarities and discrepancies between facial expressions and the integration of collected information into a decision. The present task enables to explore whether alexithymic processing deficits concern perception of angry faces, happy faces or both types of expressions.

MATERIALS AND METHODS

Participants

Patients from the Department of Psychosomatic Medicine and Psychotherapy at the University of Leipzig participated in the study. They fulfilled the criteria for a DSM-IV diagnosis of major depressive disorder as assessed by the Structured Clinical Interview for the DSM-IV Axis I (58). Exclusion criteria were other past or present bipolar, schizophrenia or psychotic disorders, abuse of alcohol or other substances within the past 6 months, medical diagnoses associated with neurocognitive impairments, treatment with sedatives, or antipsychotics as well as the wearing of eyeglasses or contact lenses. The 20-item Toronto-Alexithymia-Scale (TAS-20 (3); German version (59)) was administered to classify patients as alexithymic and non-alexithymic. The criteria proposed by Bagby and Taylor (33) were applied to define alexithymia and non-alexithymia. Patients scoring $\geq$61 were considered alexithymic ($n = 20$) and those scoring $\leq$51 were considered non-alexithymic ($n = 19$). Fifty-four percent of the sample were medicated with antidepressants ($N = 21$).

Our study was approved by the ethics committee at the University of Leipzig, Medical Faculty, and in accordance with the Declaration of Helsinki. We obtained informed consent from all patients prior to inclusion and all patients were financially compensated.

Psychological Measures

The Montgomery-Asberg Depression Rating Scale (MADRS (60)), an interviewer-administered scale, was applied to assess severity of depression. The BDI-II (61) was administered to assess severity of depressive symptoms by self-report. The State-Trait Anxiety Inventory (STAI (62)) was used in its state form to assess anxious feelings at the time of testing. The Trail Making Test Part B (TMT-B (63)) was given to the patients to control for possible differences between groups in visual search speed and cognitive flexibility.

Stimuli and Face-in-the-Crowd Task

Face stimuli comprised 24 photographs of eight individuals (four women, four men) selected from the Lifespan Database of Adult Emotional Facial Stimuli (64). Stimuli comprised three types of emotional expressions (angry, happy, and neutral faces). All photographs were processed to replace background features and to limit each facial expression to head and neck. All faces were in the same frontal orientation, similar in size and gray scaled.

In each trial, eight photographs arranged in a circle were shown simultaneously against a black background. All stimulus matrices were viewed at a distance of 70 cm with a visual angle of $\sim$22.9° × 21.6° (height × width). Each face subtended a visual angle of 6° × 3.9° (height × width). The centers of adjacent faces were located at the same distance (6.5°). Within the same trial, positions were randomly assigned, and identities did not repeat. One-third of the trials were target absent ($n = 24$), i.e., composed of only one expression condition (e.g., all faces depicted angry expressions). Two-thirds were target-present trials ($n = 48$), showing one face from an expression condition and seven faces from a discrepant condition (e.g., one angry face among seven neutral faces). All target/distractor combinations were utilized (i.e., angry target happy distractors, angry target neutral distractors, happy target angry distractors, happy target neutral distractors, neutral target happy distractors, and neutral target angry distractors). In the target-present trials, each expression condition appeared once in each of the eight possible positions, resulting in eight trials for each target-distractor combination. For each participant, the order of trials was randomized.

Eye-Tracking Procedure

Patients were tested individually by an experienced experimenter. Camera adjustments were made to best capture eyes of patients. A nine-point grid was used for calibration. Calibration was repeated in case the deviation exceeded x/y 0.7°.

Each trial began with a fixation cross, displayed until a fixation of 1,000 ms. Then, face stimuli were shown until response or, in case of no response, for 5,000 ms. Subjects were instructed on the computer screen that they would see a series of faces arranged in a circle. Their task was to press the response key quickly whenever one of the faces differed in its expression from the others.

Eye Movement Apparatus and Parameter

SMIs Experiment Center software was applied to display stimuli and to synchronize with recorded eye movements. Pictures were presented on a 22-inch TFT widescreen monitor (resolution: 1680 × 1050) running with an SMI-customized Dell laptop. Viewing behavior was continuously registered with an IView X RED250 remote system by SMI, an infrared video-based eye-tracker recording eye movements every 4 ms (250 Hz) with a gaze position accuracy of 0.4°.

Gaze data were analyzed using a velocity-based algorithm with a minimum saccade duration of 22 ms, a peak velocity threshold of 40°/s, and a minimum fixation duration of 100 ms. We used BeGaze 3.0 (SMI, Teltow) to define eight areas of interest (AOIs) in each trial corresponding to each of the eight face expressions.

Manual response times were measured, i.e., the time between picture onset and key press. The rates of correct responses and non-responses were computed for all stimulus conditions. Four main measures of gaze behavior were used. First, we calculated the latency to target face or entry time on target (i.e., the time from onset of stimulus display to first fixation on the target). Second, we analyzed whether patient groups differed concerning attention guidance to the target face. Thus, we determined the number of distractor faces fixated prior to fixating the target. When a target strongly attracts attention, only few distractors should be fixated, and many distractor stimuli should be neglected. In case a target stimulus guides attention only weakly, many distractors in a group of stimuli must be analyzed before the target is finally identified (16). Third, we wanted to investigate whether patient groups differed regarding target processing. Therefore, we analyzed the mean number of fixations on the targets. Fourth, we determined the number of distractor faces fixated after fixating the target. If many distractors are analyzed after the target has been visited search and decision-making seems to lack efficiency.

Additional analyses of gaze behavior were conducted using fixation duration parameters to determine stimulus processing of targets and distractors. Mean fixation times per distractor face before and after fixating the target were calculated, respectively. Mean fixation time on targets were also analyzed. For the sake of brevity, only the main findings of these analyses based on fixation duration will be included in this article. The relevant fixation data and statistical results are described in more detail in the **Supplementary Material**.

The analyses of reaction time and eye-movement data focus on the target present trials with correct responses. The rate of correct responses across all target present conditions was 0.98 (SD: 0.03). Reaction times and eye-movement measures were analyzed using 6 (condition) × 2 (group) mixed ANOVAs. Analysis of covariance (ANCOVA) was used to control for covariates of interest when looking at group differences in test performance and gaze behavior. One-sample *t*-tests were administered as *post-hoc* tests to assess differences in decision performance or gaze behavior between face conditions in the total sample. The Shapiro-Wilk test was used to examine if reaction-time and eye-movement variables were normally distributed. In case of (partial) violation of normality for reaction-time and eye-movement data, Mann-Whitney *U*-tests were calculated to compare performance between groups. Two-sample *t*-tests and Chi^2-tests were applied to identify group differences in sociodemographic, clinical, and psychological characteristics and test performance.

General Procedure

The experiment took place at the Department of Psychosomatic Medicine and Psychotherapy at the University of Leipzig. After the clinical screening procedure described above, patients were invited to the experimental session individually. The experiment was conducted in a sound-attenuated room shielded from sunlight. Ceiling lighting produced stable illuminance conditions. After the eye-tracking experiment, participants completed the BDI-II, the state version of the STAI, and the TMT-B.

RESULTS

Sociodemographic, Clinical, and Psychological Characteristics

Study groups did not differ in age, gender distribution, state anxiety, visual search speed (TMT-B), interviewer-rated depression (MADRS), illness onset (years since first depressive episode), and number of experienced depressive episodes (see **Table 1** for details). However, alexithymic patients had a lower level of education, $t\ (37) = -2.94$, $p < 0.01$, reported more depressive symptoms (BDI), $t\ (37) = 2.56$, $p < 0.05$, and took more frequently antidepressants, $Chi^2(1) = 4.31$, $p < 0.05$ (see **Table 1**). According to both, MADRS and BDI, patients suffered from moderate levels of depressive symptoms at time of testing.

Manual Response Data

Rates of correct responses and non-responses were high for both study groups (see **Table 2**). The results of a 6 (condition) × 2 (group) mixed ANOVA on correct response rates in target-present trials indicate a significant main effect of condition $F_{(5,\ 185)} = 5.93$, $p < 0.001$, $\eta_p^2 = 0.14$, but no main effect of group, $F_{(1,\ 37)} = 1.23$, $p = 0.27$, and no interaction effect, $F_{(5,\ 185)} = 1.15$, $p = 0.34$. The experimental conditions "angry target neutral distractors" and "neutral target angry distractors" had overall the lowest rates of correct responses. The results of one-sample *t*-tests show that correct response rate for "neutral target angry distractors" was lower than that in the conditions "happy target angry distractors," "angry target happy distractors," "happy target neutral distractors" and " neutral target happy distractors" (ps < 0.05). Similarly, correct response rate for "angry target neutral distractors" was lower than that in the conditions "angry target happy distractors," "happy target neutral distractors" and "neutral target happy distractors" (ps < 0.05).

According to two-sample *t*-tests alexithymic and non-alexithymic patients did not differ on trials with only neutral or only happy faces concerning rate of correct non-responses. However, alexithymic patients showed fewer correct non-responses than non-alexithymic patients for trials consisting only of angry faces, $t\ (37) = -2.10$, $p < 0.05$. Since rates of correct non-responses and responses were not normally distributed for all conditions in both groups, additional non-parametric

TABLE 1 | Demographic, clinical, and questionnaire characteristics of alexithymic and non-alexithymic depressed patients [means and SD (in brackets) or frequency values].

Variable	Alexithymic patients	Non-alexithymic patients	*p*
Age	28.80 (7.41)	30.11 (6.69)	n.s.
Gender (f/m)	13/7	13/6	n.s.
Level of education[a]	3.15 (1.42)	4.42 (1.26)	<0.01*
Years since first depressive episode	7.85 (6.19)	9.11 (4.75)	n.s.
Number of episodes	6.60 (7.81)	6.32 (6.73)	n.s.
Antidepressant medication (yes/no)	14/6	7/12	<0.05*
TMT-B (seconds)	62.56 (18.36)	58.96 (23.12)	n.s.
BDI-II (sum score)	25.50 (6.60)	20.47 (5.60)	<0.05*
MADRS (sum score)	25.35 (4.58)	23.18 (5.32)	n.s.
STAI-S (item score)	2.29 (0.42)	2.32 (0.55)	n.s.
TAS-20 (sum score)	66.70 (5.56)	44.32 (5.82)	<0.001*

**Significant differences between groups according to independent samples t-tests or χ^2 tests.*
[a]Coding of level of education: 1 = 9th grade, 2 = 10th grade, 3 = 11th grade, 4 = 12th grade, 5 = University bachelor degree, 6 = University master degree.
TMT-B, Trail Making Test Part B; BDI-II, Beck Depression Inventory II; MADRS, Montgomery-Åsberg Depression Rating Scale; STAI-S, State-Trait Anxiety Inventory – state version; TAS-20, 20-Item Toronto-Alexithymia Scale.

TABLE 2 | Rate of correct non-responses/responses as a function of alexithymia, emotional quality of target, and distractor face and target absence/presence [means and SD (in brackets)].

Variable	Alexithymic patients	Non-alexithymic patients
All angry faces	0.94 (0.09)	0.99 (0.06)
All happy faces	0.99 (0.03)	0.99 (0.03)
All neutral faces	0.98 (0.05)	0.97 (0.05)
Angry target happy distractors	0.99 (0.03)	0.99 (0.04)
Angry target neutral distractors	0.94 (0.08)	0.97 (0.06)
Happy target angry distractors	0.96 (0.08)	1.0 (0.0)
Happy target neutral distractors	0.99 (0.04)	0.99 (0.06)
Neutral target angry distractors	0.94 (0.09)	0.95 (0.08)
Neutral target happy distractors	1.0 (0.0)	0.99 (0.03)

analyses were calculated. According to Mann-Whitney *U*-tests, alexithymic patients had fewer correct responses than non-alexithymic patients in trials consisting only of angry faces, ($U = 127$, $p < 0.05$). Moreover, alexithymic patients showed fewer correct responses than non-alexithymic patients in trials with a happy target in angry distractors, ($U = 152$, $p < 0.05$).

A 6 (condition) × 2 (group) mixed ANOVA on response latencies revealed a significant effect of condition, $F_{(5, 185)} = 68.13$, $p < 0.001$, $\eta_p^2 = 0.65$, and a significant effect of group, $F_{(1, 37)} = 5.73$, $p < 0.05$, $\eta_p^2 = 0.13$, but no interaction effect, $F_{(5, 185)} = 1.46$, $p = 0.21$. Alexithymic patients exhibited in general slower decision latencies compared to non-alexithymic patients (see **Figure 1**). Independent of study group, participants responded slowest in the conditions "neutral target angry distractors" and "angry target neutral distractors" (see **Figure 1**). According to one-sample *t*-tests, response latencies in the condition "neutral target angry distractors" were significantly higher than those in the conditions "happy target angry distractors," "angry target happy distractors," "happy target neutral distractors" and "neutral target happy distractors" (*p*s < 0.05). Moreover, response latencies in the trials "angry target neutral distractors" were higher than those in the trials "angry target happy distractors," "happy target neutral distractors" and "neutral target happy distractors" (*p*s < 0.05).

In addition, an ANCOVA was performed entering level of education, reported depressive symptoms (BDI), antidepressant use, and sex as covariates. The ANCOVA results showed that the covariates did not have significant effects on the dependent variable, whereas, the effect of group remained significant, $F_{(1, 33)} = 5.36$, $p < 0.05$, $\eta_p^2 = 0.14$.

Eye-Movement Data

Latency to Target

A 6 (condition) × 2 (group) mixed ANOVA on entry times of gaze on target revealed a main effect of condition, $F_{(5, 185)} = 5.41$, $p < 0.001$, $\eta_p^2 = 0.13$, no effect of group $F_{(1, 37)} = 0.80$, $p = 0.38$, and no interaction effect, $F_{(5, 185)} = 0.67$, $p = 0.65$. Participants' orientation of gaze to the target face was slowest in the conditions "neutral target angry distractors" and "angry target neutral distractors," regardless of study group (see **Figure 2** for details).

Number of Distractor Faces Fixated Prior to Fixating the Target

Analyses revealed a main effect of condition, $F_{(5, 185)} = 3.41$, $p < 0.01$, $\eta_p^2 = 0.08$, but no main effect of group $F_{(1, 37)} = 0.04$, $p = 0.85$, and no interaction effect, $F_{(5, 185)} = 1.22$, $p = 0.30$. Independent of group, participants fixated more distractor faces in the conditions "angry target neutral distractors" and "neutral target angry distractors" followed by "happy target neutral distractors," and "angry target happy distractors (see **Table 3**). Participants fixated fewer distractors in the conditions "happy target angry distractors" and "neutral target happy distractors."

Number of Fixations on the Target

ANOVA revealed a main effect of condition, $F_{(5, 185)} = 32.71$, $p < 0.001$, $\eta_p^2 = 0.47$, but no main effect of group $F_{(1, 37)} = 0.43$, $p = 0.51$, and no interaction effect, $F_{(5, 185)} = 1.77$, $p = 0.12$. Study participants fixated in general the target face longest in the conditions "neutral target angry distractors" followed by "angry target neutral distractors" (see **Table 4** for details).

Number of Distractor Faces Fixated After Fixating the Target

A 6 × 2 ANOVA yielded a significant main effect of condition, $F_{(5, 185)} = 28.42$, $p < 0.001$, $\eta_p^2 = 0.43$, and a significant main effect of group, $F_{(1, 37)} = 6.79$, $p < 0.05$, $\eta_p^2 = 0.15$. No interaction effect was observed, $F_{(5, 185)} = 0.57$, $p = 0.72$. Alexithymic patients fixated more distractors after target fixation than non-alexithymic patients regardless of face condition (see **Table 5**).

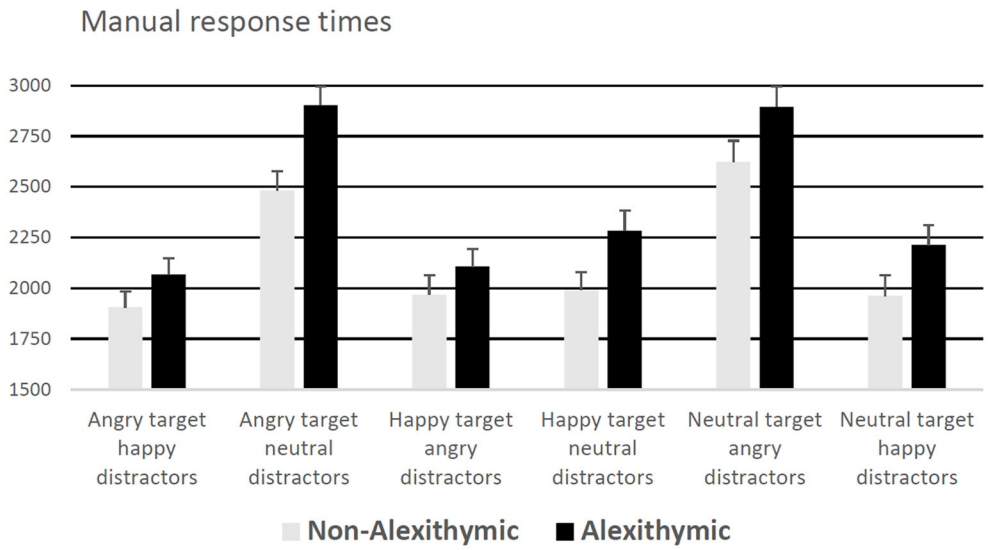

FIGURE 1 | Manual response times (for correct responses) in ms as a function of alexithymia and emotional quality of target and distractor face (error bars represent standard error).

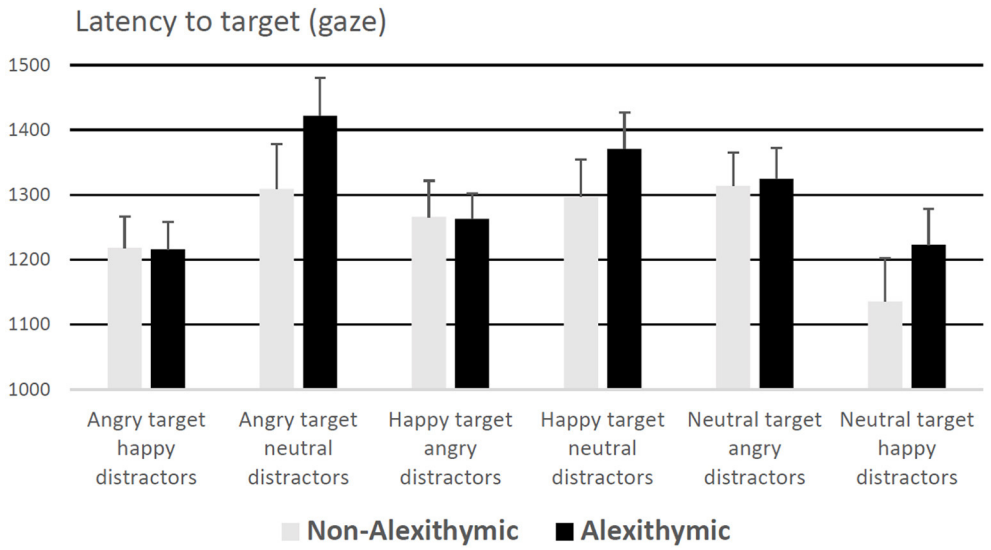

FIGURE 2 | Latency to target (for correct responses) in ms as a function of alexithymia and emotional quality of target and distractor face. Error bars represent standard error.

Independent of group, participants fixated more distractor faces after fixating the target in the conditions "angry target neutral distractors" and "neutral target angry distractors" than in the other experimental conditions.

Data for "number of distractor faces fixated after fixating the target" were in the majority of conditions normally distributed (8 out of 12). Only in case of the conditions "angry target happy distractors" (for the non-alexithymic group), "happy target angry distractors" (for both groups) and "neutral target happy distractors" (for the non-alexithymic group) data did not show a normal distribution. According to the results of additional Mann-Whitney U-tests, alexithymic patients fixated more distractors after target fixation than non-alexithymic patients in the conditions "angry target happy distractors" ($U = 101.5$, $p < 0.05$) and "angry target in neutral distractors ($U = 112$, $p < 0.05$). Moreover, they tended to fixate more distractors after fixation of the target than non-alexithymic patients in the conditions "happy target neutral distractors" ($U = 128$, $p < 0.10$) and "neutral target angry distractors" ($U = 126$, $p < 0.10$). Number of fixated distractors after target fixation did not differ between groups for "happy target angry distractors" ($U = 136$, $p = 0.13$) and "neutral target happy distractors" ($U =$

TABLE 3 | Fixation of distractor faces (number of faces) before target fixation as a function of alexithymia and emotional quality of target and distractor face [means and SD (in brackets)].

Variable	Alexithymic patients	Non-alexithymic patients
Number of fixated happy distractors before fixating angry target	3.46 (0.72)	3.60 (0.63)
Number of fixated neutral distractors before fixating angry target	3.87 (0.75)	3.80 (0.87)
Number of fixated angry distractors before fixating happy target	3.38 (0.46)	3.41 (0.79)
Number of fixated neutral distractors before fixating happy target	3.61 (0.73)	3.68 (0.54)
Number of fixated angry distractors before fixating neutral target	3.63 (0.71)	3.96 (0.75)
Number of fixated happy distractors before fixating neutral target	3.55 (0.84)	3.17 (0.68)

TABLE 4 | Number of fixations on target as a function of alexithymia and emotional quality of target and distractor face [means and SD (in brackets)].

Variable	Alexithymic patients	Non-alexithymic patients
Number of fixations on angry target in happy distractors	1.46 (0.27)	1.57 (0.32)
Number of fixations on angry target in neutral distractors	2.03 (0.39)	1.76 (0.31)
Number of fixations on happy target in angry distractors	1.59 (0.30)	1.51 (0.36)
Number of fixations on happy target in neutral distractors	1.46 (0.37)	1.43 (0.26)
Number of fixations on neutral target in angry distractors	2.16 (0.48)	2.11 (0.45)
Number of fixations on neutral target in happy distractors	1.65 (0.35)	1.64 (0.46)

163.5, $p = 0.45$). Most importantly, the number of distractor faces fixated after target fixation across all conditions differed between study groups ($U = 107$, $p < 0.05$): alexithymic patients fixated overall more distractors after fixating the target than non-alexithymic patients.

An ANCOVA was calculated with level of education, reported depressive symptoms (BDI), use of antidepressants, and sex as covariates. The results suggest that out of the covariates only education level had a significant effect on the dependent variable, $F_{(1, 33)} = 6.04$, $p < 0.05$, $\eta_p^2 = 0.15$: higher level of education was found to be associated with fewer fixated distractors after target fixation. The effect of group remained significant, $F_{(1, 33)} = 7.87$, $p < 0.01$, $\eta_p^2 = 0.19$.

Supplemental Analyses: Fixation Duration on Targets and Distractors

An ANOVA conducted on fixation time on targets suggests no difference between study groups or interaction effect. The analyses of mean fixation times per distractor face before fixating the target also revealed no difference between study groups or interaction effect. According to an ANOVA and additional ANCOVA controlling for education level, depressive symptoms, use of antidepressants, and sex alexithymic patients fixated distractor faces longer than non-alexithymic patients after target fixation, regardless of face quality (see **Supplementary Material** for details).

TABLE 5 | Fixation of distractor faces (number of faces) after target fixation as a function of alexithymia and emotional quality of target and distractor face [means and SD (in brackets)].

Variable	Alexithymic patients	Non-alexithymic patients
Number of fixated happy distractors after fixating angry target	1.30 (0.78)	0.71 (0.69)
Number of fixated neutral distractors after fixating angry target	2.90 (1.07)	2.12 (1.02)
Number of fixated angry distractors after fixating happy target	1.45 (1.02)	1.07 (0.96)
Number of fixated neutral distractors after fixating happy target	1.69 (1.01)	1.07 (0.65)
Number of fixated angry distractors after fixating neutral target	2.89 (1.34)	2.09 (1.22)
Number of fixated happy distractors after fixating neutral target	1.56 (1.14)	1.19 (0.79)

DISCUSSION

In our study, we investigated the relationship between alexithymia and visual processing of facial emotions in clinical depression. To this aim, we analyzed reaction times and gaze behavior in a face-in-the-crowd task. The concept of alexithymia refers to difficulties in identifying, describing one's feelings and an external orientation of thought (2), and is considered a major risk factor for physical and mental illness (6, 7). This is the first study on attention to multiple emotional faces as a function of alexithymia using eye-tracking methodology. Our visual search task required processes of comparison and search for discrepancies between multiple facial expressions of different individuals. Our task did not ask participants to explicitly identify or label facial emotions so that it appears plausible to assume that the processes of categorization and comparison operated primarily implicitly. Two groups of patients suffering from major depression were compared that differed substantially concerning their alexithymia scores. In our study, alexithymia was empirically measured *via* the internationally widely used 20-item Toronto Alexithymia-Scale (65, 66). Research using the TAS-20 has demonstrated adequate levels of convergent and concurrent validity of this self-report instrument (3). One patient group showed clinically relevant alexithymic characteristics whereas, the other patient group included non-alexithymic individuals according to the criteria of Bagby and Taylor (33).

There were no differences between our study groups with regard to age, sex, illness onset, number of illness episodes,

general visual search speed (TMT-B), state anxiety, and interviewer-rated depression. However, alexithymic patients took more frequently antidepressants, reported more depressive symptoms, and had a lower level of education than non-alexithymic patients. Therefore, these variables (and sex) were taken into consideration as covariates in the group comparisons. Associations of alexithymia with increased antidepressant consumption (67), heightened psychological distress (43), and lower education (4) have been observed previously. Depressed patients with alexithymia are known to often notice and report physical symptoms (68). Given alexithymic patients' tendency to describe somatic symptoms physicians might be more inclined to treat these patients with medications.

According to our reaction time findings, alexithymic depressed patients manifested in general longer decision latencies in the face-in-the-crowd task compared to non-alexithymic depressed patients. Thus, patients with alexithymia were slower in the visual search for and comparison between emotional facial expressions than patients without alexithymia. The present findings corroborate our hypothesis that patients with alexithymia manifest a less efficient performance in the face-in-the-crowd task than patients without alexithymia. In our study, rates of correct responses (and non-responses) were high for both study groups suggesting that participants understood and attentively performed the task. For target present trials, correct response rates did not differ between patient groups (except for trials with a happy target in angry distractors: here alexithymic patients gave fewer correct responses than non-alexithymic patients). Moreover, patient groups showed a similar rate of correct answers on trials with only neutral or only happy facial expressions. However, alexithymic patients made fewer correct decisions than non-alexithymic patients when only angry faces were displayed. Thus, we found some evidence for deficits in comparing threatening facial expressions in alexithymic depressed patients.

As reaction times in visual search tasks provide only a summary or final snapshot of attention processes it was a central goal of our study to decompose attention allocation into different components by analyzing gaze behavior over time. According to our results, patient groups differed neither in latency to target (i.e., the time from stimulus onset to first fixation of the discrepant facial expression in a crowd) nor in the number of fixations on target. Therefore, it appears that alexithymic patients were on the target faces as quickly as non-alexithymic patients and they fixated them as frequently as non-alexithymic ones, regardless of whether targets were emotional or non-emotional. Moreover, there were no differences between patient groups for number of distractors fixated prior to target fixation. In our sample, patients fixated on average three to four distractor faces before their gaze was directed to the target. In sum, it can be concluded from these eye-tracking data that no discrepancies were found between alexithymic and non-alexithymic depressed patients in early gaze behavior, i.e., from stimulus onset to processing of the target face. Hence, it seems that alexithymia is not associated with abnormalities in processes of attention guidance to the target face. Alexithymic patients do not have to check more distractor faces before the target is located compared to non-alexithymic patients.

The results are different when considering patients' gaze behavior after target detection. After having looked at the target face, alexithymic patients fixated more distractors than non-alexithymic patients regardless of face condition. This pattern of findings is confirmed by the results of our supplemental analyses concerning fixation duration. That is, after fixating the target alexithymic patients looked at distractor faces longer than non-alexithymic patients but there were no group differences in fixation time on distractors before target fixation and fixation time on target. The present data could indicate processing deficits only *after* target fixation in alexithymic patients. However, it cannot be excluded that a less efficient processing and identification of the target face expression has led to an increased requirement in alexithymic patients to look more often at further (distractor) faces before they came to a correct decision (i.e., that one of the faces differs in its expression from the others). At this point, it must be emphasized that the arguments presented here to explain the observed group differences have a rather speculative and tentative character and that further research and experimental evidence are needed for solid conclusions. It can also be argued that if distractor faces are fixated after the target face has been visited decision-making lacks efficiency (57). The observed deficits after target detection might suggest difficulties in the processing of similarities and discrepancies, and the integration of the gathered information into a decision. It is possible that alexithymic patients have specific problems in comparing emotional (and neutral) faces and deciding whether the expressions belong to a single category or not. The alexithymic patients might feel uncertain about the perceived expressions and could need more information before making a final decision. Lorey et al. (69) demonstrated in an experiment with video scenes of human interactions that people with high alexithymia are less confident about assessing others' emotions than those with low alexithymia. In their study, participants had to perceive emotions depicted in point-light displays and assess the confidence in these perceptions. Interestingly, people with high alexithymia were significantly less confident about their decisions but did not differ from people with low alexithymia in the valence of their ratings.

However, in our view it cannot be excluded that although alexithymic patients did not differ from non-alexithymic patients in initial distractor fixations and target fixations (regarding duration and number of fixations) they might have still processed and encoded less facial emotional information per fixation in the early phase of visual search. In general, increased fixation duration may reflect or enable more attention to and deepened processing of the fixated object (70). Consistently, it has been observed that fixation frequency during visual exploration of pictures is positively related to subsequent recall performance (71). If alexithymic patients have deficits in encoding emotional information they could need extra time during visual search for gathering more information on the composition of the crowd of faces. Findings from previous neuroimaging research on the perception of (single) emotional facial expressions show that alexithymia goes along with reduced neural response in various

parts of the brain in healthy individuals (31) and depressed patients (52). It has been argued that alexithymic individuals could manifest impairments in the perceptual encoding of emotional information at an automatic processing level (30). Yet, when looking at the specific abnormalities shown by our alexithymia patients in late (but not early) gaze behavior it appears likely that their impairments in the face-in-the-crowd task are more due to difficulties in comparing different emotional facial expressions, integrating the perceived information, and coming to a decision on dissimilarity of expressions than to general encoding deficits. Similarly, findings from a sequential affective priming study (28) indicate that alexithymic individuals could be less efficient in the use of emotional facial information when assessing subsequently shown neutral facial expressions.

In our visual search study, we investigated attention to happy and angry faces, as previous alexithymia research has revealed impairments in the identification of positive and negative facial expressions (29). The present results are consistent with the idea that alexithymic individuals' impairments in processing emotions in facial expressions are not limited to a specific affective valence. The alexithymic processing deficits seem to concern both types of expressions presented in our experiment, happy, and angry faces. Our results suggest a general, emotion-unspecific visual processing deficit in depressed patients with alexithymia.

A point worthy of note is that independent of patient group an effect of valence or valence combination was observed in our face-in-the-crowd task. Patients performed worst in face conditions where an angry target was combined with a neutral crowd or a neutral target with an angry crowd. Here, patients required substantially more time to respond and to find the target, they made more fixations on the crowd faces prior to target fixation, and they fixated the target face longer in comparison with other expression conditions. This pattern of results shows that it was much more difficult for our patients to find the target when angry and neutral faces were combined compared to other combinations of expressions. Most likely, they had difficulties to differentiate between these two categories of expression. Categorization of stimuli as target vs. distractor should take more time when distractor stimuli and target are similar to each other. The present findings indicating faster processing of happy expressions in crowds of faces are consistent with results from other research indicating a superiority effect for happy faces (14, 15). However, as mentioned earlier, it appears difficult to draw general conclusions about advantages for processing a specific facial emotion in groups of faces as some studies have reported a superiority effect for angry expressions (16, 17). It seems that the results observed in visual search for emotion faces could largely depend on the specific stimulus set applied (17).

Interestingly, even though, the processing of crowds comprising angry and neutral expressions was more difficult in our study than the processing of crowds with happy faces, there was no evidence that alexithymic patients' processing deficits were more pronounced in or limited to the most challenging task condition.

Based on the present findings, we suggest that future investigations of emotion processing in clinical depression obtain measures of alexithymia in order to determine whether any deficits or abnormalities observed are caused by depression or alexithymia. The control of alexithymia in research on emotion perception in depression seems to be of importance not least because it is fairly common in depressed patients (5, 34). Presence of alexithymia may define a subgroup of depressed patients who exhibit specific impairments in the perception of others' emotions. Interestingly, as there are elevated rates of alexithymia and emotion processing dysfunctions in a number of mental disorders (e.g., autism, substance abuse, and eating disorders) it has been suggested to assess routinely the role of alexithymia in emotion perception across different disorders (72).

According to our results, alexithymic depressed patients could be slow in the identification of discrepancies between facial emotions expressed by different individuals. Thus, in group situations alexithymic patients might be slower in noting that the emotional expression of a person deviates from the emotions expressed by the others compared with non-alexithymic patients. This could represent a disadvantage in comprehending emotional group dynamics, especially in case emotional responses of group members change fast and frequently. Alexithymic individuals' deficient emotion identification ability could be an important factor contributing to their difficulties in using interpersonal communication with others to manage distress (73). Alexithymia itself should become more often the target for psychological interventions. Findings from treatment studies suggest that it might be partly modifiable and improvements in alexithymia can be accompanied by improvements in other domains of functioning such as interpersonal abilities (74, 75). Recently, a promising psychological intervention method to reduce alexithymia has been proposed that combines psychoeducation with a smartphone-based emotion recognition skills training (76).

Limitations of our study include small sample sizes and the sole reliance on self-report for measuring alexithymia. The categorical research approach that we employed to examine the potential effects of alexithymia on visual emotion processing can be viewed critically. The comparison of extreme groups leads to the neglect of in-between participants. In our study, this neglect concerns individuals with TAS-20 scores in the range between 52 and 60. This intermediate group has been labeled as "possibly alexithymic" (77). Our investigation was limited to non-alexithymic patients (who could have scores from 20 to 51) and alexithymic patients (who could have scores from 61 to 100) applying the criteria of Bagby and Taylor (33). In clinical practice it may be helpful to label patients as having or not having an attribute. Although categorization of continuous variables as in the case of alexithymia is quite common in clinical research it can go along with several serious drawbacks. Dichotomizing continuous variables can lead to a reduction in statistical power to detect relations with other variables (78). Moreover, dichotomization might increase the risk of positive results being false positives (79). Artificial dichotomization based

on sample median poses the problem that various data-derived cut-points can be used in different studies so that their findings cannot be easily compared or processed in meta-analyses. The cut-off scores administered in our study to define alexithymia and non-alexithymia (33) have at least the advantage of being internationally recognized. Research results on the structure of the alexithymia construct have provided strong support that alexithymia is a dimensional construct. Taxometric statistical procedures produced unambiguously dimensional solutions, providing substantial evidence that the core alexithymia features are continuously distributed in the population (80, 81). Against this background, it is recommended to use dimensional analyses in future studies that examine the potential effect of the personality trait alexithymia on emotion perception in depression or other mental disorders.

A further limitation of our study is that explicit emotion identification ability of participants was not assessed. It is an interesting question whether the ability to explicitly identify and label facial emotions is related to performance in the face-in-the-crowd task which appears to measure primarily implicitly operating processes of categorization and comparison. It should be noted that when faces with intense expressions have been presented for longer durations or without time limit no impairments in emotion identification were found in alexithymic individuals (82–84). Although, we included the TMT-B to assess participants' general visual processing speed it is a limitation of our study that it did not comprise a non-social control condition requiring search for discrepancies between several complex stimuli. Thus, it remains unclear whether the observed alexithymia-related impairments are specific for social stimuli or represent general visual processing impairments. Future face-in-the-crowd research should administer complex non-social search tasks with multiple stimulus displays to enable stronger conclusions. These search tasks may consist of a texton or a non-texton target in a group of distractors (e.g., crosses, lines, or letters) that allow to assess processes of pre-attentive and attentive visual search for non-social stimuli (85, 86). A further important limitation of our investigation is that no healthy control group was included (neither non-alexithymic nor alexithymic healthy subjects). Therefore, it remains unclear whether one or both of our depressed patient groups show impairments in test performance or gaze behavior compared to healthy individuals. Future studies should investigate whether alexithymia in healthy persons is also associated with deficits in visual search for emotional faces. Finally, our study can be criticized for not having assessed patients' ratings of arousal and valence of the emotional faces presented in the experiment. However, when looking at the findings of several recent alexithymia studies on emotion face processing high alexithymia individuals' arousal and valence ratings of facial expressions did not differ from those of low alexithymia individuals (87–89). Thus, there is some evidence that intense facial expressions of basic emotions might be perceived as similarly arousing and positive (or negative) by highly alexithymic and non-alexithymic individuals.

Doubt has been expressed about the validity of self-report instruments assessing alexithymia, as such tests seem to depend on the abilities to monitor and report one's emotional states accurately (90). However, in the last 25 years, empirical studies have yielded considerable support for the reliability and validity of the TAS-20 (3). Moreover, in previous studies on alexithymia and emotion perception in which interview-based or observer-rated measures were administered in addition to self-report questionnaires self-reported alexithymia was found to be a better predictor of emotion processing than the scores derived from observer rating or interview (26, 28, 91).

In conclusion, the results from our eye-tracking study suggest that alexithymia goes along with impairments in visual processing of multiple facial emotions in clinical depression. According to the present findings, alexithymia is associated with prolonged scanning in the phase post-target detection in depression but might have no impact on the early phase of visual face processing. Thus, alexithymia seems not to be related to abnormalities in processes of attention guidance to discrepant emotional faces in clinical depression. The observed deficits could suggest difficulties in decision-making and/or target identification when processing multiple emotional facial expressions. Alexithymia might go along with a sense of uncertainty about the perceived expressions. Impairments of alexithymic depressed individuals in processing emotions in crowds of faces seem not limited to a specific affective valence. In group situations, depressed patients with alexithymia might be slowed in processing interindividual differences in emotional expressions compared with non-alexithymic depressed patients. This could be a disadvantage in comprehending non-verbal communication in groups. As alexithymia is quite common in depressed patients it appears advisable to control this personality characteristic in future research on emotion perception in clinical depression.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics committee at the University of Leipzig, Medical Faculty. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

TS, AK, and CB conceived and designed the experiment. CB collected the data. TS, TH, VG, and AK outlined the manuscript. TS and CB analyzed the data. TS wrote the first draft of the manuscript. VG, TH, AK, and CB wrote sections of the manuscript. All authors contributed to the article and approved the submitted version.

ACKNOWLEDGMENTS

The authors acknowledge support from the German Research Foundation (DFG) and Universität Leipzig within the program of Open Access Publishing.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.668019/full#supplementary-material

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Conflict of Interest: 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.

frontiers in Psychiatry

OPINION
published: 01 July 2021
doi: 10.3389/fpsyt.2021.657774

An Explanation for Repetitive Motor Behaviors in Autism: Facilitating Inventions via Trial-and-Error Discovery

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Keywords: autism, evolution, repetition, invention ability, special interests

INTRODUCTION

Restricted/repetitive behaviors is a core diagnostic criterion for autism. Motor repetitions, referred to as "lower-order," include self-stimulation, hand flapping, twirling, repeating phrases, manipulating objects, banging toys together, and repeatedly pushing buttons (1). Also included in the broad category of restricted and repetitive behaviors are cognitively advanced, "higher-level" behaviors, rituals and circumscribed or restricted interests (2, 3). These types of repetitive behaviors superficially look different. For instance, repetitive motor behaviors can cause self-injury (e.g., head banging) and interfere with learning and family life (4). In contrast, some scholars and autistic individuals themselves have relabeled restricted interests as "special interests." This follows the strength-based approach of the neurodiversity movement, including advocacy by autism individuals themselves [e.g., (5)]. Special interests can readily be understood as on a continuum with neurotypical hobbies, workplace specialization and the research interests of scientists (6, 7). Theorists have long noted that intense interests of persons with autism can be precursors to scientific discovery and achievement [e.g., (8–10)]. No comparable adaptive function has been proposed for repetitive motor actions. This is the purpose of the current paper.

What causes repetitive motor behaviors? At the level of genetic alterations, developmental heterochrony is one plausible mechanism (11). Many features of autism could result from extending the longevity of motor repetitions beyond early childhood into the juvenile years and adulthood (11, 12). Motor reflexes are integral to survival in infancy, but gradually come under voluntary control with maturation of the cortex in the first 2 years of life (13). Motor repetitions resembling those observed in autistic individuals are common in children during early childhood, but disappear by age 4–6. This is plausibly one factor for why autism is hard to diagnose before ages 3–4.

Other mechanisms for dysfunctional motor repetitions have been proposed. Parts of the brain involved in regulating motor systems have demonstrated abnormal functioning in autism. For example, the cerebellum has long been pinpointed as a likely candidate for both motor and cognitive deficits [e.g., (14)]. Striatal dysfunction has also been implicated, which is especially intriguing give that striatal circuits are important for both cognitive and social abilities (15). Whether these or other brain systems could have been altered as part of the heterochrony proposed by Crespi (11) is unknown.

Do motor repetitions serve any adaptive function, or are they only maladaptive? Motor routines allow persons with autism, especially young children, to avoid on-going social demands (16). The most frequently cited function is that motor repetitions are calming in the face of social and other stressors [e.g., (17)]. These stressors include difficulty in predicting ongoing events, resulting from weak central coherence, executive function challenges and social deficits. Self-regulation as a cause of motor repetitions is mentioned by autistic

OPEN ACCESS

Edited by:
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Reviewed by:
Michela Candini, University of Bologna, Italy

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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *25 January 2021*
Accepted: *08 June 2021*
Published: *01 July 2021*

Citation:
Caldwell-Harris CL (2021) An Explanation for Repetitive Motor Behaviors in Autism: Facilitating Inventions via Trial-and-Error Discovery. Front. Psychiatry 12:657774. doi: 10.3389/fpsyt.2021.657774

individuals themselves [e.g., (18)]. It is also plausible because humans commonly regulate both hyper- and hypo-arousal with scratching, hair/beard twirling and finger tapping; animals groom or scratch as calming strategies. Motor repetition is also heightened for animals and humans in deprived environments.

A drawback of the stress-reduction explanation is that motor repetitions in autistic individuals are not invariably or even usually associated with distress (12). Minimally verbal children often engage in repetitions with focused determination, ignoring adults' bids for attention. In addition, repeated motor behaviors observed in some autistic children can be goal directed and pursued with interest and focus. In this way, they resemble the engagement observed for pursuit of special interests, as in the mechanical tinkering of the young Isaac Newton or young Thomas Edison (8, 9).

My focus in the current paper is on motor repetitions and repetitive object use, but the ideas I present are also relevant to related motor actives, such as self-stimulatory behavior, verbal repetitions and visual repetitions [inspecting toys in an unusual manner, see taxonomy in Harrop et al. (1)]. However, the umbrella category of restricted/repetitive behaviors include sensory aversion, sensory seeking, and behavioral inflexibility (insistence on sameness). I believe these behaviors require a different explanation [see (19) for a unified approach]. For example, auditory and olfactory acuity were adaptive in the ancestral environment when humans seeking shelter needed to determine if a predator was in a cave (10).

Theorists have commented that the field needs more theories regarding the function of repetitive motor behaviors [e.g., (1, 12, 20, 21)]. I outline here an adaptive function that is plausible from the standpoint of human evolution:

Retaining motor repetitions into childhood and adulthood allowed repetitive motor sequences to fuel trial-and-error discovery.

In Temple Grandin's memorable words, "Who do you think made the first stone spear, it wasn't the social yakety-yaks sitting around the campfire" [(22); see also (23), p. 122]. Motor routines may indeed be calming or self-regulating, but they may also be pursued for their own interest and rewards. They may be pursued for the delight in the interesting variation which can result from minor deviations. What would happen if I cut this rock at an angle—would it make a sharp point? When results are interesting, and especially if predictions are correct, trial-and-error tinkering can be reinforced by the dopamine reward system (24).

During much of human prehistory, technological advances in tools, weapons, fishing craft, and shelter construction may have been fueled in part by repetitive motor explorations (and systematic observation) of sticks, stones, plants, and in rivers/lakes (10, 25). Note that autistic individuals do not need themselves to always recognize the usefulness of a novel configuration. The "aha" moment may occur in the brains of observers. Usefulness of the invention can help group members to be indulgent toward the socially-nonconforming autistic person.

I will refer to this hypothesis as *motor tinkering for trial-and-error discovery*.

The trial-and-error work of scientists fits with our intuitions about inventions (8), but the adaptive function of simple motor repetitions is less obvious. Cziko (26) documented how trial-and-error exploration of objects is a key mechanism in invention in diverse species. Genetically-specified motor programs, combined with variation to fit a specific environment, produce spider webs, beaver dams and bower displays. Crows' fixed action patterns can result in tool use (27). Human tinkering with objects also plausibly led to cultural discoveries for building shelters, creating weapons and detoxifying food (28). From this perspective, there would have been substantial selection pay-offs for a phenotype in which the repetitive behaviors of early childhood were maintained into the juvenile period and adulthood.

EVALUATING "MOTOR TINKERING FOR TRIAL-AND-ERROR DISCOVERY"

Consistent With Other Evolutionary Hypotheses

The hypothesis is consistent with Crespi's (29) characterization of autism as a disorder of imbalanced intelligence, that is, a mix of enhanced and impaired abilities. During natural section, increased analytical intelligence likely reaped fitness benefits, allowing extensive exploration in the fitness landscape. One plausible result is diverse phenotypes with pockets of enhanced ability co-existing with deficits. Motor tinkering that could result in novel useful configurations is plausibly a phenotypic variation resulting from these fitness pressures.

Bridge Between the Motor Repetitions and Restricted Interests

Although motor repetitions and narrow interests are grouped under the umbrella terms restricted/repetitive behaviors, their similarities are not obvious. I propose that repetitive motor behaviors are part of the engine that fuels systemizing of the natural world, leading to pattern extraction, if-then rules, and technological discoveries [as discussed by Baron-Cohen (8)].

An example of a bridge to circumscribed interests can be observed in cases where a motoric ritual is also a child's special interest. In videos of his young autistic son, Love (30) documents that habitual stair-climber Frumpkin must spend 15 min traversing any newly encountered staircase. Stair-climbing is both a motor preoccupation and an intense/restricted interest. But Frumpkin had other motor interests that shared a family resemblance structure with stair-climbing. In a park, he discovered picnic tables arranged to allow a complete circle to be made on table-tops and their benches. He then obsessively circumnavigated the table-tops, resistant to parental intervention. Frumpkin's father noted that Frumpkin "mixes it up"—he doesn't walk in the same manner each time, as if he is observing the variation that results from slight deviations in his path.

Frumpkin's attraction to both staircases and table-tops suggests a more abstract underlying interest: He is trying to systematize walkable, raised, man-made surfaces. From the perspective of human technological development, tables and

staircases are extremely interesting. Staircases are complex inventions whose construction is non-obvious. Generations of cultural evolution were required for invention, refinement and modern-day craftsmanship. One could conceive of Frumpkin as a future engineer obtaining sensory-motor schemes that could facilitate future innovations in design of raised wooden-surface walkways.

But: Many Motor Repetitions Are Not Geared Toward Discovery

Many behaviors in the broad category of restricted/repetitive behaviors are maladaptive and would have harsh fitness consequences during human evolution, as well as today. The plausible cause of this is that heterochrony is a blunt instrument, given that natural selection is not goal-directed. Susceptibility alleles for retaining repetitive motor repetitions beyond early childhood would need to be maintained in the population via balancing selection (31), with many individuals with autism making no fitness-enhancing discoveries.

Open questions about this include:

- What proportion of individuals with the autism phenotype must deliver fitness-enhancing discoveries in order for genes for autism to spread or be maintained in a human population?
- In what cultures or environments do repetitive motor behaviors lead to discoveries? Contemporary inventors with autism who also have high analytical intelligence (such as Elon Musk) can gain the social status consistent with reproductive benefits. But my hypothesis rests on natural selection in the ancestral environment, where discoveries included stone tools and other physical artifacts. Are there any contemporary societies in which motor tinkering leads to useful discoveries?

Heuristic Value of the Motor Tinkering Hypothesis

I propose that motor routines are information-seeking and in part driven by the reward of discovery, similar to intense interests and scientific discoveries. However, the "blunt instrument" of heterochrony and a neural system with revved-up motor programming means that many minimally verbal autistic children perform unvaried motor routines for hours a day, disrupting family life (21).

One therapeutic approach is that adults can model for children how to vary their motor routine, but in a direction that is inherently rewarding for the child. Parents and therapists can observe and participate in their child's motor activities, drawing on techniques in JASPER (32) and Floor Time Play Therapy (33). While observing, the adults use their own systemizing and prediction skills to plan a variation in the motor routine that could result in a pleasing or interesting result. The adults then assist the child in moving toward a rewarding variation, or directly model such a move. For example, for a motor routine like table-circling, the adult could tap on the table at a predictable spot, or purposefully flip over a strategically placed object (or a more spectacular result could be planned). The pay-off for the child is the inherent interest of a new event. But the behavior being reinforced is modifying the repetitive motor actions in the direction of variation and flexibility.

Alternative and/or Complementary Approaches

Two comprehensive proposals about systemizing and patterning in autism were published after the first draft of this paper. Baron-Cohen's book *The pattern seekers: How autism drives human invention*, connects his decades of work on systemizing to an evolutionary pay-off, invention. Baron-Cohen notes that autistic individuals excel at if-then reasoning, and argues that if-then reasoning allowed humans to become the top inventers in the animal kingdom. My hypothesis is complementary but distinct: Motor tinkering fosters trial-and-error discovery. Motor repetitions with slight variations (tinkering) can involve if-then conceptualization, as follows: "IF I pile my rocks his way, THEN they will form a new configuration, a vertical surface." Note that the motor behaviors of many animals amount to tinkering, as when a beaver uses trial-and-error to configure a dam. The motor-tinkering theory is otherwise similar to Baron-Cohen's approach, in that both emphasize invention as the adaptive benefit of repetitive and restricted behaviors.

Crespi (19) proposes that what is common across diverse autistic symptoms is the concept of pattern. For example, pattern seeking leads to high systemizing and interest in STEM disciplines. Highly tuned pattern perception is what underlies sensory hypersensitivity. Crespi's theory explains repetitive motor behaviors as resulting from a heightened system of pattern generation. A novel part of Crespi's theory, orthogonal to my own proposal, is that upregulating the brain's natural preference for patterns entailed a dialing-down of social information processing, given that social phenomenon are the antithesis of algorithmic patterns. Crespi's ideas about the importance of patterns are consistent with and complementary to my hypothesis that repetitive motor behaviors underwent selection pressure because of the pay-off of inventions.

SUMMARY

Clare Harrop, a leading researcher of restricted and repetitive behaviors (RRBs), wrote with her colleagues, "...as a field we do not understand what causes RRBs, and this is particularly difficult to ascertain when children are minimally verbal.." (1). The current account is a response to this request for new ideas about the cause of repetitive behaviors. Motor repetitions in autism are an alternative phenotype which has adaptive and functional consequences: fueling trial-and-error tinkering which could lead to inventions, i.e., novel, useful configurations of objects. This hypothesis is consistent with the proposed mechanism of heterochrony (11), and is complementary to other theories which take a strength-based approach to autism (8, 19). This hypothesis helps explain similarities between motor repetitions and circumscribe interests, illuminates parents' observations of their child's motor repetitions [e.g., (30)], and has heuristic value in providing ideas for therapists to introduce flexibility into the motor routines of minimally verbal children.

AUTHOR CONTRIBUTIONS

CC-H was responsible for the development of all sections of this manuscript.

ACKNOWLEDGMENTS

I thank John Elder Robison and Dr. Bernard Crespi for helpful discussions.

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

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 18 August 2021
doi: 10.3389/fpsyt.2021.724802

Validation of the Rage Attack Questionnaire-Revised (RAQ-R) in a Mixed Psychiatric Population

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Rage Attacks (RA) represent a clinically relevant symptom in patients with different psychiatric disorders. However, only recently the Rage Attack Questionnaire Revised (RAQ-R, 22 items, range, 0–66) has been developed as a new instrument for the assessment of RA. This study aimed to validate the RAQ-R in a large mixed psychiatric and psychosomatic sample. We tested internal consistency, convergent and discriminant validity as well as factor structure. In order to further explore the relationship of RA to other psychiatric symptoms, we calculated Pearson correlations between the RAQ-R and several other self-assessments including measurements for general psychological distress, quality of life, depression, anxiety, attention deficit/hyperactivity disorder (ADHD), impulsivity, and self-regulation abilities. Most relevant predictors of RA were examined in a multiple regression with stepwise elimination. In order to assess the manifestation of RA in different psychiatric disorders, group differences between diagnostic categories and healthy controls were calculated. Additionally, psychiatric patients were compared to patients with Tourette syndrome along RAQ-R scores. Data from healthy subjects and patients with Tourette syndrome were obtained from a previous study of our group. In this study, we included 156 patients with a wide and typical spectrum of psychiatric diseases. The RAQ-R was found to have excellent internal consistency and strong construct validity in this sample (Cronbach's $\alpha = 0.97$, Average Variance Extracted $= 0.58$). Thus, the RAQ-R was shown to be a psychometrically sound assessment of RA in patients with different psychiatric disorders. Close constructs to RA were found to be aggression and hostility ($r = 0.68$) as well as low frustration tolerance and impulse control ($r = 0.69$). Compared to healthy controls, RA were significantly more common in the psychiatric sample ($p < 0.001$). More specifically, RAQ-R scores in all diagnostic categories assessed were higher compared to controls. Highest scores and effect sizes were found in patients with ADHD and borderline personality disorder ($p < 0.001$). Our results suggest that RA are a common and relevant symptom in many psychiatric disorders. As depression and RA showed only a moderate relation, RA should be distinguished from the concept of anger attacks, which are described as a core symptom of depression.

Keywords: rage attacks, RAQ-R, anger attacks, outbursts, psychiatric disorders, ADHD, personality disorder, Tourette syndrome

OPEN ACCESS

Edited by:
Philipp Kanske, Technische Universität Dresden, Germany

Reviewed by:
Ömer Faruk Akça, Meram Faculty of Medicine, Turkey
Lisa Wagels, University Hospital Aachen, Germany

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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *14 June 2021*
Accepted: *16 July 2021*
Published: *18 August 2021*

Citation:
Palm L, Haas M, Pisarenko A, Jakubovski E and Müller-Vahl KR (2021) Validation of the Rage Attack Questionnaire-Revised (RAQ-R) in a Mixed Psychiatric Population. Front. Psychiatry 12:724802. doi: 10.3389/fpsyt.2021.724802

INTRODUCTION

Anger is a basic emotion with important functions like mobilization of physical and psychological resources (1). Dysfunctional levels of anger, however, are associated with negative outcomes such as poor evaluation by others, interpersonal conflicts, lower self-esteem, suicidal ideation, higher cardiovascular risk, and lower therapeutic success (1–5). Dysfunctional anger often causes psychological stress and impairment for both the affected persons and their environment. What demarcates functional from dysfunctional forms of anger are "frequency, reactivity, intensity, duration, and mode of expression" (1). Dysfunctional anger is therefore a clinically highly relevant symptom in many patients suffering from different psychiatric disorders [for an overview see (1, 5, 6)].

So far, research on dysfunctional outbursts of anger in psychiatric disorders focused on the concept of anger attacks, which was first introduced by Fava et al. (7, 8). According to them, anger attacks are defined as sudden outbursts of anger combined with autonomic arousal resembling panic attacks (i.e., sweating, trembling, tachycardia) (8, 9). Anger attacks are believed to represent a variant of depression, because of their high prevalence in patients with depression and the finding that treatment with antidepressants such as fluoxetine improves anger attacks (7, 8, 10, 11). Therefore, Fava et al. developed the Anger Attack Questionnaire (AAQ) to assess anger attacks in patients with depression (8). Not surprisingly, research on anger attacks in psychiatric disorders other than depression identified comorbid depression as predictor of anger attacks (12–14). As such, the concept of anger attacks and the AAQ as corresponding assessment seem inappropriate to examine dysfunctional outbursts of anger in psychiatric disorders other than depression and without comorbid depression, respectively.

Besides anger attacks, dysfunctional anger can alternatively manifest as rage attacks (RA), which are characterized by emotional control difficulties that are uncharacteristic of the person's personality and inappropriate with regard to the triggering situation (15). Originally, the concept of RA has been developed in relation to research in Tourette syndrome (TS) by Budman et al. (15). She was the first who described RA as a common and typical symptom in affected children and adolescents. Consecutively, Budman et al. developed the Rage Attack Questionnaire (RAQ), a parent questionnaire, to measure RA specifically in children with TS (15).

To overcome limitations of the RAQ (15), only recently, our group developed a revised version, the RAQ-R, a self-assessment for adults to measure different psychological and behavioral qualities/dimensions of RA (16). Therefore, we defined RA as "sudden, mostly short-lived, intensive, impulsive, emotional reactions to situations and/or stimuli that cannot be controlled" (16). Furthermore, the behavior must be totally out of proportion to the trigger event. According to our definition, rage attacks may manifest in inappropriate verbal utterances, property damage, or aggressive actions. Those affected must be aware of the disproportionate nature of their behavior. Finally, we specified that affected persons feel unable to change their behavior, although RA are perceived as unpleasant, unintentional, and often shame-filled (16). In this recent study, we examined face and content as well as construct validity of the RAQ-R in a sample of 645 healthy subjects (16). Discriminant validity was established on the basis of low to moderate correlations with a variety of psychiatric assessments of attention deficit/hyperactivity disorder (ADHD), TS, obsessive compulsive disorder (OCD), and general psychopathology. In terms of convergent validity, we employed scales on impulsivity. However, they all showed only low to moderate correlations so that convergent validity could not be established. In contrast, we were able to show good to excellent reliability and inter-item correlations. Finally, we were able to demonstrate that RA occur significantly more often in adults with TS ($n = 127$) compared to healthy controls ($n = 645$, $p < 0.001$). However, in both groups RA were significantly associated with reduced quality of life (16).

Although the concept of RA was first employed in patients with TS, we assumed that RA describe a more comprehensive form of outbursts that is not necessarily linked to a specific syndrome or disorder. In this study, we therefore aimed to (i) examine psychometric properties of the RAQ-R in a general psychiatric sample, (ii) explore differences in RA in a general psychiatric sample compared to healthy controls and to patients with TS, (iii) assess differences in RA between patients with different psychiatric diagnoses according to ICD-10, (iv) examine correlations of RA with a spectrum of other psychiatric symptoms as well as sociodemographic characteristics, and (v) identify possible predictors of RA.

MATERIALS AND METHODS

Patients and Study Design

Based on a power calculation, we intended to recruit 120 adult patients from out-, day-, and inpatient clinics at the Departments of Psychiatry, Social Psychiatry and Psychotherapy as well as Psychosomatic and Psychotherapy at Hanover Medical School (MHH). Inclusion criteria were: (a) the presence of at least one current ICD-10 diagnosis of a mental disorder (F00–F99), (b) age $\geq$ 18 years, (c) proficiency in German language, and (d) written informed consent. Exclusion criteria were severe cognitive or psychological impairments, which restricted understanding or answering the questions (e.g., dementia or acute delirium or intoxication).

We did not recruit a control group (CG), but used data obtained from our previous study recruited from staff and students at MHH (16). However, we excluded 34 out of the original 645 subjects, who had reported a current psychiatric diagnosis, and thus included a CG consisting of 611 healthy controls (based on self-declaration). Data from adult patients with TS ($n = 127$) was used from that same previous study without exclusion (16). These patients were recruited from our Tourette outpatient clinic and via German advocacy groups. Data from both, CG and TS were collected via an online survey between July and October 2017.

This study has been approved by the local ethics committee at MHH (no. 7781_BO_S_2018). Informed written consent was obtained from all patients before entering the study.

Assessments

The following assessments were performed in all patients independently of current or past diagnoses:

- RAQ-R consisting of 22 items on a four-point Likert scale ranging from 0 to 3 (0 = not at all/never, 1 = a little/sometimes, 2 = strong/frequent, and 3 = very strong/very common). The sum of all items generates the total score (range, 0–66) (16).
- Visual analog scale (VAS) for quality of life (QoL) (17) to assess life satisfaction.
- Barratt Impulsiveness Scale—Short Version (BIS-15) (18) to assess impulsivity.
- Impulsive behavior scale-8 (I-8) (19) to assess impulsivity consisting of four subscales: urgency, intention, endurance, and risk taking.
- Brief Symptom Inventory (BSI) (20): the BSI is an instrument to operationalize general psychological distress through a global severity index. In addition, nine subscales are used to screen for psychological strain in the areas of somatization, obsessive-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.
- Beck Anxiety Inventory (BAI) (21) to measure severity of clinical anxiety.
- Beck Depression Inventory (BDI-II) (22) to assess severity of depressive symptoms.
- German self-rating scale "ADHS-Selbstbeurteilungsskala" (ADHS-SB) (23) to screen for ADHD symptoms.
- Hannover Self-Regulation Questionnaire (HSRQ) (24) to assess ego functions and the ability of self-regulation. It consists of 35 items on a six-point Likert scale and encompasses five subscales: interpersonal disturbances, frustration tolerance and impulse control, identity disturbances, affect differentiation and affect tolerance, as well as self-esteem. The total score is generated of all subscales and ranges from 0 to 25 with high scores standing for high structure levels.

Patients were asked to complete assessments without any assistance (e.g., from staff) in order to reduce possible bias due to socially desirable response behavior. Data was collected pseudonymized in paper-based form. For all assessments used—besides the RAQ-R—good to very good psychometric properties regarding reliability, validity and internal consistency have been demonstrated.

In addition, demographic data were collected including age (in years), gender (female, male, other), country of birth (Germany vs. not-Germany), and level of education (no school degree, certificate of secondary education, general certificate of secondary education, general qualification for university entrance, university degree). Current psychiatric diagnoses according to ICD-10 (multiple entries possible) and the patient status (out-, day- or inpatient) were collected from patients' records. Diagnoses were assigned by treating physicians and psychologists based on clinical interviews, previous reports, and, whenever needed, structured interviews and disease specific assessments.

Data Analysis

All questionnaires were scanned and transformed into a digital raw data set via the survey automation software EvaSys version 7.0. Analyses were conducted in RStudio version 1.2.5033. All details of the data analysis are available as a reproducible *R* script on the Open Science Framework (doi: 10.17605/OSF.IO/73Y8P).

Due to data protection law, in our previous study performed as an online survey we were allowed to collect patients' age only in age groups. In order to present comparable demographical characteristics and being able to compare the psychiatric group (PG) to the CG and TS group, we transformed the variable "age in years" to the variable "age groups" accordingly: 1 = 18–25 years, 2 = 26–35 years, 3 = 36–45 years, 4 = 46–55 years, 5 = 56–65 years, and 6 > 65 years (16).

In case of missing values multiple imputation was used with 5 iterations (25, 26). Parameter estimates were pooled using Rubin's rule (27) if possible. Otherwise, estimates were calculated for each iteration and compared to each other.

Reliability was evaluated using Cronbach's α and composite reliability ρ_C. Contrary to α, ρ_C doesn't presuppose equal loadings of all items and a 1-factor-structure.

Given a normal distribution in the PG, we calculated Pearson correlations between the RAQ-R and other scores to assess convergent and discriminant validity. Due to lack of a German questionnaire assessing the same construct, we did not expect correlations of $r > 0.8$ between the RAQ-R and any questionnaires used. Instead, we expected correlations of assessments used for convergent validity of $r \geq 0.5$ and expected them to be higher than those used for discriminant validity. For convergent validity we used the BSI-subscale "aggression and hostility," the HSRQ-subscales "frustration tolerance and impulse control" and "affect differentiation and tolerance," and the impulsivity scales BIS-15 and I-8. To assess discriminant validity, we used the BAI, BDI-II, and BSI global severity index. In addition, Average Variance Extracted (AVE) was used to further assess discriminant validity (28). A Principal Component Analysis (PCA) was carried out to reevaluate the factor structure and loadings.

The PG was both in total and stratified by diagnostic categories (with $n \geq 4$) compared to healthy subjects along RAQ-R scores. For this, non-parametric (Wilcoxon rank-sum) and parametric (independent-samples *t*) tests were used depending on the group size and the visual data distribution in q-q-plots (29). Likewise, we compared the PG to patients with TS. To identify significant demographic differences between PG and CG as potential confounders, we carried out chi-square tests and calculated Cramér's V (29). In case of differences in demographic variables, we used a multiple linear regression to check, if differences in the RAQ-R scores remain after controlling for demographic differences between the samples.

To assess differences in the RAQ-R regarding patients' sociodemographic characteristics and status (out-, day-, or inpatient), we carried out ANOVA (for ordinal variables), independent-samples *t*-tests, and Wilcoxon rank-sum tests (for dichotomous variables). Correlations between RAQ-R and age were calculated using Pearson's *r* for age as an interval variable.

TABLE 1 | Demographic characteristics of the mixed psychiatric group (PG) compared to the control group (CG) and patients with Tourette syndrome (TS).

Characteristics		PG	CG	TS
n		156	611	127
Age, mean ± sd	Years	41.15 ± 12.84		
	Clustered in 1–6	3.06 ± 1.33	2.55 ± 1.27	2.74 ± 1.29
	V		0.166**	0.189
Gender, *n* (%) [a]	Female	99 (63.5)	486 (79.5)	38 (29.9)
	Male	57 (36.5)	125 (20.5)	89 (70.1)
	V		0.148**	0.327**
Education, *n* (%)	No school degree	7 (4.5)	0	3 (2.4)
	Certificate of secondary education	28 (18.1)	7 (1.1)	16 (12.6)
	General certificate of secondary education	63 (40.6)	105 (17.2)	36 (28.3)
	General qualification for university degree	28 (18.1)	259 (42.4)	37 (29.1)
	University degree	29 (18.7)	240 (39.9)	35 (27.6)
	V		0.471**	0.201*

*PG, psychiatric group; CG, control group; TS, Tourette syndrome. [a] "other" was indicated by none of the participants. V = Cramér's V indicating the strength of association between sample membership and demographic characteristic ranging from 0 to 1, where 0 indicates no association and 1 indicates a very strong association. P-values calculated with chi-square test: *p < 0.05, **p < 0.001.*

To identify predictors of RA in psychiatric patients, we carried out regression models. In order to find most detailed and fitting predictors, we included all demographic variables, patient status, total scores and subscores, as well as diagnostic categories with $n > 10$ in a multiple linear regression. Through stepwise elimination and Wald test we gained a regression with predictive explanatory factors of RA (30, 31). In both multiple regression models, Gauss Markov assumptions were examined via diagnostic plots. Ordinal and dichotomous scaled variables were treated as dummies. All statistical tests were two-tailed with $\alpha = 0.05$. All effect sizes were interpreted according to Cohen (32).

RESULTS

Demographics and Clinical Characteristics

Between August 2018 and April 2019, 394 patients were asked for participation. Out of 291 (74%) patients, who agreed to participate, 156 completed the questionnaires (corresponding to a response rate of 54%). Half (52%) of these participants were inpatients, 33% were day-patients, and 15% were outpatients. About two third (65%) of in- and day-patients were treated at the Department of Psychiatry, Social Psychiatry and Psychotherapy, and 35% at the Department of Psychosomatic and Psychotherapy. Eighty-four percent of patients were born in Germany, while 16 % were born in other countries.

Compared to controls ($n = 611$), patients were significantly older, less formally educated and included more men (all $p \leq 0.001$, **Table 1**) with largest differences in education.

Patients with a total of 86 different psychiatric diagnoses of ICD-10 type FXX.XX were included (average number of diagnoses per patient = 2.58, range, 1–6). With regard to ICD-10 type FXX.-, 30 different diagnoses were found (average number of diagnoses per patient = 2.47, range, 1–6). To enable meaningful analyses, diagnoses were grouped into the following eight diagnostic categories:

- F11–F19: "mental and behavioral disorders due to psychoactive substance use besides alcohol"
- F20.- and F23.-: "schizophrenia and other psychotic disorders"
- F32–F34: "depression"
- F40.- and F41.-: "anxiety disorders"
- F44.-, F45.- and F48.-: "dissociative and somatoform disorders"
- F60.- and F61.-: "personality disorders" (PD), which contained
  - F60.31: "borderline personality disorder" (BPD)
  - F60.5-8: "cluster C PD" according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (33)

Another 12 diagnoses could not be subsumed under the categories above and are thus shown as individual diagnostic categories. Thus, a total of 20 diagnostic categories is presented in **Figure 1**. Patients with more than one diagnosis of the same category were counted only once, while patients with diagnoses belonging to different categories were counted for each category separately.

Missing and Ambiguous Data

In 58 patients (37.18%) at least one item was missing [from nine single questionnaires with a total of 202 items, mean per patient = 1.51 (0.75%)]. Therefore, a combined multiple imputation method was applied. All results shown contain imputed values. Two participants answered all-in-all 26 questions by crossing between two answer options. These answers were interpreted as mean values.

Validation of the RAQ-R

We found a very high internal consistency indicated by a Cronbach's α of 0.97 and a composite reliability ρ_C of 0.97. A sensitivity analysis excluding patients with psychotic and bipolar disorders did not change the internal consistency. All instruments used for validation showed significant correlations with the RAQ-R (**Table 2**). Strong correlations were found between RAQ-R and the BSI-subscale "aggression and hostility" ($r = 0.68$) as well as the HSRQ subscales "frustration tolerance and impulse control" ($r = 0.69$) and "affect differentiation and tolerance" ($r = 0.54$) used to assess convergent validity. Weaker correlations were found with assessments used for discriminant validity (BSI global severity index: $r = 0.43$, BAI: $r = 0.24$, BDI-II: $r = 0.32$) as well as with the impulsivity scales (BIS15: $r = 0.39$, and I-8 urgency: $r = 0.47$, I-8 risk taking: $r = 0.18$, I-8 intention: $r = -0.31$, I-8 endurance: $r = -0.32$).

Discriminant validity is further demonstrated by an AVE of 58% indicating that 58% of the total variance of items quantified by their factor loadings is explained by the scale.

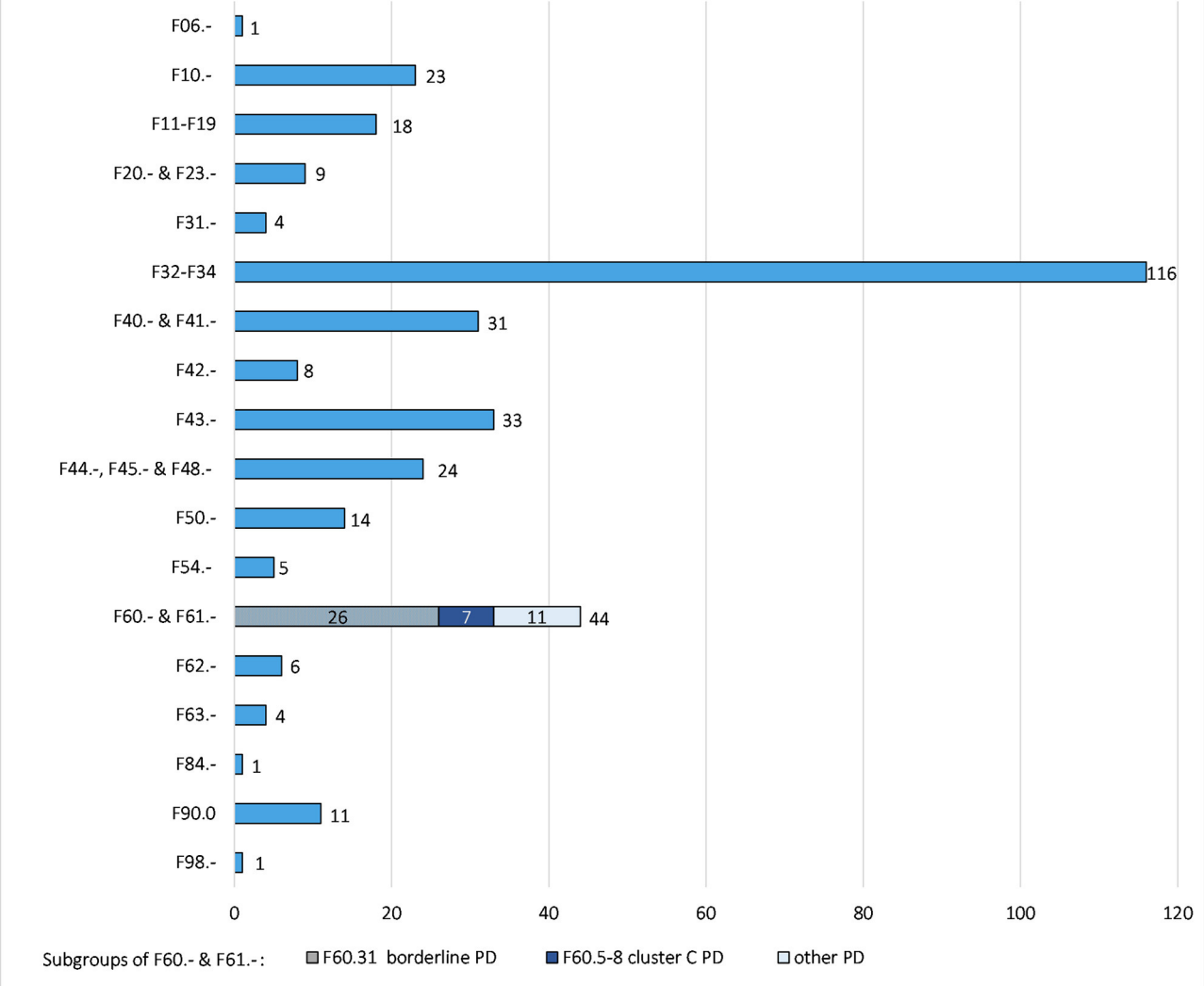

FIGURE 1 | Number of different diagnostic categories in $n = 156$ patients. F06.- = other mental disorders due to brain damage and dysfunction and to physical disease, F10.- = mental and behavioral disorders due to use of alcohol, F11–F19 = mental and behavioral disorders due to psychoactive substance use besides alcohol, F20.-and F23.- = schizophrenia and other psychotic disorders, F31.- = bipolar affective disorders, F32–F34 = depression, F40.-and F41.- = anxiety disorders, F42.- = obsessive-compulsive disorders, F43.- = reaction to severe stress and adjustment disorders, F44.-, F45.-, and F48.- = dissociative and somatoform disorders, F50.- = eating disorders, F54.- psychological and behavioral factors associated with non-mental disorders, F60.-&F61.- = personality disorders, F62.- = enduring personality changes without brain damage, F63.- = habit and impulse disorders, F84.- = pervasive developmental disorders, F90.0 = attention deficit/hyperactivity disorder, F98.- = other behavioral and emotional disorders with onset usually occurring in childhood and adolescence. PD = personality disorders. The y-axis presents the ICD-10 code of the diagnosis or diagnostic category. The x-axis presents the number of patients with that diagnosis or diagnostic category. Patients with diagnoses belonging to different categories were counted for each category separately. Patients with more than one diagnosis of the same category were counted only once in that category.

For assessing factor structure, data was proofed suitable for a PCA with a Kaiser-Meyer-Olkin coefficient of 0.95 and $p < 0.001$ in the Bartlett test for sphericity. The scree plot confirmed the 1-factor structure, which has also been found in our previous study (16). Loadings ranged from 0.45 to 0.83 (see *R* script for details).

Group Comparisons

RA as assessed by the RAQ-R were significantly more common in the PG compared to controls with a large effect size (**Table 3**; **Figure 2**). After including age, gender, and level of education as confounders the difference between PG and CG remained highly significant with $p < 0.001$ (details of the multiple regression in the *R* script). The adjusted R^2 for the model of 0.16 indicates a moderate goodness-of-fit.

Only the 17 diagnostic categories with $n \geq 4$ were used for further group comparisons. Ten out of those contained <20 patients which limits the assumption of normal distributed data despite good visual results in the q-q-plots (see the *R* script for

TABLE 2 | Pearson correlations *r* between RAQ-R and other assessments.

Assessment	*r*	*p*
VAS-QoL	−0.170	0.027
BSI global severity index	0.426	<0.001
Aggression and hostility	0.682	<0.001
BIS15	0.390	<0.001
I-8 urgency	0.470	<0.001
Intention	−0.314	<0.001
Endurance	−0.322	<0.001
Risk taking	0.178	0.008
ADHS-SB	0.428	<0.001
BAI	0.240	<0.001
BDI-II	0.316	<0.001
HSRQ total score	0.498	<0.001
Frustration tolerance and impulse control	0.689	<0.001
Affect differentiation and tolerance	0.538	<0.001

VAS-QoL, Visual Analog Scale for Quality of Life; BSI, Brief Symptom Inventory; BIS15, Barratt Impulsiveness Scale—Short Version; I-8, Impulsive Behavior Scale-8; ADHS-SB, Attention Deficit/Hyperactivity Disorder Self-Assessment Scale; BAI, Beck Angst Inventory; BDI-II, Beck Depressions Inventory II; HSRQ, Hannover Self-Regulation Questionnaire.

details). To increase reliability, we examined group differences using *t*-tests and Wilcoxon rank-sum tests for all samples and diagnostic categories (**Table 3**). Only for the diagnosis F54.- inconsistent results were found in terms of significance (*t*-test: $p = 0.013$, Wilcoxon-test: $p = 0.103$). Because of a very small number of patients included in this diagnosis ($n = 5$), *p*-value of the Wilcoxon-test was used for further interpretations. In all other categories, the two tests coincided in their assessment of significance (**Table 3**).

Compared to controls, patients of 13 out of 17 diagnostic categories demonstrated significantly higher RAQ-R scores ($p < 0.05$, in descending order of the effect sizes): ADHD, BPD, bipolar affective disorder, PD, eating disorder, cluster C PD, reaction to severe stress and adjustment disorder, mental and behavioral disorder due to use of alcohol, OCD, mental and behavioral disorder due to psychoactive substance use besides alcohol, dissociative and somatoform disorder, anxiety disorder, and depression. All these categories showed large (depression) or even very large (all others) effects. Highest mean RAQ-R scores and strongest effect sizes were found in patients with the diagnoses ADHD (F90.0), BPD (F60.31), and bipolar affective disorder (F31.-). Patients with ADHD and BPD even showed significantly higher RAQ-R scores compared to the PG without the respective disorder: ADHD: $d = 0.86$, $p = 0.007$ (*t*-test), $p = 0.02$ (Wilcoxon-test) and BPD: $d = 0.73$, $p < 0.001$ (*t*-test and Wilcoxon-test) indicating a large effect for ADHD and medium effect for BPD. For none of the diagnostic categories we found RAQ-R scores below those of the CG (**Table 3**).

Compared to PG [$n = 156$, mean = 21.67 (sd = 16.97), median: 19.50) patients with TS [as assessed in (16)] showed non-significantly higher mean RAQ-R scores [$n = 127$, mean = 25.00 (sd = 15.36), median = 24.00, $p = 0.095$].

Regarding sociodemographic characteristics within the PG, only age, but not gender, level of education, country of birth, and patient status showed a significantly negative correlation with RAQ-*R* ($r = -0.20$, $p = 0.014$).

Predictors of Rage Attacks

The data set fulfilled all Gauß-Markov assumptions as shown by diagnostic plots in the *R* script. The final model of the stepwise regression showed a very high goodness-of-fit indicated by the adjusted R^2 of 0.63 (**Table 4**). As significant predictors of rage attacks ($p < 0.05$) we identified aggression and hostility, frustration tolerance and impulse control, identity disturbances as well as the diagnostic category depression (F32–34) and the diagnosis ADHD (F90.0).

DISCUSSION

This study presents the first validation data of the RAQ-R in a psychiatric population. Getting back to the aims of this study as described in the introduction, the results demonstrate that the RAQ-R is a psychometrically sound assessment of RA in a mixed sample of psychiatric patients [aim (i)]. The RAQ-R shows excellent internal consistency and strong construct validity. In accordance with our previously proposed definition of RA (16), aggression and hostility, low frustration tolerance and impulse control as well as affect differentiation and tolerance were shown to be closely related constructs to RA. We were also able to demonstrate that depression, anxiety, general psychological distress, and impulsivity are rather distinct constructs. Impulsivity (as assessed by I-8 and BIS15) and RA (as assessed by RAQ-R) were shown to be less related than expected, which is in line with results from our previous study (16). All other validation tests met our expectations and indicate very good convergent and discriminant validity. Our data corroborate the 1-factor structure of the RAQ-R (16).

Our data clearly indicate that RA as assessed by the RAQ-R are more common in a mixed psychiatric sample compared to healthy subjects [aim (ii)]. Though the difference showed a very large effect size, the presence of a psychiatric diagnosis and demographic variables explained only 16% of variations of the RAQ-R scores. This finding as well as the high variance of RA in the psychiatric sample suggest strong influence by additional factors. Accordingly, we identified the presence of "aggression and hostility" (as assessed by BSI), "frustration tolerance and impulse control" (as assessed by HSRQ) as well as the diagnosis of ADHD as strong positive predictors of RA [aims (iv) and (v)]. These findings are in line with our definition of RA (16), since the BSI subscale "aggression and hostility" measures anger, irritability, rage, aggression and hostility (20) and the HSRQ subscale "frustration tolerance and impulse control" assesses impatience and the incomplete control of aggressive impulses (24).

Our results further corroborate that RA should be distinguished from the concept of anger attacks as defined by Fava et al. (8), although both describe phenomena of explosive outbursts in combination with emotional control difficulties. Anger attacks have consistently been found to be closely related

TABLE 3 | RAQ-R scores in controls (CG) compared to patients with Tourette syndrome (TS), the mixed psychiatric sample (PG), and diagnostic categories according to ICD-10 with $n > 1$.

Sample/ diagnostic category		*n*	RAQ-R			Cohen's d	*p* (*t*-test)	*p* (Wilcoxon-test)[a]
			Mean (sd)	Mean 95% CI	Median			
CG		611	10.09 (9.33)	9.34–10.83	7.00			
TS		127	25.00 (15.36)	22.30–27.70	24.00	1.41**	<0.001	<0.001
PG		156	21.75 (16.93)	19.08–24.43	19.40	1.03**	<0.001	<0.001
F10.-		23	23.03 (16.48)	15.91–30.16	22.00	1.34**	<0.001	<0.001
F11–F19		18	21.38 (14.91)	13.96–28.79	16.00	1.19**	<0.001	<0.001
F20.- and F23.-		9	15.44 (15.13)	3.81–27.07	10.80	0.57	0.092	0.608
F31.-		4	32.50 (16.22)	6.69–58.31	32.00	2.39*	<0.001	0.004
F32–F34		116	20.82 (17.14)	17.66–23.97	16.00	0.98**	<0.001	<0.001
F40.-, F41.-		31	20.31 (17.04)	14.06–26.56	19.00	1.04*	<0.001	0.002
F42.-		8	21.93 (12.38)	11.58–32.27	19.80	1.26*	<0.001	0.002
F43.-		33	26.07 (16.71)	20.14–31.99	26.00	1.63**	<0.001	<0.001
F44.-, F45.-, and F48.-		24	21.18 (11.78)	16.20–26.15	23.90	1.18**	<0.001	<0.001
F50.-		14	27.27 (17.47)	17.19–37.36	26.50	1.79**	<0.001	<0.001
F54.-		5	20.60 (15.68)	1.13–40.07	16.00	1.12	0.013	0.103
F60.- and F61.-		44	29.82 (16.70)	24.74–34.90	29.50	1.98**	<0.001	<0.001
	F60.31	26	31.77 (16.67)	25.04–38.50	32.00	2.23**	<0.001	<0.001
	F60.5-8	7	27.00 (21.03)	7.55–46.45	25.00	1.78*	<0.001	0.014
F62.-		6	15.67 (18.89)	(−4.15)-35.49	10.00	0.59	0.150	0.514
F63.-		4	14.50 (15.61)	(−10.34)−39.34	14.00	0.47	0.348	0.89
F90.0		11	35.00 (21.09)	20.84–49.16	37.00	2.59**	<0.001	<0.001

*CG, control group; TS, Tourette syndrome; PG, psychiatric group, F10.- = mental and behavioral disorders due to use of alcohol, F11–F19 = mental and behavioral disorders due to psychoactive substance use besides alcohol, F20.-&F23.- = schizophrenia and other psychotic disorders, F31.- = bipolar affective disorders, F32-F34 = depression, F40.-&F41.- = anxiety disorders, F42.- = obsessive-compulsive disorders, F43.- = reaction to severe stress and adjustment disorders, F44.-, F45.-, and F48.- = dissociative and somatoform disorders, F50.- = eating disorders, F54.- psychological and behavioral factors associated with non-mental disorders, F60.-and F61.- = personality disorders, F60.31 = borderline personality disorder, F60.5–8 = cluster C personality disorder, F62.- = enduring personality changes without brain damage, F63.- = habit and impulse disorders, F90.0 = attention deficit/hyperactivity disorder. Differences in RAQ-R scores compared to CG were calculated using t-test, Wilcoxon-test, and Cohen's d for effect sizes: *p < 0.05 in both t-test and Wilcoxon-test, **p < 0.001 in both t-test and Wilcoxon-test. [a]According to the five imputations five p-values were calculated. The highest p-value is shown.*

to depression (9–11, 13, 34, 35). Interestingly, even in mental disorders other than depression, comorbid depression has been identified as a predictor of anger attacks (9, 12–14). In contrast, we found only a moderate correlation between RA (as assessed by RAQ-R) and depression symptoms [as assessed by BDI-II, aim (iv)]. In addition, the effect size for depression (F32–F34) was smaller compared to all other diagnostic categories [aim (iii)]. Finally, the diagnosis of depression was even identified as a *negative* predictor of RAs when controlling for other diagnoses, symptoms, and sociodemographic characteristics [aim (v)]. Thus, based on available data, RA have to be classified as a distinct symptom, while anger attacks seem to represent a core symptom of depression.

The general relevance of RA in psychiatric patients is indicated by very large effect sizes in most and higher mean RAQ-R scores in all diagnostic categories compared to healthy controls [aim (iii)]. Significantly higher RAQ-R scores compared to CG were found for the following diagnostic categories, respectively (in descending order of effect size): ADHD (F90.0), BPD (F60.31), bipolar affective disorder (F31.-), PD (F60.-and F61.-), eating disorder (F50.-), cluster C PD (F60.5-8), reaction to severe stress and adjustment disorder, TS, mental and behavioral disorder due to use of alcohol (F10.-), OCD (F42.-), mental and behavioral disorder due to psychoactive substance use besides alcohol (F11–F19), dissociative and somatoform disorder (F44.-,F45.-&F48.-), anxiety disorder (F40.- and F41.-), and depression (F32–F34). Since sample sizes were in part very small and consisted of <10 patients (as shown in **Figure 1** and **Table 3**), caution is needed in interpreting results. Noteworthy, and in line with clinical experience and diagnostic criteria (1, 5, 33), our results suggest a high clinical relevance of RA in patients with ADHD and BPD indicated by very large effect sizes compared to healthy controls and significant differences compared to all other psychiatric patients.

Regarding demographic differences, our psychiatric sample showed significantly fewer RA with increasing age, but no significant relation between RA and gender, level of education or country of birth [aim (iv)].

In our previous study, we were able to demonstrate that patients with TS suffer from more severe RA compared to controls as assessed by RAQ-R (16). Interestingly, in TS mean RAQ-R scores were even non-significantly higher than in the mixed psychiatric population. One might argue that increased rates of RA might be influenced by comorbid ADHD, since ADHD is a common comorbidity in TS and we found highest RAQ-R scores in patients with (pure) ADHD. However, we were

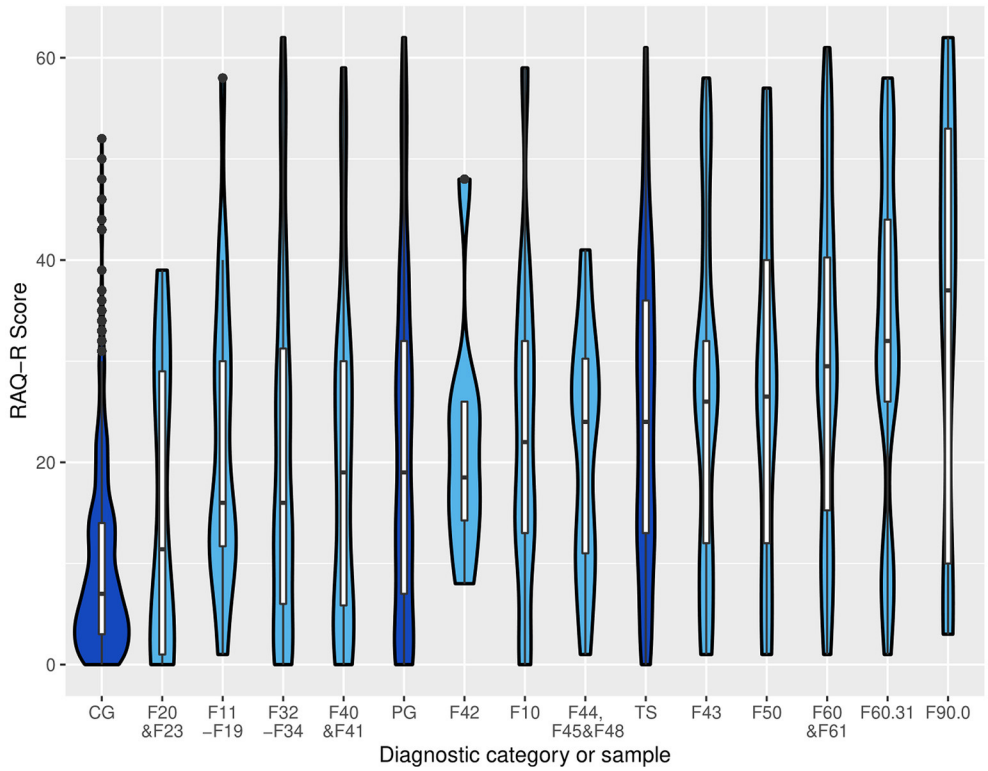

FIGURE 2 | Violin plots displaying the distribution of RAQ-R scores in controls (CG), patients with Tourette syndrome (TS), mixed psychiatric group (PG), as well as diagnostic categories according to ICD-10 with $n \geq 8$. CG = control group, F20 and F23 = schizophrenia and other psychotic disorders, F11–F19 = mental and behavioral disorders due to psychoactive substance use besides alcohol, F32–F34 = depression, F40 and F41 = anxiety disorders, PG = psychiatric group, F42 = obsessive-compulsive disorders, mental and behavioral disorders due to use of alcohol, F44, F45, and F48 = dissociative and somatoform disorders, TS, Tourette syndrome (F95.2), F43 = reaction to severe stress and adjustment disorders, F50 = eating disorders, F60 and 61 = personality disorders, F60.31 = borderline personality disorder, F90.0 = attention deficit/hyperactivity disorder. Dark blue: CG, PG, TS. Light blue: diagnostic categories within the PG. Groups and categories are sorted by median.

TABLE 4 | Multiple linear regression using RAQ-R as dependent variable.

Variable		Not-standardized coefficient	Standard error	Standardized coefficient	*p*
Constant		2.726	2.205		0.135
BSI	Aggression and hostility	9.772**	1.332	0.477**	<0.001
HSRQ	Frustration tolerance and impulse control	7.060**	0.973	0.486**	<0.001
	Identity disturbances	−2.749*	0.824	−0.198*	0.001
ADHD (F90.0)		6.740*	3.373	0.398*	0.048
Depressive disorders (F32–F34)		−4.145*	1.966	−0.245*	0.037
R squared		0.641			
Adjusted *R* squared		0.629			
F (df = 5;150)		53.562			<0.001

*BSI, Brief Symptom Inventory; HSRQ, Hannover Self-regulation Questionnaire; ADHD, attention deficit/hyperactivity disorder. *$p < 0.05$, **$p < 0.001$.*

able to demonstrate that RAQ-R scores are also increased in "TS only" without comorbid ADHD or any other psychiatric disorder (16). Accordingly, and in line with other studies (36), RA seem to represent a common and discrete symptom in TS. Our data, therefore, further supports the view that former ICD-10 classification of TS in the category "behavioral and emotional disorders with onset usually occurring in childhood and adolescence" was much more accurate compared to the new ICD-11 classification of TS in the category of "movement disorders" (37, 38).

This study has several significant strengths. We assessed a wide spectrum of common psychiatric symptoms allowing to

also analyze correlations to several close and distinct constructs. Different from most recent studies investigating clinical aspects of anger and rage attacks, we were able to compare RA in a psychiatric sample not only with healthy controls, but also between different diagnostic categories, respectively, according to ICD-10. External validity can be regarded as high for a mixed psychiatric population in a university clinic, since (a) patients from two different departments were included, (b) patients from out-, day- and inpatient clinics were included, (c) no relevant exclusion criteria have been predefined, (d) we included patients suffering from a broad and typical spectrum of different—and in many cases more than one—psychiatric diagnoses seen in psychiatric clinics, and (e) mildly to very severely affected patients were included. Another strength of our study is the availability of all raw data and analysis as reproducible *R* scripts aiming to increase the reliability and objectivity of the data processing.

The following limitations have to be taken into consideration: (a) although we included more than 150 patients, the sample size was too small to carry out a confirmatory factor analysis including an analysis of measurement invariance between groups. Nevertheless, the results of the PCA confirmed the 1-factor structure and loadings (16); (b) we used only self-assessments, but no examiner assessments; (c) for some diagnostic categories no correlations with the RAQ-R could be calculated due to small sample sizes; (d) a small number of data was missing. However, this was addressed by using multiple imputation, the gold standard approach to handle missing data (39); (e) we did not recruit a control group, but instead used data obtained from our previous study (16). Thus, an influence from different methods (paper-based vs. online survey) and time periods of data collection (7-10/2017 vs. 8/2018-4/2019) cannot completely be excluded; (f) sociodemographic characteristics between the control and patient groups slightly differed. Therefore, confounding cannot be completely ruled out, although we controlled for sociodemographic variables; (g) since no validated German version of the AAQ is available, this questionnaire could not be included in our study; (h) our validation only involves the original German version of the RAQ-R. An English version will be published in the near future, but has not been validated yet.

In conclusion, we validated the RAQ-R, a recently developed new instrument for the assessment of RA in patients with a wide spectrum of different psychiatric disorders, and found good to excellent psychometric properties. In contrast to previous assessments measuring anger or rage attacks, the RAQ-R measures the severity of RA in a dimensional way and, additionally, assesses psychological and behavioral characteristics of RA. In contrast to the AAQ (developed for the assessment of anger attacks) and the RAQ (a parents' assessment of RA only in children with TS), the RAQ-R is applicable to adult patients with the whole spectrum of psychiatric disorders. Our data provides additional support for the clinical relevance of RA in psychiatric populations, since RA were found to be a common symptom in different psychiatric disorders, but in particular in patients with ADHD and BPD.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found at: Open Science Framework (doi: 10.17605/OSF.IO/73Y8P).

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee at Hannover Medical School. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LP, KM-V, and EJ contributed to the conception and design of the study, contributed to the acquisition of data, and organized the database. LP wrote the first draft of the manuscript. LP, MH, and EJ contributed to the analysis and interpretation of data. All authors contributed to manuscript revision, read, and approved the submitted version.

ACKNOWLEDGMENTS

We thank all patients for participating in this study. We also thank Alexander Braumann, Institute for mathematical stochastics, Technical University Braunschweig, for his support with statistical analyses and Axel Weiser, patients and customer survey, quality management, MH for guiding us through the survey automation software EvaSys. We kindly acknowledge the support of PD Dr. Burkard Jäger and the opportunity to survey patients of the Department of Psychosomatic and Psychotherapy, MH.

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Conflict of Interest: In the context of other research, KM-V has received financial or material research support from EU (FP7-HEALTH-2011 No. 278367, FP7-PEOPLE-2012-ITN No. 316978) DFG: GZ MU 1527/3-1 and GZ MU 1527/3-2, BMBF: 01KG1421, National Institute of Mental Health (NIMH), Tourette Gesellschaft Deutschland e.V. Else-Kröner-Fresenius-Stiftung, GW pharmaceuticals, Almirall Hermal GmbH, Abide Therapeutics, and Therapix Biosiences. She has received consultant's honoraria from Abide Therapeutics, Boehringer Ingelheim International GmbH, Bionorica Ethics GmbH, CannaMedical Pharma GmbH, Canopy Grouth, Columbia Care, CTC Communications Corp., Demecan, Eurox Deutschland GmbH, Global Praxis Group Limited, IMC Germany, Lundbeck, Sanity Group, Stadapharm GmbH, Synendos Therapeutics AG, and Tilray. She has received speaker's fees from Aphria Deutschland GmbH, Almirall, Cogitando GmbH, Emalex, Eurox Deutschland

GmbH, Ever pharma GmbH, Meinhardt Congress GmbH, PR Berater, Spectrum Therapeutics GmbH, Takeda GmbH, Tilray, Wayland Group. She has received royalties from Deutsches Ärzteblatt, Der Neurologie und Psychiater, Elsevier, Medizinisch Wissenschaftliche Verlagsgesellschaft Berlin, and Kohlhammer.

The remaining 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.

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frontiers in Psychiatry

ORIGINAL RESEARCH
published: 23 September 2021
doi: 10.3389/fpsyt.2021.738344

High Schizotypy Predicts Emotion Recognition Independently of Negative Affect

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Introduction: Deficits in Emotion Recognition (ER) contribute significantly to poorer functional outcomes in people with schizophrenia. However, rather than reflecting a core symptom of schizophrenia, reduced ER has been suggested to reflect increased mood disorder co-morbidity and confounds of patient status such as medication. We investigated whether ER deficits are replicable in psychometrically defined schizotypy, and whether this putative association is mediated by increased negative affect.

Methods: Two hundred and nine participants between the ages of 18 and 69 (66% female) were recruited from online platforms: 80% held an undergraduate qualification or higher, 44% were current students, and 46% were in current employment. Participants were assessed on psychometric schizotypy using the O-LIFE which maps onto the same symptoms structure (positive, negative, and disorganised) as schizophrenia. Negative affect was assessed using the Depression Anxiety and Stress Scale (DASS-21). Emotion Recognition of both positive and negative emotions was assessed using the short version of the Geneva Emotion Recognition Task (GERT-S).

Results: Negative schizotypy traits predicted poorer ER accuracy to negative emotions ($\beta = -0.192$, $p = 0.002$) as predicted. Unexpectedly, disorganised schizotypy traits predicted improved performance to negative emotions ($\beta = 0.256$, $p = 0.007$) (primarily disgust). Negative affect was found to be unrelated to ER performance of either valence (both $p > 0.591$). No measure predicted ER accuracy of positive emotions. Positive schizotypy traits were not found to predict either positive or negative ER accuracy. However, positive schizotypy predicted increased confidence in decisions and disorganised schizotypy predicted reduced confidence in decisions.

Discussion: The replication of ER deficits in non-clinical negative schizotypy suggests that the association between negative symptoms and ER deficits in clinical samples may be independent of confounds of patient status (i.e., anti-psychotic medication). The finding that this association was independent of negative affect further suggests ER deficits in patients may also be independent of mood disorder co-morbidity. This association was not demonstrated for the positive symptom dimension of the O-LIFE, which may be due to low levels of this trait in the current sample.

Keywords: schizotypy, schizophrenia, psychosis, emotion recognition, affect recognition, social cognition, negative affect, mood disorder

OPEN ACCESS

Edited by:
Clare Margaret Eddy, Birmingham and Solihull Mental Health NHS Foundation Trust, United Kingdom

Reviewed by:
Gregory Fonzo, The University of Texas at Austin, United States
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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *08 July 2021*
Accepted: *20 August 2021*
Published: *23 September 2021*

Citation:
Dawes C, Danielmeier C, Haselgrove M and Moran PM (2021) High Schizotypy Predicts Emotion Recognition Independently of Negative Affect. Front. Psychiatry 12:738344. doi: 10.3389/fpsyt.2021.738344

INTRODUCTION

Schizophrenia is a chronic and potentially debilitating mental-health disorder with an estimated lifetime prevalence of 0.5% (1). The symptoms of schizophrenia can be categorised as positive negative or cognitive (2). The positive symptoms are reality distortion and disorganisation, exemplified by hallucinations, delusions, and disorganised thoughts, speech, and behaviour. Negative symptoms can be broadly categorised as expressive (restricted affect and alogia) and experiential (avolition and apathy, and asociality) (3). Negative symptoms in particular are associated with poorer functional outcomes (4, 5), including lower employment rates (6), smaller social networks (7), and poorer quality of life (8–10). Commonly, it is the negative symptoms and disorganised symptoms that are most consistently associated with poorer social cognition in schizophrenia (11).

Social cognition refers to mental processes responsible for the perception, decoding, interpretation, and regulation of responses to social stimuli (12). In schizophrenia, theory of mind, social perception, attributional bias, and emotion processing have been identified as key domains (13), with deficits reported across the prodromal, first-episode, and multi-episode stages of illness (14–16); suggesting they are an enduring trait marker. Deficits are found relative to both healthy controls (Hedge's $g = -0.89$) (15) and psychiatric controls with bipolar disorder (17), although they are less severe relative to autism spectrum disorders (18). These deficits are thought to underlie inter-personal conflict, isolation, and social disengagement (19) and contribute to poorer functioning. Social cognition may be of particular importance to improving daily functioning as it has been suggested to explain more variance in outcomes than non-social cognition (20–22). Social cognition has also been reported to explain incremental variance over non-social cognition and to mediate the association between non-social cognition (e.g., processing speed, working memory, etc.) and functioning (22). While the presence of social cognitive deficits is well-established in schizophrenia, the mechanisms behind these deficits are not well-understood. This research aims to identify potential explanatory factors in one important domain of social cognition: Emotion Recognition (ER).

In patients, ER performance is negatively associated with reality distortion, negative symptoms, and disorganised symptoms to a similar extent (11). Generally, impairments are found in the perception of negative emotions (sadness and fear) and less consistently in positive emotions, although this may be due to a lack of more varied positive stimuli beyond happiness (12). One potential contributory factor to these deficits is that patients may be hindered by confounds of patient status unrelated to the disease. Antipsychotic medication side-effects (e.g., motor slowness and poor concentration) may artificially inflate cognitive task deficits (23), while social isolation and community exclusion limits opportunities to practise social cognitive skills.

One approach to circumvent these limitations is to assess individuals varying on psychometrically-defined schizotypy; personality traits that reflect the factor structure of symptoms and are a potential marker for the transition to psychosis (24). These schizotypy "symptom" dimensions of positive, negative, and disorganised schizotypy map onto reality distortion, negative symptoms, and disorganised symptoms of schizophrenia, respectively. This dimensional viewpoint considers psychosis a spectrum of behaviour, from non-harmful schizotypy personality traits (e.g., "Do you believe in telepathy?") to clinical symptoms (e.g., persecutory delusions) that may cause disruption to daily functioning. Some psychometric assessments assess attenuated psychotic-like experiences according to diagnostic criteria (25), such as the Schizotypal Personality Questionnaire (SPQ) which bases its assessment on DSM-III-R criteria for schizotypal personality disorder (26) and the Oxford-Liverpool Index of Feelings and Experiences (O-LIFE) which is partially derived from DSM-II criteria (27). Investigating schizotypy traits allows inferences to be made to behaviour in patients in the absence of clinical confounds (25). Experimentally, if both schizotypy symptom traits in healthy controls and clinical symptoms in patients predict ER performance, this would suggest this relationship is independent of confounds of patient status. Currently, however, findings concerning schizotypy and ER are inconsistent in terms of which dimensions predict performance. Across categorical ("High" vs. "Low" schizotypy) and dimensional (associating traits with performance) approaches, the most consistently implicated traits are negative (28–32) followed by positive (reality distortion) (29, 32, 33), with fewer studies implicating disorganised traits (29, 33). However, other studies have reported no associations for these dimensions: negative (33–38), positive (28, 30, 31, 35, 36, 38–40), and disorganised (28, 30–32, 35, 36). Whether deficits are specific to positive and/or negative emotions is also unclear (28, 31, 41). Moreover, detailed assessments have found no evidence of deficits in disgust (33), but mixed evidence for happiness (36, 42), sadness (33, 36), fear (33, 36), surprise (33, 42), and anger (33, 36, 42). However, deficits have been suggested to be independent of more general face processing deficits (29). Overall, the evidence for ER deficits in schizotypy is currently inconsistent. Consequently, it is unclear whether the schizotypy literature supports the independence of ER deficits in clinical patients from clinical factors such as medication.

One potential reason for this inconsistency may be the confounding role of negative affect. Approximately 23–29% of first episode schizophrenia patients have at least one co-morbid mood disorder (43). For example, Major Depressive Disorder has been associated with poorer recognition of all six basic emotions except sadness ($g = -0.42$ to -0.17) (44). Schizotypy has also been associated with negative affect (45–47). Assessing negative affect in schizotypy may help explain some of the literature inconsistencies. Specifically, if negative affect were to moderate ER deficits in schizotypy, samples high in negative affect would report significant associations while samples low in negative affect may not. Alternatively, both schizotypy and negative affect may contribute to deficits.

Previous research has suggested statistically controlling for negative affect when assessing both schizotypy and ER performance (29, 33). However, only one study to our knowledge has done so. This study found correlations between schizotypy and ER performance remained significant when negative affect

Abbreviations: ER, Emotion Recognition.

was controlled for (28). However, this methodological approach did not allow a comparison of the relative impact of schizotypy and negative affect on ER e.g., by use of a mediation analysis or by comparing standardised effect sizes. Moreover, the tasks used in both this investigation and other previous investigations are limited by the range of positive emotions presented. Commonly, assessments in both schizotypy and schizophrenia use stimuli reflecting Ekman's six basic emotions (48) which includes happiness as a positive emotion. This has been highlighted as a limitation of current research (12) and a potential explanation for inconsistent associations with positive emotions. It is therefore important to include a wider variety of positive emotions (i.e., relief, pleasure, amusement, etc.) which was implemented in the current study.

Consequently, this report aimed to assess whether the literature inconsistencies of ER deficits in schizotypy may be partially explained by increased levels of negative effect. This was investigated by assessing whether negative affect mediates the relationship between schizotypy and ER performance. Normative comparisons of negative affect were also planned to determine whether any lack of mediation may be due to low levels of negative affect in the current sample. If ER deficits are both present in schizotypy and are independent of negative affect, this would suggest deficits in patients are not fully explainable by confounds of patient status (e.g., anti-psychotic medication and social isolation) nor mood disorder co-morbidity, respectively.

Therefore it was hypothesised that: (1) high negative schizotypy (28–32) will predict lower Emotion Recognition accuracy and that (2) if this association is attributable to negative affect it will be reduced if negative affect is controlled for.

METHODS

Participants

From an initial 232 participants, 23 were excluded (see Data Preparation). The final sample of 209 participants was recruited through the University's recruitment system (15.8%), Call for Participants (15.8%), social media (38.8%), and Prolific (29.7%). In this sample, 66% were biologically female, ages ranged between 18 and 69 years old ($M = 27.4$, $SD = 10.2$), 79.4% had at least an undergraduate level qualification, 44.0% were current students, and 45.9% were currently employed. Of the 148 participants that volunteered responses, 51.6% reported no current medication, 10 participants reported taking anti-depressants, one participant reported taking lithium (a mood stabiliser), but no participant reported anti-psychotic medication. The following analyses did not differ in interpretation when excluding these 11 participants and the remaining participants reported medication such as antihistamines or the contraceptive pill. This study achieved a power of 0.99 for a medium effect size and 0.37 for a small effect size (multiple regression analysis with three predictors) (49).

Materials

The first three scales of the Oxford-Liverpool Index of Feelings and Experiences (O-LIFE) (50) were used to assess schizotypy. These scales were Unusual experiences (Unex, "Do you believe in telepathy"), Introvertive anhedonia (Intan, e.g., "Do you feel that making new friends isn't worth the energy it takes?), and Cognitive disorganisation (Cogdis, e.g., "Are you easily distracted when you read or talk to someone?") which correspond to positive (reality distortion), negative, and disorganised schizotypy, respectively. The fourth scale of Impulsive non-conformity was not included as it may not be central to schizotypy (50). Negative affect was assessed using the total score of the Depression, Anxiety, and Stress Scale (DASS-21) (51). A psychometric measure of pre and post-task motivation was also taken using the motivation scale of the Momentary Influences, Attitudes and Motivation Impact (MIAMI) on Cognitive Performance Scale (52). The GERT-S (53), an emotion identification task consisting of 42 items and 14 emotions, was used to assess ER (**Figure 1**). Stimuli were 1 to 3 s videos of 10 male and female actors. Actors spoke non-sense syllables, meaning recognition was from dynamic facial expression, upper body language, and prosody (but not semantic meaning). Consequently, the task assessed more general emotion recognition. The GERT-S includes high arousal positive (pleasure, relief, interest) and low arousal positive emotions (joy, amusement, pride), and high arousal negative (anger, fear, despair) and low arousal negative items (irritation, sadness, anxiety). Disgust was categorised as negative consistent with most previous reports in schizotypy. Surprised was not categorised as positive nor negative due to conflicting evidence in the wider social cognitive literature. However, as reports on ER in schizotypy primarily consider surprise as positive (28, 32, 41) the analyses were repeated including surprise as a positive emotion, but they did not differ in implication. On each trial participants had to identify which one of the 14 emotions was being presented. To gather more information on decision making an additional scale was added requesting response confidence judgments (from 1 "low confidence" to 7 "high confidence") that was not present in the original GERT-S. The GERT-S presents good internal consistency ($\omega_T = 0.89$) and has been critically reviewed elsewhere (53, 54).

Procedure

This study was part of a larger cognitive battery also administering two tasks of executive function. All participants complete the study online via Qualtrics between March and August 2020. Psychometric information was collected from one survey while the GERT-S was administered on a separate survey provided by the original authors. The questionnaires were administered first followed by the GERT-S. The GERT-S includes two practise trials, clear definitions of each emotion, and the option to repeat the practise. "Prefer not to say" options were added to all questionnaires for ethical reasons as well as two awareness items which asked participants to select "Prefer not to say." Psychometric motivation assessments were taken both pre- and post-task (52). Before being debriefed, participants were given the option to withdraw their data if they experienced technical issues or for any other reason (with no justifications required). Participants were compensated with University credits or monetary incentives irrespective of whether they withdrew their data. This study was approved by the University of

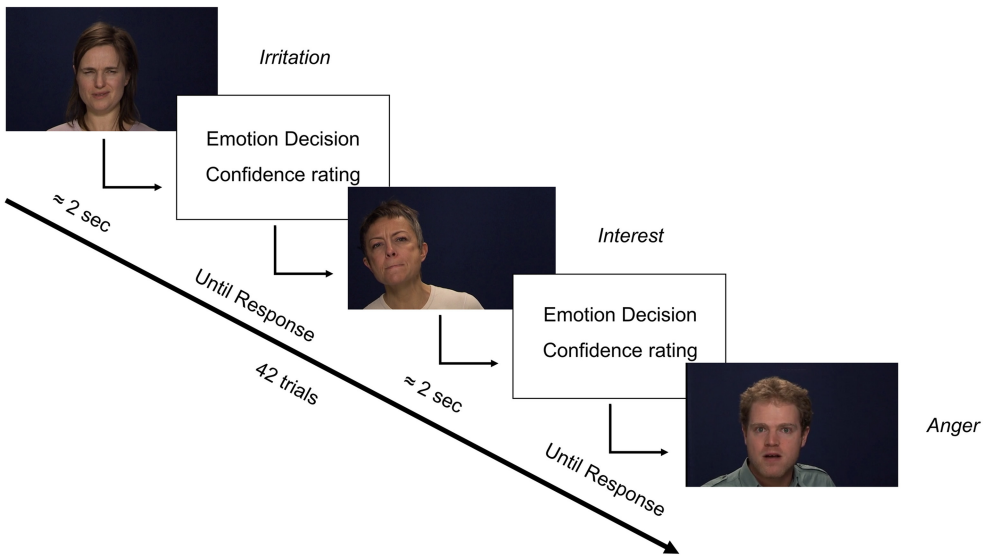

FIGURE 1 | Trial format of the GERT-S with the addition of confidence ratings. Italics represent the emotion displayed by each person. Original materials adapted from (54).

Nottingham's Ethics Committee (S1214) and all participants gave informed consent.

Data Preparation

From the original sample, 17 participants were excluded due to failing either awareness item (not selecting "Prefer not to say"), one participant withdrew their data, and one participant was excluded due to excessive "Prefer not to say" responses. Six more were excluded due to outlier performance (total accuracy < median – 2.5 * Median Absolute Deviation). The exclusion of these participants more readily satisfied model assumptions and but did not affect the current conclusions. Missing data including "prefer not to say" were imputed using the missForest R package (55). Missing data accounted for 0.4, 0.5, and 1.2% of single-item responses for the DASS-21, O-LIFE, and MIAMI respectively.

Analysis Strategy

The primary outcome was Emotion Recognition accuracy (ER; 0–100%) divided into positive and negative items. To address the first hypothesis each of the O-LIFE scales were added simultaneously to two multiple regressions predicting positive ER and negative ER performance. To assess a potential mediatory role of negative affect, the DASS-21 total score was then added to these multiple regression models. Bayes Factors (BF) were calculated for each regression coefficient to differentiate between data insensitivity and a true null effect (56). BFs were interpreted as follows for the alternate hypothesis (BF_{10}): a BF between 3 and 0.333 was insensitive (more data required), BF > 3 moderate evidence, BF > 10 strong evidence, BF > 30 very strong evidence, and BF > 100 decisive evidence (57). As accuracy scores are bound between 0 and 100%, a beta-binomial distribution regression was applied as a robustness cheque. As each approach was identical in conclusions the more readily interpretable Ordinary Least Squares approach is presented. The accuracy of each emotion was correlated with all psychometric scales. Finally, all regression analyses passed the assumptions of normally distributed residuals, linearity, homoscedasticity, lack of influential values (Cook's distance < 1), and no multicollinearity (VIF < 5). Analyses were conducted in R studio (58), Jamovi (59), and JASP (60) using several statistical (61, 62) and data visualisation packages (63, 64).

RESULTS

Descriptives

Descriptive summaries of psychometric and GERT-S scores can be found in **Table 1** and **Supplementary Table 1**, respectively. The total sample presented lower accuracy score for negative emotions relative to positive emotions [$t_{(208)} = 7.825$, $p < 0.001$, $d = 0.541$]. Normative comparisons were conducted to assess whether current levels of traits were representative of the wider population. As Shapiro-Wilk tests suggested all variables were non-normally distributed (all $p < 0.011$), normative comparisons of the O-LIFE (extracted from the 21 to 30 age category, $N = 402$) (50) and DASS-21 (51) were conducted using One-Sample Wilcoxon signed-rank tests as medians were available. As normative medians are not available for the GERT-S (53) One-Sample *t*-tests were required. Effect sizes for non-parametric tests were rank-biserial correlations (r_{rb}) while *t*-tests used Cohen's *d* (**Table 1**). Positive schizotypy was lower in the current sample ($p = 0.004$, $r_{rb} = -0.27$), negative schizotypy ($p < 0.001$, $r_{rb} = 0.76$), DASS-21 ($p < 0.001$, $r_{rb} = 0.80$), and total GERT-S were higher ($p < 0.001$, $d = 1.09$), but disorganised schizotypy did not differ ($p = 0.536$, $r_{rb} = 0.04$). Scale internal consistency was calculated using McDonald's Omega Total (ω_T) following recommendations (65). Cronbach's α is presented for completeness but is not appraised due to being unsuitable for psychometric (66) and non-normal data (67). The O-LIFE and

DASS-21 presented excellent internal consistency ($\omega_T > 0.80$), but the GERT-S was questionable to poor, unlike the original validation. GERT-S scores presented a good range of difficulties and a lack of floor or ceiling effects (**Supplementary Table 1**). Spearman correlations were also conducted between the three schizotypy scales and both pre and post-task motivation (FDR corrected). The correlations found disorganised schizotypy was significantly associated with lower post-task motivation ($r_s = -0.215$, $p = 0.012$) and presented a trend association to lower pre-task motivation ($r_s = -0.164$, $p = 0.054$), but the remaining associations were non-significant ($p > 0.138$).

Emotion Recognition Accuracy

Two multiple regression analyses (**Table 2**) entered the three O-LIFE scales as predictors of positive and negative accuracy. For negative emotions, negative schizotypy predicted poorer performance (β = −0.192[−0.333, −0.052], $p = 0.007$, $BF_{10} = 3.238$, $R^2_{partial} = 3.5\%$), disorganised schizotypy predicted improved performance at a larger effect size (β = 0.256[0.096, 0.417], $p = 0.002$, $BF_{10} = 4.387$, $R^2_{partial} = 4.6\%$), but positive schizotypy returned non-significant with the BF_{10} suggesting more data were needed to accept the null hypothesis ($p = 0.094$, $BF_{10} = 0.671$) (hypothesis 1). All significant associations survived FDR correction for multiple comparisons (all $p < 0.021$). For positive emotions, no O-LIFE scale significantly predicted performance (all $p > 0.090$). The BFs suggested there was moderate evidence for null hypothesis for positive schizotypy ($BF_{10} = 0.191$) and disorganised schizotypy ($BF_{10} = 0.256$), but more data were needed to conclude about negative schizotypy ($BF_{10} = 0.477$). Both sex and age were not significant predictors of performance when added to these two regression models and did not affect the significant associations between schizotypy and performance.

Total DASS-21 score did not predict positive (β = −0.037 [−0.174, 0.100], $p = 0.591$, $BF_{10} = 0.172$) nor negative ER accuracy (β = 0.014[−0.123, 0.151], $p = 0.843$, $BF_{10=}$ 0.153). Unplanned exploratory analyses additionally confirmed no DASS-21 subscale predicted performance on the GERT-S that would warrant more detailed investigation (positive ER: Depression, $p = 0.536$, Anxiety, $p = 0.333$, Stress, $p = 0.922$; negative ER: Depression, $p = 0.867$, Anxiety, $p = 0.890$, Stress, $p = 0.638$). The inclusion of DASS-21 total score these regression models in **Table 2**. did not change the associations between schizotypy and both positive and negative ER accuracy. Consequently, this suggested negative affect does not mediate the relationship between schizotypy and ER performance (hypothesis 2). Marginal effects were plotted to illustrate the independent effects of each O-LIFE scale on negative ER accuracy (**Figure 2**). Participants scoring in the 90th percentile of positive schizotypy, negative schizotypy, or disorganised schizotypy were predicted to have changes in accuracy of −4.52%, −7.1%, and +9.08% respectively, relative to participants scoring in the 10th percentile (a common cut-off criterion for categorical studies).

Individual Emotion Recognition Accuracy

A spearman's correlation matrix was calculated between the O-LIFE, DASS-21, and emotion recognition accuracy (**Table 3**). The

TABLE 1 | Descriptive statistics of psychometric measures compared against normative values.

	Current							Normative					Comparison		
Scale	**Range**	**M**	**SD**	**Med**	**MAD**	**IQR**	**ω_T**	**α**	**Range**	**M**	**SD**	**Med**	**IQR**	**α**	***p***	**ES [Low, High]**	**Norm**
Pos Scz	0–23	8.105	5.587	7.042	5.930	7.967	0.869	0.932	–	10.159	6.304	9[a]	10	0.89	=0.004	−0.27 [−0.16, −0.41]	<0.001
Neg Scz	0–24	8.455	5.594	7.727	5.930	8.425	0.866	0.916	–	5.444	4.000	4.5[a]	6.5	0.82	<0.001	0.76 [0.68, 0.82]	<0.001
Dis Scz	0–24	13.177	6.218	13.600	7.413	9.375	0.899	0.942	–	12.391	5.690	13[a]	–	0.87	=0.536	0.04 [−0.12, 0.20]	<0.001
Depression	0–21	7.153	5.610	5.846	5.930	9.117	0.916	0.940	0–21	2.83[b]	3.87	1	–	0.88	<0.001	0.77 [0.62, 0.92]	<0.001
Anxiety	0–20	4.746	4.580	3.175	4.448	7.099	0.858	0.900	0–20	1.88[b]	2.95	1	–	0.82	<0.001	0.63 [0.48, 0.77]	<0.001
Stress	0–21	7.388	5.154	6.972	5.930	7.982	0.866	0.894	0–21	4.73[b]	4.20	4	–	0.90	<0.001	0.52 [0.37, 0.66]	=0.008
DASS Total	0–54	19.287	13.781	15.417	13.343	20.350	0.966	0.958	0–61	9.42[b]	9.66	7	–	0.93	<0.001	0.80 [0.74, 0.85]	=0.011
GERT-S Tot	38–83	62.930	10.063	64.172	10.590	12.616	0.535	0.691	–	52[c]	15.318	–	–	0.81–0.83	<0.001	1.09 [0.91, 1.27]	=0.005
GERT-S Neg	29–90	60.059	13.748	61.499	14.120	19.294	0.503	0.628	–	–	–	–	–	–	–	–	=0.002
GERT-S Pos	39–100	68.979	13.079	71.871	16.473	17.108	0.400	0.562	–	–	–	–	–	–	–	–	=0.001

IQR, interquartile range; MAD, median absolute deviation, medians are interpolated medians; **ωT**, *McDonald's Omega total; Norm, Shapiro-Wilk tests. Group comparisons are One-Sample Wilcoxon Sign-Rank tests for both the O-LIFE and DASS-21 and a One Sample t-tests for the GERT-S (all p-values are False Discovery Rate corrected), ES = rank-biserial correlations for Wilcoxon and Cohen's d for t-tests.* [a]*Mason and Claridge (60),* [b]*Henry and Crawford (61),* [c]*Schlegel and Scherer (53).*

TABLE 2 | Multiple linear regressions predicting positive and negative emotion recognition accuracy from positive (Unex), negative (Intan), and disorganised (Cogdis) schizotypy.

	Pos Accuracy								95% Conf Int	
Predictor	**B**	**SE**	**t**	***p***	**BF_{10}**	**$R^2_{partial}$**	**VIF**	**β**	**LC**	**HC**
Intercept	69.480	2.337	29.727	< 0.001						
Pos Scz	−0.106	0.187	−0.565	=0.572	0.191	1.156	1.326	−0.045	−0.202	0.112
Neg Scz	−0.290	0.170	−1.706	=0.090	0.477	1.399	1.105	−0.124	−0.268	0.019
Dis Scz	0.213	0.175	1.217	=0.225	0.256	0.718	1.447	0.101	−0.063	0.266
	Neg Accuracy								**95% Conf Int**	
Predictor	**B**	**SE**	**t**	***p***	**BF_{10}**	**$R^2_{partial}$**	**VIF**	**β**	**LC**	**HC**
Intercept	59.202	2.400	24.666	< 0.001						
Pos Scz	−0.323	0.192	−1.683	=0.094	0.671	1.362	1.326	−0.131	−0.285	0.023
Neg Scz	−0.473	0.175	−2.706	=0.007	3.238	3.449	1.105	−0.192	−0.333	−0.052
Dis Scz	0.567	0.180	3.152	=0.002	4.387	4.622	1.447	0.256	0.096	0.417

Positive: $F_{(3, 205)} = 1.152$, $p = 0.329$, $R^2 = 1.7\%$, $R^2_{adjusted} = 0.2\%$. ***Negative:*** $F_{(3, 205)} = 4.469$, $p = 0.005$, $R^2 = 6.1\%$, $R^2_{adjusted} = 4.8\%$. *VIF, Variance Inflation Factor. Bayesian priors are full Cauchy (location = 0, scale = 0.354).*

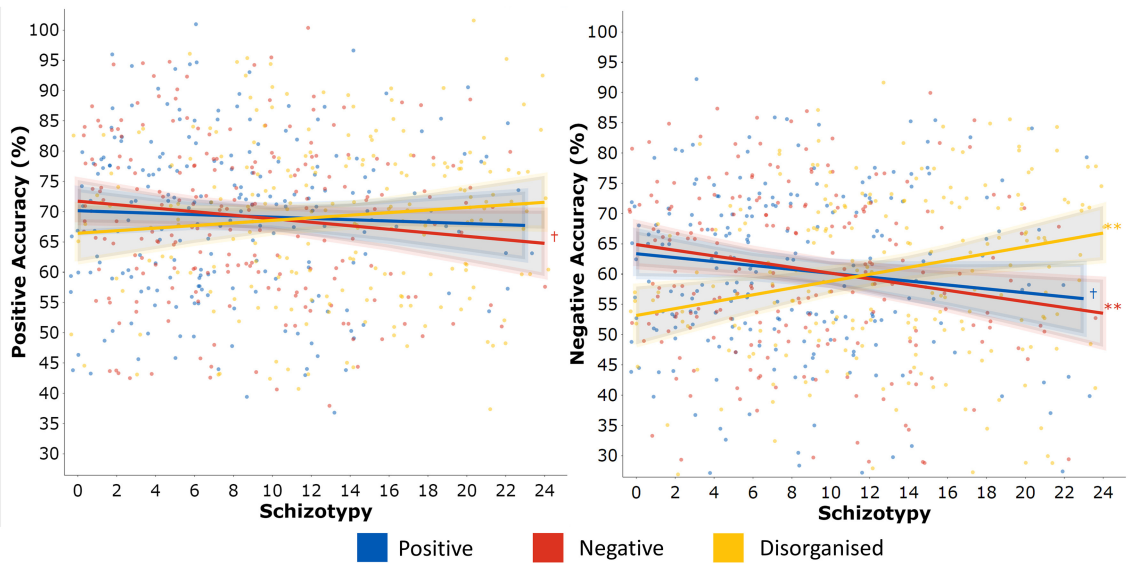

FIGURE 2 | Post estimation of multiple linear regressions predicting positive (left) and negative (right) emotion recognition accuracy from positive (Unex), negative (Intan), and disorganised (Cogdis) schizotypy.

effect of negative schizotypy for negative items may have come from anger and fear (both $p < 0.074$), although these analyses were both trend and did not survive FDR correct (both $p < 0.395$). The effect of disorganised schizotypy for negative items likely came from disgust ($r_s = 0.254$, $p < 0.001$, $p_{FDR} = 0.007$). To assess the latter, the multiple regression analysis was repeated with the exclusion of disgust. Disorganised schizotypy remained a significant albeit weaker predictor (β = 0.196 [0.034, 0.357], $p = 0.018$). A conflicting negative correlation between disorganised schizotypy and relief accuracy was also found (r_s= −0.139, $p = 0.045$), but this did not survive FDR correction (p =0.277). This association may be an indirect result of the association between disorganised schizotypy and DASS-21 total score ($r_s = 0.681$, $p_{FDR} = 0.007$), as the DASS-21 was also correlated with relief accuracy in the same direction ($r_s = -0.186$, $p_{FDR} = 0.050$). In keeping with the regression results, positive schizotypy was not correlated with any emotion. Correlations between psychometric scales and reaction time are provided in **Supplementary Table 2**.

Response Confidence

Regression analyses were repeated with GERT-S decision confidence as the outcome. Originally, four multiple regressions were conducted dividing responses between both valence

TABLE 3 | Spearman correlations between the accuracy of each emotion and schizotypy.

			Schizotypy				Negative Affect
Valance	**Arousal**	**Scale**	**Total**	**Pos**	**Neg**	**Dis**	**DASS Total**
		Pos	0.718***	–			
		Neg	0.608***	0.122†	–		
		Dis	0.834***	0.490***	0.300***	–	
		DASS Total	0.634***	0.404***	0.309***	0.681***	–
Positive	High	Interest	−0.100	−0.106	−0.091	−0.071	−0.065
		Pleasure	0.074	0.046	0.065	0.049	0.012
		Relief	−0.113	−0.047	−0.038	−0.139*	−0.186**
	Low	Amusement	0.034	0.035	−0.079	0.097	0.069
		Joy	−0.040	−0.011	−0.105	0.036	0.059
		Pride	0.035	−0.016	0.002	0.061	−0.036
Negative	High	Anger	−0.018	0.058	−0.124†	0.050	0.054
		Fear	−0.024	−0.009	−0.131†	0.069	0.067
		Despair	0.009	0.000	−0.024	0.020	0.047
	Low	Anxiety	0.021	0.024	0.027	0.025	−0.038
		Irritation	0.003	−0.076	0.001	0.083	0.011
		Sadness	−0.083	−0.001	−0.109	−0.050	−0.016
	NR	Disgust[a]	0.167*	0.072	−0.012	0.254***	0.068
	NR	Surprise	−0.030	0.023	−0.037	−0.054	−0.013

[a] *Schlegel and Scherer (53) did not suggest arousal of disgust,* † *p < 0.1, *p < 0.05, **p < 0.01, ***p < 0.001. Unex, Unusual Experiences; Intan, Introvertive Anhedonia; Cogdis, Cognitive Disorganisation; DASS Total, Depression, Anxiety, and Stress Scale total score. Significant correlations between Intan and both anger (p = 0.395) and fear (p = 0.337) recognition and Cogdis and Relief accuracy (p = 0.277) do not survive correction for multiple comparison (False Discovery Rate, FDR). However, the associations between Cogdis and disgust (p = 0.007) and DASS total score and Relief accuracy (p = 0.050) do survive correction.*

(positive vs. negative) and veracity (correct vs. incorrect decisions). However, as the relationship between schizotypy and confidence rating were unaffected by these variables and splitting the analyses violated several model assumptions, only overall confidence is presented. A multiple regression analysis (**Table 4**) reported that positive schizotypy marginally predicted greater confidence, but the BF_{10} suggested more data were needed ($\beta = 0.166$ [0.012, 0.320], $p = 0.035$, $BF_{10} = 1.358$) and the association became trend under FDR correction ($p = 0.053$). In contrast, disorganised schizotypy predicted reduced confidence ($\beta = -0.220$ [−0.381, −0.059], $p = 0.008$, $p_{FDR} = 0.024$, $BF_{10} = 3.892$). More data were needed to conclude about negative schizotypy which returned non-significant (p_{FDR} =0.453, $BF_{10} = 0.497$). Total DASS-21 was not found to predict confidence judgements, but the BF_{10} suggested more data were needed ($\beta = -0.107$ [−0.244, 0.029], $p = 0.122$, $BF_{10} = 0.465$).

DISCUSSION

This study assessed Emotion Recognition (ER) in psychometrically-defined schizotypy (measured using the O-LIFE). The first hypothesis that negative schizotypy would predict poorer ER performance was supported. The second hypothesis that negative affect (measured using the DASS-21 total score) would mediate deficits in schizotypy was not supported. Unexpectedly, we found that disorganised schizotypy predicted improved performance and whether positive schizotypy was related to performance was inconclusive. The effects of negative schizotypy and disorganised schizotypy were statistically significant for negative but not positive emotions. The standardised effect sizes of negative and disorganised schizotypy here ($\beta = -0.192$ to 0.256) were much larger than one previous study using a similar approach ($N = 2{,}332$, $\beta = -0.04$ to -0.10) (29). Positive schizotypy marginally predicted higher confidence in decisions, while disorganised schizotypy predicted reduced confidence in decisions.

The finding that schizotypy was associated with performance on negative emotions is consistent with reviews using a variety of emotion recognition instruments in patients with schizophrenia (12). This replication may suggest ER is a valid construct to investigate the dimensional aspects of schizophrenia in the absence of clinical confounds. As the schizotypy literature is equivocal, these findings confirm some but not all studies (28, 31, 33, 34, 36, 38, 41, 42). One reason why only negative emotions may have shown differential effects is that they may activate unpleasant internal states in participants; producing excessive anxiety that can be detrimental to performance. Although negative affect was unrelated to performance, the DASS-21 is not suitable to determine this as it assesses trait rather than state disturbances. To test this hypothesis, state anxiety questionnaires or physiological measures (e.g., Galvanic Skin Response) could be applied. Alternatively, perhaps the GERT-S itself is not sensitive to detect deficits, as the use of multi-modal stimuli (prosody, body language, facial expression) may provide adequate information for processing. This may be consistent with only the more difficult negative emotions being predicted by

TABLE 4 | Multiple linear regressions predicting response confidence to either correct or incorrect decisions from positive (Unex), negative (Intan), and disorganised (Cogdis) schizotypy dimensions.

	Confidence								95% Conf Int	
predictor	β	SE	t	*p*	BF_{10}	$R^2_{partial}$	VIF	β	LC	HC
Intercept	5.190	0.147	35.385	< 0.001						
Pos Scz	0.025	0.012	2.122	=0.035	1.358	2.150	1.326	0.166	0.012	0.320
Neg Scz	−0.011	0.011	−1.061	=0.290	0.497	0.546	1.105	−0.076	−0.217	0.065
Dis Scz	−0.030	0.011	−2.695	=0.008	3.892	3.421	1.446	−0.220	−0.381	−0.059

$F_{(3, 205)} = 3.910$, $p = 0.010$, $R^2 = 5.4\%$, $R^2_{adjusted} = 4.00\%$. *VIF, Variance Inflation Factor. Bayesian priors are full Cauchy (location = 0, scale = 0.354).*

schizotypy and not the less difficult positive emotions. The lack of significant association between positive emotion recognition and schizotypy is also consistent with some (31, 38, 41) but not all past investigations (28, 32, 34, 42). As there are currently no investigations in schizotypy or schizophrenia that compares performance to controls on the GERT-S, it cannot be ruled out that our findings are due to the ER instrument used. However, one study has assessed patients using the GERT-S (with no control group) and reported an average score of 53.5% (68). The average score in this control sample was 62.9% which may suggest the GERT-S is sensitive to detect ER deficits in psychosis patients. However, non-clinical participants in the original validation of the GERT-S (averaged across both studies) scored 52%, thus indirect comparisons in this case may not insightful. Consequently, future research should aim to replicate these ER deficits in clinical patients relative to a control group. Due to the employment of the GERT-S, however, a lack of diverse positive stimuli is an unlikely explanation for our findings, which is a commonly cited limitation of previous emotion recognition research (12).

The explanations above are likely only applicable to negative schizotypy, which predicted poorer ER performance consistent with previous research in patients (11) and adds to equivocal research in schizotypy (28–32). One clinical study reported 20% of the variance in ER performance was explained by negative symptoms (69). The effect of negative schizotypy in our non-clinical sample was lower (3.5%) which was expected given the dimensional view of psychosis as a spectrum (i.e., less severe deficits should occur with less severe schizophrenia-like experiences). The correlational analysis suggested the deficits in ER were potentially due to poorer fear and anger recognition (but these correlations did not survive correction for multiple comparisons). These potential associations are, however, consistent with previous findings in patients (12). Previous research has found items on social anxiety may primarily drive the effect in negative schizotypy (30). It has been suggested that poor ER may increase social anxiety through reduced confidence in social cognitive abilities (29), perhaps leading to increased social withdrawal and negative traits (35). However, in this study, negative schizotypy did not predict confidence in decisions which conflicts with this suggestion.

Another explanation could be that this relationship is mediated through increased alexithymia, which is increased in clinical samples (70) and correlates with all three schizotypy trait dimensions (71, 72). This initially contradicts the current explanation being specific to negative schizotypy. However, without controlling for scale inter-correlation, it is unclear whether these associations are general or scale specific. If this suggestion were accurate, the experiential rather than expressive negative traits would correlate with self-reported alexithymia. To the best of our knowledge, no study has controlled for alexithymia in this context. One study has assessed alexithymia, but because performance was unaffected by schizotypy, further investigation was unnecessary (39).

The replication of ER deficits in negative schizotypy may suggest the association between negative symptoms and poorer ER in clinical samples may not an artefact of patient status. Moreover, as these deficits were found to be independent of negative affect this may also suggest that mood disorder co-morbidity may not completely explain ER deficits in schizophrenia patients. However, it should be stated that the internal consistency for both positive and negative emotion was low (**Table 1**), which should caution interpretation.

This study is the first to report a positive association between disorganised schizotypy and ER. This conflicts with previous research in schizotypy commonly reporting no associations (28–31, 33, 35, 36) and patient samples finding negative associations (11). The improved performance in this study was driven primarily through disgust recognition, which contradicts impaired disgust recognition in patient samples (12) and schizotypy samples (29, 33). Both increased deliberation time and improved motivation are unlikely explanations for this improved performance as all schizotypy dimensions generally correlated with increased reaction time (**Supplementary Table 2**) and disorganised schizotypy correlated with reduced post-task motivation. Studies have reported that schizotypy can exaggerate the perceived emotion expressed in ER tasks (73), which may lead to improved ER performance. However, performance benefits are commonly found in the paranoid subtype of patients (74) and paranoia-related (positive) schizotypy (73), rather than disorganised schizotypy. Alternatively, perhaps participants that can more accurately identify negative emotions have a negatively biassed perception of social interactions. This psychological stress may in turn lead to reports of disorganised thinking. Finally, as this is the only study in schizotypy to use the O-LIFE (rather

than the SPQ) or the GERT-S, these results may be specific to the conceptualisations of these measures.

Previously, it has been suggested that positive schizotypy traits such as paranoia may bias participants to expect negative facial emotions and response, or that poorer ER may make individual highly suspicious (32). This is consistent with ER deficits correlating with positive symptoms in patient samples (11) but contrasts with the majority of non-clinical samples (28, 30, 31, 35, 36, 38–40). However, the Bayesian analyses in the current study suggested more evidence was needed to support a lack of relationship. The disparity between clinical and non-clinical studies may be explained by very high levels of positive schizotypy traits being necessary to produce deficits. Indeed, negative schizotypy has been reported to only correlate with FER performance in those classified as being high in schizotypy (31). In this study the normative comparisons found that the levels of positive schizotypy were significantly lower in the current sample, but negative schizotypy and disorganised schizotypy were not, which both predicted performance.

Positive schizotypy predicted increased confidence in decisions while disorganised schizotypy predicted decreased confidence. Clinical studies using both social and non-social stimuli have suggested patients are underconfident in correct responses and overconfident in errors (75); which may underlie impaired functioning and delusion formation, respectively. However, confidence here was unaffected by both valance and veracity, suggesting a divergence with past research in patient samples (75). The discrepancy between patient and schizotypy samples may highlight a potential cognitive mechanism subject to deterioration at illness onset. As a clinical diagnosis is often the result of positive symptoms and is associated with a decline in social cognition, this overconfidence would likely be applied to now impaired performance. This overconfidence in positive schizotypy may be highly relevant to delusion formation. However, it is important to state that the BF_{10} suggested only anecdotal evidence of this association which should caution interpretations. The under-confidence associated with disorganised schizotypy may potentially explain the beneficial effects of this trait in the current study. Although deliberation time and motivation were unlikely explanations, under-confidence may produce more effortful deliberation. This would suggest disorganised schizotypy may relate to a more general cognitive thinking style that is independent of judgement veracity. When combined with the results on accuracy, this suggests (a) positive schizotypy predicts ER overconfidence but intact accuracy, (b) disorganised schizotypy predicts ER underconfidence but improved accuracy, and (c) negative schizotypy predicts poorer ER accuracy with unaffected confidence judgments. If the beneficial effect of disorganised schizotypy can be replicated, improving decision confidence for those high in disorganised schizotypy may improve the transferal of skills to real-world functioning, which may also be relevant to patient samples. This finding of alternated metacognitive processing in schizotypy merits further investigation, potentially with the addition of psychometric metacognitive scales.

Several limitations of this study should be highlighted. Firstly, while the advantage of using a schizotypy sample is the removal of clinical confounds, caution must be applied when applying conclusions directly to clinical samples. Secondly, the cross-sectional nature of this study means that the results are associative and causality cannot be determined. Thirdly, we used single assessments of ER, schizotypy and negative affect which may limit this pattern of results to the specific instruments used.

CONCLUSIONS

This study demonstrated Emotion Recognition deficits were associated with negative schizotypy, suggesting an association between negative clinical symptoms and emotion recognition deficits may be independent of confounds of patient status (i.e., anti-psychotic medication). Inconclusive evidence was found for an association with positive schizotypy ($BF_{10} = 0.671$), which may be explained by the low levels of positive schizotypy traits in the current investigation. Unexpectedly, disorganised schizotypy predicted improved recognition which may be due to under-confidence in decisions increasing effortful deliberation. Negative affect was found to not mediate reduced Emotion Recognition performance; potentially suggesting that impairments in clinical patients may be independent of co-morbid mood disorders. This has implications for therapeutic interventions and merits further investigation in a clinical sample.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Nottingham Ethics Committee (S1214). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CDaw designed the study, conducted the literature review and statistical analyses, and wrote the first draft. PM designed the study and reviewed both the first draft and final manuscript. MH and CDan reviewed early conceptualisations of the project and contributed to academic discussion and reviewed several draughts of the manuscript. All authors have reviewed and approved the final manuscript.

FUNDING

CDaw was funded by a University of Nottingham Economic and Social Research Council Doctoral Training Centre grant [ES/J500100/1] as part of their Ph.D. All other authors report

their contributions were supported by no specific grant from any funding agency, commercial or not-for-profit sectors.

ACKNOWLEDGMENTS

We would like to thank the original authors of the GERT-S (Katja Schlegel and Klaud Scherer) for providing us with the GERT-S for this study, all participants who took part, and the ESRC for financially supporting CDaw's research. We also thank the three reviewers for their helpful comments.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.738344/full#supplementary-material

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Conflict of Interest: 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.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 07 February 2022
doi: 10.3389/fpsyt.2022.819143

How Social Experiences Affect Interpretation Bias Among Individuals With Non-clinical Depression: The Role of Ostracism

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Background: Extensive knowledge and research indicate that interpretation bias is very common among individuals with sub-clinical and clinical levels of depression. Nevertheless, little is known about the role of social experiences in enhancing interpretation bias. Given the major relevance of social experiences in the context of depression, the present study investigated the role of potential interactions between social experiences and levels of depression symptoms in the interpretation of ambiguous information.

Method: Seventy participants underwent a laboratory controlled manipulation either of social ostracism or of overinclusion. Participants completed a computerized task that measured both direct and indirect interpretation bias and reported their level of depression symptoms.

Results: The findings show that ostracism enhanced interpretation bias when symptom levels were higher, while overinclusion did not. This interaction effect between social ostracism and symptom level was found both for direct and for indirect interpretation bias.

Conclusion: Whereas previous research showed the existence of interpretation bias among people with symptoms of depression, the present study expands previous knowledge by shedding light on the conditions under which interpretation bias emerges, suggesting that ostracism enhances negative interpretation of ambiguous information when levels of depression symptoms are higher.

Keywords: interpretation bias, ostracism, depression, Cyberball task, social cognition, cognitive bias

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *20 November 2021*
Accepted: *03 January 2022*
Published: *07 February 2022*

Citation:
Bar-Sella A, Richter T, Zilcha-Mano S and Okon-Singer H (2022) How Social Experiences Affect Interpretation Bias Among Individuals With Non-clinical Depression: The Role of Ostracism. Front. Psychiatry 13:819143. doi: 10.3389/fpsyt.2022.819143

INTRODUCTION

Our perceptions of reality can be highly subjective and can change as our experiences change. When these experiences are negative, we may interpret information in a negative manner, regardless of its objective manifestation. Beck and Clark (1) defined this tendency as *interpretation bias*: the tendency to selectively interpret ambiguous information in a negative manner. Interpretation bias has been widely studied in sub-clinical and clinical populations and found to be highly related to mental disorders such as depression (2, 3). Accumulating evidence shows that individuals with symptoms of depression, even sub-clinical populations, tend to

systematically interpret ambiguous information in a negative manner (2, 4). This association has been replicated in a large number of studies and was found to have a medium effect size, as revealed in a recent meta-analysis (4). Yet, while the existence of interpretation bias among individuals with symptoms of depression is well-established, little is known about the conditions under which this maladaptive cognitive performance may be enhanced.

Theoretical knowledge suggests that external events such as social experiences may enhance interpretation bias among individuals with depression symptoms (5). According to these theories, individuals who exhibit symptoms of depression process information through latent negative cognitive schemas (5). Cognitive schemas, which are defined as internally stored representations of stimuli, ideas, or experiences (6), constitute the central structure in information processing, through which the individual unconsciously grants meaning to new information. When depressed individuals undergo adverse experiences, their negative cognitive schemas are activated and guide their interpretation of the situation, consequently reinforcing negatively biased forms of interpretations (i.e., "She doesn't wave back at me because she doesn't like me, I am so faulty, why should she like me"). One negative experience that may affect interpretation among individuals with depression symptoms is social ostracism (7). Social ostracism is considered aversive and stressful since it interferes with the individual's sense of belongingness, a major motivation defined as a universal human need (7, 8). Moreover, a recent meta-analysis revealed that ostracism can have an aversive and stressful impact on various psychological conditions (interpersonal, e.g., aggressive behavior, and intrapersonal, e.g., self-esteem). This impact has a large effect size (9).

Beyond the extensive effect of ostracism in the general population (9), studies suggest that ostracism may be especially aversive for individuals who exhibit symptoms of depression [e.g., (10)]. These individuals have been found to be highly sensitive to external cues of rejection (10) and to exhibit extensive concern about being rejected [e.g., (11)]. Corresponding with Beck's theory of cognitive schemas (5), a recent study suggests that sensitivity to ostracism may be partially explained by the interaction of external cues with schema-congruent information processing [i.e., a friend who doesn't wave back reinforces the person's internal belief about being faulty and unlovable; (12)]. This information is instrumental in demonstrating the sensitivity of individuals with symptoms of depression to ostracism. Yet whether the interaction between actual cases of ostracism and symptoms of depression plays a causal role in interpretation bias has yet to be examined.

Therefore, the main aim of the current study was to investigate the potential effect of ostracism on the interpretation of ambiguous information among individuals with depression symptoms. We hypothesized that ostracism, as opposed to other social experiences such as overinclusion, would lead to greater interpretation bias among individuals with high levels of depression symptoms. To examine the effect of social experience, we used a lab-controlled paradigm that manipulated ostracism and overinclusion (13). This paradigm enabled us to compare ostracism to another social experience in which the participant may feel conspicuous and self-aware *but not ignored or excluded* [i.e., overinclusion; (13)]. After undergoing the social manipulation, participants completed a computerized interpretation task that measured both direct (i.e., overt selection among two possible interpretations of an ambiguous sentence) and indirect [i.e., reaction time (RT)] selection of interpretation. Participants also reported their level of depression symptoms over the last week, thus enabling us to examine how the interaction between ostracism and depression symptoms affects interpretation bias.

METHOD

Participants

Seventy-one participants took part in the current study. One participant was removed from the analysis because of a lack of self-report measures due to technical problems. Power analysis using G*POWER software [version 3.1.9.7; (14)] confirmed that a sample size of 70 participants, alpha of 5% and medium effect size ($f^2 = 0.15$), provided sufficient power (Power = 0.89) to conduct the study's analysis. Since ostracism has been found to affect men and women differently [e.g., (15)], only female participants took part in the study. Participants were students at the University of Haifa between the ages of 18 and 39 ($M = 24.41$, $SD = 3.15$). All were native speakers of Hebrew. Participants signed an informed consent form prior to participation and were debriefed at the end of the experiment. They received monetary compensation or course credit in exchange for their participation. They were randomly assigned by GraphPad software (16) to one of the two experimental social conditions: ostracism or overinclusion. The study was approved by the local ethics committee (approval no. 385/17).

Materials

Social Experience (Ostracism/Overinclusion)

Social experience was manipulated using the Cyberball game, a computerized ball tossing game (13). The manipulation was conducted in line with the work of Zadro et al. (17), such that participants were misled to believe they were playing simultaneously with two other participants sitting in different rooms. In both conditions, the game lasted for 30 ball tosses. In the ostracism condition, participants obtained the ball only three times at the beginning of the game, while in the overinclusion condition they obtained the ball 15 randomly distributed times, more than any other "participant" in the game. We checked the manipulation in line with Zadro et al. (17): Participants reported the percent of throws they obtained in the game and used a 5-point scale to rate the level at which they believed they were included and/or ignored during the game.

Interpretation Bias

Interpretation bias was measured by the interpretation task used by Richter et al. (18); for a graphical description of a typical trial in the task, see **Figure 1**. The task is a modification of the Word Sentence Association Paradigm [WSAP; (19, 20)], and was previously validated in Hebrew in subclinical (18) and

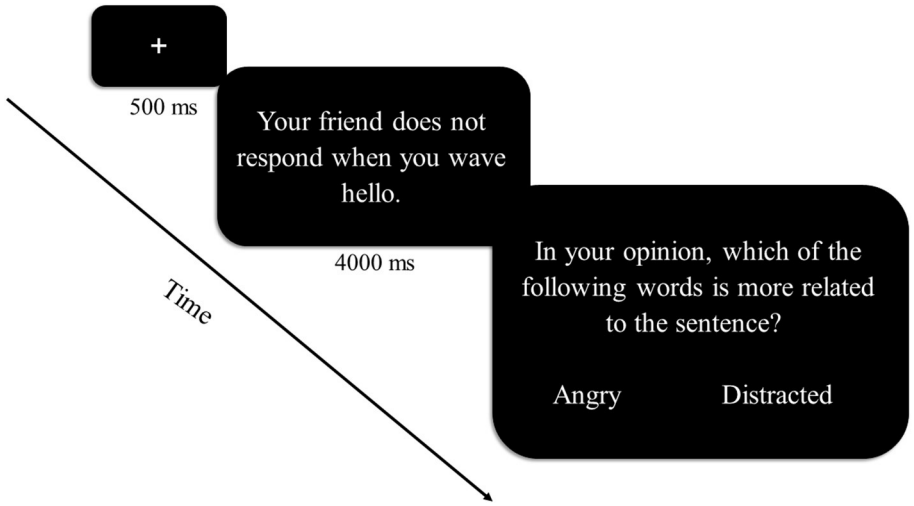

FIGURE 1 | Sequence of a typical trial in the interpretation task. The sequence of a typical trial in the interpretation task is represented graphically. On each trial, a fixation point is followed by an ambiguous sentence describing a situation in which another person is involved. Participants are instructed to imagine themselves in the described situation. Each sentence is followed by negative and benign associative words that may be related to the sentence. Participants are asked to choose, as rapidly as possible, which word they believe is more related to the sentence.

clinical (21) samples of depression [for a detailed description of task validation please see (18)]. In this task, participants were shown 40 ambiguous sentences that appeared on the screen one at a time. Participants were instructed to try to imagine themselves in the described situations. All sentences described situations in which another person is involved. Each sentence was followed by presentation of negative and benign associative words related to the ambiguous sentence (e.g., "A friend has not returned your call" "busy/dodging"). Participants were asked to choose, as rapidly as possible, which word they believe is more related to the sentence. Four sentences were given at the beginning of the task as practice trials. For each participant, we calculated the percentage of selecting negative interpretations and the RT for selecting negative or benign interpretations. A *higher* percentage of negative interpretation selections, *lower* RTs for selecting *negative* interpretations and *higher* RTs for selecting *benign* interpretations are considered to be indicators of greater negative interpretation bias.

Depression Symptoms

Levels of depression symptoms were measured by the Depression and Anxiety Stress Scales [DASS-21; (22)]. The DASS-21 is a self-report questionnaire used to assess symptomatic levels of depression, anxiety and stress. The depression subscale consists of seven items, each rated on a 4-point scale. Participants reported their level of symptoms during the past week. Cronbach's alpha for internal consistency in the current sample was 0.85.

Procedure

After signing a consent form, participants were told they were going to play an internet game known as Cyberball with two other participants playing in two different rooms. Participants then played the Cyberball game and subsequently completed the interpretation task. After that, participants completed the manipulation check and the DASS-21 questionnaire. To better characterize the sample, participants answered demographic questions, including country of origin, years of education, age, use of psychiatric medications and previous or current psychiatric diagnosis. The entire experimental procedure lasted about 30 min. At the end of the experiment, participants were debriefed and told that ostracism was part of the experiment (if they were in the ostracism condition).

Data Analysis

Direct Measurement of Interpretation Bias (Model 1)

To examine the moderation effect of social experience (ostracism/overinclusion) on the association between levels of depression symptoms and interpretation bias, we conducted a two-step hierarchical regression on the direct measurement (i.e., selection of negative/benign interpretation). Levels of depression symptoms and social experience (ostracism/overinclusion) were entered into the regression as main effects in the first step, their interaction was entered in the second step, and the percentage of selecting negative interpretations was entered as the outcome.

Indirect Measurement of Interpretation Bias (Model 2–3)

Additional models focusing on indirect measures (i.e., selection RT) were further used to examine the moderation effect of social experience (ostracism/overinclusion) on the association between levels of depression symptoms and interpretation bias. Two models were conducted, one with mean RTs for selecting *negative* interpretations as an outcome (Model 2) and the other with mean RTs for selecting *benign* interpretations as an outcome (Model 3). Trials in which the RT measurement was above

TABLE 1 | Descriptive statistics of depression symptoms and interpretation, by condition (ostracism/overinclusion).

	Ostracism			Overinclusion		
	Mean	**Std**	**Range**	**Mean**	**Std**	**Range**
Depression Symptoms	9.6	9.2	0.0–36.0	7.5	6.6	0.0–26.0
Percent of Selection of Negative Interpretation	30.6	14.6	08.0–60.0	28.9	12.9	0.0–63.0
RT for Selection of Negative Interpretation	2441.3	1047.1	1105.3–4934.5	1937.8	675.5	614.6–3811.1
RT for Selection of Benign Interpretation	1972.4	713.9	997.0–4401.1	1681.5	523.5	564.2–3042.3

N = 70. RTs are shown in milliseconds.

or below 2.5 standard deviations from the participant's mean RT were considered outliers and eliminated from the data. Nevertheless, even after cleaning RT outliers, fewer than 3% of each participant's total trials were eliminated.

Regression models were selected for the study's analysis in line with the statistical recommendations of Leppink (23).

RESULTS

Manipulation Check

A series of *T*-tests indicated that the manipulation was effective. Participants in the ostracism condition reported feeling less included $\{t_{(56,\ 33)} = 14.15,\ p = 0.001$, Cohen's $d = 6.22$, 95% CI [3.01, 3.51]$\}$ and more ignored during the game $\{t_{(61,\ 42)} = 25.99, p = 0.001$, Cohen's $d = 3.38$, 95% CI [2.40, 3.19]$\}$ than participants in the overinclusion condition. Additionally, they reported obtaining fewer ball tosses during the game $\{t_{(41,98)} = -10.88, p = 0.001$, Cohen's $d = 2.60$, 95% CI [−38.78, −26.65]$\}$.

Descriptive Statistics and Pre-analysis Tests

Table 1 shows the descriptive statistics for symptoms of depression and direct and indirect interpretations in the two condition groups (ostracism/overinclusion). No between-group differences were observed in levels of depression symptoms $[t_{(68)} = 1.10, p = 0.273]$.

Direct Measurement of Interpretation Bias

Model 1

The entire model was significant in predicting the percentage of selecting the negative interpretation $[F_{(3,66)} = 12.61, p = 0.0001$, Adjusted $R^2 = 0.33]$. Levels of depression symptoms significantly and positively predicted the percentage of selecting the negative interpretation ($\beta = 0.52$, $p = 0.000$, 95% CI [0.04, 0.10]). Social experience (ostracism/overinclusion) by itself was not found to predict the percentage of selecting the negative interpretation ($\beta = 0.06$, $p = 0.540$, 95% CI [−0.02, 0.03]). In contrast, the social experience × depression symptoms interaction significantly predicted the percentage of negative interpretation selection (β =0 0.31, $p = 0.003$, 95% CI [0.01, 0.07], R^2 change = 0.094).

To better understand the interaction, we conducted two simple regressions that examined prediction of percentage of negative interpretation selection by levels of depression symptoms under the different social conditions (ostracism/overinclusion; see **Figure 2**). The regressions revealed that among individuals in the ostracism condition, levels of depression symptoms significantly and positively predicted percentage of negative interpretation selection ($\beta = 0.78$, $p = 0.000$, 95% CI [0.08, 0.1]; **Figure 2A**). In contrast, among individuals in the overinclusion condition, depression symptoms did not predict the percentage of negative interpretation selection ($\beta = 0.22$, $p = 0.196$, 95% CI [−0.02, 0.07]; **Figure 2B**). These results suggest that higher levels of depression symptoms predict higher levels of directly measured interpretation bias under conditions of ostracism but not under conditions of overinclusion.

Indirect Measurement of Interpretation Bias

Model 2

The entire model was significant in predicting mean RTs for selecting a negative interpretation $[F_{(3,65)} = 4.78$, $p = 0.005$, Adjusted $R^2 = 0.14]$. Levels of depression symptoms did not predict the mean RTs for selecting a negative interpretation ($\beta = -0.08$, $p = 0.454$, 95% CI [−282.57, 127.77]). In contrast, the social experience condition (ostracism/overinclusion) significantly and positively predicted mean RTs for selecting a negative interpretation ($\beta = 0.28$, $p = 0.015$, 95% CI [50.07, 456.63]): Participants in the ostracism condition selected a negative interpretation of ambiguous information faster than did participants in the overinclusion condition. Moreover, the social experience × depression symptoms interaction significantly predicted mean RTs for negative interpretation selection ($\beta = -0.31$, $p = 0.007$, 95% CI [−489.23, −78.89], R^2 change = 0.096).

To better understand the interaction, we conducted two simple regressions that examined prediction of mean RTs for selection of a negative interpretation by levels of depression symptoms under the different social conditions (ostracism/overinclusion; see **Figure 3**). The regressions revealed that among individuals in the ostracism condition, levels of depression symptoms significantly and positively predicted the mean RTs for selection of a negative interpretation ($\beta = -0.34$, $p = 0.042$, 95% CI [−709.49, −13.42]; **Figure 3A**). In contrast, among individuals in the overinclusion condition, depression symptoms did not predict the mean RTs for selection of a negative interpretation ($\beta = 0.31$, $p = 0.07$, 95% CI [−22.19, 435.51]; **Figure 3B**). These results suggest that higher levels of

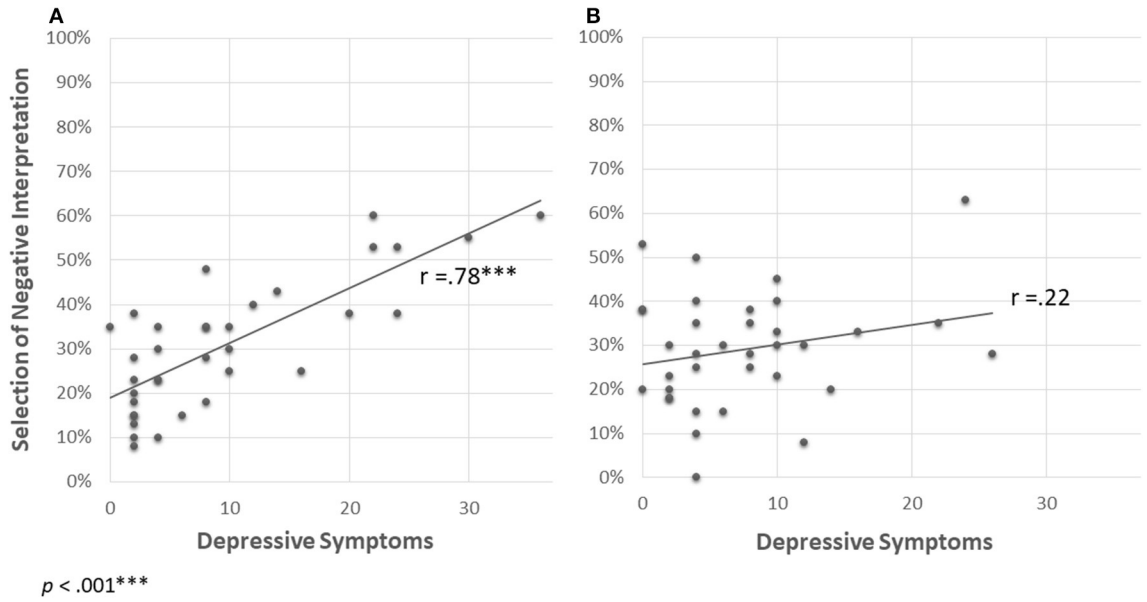

FIGURE 2 | Prediction of selecting negative interpretation by levels of depression symptoms in each social experience condition [**(A)** ostracism, **(B)** overinclusion].

depression symptoms predict higher levels of interpretation bias, as measured by indirect measurements after experiencing ostracism but not after experiencing overinclusion.

Model 3

Levels of depression symptoms, social experience (ostracism/overinclusion) and their interaction were not found to be predictors of mean RTs for selecting benign interpretations [$F_{(3,66)} = 2.15$, $p = 0.102$].

DISCUSSION

Given the role of interpretation bias in the etiology and maintenance of depression (2), it is especially important to understand *under which conditions* interpretation bias may emerge. The present findings suggest that social experiences contribute to interpretation bias. Specifically, ostracism—though not overinclusion—results in more and faster selection of *negative* interpretations of ambiguous social situations among individuals with higher levels of depression symptoms. Thus, when individuals with more intense symptoms of depression are socially ostracized, they are likely to interpret ambiguous situations in a negative manner more frequently and quickly than individuals who exhibit less intense symptoms of depression. These findings are consistent with theoretical knowledge, according to which social experiences may increase interpretation bias (5). These findings are also consistent with a previous study showing that greater sensitivity to ostracism is related to higher levels of depression symptoms and greater interpretation bias (24). Yet, whereas previous research contributed to understanding the aforementioned association, the present study expands previous knowledge by suggesting that ostracism enhances more negative interpretations of ambiguous information when levels of depression symptoms are higher. In line with Beck's theory of cognitive schemas (6), it is possible that among individuals with high levels of depression symptoms, social ostracism confirms latent negative cognitive schemas, which in turn increase their negative interpretations.

Replicating previous studies (4), the present findings suggest that levels of depression symptoms predict the selection of negative interpretations, such that higher levels of symptoms predicted a greater tendency to select negative interpretations. Yet whereas ostracism led to greater and faster selection of negative interpretations when levels of depression symptoms were higher, it did not affect RTs for the selection of *benign* interpretations. Additionally, levels of depression symptoms were not found to predict RTs for the selection of either negative or benign interpretations. This inconsistency between the direct and indirect measurements corresponds to the findings of previous studies that used indirect measurements of interpretation bias [i.e., (25)]. These studies showed interpretation bias in RTs for selection of negative but not of benign interpretations. This inconsistency is also in line with the findings of reviews [i.e., (26)] and meta-analyses [i.e., (4)] suggesting that the association between symptom levels and interpretation bias using direct measurements is consistent across studies, whereas the association between symptom levels and interpretation bias using indirect measurements yields mixed results.

The role of interpretation bias in the maintenance of depression symptoms has been emphasized and targeted across a variety of psychological treatments [i.e., Interpretation Bias Modification—(27); Cognitive Behavioral Therapy—(28); and psychodynamic therapy—(29)]. While these treatment orientations use different therapeutic interventions, they all invest major efforts in converting patients' maladaptive interpretations to more adaptive ones. By highlighting the effect of social ostracism on interpretation bias, the present findings

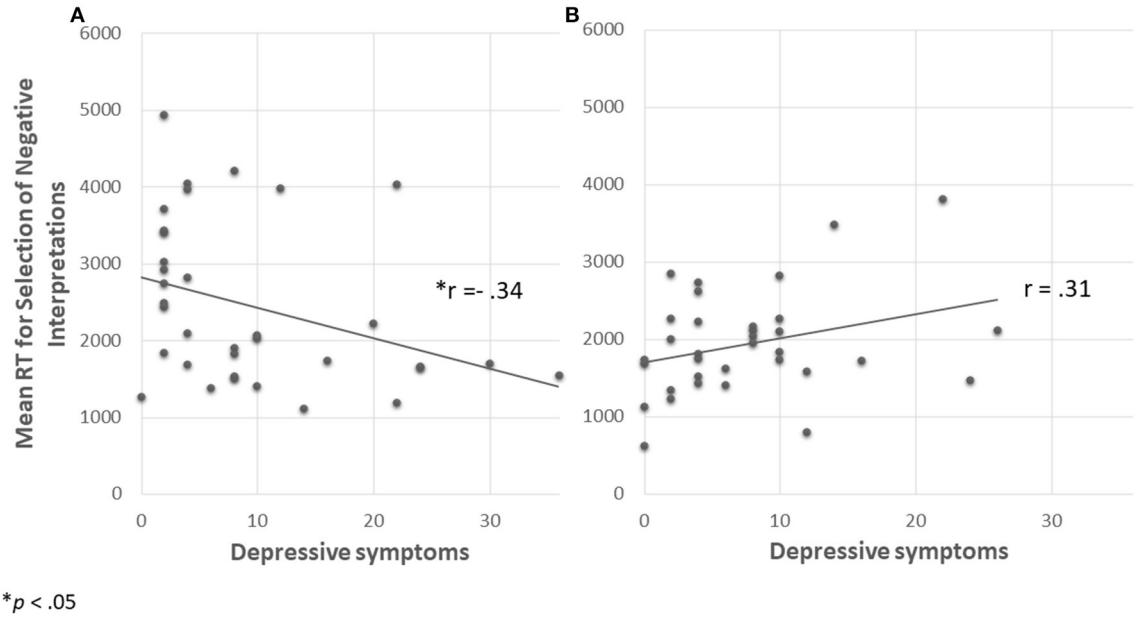

FIGURE 3 | Mean RTs for selection of negative interpretation predicted by depression symptoms in each social experience condition [**(A)** ostracism, **(B)** overinclusion] Note that participants with higher depression symptoms selected negative interpretations faster in the ostracism than in the overinclusion condition.

add to accumulating knowledge regarding the possible factors by which interpretation bias maintains a depressive state [i.e., (30)]. Such knowledge may be utilized to treat individuals with depression symptoms by increasing the focus on maladaptive interpretations among patients reporting social ostracism.

The present findings also add to the accumulating literature on cognitive biases in psychiatric disorders and states, and particularly in depression [see (31), for elaboration]. Individuals with depression symptoms exhibit evidence of biased attention, interpretation, expectancy and memory (18). Beyond examining whether biased cognitions exist in psychiatric disorders, research has also placed emphasis on understanding the causal relations among cognitive biases [e.g., the effect of manipulated expectancies on participants' attention bias; (33)] and the relationships between the factors moderating cognitive biases [e.g., (32, 33)]. Studies also seek to use accumulating knowledge regarding cognitive biases to improve diagnosis of psychiatric disorders [e.g., see (18, 21) for an example of a diagnostic support system based on cognitive performance aimed at better differentiating between depression and anxiety diagnoses]. By shedding light on the interactive role of depression symptoms and aversive social experiences in the emergence of interpretation biases, the present study contributes to knowledge regarding the possible moderators of cognitive biases.

This study has several limitations. First, the examination was restricted to women, leaving open the question of whether and how the combined effect of depression symptoms and social experience (ostracism/overinclusion) may affect interpretation bias among men. The present study also examined levels of depression symptoms as distributed in the general population, whereas the findings may be different in a clinical sample. In addition, the present study used overinclusion as a control condition and not the more common inclusion condition (33% ball tosses for each "participant"). It is possible that the study's results would be different when using other control conditions. Additionally, overinclusion may not necessarily be a positive experience for everyone (34). Therefore, future studies should examine the combined effect of depression symptoms and social experience on interpretation bias among both men and women, while also considering clinical levels of depression symptoms and controlling for complicated feelings that may raise under conditions of overinclusion. Furthermore, the study's design does not allow us to infer whether the interaction between depression symptoms and ostracism directly affects interpretation bias or whether this effect is mediated by other factors, such as negative feelings or schemas elicited by ostracism. Future studies should further examine this issue.

The present findings highlight the importance of examining how social experiences such as ostracism interact with depression symptoms in order to understand the conditions under which interpretation bias may emerge. By doing so, the current research broadens our understanding regarding the role of interpretation bias in the maintenance of depression symptoms. Such an understanding may be utilized in the future to develop treatments tailored to each individual's cognitive biases and personal experiences.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee, School of Psychological Sciences, University of Haifa, Israel. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AB-S ran the research, analyzed the data, and wrote the first draft of the manuscript. HO-S initiated and supervised the study. TR participated in the design, data analysis, and writing. SZ-M advised in the process of designing and implementing the study. All authors participated in the design and planning of the study and approved the final manuscript.

FUNDING

This research was supported by a grant from the Ministry of Science & Technology, Israel, Ministry of Europe and Foreign Affairs (MEAE) and the Ministry of Higher Education, Research and Innovation (MESRI) of France awarded to HO-S.

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frontiers in Psychiatry

PERSPECTIVE
published: 10 March 2022
doi: 10.3389/fpsyt.2022.797952

The Transdiagnostic Relevance of Self-Other Distinction to Psychiatry Spans Emotional, Cognitive and Motor Domains

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Self-other distinction refers to the ability to distinguish between our own and other people's physical and mental states (actions, perceptions, emotions etc.). Both the right temporo-parietal junction and brain areas associated with the human mirror neuron system are likely to critically influence self-other distinction, given their respective contributions to theory of mind and embodied empathy. The degree of appropriate self-other distinction will vary according to the exact social situation, and how helpful it is to feel into, or remain detached from, another person's mental state. Indeed, the emotional resonance that we can share with others affords the gift of empathy, but over-sharing may pose a downside, leading to a range of difficulties from personal distress to paranoia, and perhaps even motor tics and compulsions. The aim of this perspective paper is to consider how evidence from behavioral and neurophysiological studies supports a role for problems with self-other distinction in a range of psychiatric symptoms spanning the emotional, cognitive and motor domains. The various signs and symptoms associated with problematic self-other distinction comprise both maladaptive and adaptive (compensatory) responses to dysfunction within a common underlying neuropsychological mechanism, compelling the adoption of more holistic transdiagnostic therapeutic approaches within Psychiatry.

Keywords: empathy, social cognition, self-other distinction, Tourette syndrome, obsessive-compulsive disorder, schizophrenia, autism, personality disorder

OPEN ACCESS

Edited by:
Frieder Michel Paulus,
University of Lübeck, Germany

Reviewed by:
Benjamin Straube,
University of Marburg, Germany
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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *19 October 2021*
Accepted: *14 February 2022*
Published: *10 March 2022*

Citation:
Eddy CM (2022) The Transdiagnostic Relevance of Self-Other Distinction to Psychiatry Spans Emotional, Cognitive and Motor Domains. Front. Psychiatry 13:797952. doi: 10.3389/fpsyt.2022.797952

INTRODUCTION

What Is Self-Other Distinction and Why Is It Important?

Humans are innately wired to respond to others' emotional states. Most of us understand what it is to vicariously feel other's pain, and if we are lucky, their happiness. This emotional resonance that we can share with others appears automatic, and its greatest gift is that of affective empathy and our ability to respond sensitively to the needs of others. However, successful navigation of the social world also requires that we can contemplate the contrasting perspectives of self and other, and too much sharing may have a downside.

Self-other distinction refers to the ability to distinguish between our own and other people's physical and mental states, including actions, perceptions, emotions etc. Low self-other distinction (or self-other blending/merging) is associated with processes that contribute to the recognition

TABLE 1 | Self-other distinction and two approaches to social cognition.

Mirroring	Mentalizing
Embodied: external focus of attention	Abstract: internal focus of attention
Relies on non-linguistic cues (expression/tone)	Can rely on linguistic cues
Innate, more automatic	Develops in childhood, more effortful
Concrete: mental states must be directly inferred from action	Theoretical: accommodates unobservable mental states
Motion, emotion	Cognition
Reflexive/reactive—lower self control	Calculating/reasoning—higher self control
Emotion contagion, affective empathy	Cognitive empathy, theory of mind
Observer resonates with and becomes one with the externally perceived other: sense of a separate self is momentarily lost (low self-other distinction)	Observer actively constructs imaginary representation of other within the larger construct of the self: maintaining separate self (higher self-other distinction)

of mental states in others including imitation or mirroring. However, low self-other distinction can be associated with misattributions of mental states when these differ for self and other, a situation when abstract mentalizing that holds in mind these opposing perspectives is important. Mirroring tends to occur in response to visual stimuli and for embodied mental states, whereas mentalizing is critical when visual cues to mental states are potentially misleading or not readily observable (e.g., verbal tasks; understanding beliefs; deception etc.). The appropriate degree of self-other distinction will therefore vary according to the exact social situation e.g., affective empathy may involve low self-other distinction, whereas understanding false belief requires higher self-other distinction (**Table 1**).

Which Brain Regions Contribute to Self-Other Distinction?

One neural network highly relevant to self-other distinction is the Mirror Neuron System [MNS: (1)] which was first identified in primates (2–4). The MNS is thought to underpin motor simulation of observed actions, providing a basis for imitation, and to draw upon visual cues to support the understanding of action goals [e.g., (5, 6)], in turn facilitating inferences about emotions, and perhaps beliefs and intentions (7, 8), although its exact contribution to empathy continues to be investigated (9). In humans, the MNS includes the inferior frontal gyrus (BA44/45), superior temporal and inferior parietal lobe (10–12). This network develops very early in childhood (13), and may be automatically activated before the second network, the mentalizing system (14, 15), which includes the medial prefrontal cortex, precuneus, and right temporal parietal junction (rTPJ). The mentalizing network supports more conscious reasoning about mental states (15, 16).

The rTPJ is of particular importance in self-other distinction, given its role in multi-sensory integration and sense of embodiment (17), and activation during tasks where the differing beliefs of self and other are salient (18, 19). Further evidence comes from the effects of rTPJ stimulation on tasks that require self-other distinction such as imitation inhibition tasks (20–22). Most studies suggest that rTPJ activity is positively associated with self-other distinction (8), such that activations may emphasize incongruence between self and other, or allow for switching between their related representations [e.g., (23)].

What Might Happen If Self-Other Distinction Goes Wrong?

Within the social cognitive domain, indicators of low self-other distinction include motor imitation, and emotion contagion, when we effectively take on the physical and emotional states of others. These acts of mirroring encourage the automatic sacrifice of a sense of separate self as the observer becomes one with the perceived other. This loss of self-other distinction could be less likely to occur in the context of mentalizing, which may involve the conscious and controlled construction of an imaginary other (or alternative self) perhaps subordinate to and easily distinguishable from the one's true self. In sum, sense of oneself as a unique individual entity, and as the originator or controller of perceived internal and external states (e.g., actions and emotions), may be vulnerable to the effects associated with loss of self-other distinction and the mirroring experience. On the other hand, in some cases, too much self-other distinction could be problematic.

The aim of this perspective paper is to synthesize the evidence suggesting that problems with self-other distinction are relevant to the development of numerous psychiatric disorders, building on previous research (8, 17) through the integration of additional evidence in the form of both behavioral and neurophysiological studies within the field of psychiatry. While many factors may influence self-other distinction (e.g., executive dysfunction; self-efficacy; sensory impairments), this opinion piece focuses on processes that are typically associated with mirroring, with reference to the contrast with conscious mentalizing. Key questions were: 1. Is it possible to identify primary (direct) vs. secondary (indirect) signs of problematic self-other distinction? 2. Are there secondary signs with opposing/compensatory effects? I will argue that a range of clinical symptoms across emotional, cognitive and motor domains constitute various manifestations of impaired self-other distinction, resulting from dysfunction within a common underlying neural mechanism, with important implications including in terms of treatment approaches.

RELEVANCE OF SELF-OTHER DISTINCTION TO PSYCHIATRY

Self-Other Distinction Within the Emotional Domain

The primary cause of loss of self-other distinction within the emotional domain is likely to be high emotion contagion. MNS responses are emotion specific and more sensitive to negative valence (24, 25), therefore excessive resonance with others experiencing negative emotion is likely to result in increased personal distress. High personal distress is common in psychiatric disorders but is not usually accompanied by high

empathic concern (**Table 2**). Perhaps continued experience of personal distress can prove aversive, leading individuals to self-report lower empathic concern as they become more focused on resolving their own internal emotional state. The unpleasantness of excessive emotional resonance could also contribute to social anxiety and social anhedonia (8). Furthermore, the relationship between performance on social cognitive tasks and emotional resonance may fall on an inverted U-curve helping to explain patterns of social cognitive performance (e.g. inconsistent impairment across tasks) in numerous psychiatric disorders (8, 17).

Frequent unregulated emotional contagion may encourage confusion around the source (self/other) of experienced emotional states. Alexithymia (286), or difficulty identifying and expressing emotions, could be one consequence of this confusion stemming from vicarious experience of other's emotions in the absence of a linking situational cause for that emotion in oneself (8). However, alexithymia could indicate reduced attention to internal states which in turn reduces the salience of excessive emotional resonance or personal distress (8, 287). Other forms of emotional blunting (e.g., constricted/flat affect), and perhaps dissociation, could support similar regulatory functions in terms of avoiding exposure to problematic emotions of self and/or other. Such emotional responses may be largely unconscious conditioned responses to the primary problem of loss of self-other distinction within the emotional domain.

Some psychiatric disorders feature anti-social behaviors which should prompt an emotional reaction in others, such as the compulsive socially inappropriate urges seen in Tourette syndrome (TS). TS is associated with heightened personal distress and increased emotional reactivity to emotional facial expressions (26, 36), and patients who experience urges to make offensive remarks/gestures find them troubling as they don't consciously wish to cause distress (288). On the surface, socially inappropriate actions imply emotional disregard, and emphasize self-other distinction because the patient's transgression is in direct antagonism to the others' emotional needs (8) i.e., the anti-social action (at least momentarily) separates the perpetrator from the victim because the intention and action goals associated with their anti-social act conflict with the desired mental state of the victim. However, in addition to counteracting any feeling of excessive emotional resonance, such actions promote control over the emotional state of others. Therefore, rather than emphasizing self-other distinction, anti-social urges could arise from an unconscious urge to prompt a negative emotional mental state within another that matches the patient's own negative internal state (i.e., reduced self-other distinction). This may provide a better explanation for some emotionally provocative and antagonistic behaviors seen in Borderline Personality Disorder (BPD) and Narcissistic Personality Disorder (NPD).

Self-Other Distinction Within the Cognitive Domain

Excessive emotional resonance with others and arising difficulties with self-other distinction could have a broader effect on conscious experience of cognitive mental states including judgments about the origin of these. Difficulty knowing whether a thought or intention arose from the self explains many symptoms of psychosis [e.g., (155)] including delusions relating to thought transfer and telepathy. Incorrect assumptions that one is aware of the cognitive mental state of another could also reduce mentalizing leading to egocentric errors (289). Projection of negative emotions or intentions onto others, as seen in disorders such as BPD and schizophrenia (including on social cognitive tasks: **Table 2**), is likely to prompt social anxiety and paranoia. If a projected thought is positive, it could encourage grandiosity. Doubts about whether thoughts are internally generated may also underlie magical thinking as seen in Obsessive-compulsive Disorder (OCD), explaining the association between negative sense of agency and likelihood thought action fusion (287) i.e., the belief that thinking about events makes those events more likely to happen.

In some cases, loss of self-other distinction may weaken the stability of our overall conscious construct of self, as most clearly seen in BPD and schizophrenia. When this occurs, it appears all the more important to develop cognitive strategies that help restore self-other boundaries. Strategies are likely to include conscious avoidance of mentalizing, helping to explain the low self-reported perspective taking that often accompanies high personal distress (**Table 2**), and perhaps poor performance on social cognitive tasks. In addition, impulsive non-conformity, whereby individuals with schizophrenia express strong opposition to convention and the opinions or expectations of others, even where this would seem harmful or irrational, may enhance cognitive self-other distinction. Similar characteristics can be seen in NPD, where rivalry and entitlement emphasize one's own uniqueness, and deception may be used to maintain differentiation between the cognitive mental states of self and other (152).

Self-Other Distinction Within the Motor Domain

Excessive motor resonance in the form of echophenomena is likely to indicate loss of self-other distinction within the motor domain. Similar more subtle characteristics may be observed during imitation inhibition tasks, through magnetoencephalography, or perhaps when exploring susceptibility to the rubber-hand illusion (**Table 2**). Given the role of the MNS in emotion contagion there is likely to be a link between motor resonance and neural limbic response [e.g., (290, 291)], and therefore greater motor resonance and a tendency to emotional dysregulation (although MNS activity may not always manifest as observable movement). Difficulties in deciding whether the self is the agent of movements and related sensory events could help to explain the perception of involuntary movements, and perhaps depersonalization, in some psychiatric disorders. Weakened sense of ownership of personal actions could encourage impulsivity, and in more severe cases, delusions of control.

One proposed mechanism thought to influence self-other distinction is based on movement efference and predictive sensory feedback [e.g., (292, 293)], whereby dysfunction

TABLE 2 | Evidence for problems with self-other distinction in psychiatric disorders.

Domain	Symptom/sign	Disorder	Study findings
Emotional	Emotion contagion*	TS	Heightened neural response to facial expressions (26, 27)
		SZ	Higher than HCs (28). Empathizing v systematizing bias associated with paranoia (29)
		OCD	Higher emotional response to observed emotions (30)
		ASD	Can be lower than HC but influenced by target familiarity and eye gaze (31). Emotion contagion for pain is intact (32)
		BPD	Higher that HCs (33) with one study showing this using EMG while patients viewed negative facial expressions (34)
		NPD	Mix of no difference/lower self-report in association with grandiose subtype traits in non-clinical sample (35)
	Personal distress	TS	Higher personal distress (but lower IRI perspective taking) than HCs (36)
		SZ	Higher personal distress (but lower IRI perspective taking) than in controls (37). Personal distress positively related to symptoms (38)
		OCD	Higher personal distress than HCs (39) and lower perspective taking (40)
		ASD	Higher personal distress than HCs (41). Autistic traits linked to high personal distress in general population (42)
		BPD	Higher personal distress than HCs (43–47)
		NPD	High personal distress in covert/vulnerable narcissism (48, 49)
	General emotion dysregulation	TS	Correlates with tic severity (50), high in more complex cases (51)
		SZ	Overwhelming/lack of control over emotions (28); mediates symptom expression (52, 53)
		OCD	Heightened affective responses and poor emotion regulation, but perhaps lower motor resonance (54)
		ASD	High levels in autism (55–57) and Asperger's (58)
		BPD	Low cognitive empathy in high vs. low borderline traits, associated with emotional dysregulation (59)
		NPD	Rivalry (60) and vulnerable narcissism associated with more problems vs. grandiose (35, 61–63)
	Social anxiety/ social anhedonia	TS	Higher social anxiety than HC (64). Attentional bias toward social threat (65)
		SZ	Linked to perception of negative valence in facial expressions (66, 67) and empathy/emotion contagion (68)
		OCD	Higher social anxiety than HC (69). Linked to altered activity in right STG (70)
		ASD	Both seen in adults (71); social anxiety in adolescents (72); social anhedonia correlates with autism severity (73)
		BPD	High social anxiety in clinical sample (74) and associated with traits (75)
		NPD	More likely in vulnerable narcissism (76)
	Alexithymia†; flat/ constricted affect	TS	May be related to strength of sensory urges to tic (77, 78)
		SZ	Difficulty describing and identifying feelings (79). Flat affect related to ToM tasks (80), despite heightened automatic sensitivity to facial affect (81), increased amygdala reactivity (82) and altered IPL activity (83)
		OCD	Higher alexithymia than HCs (84, 85) and more blunted affect (69). Associated with mental neutralizing (86) and suicide risk (87)
		ASD	High alexithymia (88) associated with emotional dysregulation (56). Reduced facial expression in children (89, 90)
		BPD	Higher alexithymia than HCs (46, 91–94). Linked to non-suicidal self-injury (95). Less facial expression of emotion (96)
		NPD	Seen in clinical and non-clinical samples and associated with empathy (97–99)
Cognitive	Misattribution of origin of mental states i.e., projection; paranoia; hyper-mentalizing	TS	Projection could explain performance on ToM tasks (77, 100). Some paranoid thoughts more common than in HC (101, 102)
		SZ	Projection could explain performance on ToM tasks e.g., attributions of mental states to non-social stimuli [e.g., (103)] and neutral expressions appearing negative (104). Hyper-mentalizing errors (105) including self-referential hyper-mentalizing in schizotypy (106)

(Continued)

TABLE 2 | Continued

Domain	Symptom/sign	Disorder	Findings/specific observations
		OCD	Paranoia associated with OCD symptoms in non-clinical (107) and clinical (69, 108) samples. Hoarding associated with anthropomorphising (109)
		ASD	Autistic traits associated with anthropomorphising (110, 111). Characteristics linked to paranoia (112, 113) and persecutory ideation (58) can present
		BPD	Projection and projective identification (114). Paranoia (115) including more severe non-delusional paranoia than SZ (116)
		NPD	Paranoia associated with low mood (117), rejection sensitivity (118) and the proposed diagnosis of malignant narcissism (119, 120)
	Difficulty with self (i.e., coherent, stable self concept)	TS	Lower self-concept reported in TS (121) or TS+OCD (64) although measures seem closely related to self-esteem
		SZ	Poorer self-definition and negative self-regard (122) linked to emotional experience (123). Fundamental loss of sense of self (124)
		OCD	Sensitive self-concept, negative view of self (125, 126) or feared self (127)
		ASD	Weaker self-concept (128, 129) and hoarding has been suggested to help maintain continuity of self in autistic spectrum (130)
		BPD	Identity confusion (131, 132) and self and other representational disturbances (133, 134)
		NPD	Impaired sense of self (135) including lack of integration of self (136)
	Altered sense of agency/magical thinking	TS	Jumping to conclusions bias (137) and greater tendency than controls to ascribe intentions to randomly moving shapes (77). Symptoms of OCD (which often include magical thinking) frequently comorbid with TS (138)
		SZ	Tendency to thought action fusion (139). Alterations to self agency and relatedness (122) and decreased sense of self-causation (140). Lower sense of agency in high schizotypal non-clinical sample (141)
		OCD	Tendency to thought action fusion (142, 143). Belief that one has excessive ability and responsibility to prevent harm (144). Lower use of agency related language vs. HCs (145)
		ASD	Reduced intention attribution (146) and altered sense of agency in mystical experience (147)
		BPD	BPD v HC less agentic in their descriptions for self and other stories seeing people as powerless (148).
		NPD	High vs. low sense of agency and self-esteem associated with grandiose traits vs. vulnerable traits respectively, in non-clinical sample (149)
	Reduction in conscious perspective taking†	TS	Lower self-reported perspective taking vs. HCs (36)
		SZ	Lower self-reported perspective taking vs. HCs (37)
		OCD	Lower self-reported perspective taking vs. HCs (40)
		ASD	Problem with explicit perspective taking but not necessarily empathy (150)
		BPD	Cognitive perspective taking can be reduced (151)
		NPD	Most likely to be reduced when affect is involved and may depend on subtype (152–154)
	Antagonistic (including egodystonic) impulses and actions†	TS	Coprophenomena and non-obscene socially inappropriate urges that tend to be ego-dystonic (155–157)
		SZ	Impulsive non-conformity is associated with atypical emotional prosody processing (158); high in schizotypy in association with reasoning about actions based on emotions (159); negatively correlated with anhedonia (160)
		OCD	Ego-dystonic intrusive thoughts about harming others (161) associated with proposed 'self-defeating' personality disorder (162, 163)
		ASD	Acute agitation and aggression (164) and problem behaviors which may be related to coping skills (165)
		BPD	Emotional dysregulation linked to splitting, projection and acting out (166). Low compliance (167) and self-defeating behavior (168)
		NPD	Antagonism is at the core of narcissism (169, 170) low compliance (167) and self-defeating traits (171) are also associated

(Continued)

TABLE 2 | Continued

Domain	Symptom/sign	Disorder	Findings/specific observations
	Narcissism/ grandiosity†	TS	Features linked to vulnerable narcissim more likely to occur and associated with depression (172)
		SZ	Grandiosity may have a defensive or protective role (173, 174)
		OCD	Can get a proportion of people with obsessive-compulsive traits who are diagnosed with NPD (175)
		ASD	NPD can be co-morbid (176) and tendency to self-enhance (177)
		BPD	Vulnerable traits are more closely related (178–180)
		NPD	Grandiosity is often central to NPD, though less prominent in vulnerable than grandiose subtype (149, 170, 181)
Motor	Echophenomena/excessive motor resonance*	TS	Echophenomena are characteristic of TS (182, 183). Severity associated with TPJ activity during social cognitive tasks (26, 184). Poor inhibition of imitation (185, 186)
		SZ	Echophenomena classified as a form of catatonia and seen in drug naïve cases (187, 188). Both enhanced (189) and impaired imitation (190): effort/medication may influence
		OCD	Reported deficits in imitation of meaningless movements (191) vs. contrasting evidence of more vicarious experience from others' movement (30). OCD is often comorbid with TS
		ASD	Echophenomena may present (192, 193). Greater automatic imitation associated with reduced activity in med PFC and TPJ in autism (194)
		BPD	Higher MEG response to facial expressions (34). Poor imitation inhibition i.e., interference from observed movements (195)
		NPD	Stronger motor-emotional resonance when observing physical pain despite lower self-reported empathy (196)
	Sensing loss of agency over movements/ actions	TS	Sense of tics as being involuntary [e.g., (197)], and reduced accuracy in action monitoring (198–200)
		SZ	Delusions of control over actions seen in association with psychosis (201). Greater susceptibility to illusions of body ownership in schizotypy (202)
		OCD	Low intentional binding but higher illusory control (203). Altered sense of motor agency (204, 205)
		ASD	Larger temporal window of integration and potential excessive binding between unrelated stimuli (206). In addition, reduced intentional binding may be seen (207), perhaps affecting sense of agency (208)
		BPD	Greater susceptibility to illusions of body ownership vs. HC (195, 209–211) but can self-report higher sense of agency (210)
		NPD	Narcissistic traits have a positive relationship with intentional binding and sense of agency (212) despite link to impulsivity (213), which may reflect grandiose vs. vulnerable difference (149)
	Motor compulsions (including tics)†	TS	Motor compulsions include symmetry and evening up compulsions (214), and self-injurious behavior [e.g., (215)], plus more general difficulties with motor inhibition [e.g., (216)]
		SZ	Tics can precede typical symptoms of SZ and related treatments [e.g., (188, 217)]
		OCD	Compulsions are related to sensori-motor issues (205, 218). Reduced motor inhibition/enhanced tendency to action (219)
		ASD	Tics (220) and motor stereotypies and compulsions are often present, including self-injurious behaviors (221, 222)
		BPD	Impaired motor inhibition related to general impulsivity and dissociation (223, 224). Self-harm linked to compulsivity (225)
		NPD	Occasionally associated with exercise (226) and sexual (227) compulsions but not simple motor compulsions
	Impulsivity	TS	Impulsive behaviors are common in TS (228) and can involve self-harm (215). There may be a predisposition toward motor impulsivity in general (229, 230)
		SZ	Impulsive behaviors can occur in response to command hallucinations (231). Less impulsive than BPD or OCD (232) but impulsive non-conformity linked to risk-taking behavior in schizotypy (233)

(Continued)

TABLE 2 | Continued

Domain	Symptom/sign	Disorder	Findings/specific observations
		OCD	Motor impulsivity linked to hoarding symptoms (234) but most behaviors more closely linked to compulsivity (235)
		ASD	Impulsivity linked to self-injurious behavior (236, 237)
		BPD	Phenotypic trait according to longitudinal studies (238). High impulsivity (239, 240) especially if in negative emotional state (241) related to alexithymia (242) and anhedonia (243)
		NPD	Linked to impulsive buying (244) but may vary according to subtype (149, 245, 246)
Neuro	MNS: Atypical activity/ structure	TS	Atypical activity within IPL/TPJ and IFG during observation of facial expressions (26), altered structural connectivity between these areas, basal ganglia and thalamus (247), and lower volume of IFG (248).
		SZ	Greater MNS activity when observing movement in association with psychosis (249), linked to both positive (250) and negative (251) symptoms. Resting state connectivity is also atypical (252, 253)
		OCD	Altered activity in MNS regions when perceiving biological motion (254). Structural changes in IPL (58, 255) and IFG (58, 256) and thickness of right IFG can be associated with symptoms (257)
		ASD	IPL responses negatively correlated with autism symptom severity in adults (258) and MNS abnormalities include reduced IFG activity (259, 260)
		BPD	Atypical activity in frontal and/or parietal components of the MNS (261–263) including during pain processing (264) and emotion contagion (265)
		NPD	EEG differences to HC during empathy for pain involving somatosensory cortex (196). Reduced cortical thickness in right IFG (266)
	rTPJ: Atypical activity/ structure	TS	Hyperactive for facial expressions (26) but hypoactive during false belief task (184). Activity correlates with echophenomena and global tic severity (26, 184). Atypical structural connectivity (247, 267). Atypical activity for imagined and executed movements (268)
		SZ	Hyperactive during ToM task when high risk (269); hypoactive after diagnosis (269, 270). Hypoactive during other vs. self reflection (271) and during naturalistic social cognitive tasks (272). Functional connectivity and structural differences to HC (273, 274)
		OCD	Altered resting state functional connectivity (275) including MEG study (276). Increased volume (58)
		ASD	Dysfunction during imitation (277), observation of social interaction (278, 279), belief reasoning (280) and perspective taking (281). Reduced selectivity for mental vs. physical states (282). Activity linked to impaired communication (283)
		BPD	Both hypoactivity during perspective taking (284) and hyperactivation while evaluating own and others' personality traits (285)
		NPD	No studies identified (few imaging studies overall)

Proposed to result from low self-other distinction; may help to increase self-other distinction†.*
ASD, autistic spectrum disorder; BPD, borderline personality disorder; EEG, elctroencephalography; EMG, electromyography; HC, healthy controls; IFG, inferior frontal gyrus; IPL, inferior parietal lobe; IRI, Interpersonal Reactivity Index; MEG, magnetoencephalography; MNS, mirror neuron system; NPD, narcissistic personality disorder; OCD, obsessive-compulsive disorder; PFC, prefrontal cortex; SZ, schizophrenia; ToM, theory of mind; rTPJ, right temporo-parietal junction; TS, Tourette syndrome.

impairs determination of self-produced actions and effects, with relevance to conditions such as psychosis (294–296). Disrupted sensory feedback (alike excessive motor resonance) could have a conscious cognitive correlate in the form of altered sense of agency. Indeed, sense of agency appears to consist of both intrinsic (i.e., a more conscious, cognitive experience of agency) and extrinsic (i.e., sensorimotor experience of body ownership) aspects, and differences in integrating or balancing intrinsic and extrinsic self-representation networks could impair self-other distinctions (297).

Tics and compulsions can be associated with sensorimotor abnormalities (298, 299) and alterations in sense of agency for action (**Table 2**). While tics are reported as feeling at the most semi-voluntary, and tend not to appear goal directed, one effect of these internally generated fragments of motor activity is to interrupt motor resonance with external others, helping to support self-other differentiation, and perhaps developing into a habit conditioned to the experience of internal emotional stress. That is, the sensory fulfillment associated with tics and motor compulsions may arise through the acting out of a self-initiated

action which helps to confirm (perhaps subconsciously) internal control over movement and related neural motor activity, counterintuitively helping to re-establish sense of agency. Given that both emotion and sense of self are relevant to self-harm (300), compulsive self-harm may be another symptom through which a self-initiated motor act enables a sense of self-control or internal agency over a perceived emotional or sensory state.

Self-Other Distinction Within the Brain

Excessive resonance with others is perhaps most likely to be reflected in atypical activity within the MNS, as seen in disorders including TS and schizophrenia (26, 249). More generally, inferior parietal and inferior frontal activations have been shown to be atypical during social cognitive tasks in TS, ASD and BPD; unusual resting state activity has been revealed in schizophrenia; and structural changes have been associated with symptoms of OCD and NPD (**Table 2**). Problems with self-other distinction may also manifest as atypical activity within the mentalizing system, perhaps as hypo-activation of rTPJ when mentalizing is cued or hyper-activation when it is not [e.g., 29, 46]. Many studies have revealed that the right TPJ in particular, may demonstrate atypical activity during social cognitive tasks in patient populations with symptoms linked to problems with self-other distinction.

Perhaps the best evidence links brain dysfunction directly to behavioral signs of self-other distinction problems or related symptoms. For example, in TS, global measures of echophenomena and urges to tic have been associated with rTPJ activity during two different social cognitive tasks (26, 184). In schizophrenia, psychosis has been linked to negative symptoms (249) and excessive activity within the MNS (83), while reduced neural synchrony involving rTPJ has been implicated in impaired social communication in autism (283). Overall however, few studies have attempted to explore specific associations.

DISCUSSION

Primary Effects, Secondary Symptoms and Coping Strategies

Many neuropsychiatric disorders feature emotional, cognitive and/or motor features that are likely to indicate problems with self-other distinction. Within each of these domains, we may identify both signs of low self-other distinction, and characteristics or behaviors that could constitute secondary effects or coping strategies which serve to increase self-other distinction. For example, frequent emotion contagion may lead to emotional dysregulation, and detachment from emotional experiences may combat personal distress. Cognitive features associated with poor self-other distinction may manifest as paranoia or projection, and potential coping strategies include avoidance of perspective taking or buffering sense of self through grandiosity or impulsive non-conformity. Excessive motor resonance with others (e.g., poor imitation inhibition) may reduce sense of physical agency and encourage the development of tics and compulsions that may help to restore this.

A novel contribution of the hypotheses presented herein is that they can account for a range of seemingly contradictory behaviors and self-defeating symptoms. There is irony in that many of the symptoms that arise through difficulties with self-other distinction, and reflect greater resonance with others' mental states, could appear to suggest hypo-mentalizing or antagonism toward others. This highlights the importance of considering both ability and application. Where over-application occurs, resulting difficulties may be as great as in cases of under-application.

While the concept of self-other distinction can be applied to cognition, emotion or movement, it's also important to consider automaticity, or implicit vs. explicit processes and skills, where possible. For example, processes that reduce self-other distinction and involve the motor and limbic system (e.g., emotion contagion) appear fairly implicit or automatic (301, 302), although some individuals may be more susceptible to the cues that initiate this. In contrast, complex higher level mentalizing may be to some extent more explicit or controllable (16, 186, 303). An over-responsive MNS leading to frequent limbic dysregulation may initiate confusion around sense of agency, which then becomes more generalized to thought and action. In general, as we cannot directly observe another person's thought, it makes sense for cognitive signs to occur further downstream. For example, while excessive automatic emotion contagion is often a primary sign, secondary effects such as reduced perspective taking or conscious attention to other's emotions, may help to compensate for the primary problem (i.e., low self-other distinction). Other indirect signs (e.g., tics and motor compulsions) may seem less conscious, although differentiating between conscious strategies and automatic compulsive responses can be challenging. Furthermore, regulatory or compensatory effects may occur across domains, supported by the finding that both cognitive (thought action fusion; sense of agency) and emotional (personal distress) factors mediate the relationship between emotion contagion and alexithymia (287).

Therapeutic Implications, Limitations and Remaining Questions

The struggle to achieve a healthy and functional balance of self-other distinction may manifest in a range of forms, from tics in TS, to repetitive cycles of affiliation followed by antagonism in BPD. The theory presented suggests while those with neurodevelopmental, anxiety and personality disorders express differing constellations of internalizing and externalizing symptoms, overlapping difficulties with self-other distinction imply shared dysfunction within a common underlying neuropsychological mechanism. Therefore the potential therapeutic benefit of addressing difficulties with self-other distinction should be extensive, once the specific associations between self-other distinction and the suggested related symptoms and coping mechanisms have been established. Psychological interventions have begun to consider factors which overlap with the self-other distinction theme (e.g., self-awareness; emotion regulation; mentalizing), including metacognitive approaches for psychosis [e.g., (304, 305)], and personality disorders (306, 307). Other emerging interventions combine

non-invasive brain stimulation with social cognitive (308) or sensori-motor (309) related training. Future related research should seek to first fully define and operationalise the construct of self-other distinction, before identifying reliable measures (e.g., self-other overlap index) that can be used in assessment and evaluation. Ultimately we should seek to harness what we can from behaviors that appear to counteract a problem with self-other distinction in order to inform therapeutic strategies.

The proposed hypotheses prompt further unanswered questions. For example, longitudinal studies are necessary to test whether suggested primary signs of low self-other distinction (e.g., emotion contagion; echophenomena) precede the development of other symptoms such as alexithymia, blunted affect, paranoia, antagonistic behaviors. This would identify risk factors and targets for early intervention. While there should be common overlap in the underlying mechanisms, individual differences in neural organization or stage of development of self-other distinction difficulties or compensatory responses, would help to explain the predominance of features within a given domain e.g., motor in TS vs. cognitive in schizophrenia. Diagnostic and therapeutic approaches would also be informed by a better understanding of the specific neural networks and structures involved, as well as factors such as the relationship between self-other distinction and executive dysfunction (e.g., cognitive flexibility). Can most of the symptoms described be linked to dysfunction of rTPJ, and is this synonymous with over-activation of the MNS or altered functional connectivity between the mirroring and mentalizing networks? Recent studies have revealed rTPJ activation in relation to forward predictions in both highly social (310) and less social (311) contexts, so further related clinical research using carefully selected experimental tasks is needed.

Many psychiatric symptoms appear likely to stem from low self-other distinction. However, some behavioral problems may reflect excessive self-other distinction as a primary effect. For example, the data on autism seems to suggest a mixed pattern, which could be linked to motor and/or MNS dysfunction [(312–314); but see (315)]. Social cognition is frequently impaired in movement disorder (316) and an impaired motor system will likely impair self-other distinction through loss of feedback between motor resonance and emotional processes (317). In relation to primary and secondary effects, primary psychopathy is thought to involve a fundamental deficit in affective empathy and therefore high self-other distinction, whereas secondary psychopathy may involve indirect symptoms or those arising through a coping strategy (318). It is possible that some of the signs and symptoms presented here that are suggestive of high self-other distinction constitute primary rather than secondary effects. Furthermore, some behaviors could reflect either high or low self-other distinction [e.g., hypo-imitation: (319)] and whether an individual may fluctuate between polarized high or low self-other distinction (e.g., due to rTPJ dysfunction) remains to be explored. Other more general limitations include the challenges in reviewing the literature and drawing comparisons across different studies and disorders, because of variations in terms used, co-morbidities, reliability of self-report and unknown impact of medications.

CONCLUSION

In conclusion, impaired self-other distinction, potentially underpinned by excessive mirroring, and/or hypoactivation of rTPJ, appears to lead to a disturbed sense of agency and the manifestation of a range of psychiatric symptoms across emotional, motor and cognitive domains. These symptoms variously reflect, or attempt to redress, the problematic level of self-other distinction. Understanding the hidden relationship between self-other distinction and symptoms as diverse as paranoia, self-harm, tics and narcissism, and considering the potential compensatory value of compulsive and antagonistic behaviors that are typically viewed as dysfunctional, will enhance our global understanding of mental health and expedite the development of more effective and innovative interventions.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

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

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frontiers | Frontiers in Psychiatry

MINI REVIEW
published: 05 April 2022
doi: 10.3389/fpsyt.2022.845492

The Social Connectome – Moving Toward Complexity in the Study of Brain Networks and Their Interactions in Social Cognitive and Affective Neuroscience

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Over the past 150 years of neuroscientific research, the field has undergone a tremendous evolution. Starting out with lesion-based inference of brain function, functional neuroimaging, introduced in the late 1980s, and increasingly fine-grained and sophisticated methods and analyses now allow us to study the live neural correlates of complex behaviors in individuals and multiple agents simultaneously. Classically, brain-behavior coupling has been studied as an association of a specific area in the brain and a certain behavioral outcome. This has been a crucial first step in understanding brain organization. Social cognitive processes, as well as their neural correlates, have typically been regarded and studied as isolated functions and blobs of neural activation. However, as our understanding of the social brain as an inherently dynamic organ grows, research in the field of social neuroscience is slowly undergoing the necessary evolution from studying individual elements to how these elements interact and their embedding within the overall brain architecture. In this article, we review recent studies that investigate the neural representation of social cognition as interacting, complex, and flexible networks. We discuss studies that identify individual brain networks associated with social affect and cognition, interaction of these networks, and their relevance for disorders of social affect and cognition. This perspective on social cognitive neuroscience can highlight how a more fine-grained understanding of complex network (re-)configurations could improve our understanding of social cognitive deficits in mental disorders such as autism spectrum disorder and schizophrenia, thereby providing new impulses for methods of interventions.

Keywords: social cognition, network neuroscience, connectome, network interaction, mental disorders

OPEN ACCESS

Edited by:
Martin Schulte-Rüther, University Medical Center Göttingen, Germany

Reviewed by:
Yuan Zhou, Institute of Psychology (CAS), China

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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *29 December 2021*
Accepted: *11 March 2022*
Published: *05 April 2022*

Citation:
Maliske L and Kanske P (2022) The Social Connectome – Moving Toward Complexity in the Study of Brain Networks and Their Interactions in Social Cognitive and Affective Neuroscience. Front. Psychiatry 13:845492. doi: 10.3389/fpsyt.2022.845492

THE MODULAR SOCIAL BRAIN

We live in a social world requiring constant behavioral adaptation to changing socio-environmental demands. Socio-affective and -cognitive functions have been distinguished as crucial for coping with these demands and appropriately updating behavior in social situations. Our understanding of how these processes are represented in the brain has evolved quite substantially. In the 19th

century, researchers relied on lesion-based approaches to infer the coupling of brain areas and behavior [a prominent example is that of Phineas Gage, a railroad worker that received extensive damage to parts of the frontal lobe after a workplace accident, and showed pronounced personality changes, (1)]. The development of increasingly sophisticated methods of non-invasive functional neuroimaging starting from the end of the last century on allowed researchers to arrive at studying the online coupling of social processes and neural activation at certain areas of interest.

The past two decades have yielded somewhat of a consensus regarding the brain areas associated with socio-affective and -cognitive functions (2). These social processes and the associated neural activations have classically been investigated as isolated functions and related neural networks. The underlying assumption has been that specialized "social brain regions" can be identified, potentially leading to an atlas of specific brain regions associated with social processes. A strength of this first wave of social neuroscience viewing social affect and cognition as separate and modular is that it allowed researchers to identify "core elements" guiding behavior in social situations, such as empathy [the affective representation of another's emotions, (3)] and Theory of Mind [ToM, the cognitive representation of others' mental states, (4)].

A large body of work has investigated the association of individual areas (such as the insula, temporoparietal junction, TPJ) with these socio-affective and -cognitive processes. While it has been crucial to build a base of understanding related to social affect and cognition as individual processes, it is becoming clearer that this does not seem to be the whole story. In naturalistic social interactions, we are confronted with a multitude of social and non-social information, which must be processed simultaneously to react appropriately [e.g., (5)]. Investigating pieces of social information processing in isolation, but also brain activation related to only one aspect of social information processing, appears to be too simplistic to understand actual social behavior. At the neural level, knowledge about the functional profiles of an individual area is the cornerstone on which to build on, however, understanding how an area is embedded within the overall brain architecture and how it is communicating with other areas of the brain can bring about another level of understanding [see (6) for an account of connectivity-based valence-specificity of the anterior insula]. Note that for reasons of simplicity, in the following we will refer to the neural representation of social affect and cognition, and the underlying neural networks [see e.g., (2, 7–10)], as "the social brain." However, we want to stress that this is merely a simplification for illustrative purposes; we believe that the actual neural representation of social affective and cognitive processing requires an intricate pattern of interactions among components of the entire brain. **Figure 1** gives an illustrative overview of regions previously associated with socio-affective and -cognitive processes.

A bit like moving from inspecting only a snippet of a painting to stepping back and observing it in its entirety, there is a chance to better understand and predict social behavior by considering the inherently interconnected, dynamic nature of information processing in the brain. Recent advances in the field of connectomics and network neuroscience – studying the brain in terms of a comprehensive map (11) – make methods that allow for a more holistic view of the brain accessible to a wider scientific community. In the following, we are employing ideas from the field of connectomics to describe interactions among modular brain networks associated with social affect and cognition [for a comprehensive introduction to the field of connectomics, see e.g., (11, 12)]. We want to highlight the added value of employing these ideas and methodology which allows to describe neural representation of social affect and cognition in terms of their network organization, especially for the field of (clinical) social cognitive neuroscience.

THE CONNECTED SOCIAL BRAIN

The aim of the current review is to outline recent, promising avenues to describing the social brain at the network level, and how these networks interact in complex social situations.

Network Organization of the Social Brain

Alcalá-López et al. (13) describe the social brain across a wide range of different (social and non-social) behavioral domains and experimental setups. The authors identified key social cognition hubs from the neuroimaging literature, and investigated neural networks associated with these hubs using meta-analytic connectivity modeling (MACM) and resting-state functional connectivity mapping. Furthermore, they performed hierarchical clustering and functional decoding of their identified networks to describe commonalities of the observed networks, as well as compare their results with a wide range of topics from neuroimaging research. We want to highlight two findings from their extensive analysis: (a) the authors identified a hierarchical organization of the social brain's functional connectivity profiles into four dimensions (visual-sensory, limbic, intermediate-, and higher-level seeds). The authors observed considerable cross-network interactions for intermediate-level seeds, while the higher-level seeds displayed mostly connections within their respective network. Furthermore, the authors found (b) no one-to-one mapping for a seed region onto only one behavioral and experimental domain. In fact, the authors showed that activation in each seed region corresponded to a wide range of social and non-social topics, suggesting that the notion of specialized "social brain regions" is too simplistic [with possible exceptions like the fusiform face area, (14)].

In a similar vein, we performed a meta-analysis and hierarchical clustering analysis across empathy and ToM task groups (2). We observed a tripartite hierarchical organization of the networks associated with empathy and ToM tasks: neural activation of the task clusters typically associated with empathy and ToM corresponded well with previously described neural empathy and ToM networks [e.g., (9, 15)]. Interestingly, we also observed a third task cluster: this cluster was comprised of more complex social tasks including both affective and cognitive stimulus elements (e.g., inferring a character's next actions based on their mental or emotional state). The neural activation pattern associated with this cluster showed activation in regions

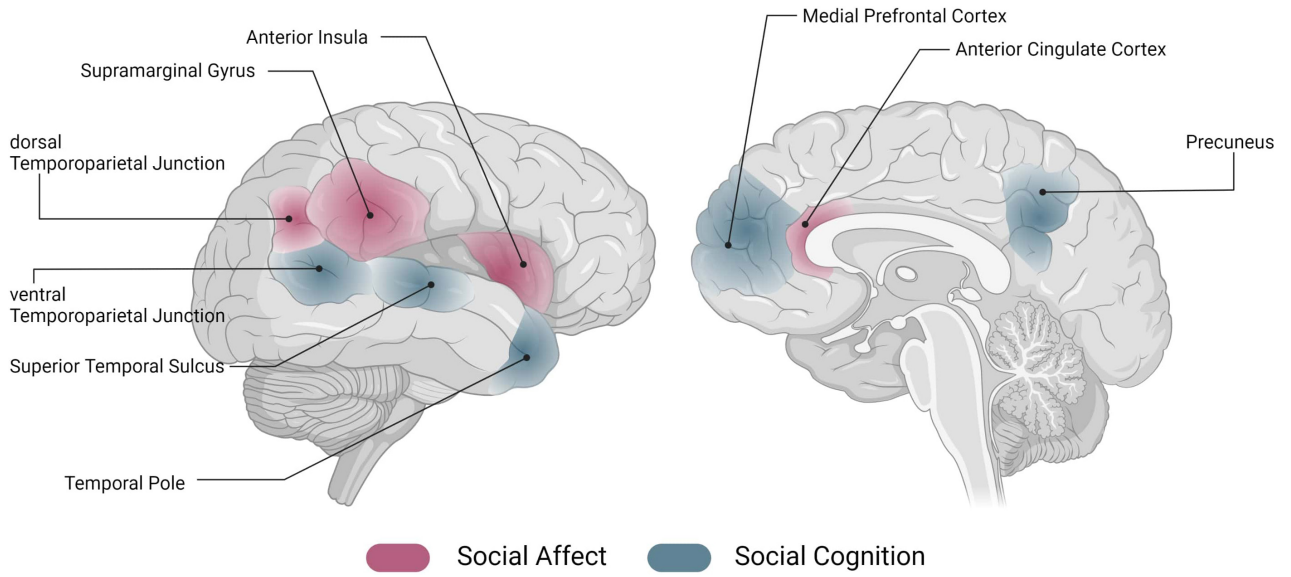

FIGURE 1 | Networks of the social brain. Schematic overview of activation in regions that have previously been associated with social affect (red) and social cognition (blue) [for an overview, see e.g., (7–10)]. Image generated using biorender (www.biorender.com).

previously associated with empathy and ToM [see also (16)], networks previously described as independent [e.g., (17–19)].

While these studies only represent a small excerpt from the field of social affect and cognition, they summarize important new developments, showing how a more network-based perspective on social cognitive neuroscience can give new insights into the underlying neural architecture, but also the processes themselves [similar to other research areas, like intelligence, e.g., (20), or working memory, e.g., (21)].

Interaction Between Networks of the Social Brain

Previous research has found substantial overlap between networks of social affect and cognition and selected canonical resting-state networks of the brain, which might enable closely related or compatible cognitive functions (22). A prime example for this is the overlap of the default mode network (DMN) with areas typically associated with ToM. The DMN is assumed to mediate self-generated cognition decoupled from the surrounding environment (23), which might be compatible with certain processes engaged during mental state reasoning. Recently, we systematically investigated the overlap of basic networks of the brain and social affect and cognition networks (24). We computed an overlap of canonical resting-state networks of the brain (25) with meta-analytically derived network maps associated with different social affect and cognition tasks. While ToM tasks primarily overlapped with the DMN [an interesting exception being the Reading the Mind in the Eyes task, see also (2)], overlap for complex social and empathy tasks was more heterogeneous: classical empathy tasks showed largest overlap with the ventral attention network (VAN), however there was also sizable overlap with other higher-level cognitive (e.g., frontoparietal network, FPN) and lower-sensory networks (e.g., visual network), pointing to increased cross-network interaction.

Having established that these seemingly independent neural networks do in fact interact, the next question might be how these networks interact. Studies of directed connectivity allow us to investigate how activity in one region causally influences activity in another region (26). A handful of studies investigated directed connectivity between regions of different canonical resting-state networks related to social cognition. Kanske et al. (18) found an inhibitory relationship from the insula (located in the FPN) onto the TPJ (located in the DMN) mediated by emotional content in a naturalistic social cognitive paradigm. Activity in the insula seemed to downregulate activity in the TPJ when participants viewed emotionally negative videos, which went along with impaired performance on an associated ToM-measure. The authors argue that this might be due to the emotional content of the video being more salient and requiring the most immediate response. Similarly, Regenbogen et al. (27) observed up-regulatory effects of a visual network onto a DMN region in the same experimental condition. In contrast, Schuwerk et al. (28) observed reciprocal down-regulation of DMN- and VAN-related regions for a false belief video task in conditions wherein a demonstrator and participant's belief are incongruent. As a last example, social cues in an attentional re-orienting task (29) were associated with up-regulation of a VAN- onto a DMN-related region.

The interaction and reconfiguration of brain region interactions is rather complex and seems largely context-dependent [for a review, see (30)]. Rich, naturalistic social situations present us with a plethora of different cognitive and affective information, which must be processed simultaneously (31, 32). To react appropriately, certain information must be integrated while other information must be blocked out (33,

34). The notion of network integration, that is, the interaction of modular sub-components of different networks, has been associated with tasks that require more effortful and controlled processing (35), including more complex social tasks (36). Network integration might be a relevant mechanism, especially for complex and naturalistic social tasks, as it provides a means of integrating different mechanisms across unique behavioral domains (30).

Malleability of the Connected Social Brain

Measures of network interaction cannot only be contextually reconfigured (30), but also altered by interventions or training. In one such study, Valk et al. (37) investigated reorganization in networks relevant to attention, socio-affective, and socio-cognitive processing after intensive 9-month meditation training, that did indeed improve behavioral measures of the respective functions (38). Using gradient-based approaches to measure network integration, Valk et al. (37) could show that training in different meditation practices went along with differential patterns of network reorganization. After socio-cognitive meditation training, the authors observed increased functional integration of regions in the DMN, FPN, and dorsal attention network (DAN). Furthermore, the organization of task-based neural networks associated with attention and social cognition became more similar to other networks within the overall connectome after socio-cognitive meditation training. Alterations in network organization after socio-affective meditation training resulted in increased network integration of areas of the VAN with the DMN, FPN, and DAN along the hierarchical organization of the first gradient. These changes in large-scale network organization could furthermore predict changes in behavioral ToM and compassion measures.

Taken together, these data can greatly enhance our understanding of (a) how the brain represents social affect and cognition, (b) the nature of social affect and cognition, and how they relate to one another, (c) the context-dependency of how the brain represents social affect and cognition, and (d) the flexibility, adaptability, and malleability of how the brain represents social affect and cognition. Just like social encounters in real-life interactions, the relationship between social affect and cognition, and their representation in the brain, is marked by a complex, interconnected pattern of excitatory and inhibitory connections.

THE DISCONNECTED SOCIAL BRAIN

If we understand the organization of social processes in the brain in terms networks and argue that their interaction underlies successful social interactions, we should also be able to use this network-based perspective to enhance our understanding of failures and disorders of social cognition.

A growing body of research has investigated alterations of brain network organization in different neurological and mental disorders (39–41). Evidence suggests that brain structural and functional alterations associated with neurological and mental disorders are more likely to be located in densely interconnected regions of the brain (42) and at white matter pathways relevant for cross-network interaction and global communication (43). In the following, we want to pinpoint relevant studies discussing network-based alterations in subgroups of mental disorders that might shed light on disorder-specific and more general pathophysiological neural or behavioral dysfunctions.

Patients with bipolar disorder (BD) have been found to show altered socio-cognitive and emotional processing and perception (44), which has furthermore been associated with altered functioning in a central-limbic network and decreased activity in dorsal brain areas (45, 46). Recently, Roberts et al. (47) found decreased structural connectivity in networks centered on the inferior frontal gyrus and left insular cortex in youths at high risk for developing BD, as well as increased connectivity in the limbic network. These regions have been shown to be implicated in altered neural functioning in individuals with BD (48) and are also core regions associated with socio-affective and -cognitive functioning (2). A recent study associated altered functional connectivity with socio-cognitive task performance in participants with BD and schizophrenia (49). Here, the authors compared network connectivity between patients with BD, schizophrenia, and healthy controls, and related network connectivity to measures of social affect and cognition. Altered network connectivity was observed in networks related to visual processing in BD and schizophrenia, which was associated with differential performance in socio-cognitive tasks in both patient groups. The authors argue that compensatory mechanisms might cushion behavioral deficits in BD, while this was not the case for participants with schizophrenia, elegantly demonstrating how measures of network organization might be a transdiagnostic marker of socio-cognitive deficits in mental disorders.

It is generally agreed upon that brain network organization is altered in individuals with autism spectrum disorder (ASD), however, the nature of these alterations remains a topic of ongoing debate. It seems that neural patterns of connectivity in individuals with ASD are a complex phenotype, with studies reporting both hyper- and hypoconnectivity [e.g., (50, 51); for a developmental account, see (52)], as well as reduced functional integration and segregation in networks related to social information processing (53). A recent study comparing functional connectivity in a complex social task across ASD, attention-deficit/hyperactivity disorder, and a comorbid group found distinctly altered connectivity profiles related to socio-cognitive processing (54). More specifically, while the three groups did not differ in terms of task performance, they did show decreased connectivity in a key region of what the authors term the social cognitive network (centered on the right temporoparietal cortex). Participants with ASD showed decreased connectivity between nodes of this network, which the authors attribute to atypical informational transfer during social cognition.

These studies highlight how a network-based perspective might explain previously heterogeneous findings, or might shed light onto underlying mechanisms associated with altered neural processing and overall social cognitive dysfunctions. Especially moving toward fully socially interactive experimental paradigms

to better understand real-life social deficits will necessitate more complex analyses of the related brain activity (55). Additionally, network-based characteristics might serve as an additional transdiagnostic marker of mental disorders of social cognition, in line with the growing interest in dimensional approaches to mental disorders [like the RDoC framework, (56)], or might offer up new explanatory models for mental disorders (57).

THE FUTURE OF THE CONNECTED SOCIAL BRAIN

Our understanding of the processes underlying social affect and cognition, as well as how they are represented in the brain has undergone a tremendous evolution. From a modular, isolated understanding of these processes, the field has now arrived at a more interconnected, complex view. Among others, developments in methodology are making more advanced analyses and representations of social brain activity accessible to the scientific community. Overall, the field is moving from the search of an individual "social seed" in the brain (areas specifically dedicated to orchestrating one specific function) toward a more large-scale investigation of how the social brain is organized.

In this review, we highlighted individual studies that showcase how this move toward a network-based investigation of the social brain might reshape our understanding of social affect and cognition in terms of overall network organization (2, 13), network configuration and interaction (18, 27), flexible network reconfiguration (37), and disorders of the social brain (49, 54). This approach offers promising avenues for the field of (clinical) social neuroscience, which will allow us to gain a more holistic understanding of how the brain represents social processing, and social processing in itself. Analogous to the move toward a second-person neuroscience (58), moving toward a network-based perspective of the social brain might help sharpen our understanding of different areas of the brain as interacting, interconnected networks.

Beyond basic research, a move toward a network-based understanding of the social brain could open up crucial avenues especially in the context of clinical research, similar to how connectome-based decoding is now used in, for example, neurological or psychiatric research. To illustrate, in neurological research, information about connectome-level organization of the brain was successful in diagnosing disorders or predicting long-term outcome (59, 60). But also in the context of mental health, information about connectome organization has been shown to aid diagnosis of disorders (61), classify patient subgroups (62), and predict symptom severity (63). Correspondingly, information about the connectome-level representation of social affect and cognition in the brain might help to predict alterations in interpersonal behavior and social cognitive functioning associated with a wide range of mental disorders. Similar to the approach of precision medicine, adopting a perspective of "precision connectomics" could support clinical work substantially (57).

While the classically held view of an isolated and modular social brain paved the way for our currently held understanding of social affect and cognition, we believe that the field is ready to move toward a more holistic account of the social brain – in terms of both, how we probe social affective and cognitive processing (the employed task paradigms) and how we map their neural representation. Adopting a network-based perspective on social affect and cognition cannot only enhance our understanding of the social brain itself, but also of the underlying processes, their relationship with each other, and possible alterations in them.

AUTHOR CONTRIBUTIONS

LM and PK conceived the manuscript and contributed to writing and editing. Both authors contributed to the article and approved the submitted version.

FUNDING

LM was supported by a scholarship of the Friedrich-Ebert-Foundation. PK was supported by the German Research Foundation (KA 4412/2-1, KA 4412/4-1, KA 4412/5-1, KA 4412/9-1, Project C07 in CRC 940).

ACKNOWLEDGMENTS

LM and PK would like to thank Caroline Surrey and Maike Salazar-Kämpf for their invaluable feedback on previous versions of this article.

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Conflict of Interest: 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.

frontiers | Frontiers in Psychiatry

REVIEW
published: 18 April 2022
doi: 10.3389/fpsyt.2022.846535

Characterization of the Core Determinants of Social Influence From a Computational and Cognitive Perspective

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Most human decisions are made among social others, and in what social context the choices are made is known to influence individuals' decisions. Social influence has been noted as an important factor that may nudge individuals to take more risks (e.g., initiation of substance use), but ironically also help individuals to take safer actions (e.g., successful abstinence). Such bi-directional impacts of social influence hint at the complexity of social information processing. Here, we first review the recent computational approaches that shed light on neural and behavioral mechanisms underlying social influence following basic computations involved in decision-making: valuation, action selection, and learning. We next review the studies on social influence from various fields including neuroeconomics, developmental psychology, social psychology, and cognitive neuroscience, and highlight three dimensions of determinants—who are the recipients, how the social contexts are presented, and to what domains and processes of decisions the influence is applied—that modulate the extent to which individuals are influenced by others. Throughout the review, we also introduce the brain regions that were suggested as neural instantiations of social influence from a large body of functional neuroimaging studies. Finally, we outline the remaining questions to be addressed in the translational application of computational and cognitive theories of social influence to psychopathology and health.

Keywords: social influence, computational modeling, individual differences, computational psychiatry, context dependence

OPEN ACCESS

Edited by:
Sören Krach,
University of Lübeck, Germany

Reviewed by:
Shinsuke Suzuki,
The University of Melbourne, Australia
Christoph W. Korn,
University Medical Center Hamburg-Eppendorf, Germany

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Specialty section:
This article was submitted to Social Cognition, a section of the journal Frontiers in Psychiatry

Received: *31 December 2021*
Accepted: *22 March 2022*
Published: *18 April 2022*

Citation:
Lee H and Chung D (2022) Characterization of the Core Determinants of Social Influence From a Computational and Cognitive Perspective. Front. Psychiatry 13:846535. doi: 10.3389/fpsyt.2022.846535

INTRODUCTION

Most human decisions are made among social others. It is broadly observed that individuals' choice patterns sometimes vary and reflect the social information (1, 2). These phenomena highlight the importance of the social context at which the decision-making is taking place. Individuals being exposed to such "social influence" may have positive consequences; the decision maker whose actions were swayed by observing others' choices may benefit from the influence (e.g., joining others in following daily athletic routine) or get oneself to participate in spreading the good deed (e.g., ALS Ice bucket Challenge). However, in many other occasions, social influence is considered as a crucial factor that affects individuals negatively. For example, negative peer influence is known as a major risk factor for early initiation of substance use and other risky behaviors (3), and in line with this, having close friends and family members who suffer from substance use disorder is one of the

prominent predictors for individuals' substance use problem (4). These bi-directional impacts of social influence suggest that the mechanisms how social information affects individuals could be quite complex.

There has been abundant amount of research carried out to understand the breadth and levels of social influence in individuals' choices. In classic social psychology studies, researchers largely focused on the impact of social environment in adolescents, given that adolescence is a critical neurodevelopmental period (5, 6). Due to the complex nature of the natural settings, analyzing questionnaire data based on self-reports was not sufficient to answer why the impacts of social environment on adolescents' delinquent behavior sometimes are positive (7) but some other times negative (8, 9). Addressing this issue, over the recent two decades, various types of experimental paradigms have been suggested to examine the impact of overt (e.g., advice from an expert) (10, 11) and covert (e.g., presence of peers) (12) social contexts. In parallel, computational modeling of behavioral data from laboratory settings has been found useful in disentangling potential factors and plausible neurobehavioral mechanisms underlying social influence. Yet, experimental designs in laboratory settings are typically restricted by the specific factors-of-interest (e.g., age group, delivery methods or contents of social information) in line with their hypotheses, and thus suggested computational models still have room for improvement.

In this review, we aim to review previous research on social influence from various fields of studies, and to suggest core factors that would play key roles determining how individuals process and respond to social contexts. In the next section, we overview the recent computational approaches suggested to explain why and how individuals are affected by social contexts. In the following three sections, we review three dimensions of determinants that are known (or expected) to modulate the extent to which individuals are influenced by others: characteristics of the individuals who are receiving the social influence, the forms that the influence is conveyed, and the domains and processes of decisions that the influence is modulating. In the last section, we discuss about future directions in understanding of social influence and its translational application to mental illness. Large proportion of the studies we include here also provided functional neuroimaging results, which further supported their suggested cognitive and computational models explaining how social information is involved in decision processes. Thus, whenever found necessary, throughout the current review, we also introduce the brain regions that were suggested as neural instantiation of social influence.

COMPUTATIONAL MODELS OF SOCIAL INFLUENCE

How does an individual make decisions under social influence? To answer this question, we need a better approach than simply observing individuals' behavioral patterns, because there could be different paths of decision processes that underlie the same exact choice. To shed light on the question, various studies in social influence used computational modeling approaches in conjunction with functional neuroimaging (13–20). Given that social information contributes to change of individuals' initial decisions, the extent to which individuals use or respond to social information is often explained within the framework of learning. However, depending on the specific goal of the task and the way how the social information is framed, potential motives that individuals are expected to show differ (e.g., following the norm, or collecting more information) and moreover, different learning models are suggested to best explain individuals' choice patterns (e.g., Rescorla-Wagner type reinforcement learning model, or Bayesian learner model) [for review, see (21, 22)]. In this section, we review putative mechanisms of social influence suggested in these recent studies following basic levels of computations involved in decision-making (23): valuation, action selection, and learning. Of note, we focus on cognitive processes that occur within individuals who are on the receiving end of the social information, and the mechanisms how one may decide to exert influence over others [e.g., (24)] or how social information diffuses over a large group of people [e.g., (25)] are out of the scope of the current review.

Adjustment of Individuals' Preferences

Under social context, on average, people tend to follow others' choices [(2); c.f., (26)]. One of the simplest explanation why people follow others' choices is that individuals become similar to social others who they are with. Previous studies suggested that having chances to observe others' choices sways individuals to change their own preferences—behavioral tendency how they make choices (*action selection*) in a particular context—to match that of social others. Individuals showed shifts in the extent to which they discount delayed rewards after observing the choices of the majority of the social group (27). Such a "contagion" of preference was observed even in the case when individuals were presented with choices from anonymous few social others rather than from a representative group. Individuals changed their choice behaviors (e.g., delayed reward, uncertain gambles, moral choices) after participating in a task phase where they were asked to predict others' choices, and the changes were explained by computational models that assumed shifts in individuals preferences toward the observed social others (19, 28, 29). These modeling results were corroborated by model-based neuroimaging results. Specifically, event-related blood oxygen-level-dependent (BOLD) responses in the dorsomedial prefrontal cortex (dmPFC), a brain region known to be recruited for social information processing (30–32), tracked individuals' beliefs about others' choices (19, 27). This set of results suggested that individuals adjust their preferences in the direction that matches with social others, and in turn, show conforming behaviors.

Social Valuation

As any other decisions individuals make in life, choices under social contexts can be attributed to individuals' *subjective valuation* (33). This view assumes that individuals place value on the information obtained from social others and this additional social value can explain why they tend to make the

same choices as social others. In contrast to the studies that reported individuals' preference change under social context, task contexts where individuals had a brief chance to observe others' choices successfully showed evidence for a transient use of social information. In recent studies, Chung et al. (17, 20) used a formal model comparison and showed that a brief observation of social others' choices may affect individuals in their valuation rather than changing their preferences; the impact of observing others' choices on valuation was defined as "other-conferred utility". Consistent with their model-based results, it was observed that the ventromedial prefrontal cortex (vmPFC), a brain region known to encode subjective values of social and non-social choices (13, 34, 35), tracked trial-by-trial decision values combining the social values in individuals' decision processes (17). Such an impact of social valuation was also observed in a learning context where individuals made choices whether or not to follow social others' advice (15). Specifically, individuals' advice following behavior was explained by their adaptive learning process in which the value of obtained reward (or punishment) gets modulated for the choices advised by others. This value level premium, termed as "outcome-bonus", was tracked in the septal area and the caudate, brain regions implicated in signaling rewards and reward prediction errors (36–38). Another recent study suggested that individuals may encode social value in the anterior cingulate cortex (ACC) through vicarious simulation conducted from observing others' choices, and that this distinct value signal is combined with experience-based value signal in the vmPFC for subsequent decision-making (39). These results suggest that individuals' motivations to conform emerge from their computations of the value of social information and/or the value of sharing membership with the social group.

Learning From Social Others

The two perspectives introduced above are not mutually exclusive, but rather intertwined one another (22, 23). At a first look, the results would seem contradictory such that some studies suggest stable and non-changing individual preferences [e.g., (17)] whereas others suggest changes in preferences under social context [e.g., (19)]. However, social *learning* framework provided explanation why and how such subtle differences in the contexts may trigger differential responses from individuals. When individuals receive social information that is deviant from their own, BOLD responses in the dorsomedial prefrontal cortex (dmPFC) associated with social and cognitive conflicts were observed (14, 40, 41). Moreover, it was shown that this error signal is used as social prediction error, which individuals use to reduce the difference between self and others by learning from social others (14, 40, 42, 43). When individuals do not have a full access to social others' choice preferences or intentions (as in most of the social interactions), but believe others' choices are informative, individuals have to infer what others would be thinking to optimize one's own actions. In these contexts, individuals make inference about reliability of others' choices (44, 45), emulate others' intention (46), and combine the inferred social information with their own (44–47). This set of results suggests that individuals are influenced by social contexts because they use the information in learning how to adjust their choices at a specific context (e.g., interacting with the same social partner repetitively, observing choices of randomly assigned partner).

Summary

As briefly reviewed above, cognitive mechanisms of social influence may take different forms depending on the context in which its impact is examined. Depending on how the social information is provided, individuals may use the information as a transient nudge toward others' opinion or as a normative guide directing them to be changed. To date, computational modeling approach has been found useful in delineating such variant mechanisms (21, 22, 48, 49). However, there are still many remaining questions regarding the mechanisms, such as why some individuals are more susceptible to social information, and how does the value of a certain type of social information determined. To address these, we suggested that further practices in quantifying potential modulatory effects of latent variables are crucial. In the following sections, we review studies on social influence from various fields of studies and highlight three dimensions of determinants that are known to modulate the extent to which individuals are influenced by others.

COGNITIVE, PSYCHOLOGICAL, AND CONTEXTUAL DETERMINANTS OF THE IMPACTS OF SOCIAL INFLUENCE

Who Is More Susceptible to Social Influence

Everyone is bound to live under social influence, but some are more affected by others. Over the decades, a considerable amount of literature in social psychology has been published on the association between individual-specific characteristics and the extent to which individuals are influenced by social influence [e.g., (50, 51)]. The individual-specific characteristics that have been investigated across various fields of studies include demographics (e.g., age, socioeconomic status) and individuals' psychological characteristics (e.g., anxiety level, self-esteem). In this section, we review major factors that may mediate or modulate the impact of social influence on individuals' decision processes.

Demographic Factors: Age and Socioeconomic Status

Age has been considered as one of the most salient determinants that modulate social influence. Early pioneering research focused on the negative impacts of peers on adolescents' behavior. A seminal work by Gardner and Steinberg (10) showed that adolescents, compared to adults and young adults, take more risks when in peer groups. Adolescents' increased risk-seeking behavior was accounted for by the imbalance between adolescents' reward and cognitive control circuits (52, 53). In line with this neurodevelopmental model, their heightened social susceptibility was suggested to be associated with socio-emotional neural system (54, 55). Supporting these neural sensitivity models for adolescents, adolescents who exhibited

increased risk-taking choices under the presence of peers indeed showed increased BOLD responses in the reward circuit, including the ventral striatum and orbitofrontal cortex (12).

In contrast to classic studies on social influence in adolescents, recent studies gave more attention to positive impacts of social influence (56). Do et al. (57) specifically compared adolescents' conforming behaviors toward different types of social influence. In this study, adolescents tended to stick to their original attitudes toward various types of behaviors, but on the cases when they change their attitudes, adolescents conformed to constructive behaviors (e.g., working hard in school) more than unconstructive behaviors (e.g., smoking a cigarette). Another study used computational modeling approach and showed neural and behavioral evidence for positive peer influence in adolescents (20). Adolescents were making a series of gamble choices and presented with social others' choices before they made each choice. Consistent with the results observed in adults (17), adolescents followed others' choices on average, and such conformity was explained by added social value to the option others chose. In particular, adolescents who never used any types of substances were influenced by others' safe choices, whereas adolescents who have used were not. Although these studies did not directly compare adolescents' decision patterns from those of adults, the results suggested the mechanisms how individuals use social information in their adolescence, a sensitive period for sociocultural processing (6).

Considering the hormonal effects on biological development of the brain, one should consider pubertal stage as a determinant as important as age in developmental research. Indeed, across many adolescent studies, it has been reported that the extent to which individuals are susceptible to social influence is heightened during adolescence and usually diminished after pubertal growth (55, 58, 59). Moreover, recent functional neuroimaging studies suggested that puberty might play a more important role than chronical age in structural and functional development of the brain [(60); for review, see (61)]. This set of studies again highlights that individuals' age would explain considerable variability in their neural and behavioral patterns reflecting individual differences in social information processing.

Another noteworthy demographic factor is socioeconomic status (SES). There have been fairly consistent results suggesting that individuals' socioeconomic status has a significant effect on their behavior in social context. Psychological research suggested the association between individuals' social class and their perspectives over the social environmental (62). Specifically, individuals' high and low classes were considered to be shaped by abundance (or scarcity) of available resources, which in turn may underlie their behavioral tendencies either to focus on one's own internal states or to external factors (62). Consistent with this view, empirical research on social influence among marginalized groups also reported that they tend to conform to their peers more not to be excluded from their community and assert their identity in the group (63).

Recent neuroimaging research further supported the role of SES in individuals susceptibility to social influence. Casio et al. (64) examined whether individuals' SES moderates the relationship between brain responses to social exclusion and the extent to which they conform to peer influence. Specifically, individuals who had low SES showed positive association between neural sensitivity to social exclusion measured in the "social pain" network regions [including dorsal anterior cingulate cortex (dACC), anterior insula, and subgenual cingulate cortex (subACC)] and their conforming tendencies, whereas individuals who had high SES showed the opposite association. Comparable moderating effects of SES were observed for the brain regions implicated in mentalizing [e.g., medial prefrontal cortex (mPFC), temporoparietal junction (TPJ)] (64, 65). These results together imply that SES is neurocognitively linked to the way people process social information.

Of note, the measurements of SES vary across studies and these results should be interpreted with caution. The most common indices include income and educational levels (64, 66), and subjective assessments, such as perceived neighborhood quality (67) and the MacArthur ladder, which measures individual belief about one's location in a status order (65). Although these assessments are usually correlated, they should not be used interchangeably, because they might have enough differential effects on the brain development (68).

Psychological Characteristics: Anxiety and Self-Esteem

Among individuals who have the same demographic profiles, social influence still may have very different impacts, contingent upon individuals' psychological characteristics. Given the social characteristic of the information processing, social anxiety is one of the closest psychological factors that may modulate the effect of social influence. A recent study reported that individuals' social anxiety was positively associated with their conformity to bullying under social influence, such that individuals who show highest social anxiety level conforms to others the most (69). Even in learning directly from experience, highly anxious individuals showed a negative bias (i.e., learning better from bad news) when social others were observing (70). Another study examined social influence differences between healthy individuals and individuals with social anxiety disorder (71). Consistent with the results from the subclinical population, individuals with social anxiety disorder showed higher susceptibility to social influence particularly when social others rated presented face as more attractive than they originally reported. This result was interpreted as evidence for increased motivation to pursue social acceptance and avoid social rejecting in individuals with high social anxiety.

Self-esteem is another psychological characteristic that may be associated with the extent to which one is swayed by others' opinion. Indeed, various classic social psychology research have examined whether individuals' self-esteem is a major moderator of social influence (72–74). Despite the general results showcasing negative association with individuals' susceptibility to peer influence—individuals with low self-esteem are more susceptible to others' influence (72, 74)—, other studies suggested that the relationship is rather more complex. Nisbett and Gordon (73) suggested that modulating effect of self-esteem may differ depding on the type of social influence. Particularly, individuals' self-esteem was negatively associated with the extent to which

they are influenced by others for the type of social influence that is relatively easy to comprehend but implausible, while the association was non-monotonic or even opposite for a difficult but plausible message.

Recent neuroimaging studies corroborated this suggested association between self-esteem and their susceptibility to social information. Somerville et al. (75) reported that individuals who had low self-esteem not only reported that they received positive feedbacks less from others, but also were more sensitive to positive feedbacks received by others compared with individuals who had high self-esteem. This result implied that social feedbacks might be exaggerated in low self-esteem individuals, and thus have increased susceptibility to social influence. Will and colleagues (76) used computational modeling approach and suggested that individuals' self-esteem is established through the way how they learn about social others. These results altogether hint a possibility that self-esteem is more than a modulator for individuals' social susceptibility, but rather a dynamically changing characteristic shaped by the history of social interactions.

Summary

We reviewed various individual characteristics that are associated with the extent to which individuals are influenced by social contexts. As introduced above, vast amount of studies showed that a large variance of individual differences exists in susceptibility to social influence. However, only few studies directly took these associated factors into account in constructing a cohesive computational model of social influence. Individual characteristics such as age and socioeconomic status may be closely tied to developmental changes or differential learning experiences, while other characteristics (e.g., anxiety and self-esteem) may be linked to baseline traits each individual has and to a specific state individuals reside at the moment. Better mechanistic understanding of social influence spanning across these individual characteristics may provide explanation why minorities who are most vulnerable (e.g., adolescents), or marginalized and stigmatized cohorts are more susceptible to their social environment (3, 12) and even likely to experience mental health problems (77, 78).

How Is the Social Influence Conveyed

Sometimes what matters is how you say it, rather than what you say. In the same vein, the exact same content can have a very different impact on people's behavioral changes depending on from whom or how it is delivered. Characteristics of the group (e.g., social distance, expertise) may shape the credibility of the social information, and thus individuals may be more (or less) influenced by a particular social group. Two distinctive ways of being exposed to social information includes directly observing others and in reverse, realizing that one is being observed by others. Depends on these specific circumstances, individuals may obtain different types of social information and in turn, be influenced differently. In this section, we review previous research that examined how the forms of social influence modulate the way how or the extent to which social influence affects individuals' choices.

Characteristics of Others: Social Closeness, Credibility, and Competence

When one has a chance to decide on the team members to work together, one would usually prefer others who he or she shares similar perspectives and relates one another easily. A biased behavioral tendency of being assorted based on individuals' preference is often observed in social context, such that individuals who are closer in their social network are more likely to have similar preference (79). Moreover, social closeness, a psychological construct that is well-described as a shared variance between oneself and others (80), was shown to have a significant effect on individuals' judgement about others (81). In other psychology studies where a dichotomous classification of social relationship is adopted (in- vs. out-group) showed consistent results, such that individuals showed a biased preference toward in-group members (82). Such biases toward socially intimate others might be accounted for by their motivation to keep their membership stable and to enhance self-esteem (2).

Recent neuroimaging studies presented further evidence explaining why and how such biases exist. Sip et al. (83) examined whether social feedbacks from a gender-matched close friend vs. from a confederate have differential impacts on individuals' decision pattern and on their neural responses. Individuals were responsive to social feedback and showed changes in choice patterns accordingly, but only when the feedback came from a close friend. This effect was reflected in BOLD responses in the vmPFC and posterior cingulate cortex (PCC), which they presented as supporting evidence for modulatory impact of social closeness on decision-making processes. A similar study that examined individuals' neural responses to social influence revealed differences when the influence originated from in- vs. out- group (84). Particularly, a set of brain regions including the medial prefrontal cortex (mPFC), amygdala, and ventral striatum (vStr) showed higher BOLD responses for the social influence from in-group than out-group members. Consistent with these findings, the default mode network (85), a set of brain regions including the medial PFC and PCC, and its interaction with subcortical regions are known to be closely associated with mental representation about self-other relationship (86). These studies together highlight that social closeness is an important determinant for social information processing.

Another very closely related factor is whether the achieved social information is perceived useful or not. When expertise of social others is explicitly informed, one can use this knowledge to judge whether social information from them is reliable or not. Supporting this view, various studies have shown that people tend to follow opinion and advice from people with expertise than from novice (87, 88). Klucharev et al. (89) suggested that presenting an object paired with an expert enhances memory performance and moreover has a positive impact on the attitude toward the object. Such an impact of perceived expertise was associated with re-evaluation of an item (89, 90), which may account for the reason why people are more likely to follow experts' opinion.

It is important to note that in most of the cases, it is not obvious whether the social information is useful or not. Thus, individuals should estimate how useful the social information is to maximize one's own benefit (or minimize the harm). As crude heuristics, opinion from larger group of people can be taken into account more heavily (45), and others' faster responses are considered more informative (91). Independent of the true usefulness of the information, individuals were more likely to be persuaded by others when presented with higher confidence (92, 93). Evaluation of the confidence that is presented for (or estimated to be associated with) the social information was tracked in the vmPFC, an area dissociable from the region that encoded subjective value signal combining one's own and others' preference (44, 94). These results support the view that by estimating who knows better or whether the social information is useful, individuals can choose their strategy to learn from social others (13, 95).

The Way Social Information Is Given: Observing and Being Observed

When being around social others, there are different ways to acquire additional social information. The type of information one can achieve is yoked to the methods how social influence is acquired, and thus how one processes and uses the information naturally should be different accordingly. The most direct way to acquire social information is through a chance to observe others' choices which inform others' preferences and social norms. Chung et al. (17) showed that individuals tend to follow others' choices during risky decision-making. By conducting a formal model comparison, they suggested that such conformity is explained by a value-based decision process combining additional utility to the option chosen by others, rather than by changing individuals' original preferences. The mechanisms how individuals combine their own knowledge and preference with social information may vary. Individuals may project their own preference in predicting that of others (96), and also track whether others' intentions underlying the observed actions of others change over time (97). Other studies suggested that individuals use social information to adjust their own opinion and intend to match with that of others. Specifically, when individuals were asked to report attractiveness of a series of faces after viewing others' responses, their original attractiveness reports were adjusted toward the others (40, 98). These results suggested that individuals are able to track the difference of the values (or preference) between their own and others (17, 40, 41), and change their choices (or ratings) accordingly to minimize the difference (40).

On other occasions, one can be mindful of being around others, but have no chance to directly observe others' choices. The impact of simple presence of others is largely investigated in adolescents, where presence of friends were found to increase adolescents' risk seeking behavior (10, 12, 99). Individuals tended to show higher sensitivity to rewards and more impulsive choices under presence of others even if the social others were not friends, but strangers (100). Such social influence was attributed to social reward, associated with approval from others (101). In a recent study, Powers et al. (102) also examined impacts of the contexts where friends were simply present at the same room or monitoring participants' choices. Particularly, options were more likely to be chosen when they were paired with friends' monetary gains compared with when they were paired with friends' losses. In adults, such adjustment of individuals' choice attitudes were more pronounced when friends were monitoring the choices than merely present, while adolescents showed comparable responses to the social contexts regardless of whether friends could witness the choices or not. These results suggested that individuals may take into account wellbeing of friends, particularly when others can immediately witness the choices.

Individuals may infer what others would expect from their choices and place social values toward meeting the inferred expectation (13, 46). This perspective was closely examined in a recent study where participants were asked to predict others' choices (19). After successfully learning others' choices, individuals' preferences for risky choices changed toward that of others as if there was a "behavioral contagion". The main goal of predicting others' choices might have motivated individuals to simulate others' preferences and mentalize (103), which may underlie why social context affects individuals differently.

Summary

We reviewed that how social influence is conveyed may shape the mechanism how a social context would affect individuals' choices. When individuals are under a social context, they may start extracting a set of information ranging from whether others share the same goal as them to whether others have more amount of information. In the inference process figuring out social others' goals, individuals may recalibrate their subgoals [e.g., to collaborate or compete with others, to mimic others' actions (104), to meet a consensus (105)]. Given that real world is largely uncertain and volatile, we, as social agents, must be constantly solving such an inference problem to first evaluate the usefulness of social information and next alternate how to use the information (46).

What Decision Domains and Processes Is the Social Influence Applied to

Would a person who is susceptible to one type of social information always be sensitive to other types of social contexts? It is not uncommon in real life that the extent to which individuals respond to social information differs depending on the type of behavioral choices which are subject to the influence. For example, an adolescent who is not swayed by aberrant behaviors of peers may show tendencies to join her friend for volunteer opportunities, and an addict who easily gives in to craving around other substance users may not respond to intervention of social support groups. In this section, we review previous studies in social influence across different decision domains and processes. In addition, we discuss whether or not social influence is domain-general and if not, whether there are any latent variables that explain why individuals show domain-specific responses to social information.

Domain-Specific and Domain-General Mechanisms of Social Influence

Social influence can be readily observed in almost every kind of decision process in our life. Mirroring this, there were many empirical studies ranging from the simplest perceptual decision-making to complex moral decision-making where they used a variety of task paradigms to show the effects of social influence on human information processing. Perceptual decision-making tasks are based on the evaluation of sensory information, such as the length of lines (106), the dominant color of the presented patches (107), or the shape of three-dimensional objects (108). Personal preference tasks include variety of options, such as preference for t-shirts (41), faces (40, 98), and works of art (108, 109). In monetary reward tasks, there are explicit gains and losses of money associated with each of the choice option (17, 19, 110). Lastly, in social preference tasks, individuals encounter decision-making situation where they have to consider explicit losses and gains of social others and their own simultaneously (29, 101). On average, behavioral changes indeed were observed under social influence across all of these studies that probe different levels of cognitive processing in humans. However, due to the variety of contexts each study adopted (e.g., cover stories) and the differences in the targeted cognitive processes (e.g., perception, valuation), there is no universal computational framework that explains the mechanism of social influence across domains.

There are a few computational frameworks that provided cross-domain accounts for social influence (21, 22). First, individuals may be trying to learn others' preferences and values under social influence. Such "normative influence" of social contexts, where social others' choices are not necessarily based on a better set of information, were explained by reinforcement learning (RL) framework capturing individuals' change of behaviors toward others [(40, 98), c.f., (111)]. Consistent with this perspective, individuals under social context were sensitive to the opinion differences between them and the others (41, 112), and it was shown that a set of brain regions involved in social and monetary reward learning overlap (113, 114). The RL framework successfully captured the extent to which individuals conform to others' preference-based choices over primary and social rewards (40, 115). Second, individuals may be collecting more information from others' choices. Following such "informational influence" of social contexts, individuals seemed to be using others' responses and choices to appropriately adjust their original responses. To integrate information from two sources, individuals computed the importance and reliability of each piece of information (44, 45, 47). Such a Bayesian learner framework successfully explained individuals' conformity not only in perceptual, but also in value-based decision-making particularly when statistical inference was available.

It is worth noting that behavioral patterns which are well-explained by the same computational framework may in fact induced by different neural mechanisms; differential implementation level explanation as per Marr's three levels of analysis (116). For example, a recent study directly compared multivoxel neural patterns for social conformity with that for classic reward learning, and suggested that neural responses in the brain regions typically involved in non-social RL (e.g., striatum) do not explain whether or not individuals conform to social information (111). This emphasizes again the importance of interdisciplinary approaches in understanding human information processing. A careful consideration of specific contexts will shape individuals' motivation ("computation level"), but why and how individuals process social information in the context need thorough examination not only in algorithmic level (e.g., computational modeling) but also in implementational level (e.g., functional neuroimging) (117).

Summary

We briefly reviewed plausible mechanisms suggested to date of social influence over different decision domains. Although cognitive motivations defined over psychological constructs including value and information maximization accounted for neural and behavioral mechanisms under social influence (33), applying the same mechanism to different levels of cognitive processing has been challenging, because task settings (e.g., goal, order, amount of information) also varied across different studies. Future studies may tailor the study design to specifically examine individuals' cross-domain susceptibility to social information. By using the same task settings, but over different domain, we would get a direct chance to address whether individuals' domain-specific sensitivity and confidence, which will be manifested as preference for social information, affect the extent to which individuals use social information.

CONCLUDING REMARKS AND FUTURE CHALLENGES

Research on social influence has been conducted across various fields of studies. Recent computational approach in conjunction with functional brain imaging technology provided new impetus for the study of social influence, and shed light on underlying mechanisms of individual cognitive processes under social context. Still, there are major challenges remaining given the sheer diversity of social contexts. In this review, we overviewed previous studies in social influence along the three axes of determinants (who are the receivers, how is the influence provided, and to what is the influence applied) that may modulate and mediate the impacts of social influence. These three dimensions are not mutually exclusive one another and thus, they would not completely compartmentalize the impacts of one axis from the other. Still, we hope that our review would highlight potential co-factors crucial to consider for expanding our mechanistic understanding of social influence to translational applications (e.g., intervention design) (118, 119).

Given the complex nature of social contexts, simply adding up all the plausible factors into one experiment might not bring solutions. To address this issue, coherent and theory-driven computational modeling approaches should be proceeded (22, 120, 121). In parallel with this formal theory-driven approach, individual differences and extreme cases (e.g., cultural differences, race and gender discrimination, mental illness) cannot be overlooked as described herein. Thus, hypothesis

testing in special population may provide further insights in examining the generalizability and transferability of the model (122–125). As an equally important research direction, data-driven understanding of behaviors in social contexts may provide complementary insights for latent variables. Nowadays, taking advantage of large-scale studies and open science practices, we now have better access to big data including personal habits and their social network (126–128). However, we still have to interpret the results with caution considering the sparsity and multi-dimensionality of the data (129).

Considering the importance of both theory-driven and data-driven approaches in mind, there are at least two issues to take into account when in designing future studies in social influence. First, dimensional measurements of potential determinants are preferrable than to have dichotomized classes. For example, most of the studies that investigated the impact of social closeness took contrast approach where the effects of a close friend vs. a stranger were examined (82–84). However, social closeness is not only associated with perception of social membership, but also trust and competence (130, 131). That is, we cannot disentangle potential effects of social distance and other co-varying factors by having only two categories along the dimension. Second, volatility of the social context should be considered to better mimic real world interactions. Social environment and relationship between people constantly change and how we perceive the context gets adjusted accordingly. In perspective of formalizing its impacts in the model, changes in belief about others' advice (13) or active alterations between utilized strategies for social information (46) can be implemented. Alternatively, to explore naturally emerging dynamics in rich environment, new experimental designs may target for collecting neural and behavioral data from interactions between uncontrolled real dyads simultaneously (132–134), and even further, using naturalistic social stimuli such as real-time videos and virtual reality (135). Using naturalistic social environment would get us closer to directly simulate the impacts of social contexts simulating translational applications. However, as reviewed above, there are numerous factors that are already known to affect social processing, but we have close to no understanding how these factors interact and interfere each other. Thus, for broader generalizability and future individualized translational applications, it cannot be emphasized enough the importance of compartmentalized and computational understanding about the underlying determinants of social influence.

AUTHOR CONTRIBUTIONS

HL and DC conceptualized the study, wrote the first draft of the manuscript, and contributed to manuscript revision, read, and approved the submitted version. All authors contributed to the article and approved the submitted version.

FUNDING

DC was supported by UNIST internal funding (1.220032.01) and the National Research Foundation of Korea (NRF-2020S1A3A2A02097375). The funders had no role in study design, decision to publish, or preparation of the manuscript.

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