"NO WORDS FOR FEELINGS, YET!". EXPLORING ALEXITHYMIA, DISORDER OF AFFECT REGULATION AND "MIND-BODY" CONNECTION

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"NO WORDS FOR FEELINGS, YET!". EXPLORING ALEXITHYMIA, DISORDER OF AFFECT REGULATION AND "MIND-BODY" CONNECTION

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EDITORIAL
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Editorial: "No Words for Feelings, Yet!" Exploring Alexithymia, Disorder of Affect Regulation, and the "Mind-Body" Connection

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Keywords: alexithymia, emotional regulation, mind-body connection, affective dysregulation, psychosomatic and emotional difficulties

Editorial on the Research Topic

"No Words for Feelings, Yet!" Exploring Alexithymia, Disorder of Affect Regulation, and the "Mind-Body" Connection

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> "*Unexpressed emotions will never die.*
> *They are buried alive and will come forth later in uglier ways.*" (Sigmund Freud)

The term "alexithymia" was introduced by Peter Sifneos in 1973, to designate a cluster of cognitive and affective characteristics that were observed among patients with classical psychosomatic diseases (1). The alexithymia construct was further expanded over the years, resulting from many clinical investigations (2, 3). The construct is multifaceted and dimensional and includes several distinct characteristics: (a) difficulty in identifying and describing feelings, (b) difficulty in distinguishing feelings from the bodily sensations, (c) diminution of fantasy, and (d) concrete and poorly introspective thinking (4). The persons with alexithymia may show affective dysregulation, the inability to self soothe, and manage emotions because of a lack of awareness of emotions (5). Therefore, the adaptive informational meaning of emotions that is essential for emotion regulation often lacks in these individuals (6).

These cognitive features have been ascribed to a compromised capability to elevate emotions from a sensorimotor level of experience to a representational level, where they can be used as signaling reactions to internal or external events and moderated by psychological mechanisms (7). It has been demonstrated in several studies that often persons with alexithymia show significantly higher levels of psychological distress than persons without alexithymia and may develop "functional" somatic symptoms and complaints (8).

As a distinctive trait, the classical features of alexithymia are more evident during meaningful social interactions with high emotional valence (9). The affect-avoiding relational pattern behavior exhibited

by the persons with alexithymia is habitually maladaptive. It may stimulate problems and conflicts in significant relationships, finally subsidizing the risk of the emergence of psychiatric symptoms such as depression and anxiety (10).

Moreover, alexithymia is a relatively stable personality trait, enhancing vulnerability to depressive symptoms, and is generally associated with a higher risk of death for several causes (suicide, accidents, injury, or violence) and is accompanied by an affective dysregulation (11, 12). The affective dysregulation may further impair emotion recognition, further increasing the risk of impulsive/addictive behaviors and the emergence of suicidal ideation and behaviors (13).

As an ideal introduction to the Research Topic, López-Muñoz and Pérez-Fernández provided a comprehensive and intriguing history of the alexithymia concept. They pointed out that the alexithymia construct may be understandable when observed from an epistemological perspective, and it mainly involves a rerun of the age-old conflict between basic and applied science, which in this case takes the form of a confrontation between the therapist's clinical reflection and the critical judgment of experimental methodology.

Alexithymia is the quintessence of impairment of "mind-body connection," and its recognition is crucial in everyday clinical practice to develop *ad hoc* interventions, considering that persons with alexithymia and concurrent psychiatric disorders are often treatment-resistant (not only to pharmacotherapy but also to psychotherapy) (14, 15). Concerning this point, several papers have explored the issue of treatment resistance and possible interventions. Pinna et al. performed a systematic review to evaluate the shreds of evidence on the role of alexithymia role in influencing the treatment outcome in several psychiatric disorders. They found that the existing data tend principally to correlate low baseline, and/or post-treatment levels of alexithymia and/or an improvement in levels of alexithymia throughout treatment, with a more satisfactory outcome of the treatment of the psychiatric disorders considered. Following this observation, Gramaglia et al. reviewed the treatment outcome in Anorexia Nervosa (AN) in terms of changes in alexithymia as assessed by its most commonly used self-report measure, the Toronto Alexithymia Scale (TAS). They found that a relevant percentage of persons with AN and comorbid alexithymia reached only partial recovery following treatment. Therefore, the identification of outcome predictors such as alexithymia is essential, as well as that of treatments specifically targeting such predictors.

Accordingly, one can argue that pre- and during-treatment interventions aimed to reduce alexithymia levels may be somewhat beneficial to achieve an excellent therapeutic response (16, 17). Aaron et al. assessed the relationships between alexithymia and interoceptive accuracy and sensibility in a sample of healthy young adults and the outcomes of a brief mindfulness-based body scan intervention. The results showed that higher alexithymia levels might be associated with either relatively high or low interoceptive accuracy. They also showed that the meditation mindfulness-based body scan intervention did not result in improved interoceptive accuracy or sensibility above and beyond that of a control group. Therefore, improvements in interoceptive accuracy, interoceptive sensibility, and emotional awareness may require longer or more interactive intervention approaches.

Interestingly, in a Perspective Article of this Research Topic, Shalev suggested that clinicians and neuropsychologists could help individuals who suffer from alexithymia by coaching them to use awareness-of-sensation practices. She argued that these techniques might promote relaxation or self-acceptance, also facilitating interoceptive improvement through an improved distinction between bodily perceptions and psychological interpretation. Besides, as demonstrated by Fournier et al., difficulties in interoceptive abilities (DIA) were predictive of the presence of irritable bowel syndrome (IBS), suggesting that when faced with a new stressful situation, patients in remission would have difficulty in perceiving their internal body changes and thus would have difficulty properly regulating their emotions. On the other hand, in the Crohn's disease group, difficulties in describing feelings dimension of alexithymia were found a predictor of the presence of this disorder. In contrast, in the Ulcerative Colitis group, predictors seem to belong more to the physiological sphere rather than alexithymia. These results were encouraging and opened new perspectives for the healthcare of patients with gastrointestinal diseases, such as the use of Cognitive Behavioral Therapy. Duquette presented a very interesting case series describing the disturbances in emotional awareness in alexithymia, trying to integrate psychotherapeutic and neuroscience findings. Considering the current advances in neuroscientific theory and its application to psychotherapy, she argued that persons with alexithymia should be trained and enhanced in the ability to switch their attention between: their inward interoceptive sensations flexibly; exteroceptive sensory signals from the world, in the present moment (i.e., the context); and their own usual and deeply held prior beliefs about the causes or meanings of sensations.

Several contributions in this Research Topic also aimed to evaluate alexithymia in clinical and non-clinical samples, further contributing to its understanding.

Concerning non-clinical samples, Elkholi et al. evaluated the rates of alexithymia and its relationship with smartphone addiction in a cross-sectional study on a sample of 200 university students and found a strong association between both. These results were consistent with most of the previous literature that pointed out that persons with alexithymia tend to regulate their emotions through several forms of addictive behaviors. Kajanoja et al. examined the relationships of alexithymia and hair cortisol concentrations (HCC), a measure of long-term cortisol levels, and a biomarker for chronic stress in pregnant women. They found that among pregnant women, moderate to high alexithymia was associated with elevated HCC levels, and this association was driven by the subjective difficulty in identifying feelings (DIF) dimension of alexithymia, the only associated with HCC in the whole sample, after controlling for potential confounders. These results are in line with the so-called "stress-alexithymia hypothesis" (18, 19). Ma et al. explored the relationships between schizotypal traits, alexithymia, and sleep problems in 2,626 first-year students of a medical university. They found positive correlations between schizotypal traits,

alexithymia, and sleep difficulties, although alexithymia was found to mediate the relationship between schizotypal traits and sleep difficulties partly. They also suggested that training the ability to express emotion may be capable of improving the sleep quality of persons with higher schizotypal traits.

Concerning clinical samples, Raffagnato et al. evaluated 134 adolescents with "nonsuicidal self-harming, or self-injury" (NSSI). They found that individuals who engaged in NSSI had more problems in the internalizing and externalizing domains than the control group, and internalizing disorders (and affective disorders in particular) was the factor that most strongly characterized the clinical group. Moreover, self-harming persons had more severe somatic disorders and alexithymia. These findings demonstrated that alexithymic traits are linked to the use of the body instead of words to express emotion in the case of psychological disease and may explain body NSSI when the emotional dysregulation and negative feelings are overwhelming. Bileviciute-Ljungar and Friberg investigated the connections between the alexithymia (using the TAS-20) and the level of emotional awareness, as well as depression and anxiety, with objective sleep parameters from polysomnography in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). The results of this pilot study indicated a biological mechanism such as sleep fragmentation that may affect emotional awareness.

Moreover, they hypothesized that alexithymia and emotional awareness might have different associations with sleep and probably are regulated in different ways, though overlapping each other. On the other hand, Šago et al. assessed the difference in the prevalence of alexithymia in panic disorder (PD) and other anxiety disorders (OAD). They found that the prevalence rate of alexithymia in PD was 27%, and the difficulty identifying feelings (DIF) subscale scores of TAS-20 DIF was significantly higher in the PD group than in the OAD. Because of these results, they argued that higher rates of alexithymia in PD might reflect a person's disposition to tighten their emotional experience to elude affect-based psychological sensations. These results are in line with those of previous studies on PD (20, 21).

As an ideal conclusion of the present Research Topic, the paper by Tonello et al. explored fascinatingly the "mind-body connection" and investigated the relationships between depression and objective measures of body fatness, autonomic indices, cardiorespiratory fitness and physical activity levels in 35 non-exercising women. They found that that cardiorespiratory fitness was the best predictor of depressive symptoms independently of body fatness, with maximum oxygen consumption (VO2max) and the sum of skinfolds moderately related to depression scores and VO2max the only independent predictor of depression in several stepwise multiple linear regression models.

In conclusion, all the papers in the present Research Topic provided clarification on the alexithymia construct and the "mind-body connection," also trying to give practical and useful information on their evaluation and possible treatment options. We believe that alexithymia and its impact on "mind-body connection" still represent a challenge for all mental health and healthcare workers. Still, there is a silver lining as early detection of alexithymia has become more frequent in everyday "real-world" clinical practice (22). We hope that the research on these fundamental topics in mental and general health will proceed to explore this construct further and to find an appropriate and reliable therapeutic strategy.

AUTHOR CONTRIBUTIONS

The Editorial has been written by DB, MF, and LO.

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ORIGINAL RESEARCH
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Prediction of Depression Scores From Aerobic Fitness, Body Fatness, Physical Activity, and Vagal Indices in Non-exercising, Female Workers

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Background: Depression is associated with a decreased cardiorespiratory fitness, and physical activity [PA] levels, higher rates of obesity, and dysfunction in autonomic control of heart rate [HR]. However, these parameters were mostly recorded with indirect methods. Thus, the aim of the current study was to investigate the relationships between depression scores and objective measures of body fatness, autonomic indices (i.e. HRV and HRR), cardiorespiratory fitness and PA levels; and subsequently to present the best predictive models of depression scores for this population, based on these variables.

Methods: Thirty-five non-exercising women (26–43 years; maximal oxygen consumption [VO_2max] ∼ 17.4–38.3 mL/kg/min) volunteered for participation in this study. All participants responded to the Beck Depression Inventory [DBI] and were evaluated for body mass index [BMI], percentage of body fat, sum of skinfolds, and VO_2max. Subsequently, over four consecutive days, an orthostatic test and a submaximal exercise on a cycle ergometer were performed to record HRV and HRR, respectively. In addition, incidental PA was recorded during 5 consecutive days using accelerometers.

Results: depression scores were related to VO_2max ($r = -0.446$, $p = 0.007$) and the sum of skinfolds ($r = 0.434$, $p = 0.009$). Several stepwise multiple linear regression models were performed and only VO_2max was revealed as an independent predictor of the Beck scores (ß $= -0.446$, $R^2 = 0.199$, $p = 0.007$).

Conclusion: The present study revealed that VO_2max and the sum of skinfolds were moderately related to depression scores, while VO_2max was the only independent predictor of depression scores in female workers.

Keywords: depression, physical activity, autonomic control of HR, body composition, physical fitness, women

INTRODUCTION

Depression is a multifactorial disease that affects 322 million people worldwide (1). Between 2005 and 2015, there was an increase of more than 18% in the number of cases (1). The global prevalence is 4.4%, however, women suffer more from the disease, with 5.1% compared to 3.1% of men (1). In Brazil, depression affects 7.6% of the population, which represents about 11.2 million people, with a prevalence of 10.9% in women and 3.9% in men (2), therefore ranking Brazil as the 5th country in the world in depression prevalence (2).

Depression is a prevalent risk factor for the development of cardiovascular and metabolic (3–5) diseases (CVDs) (6–10). For example, people with depression presents an increased risk (relative risk [RR] = 1.72, 95% CI 1.48–2.00) of developing any cardiovascular disease when compared to non-depressed controls. In addition, people with subsyndromal depressive symptoms are already in increased risk for developing cardiovascular disease (11). Although the underlying mechanisms of this relationship are not fully understood, there are several factors that act bidirectionally and independently, increasing both depression and CVDs risk, including aerobic capacity (12), obesity (13), physical activity (14), and heart rate variability (HRV) (15).

Cardiovascular diseases are the main cause of death in women (7, 16) and present an inverse relationship with cardiorespiratory fitness (17, 18). Moreover, cardiorespiratory fitness is inversely related with depressive symptoms severity, regardless depression diagnosis, and this association has been demonstrated to be moderated by sex (12). Thus, people with depression have decreased fitness when compared to people without depression (19, 20). Moreover, a possible relationship between depression, lack of exercise and cerebrovascular disease comorbidity has also been suggested (21).

Overweight and obesity has been associated with depression, in addition to be an aggravating factor for overall health status (13, 22–24). The association between obesity and depression is bidirectional: depressed people are at an increased risk of being obese and, in turn, obese people have a risk of developing depression (25). Interestingly, although the percentage of fat increases the risk for developing depressive symptoms, this association disappears when adjusted for cardiorespiratory fitness levels in both men and women (23), with some sex differences identified in the association between obesity and depression (22).

Individuals with depression have a decreased HRV when compared to healthy controls (15, 26–29), and this inverse association between HRV and depressive symptoms has also shown different sex related interactions (30). The severity of depressive symptoms is an independent factor for decreased HRV and vagal tone in patients with unipolar and bipolar depression (31). The reduction in HRV is commonly associated with cardiovascular morbidity and mortality, thus, depressive symptoms, decreased HRV, and risk of developing cardiovascular disease are closely related (32). In addition, autonomic activity could be also assessed with HRR, which is an index of vagal reactivation after different exercises (33–38). Heart rate recovery has been also found to be inversely related with depression scores (39, 40).

Finally, PA has been previously associated with all of the aforementioned factors and has been recommended as a complement to pharmacotherapy for the treatment of depression (41). Previous studies have also shown that the association of PA with other forms of treatment is a determinant for a decrease in depression scores (42). People with higher PA levels have 17% less risk of developing depression (43). However, these previous studies did not account for the difference between PA (i.e., any movement of the body that is produced by muscle contraction and which increases energy expenditure above basal levels) and physical exercise (i.e., a repetitive structured PA designed to improve or maintain one or more components of the physical condition) (44–48).

Although several studies have independently investigated the relationship between the above-mentioned variables (i.e., PA, HRV, HRR, body fatness) and depression scores, to the best of our knowledge, there are no studies investigating the relationship of all these physical and physiological variables, and their interactions, with depression scores in a homogenous sample of women. Thus, the aim of the current study was to investigate the relationships between depression scores and objective measures of body fatness, autonomic indices (i.e., HRV and HRR), cardiorespiratory fitness and PA levels; and subsequently, to present the best predictive models of depression scores for this population, based on these variables.

METHODS

Participants

All participants were employees of two private Universities in Brazil. All of them worked in the cleaning service or administrative staff. The inclusion criteria were: absence of health related problems or physical conditions; no medications that could interfere with independent and dependent variables; and no practice any form of regular exercise at the time of the study. Thus, 35 adult female workers, aged 34.5 ± 5.1 years (26–43 years), were finally included in this study. All of them were classified as irregularly active or sedentary by the short version of the international PA questionnaire (IPAQ) (49), a short validated questionnaire with eight questions regarding the weekly time devoted to different levels of PA and sedentary time. This research was approved by the ethics committee of the Catholic University of Brasília and all volunteers signed the consent form after detailed explanation of procedures.

Study Design

All participants were evaluated for 14 days following the methods of a previous study (36). The schedule of evaluations is presented in **Figure 1**. During the first week, participants were familiarized with all the procedures, completed the IPAQ and Beck Depression inventory (BDI) (50), and were evaluated for body fatness and cardiorespiratory fitness. During the second week, participants went to the laboratory on a daily basis and were evaluated for HRV and HRR. PA was recorded over 7 days,

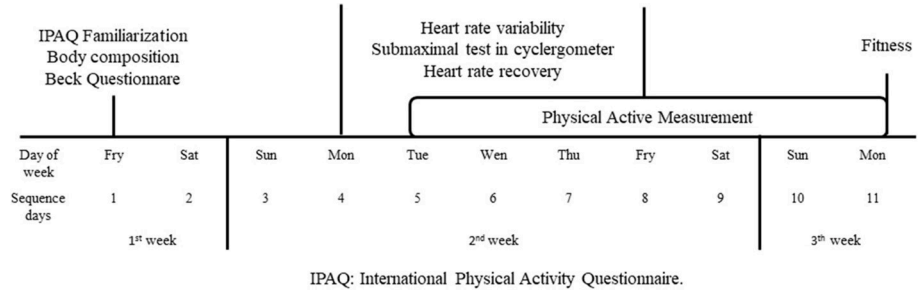

FIGURE 1 | Schedule of evaluations.

but only measures from five days (Wednesday to Sunday) were used for further analyses (36). During the third week, participants completed the cardiorespiratory fitness test.

Measures

Body Composition

Body mass (kg) was evaluated using a digital scale (Model 05, G-Tech®, China), and height (cm) through a stadiometer (Sanny®, ES2040, Brazil) to determine body mass index (BMI). Adiposity was evaluated using the sum of the skinfolds ($\sum$S) (i.e., pectoral, mid axillary, abdominal, supra iliac, thigh, triceps and subscapular) (47), with % of body fatness determined with the equations of Jackson and Pollock (51) and (52).

Cardiorespiratory Fitness

Maximum oxygen consumption (VO_2max) was assessed as a measure of cardiorespiratory fitness, during a maximal incremental test on a cycle ergometer (Lode Excalibur, Lode, Netherlands; or Monark model 8348, Monark, Sweden). The test started with a load of 0 W and thereafter it was increased at a rate of 20 W·min^{-1}, maintaining a constant cadence of 60 rpm. HR was continuously recorded using a telemetric monitor (POLAR Electro Oy, Finland), while ventilatory parameters were assessed breath-by-breath with a metabolic cart (Metalyzer 3B, Cortex, Germany) that was previously calibrated following manufacturer's instructions.

Beck Depression Inventory

The BDI is a valid questionnaire with 21 questions that include cognitive and affective behavioral symptoms and attitudes related to depression. The subjects selected the sentence that best described their answer during their previous two weeks. The sum of the final score can be from 0 to 63 (53). All the questionnaires were individually applied by the same clinician, in a closed room, under a calm environment and without the possibility of any interruption by other people. The cut-off scores for the BDI are: none or minimal depression with <10; mild to moderate depression with 10–18; moderate to severe depression with 19–29; and severe depression with 30–63.

Autonomic Indices

The evaluation of HRV was performed during four consecutive days, through an orthostatic test, performed in the laboratory (07:00–08:00 a.m.) under standard environmental conditions. During the orthostatic test, participants remained seated for 3 min followed by 4 min in standing position. All HR recordings were obtained using a HR monitor (RS800cx, Polar Electro Oy, Finland) previously validated for this purpose (54). Subsequently, HR data were transferred to a computer and filtered using the customer's specific software (Polar ProTrainer® 5, Polar Electro Oy, Finland). If a record presented error >5%, it was discarded (55). After visual inspection, filtering and correction, the data was transferred and analyzed on a specific HRV analysis software (Kubios 2.2, The Biomedical Signals Analysis Group, Finland). Vagal modulation was assessed via the root mean square of successive R-R intervals differences (RMSSD) during the last 2 min of each position ($RMSSD_{seated}$ and $RMSSD_{standing}$, respectively). Following a previous study (36), we used the average values over the four days of evaluation.

For HRR determination, the volunteers performed a 6-min submaximal cycle ergometer exercise (model 8,348, Monark, Sweden) immediately after HRV evaluations. At the end of the exercise, the volunteers remained seated and relaxed on the cycle ergometer for 5 min for determination of HRR at 1 min (HRR_{1min}) and at 5 min (HRR_{5min}). As in the case of HRV analyses, we used the average values over the four days of evaluation (36).

Incidental Physical Activity

The PA was recorded with an accelerometer (GT1M, Actigraph, USA), being considered the values of five consecutive days, which is enough to reflect weekly AF patterns in adults (56). The devices were placed on the right hip of participants and PA was recorded continuously, except during bathing, sleeping and the cycle ergometer submaximal exercise. Following the procedures of a previous study (36), the parameters analyzed were: steps per day (Steps), and moderate to vigorous PA (MVPA).

Statistical Analyses

The distribution of the data was verified for normality with Shapiro Wilk's test. Scaterplot of the predicted values vs. the standard residuals of the variables were verified for homoscedasticity and presence of outliers. To achieve the statistical assumptions above mentioned, some variables were log-transformed. Subsequently, Pearson product correlation coefficient was used to verify independent associations with the dependent variables, and for multicolinearity of the independent

variables. Multicolinearity was considered when independent variables presented correlations with $r \geq 0.7$. Then, a stepwise regression was applied with Beck scores as the dependent variable, and with all other parameters as independent variables. Thereafter, due to the number of subjects in the final sample, some multiple linear regression models were constructed using a combination of up to four variables, one from each different domain (e.g. body composition, aerobic fitness, PA, and autonomic indices) to achieve the better model of prediction of depression scores, preserving an sufficient statistical power for the analyses. A 5% level of significance was adopted.

RESULTS

Characteristics of adiposity, aerobic fitness, PA levels, autonomic indices, and depression scores of participants are presented in **Table 1**.

Significant correlations were found between some independent variables (see **Table 2**). Although multicollinearity was observed in some of the independent variables, none of the regression models included those variables simultaneously. Besides that, ΣS and VO_2max were significantly and independently correlated with the dependent variable (Beck scores), as reported in **Figures 2A,B**, respectively.

The stepwise multiple linear regression model selected only VO_2max as a predictor of Beck scores, with standard $\beta = -0.446$, $R^2 = 0.199$, and $p = 0.007$. Then, another 16 models were tested, and the better model achieved $R^2 = 0.278$ and $p = 0.039$, including VO_2max (std.$\beta = -0.283$, $p = 0.180$), SS (std.$\beta = 0.224$, $p = 0.279$), MVPA (std.$\beta = 0.154$, $p = 0.338$), and $RMSSD_{standing}$ (std.$\beta = 0.117$, $p = 0.472$). Although that model reached statistical significance, none of the independent variables adopted were found to be significant independent predictors of Beck scores. As expected, for other models tested, the only variable who independently predicted Beck scores was VO_2max. The models are presented in **Table 3**.

TABLE 1 | Demographic characteristics and physical activity levels of participants.

Parameters	Mean ± SD	Range
BDI-scores	12.3 ± 7.1	0.0–28.0
Age (years)	34.5 ± 5.1	26–43
Body mass (kg)	65.5 ± 13.7	48.6–110.0
Height (m)	1.57 ± 0.09	1.28–1.68
BMI ($kg{\cdot}m^{-2}$)	26.01 ± 4.9	18.1–36.5
Body fat (%)	33.98 ± 6.7	19.9–43.1
ΣS (mm)	206.2 ± 55.8	102–293
VO_2max ($mL{\cdot}kg^{-1}{\cdot}min^{-1}$)	25.2 ± 5.2	17.4–38.3
Steps·day^{-1} (Steps)	8597 ± 3204	3257–15464
MVPA ($min{\cdot}day^{-1}$)	41.5 ± 22.4	7–84.1
$RMSSD_{seated}$ (ms)	25.8 ± 9.0	8.6–46.5
$RMSSD_{upright}$ (ms)	17.9 ± 5.7	9.8–31.9
HRR_{1min} (bpm)	31.3 ± 7.2	18.7–49.7
HRR_{5min} (bpm)	53.6 ± 5.2	45.5–64.7

SD, standard deviation; BDI-scores, beck depression inventory scores; BMI, body mass index; Body Fat%, percentage of body fatness; ΣS, sum of 7 Skinfold; VO_{2max}, maximum oxygen consumption; Steps·day^{-1}, mean daily steps; MVPA, mean daily moderate to vigorous PA of 4 days of data collection; RMSSD, root Mean Square of the differences between successive R peak intervals; HRR_{1min}, heart rate recovery of the first minute; HRR_{5min}, heart rate recovery of the fifth minute.

DISCUSSION

To the best of our knowledge, this is the first study evaluating the relationship and interaction of depression scores with the autonomic control of HR, PA, cardiorespiratory fitness and body fatness in the same sample. Several models were tested to investigate what variables were able to predict depression scores (see **Table 3**). Thus, we observed that in women who do not exercise regularly, the depressive symptoms are related to the level of cardiorespiratory fitness and body fatness. However, the only variable able to predict independently depression scores was VO_2max. In contrast, and contrary to our hypotheses, incidental PA or autonomic control of HR were not associated with depression scores.

As shown in previous studies (12, 19, 23, 57–60), depression scores demonstrated an inverse association with cardiorespiratory fitness. In addition, our main finding is that cardiorespiratory fitness is the best predictor of depressive symptoms independently of body fatness, confirming the previous findings of the prospective study of Becofsky et al. (23). According to our model, changes in VO_2max values may explain up to 19.9% of the variance in the depression scores, therefore, an increase of ∼2 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ of VO_2max would imply ∼1.2 points less in the depression score. While the relationship between aerobic fitness and depression has been previously suggested to be mediated by PA, this is not the case in the current study. In this regard, exercise has been previously demonstrated to influence depression independently of its intensity (61), perhaps implying that the impact of aerobic fitness *per se* on depression scores and symptoms could be mediated by other factors. Thus, we may suggest the possible association between aerobic fitness and other biological mediating factors related to mental health and cognition. For instance, previous reports have found a relationship between VO_2max, inflammation, and brain-derived neurotrophic factor (BDNF) in different populations (62–64), factors also recognized to be related to depression (65). Therefore, future studies are needed to better clarify the mechanistic link between VO_2max, other aerobic fitness parameters and depression.

In our study, body fat did not correlate with depression scores, however, they were associated with the sum of skinfolds. The association between body composition parameters with depression scores has presented contradictory results in literature, a fact that can be attributed to differences in methods to characterize overweight and obesity, in addition to the existence of a number of confounding variables. For instance, previous studies identified an association between BMI and depression scores (13, 24, 66). In addition, women with % of body fatness greater than 30 were more likely to develop depressive symptoms (23). Our results may be also explained by the fact that % of body

TABLE 2 | Correlation matrix of dependent and independent variables ($n = 35$).

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Beck scores	–	−0.446‡	0.351	0.435‡	0.056	0.173	0.136	0.237	0.188	0.001
2. VO_2max	−0.446‡	–	−0.528‡	−0.642‡	−0.038	0.041	−0.088	−0.215	−0.235	−0.138
3. Body Fat (%)	0.351	−0.528‡	–	0.816‡	0.243	0.124	0.042	0.035	0.183	0.211
4. ∑S	0.435‡	−0.642‡	0.816‡	–	0.110	0.060	0.156	0.163	0.198	0.090
5. Steps·day^{-1}	0.056	−0.038	0.243	0.110	–	0.731‡	0.201	0.090	0.567‡	0.536‡
6. MVPA	0.173	0.041	0.124	0.060	0.731‡	–	0.319	0.143	0.383*	0.123
7. $RMSSD_{seated}$	0.136	−0.088	0.042	0.156	0.201	0.319	–	0.564‡	0.419*	0.171
8. $RMSSD_{standing}$	0.237	−0.215	0.035	0.163	0.090	0.143	0.564‡	–	0.435‡	0.199
9. HRR_{1min}	0.188	−0.235	0.183	0.198	0.567‡	0.383*	0.419*	0.435‡	–	0.707‡
10. HRR_{5min}	0.001	−0.138	0.211	0.090	0.536‡	0.123	0.171	0.199	0.707‡	–

*Beck, Beck inventory depression scores; VO_{2max}, maximum oxygen uptake; Fat%, Body percentage of fatness; ∑S, sum of skinfolds; Steps/Day, mean daily steps; MVPA, minutes per day on moderate to vigorous PA; sRMSSD, Root Mean Square of the differences between successive R peak intervals recorded in seated condition; uRMSSD, Root Mean Square of the differences between successive R peak intervals recorded in the standing condition; 1minHRR, one minute heart rate recovery; 5minHRR, five minutes heart rate recovery. *$p < 0.05$; ‡$p < 0.01$.*

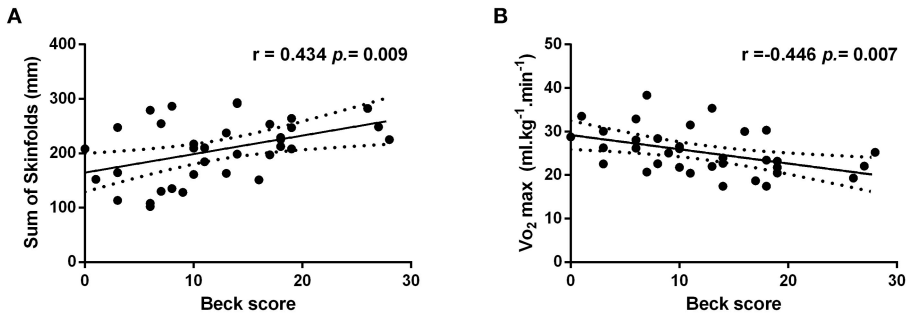

FIGURE 2 | Correlation between Beck scores and the sum of skinfolds **(A)** and VO_2max **(B)**.

fatness is an estimated measure, while the sum of skinfolds is an objective measure. Future studies should consider these aspects when verifying these associations in further studies.

Our data did not reveal any relationship between objective measured PA and depression, which is in contrast to previous literature (14, 43, 67–72)]. The lack of association may be attributed to the different protocols used for evaluation of depression scores and PA levels (e.g., selection of cut-off points for different PA levels). However, a strength of the current study is the use of objective measures of PA along with the isolation of incidental PA from exercise, as participants who exercised regularly were not included in the current investigation. Therefore, it may be suggested that this finding is not necessarily in contradiction with previous studies that mostly used indirect measures of PA levels, while they did not differentiate between exercise and overall incidental PA levels. In this respect, it should be pointed out that women in the current study averaged 41 min/day of moderate to vigorous PA. Meanwhile, previous studies showed that 30 min/day, three times a week, of moderate PA is enough to reduce the risk of developing depression by 22% (43). In addition, although the number of daily steps has not been shown to be associated with depressive symptoms, mean values in the current study are above the recommendations of 6,500-8,500 steps for special populations (73, 74). In this regard, given that our sample was composed of female workers, and that probably most PA was performed at work, future studies differentiating between leisure time and occupational PA are needed as these two PA dimensions have both been demonstrated to influence cardiovascular health in different ways (75).

The use of PA and physical exercise for the treatment of depression is currently increasing (42, 73, 74, 76–79). The improvement of cardiorespiratory fitness in a short period of time with regular physical exercise could be suggested as an effective means for this purpose (59). However, PA performed in daily life could also be important in order to improve levels of cardiorespiratory fitness (80). Stimulating the participation of individuals with depression in physical exercise programs can be an effective treatment alternative, given the low barriers associated and their effectiveness for improving depressive symptoms (81). Recently, Busch et al. (82) evaluated the preferences and barriers of exercise for the treatment of depression. The results of this study (82) indicated that the lack of motivation and fatigue are the main barriers to exercise (82). Therefore, in order to identify the best exercise model and the amount of incidental PA for the treatment of depression, it is

TABLE 3 | Regression analysis for variables predicting Beck Scores ($n = 35$).

Model	Regression R^2 (*p.*)	VO_{2max} Std.*B* (*p.*)	Body Fat (%) Std.*B* (*p.*)	$\sum S$ Std.*B* (*p.*)	Steps·day^{-1} Std.*B* (*p.*)	MVPA Std.*B* (*p.*)	RMSSDseated Std.*B* (*p.*)	RMSSDstanding Std.*B* (*p.*)	HRR_{1min} Std.*B* (*p.*)	HRR_{5min} Std.*B* (*p.*)
1-Stepwise	0.199 (0.007)**	−0.446 (0.007)**	-	-	-	-	-	-	-	-
02-Insert	0.227 (0.092)	−0.350 (0.077)	0.166 (0.404)	-	−0.018 (0.915)	-	0.102 (0.539)	-	-	-
03-Insert	0.242 (0.073)	−0.330 (0.095)	0.173 (0.380)	-	−0.010 (0.951)	-	-	0.158 (0.335)	-	-
04-Insert	0.226 (0.095)	−0.332 (0.104)	0.170 (0.396)	-	−0.063 (0.760)	-	-	-	0.115 (0.576)	-
05-Insert	0.227 (0.092)	−0.374 (0.060)	0.162 (0.414)	-	0.067 (0.734)	-	-	-	-	−0.121 (0.535)
06-Insert	0.248 (0.065)	−0.380 (0.054)	0.128 (0.504)	-	-	0.157 (0.364)	0.047 (0.780)	-	-	-
07-Insert	0.263 (0.051)	−0.358 (0.068)	0.138 (0.468)	-	-	0.150 (0.362)	-	0.131 (0.423)	-	-
08-Insert	0.246 (0.067)	−0.385 (0.056)	0.125 (0.515)	-	-	0.169 (0.344)	-	-	0.010 (0.956)	-
09-Insert	0.257 (0.057)	−0.393 (0.044)	0.143 (0.458)	-	-	0.184 (0.262)	-	-	-	−0.106 (0.518)
10-Insert	0.242 (0.073)	−0.286 (0.179)	-	0.239 (0.264)	0.004 (0.981)	-	0.073 (0.659)	-	-	-
11-Insert	0.255 (0.058)	−0.258 (0.224)	-	0.245 (0.245)	0.006 (0.968)	-	-	0.140 (0.393)	-	-
12-Insert	0.243 (0.072)	−0.264 (0.222)	-	0.250 (0.241)	−0.037 (0.852)	-	-	-	0.097 (0.630)	-
13-Insert	0.244 (0.071)	−0.302 (0.160)	-	0.242 (0.256)	0.072 (0.708)	-	-	-	-	−0.101 (0.600)
14-Insert	0.266 (0.049)*	−0.307 (0.145)	-	0.224 (0.286)	-	0.165 (0.329)	0.022 (0.896)	-	-	-
15-Insert	0.278 (0.039)*	−0.283 (0.180)	-	0.224 (0.279)	-	0.154 (0.338)	-	0.117 (0.472)	-	-
16-Insert	0.265 (0.049)*	−0.306 (0.154)	-	0.169 (0.334)	-	0.169 (0.334)	-	-	0.006 (0.972)	-
17-Insert	0.272 (0.043)*	−0.321 (0.130)	-	0.225 (0.279)	-	0.183 (0.258)	-	-	-	−0.086 (0.592)

*VO_{2max}, maximum oxygen consumption; Body Fat (%), body percentage of fatness; $\sum S$, sum of 7 Skinfolds; Steps·day^{-1}, mean daily steps; MVPA, mean daily moderate to vigorous PA daily mean for the 4 days data collection; RMSSDstanding, HR recorded in upright position; RMSSDseated, HR recorded on seated position; HRR_{1min}, heart rate recovery of the first minute after de exercise; HRR_{5min}, heart rate recovery of five minutes after de exercise. *$p < 0.05$; **$p < 0.01$.*

necessary to take into account the effectiveness of every exercise program to improve cardiorespiratory fitness, highlighting the inverse relationship between aerobic fitness and scores of depression.

Although, Busch et al. (82) addressed some characteristics of an exercise model for this population, it is clear that there is no unanimity for the choice of intensities, duration and type of exercise. For instance, high-intensity training could be an interesting option as it has been shown to be effective for improving VO_2max and other health related parameters in a short period of time in different populations (83–85). Therefore, PA and physical exercise should be evaluated separately or in conjunction in future investigations to determine the better dose-response for the improvement of cardiorespiratory fitness in people with depression.

Previous studies have suggested that autonomic control of HR is directly related to depression scores (15, 29, 86–89). In contrast, the current study did not reveal any association between HRV or HRR and depression scores. Cardiac autonomic modulation, assessed with HRV, besides important associations with cardiovascular diseases (90), has also been suggested as an indicator of the body's ability to adapt to stress (91), thus playing an important role in the interpretation and response to emotional stimuli (92). In the case of people with depression, the reduction of HRV has been demonstrated to be linked to the severity of the disease (15, 29, 89), with sympathetic predominance and reduction of parasympathetic activity, resulting in reduced HRV (86, 87). In this regard, PA and exercise have been highlighted for the improvement of HRV (93, 94). This adaptation is thought to be related to improvements in VO_2max (80). However, the current study did not reveal any relationship between PA, HRV and VO_2max. In contrast, the current results showed some relationships between HRV, HRR, and PA, which is partially in agreement with a previous study of our group (36). Therefore, given the unique characteristic of the current study with objective measures of these parameters, and with participants not involved in physical exercise, it may be speculated that the inclusion of participants practicing exercise would result in higher VO_2max levels, and thus some correlations between aerobic fitness and HRV.

This study is not free from limitations. First, given the cross-sectional design, causal relationships cannot be established. Second, the low number of participants may be another limitation. However, the use of objective measures for all the parameters investigated, with average values over various days for HRV and HRR, in conjunction with stringent criteria for inclusion of adult female participants, reduce the noise importantly when compared to previous studies looking for similar relationships with greater but very heterogeneous samples with unknown confounders. Finally, from a biopsychosocial perspective, other factors such as socioeconomic status were not recorded, therefore, further studies should verify the possible interaction between physical and physiological variables with other psycho-social influences on depression scores and symptoms (95).

CONCLUSIONS

The present study revealed that VO_2max and the sum of skinfolds were moderately related to depression scores, while VO_2max was the only independent predictor of depression in female workers. However, incidental PA, HRV, and HRV were not related to depression scores in this small but homogenous sample. Future studies with greater samples

should identify the best models of physical exercise, while monitoring levels of incidental PA, for promoting improvements in cardiorespiratory fitness and other health-related parameters as body composition and autonomic indices. The mechanistic link between aerobic fitness and depression remains to be clarified.

ETHICS STATEMENT

Ethical approval was obtained from the Ethics Committee of the Catholic University of Brasília. In addition, a consent from was obtained from every participant.

AUTHOR CONTRIBUTIONS

LT and DB: study design. LT, IO-S, and ARM: data collection. LT, DB, IO-S, and ARM: data analyses. LT, IO-S, ARM, ANAD, FS, LD, and DB: interpretation of the results, manuscript writing, and approved the final manuscript version.

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Motivated Cue Integration in Alexithymia: Improving Interoception and Emotion Information Processing by Awareness-of-Sensation Techniques

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Recent findings indicate that alexithymia is the result of a multidomain, multidimensional failure of interoception. Whereas much of the literature addresses the cognitive and affective aspects of alexithymia, less is known about the association between the failure of interoception and the process of motivated cue integration. The theory of motivated cue integration integrates high-level control processes with low-level embodied and contextual cues, suggesting that selective attention to internal and contextual cues results in the creation of meaning that, in turn, influences judgment and action generation. Conceptualized as a special case of the cue integration problem, alexithymia may be associated with restricted access to emotional cues, indicating impaired connectivity between low-level embodied cues and top–down goals and values. This problem may also be viewed as a means substitution problem, indicating the individual's need for alternative multisensory information. Based on this reasoning, interventions that exploit awareness-of-sensation techniques (e.g., mindfulness, experiential approach, focusing) may help to improve the distinction between bodily sensation and interpretation and to create meaning of situational state by substitution of inaccessible affective cues with alternative cues. Accordingly, clinicians and neuropsychologists can help individuals who suffer from alexithymia by training them to use awareness-of-sensation techniques and directing their attention to alternative multisensory cues as well as alternative cognitive configurations (e.g., mental images). Integrating peripheral cues in the moment-by-moment generation of meaning and self-regulation can improve affective judgment through the exchange of inaccessible affective cues with alternative ones.

Keywords: alexithymia, interoception, embodied cognition, focusing, mindfulness, awareness, motivated cue integration

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ALEXITHYMIA AS A MARKER OF ATYPICAL INTEROCEPTION

Alexithymia is a personality trait characterized by difficulty in experiencing and expressing emotions (1, 2). Viewed as a continuum (3, 4), alexithymia manifests as difficulty in identifying feelings and in distinguishing them from bodily sensations of emotional arousal; difficulty in describing one's own feelings; and an externally oriented cognitive style, i.e., a focusing of one's attention externally

with little introspection or insight into one's own feelings (5). Recent findings indicate that alexithymia is the result of a multidomain, multidimensional failure of interoception (6, 7). Garfinkel and Critchley (8) differentiated between the different dimensions of interoception. Accordingly, they defined interoceptive accuracy as the ability to detect signals from within the body and interoceptive sensibility as the ability to report on body states (9). Lastly, interoceptive awareness refers to both the awareness of body states and confidence in the accuracy of interoceptive states [see Ref. (10)]. From the perspective of the dimensional elements of interoception and in light of the results of recent research, the impairment in alexithymia may be associated both with reduced interoceptive accuracy and with poor integration of interoceptive information with ongoing cognition, regardless of the interoceptive signal under consideration (7).

There is evidence that both the symptom commonalities between psychiatric disorders and the symptom heterogeneity within disorders may be based on interoception (11, 12). The link between interoception and alexithymia accounts for symptom intercorrelations, suggesting that interoceptive ability may underpin the p-factor, a first-order umbrella factor that describes the severity of psychopathology and its associated neural dysfunction and that is found by performing confirmatory factor analysis on the co-occurrence of particular symptoms across diagnostic categories (6, 13–15). Accordingly, the failure of interoception found in alexithymia has been shown to affect functions of higher cognition such as learning (16), decision-making (17), emotion processing (18–21), and cognitive control (22).

Following this view, the neural processing in alexithymia is activated mainly on the physiological, motor-expressive level and less in associating the produced information with cognitive and emotional response domains (22, 23). These and similar findings suggest that alexithymics exhibit amplified activity—shown by greater hormonal arousal responses during visceral pain—in brain areas believed to be involved in physical sensation. Likewise, increased activity has been reported in the insula, anterior cingulate cortex, and midbrain (22, 23). These structural deficits reveal themselves in complex social situations, indicating that alexithymia presents with limited subjective awareness of the internal state of the body along with impaired cognitive processing of emotion. Alexithymics thus may be unable to use affective signals as guidance for their behavior. Following this view, affected individuals are characterized by exaggerated concentration on and amplification of the somatic sensations associated with the emotional arousal caused by alexithymia. The misinterpretation of these sensations can foster hypersensitivity to bodily sensations and somatic complaints and can lead to hypochondriasis or somatization disorder (24). Indeed, the failure to cognitively regulate distressing emotions may cause prolonged states of sympathetic nervous system arousal (25) that, in turn, could contribute to the development of certain types of somatic illness, such as functional gastrointestinal disorders (26) and essential hypertension (27).

At the neuropsychological level, findings demonstrate that processing and automatically using high-arousal emotional information to respond to concomitant behavioral demands is difficult in alexithymia (28). Likewise, there are strong indications that alexithymic characteristics are associated with impairments in the controlled processing of facial and lexical emotion stimuli. Research has shown that alexithymic individuals suffer from deficits in the automatic recognition of affective valence and reduced involuntary allocation of attention toward emotional information. Such deficits are associated with difficulty in developing healthy emotional reactions and in understanding emotional stimuli at a conscious or controlled level of processing (29).

These findings help explain the feelings of stress, ambiguity, and indecision reported by individuals who suffer from alexithymia. The difficulty alexithymic people have in learning and in decision-making may exacerbate the levels of stress they feel when confronted with the constantly changing environmental demands of daily life. Likewise, the mismatch between physiological arousal and emotional awareness that manifests in alexithymia may inhibit decision-making in alexithymic individuals (30).

Theory of Motivated Cue Integration

The theory of motivated cue integration (MCI) (31, 32) explains how individuals integrate goals, embodied cues, and multisensory information to create meaning. On the one hand, active goals influence the feasibility of relevant embodied cues (31). On the other hand, the perceiver's likelihood of drawing a specific inference may be proportional to the strengths of the associations between the contextual cues and multisensory data encountered by the individual (33). The MCI theory integrates high-level control processes with low-level embodied and contextual cues. Thus, according to MCI, selective attention to internal and contextual cues results in different patterns of organization that, in turn, influence judgment and action generation. From a neurophysiological perspective, MCI explains the interaction between the dorsolateral areas of the brain involved in the control process associated with goals and action generation and the ventromedial areas involved in motivation and value.

In line with control theories, goal systems theory (34) suggests that the individual's choice of actions is driven by the mental representation of goals that they chronically hold or is elicited by the contextual cues of the given situation [e.g., Ref. (35, 36)]. Goals are defined as cognitive representations of desired end points that affect evaluations, emotions, and behaviors (37). The relations between goals and means are depicted in terms of an interconnected cognitive architecture [see also Ref. (38)], wherein a superordinate goal is connected to lower-level, or subordinate, goals that, in turn, are linked to their own means of attainment (35, 39). There potentially exist several alternative means to the same goal that could substitute for each other. Whereas goal systems theory has demonstrated the role of the control process to address situational demands (34), little is known of the integration between control processes and homeostatic and embodied signals. Some research of the socio-emotional aspects of embodied cognition has demonstrated the association between physical sensation and active goals. For example, the findings of Bargh and Shalev (40) indicated that physical and social warmth are substitutable to address the problem of loneliness. Zhang and Risen (41) found that feeling

physically cold motivated people to seek social warmth. Likewise, the results of Fay and Maner (42) indicated that warmth satisfied active affiliative motives. Whereas these findings indicate the association between embodied homeostatic cues and interpretation of psychological situational state [see Refs. (43–45)], little is known about the general process of MCI, especially under conditions of affective cue deficits.

To fill this gap in knowledge, from the perspective of MCI, Shalev (31, 32) suggested that individual differences could be partially explained by the types of integration they make between accessible perceptual cues and their unique cognitive configurations (e.g., multisensory input, emotions, mental images). Individuals' patterns of structural and motivational constraints influence the way they organize semantic information, which shapes the meaning of the psychological experience. Some representative examples of structural and motivational constraints include the unique associations between goals and means (31), the repeated coupling of sensory signals (46), and the strength of the association between specific bodily sensations and psychological concepts such as the association between homeostatic cues (e.g., temperature, dryness) and psychological concepts (40, 43–45, 47). The cue integration process is influenced by situational demands, past experience, and psychiatric and neuropsychological deficits (e.g., cognitive flexibility) (31).

Alexithymia and the Theory of Motivated Cue Integration

MCI thus provides a framework within which to understand the problem of interoception and affective information processing in alexithymia. Conceptualized as a special case of the cue integration problem, alexithymia may be caused by individuals' restricted access to the contribution of emotion to their means for goal attainment and by a lack of connectivity between their low-level embodied cues and their top–down goals and values.

That is because emotions are the instantaneous, moment-to-moment output of a continuous sequence of behavior and evaluations of situational demands that enable rapid mobilization and action initiation (48). Put differently, emotions are self-regulatory responses that people exploit to efficiently coordinate themselves toward goal-directed behavior. As Frijda (49) noted, specific emotions imply specific eliciting stimuli, specific action tendencies, and specific reinforcers. When it functions properly, this system allows one to flexibly adapt to changing environmental demands. Inefficient affective information processing or lack of association between embodied cues and top–down goals, in contrast, leads to affective dysregulation and inaction. When this inefficiency becomes severe, various forms of pathology are said to exist (50).

The theory of MCI suggests that the problem of low access to emotional information be viewed as a means substitution problem (34), indicating the individual's need to switch to alternative means when goal progress *via* a prior means was thwarted. Accordingly, MCI suggests that selective attention to low-level sensory data and mental images may help fill the gap created by the lack of access to emotion among alexithymic individuals.

The difficulty accessing affective signals that is described for alexithymia dovetails well with the skills that are targeted for development in mindfulness and other awareness-of-sensation techniques.

Use of Awareness-of-Sensation Techniques to Reduce Alexithymia

Mindfulness and other awareness-of-sensation techniques promote an open and conscious awareness of experience that is achieved by observing and acknowledging subjective experiences. Furthermore, it encourages individuals to develop a qualitative and articulated appreciation of their present experiences (51) that enables one to direct selective attention to peripheral cues and to re-integrate these cues to create meaning. Although initial evidence from a meta-analysis of 17 studies suggests that deficient emotional clarity, a major characteristic of alexithymia, may be enhanced by mindfulness-based interventions, there is a need for additional research (52). Research in the practice of mindfulness termed one's experience of an openness to sensory data "decentering" (53), which describes how an individual increases his or her awareness of his or her unique motivational constraints (e.g., strength of association, type of mental images, metaphors) and of multiple sporadic multisensory signals. As such, decentering functions to reset the emotional context associated with prior judgment to a state of low arousal grounded in visceral sensations. Based on this reasoning, decentering enables the neural principle of interoceptive recovery or the restoration of suppressed viscerosensory brain circuits after emotional challenge (54). A similar process of attention to the flow of internal cues that was recognized early by the humanistic approach was termed "experiencing" (55), which was defined as the manner in which the individual attends to the continuous flow of sensory data, known as feeling. While Rogers' conceptualization placed a strong emphasis on how the person's feelings and constructs combined to contribute to his or her notion of self, the approach of others like Gendlin (56) stressed the perceived shifts in the actual bodily sensations associated with the person's feelings and the insights that emerged from these changes in bodily experience. In line with this view, the practice of focusing suggests that in attending to bodily sensations, the focuser assigns to them words, mental images, or phrases that express the present sensory experience. These words or images can be tested against the bodily sensations, which will not resonate with words or phrases that do not adequately describe them. Once the focuser has accurately linked sensations with words, new words or images emerge that provide the focuser with new insight into the experienced context. Eventually, there will be a shift in experiencing as the person gains some clarity about his or her emotional state and begins to move forward (57).

Following this reasoning, clinicians and neuropsychologists can help individuals who suffer from alexithymia by coaching them to use awareness-of-sensation techniques. Not only can this promote relaxation or self-acceptance; it can also facilitate interoceptive improvement by better distinction between bodily sensation and psychological interpretation. Likewise, integrating peripheral cues in the moment-by-moment creation of meaning can improve affective judgment through the exchange of inaccessible affective cues with alternative ones. Future research will focus on evaluating the effectiveness of these techniques in improving judgment that

results in appropriate action generation in contexts involving emotion. Such investigations will contribute to the state of the art of evidence-based research in the area of moment-by-moment self-regulation (32) and interoceptive awareness and the possible synergy between the two.

DATA AVAILABILITY STATEMENT

No datasets were generated or analyzed for this study.

AUTHOR CONTRIBUTIONS

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

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REVIEW
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A History of the Alexithymia Concept and Its Explanatory Models: An Epistemological Perspective

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Alexithymia, as a theoretical psychotherapeutic construct, finds its origins in psychosomatic medicine, actually being quite old. However, beyond the specific observations and case studies, their characterization and systematization is relatively recent. However, from an epistemological point of view, it remains the subject of debate and therefore remains outside the conventional diagnostic guidelines. Possibly, its history, closely linked to psychoanalysis, as well as the lack of clear empirical references, has turned the alexithymia construct before into a good descriptive and comprehensive framework than in a precise diagnostic model. In this article it is, following the thread conduits of the historical perspective, to deepen these epistemological aspects.

Keywords: alexithymia, history, therapeutic models, psychosomatic medicine, theoretical constructs

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INTRODUCTION

Psychosomatic medicine in general is based on the principle that emotions and personality have an impact on bodily functions, and thereby play a part in physical wellbeing or illness. Nevertheless, because the mechanisms of these interactions are not clear, very few of its explanatory models have gained the consideration of research paradigm (1). In fact, today's psychosomatic model dates back to the explanations provided by Sigmund Freud (1856–1939) on the understanding of neurosis, whereby it has its origin in the theoretical bases of the orthodox psychoanalytical model that summarily contends that the intrapsychic conflict that explains both the genesis and development of the structuring of personality, together with its pathologies, prompts a high level of emotional activation that may cause more or less serious damage to the organism (2). This hypothesis has been widely debated for decades inasmuch as it was complicated to establish clear empirical references to support it, which gave rise to far-reaching controversies that even affected the very development of psychoanalysis as a school, giving rise to a broad diversification of the heterodoxy (3). Nevertheless, the appearance of the construct of alexithymia appeared to go some way to resolving many of these inconsistencies by finding quantifiable empirical referents that rekindled the interest in different biological aspects of Freud's controversial theory (4).

Nonetheless, and beyond Freud, the issue enjoys a long-standing medical tradition, which would in due course be consolidated within the field of psychiatry, as throughout the 19th century it seemed clear that emotion, personality, and health were closely related. This meant that professionals soon raised the

question of how to establish a two-way nexus between mental functions and physical states (5). Thus, for example, the US surgeon William Beaumont (1785–1853) established that fear and anger reduced the amount of gastric mucus secreted (6). The same may be said in relation to the first controlled studies on hypnosis, as a British surgeon called James Braid (1795–1860) used experimental means to prove that patients subject to hypnotic suggestion suffered less physical pain during surgical procedures (7). It therefore stands to reason that a school of medical inspiration in origin, such as Freudian psychoanalysis, and inspired by the work undertaken by the neurologist Jean-Martin Charcot (1825–1893) in La Salpêtrière Hospital in Paris, should embrace these and other findings in its explanation of the causes and consequences of neurotic processes.

The widespread dissemination of approaches of this nature, which converged in the psychosomatic hypothesis, specifically took place in the 1940s and 1950s by the hand of doctors trained in psychoanalysis, such as Franz Gabriel Alexander (1891–1964) and Felix Deutsch (1884–1964), among others (1). Indeed, the psychosomatic paradigm added emphasis to the role of conflicts of the unconscious by generating states of chronic activation in patients in physiological pathologies, and even in some kind of tissue alterations. As is logical, this hypothesis, focusing on the organic effects of emotion, involved a new approach to therapy, inasmuch as it was assumed that together with psychogenic and biological aspects, environmental stresses would also have an important part to play in the origin and development of all nature of complaints, as factors that would also alter an individual's emotional state to a greater or lesser extent (8). We should note, however, that despite the importance these authors gave to the intrapsychic conflict, the aim here was not to uphold a psychoanalytical approach linked to Freudian orthodoxy, as the pathogenic mechanism would not be actually symbolic, but instead of a psychobiological nature (9).

Whatever the case, the psychosomatic model based on an individual's internal conflict was backed by scant empirical evidence, whereby it began to be seriously questioned toward the end of the 1950s; above all because the therapeutic model based on psychoanalytical models did not appear to provide results that were both uniform and consistent. Although certain patients made headway in reducing the physical symptoms of their disorders, others, especially when they manifested development-related problems, only appeared to record clear benefits related to their physiological problems when they underwent other kinds of psychodynamic therapies of psychological support, such as the well-known brief psychodynamic therapy. In fact, some even worsened when they were prompted to look for the unconscious reasons for their motivations, a situation that ultimately raised doubts about the psychosomatic approach itself (10, 11).

ALEXITHYMIA AS A MODEL

The crisis of the therapeutic model based on psychoanalysis for addressing psychosomatic problems did not question the existence of such problems, as their clinical evidence seemed clear and consistent, but instead the way of explaining them with a view to seeking alternative approaches. This means that the concept of alexithymia was not the result of an eureka moment, but instead emerged in the early 1970s following a protracted period of reflection and the evaluation of sundry alternative hypotheses (1).

Back in 1948, a psychiatrist of Swiss origin called Jürgen Ruesch (1910–1995) reported finding a unique casuistic among his patients: those that experienced topical psychosomatic complaints—such as migraines, abdominal disorders, and hypertension, as well as other chronic physiological complaints, were characterized by being scarcely imaginative, as well as having problems with the verbal and symbolic expression of emotions different to those usually found in patients with disorders other than somatic symptoms (12). Before being seen as a disorder of neurotic origin, this problem was considered a difficulty arising from a deficient personality development, understanding this to be the main cause of psychosomatic disorders. Along these same lines, and around the same time, authors such as the US neuroscientist Paul MacLean (1913–2007), known for his popular triune brain theory, contended that patients with psychosomatic complaints encountered difficulties in expressing their feelings, speculating with the possibility that this might be due to a weak consolidation of the areas of the neocortex related to language processing: the emotions that caused the patient significant distress were not suitably symbolized, whereby they were manifested through what was referred to as "organic language" (13).

In the early 1950s, even psychoanalysts themselves began to encounter a growing number of cases that broke with the traditional model of intrapsychic conflict. Thus, for example, Karen Horney (1885–1952) first reported that some of her patients were immune to psychoanalytical treatment due to a significant lack of emotional awareness, little expression of their internal states, a minimal interest in their dreams and fantasies, excessive focus on thoughts and, as a result, pursued a superficial life-style focused on outside experience (14). Nonetheless, what was of interest to Horney was that this type of patient was prone to develop psychosomatic problems, eating disorders, polydrug use and, in general, all kinds of compulsive behaviors that, it seems, were closely related to the systematic avoidance of the understanding of their own emotions and a profound feeling of emptiness. What is important, at this point, is that despite admitting that these people did not fit into the traditional model for explaining neurosis, nor respond well to psychoanalytical therapy, Horney sought to attribute their behavior to the existence, in these individuals, of powerful and deeply rooted defenses against unconscious conflicts (1). This approach began to change among the advocates of psychoanalysis barely a decade later, with the appearance of specialists that began to reject the model of neurotic defense in favor of a more eclectic approach. This was when the notion began to be accepted that these patients' behavior would involve, above all, personality deficits: given the lack of a rich inner life, these people focused their concerns on their organic symptoms

and the medium's influence, thus generating a model of "operational thinking", which ended up having a very negative impact on their interpersonal skills (15, 16).

Nevertheless, and despite the increasing amount of data on this specific type of patient in the clinical literature, it was not until the mid-1960s that the US psychiatrist John Case Nemiah (1918–2009) and his Greek-born colleague Peter Emanuel Sifneos (1920–2008) jointly embarked upon a systematic study of the cognitive style of a sample of individuals with common and persistent psychosomatic problems (17, 18). They came to the conclusion that compared to individuals with standard mental disorders, many of those that reported these associated physiological complaints found it extremely difficult to describe their subjective feelings, apart from having an impoverished fantasy, as well as a utilitarian cognitive style focusing on the outside. This unusual psychological concept was what in 1972 Sifneos coined as 'alexithymia', which is formed by the roots of several Greek words, and literally means "lack of words for emotion" (18–20).[1]

Following the publication of these initial empirical findings, alexithymia began to quickly gain in popularity among practitioners of psychiatry and psychology. This was especially the case after two international conferences; the first held in London in 1972 and the second in Heidelberg in 1976, which established the importance of the alexithymia model in research into states of emotional deficit (18). In fact, following the London conference, it became clear that despite the contradictory views held by clinical and non-clinical specialists, there was a need to give the term uniformity when addressing problems of this kind if the aim was to ultimately find a framework of consensus that would pave the way for communication between basic and applied science. Hence it was agreed to replace the fuzzy concept of 'affection' by the more precise term of 'emotion' for all its somatic aspects, while the term 'feeling' was reserved for its cognitive components (18).

The truth is that a clear convergence swiftly appeared in the literature between a vast number of therapists and the model propounded by Nemiah and Sifneos. But it was not alone. The result was that the first empirical studies on alexithymia provided unidirectional results that soon consolidated a clear explanatory model based on four elementary premises: 1) difficulty in identifying and describing feelings; 2) difficulty in distinguishing between feelings and bodily sensations related to emotional activation; 3) restrained and limited imaginative processes, adopting the guise of an impoverished fantasy; and 4) a cognitive style oriented toward the outside (1). It is worth stressing, nonetheless, that alexithymia seemed to manifest itself in an unusual and paradoxical manner, as at first glance the patients appeared to express a strong sense of melancholy, with chronic dysphoria, or else outbursts of tears and anger. Nevertheless, following an in-depth interview, a specialist found that in reality these people knew quite little about their internal states and were often incapable of effectively relating them to memories, specific situations, or recurring fantasies (9). The important thing is that the approach taken by Nemiah and Sifneos allowed superseding the classical psychoanalytical proposal that used the link between the repressed effect and the somatic symptoms to shift the understanding of alexithymia toward a view close to developmental psychology: an alexithymic one, due to an inefficient psychological development that converged in a dysfunctional adult personality, would experience serious difficulties when cognitively integrating the effects, which would stop the patient being properly regulated and modulated. This would prompt, on the one hand, the usual communicative problems that are typical of the disorder and, and on the other, a clear vulnerability to experience a growing tension informed by non-differentiated states of unpleasant emotional activation (22).

Indeed, certain cases of alexithymia provided evidence of neurotic conflict in the classical sense of the concept, but it was soon evident that alexithymia could both be found in the very origin of these conflicts and strengthen others arising during its development, thereby revealing that the main problem of alexithymia was not so much one of neurosis, but the poor emotional regulation that its emotional deficits caused and, furthermore, pointed to an organic substrate (23). In view of this state of affairs, it was perfectly possible that intrapsychic conflicts could be one of the causes of the disorder, although they were undoubtedly not the main one, as psychoanalysts had believed for decades. In fact, alexithymia had transformed, largely, into describing someone with problems when cognitively processing emotions with complete independence of their origin and intensity. In fact, subsequent research both from the field of developmental psychology and from neuropsychology has found that the root of alexithymia could lie in either a problem of cerebral organization, or in a marked lack of suitable emotional models during the passage from childhood to adulthood, or else a combination of both factors (24, 25).

A DEBATED MODEL

In view of the approaches considered, Sifneos soon proposed a general etiological model for alexithymia that, to begin with, subdivided it into two types: primary and secondary. The primary one had its origin in a neuroanatomical or physiological defect, possibly hereditary in nature, whereby the communication between the limbic system and the neocortex would not function properly, affecting hemispherical lateralization, which would lead to an inability to associate fantasies, thoughts, and languages with emotions. The secondary one, in turn, is associated with psychological traumas in childhood, serious and prolonged traumatic aggressions in adulthood, or psychodynamic sociocultural factors that prompt an overuse of defensive mechanisms such

[1] α (a) or "no"; λέξις (lexis) or "speech/word"; θυμός (zümós) or "emotion/mind". While the noun λέξις in turn comes from the verb λέγω, which means "read", which provides the double meaning (adapted from the Spanish version by Lusiardo and Rodrigo (21).

as repression or negation (19, 21). Whatever the case, and without a clear empirical corroboration, this etiological explanation was based solely on clinical observations and case studies. Hence the reason that, in the first instances, the model of alexithymia proposed by Nemiah and Sifneos faced major opposition.

The first thing that was challenged was the fact that the proposal was based, as we have already stated, on scant empirical information, which meant there was no point in validating it inasmuch as it had not been properly verified (1). Indeed, it was a valid criticism insofar that many clinicians believed they had found an explanatory panacea for the somatic symptoms, which led to the misinterpretation of their own particular clinical experiences as a corroboration of the construct's validity when, in reality, what was happening was that they appeared to be fitting them subjectively to a pre-established model that had never been verified (26). Yet the second great reticence caused by the model of alexithymia was that it led to the commission of a serious mistake in interpretation: many researchers assumed the existence of a specific and consolidated relationship between alexithymia and the whole known raft of classic psychosomatic symptoms, when the truth is that the construct had been defined, rather than as a cause, as a factor of risk. Alexithymia thus heightened the patient's vulnerability toward psychosomatic disorders, but the efficient variables that prompted were others linked to the management of emotions, such as badly resolved situations of grief, poverty, and abandon, for example (2). In view of this, the most critical views estimated that the so-called "alexithymic characteristics" could be explained more effectively through directly observable factors, such as socioeconomic status or other variables of a situational nature, such as adverse life events, which prompted the patient to adopt systemized defensive strategies of resistance, negotiation, and negation, which again opened the door to a psychodynamic interpretation of the problem (27). This is the context that gave rise to new and popular psychoanalytical reviews of the construct, such as the one proposed by the New Zealander Joyce McDougall (1920–2011), who coined the phrase "emotionally deaf and dumb" to refer to patients suffering from alexithymia. McDougall, who chose to elude the intrapsychic conflict to concentrate on the problem of symbolic linguistic representation, linked alexithymia, and psychosis when finding that a psychotic and alexithymic patient treated language in a similar, but opposite way, which possibly means that both their pathological manifestations had a common origin. She thus explained that the psychotic patient tries to make up for their psycho-emotional deficits through the delirious use of words in order to overcome their anxiety, while the alexithymic patient tackled their anxiety by emptying their words of emotional meanings, which induced the psychosomatic disorder. This explained, in her view, why the psychotic patient expressed their delirium in a mental order, while the alexithymic one expressed their delirium in a physiological way (28).

On the other hand, and as an alternative critical pathway, transcultural studies had established the notion that neither the psychosomatic symptoms nor the verbal expression of emotions were universal, being mediated by specific cultural attitudes toward life events, as well as by the restrictions imposed by language in each case. Nevertheless, the response to this objection by the advocates of the model of alexithymia was that it was unlikely that sociocultural and language aspects could explain manifestations of alexithymia such as the reduction in imagination, impoverished fantasy, or poor symbolization, and they reproached their critics, who were generally behavioral therapists, that their analysis model did not even consider these kinds of hypotheses insofar as it had either clearly ignored them or studied them only superficially and with little theoretical rigor (1). Accordingly, those that defended the construct would say that they were not in this case faced with a question of "believing or not believing" in it, or of a problem intrinsically related to its internal validity, but instead with an epistemological difficulty that was due rather to the type of scientific paradigm it was analyzed from (29). In fact, other dimensional models based on internal hypotheses had proven their utility within the clinical field and in psychopathological research such as, for example, that of introversion-extroversion, and this was due to the fact that, like alexithymia, they should not be understood as a mere diagnosis, but instead as a personality trait (1). Nevertheless, Sifneos was convinced of the construct's validity, and of the fact that sooner or later he would find empirical proof of the same, as in 1973 he introduced a simple questionnaire, the *Sifneos Alexithymia Questionnaire* (SAQ) to be administered to patients in daily clinical practice. This screening test consisted of 17 items, of which eight referred to key issues for revealing a patient's symptoms of alexithymia (30). This instrument was subsequently reformulated by Sifneos himself, converting it into the *Beth Israel Hospital Questionnaire* (BIQ-1), comprising 21 items to be completed by the actual therapist based on their observations, which raised doubts about its objectivity insofar as the possibility of obtaining emotional results from the patient varied depending on the interviewer's experience (20, 31).

Indeed, neuropsychological research came to the aid of the alexithymia paradigm inasmuch as it detected, for example, that those patients that underwent a commissurotomy, or surgical incision into the callosal commissure, experienced, as the model predicted, many of the cluster of symptoms traditionally associated with the complaint: the visual-spatial information, with a major emotive content, processed by the right hemisphere of the brain, no longer travelled freely to the left hemisphere to be sequentially segmented and reformulated in a verbal format. These patients therefore encountered all kinds of difficulties when symbolizing, imagining, fantasizing, or expressing themselves emotionally, which made alexithymia, at least in functional terms, into a phenomenon that was the complete opposite to creativity (32).

In sum, the verbalization and use of emotions involved a transfer of data, with a transduction or change in the type of information contained in the same, between the limbic system and the cortex, as well as between both hemispheres of the brain, which is precisely the problem affecting the alexithymic patient. Consequently, the progressive clarification of the brain structures

involved in the processing of emotional activation shed empirical light on the model, at least in part, and helped to explain the fact that alexithymia often appeared in patients linked to substance abuse, sociopathic or borderline personality traits, eating disorders, panic attacks, somatoform disorders, or psychogenic pain (18). Moreover: as opposed to Horney's aforementioned opinion, attributing the shortcomings of psychoanalysis in these individuals to a firmly entrenched resistance to the unconscious, what really explained why traditional psychodynamic therapies fell short with these patients, specifically those of a primary nature, was that because of their organic difficulties for imagining, fantasizing, or visualizing situations, such therapeutic approaches were of little use and could even be counterproductive.

THE CONSOLIDATION OF THE CONSTRUCT

The advancement in the understanding of the neurological bases of alexithymic manifestations, as well as the slow but steady progress made in the clinical field, prompted numerous attempts to strengthen it through theoretical refinement and the collation of data gathered from exploratory sample studies. The first attempt, barely concealed among many professionals, involved dissociating insofar as possible alexithymia from the temptation to explain it solely in psychoanalytical terms and, of course, reinforce it in such fields as neuropsychology, developmental psychology, and personality psychology. This gave rise, to mention just one example, to studies that sought to influence the emotional symbolic development of children and adolescents, as well as their expression of emotions, in connection with the stages of development described by Jean Piaget (1896–1980). As is common knowledge, Piaget contended that psychological growth began with the acknowledgement of one's own physiological bodily conditions, and culminated in the cognitive recognition of the psychological states of others, whereby psycho-emotional development and the communication of emotions were key elements both in individuals' cognitive development and in the proper formation and consolidation of their personality (33). In short, the well-consolidated higher psychological processes that are the hallmark of the healthy adult, as propounded early on by the Austrian doctor Max Schur (1897–1969), were only possible largely through a progressive desomatization of the individual (34).

Based on these approaches, of psychoanalytical resonance in origin, subsequent developmental psychology focused its attention on, among other things, the way of symbolizing and integrating emotions, as well as their communicative functions, in keeping with the cognitive mechanisms involved in their regulation and modulation (22). This involved a basic line of research for the theoretical consolidation of the model of alexithymia inasmuch as, it seems, these mechanisms were absent, or were at least dysfunctional, in alexithymic patients, which rendered them vulnerable to the stresses generated in the non-differentiated states of emotional excitement that explained the disorder (1). Nevertheless, and in view of its own diagnostic conditions, given that it involved a descriptive concept based not on an illness but instead informed by the patient's complaint of one or more basic pains, there persists—and still persists in some way—the handicap of deciding whether alexithymia could be considered a personality trait in the true sense of the meaning or a state, which prompted the need to suitably evaluate both aspects (35). The fact that alexithymia was linked to different psychosomatic complaints may have led to its premature acceptance, and not necessarily the right one, of the existence of a direct relationship between alexithymia and psychosomatic illness, which constituted a problem when assessing the construct because the clinical observation found both psychosomatic patients that were not alexithymic and alexithymic patients that did not record any psychosomatic malaise whatsoever (31). In fact, a constant when addressing therapy with these kinds of patients was the scant literature on their treatment, as individuals with alexithymia rarely sought help on their own accord, and generally ended up visiting a specialist at the behest of someone close to them who was frustrated by their communicative shortcomings or on the advice of a medical practitioner confused by their constant physical complaints that were difficult to determine and resisted traditional medical treatment (36).

This may explain why it was thought that the solution for addressing alexithymia, which in clinical practice was both a recurring and unquestionable phenomenon, would come from its controlled assessment through instruments. Sifneos himself, aware of the methodological limitations inherent to BIQ-1, did not take long to present BIQ-2, in this case a self-assessment scale consisting of semi-structured questions that patients were required to answer and, in theory, provided the therapist with first-hand information over and above that gathered during the clinical interview (37). This led to other measures such as the *Schalling-Sifneos Personality Scale*, the *Alexithymia Scale of Noël,* and the widely used *Toronto Alexithymia Scale* (TAS) (38). They were accompanied by structured interview procedures, such as the *Alexithymia Provoked Response Questionnaire* (APQR) (39), as well as the combined use of the appropriate tools with other common psychodiagnostic tests such as MMPI, TAT, and AT-9 in order to obtain more complete observations (31). All this led to a fairly accurate profile of an average person with alexithymia —generally a male who reported their first complaints at a mature age—as well as an epidemiological interest that revealed that this complaint was more frequent among the general population than initially thought, with the impact of alexithymia, furthermore, varying depending on the specific populations under study, but not in transcultural studies: more common among patients with psychosomatic complaints than among patients with other health issues; more common among those addicted to psychoactive substances and, in general, with an impact of between 8% and 10% in the normal undiagnosed population (31).

The gradual severance of the close bond that had historically been forged between alexithymia and psychosomatic pain

allowed extending the problem's horizon and, therefore, calibrating the construct's validity in sundry fields, both psychosociological and cultural ones and regarding the field of health. Indeed, the focus began to turn toward alexithymia as a personal condition and not simply as a mere medical problem, or solely due to a diagnosable medical disorder. Thus for example, and given the shortcomings in the emotional management of alexithymia, it was thought that a parallel model of analysis could be established between alexithymia and psychopathy given the latter's popular characterization by Hervey Cleckley (1903–1984), who among other things described a psychopath as having a significant deficit in the management and understanding of emotions. This led to a systemic study of the relationships between psychopathy and alexithymia in a sample of women by comparing the results obtained on the PCL-R psychopathy checklist of Robert Hare (b. 1934) and the measure of alexithymia provided by the TAS scale (40). Despite the similarity in the deficiency of the emotional manifestations affecting both constructs, and possibly constituting one of its main symptoms, it was found that they were not interchangeable insofar as they did not refer to the same thing, nor did they measure equivalent or correlative aspects of emotion.

The end result was a set of evidence that was difficult to doubt regarding the construct of alexithymia. The first and key piece of evidence was its undoubtable entity. In fact, although subject to permanent criticism, even its detractors had to accept its advantageous nature as an operational element, whereby a raft of clinical features subsumed beneath a single concept and systematically affected a specific group of disorders and patients with very specific characteristics (41). Thus, and despite its non-introduction—at least for the time being—in standard diagnostic classifications because of its debated status—trait versus state—those in favor of the model found a way of defending with assurances that although it could not be acknowledged as a diagnostic entity in its own right, it had the intrinsic value of characterizing and operationalizing a long history of psycho-medical observations of great social import which, until their appearance and systematization, had remained within the sphere of the undefined, thereby generating some considerable perplexity among specialists and the inconsistent treatment of patients (42).

RECENT DEVELOPMENTS IN ALEXITHYMIA

From the described perspective, recent research has focused on exploring the links of alexithymia, understood as a stable personality trait present in some patients, and various medical and psychiatric conditions. For example, a study of relationships between insight and alexithymia in adult outpatients diagnosed with obsessive-compulsive disorder (OCD) showed that the subjects of the sample that obtained higher scores on the TAS-20 scale also reflected poor or absent insight (43). Similarly, further work has established clear connections between body image disturbances and alexithymia in women with severe premenstrual dysphoric disorder (PDD) and patients with serious binge eating disorder (BDD). In the last case, moreover, the presence of alexithymia not only impoverished the evaluation and bodily satisfaction of individuals, but also seemed to increase depressive symptoms (44–46).

The relationships between alexithymia and other organic conditions have also been investigated, such as the presence of acute phase proteins—especially C-reactive protein— lipid levels, cholesterol, and cytokine imbalance, with special attention at the area of drug naïve outpatients diagnosed with other pathologies, such as OCD, major depression (MD), or panic disorder (PD). The results seem to establish links between alexithymic patients with OCD, MD, and PD and the presence of poor cholesterol regulation and high suicide ideation (47–49). Also, in line with the "stress-alexithymia hypothesis", there seems to be a clear relationship between the high presence of C-reactive protein in blood and alexithymia. This connection motivates that the pro-inflammatory and anti-inflammatory cytokine balance may be tuned toward a pro-inflammatory imbalance with a concomitant altered cell-mediated immunity. These results point to the idea that the presence of alexithymic features in the patient should encourage more comprehensive therapeutic approaches, both medical and psychological, that could prevent the development of more severe diseases in alexithymic patients and, logically, improve their quality of life (50).

However, one of the main lines of research in the field is the risk of suicide, and there is a wide literature that seems to coincide in the fact that the presence of alexithymic traits in the individuals significantly increases suicidal behavior. Initially, it was thought that alexithymia, in suicides, would be associated mainly with depressive symptoms, so it could operate as a predictive factor for this type of behavior (51). Subsequent integrative studies have also shown that suicidal depressants with alexithymic traits—a fact that has also been found in relation to other psychiatric disorders as already indicated—showed elevated blood cholesterol levels, as well as deregulation of C-reactive protein and homocysteine. Consequently, this would confirm to some extent, and in the absence of further evidence, the predictions of "stress-alexithymia hypothesis" (52, 53): alexithymia could be a chronic condition of the patient, possibly due to childhood or early adolescence in that there were systematic abuses and/or abandonment, which would cause in the subject a state of pronounced inflammation with an impaired hypothalamic-pituitary-adrenal axis reactivity toward the usual stressors of daily life. Thus, the manifestation of alexithymia would operate as a chronic response to stress that would complicate both psychiatric disorders and other medical conditions (54).

CONCLUSION: BRIEF FINAL THOUGHTS

To a certain extent, the historical debate on the issue of alexithymia is readily understandable when observed from an epistemological perspective, as it actually involves a rerun of the age-old conflict between basic and applied science,

which in this case takes the form of a showdown between the therapist's clinical observation and the critical eye of experimental methodology. Although it is true to say that Nemiah and Sifneos do not "discover" alexithymia—in fact, the latter has earned greater fame than the former by given it its name and investing more effort in its definition and disclosure— they should be granted the merit of managing to formulate a coherent explanatory model that integrates a long tradition of real and systematic medical observations that pointed toward a problem that basic research not only had failed to resolve, but had not even detected.

The collateral circumstance whereby the problem that Sifneos systemizes, more than psychological, constitutes a basically medical matter, had a great influence in its subsequent treatment when one considers the fact that, at least in its orthodox origin, psychoanalysis was the medical school of psychology par excellence. This was not only because it was inspired by a doctor such as Freud, but also because of its profoundly organic and deterministic approach incapable of understanding a mental problem that had not previously had a biological cause. Hence the reason that for a long time it attracted the interest of the general medical profession—and of psychiatry in particular—and also that the first treatments of these observations that would end up constituting alexithymia acquired a marked psychoanalytical and psychosomatic bias, closely interrelated, that would define its future. Possibly, the resistance that the psychopathology of a more empirical bias initially faced regarding the construct's acceptance therefore involved a great deal of prejudice. It is possible that the issue in this case, more than its operative value, its empirical referents, or its epistemological underpinnings, lay in its debated and debatable origins.

The natural, and logical, tendency of basic research of not accepting models and approaches that do no not arise from within it led in this matter—as in others—to fierce discussions that, if we pay attention to the precedent, have less to do with the real therapeutic problem that alexithymia sought to define and operationalize than with its possible explanation and subsequent fit within the framework of the theoretical underpinnings of psychology and psychiatry. In fact, and this is very common among the more reductionist sectors of the psychological explanation, there is a tendency to forget with consummate ease that the psychological and the organic mutually influence each other, considering materialist explanations a single direction in this relationship, which tends to mean that they are often partial and confusing. It therefore involved, as is often the case with these confrontations that reignite the perennial conflict between science and practice, a debate on scientific primogeniture. Or, to put it another way, of a potentially sterile discussion between the nature of things and their value of use. Both questions may be perfectly legitimate, yet what is certain, as in the case that concerns us here, is that they are doomed to understand each other.

AUTHOR CONTRIBUTIONS

Both authors took part in planning the theoretical and conceptual basis for the study. FP-F wrote the first draft. Both authors took part in critically reviewing and editing the manuscript.

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Alexithymia and Treatment Outcome in Anorexia Nervosa: A Scoping Review of the Literature

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Alexithymia is of great interest as an outcome predictor of recovery from anorexia nervosa, since it may interfere with both treatment compliance and patients' ability to benefit from the adopted interventions. For this reason, in the last years new treatment approaches targeting emotion identification, expression, and regulation have been applied and tested. Using the PRISMA methodology, we performed a scoping review of the literature about treatment outcome in anorexia nervosa, in terms of changes in alexithymia as assessed by its most commonly used self-report measure, the Toronto Alexithymia Scale (TAS). The Medline and Scopus databases were searched, and articles were included if matching the following criteria: dealing with patients affected by anorexia nervosa, without limits of age; involving the application of any kind of targeted therapy or treatment; assessing alexithymia and the effect of a treatment intervention on alexithymia, using the TAS. Ten studies were eventually included; overall, according to the selected studies, alexithymia levels often remain high even after specific treatment. Further research aimed at a deeper understanding of the actual impact of alexithymia on the outcome of anorexia, as well as exploring alternative treatment strategies for alexithymia in eating disorders (EDs), are warranted.

Keywords: alexithymia, anorexia nervosa, systematic review, PRISMA, treatment, outcome

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INTRODUCTION

Alexithymia is defined as a difficulty and inability in identifying and describing feelings and emotions (1): alexithymic individuals usually show a paucity of words to describe their affective status, and find it difficult distinguishing feelings from physical sensations. Furthermore, alexithymia is characterized by a diminution of fantasy and a concrete and externally-oriented thinking style (2). It is likely a stable personality trait reflecting an impairment of emotion regulation (3, 4), rather than a state-dependent phenomenon linked to depression or to clinical status (5, 6).

Impaired emotional functioning and alexithymic traits are core features of anorexia nervosa, both in the adolescent and adult population (7–15): they seem to be independent from depressive symptoms and eating disorder severity (16–18) and express themselves as a concrete, reality-based cognitive style and a poor inner emotional and fantasy life.

A "cognitive-affective" division (19) has been suggested to describe the experience of patients with eating disorders (EDs) when trying to translate their thoughts at a cognitive level into what is felt from an emotional standpoint. The emotional difficulties of individuals with anorexia nervosa (AN) may not depend on a primary impairment in emotion recognition, but rather on inhibition or avoidance occurring after a proper acknowledgment of others' emotions (20), possibly due to patients' feelings of being overwhelmed by over-control and anxious worry (21). Alexithymic traits in AN may cause patients avoiding or regulating the experience of emotions, especially those perceived as negative or disruptive (22), with inappropriate behaviors (restriction, binges, purges, body checking behaviors) (23), leading to a gap between the inner experience of negative affect and its expression (13). Actually, also in a non-clinical sample of undergraduate women, alexithymic individuals, compared to non-alexithymic ones, had more body checking behaviors, greater body dissatisfaction, and higher potential risk for EDs (24).

Implications at the social level of alexithymia and emotional difficulties (such as emotional avoidance and poor regulation), include low social emotional intelligence (25), problems with intimacy, attachment and social communication or interactions (26–29), and social anhedonia (30, 31).

Moreover, alexithymia and emotion regulation difficulties have been shown to have an impact on the course and maintenance of anorexia (12, 15, 32, 33), and on treatment outcome and recovery (34, 35). Actually, the lack of insight and the externally-oriented thinking style typical of alexithymia may interfere with treatment compliance and with patients' ability to benefit from interventions, especially psychotherapy ones (36).

According to these clinical observations, in the last years the need to explore new treatment approaches targeting emotion identification, expression and regulation has emerged, with the aim of fostering the process of recovery, enhancing quality of life (27) and improving long-term outcomes in the ED population (32). Another issue which should not be overlooked is that, notwithstanding patients' primary psychiatric diagnosis, increasing evidence suggests that alexithymia may play a role as risk factor for suicide, often mediated by depressive symptoms (37, 38). Biological correlates of the relationship between alexithymia and suicidal behaviors have been suggested, including for instance homocysteine dysregulation (39). This evidence further supports the importance to screen for alexithymia in the everyday clinical practice with psychiatric patients, including those suffering from EDs (40). The aim of the current scoping review was to assess treatment outcome in AN in terms of changes in alexithymia as assessed by its most commonly used self-report measure, the Toronto Alexithymia Scale (TAS).

METHODS

A scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA Statement; (41)]. The Medline and Scopus databases were searched on August 30th, 2019, and on September 2nd, 2019. For Medline, the following keywords were used: [(anorexia nervosa) AND (Toronto Alexithymia Scale)] AND ((therapy) OR treatment). Scopus was searched with the following research string: [ALL ("anorexia nervosa") AND ALL (Toronto AND Alexithymia AND Scale) AND ALL (treatment OR therapy)] AND [LIMIT-TO (DOCTYPE, "ar")] AND [LIMIT-TO (LANGUAGE, "English")].

Two independent reviewers (EG and CG) assessed the articles identified by the above described key words. To be included in the review, studies had to: (a) be clinical trials dealing with patients affected by AN, without limits of age; (b) involve the application of any kind of targeted therapy or treatment; (c) assess alexithymia and the effect of a treatment intervention on alexithymia, using the TAS. Only articles in English were considered eligible. The presence of a control group was not considered an inclusion criterion. Studies which did not match the inclusion criteria described above were excluded. Possible disagreement between reviewers was resolved by joint discussion with a third review author (PZ). Quality of studies was assessed with the Newcastle Ottawa Scale (NOS) (42) by the reviewers who assessed the articles (EG and CG).

Data extracted from the selected studies were recorded in a datasheet using a standardized coding form, including the following categorical and numerical variables: general information about the study (author/s, year of publication, title, journal title, volume, pages, country, study type), sample features (sex, age, BMI, years of illness, diagnosis, treatment; medical and psychiatric comorbidities; sample size, number in experimental group, number in control group, lost at follow-up), setting (inpatient, outpatient…), type of intervention (group, individual, setting…), questionnaires used, study outcome (primary or secondary), main study results.

RESULTS

Selection Process

As described in the PRISMA flow diagram (**Figure 1**) (43), the initial search identified 384 titles (17 from Medline, 367 from Scopus); after removing 13 duplicates, titles were screened first, and those clearly not in line with the purpose of the review were excluded (N = 276). Then abstracts were assessed, leading to the exclusion of 71 records, and last full texts were read, eventually leading to the inclusion of 10 papers (2, 15, 32, 44–50) in the qualitative synthesis.

Quality Assessment

The NOS scores for the included studies ranged from 1 to 6, with a mean score of 3.9 ± 1.59 (SD).

Description of Study Features

The main features of the selected studies are shown in **Table 1**.

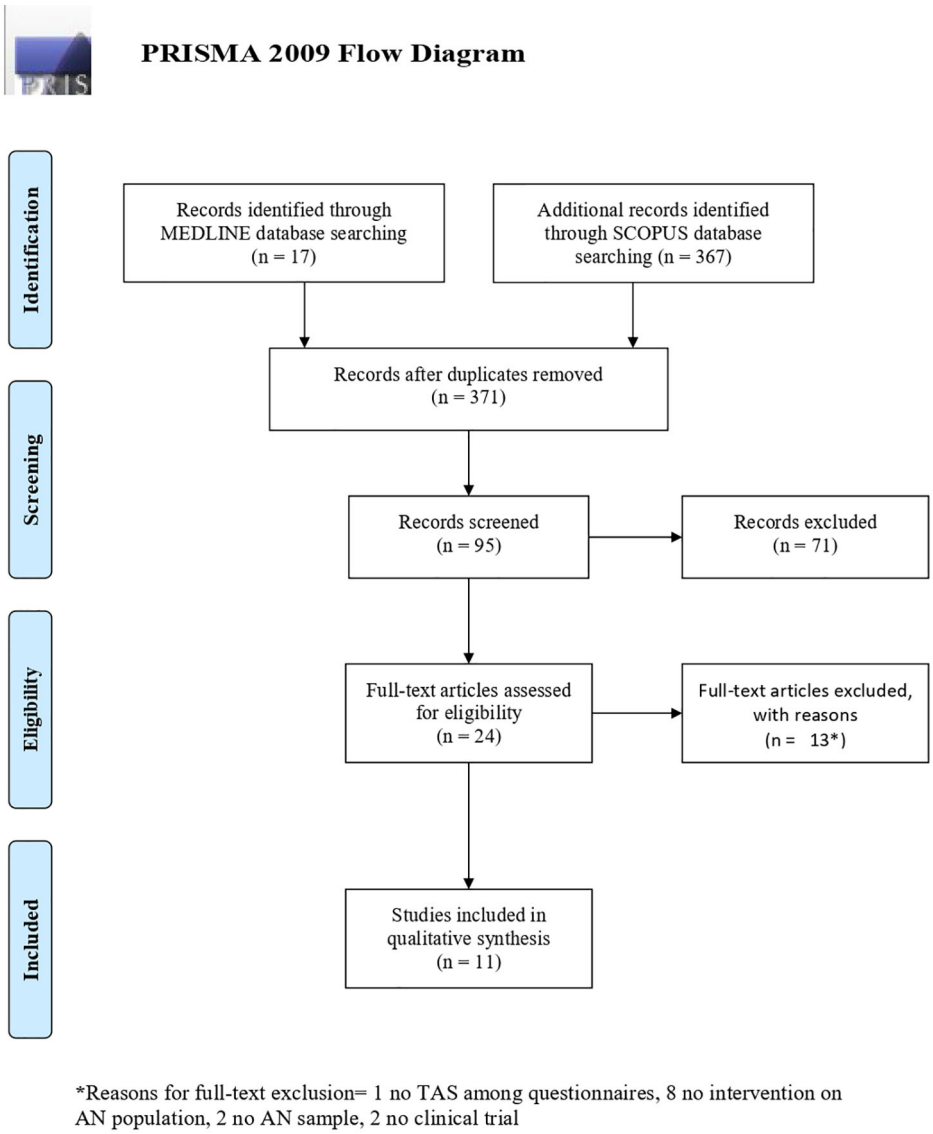

FIGURE 1 | PRISMA 2009 Flow Diagram.

Details about treatment were reported for the approaches described below; in the other cases, no specific details were described apart from those reported in **Table 1**.

CREST (15, 51–53) is a low-intensity individual manualized treatment for inpatients with severe AN, based on the cognitive interpersonal model. It targets rigid and detail-focused thinking styles but also has a strong emphasis on emotion recognition skills and emotion management and expression. The aim is to help patients learn about the function of emotions (including the communication of needs to self and others), and to improve skills in emotion labeling, identification, and tolerance in self and others.

Lunbad and coworkers (47) described in detail the group psycho-pedagogic method applied at the Anorexia & Bulimia Clinic for Adults at the Sahlgrenska University Hospital. According to the theoretical premise that alexithymia implies an inability to handle negative feelings, eventually requiring a "protective" or "blocking" ingredient (ED symptoms). The aim of the method is to help patients cope with negative feelings.

Group Cognitive-Behavior Therapy (G-CBT) as described by Ohmann et al. (45) includes the following modules: therapeutic motivation, psycho-education, individual problem analysis, (teaching of) problem solving strategies, soft and communication skills, hedonistic training, elements of awareness, body and schema psychotherapy (54). While the primary therapeutic goals are weight gain and improvement of eating behavior, the secondary goal is improved emotional functioning, including alexithymia measures.

Becker-Stoll and Gerlinghoff (48) described a three-phase treatment program (4-week outpatient motivation phase, 4-month

TABLE 1 | Main features of the clinical studies included in the review.

Author, year	Sample features	Setting	Intervention assessed	Assessment	Outcome	Main results	NOS
Speranza et al. (2)	N = 102 with complete assessment (initial sample N = 144; directly interviewed N = 109) Gender 100% females Age, mean 21.5 (± 5) Diagnosis AN (N = 63) or BN (N = 39) (DSM-IV) BMI n.s. Illness duration, mean 4.3 (± 4.8) Comorbidities, anxiety and depressive disorders, substance-related disorders diagnosed with Mini International Neuropsychiatric Interview (MINI).	Multicenter research project involving academic psychiatric hospitals.	Treatments could include (1) pharmacotherapy, any kind, for at least 3 months; (2) Psychotherapy, any kind, for at least 6 months; (3) Hospitalization, either full or partial; (4) Pharmacotherapy + psychotherapy.	Assessment at baseline and 3-year follow-up with: clinical interview BDI-13 CGI MINI MMPI-2 (Negative Treatment Indicators scale) TAS (cutoff ≥56)	Explore the relationship between alexithyimic features and treatment choices in a naturalistic prospective study.	Global improvement of alexithymia and depression. TAS scores not influenced by antidepressants, psychotherapy, or both. Patients received different treatments (number, type) according to their alexithymic profile. Patients with high levels of alexithymia: more treatments and more antidepressants. Patients who became alexithymic during follow-up: more often re-hospitalized; fewer psychotherapies.	4
Tchanturia et al. (15)	N = 33 who attended all 10 sessions and completed both pre- and post-intervention assessments (63% of the sample who completed baseline measures) Gender n.s. Age, mean 24.5 (± 8.2) Diagnosis AN (n.s.) BMI, mean 15.1 (± 1.95) Illness duration, mean 8 (± 7.2) Comorbidities (n.s.)	Inpatient, South London and Maudsley National Adult EDs Service.	CREST: manualized 10-session intervention addressing emotion processing, in individual format. Includes psycho-education, experiential exercises, homework tasks.	RSAS TAS Motivational ruler exploring importance to change and perceived ability to change	Primary: RSAS and TAS scores. Secondary: perceived "importance to change" and "ability to change"; BMI	Decrease of anhedonia (RSAS) and alexithymia (TAS) after CREST. Increase of perceived "ability to change" and of BMI.	3
Giombini et al. (32)	N = 32 who completed the group cycle Gender 87.5% females Age, mean 14.03 (± 1.75) Diagnosis AN (DSM-5 criteria) Weight for height %, mean 75.68 (± 6.44) Illness duration n.s. 28.1% comorbidities.	Inpatient child and adolescent EDs unit offering multi-disciplinary treatment (individual, family, and group therapy).	CREST-YP: manualized 5-session intervention, weekly, in group format. Includes psychoeducation, experiential exercise, homework.	Semi-structured qualitative interview created *ad hoc*. SQ ERQ-CA RSAS TAS Motivational ruler assessing self-reported importance to change and ability to change. Data collected at the beginning	Suitability of CREST-YP. Experience of YP receiving CREST-YP. Emotional functioning pre- and post- intervention.	Themes reported by IP: Exploring emotions; Emotions and ED; Homework, Suggestions for improvement. Quantitative results only partially supporting qualitative ones: no significant change in ERQ-CA, RSAS, TAS, and motivational ruler scores. CREST-YP is a suitable intervention for YP with AN.	4

(Continued)

TABLE 1 | Continued

Author, year	Sample features	Setting	Intervention assessed	Assessment	Outcome	Main results	NOS
				and at the end of the cycle.			
Beadle et al. (44)	N = 20 AN patients tested both during starvation and after weight restoration (out of N = 26 tested at baseline); compared to 16 age-matched healthy women at comparable timepoints. Gender 100% female Age in the AN sample, mean 24.4 (± 5.5). Diagnosis AN (ANP or ANR) BMI: mean 15.7. Weight restoration defined as a BMI of at least 18.5 (in the 20 patients sample, mean BMI at time 2, 20.16 (± 1.24). Illness duration = n.s. Comorbidities n.s.	Inpatient or outpatient day program following hospitalization.	Inpatient eating disorder program: daily cognitive behavioral therapy, group and individual therapy, supervised eating, occupational and recreational therapy, physician supervision.	EAT EDI-3 YBC-EDS HDRS HARS WAIS-IV CPT II Stroop Color and Word Test WCST TAS-20 IRI MMPI-2 (37 items).	Differences (demographic, cognitive, clinical, and personality characteristics) between participants with AN and healthy controls. Differences between the starvation and weight restoration phases within the AN group. Examination of relationships between alexithymia, emotional empathy, and self-regulation, controlling for depression and/or BMI when relevant.	In the group of AN patients, decrease of DIF and EOT from the starvation to the weight restoration phase. No change in DDF. Overall improvement in alexithymia.	6
Ohmann et al. (45)	N = 29 Gender 100% female Age, mean 14.3 (range 13–17) Diagnosis AN (ICD-10 Criteria): N = 22 ANR; N = 7 ANB BMI, mean 15 (range 13–17) Illness duration, mean 7.2 months (range 2–18). Comorbidity in N = 23 cases N = 5 patients (17%) treated with antidepressants. N = 3 had previous psychotherapy.	Eating Disorder Outpatient Clinic, Department of Child and Adolescent Psychiatry, Medical University of Vienna (recruitment between May and September 2003–2006).	A maximum of 40 weekly sessions (90 minutes each) of Multimodal G-CBT program, including 9 modules: therapeutic motivation, psycho-education, individual problem analysis, (teaching of) problem solving strategies, soft and communication skills, hedonistic training, elements of awareness, body and schema psychotherapy. Family sessions once monthly.	YSR (baseline and 9-months after) At baseline and 3-6-9 and 12-months follow-up: EDE BDI FBA ASW MUM EV-H EV-A MUM-SOC SPS SIAS BIKS TAS	To assess changes of the psychopathological measures during the course of G-CBT and 1-year follow-up. To investigate whether G-CBT is effective for the treatment of adolescent AN and whether emotional risk factors might complicate the course of the disorder. Hypothesis: patients with less disturbed handling of emotions would have a better treatment outcome.	Severe and multiple emotional deficits, difficulties of emotional control, problems in self-confidence and self-efficacy in AN. Especially in patients with poor outcome: problems in intrafamilial communication and expression of emotions. Alexithymia and SOC were disturbed and resistant to change in all patients. Problems in handling, detecting, and expressing emotions are involved in promoting and maintaining anorexic behavior, and are resistant to change, especially in the patients with poor outcome.	4
Iancu et al. (46)	N = 30 soldiers with ED Gender 90% female. Age, mean 19.5 (range 18–21). Diagnosis N = 10 AN (33%); N = 15 BN (50%); N = 5 EDNOS (17%) (DSM-IV).	Eating Disorder Clinic at the Zeriffin Mental Health Clinic, Israel Defense Forces (2001–2003).	Weekly group meetings (90 minutes) 6 months (lead by a social worker with a social worker and a dietitian as cotherapists) Meetings included: psychoeducation; cognitive behavioral therapy combined with a dynamic approach.	Assessment before and after the intervention with: EDI-2 EAT-26	To examine the efficacy of treatment program. To evaluate the rate of alexithymia and dissociation proneness in the sample (before and after treatment).	Treatment was associated with a significant improvement in eating symptoms (50% decrease in the EAT-26 and EDI- 2 scores), but not with a significant decrease on the DES and TAS-26 scores.	5

(Continued)

TABLE 1 | Continued

Author, year	Sample features	Setting	Intervention assessed	Assessment	Outcome	Main results	NOS
	BMI n.s. Illness duration n.s. Comorbidities, No Axis I comorbidity 90% had a personality disorder (mostly borderline or narcissistic) according to the SCID-II questionnaire			TAS-26 DES			
Lundbad et al. (47)	N = 30 Gender 100% female Age range 25–40. Diagnosis AN and/or BN (type of eating disorder described by patients and EDI-2 questionnaire) BMI n.s. Illness duration, > 5 years Comorbidities, n.s.	Referred from the Department of General Psychiatry, Sahlgrenska University Hospital (Anorexia and Bulimia Clinic for Adults), Sweden.	Psycho-pedagogic method facilitating the ability of patients to cope with negative feelings: 8 weekly written and oral sessions teaching and coaching about emotional/affective status, in a group format.	TAS	TAS scores changes after intervention.	Significant reduction (pre- to post- intervention) of alexithymia (TAS). Alexithymia negatively correlated with education; no correlation with illness duration, weight loss, depression, general psychoneurotic pathology.	1
Becker-Stoll and Gerlinghoff, (48)	N = 47 (N = 18 AN; N = 25 BN; N = 4 EDNOS) Gender 100% female Age, mean 21.7 (± 3.4; range 16–30). Diagnosis AN and BN (DSM-IV criteria). BMI, mean in AN 16.2 (± 1.5); mean in BN 22.8 (± 6.1) Illness duration n.s. Comorbidities n.s.	Day Hospital at the TCE, Max Planck Institute of Psychiatry, Munich (2001).	TCE: three-phase treatment program consisting of a 4-week outpatient motivation phase, a 4-month day hospital phase, and a 4-month outpatient follow-up treatment phase. Group psychotherapy includes cognitive-behavioral, psycho-educational and interpersonal interventions. Exercises to support body acceptance, including video-confrontation, relaxation techniques, and dance therapy.	Pre- and post-treatment assessment with: EDI (total score) TAS-20	To determine whether a 4-month treatment program has an influence on alexithymia in ED patients. To assess whether alexithymia predicts treatment outcome in the ED population.	High levels of alexithymia in AN and BN patients, without any difference in TAS scores between AN and BN. TAS scores decreased from pre- to post- treatment as well as EDI ones. Baseline scores for alexithymia did not predict post-treatment outcome.	4
Elzakkers et al. (49)	N = 70 (N = 56 assessed at 1-year follow-up; N = 50 at 2-year follow-up) Gender 100% female Age, mean 27.3 (± 9.7) Diagnosis, % ANR/ANP 49/51 (Severity of eating disorder symptoms was rated with the EDEQ BMI, mean 15.5 (± 1.9) Illness duration, mean 8.6 (± 8.1) Comorbidities n.s.	National specialist center for the treatment of eating disorders.	Treatment including individual and group therapies, psychomotor therapy, rehabilitation on and outpatient, day-hospital or inpatient basis.	Baseline, 1- and 2-year follow-up. BMI BDI-II EDEQ IGT MacCAT-T STAI TAS Full remission defined as having: BMI range 18.5–25; resumed menses; no disabling anorectic conditions. Partial remission	Mental capacity. Relation of the disorder course with psychological variables and decision making.	Full mental capacity group: mild AN at follow-up; improvement in alexithymia score (below the cutoff of 52 for possible alexithymia); improvement of BMI. Diminished mental capacity group: moderately ill category (DSM-5) at follow-up; no improvement of alexithymia; improvement of BMI; higher likelihood of inpatient treatment.	6

(Continued)

TABLE 1 | Continued

Author, year	Sample features	Setting	Intervention assessed	Assessment	Outcome	Main results	NOS
				defined as satisfying 2 out of the 3 criteria described above.			
Adamson et al. (50)	Individual CREST, N = 66 Gender 100% female Age, mean 25.8 (range 18–53) Diagnosis AN, (DSM-5) BMI, mean 14.8 (± 1.3) Illness duration, mean 8 (± 8.5) Score above the AQ10 cutoff 32% Group CREST, N = 62 Gender 100% female Age, mean 25.5 (range 18–63) Diagnosis AN, DSM-5 BMI, mean 14.8 ± 1.4) Illness duration, mean 7.6 (± 8.3) Score above the AQ10 cutoff 34% Comorbidities, n.s.	Inpatient.	CREST in individual (N = 66) and group formats (N = 62). Individual format: manualized 8 weekly sessions, 40–45 minutes. Psychoeducation and experiential exercises. Group format: 5 weekly sessions, 60 minutes. Optional, participants can drop out at any time.	Assessment before and after individual and group interventions with: RSAS TAS Motivational ruler (ability to change, importance to change) AQ-10 BMI	Effectiveness of CREST interventions. TAS and RSAS scores. ASD symptoms.	Individual CREST: improvement in patients' alexithymia; increase in motivation; no impact on social anhedonia; significant effect of ASD symptoms on RSAS and TAS scores. Group CREST: increase in motivation; no impact on social anhedonia and alexithymia; significant effect of ASD symptoms on TAS scores.	2

AN, Anorexia Nervosa; ANP, Anorexia Nervosa Purging Type; ANR, Anorexia Nervosa Restrictive Type; AQ, Autism Questionnaire; ASD, Autism Spectrum Disorder; ASW, Assessment of Self-Efficacy; BDI, Depression Inventory; BIKS, Beck Inventory of Cognitive Schemata; BMI, Body Mass Index; BN, Bulimia Nervosa; G-CBT, Cognitive Behavioral Group Therapy; CGI, Clinical Global Impression; CPT II, Conners' Continuous Performance Test-II; CREST, Cognitive Remediation and Emotion Skills Training; CREST-YP, Cognitive Remediation and Emotion Skills Training—Young People; DES, Dissociation Experience Scale; DDF, Difficult Describing Feelings; DIF, Difficult Identifyng Feelings; DSM, Diagnostic and Statistical Manual for Mental Disorders; EAT, Eating Attitudes Test; EDEQ, Eating Disorder Examination Questionnaire; EDI-3, Eating Disorder Inventory; EOT, Externally Oriented Thinking; ERQ-CA, Emotional Regulation Questionnaire for Children and Adolescents; FBA, General Family Questionnaire; HARS, Hamilton Anxiety Rating Scale; HDRS, Hamilton Depression Rating Scale; IGT, Iowa Gambling Task; IRI, Interpersonal Reactivity Index; MacCAT-T, MacArthur Competence Assessment Tool-Treatment; MINI, Mini International Neuropsychiatric Interview; MMPI, Minnesota Multiphasic Personality Inventory; MUM, EV-H, EV-A, Marburg Scale of Euthymic Disorder; MUM-SOC, Marburg Sense of Coherence Scale; n.s., not specified; RSAS, Revised Social Anhedonia Scale; SIAS, Social Interaction Anxiety Scale; SPS, social phobia scale; SQ, Satisfaction Questionnaire; STAI, Spielberger State Trait Anxiety Inventory; TAS, Toronto Alexithymia Scale; TCE, Treatment Center for Eating Disorders; WCST, Wisconsin Card Sorting Test Version 4; YSR, Youth Self Report; YBC-EDS, Yale-Brown-Cornell Eating Disorder Scale.

day hospital phase, 4-month outpatient follow-up), including group cognitive-behavioral psychotherapy, psycho-educational and interpersonal interventions.

Iancu et al. (46) adopted a group therapy combining a cognitive-behavioral and a dynamic approach; with more detail, the latter proposes a dynamic understanding of ED symptoms as an externalization of an unsolved conflict.

DISCUSSION

Overall, according to the studies included in the review, alexithymia levels sometimes remain high even after specific treatment, while changes and improvements may occur in other outcome indicators (e.g. body mass index, eating symptomatology, motivation).

Some studies clearly failed to find a positive impact of treatment on alexithymia as assessed with the TAS (32, 45, 46). On the other hand, others supported an improvement of alexithymia after treatment (2, 15, 44, 47, 48), which was represented by CREST (15), a mixed approach including different types of treatment (2, 44), a 4-month day hospital treatment (48), and a psycho-pedagogic intervention (47), respectively (see **Table 1** for more details). Last, mixed findings have been reported by a couple of studies. An improvement of TAS scores was reported in a subgroup of patients with AN (full mental capacity) but not in another (diminished mental capacity) (49). Furthermore, CREST was described as effective in reducing alexithymia when offered in an individual format, but not in a group one (50).

General Information

All studies but one (2) involved a single center. Most studies were performed in a hospital setting, on inpatients; only four studies included outpatients (44, 45, 48, 49). Samples size ranged from 29 to 168 patients. One study (44) included also a control group, composed by 16 age-matched healthy women.

Participants' Features

The studies included in this review involved patients with an age range from 12 to 63 years old; two studies (32, 45) were specifically focused on an adolescent population. Most studies included only female patients, while two (32, 46) assessed both genders. From a clinical standpoint, four of the 10 studies selected for this review involved patients with different types of EDs: AN-R; AN-P; BN; EDNOS (2, 46–48), while six studies included only AN patients (15, 32, 44, 45, 49, 50). More specifically, diagnosis was made according to DSM-IV criteria in three studies (2, 46, 48), to ICD-10 criteria in one study (45) and to DSM-5 criteria in another one (50). In 2 studies (47, 49) the type of ED was assessed using different questionnaires (respectively EDI-2 and EDEQ). The remaining five studies did not specify the diagnostic criteria used (15, 32, 44, 47, 49). Patients' BMI ranged from 13 to 21.4; illness duration, when specified, ranged from 1 month to more than 5 years. Comorbidities were specified in four studies (2, 32, 45, 46).

Intervention Features

All studies but two (2, 47) applied cognitive interventions (15, 32, 44–46, 48, 50). More specifically, patients enrolled in three studies (15, 32, 50) were treated with CREST, in a group format; furthermore, Adamson et al. (50) used CREST in an individual therapy setting as well. Seven studies (15, 32, 45–48, 50) included psycho-pedagogic methods to facilitate the ability of patients to cope with negative feelings, particularly associated to body appearance and food assumption. Speranza et al. (2) provided different treatment approaches, such as pharmacotherapy (for at least 3 months), psychotherapy (for at least 6 months), hospitalization (either full or partial), and a combination of pharmacotherapy with psychotherapy. Ohman and coworkers (45) also offered once-monthly family sessions, in the context of 40 weekly sessions of multimodal cognitive behavioral group therapy (G-CBT) program.

Assessment

All studies but one (2, 15, 32, 45–50) assessed patients with several questionnaires (either self-report measurers or clinician-rated interviews) both at baseline and after the intervention. Beadle et al. (44) tested patients with the TAS only.

Outcomes

In line with the inclusion criteria adopted, alexithymia as outcome after the intervention was assessed by all studies (2, 15, 32, 44–50). Moreover, four studies (2, 45, 46, 48) evaluated its possible role as predictor of treatment outcome in the AN population.

Strengths and Limitations

The current paper provides an up-to-date review of the literature on alexithymia and treatment outcome in AN. Despite the clinical relevance of alexithymia, the number of published studies about its changes after treatment are somewhat limited; the possibility to compare the results of these studies is hindered by their heterogeneity and by methodological issues. Besides the previous review study by Pinna et al. (55), that focused on the implications of alexithymia as a predictor of treatment outcome in subjects affected by ED, there are no similar studies on interventions for alexithymia in anorexic patients, making the current review useful to the community of researchers in the field of EDs. Some limitations of this scoping review should be underscored: first, only two databases (i.e., Medline and Scopus) were searched to identify relevant articles written in English language, with potential loss of valuable additional information. The restriction to published studies could *per se* represent a bias in systematic reviews of effectiveness. Despite we focused on TAS as outcome measure in patients with AN undergoing any kind of treatment, samples sometimes included also patients with other EDs, and it was not always possible to rule out results pertaining only those with a diagnosis of AN. Last, while we focused on the TAS as the most used tool for the assessment of alexithymia, and this ensures the homogeneity of results, this choice obviously lead to the exclusion of all those studies using other rating scales for alexithymia.

On the other hand, we adopted restrictive inclusion criteria and applied the PRISMA methodology for the selection process; furthermore, we assessed the quality of the studies included in this review.

Nonetheless, since our aim was to conduct a scoping review of the literature we did not perform a quantitative data synthesis nor meta-analysis. This represents a further limitation of the current study; a meta-analytic approach would certainly represent an interesting research direction for the future to allow drawing clear, evidence-based conclusions about the clinical implications of the findings that have emerged from our research.

CONCLUSIONS

A high rate of individuals with AN achieve incomplete recovery following treatment. The identification of outcome predictors such as alexithymia is crucial, as well as that of treatments specifically targeting these predictors (56–62).

Further studies aimed at a deeper understanding of the actual impact of alexithymia on the outcome of anorexia are warranted, as well as researches exploring alternative treatment strategies for alexithymia in EDs.

DATA AVAILABILITY STATEMENT

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

AUTHOR CONTRIBUTIONS

CG and PZ contributed to the conception and design of the work. EG and CG independently triaged the titles and abstracts to remove those that were clearly inappropriate. The remaining papers, to be included, had to satisfy all the predetermined eligibility criteria. Possible disagreements regarding study inclusion were resolved by discussion with PZ. After selection of the relevant studies, EG and CG independently extracted and tabulated data on study design and outcome data using a standard form. CG and EG drafted the manuscript. PZ revised it critically for important intellectual content.

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The Mediating Effect of Alexithymia on the Relationship Between Schizotypal Traits and Sleep Problems Among College Students

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A body of research has investigated the relationship between alexithymia and sleep problems, as well as the relationship between schizophrenia and alexithymia. However, there have been few studies on the relationships between the three. The current study explored the relationship between schizotypal traits and sleep problems among college students, and the potential role of alexithymia as a mediator of this relationship. The participants were all first-year students at a medical university in Guangdong province, China. A total of 2,626 college students participated. They were asked to complete a questionnaire that incorporated the Schizotypal Personality Questionnaire (SPQ), the Toronto Alexithymia Scale (TAS-20), and the Insomnia Severity Index (ISI). The results revealed a relatively high percentage of students with mild insomnia (74.8%) and a smaller percentage with moderate to severe insomnia (7.9%). Correlation analysis revealed that both the TAS-20 and ISI scores had significant positive correlations with the SPQ score ($p < 0.01$). There was also a significant positive correlation between the TAS-20 and ISI scores ($p < 0.01$). The ISI score was significantly influenced by the SPQ score in a direct way, and increased considerably with increases in the TAS-20 score, indicating the importance of alexithymia as a mediator. The mediation model was tested via regression analysis and the bias-corrected bootstrap method, and these results further confirmed the role of alexithymia as a mediator.

Keywords: alexithymia, schizotypal traits, insomnia, sleep problems, college students, mediating effect

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INTRODUCTION

Sleep problems can be found in 30–80% of schizophrenia patients (1). They are defined as increased sleep latency, frequent night waking, shorter sleep duration, and other parasomnias (2). Additionally, studies have found that schizotypal traits are present in people without schizophrenia, including offspring with parental psychiatric disorders and the general population (3). Schizotypal traits are of interest and importance in their own right but also have theoretical and clinical relevance to schizophrenia (4). Individuals with schizotypal traits show similar symptoms to schizophrenia patients but to a milder degree. These traits include social withdrawal, reduced cognitive capacity, and affective dysregulation. Most researchers in psychopathology hold the view that schizotypy is a construct that is intimately connected to a schizophrenia-related liability (5).

Evidence also suggests that individuals with high levels of schizotypal traits resemble schizophrenia patients in experiencing much more vivid nightmares or pleasant dreams than other individuals (6). Moreover, sleep problems have been associated with psychosis-like experiences in epidemiological studies (7). A growing amount of evidence suggests that recognizing and addressing early signs and symptoms of psychosis can lead to better outcomes (8). However, few studies have examined directly the relationship between schizotypal traits and sleep problems.

Research has also found a close correlation between alexithymia and sleep problems (9). Alexithymia is a type of emotional disorder, and the alexithymia personality construct includes the following features: difficulty in identifying and describing feelings, difficulty in distinguishing between feelings and bodily sensations, a constricted imagination, and an externally oriented cognitive style (10). Researchers have recently suggested that internalized psychic conflicts and an inability to verbalize these problems result in increased nocturnal arousal and subsequent insomnia in individuals with alexithymia (11). Moreover, a recent study has shown that difficulties in identifying feelings are related to increased general sleep experiences such as hallucinations, frequent waking, and insomnia, leading to the suggestion that general sleep experiences represent a nocturnal manifestation of unprocessed emotions (12); the same study also found that externally oriented thinking is related to decreased general sleep experiences. Meanwhile, schizophrenia also has a strong correlation with alexithymia (13). A considerable amount of research has found that schizophrenia patients exhibit higher levels of alexithymia, and that individuals with higher levels of alexithymia may be more prone to schizophrenia spectrum disorders (14).

Although there has been much research on the relationship between alexithymia and sleep problems, as well as on the relationship between schizophrenia and alexithymia, a review of the literature shows that there have been few studies on the relationships between schizophrenia, alexithymia, and sleep problems. The role of alexithymia in the relationship between schizophrenia and sleep problems is therefore unclear. The purpose of the current investigation was to explore the relationships between schizotypal traits, alexithymia, and sleep problems among college students. We hypothesized that schizotypal traits play an important role in the sleep problems of college students, and that alexithymia is a mediating variable between the two.

MATERIALS AND METHODS

Participants

In this study, 2,811 questionnaires were issued to first-year students at a medical university in Guangzhou, Guangdong, China, of which 2,626 were returned as valid and analyzed, showing an effective response rate of 93.42%. Of the 2,626 participants, 1,601 were female and 1,025 male, with a mean age of 18.34 years ($SD = 0.83$). The study was approved by the ethics committee of Southern Medical University and all participants provided informed consent.

Measures

Schizotypal Personality Questionnaire (SPQ)

The SPQ is a 74-item self-report questionnaire consisting of three dimensions: positive, negative, and disorganized (15). Participants respond to statements with "yes" or "no" answers, depending on their agreement with each item. A "yes" is scored as 1, a "no" is scored as 0, and the total score ranges from 0 to 74. The higher the score, the higher the levels of schizotypal personality traits. According to Raine (16), people scoring in the top 10% can be identified as exhibiting schizotypal traits. A threshold of 36 is considered an acceptable standard in China and has been used in our previous studies [e.g., (17, 18)]. In our sample, 91 individuals who scored higher than 36 were classified as individuals with schizotypy. The Chinese version was revised by researchers in Taiwan and has good reliability and validity, with Cronbach's alpha ranging from 0.9 to 0.91 (19).

Toronto Alexithymia Scale (TAS-20)

The TAS-20 consists of 20 items and measures three dimensions of the alexithymia construct: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking (20). Participants respond to items on a five-point scale, ranging from 1 ("strongly disagree") to 5 ("strongly agree"). The total score ranges from 20 to 100. For the English version of the scale, cutoff scores have been established empirically; total scores >60 indicate a high degree of alexithymia and scores <52 indicate a definite absence of alexithymia (21). However, the cutoff score must be determined as appropriate in the Chinese population and we referred to the criteria from the Chinese translation of the 20-item TAS. For the TAS-20-C, it is preferable for researchers to use alexithymia as a dimensional variable rather than to apply categorical cutoff scores (22). The Cronbach's alpha for this scale in a student sample is 0.79, indicating good reliability and validity (22).

Insomnia Severity Index (ISI)

The ISI consists of seven items and was developed by Bastien et al. (23). It has been used widely to assess the severity of insomnia symptoms. Participants respond to items on a five-point scale, scored on a range of 0–4 (0 = "not at all"; 1 = "mild"; 2 = "moderate"; 3 = "severe"; and 4 = "extremely severe") (24). The total score ranges from 0 to 28. A score of 0–7 represents no clinically significant insomnia; a score of 8–14 indicates mild insomnia, a score of 15–21 indicates moderately clinical insomnia, and a score of 22–28 indicates severe clinical insomnia. The Cronbach's alpha of this scale is 0.83, indicating high internal consistency (23).

Data Analysis

Statistical analyses were performed using SPSS 23.0. First, a Harman single-factor test was used on all the variables combined in the questionnaire for factor analysis. The results showed that 15.03% of the variation was explained by the first principal component, which is lower than the critical value (40%) and indicates that there is no common method bias effect among the variables measured in this study. Second, associations between variables were tested with Pearson correlations. AMOS 20.0

TABLE 1 | Sample screening status.

	Groupings	Number of students	Percentage
SPQ score	SPQ < 14.94 (low schizotypal)	1,466	55.8%
	SPQ ≥ 36 (high schizotypal)	91	3.50%
ISI score	ISI ≤ 7 (no clinical significance)	427	16.30%
	8 ≤ ISI ≤ 14 (mild insomnia)	1,965	74.80%
	15 ≤ ISI ≤ 21 (moderate insomnia)	220	8.40%
	22 ≤ ISI (severe insomnia)	14	0.50%

SPQ, schizotypal personality questionnaire; ISI, insomnia severity index.

was then used to fit the mediation model. The bootstrap mediation technique was adopted to conduct 5,000 samples with replacement, and the maximum likelihood estimation method was used to fit the global model; $p < 0.05$ was used to confirm statistical significance.

RESULTS

Prevalence of Schizotypal Traits, Alexithymia, and Insomnia

As shown in **Table 1**, 91 college students with high schizotypal traits were found, accounting for 3.5% of the overall sample. There were 1,466 individuals with low levels of schizotypal traits, accounting for 55.8% of the overall sample. Meanwhile, the numbers of individuals with mild, moderate, and severe insomnia were 1,965, 220, and 14, respectively, accounting for 74.8, 8.4, and 0.5%, respectively, indicating that a relatively large percentage of the participants had mild insomnia.

Relationships Between Schizotypal Traits, Alexithymia, and Insomnia

The mean scores for the SPQ, TAS-20, and ISI were 14.94 ($SD = 9.38$), 54.77 ($SD = 6.82$), and 10.41 ($SD = 2.98$), respectively. Pearson correlations were used to explore the relationships between schizotypal traits, alexithymia, and insomnia, as shown in **Table 2**. As predicted, the total SPQ score was significantly positively correlated with the ISI score, the TAS-20 score, and the scores for each dimension of the alexithymia construct ($p < 0.01$). The ISI score was also significantly positively correlated with the TAS-20 score and the scores for each alexithymia dimension ($p < 0.01$).

The Mediating Effect of Alexithymia

The Mediating Effect of Alexithymia on the Total SPQ Scores and ISI Scores

The mediating effect model was constructed by taking the total ISI score as the dependent variable, the total SPQ score as the independent variable, and the total TAS-20 score as the mediating variable (see **Figure 1**). The process of testing the mediating effect then followed the procedure proposed Wen and Ye (25). In the first step, to conduct regression analysis and test coefficient *c*, the total SPQ score was taken as the independent variable and the total ISI score as the dependent variable. Second, to conduct the regression analysis and test coefficient *a*, the total SPQ score was taken as the independent variable and the total TAS-20 score as the dependent variable. Third, to conduct the regression analysis and test coefficient *b*, the total SPQ score and total TAS-20 score were taken as the independent variables, and the total ISI score was taken as the dependent variable. As shown in **Table 3**, the results revealed that the coefficients *a*, *b*, and *c* were all significant, indicating that alexithymia is a mediating variable between schizotypal traits and insomnia; i.e., schizotypal traits were found to affect sleep problems through alexithymia.

Due to these regressions being significant, the indirect effect of alexithymia was tested using the bias-corrected bootstrap method. As shown in **Table 4**, the results show, first, that the bootstrap 95% confidence interval for the total effect of the model did not contain a zero value [B = 0.144, 95% CI = (0.133, 0.155)]. Second, the direct effect of schizotypal traits on the insomnia severity index did not include a zero value [B = 0.103, 95% CI = (0.090, 0.116)]; and, third, the bootstrap 95% confidence interval for indirect effect did not contain a zero value [B = 0.041, 95% CI = (0.032, 0.049)]. This further indicates that alexithymia had a significant mediating effect on the relationship between schizotypal traits and sleep problems. The effect size of the mediating effect was 28.47%.

The Mediating Effect of Alexithymia on Each Dimension of the SPQ Scores and ISI Scores

For the SPQ subscales scores, the mediating effect model was constructed by taking the total ISI score as the dependent variable, and the positive SPQ score, negative SPQ score, and disorganized SPQ score as the independent variables, and the total TAS-20 score as the mediating variable (see **Figures 2–4**). The process of testing the mediating effect was the same as above. As shown in **Table 5**, for the positive dimension, the results revealed that the total effect on the model was 0.224 ($p < 0.001$). The direct effect of the positive dimension of schizotypal traits on the ISI was 0.070 ($p < 0.001$) and the indirect effect was 0.154 ($p < 0.001$). For the negative dimension, the total effect on the model was 0.255 ($p < 0.001$). The direct effect of the positive dimension of schizotypal traits on the ISI was 0.092 ($p < 0.001$) and the indirect effect was 0.163 ($p < 0.001$). For the disorganized dimension, the results revealed that the total effect on the model was 0.411 ($p < 0.001$). The direct effect of the positive dimension of schizotypal traits on the ISI was 0.158 ($p < 0.001$) and the indirect effect was 0.253 ($p < 0.001$). In summary, the results for the three dimensions of the SPQ further confirm the hypothesis that alexithymia has a significant mediating effect on the relationship between schizotypal traits and sleep problems.

DISCUSSION

This survey identified that insomnia afflicts 83.7% of a group of first-year students at a medical university, with 74.8% reporting mild insomnia, and 8.9% reporting moderate and severe insomnia. In contrast to a previous study (26), the percentage of first-year students with sleep problems in this study was relatively higher (83.7 vs. 74.00%), which can possibly be explained by the fact that near half of the participants were

TABLE 2 | Descriptive statistics and correlation analysis for SPQ, TAS-20, and ISI.

Variable	M ± SD	SPQ total	SPQ pos	SPQ neg	SPQ dis	TAS-20 total	DIF	DDF	EOT	ISI total
SPQ Total	14.94 ± 9.38	1								
SPQ Positive	6.92 ± 4.15	0.812**	1							
SPQ Negative	5.55 ± 5.02	0.868**	0.511**	1						
SPQ Disorganized	3.24 ± 2.93	0.835**	0.564**	0.624**	1					
TAS-20 Total	54.77 ± 6.82	0.581**	0.427**	0.540**	0.493**	1				
DIF	14.92 ± 4.50	0.606**	0.444**	0.555**	0.523**	0.856**	1			
DDF	13.10 ± 2.19	0.455**	0.295**	0.454**	0.393**	0.767**	0.595**	1		
EOT	26.74 ± 2.80	0.084**	0.096**	0.069**	0.050**	0.459**	0.011	0.128**	1	
ISI Total	10.41 ± 2.98	0.454**	0.312**	0.430**	0.404**	0.410**	0.486**	0.306**	−0.021	1

*SPQ, schizotypal personality questionnaire; Pos, positive; Neg, negative; Dis, disorganized; TAS-20, Toronto Alexithymia Scale; DIF, difficulty feelings; DDF, difficulty describing feelings; EOT, externally oriented thinking; ISI, insomnia severity index. **$p < 0.01$.*

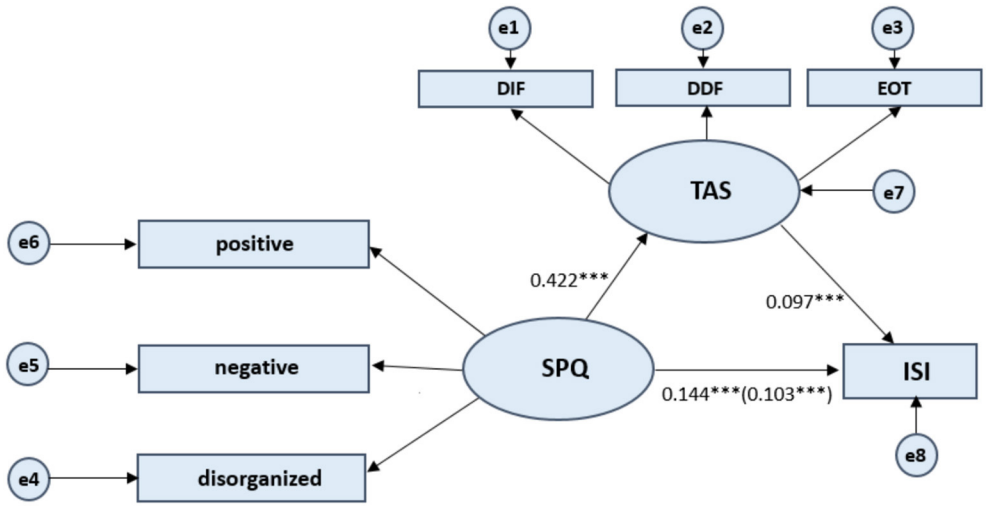

FIGURE 1 | Test of mediation model. Schizotypal Personality Questionnaire (SPQ) consists of three dimensions: positive, negative, and disorganized. Toronto Alexithymia Scale (TAS-20) measures three dimensions of the alexithymia construct: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking (EOT). ISI refers to Insomnia Severity Index. Values presented are standardized regression coefficients. The value in parentheses represents the coefficient for the direct path. e1 to e8 represents each error. Latent Variables use ellipses and Observable Variables use rectangular boxes. ***$p < 0.001$.

TABLE 3 | Test of mediation effect of alexithymia on relationship between schizotypal trait and insomnia.

Procedure	Dependent variable	Independent variable		*B*	*SE*	*t*	*R*	R^2	*F*
Step 1	ISI	schizotypal trait	c	0.144	0.006	26.09***	0.454	0.206	681.113***
Step 2	TAS-20	schizotypal trait	a	0.422	0.0115	36.608***	0.581	0.338	1340.132***
Step 3	ISI	alexithymia	b	0.097	0.009	10.569***	0.488	0.238	410.781***
		schizotypal trait	c′	0.103	0.007	15.531***			

*TAS-20, Toronto Alexithymia Scale; ISI, insomnia severity index. ***$p < 0.001$.*

medical students who with a heavy academic workload in our study. Thus, adaptation to a new environment and the academic workload may have contributed to sleep problems.

The results indicated a positive correlation between schizotypal traits and insomnia severity levels among the students. This is consistent with previous studies (27). Benson (28) found that people with schizophrenia had longer sleep latencies, frequent awakenings, and shorter sleep durations. Another study of schizophrenia patients indicated that most of the participants preferred to stay awake at night and sleep during the day (29). These findings further support the idea that the greater the levels of schizotypal traits, the more severe the sleep problems. Schizophrenia is a complex disorder, caused by both genetic and environmental factors and their interactions (30). It is thought that there is an overlap between the causes of both schizophrenia and sleep problems (31). Compared to people with

TABLE 4 | Bias-corrected bootstrap test of indirect effect of alexithymia on relationship between schizotypal trait and insomnia.

	Effect of value	Boot standard error	Boot CI limit	Boot CI ceiling
Total effect	0.144	0.005	0.133	0.155
Direct effect	0.103	0.007	0.090	0.116
Indirect effect	0.041	0.004	0.032	0.049

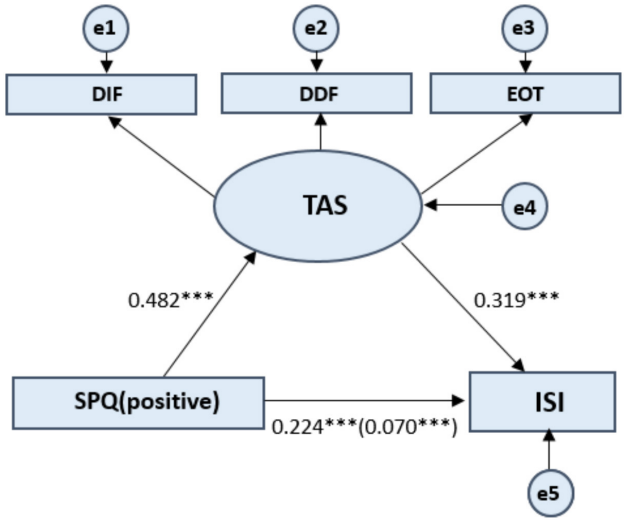

FIGURE 2 | Standardized beta coefficient in TAS partially mediated pathway from SPQ (positive) to ISI. SPQ (positive) represents the positive dimension of the Schizotypal Personality Questionnaire. Toronto Alexithymia Scale (TAS-20) measures three dimensions of the alexithymia construct: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. ISI refers to Insomnia Severity Index. The value in parentheses represents the coefficient for the direct path. e1 to e5 represents each error. Latent Variables use ellipses and Observable Variables use rectangular boxes. ***$p < 0.001$.

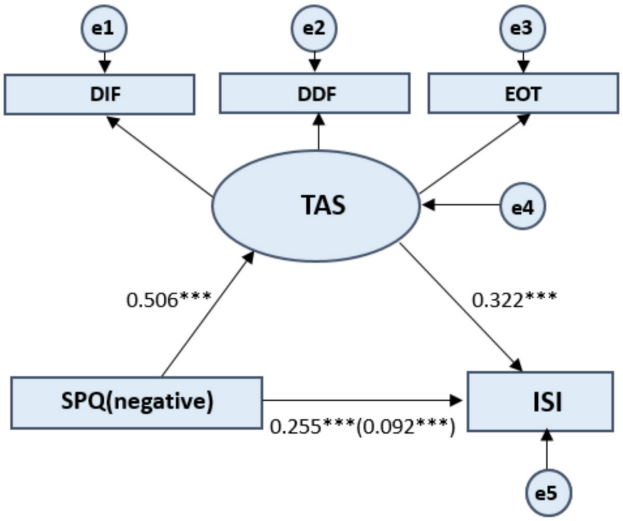

FIGURE 3 | Standardized beta coefficient in TAS partially mediated pathway from SPQ (negative) to ISI. SPQ (negative) represents the negative dimension of the Schizotypal Personality Questionnaire. Toronto Alexithymia Scale (TAS-20) measures three dimensions of the alexithymia construct: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. ISI refers to Insomnia Severity Index. The value in parentheses represents the coefficient for the direct path. e1 to e5 represents each error. Latent Variables use ellipses and Observable Variables use rectangular boxes. ***$p < 0.001$.

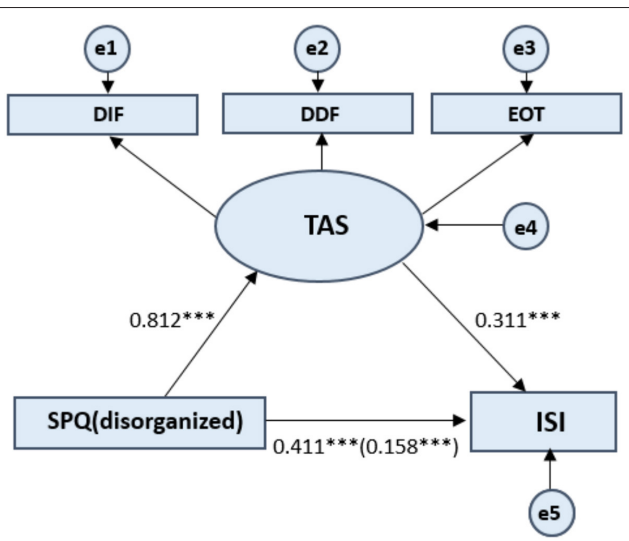

FIGURE 4 | Standardized beta coefficient in TAS partially mediated pathway from SPQ (disorganized) to ISI. SPQ (disorganized) represents the disorganized dimension of the Schizotypal Personality Questionnaire. Toronto Alexithymia Scale (TAS-20) measures three dimensions of the alexithymia construct: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. ISI refers to Insomnia Severity Index. The value in parentheses represents the coefficient for the direct path. e1 to e5 represents each error. Latent Variables use ellipses and Observable Variables use rectangular boxes. ***$p < 0.001$.

schizophrenia, sleep problems are relatively easy to study in the general population, and future studies could include the study of the relevant biological factors to elucidate the mechanisms of the link between schizophrenia and sleep problems.

In addition, the results showed a positive correlation between schizotypal traits and alexithymia among the students, which indicated that the greater the levels of schizotypal traits, the more serious the alexithymia. Studies have shown that schizophrenia is a neurocognitive disease, and that abnormalities in key sections of the brain responsible for emotional processing lead to emotional disorders, making it difficult for individuals to process emotions, resulting in alexithymia (32). This explains why individuals with greater levels of schizotypal traits also show more serious alexithymia.

The structural equation modeling further demonstrated that alexithymia played a partial mediating role between schizotypal traits and sleep problems among the students. This means that schizotypal traits could predict directly the sleep quality of the students. However, schizotypal traits also exerted an indirect influence on sleep problems through the mediating effect of alexithymia. This appears to be consistent with some previous studies. For instance, Rehman et al. suggested that sleep problems are associated with psychotic disorders such as paranoia, and that alexithymia may be a potentially important mediating

TABLE 5 | Test of mediation effect of alexithymia on relationship between each dimensions of schizotypal trait and insomnia.

	Positive dimension	Negative dimension	Disorganized dimension
Total effect	0.224	0.255	0.411
Direct effect	0.070	0.092	0.158
Indirect effect	0.154	0.163	0.253

Schizotypal Personality Questionnaire (SPQ) consists of three dimensions: positive, negative, and disorganized.

variable (33). However, other studies have shown that, although alexithymia is significantly correlated with sleep symptoms such as prolonged sleep latencies and frequent awakenings, these correlations disappear when the effects of depression are excluded (34). This suggests that sleep problems may also be associated with mood disorders such as depression.

The mediating effect of alexithymia on each dimension of the SPQ and the ISI scores demonstrates that all the three dimensions exerted influences on insomnia through alexithymia, but the disorganized dimension had the greatest impact. This seems to be consistent with some previous studies. For example, negative symptoms are correlated with generalized impairment (35), psychomotor speed, and poor attention (36, 37). This suggests that negative symptoms may be associated with alexithymia (38) and rapid eye movement sleep abnormalities (39). In addition, positive symptoms are correlated with verbal memory and language comprehension deficits (40) which can lead to inner emotions being difficult to release and deal with, resulting in insomnia at night. Finally, disorganized symptoms are correlated with global impairment, as well as language and memory problems (41). This means that disorganized symptoms experiences almost all of these cognitive impairment, including those that have occurred on both the positive and negative dimensions. Therefore, the disorganized dimension has the greatest impact on sleep problems through the partial mediation effect of alexithymia.

In any case, the causes of sleep problems still need further exploration, including investigation of the impact of depression on alexithymia, and the independent effect of other emotional disorders. Additionally, in order to improve the sleep quality of college students, and to enhance the pertinence and effectiveness of psychological health education, findings from the current study may suggest that psychological counseling might help students develop the ability to express their inner feelings and to understand others' emotions from the perspective of alexithymia.

The limitations of this study are as follows. First, this is a cross-sectional study, so it is still not known how is the dynamic relationship among alexithymia, schizotypal traits and sleep. Future study need to address this issue. Second, alexithymia is generally assessed by self-report or interview, but individuals with schizotypal traits often have low levels of self-awareness. Relying on these subjective approaches can, therefore, be problematic. In future research, self-report approaches should be combined with objective measures. Third, the evaluation of sleep quality in our study relied on the single source of a self-report questionnaire. The data obtained could be combined with polysomnography and the use of sleep diaries to obtain more comprehensive sleep data. Lastly, the participants surveyed in the current study were all college students. Therefore, they are not sufficiently representative of the general population, and the extrapolation validity of this research is poor. To be more representative of the general population, future research would need to replicate the results using larger samples, and the samples expanded to include different demographic groups.

In conclusion, we found positive correlations between schizotypal traits, alexithymia, and sleep problems, while alexithymia was found to partially mediate the relationship between schizotypal traits and sleep problems. We may be able to improve the sleep quality of those with a high level of schizotypal traits by training their ability to express emotion.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committees of Southern Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

QM and XZ collected and analyzed the data, and wrote the first draft of the manuscript. LZ generated the idea, designed the study, interpreted the data, and wrote the manuscript.

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Quadratic Relationship Between Alexithymia and Interoceptive Accuracy, and Results From a Pilot Mindfulness Intervention

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Alexithymia, or a reduced ability to label and describe one's emotions, is a transdiagnostic construct associated with poor psychosocial outcomes. Currently, the mechanisms underlying affective deficits associated with alexithymia are unclear, hindering targeted treatment delivery. Recent research suggests deficient interoceptive awareness, or reduced awareness of one's internal bodily state, may be key in the etiology of alexithymia. It has long been demonstrated that mindfulness meditation can alter perceptions of one's own emotions and bodily cues. Therefore, it is possible that mindfulness meditation may reduce affective deficits associated with alexithymia by improving interoceptive awareness. In this study, we aimed to (1) elucidate the role of interoceptive accuracy and sensibility, two dimensions of interoceptive awareness, in alexithymia, and (2) test the efficacy of a brief mindfulness meditation for improving interoceptive accuracy, interoceptive sensibility, and emotional awareness. Seventy six young adults completed a baseline heartbeat detection task, to assess interoceptive accuracy and sensibility, and the Toronto Alexithymia Scale—20 item. They were randomly assigned to a brief mindfulness-based body scan meditation intervention or control condition. Afterwards, participants completed tasks assessing emotional awareness (i.e., affect labeling, emotional granularity) and follow-up heartbeat detection task. Relationships between alexithymia and interoceptive accuracy and sensibility were best described as quadratic ($p = 0.002$) and linear ($p = 0.040$), respectively. Participants in both conditions showed robust improvements in interoceptive accuracy from baseline to follow-up ($p < 0.001$; $\eta_p^2 = 0.15$); however, there were no group (meditation or control) differences in degree of improvement. Similarly, there were no group differences in affect labeling or emotional granularity. These preliminary results suggest that heightened alexithymia may be associated with either relatively high or low interoceptive accuracy. The meditation condition did not result in improved interoceptive accuracy or sensibility above and beyond that of a control group. Improvements in interoceptive accuracy, interoceptive sensibility, and emotional awareness may require longer or more interactive intervention approaches. More research is needed to parse the potentially complex relationship between alexithymia and interoceptive awareness, and to develop targeted treatment approaches to ameliorating associated affective deficits.

Keywords: alexithymia, interoception, mindfulness meditation, interoceptive accuracy, interoceptive sensibility, emotional awareness, emotional granularity, affect labeling

INTRODUCTION

Alexithymia is a dimensional and transdiagnostic construct, defined by an inability to label and describe one's own emotional experiences, and a preference for externally-oriented thinking (1). Elevated alexithymia is problematic as it is associated with deficits in emotion regulation (2) and relatedly, elevated mental health risk (3). Alexithymia was once considered a stable personality trait; however, recent research suggests both targeted and general psychosocial interventions result in reductions of alexithymia (4–6). It is now exceedingly important to clarify the nature of alexithymic deficits and how to effectively target them in intervention. The current study takes steps toward this goal by investigating the relationship between alexithymia and interoceptive accuracy and sensibility, and piloting a mindfulness intervention to improve interoceptive accuracy, interoceptive sensibility and emotional awareness.

Interoception refers to one's perception of internal physiological sensations within their body (7). The capacity to accurately detect interoceptive cues is thought to be critical in facilitating the experience of subjective emotional states (8–10). Some propose that alexithymia is fundamentally a deficit in interoceptive accuracy (10–12). Thus, clarifying the relationship between alexithymia and aspects of interoception is essential. The umbrella of interoceptive awareness includes multiple related, but distinct processes including "interoceptive accuracy" and "interoceptive sensibility" (13). Interoceptive accuracy refers to one's *objective* accuracy in detecting interoceptive signals. In the laboratory, this is typically measured using heartbeat detection paradigms; for example, in Schandry's (14) mental tracking task, participants are instructed to estimate how many times their heart beats over various time intervals. Meanwhile, their actual heartrate is measured using a tracking device, allowing direct comparison of estimated and objective heartbeat data. The ratio of these values forms an index of interoceptive accuracy. Interoceptive sensibility refers to one's *perceived* dispositional tendency to focus on interoceptive signals, and is typically measured using self-report questionnaires that assess an individual's belief in their interoceptive ability (13). In the laboratory, this is often assessed by measuring one's confidence in performance on heartbeat detection paradigms.

Despite theoretical conjecture that alexithymia should be negatively related to interoceptive accuracy and sensibility, empirical findings testing this linear relationship are mixed. While some studies have shown significant negative relationships between alexithymia and interoceptive sensibility, assessed with self-report questionnaires (15, 16), others have reported significant positive relationships between alexithymia and interoceptive sensibility (17, 18).

Similarly, on heartbeat detection tasks, investigators have reported statistically significant negative [e.g., (12)], positive [e.g., (19)], and statistically non-significant relationships [e.g., (16)] between interoceptive accuracy and alexithymia. Murphey et al. (20) suggests inconsistent findings may result from failure to account for key covariates. They show alexithymia and interoceptive accuracy are significantly negatively correlated, but only after accounting for relevant covariates such as BMI [associated with lower interoceptive discrimination; (21)], depression and anxiety, and gender.

Another source of variance might be non-linear relationships between alexithymia and interoceptive accuracy and sensibility; consideration of specific clinical examples marked by elevated alexithymia raises this possibility. Some clinical examples are conceptually consistent with the theory that reduced interoceptive awareness relates to reduced emotional awareness. For example, eating disorders are characterized by elevated alexithymia (22) and abnormal internal bodily representations; it is perhaps unsurprising that individuals with eating disorders (compared to non-clinical controls) are characterized by interoceptive deficits (23). Other clinical populations do not present as consistent with this intuitive account. For example, compared to healthy controls, individuals with anxiety disorders have higher levels of alexithymia (3) but also increased interoceptive accuracy (24). Domschke et al. (24) argue that rather than provide useful knowledge about one's internal affective state, heightened interoceptive accuracy may create more frequent opportunities for catastrophic interpretation, perpetuating a cycle of anxiety. Longarz et al. (18) showed significant positive associations between alexithymia, interoceptive sensibility and an index of hypochondriasis. They conclude that heighted interoceptive sensibility can sometimes occur at the expense of emotionally relevant cues. Taken together, the literature suggests that reduced or elevated interoceptive accuracy or sensibility may be problematic in individuals characterized by difficulties with emotional awareness. This suggests the possibility of quadratic relationships between alexithymia and interoceptive accuracy and sensibility. Ultimately, understanding mechanisms underlying accurate, and healthy (e.g., non-catastrophic) interoceptive awareness may be key to ameliorating deficits associated with alexithymia.

Research highlights specific deficits in emotional awareness that are associated with alexithymia, and potentially modifiable in response to focused intervention. Alexithymia is associated with distinct patterns of labeling one's own emotions (i.e., affect labeling): in response to evocative images and videos, those with heightened alexithymia generate fewer or no emotion words to describe their feelings (25, 26). Alexithymia is also associated with reduced negative emotional granularity (26, 27), or the ability to make fine-grained distinctions between various negative emotional states. For example, an individual with low emotional granularity might describe feeling "bad," while someone with high emotional granularity might describe the same feeling as "ashamed, embarrassed, and irritated" (28). Affect labeling and granularity are related to successful emotion regulation (28); knowing what one feels is critical for taking active steps to regulate that emotion (29). This link might help explain robust associations between elevated alexithymia and poor mental health outcomes (3). Critically, affect labeling and emotional granularity are modifiable and thus potential targets of intervention: affect labeling interventions have been shown to improve physiological recovery following a stressful speech task (30). Undergoing an 8-week mindfulness based stress reduction course has been shown to result in increased emotional

granularity (31). In dialectical behavioral therapy (DBT), patients learn to increase awareness and acceptance of varied emotional states, which promotes successful emotion regulation (32).

An essential next step in alexithymia research is developing and testing targeted interventions to ameliorate specific deficits. A primary goal of mindfulness-based interventions is to cultivate non-judgmental and present focused awareness of internal experiences including bodily sensations, thoughts, and emotions (33); as such, mindfulness-based interventions, particularly those that are bodily-focused, may be ideally suited to foster accurate detection of both interoceptive and emotional cues. This is again demonstrated in DBT interventions, which use mindfulness-based approaches to increase emotional awareness (32). Results from two recent mindfulness-based interventions highlight the utility of applying these techniques to improve alexithymia specifically. In a large, non-clinical sample, Bornemann and Singer (6) showed increased interoceptive accuracy in response to a 9-month mindfulness-based training. These improvements were directly related to reductions in alexithymia over time. Edwards et al. (34) developed a brief mindfulness-based intervention delivered to individuals with high alexithymia, which resulted in more precise and complex affect labeling. In the current study, we examined the benefits of a brief mindfulness-based body scan meditation on interoceptive accuracy, interoceptive sensibility, and emotional awareness in a healthy population.

The current study aimed to (1) explore the relationship between alexithymia and interoceptive accuracy and sensibility in a sample of healthy young adults while accounting for key covariates of BMI and gender, and (2) pilot a brief mindfulness-based body scan intervention and determine whether it results in improved emotional awareness and interoceptive accuracy and sensibility, compared to a control task. To test our first aim, participants completed a heartbeat tracking task and an alexithymia questionnaire. We hypothesized alexithymia would be related to interoceptive accuracy and sensibility and we explored both linear and quadratic relationships. In the interest of transparency, it is important to acknowledge that although the heartbeat tracking task is widely utilized, recent empirical evidence highlights significant limitations of this method (35); we discuss the implications of these limitations in the discussion section. To address our second aim, we randomized participants to receive either a mindfulness-based body scan meditation intervention or to complete a control task. Similar meditations have been successful in increasing accurate perception of bodily sensations in prior research (36). We hypothesized that those in the mindfulness (vs. control) group would demonstrate greater improvements in interoceptive accuracy and sensibility from baseline to follow-up, and improved performance on affect labeling and emotional granularity tasks.

MATERIALS AND METHODS

Participants

Participants were recruited from the university's undergraduate research pool. They responded to a general advertisement describing a laboratory visit entailing questionnaires and laboratory tasks. Seventy six participants were recruited and received course credit for their participation. To account for the potentially confounding effect of mood disorders on study variables, we excluded participants with a past or current self-reported diagnosis of depression, anxiety, or substance use disorder. This study was approved by the Vanderbilt University Institutional Review Board, and participants provided written informed consent.

Procedure

Prior to attending a scheduled laboratory visit, participants were randomized to either a mindfulness-based body scan meditation intervention condition or a control condition using a random number generator. When they arrived to the laboratory, they first completed questionnaires and a heartbeat detection task (14), used to measure interoceptive accuracy and interoceptive sensibility. Next, they received either a mindfulness-based body scan meditation intervention or control condition, depending on prior randomization.

Both conditions were delivered via a 10-min audio recording, and participants were instructed to simply follow along with instructions in the recording. The mindfulness intervention conditions consisted specifically of a body scan mediation; participants were instructed to sequentially attend to specific parts of their body with non-judgmental and present-focused attention; in the control condition, participants were instructed to listen passively to a reading from a natural history text book. Both recordings were originally developed for use in a smoking cessation intervention (37). Afterwards, participants completed tasks designed to assess multidimensional aspects of emotional awareness [for details on this "INduction-based multiDimensional Emotional Experiences Paradigm" see previous work; (26)]. Finally, they completed a follow-up heartbeat detection task.

Materials and Tasks

Questionnaires

Participants completed the Toronto Alexithymia Scale 20-item [TAS-20; (38)], which yields a total alexithymia score, summed from scores on three subscales, difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally-oriented thinking (EOT). Participants responded to questions on a 1–5 Likert scale; higher scores indicate greater alexithymia. Participants also completed a brief demographics questionnaire to assess age, gender, race, height, and weight (the latter two used to calculate BMI).

Heartbeat Detection Task

Interoceptive accuracy and interoceptive sensibility were assessed using the heartbeat tracking task (14). A Polar H7 Bluetooth Smart Heart Rate Sensor (Polar Electro Oy, Kempele, Finland) was utilized to measure heartrate during the heartbeat tracking trials. Heartrate data was transmitted using Bluetooth technology to a 4th generation iPad using the Polar Beat App (Apple Inc., Cupertino, CA, USA). To avoid references to the passing of time, participants were asked to remove watches for the duration of the heartbeat detection task, which were stored in a safe place outside of the data collection room; all clocks were also removed from the room. Participants were instructed to sit with their eyes closed,

hands on the table, and palms face up, to avoid using visual cues or pulse detection as a proxy for heartbeat. Participants were asked to estimate the number of times their heart beat over various time intervals. First, they completed a 30 s practice trial and were given the opportunity to ask questions. Next, the completed 25 s, 35 s, and 45 s trials, with trial order randomized across participants. After each trial, they were asked "how many times did your heart beat?" After completing all four trials, they rated confidence in their estimation on a 1–10 scale (1 = "not at all confident," 10 = "completely confident").

Interoceptive accuracy was calculated as the mean score across the three trials using the following transformation: 1/3 $\sum$[(1-|recorded heartbeats—counted heartbeats|)/recorded heartbeats; (14)]. Confidence ratings were used as an index of interoceptive sensibility (13). Participants were not given any feedback on their performance after completing the task.

Emotional Awareness Tasks

After the mindfulness intervention or control task, participants completed the INduction-based multiDimensional Emotional Experiences Paradigm [IN-DEEP; (26)] to assess aspects of emotional awareness. Participants viewed 14 film clips identified as reliably eliciting 6 prototypical emotions by Gross and Levenson [(39); amusement, anger, contentment, disgust, fear, sadness, and surprise]. After each clip, they selected the emotion they experienced "the most" from a list including 16 emotion words and two additional options of "the emotion I experienced is not listed here" and "I did not experience any emotion." Consistent with our prior research (26), the frequency with which participants selected the standardized emotion was used to compute an index of "consistent affect label." The frequency with which they chose an affect label that did not correspond with the standardized emotion was used to form an index of "non-standard affect label," and the frequency of selecting "I did not experience any emotion" formed an index of "no affect label."

After providing an affect label, participants were presented with 29 emotional words sequentially, and asked to report the intensity with which they experienced each on a 1–9 Likert Scale. These ratings were used to form an index of emotional granularity. We calculated the degree to which each participant made granular distinctions between specific negative and specific positive emotions using a standard approach (28). First, interclass correlations with absolute agreement were calculated between the intensity ratings of each individual's endorsement of all negative or positive emotions across the entire experiment. For each participant, these ICCs were averaged together to form a single index representing average positive or negative granularity. At this stage, a high average ICC suggests a tendency to rate all positive or all negative emotion words similarly, reflecting a lower degree of granularity. However, to aid interpretation of these results, and in line with standard procedures, we then subtracted the average ICC from one, such that higher scores reflect a higher degree of granularity. Finally, scores were transformed to Fisher's *z*.

Of note, the full IN-DEEP paradigm assesses other domains of emotional experiences (e.g., subjective arousal, response time). We isolated affect labeling and emotional granularity to facilitate group comparison: for these variables, higher scores indicate report of more normative experiences or greater degree of emotional awareness. These two variables have been shown to be most tightly linked to the alexithymia construct (26, 27).

Data Analysis

Power Analysis

A power analysis was conducted to determine the number of participants needed to sufficiently power our primary aim (determining the relation between interoceptive accuracy and alexithymia). One previous study reported a correlation of −0.37 between alexithymia and interoceptive accuracy in a sample from the general population (12). Thus, approximately 73 participants were needed to have 90% power to detect a similar, moderate, effect.

Missing Data

Heart rate data was missing from three participants at both time points (due to equipment failure or preference not to participate), and two participants at follow-up (due to time constraints). These data points were removed case-wise from our analyses.

Statistical Approach

To test our first aim, hierarchical regression models were conducted to examine relationships between (1) alexithymia and interoceptive accuracy, and (2) alexithymia and interoceptive sensibility. We tested relationships between total alexithymia and alexithymia subscales in relation to interoceptive accuracy and sensibility. In all models, BMI and gender were entered as the first step in each model. In the second step, baseline interoceptive accuracy (model 1) or interoceptive sensibility (model 2) were added to the model. In the third step, the quadratic term of baseline interoceptive accuracy (model 1) or interoceptive sensibility (model 2) was added to the model. Step two yielded estimates for a linear model, and step three yielded estimates for a quadratic model. We examined the significance and effect size (f^2) of the overall model at each step. We also examined the significance of the individual items within. Finally, we examined the change in the effect of the overall model and the statistical significance of that change at each step, to determine whether a quadratic model was a better predictor of alexithymia, compared to linear effects. Of note, our decision to test a quadratic relationship between interoceptive accuracy and sensibility and alexithymia was a posteriori, driven by literature that emerged after the planning of this study. For example, a meta-analysis from our group that concluded that chronic pain—a condition characterized by hypervigilance toward bodily sensations—was consistently and robustly associated with elevated levels of alexithymia (40). Because this was not an *a priori* analysis, there is increased risk of Type I error.

Our second aim examined whether exposure to mindfulness-based body scan meditation intervention resulted in improved interoceptive accuracy and sensibility, and greater emotional awareness, compared to a control task. We conducted mixed repeated measure analysis of variance (RM-ANOVA) to examine the effect of time (baseline, follow-up) on interoceptive accuracy

and sensibility, considering group (meditation, control) as a between-groups factor. Where significant interactions emerged, we conducted *post-hoc* paired sample *t*-tests to examine group differences. Finally, we performed *t*-tests comparing group differences in affect labeling and positive and negative emotional granularity, and report Cohen's *d* to describe effect size.

RESULTS

Descriptive

Sample Characteristics

Of the included 76 participants, 66% identified as women and 34% as men (Mean age = 19.70, *SD* = 0.95). Fifty four percentage of participants identified as Caucasian, 16% African American or African, 15% Asian or Asian American, 3% Hispanic, and 10% "Multiracial" or "other." The meditation and control groups did not differ on these demographic factors.

Alexithymia

Mean TAS-20 total score was 44.57 (SD = 9.36). There were no group differences (meditation vs. control) on TAS-20 total score ($t_{(75)} = 0.04$, $p = 0.97$). There were significant correlations between TAS-20 subscales; subscale score means, standard deviations and inter-correlations coefficients are reported in **Table 1**.

TABLE 1 | Descriptive statistics and inter-correlations of alexithymia subscale scores.

Alexithymia subscale	Mean (SD)	Inter-correlations		
		1	2	3
Difficulty describing feelings	11.88 (3.63)		**0.715**	**0.247**
Difficulty identifying feelings	14.92 (4.33)	**<0.000**		**0.238**
Externally oriented thinking	17.76 (4.15)	**0.032**	**0.038**	

Values above the diagonal indicate correlation Pearson Correlation coefficient (r). Values below the diagonal indicate p values. Statistically significant values (p < 0.05) bolded.

Relationship Between Alexithymia and Interoceptive Accuracy and Sensibility

Interoceptive Accuracy

We used hierarchical regression models to examine linear and quadratic relationships between baseline interoceptive accuracy and total alexithymia, controlling for BMI and gender. See **Table 2** for full results. The first step, including covariates (BMI, gender) was not statistically significantly related to total alexithymia (step 1; $R^2 = 0.02$, $p = 0.460$). The second step, which added a linear interoceptive accuracy term was also not statistically significantly related to total alexithymia (step 2; $R^2 = 0.03$, $p = 0.612$). The third step, which added a quadratic interoceptive accuracy term, was statistically significant (step 3; $R^2 = 0.17$, $p = 0.017$) and moderate in effect ($f^2 = 0.20$). The addition of a quadratic term to the overall model resulted in statistically significant improvement in R^2, highlighting the statistical superiority of a quadratic vs. linear relationship between alexithymia and interoceptive accuracy ($\Delta R^2 = 0.14$, $p = 0.002$). Examination of individual items revealed that after accounting for covariates and the linear interoceptive accuracy term, there was a statistically significant quadratic relationship between interoceptive accuracy and alexithymia ($\beta = 2.62$, $p = 0.002$); see **Figure 1**. Of note, a single outlying TAS-20 score (TAS-20 = 80; greater than three standard deviations above the mean) was identified. We explored the quadratic relationship when this outlier was removed: After accounting for covariates and the linear interoceptive accuracy term, the relationship between interoceptive accuracy and alexithymia remained statistically significant ($\beta = 1.89$, $p = 0.034$).

We also conducted a series of models examining the relationship between alexithymia subscales and interoceptive accuracy, which yielded similar patterns of results. The relationship between DDF and DIF and interoceptive accuracy

TABLE 2 | Hierarchical regression models of linear and quadratic relationships between alexithymia and baseline interoceptive accuracy.

		β	t	p	R^2	p	f^2	Change	
								ΔR^2	$p(\Delta F)$
Step 1					0.02	0.460	0.02	0.02	0.460
	BMI	−0.16	−1.24	0.218					
	Gender	−0.07	−0.553	0.582					
Step 2					0.03	0.612	0.03	0.00	0.605
	BMI	−0.15	−1.14	0.259					
	Gender	−0.07	−0.54	0.594					
	IA_b	−0.06	−0.52	0.605					
Step 3					**0.17**	**0.017**	**0.20**	**0.14**	**0.002**
	BMI	−0.09	−0.70	0.489					
	Gender	0.04	0.34	0.732					
	IA_b	**−2.66**	**−3.35**	**0.001**					
	IA_b^2	**2.62**	**3.30**	**0.002**					

BMI, Body Mass Index; IA_b, Baseline Interoceptive Accuracy. Statistically significant values (p < 0.05) bolded.

were best characterized as quadratic, effects which were moderate in magnitude. The relationship between EOT and interoceptive accuracy was also best characterized as quadratic, an effect which was small in magnitude. See **Supplemental Material A** for full results.

Interoceptive Sensibility

We conducted a similar series of models to examine relationships between baseline interoceptive sensibility and total alexithymia (**Table 3**). The first step, including covariates (BMI, gender) was not statistically significantly related to total alexithymia (step 1; $R^2 = 0.02$, $p = 0.478$). The second and third step, which added first linear (step 2; $R^2 = 0.08$, $p = 0.124$) and then quadratic (step 3; $R^2 = 0.09$, $p = 0.214$) interoceptive sensibility terms, were not statistically significantly related to total alexithymia. However, examination of individual items revealed a statistically significant linear relationship between interoceptive sensibility and total alexithymia, after accounting for covariates ($\beta = -0.26$, $p = 0.040$). We explored this same relationship after removing the single outlying TAS-20 score (TAS-20 = 80), and the result was trending significance ($\beta = -0.23$, $p = 0.074$).

We also conducted a series of models examining the relationship between interoceptive sensibility and alexithymia subscales, which yielded similar overall patterns for DDF and DIF. Both relationships were best characterized as linear, although the relationship between subscales and the linear term were both trending significant ($0.10 > p > 0.05$). In contrast, there was no statistically significant relationship between EOT and interoceptive sensibility. See **Supplemental Material B** for full results.

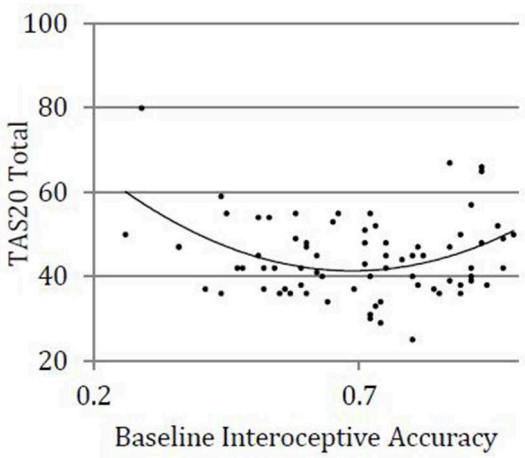

FIGURE 1 | Quadratic relationship between alexithymia and interoceptive accuracy.

Change in Interoceptive Accuracy and Sensibility

Means and SD's of interoceptive accuracy and sensibility at baseline and follow-up by group are presented in **Table 4**.

Interoceptive Accuracy

Mixed RM-ANOVAs examining change in interoceptive accuracy from baseline to follow-up revealed a main effect of time on interoceptive accuracy [$F_{(1, 70)} = 12.22$, $p < 0.001$], suggesting statistically significant and large in magnitude improvements in interoceptive accuracy from baseline to follow-up ($\eta^2 = 0.15$). However, there was no interaction of time and group [$F_{(1, 70)} = 0.02$, $p = 0.88$, $\eta^2 = 0.00$) on this relationship, suggesting that these improvements were statistically similar for both meditation and control groups.

Interoceptive Sensibility

There was no main effect of time on interoceptive sensibility [$F_{(1, 70)} = 0.00$, $p = 0.96$, $\eta^2 = 0.00$], suggesting that there were no overall improvements in interoceptive sensibility, across the two groups. However, there was a significant time by group interaction [$F_{(1, 70)} = 4.41$, $p = 0.039$], an effect that

TABLE 3 | Hierarchical regression models of linear and quadratic relationships between alexithymia and baseline interoceptive sensibility.

		β	t	p	R^2	p	f^2	Change	
								ΔR^2	$p(\Delta F)$
Step 1					0.02	0.478	0.02	0.02	0.478
	BMI	−0.16	−1.21	0.230					
	Gender	−0.07	−0.53	0.597					
Step 2					0.08	0.124	0.09	**0.06**	**0.040**
	BMI	−0.18	−1.40	0.165					
	Gender	−0.02	−0.13	0.900					
	IS_b	**−0.26**	**−2.10**	**0.040**					
Step 3					0.09	0.214	0.10	0.00	0.758
	BMI	−0.18	−1.43	0.159					
	Gender	−0.02	−0.12	0.902					
	IS_b	−0.45	−0.71	0.480					
	IS_b^2	0.19	0.310	0.758					

BMI, Body Mass Index; IS_b, Baseline Interoceptive Sensibility. Statistically significant values ($p < 0.05$) bolded.

TABLE 4 | Interoceptive accuracy and sensibility means and standard deviations at baseline and follow-up.

	Control group		Meditation group	
	Baseline	Follow-up	Baseline	Follow-up
Interoceptive accuracy (%)	0.69 (0.17)	0.76 (0.14)	0.71 (0.18)	0.78 (0.16)
Interoceptive sensibility (0–10)	5.66 (1.77)	5.97 (1.66)	6.19 (2.07)	5.89 (1.98)

TABLE 5 | Group differences (meditation intervention vs. control condition) in emotional awareness.

	Control mean (SD)	Meditation mean (SD)	*t*	*p*	*d*
Affect label					
Consistent affect label	9.18 (1.67)	8.82 (2.30)	0.80	0.420	0.18
Non-standard affect label	3.87 (1.47)	4.58 (2.33)	−1.59	0.117	−0.36
No affect label	0.95 (1.14)	0.61 (0.72)	1.57	0.121	0.36
Granularity					
Negative granularity	0.68 (0.12)	0.66 (0.14)	0.36	0.719	0.15
Positive granularity	0.65 (0.17)	0.65 (0.20)	−0.12	0.904	0.00

was moderate in magnitude ($\eta^2 = 0.06$). This suggests the presence of group differences (meditation vs. control) in changes in interoceptive sensibility from baseline to follow-up. We further explored this finding with *post-hoc* paired sample *t*-tests. Participants who received the mindfulness-based body scan intervention demonstrated a statistically non-significant reduction in interoceptive sensibility from baseline to follow-up [$t_{(34)} = 1.25$, $p = 0.22$, $d = 0.15$]. Those who received the control task recording demonstrated a statistically non-significant increase in interoceptive sensibility [$t_{(33)} = -1.92$, $p = 0.063$, $d = 0.18$].

Group Difference in Emotional Awareness

There were no significant group differences on IN-DEEP performance between the control group and meditation groups (**Table 5**).

DISCUSSION

The current study examined the relationship between alexithymia and both interoceptive accuracy and sensibility in a non-clinical sample of young adults. We tested whether individuals who underwent a brief mindfulness-based body scan meditation demonstrated improved interoceptive accuracy and sensibility, as well as greater emotional awareness, relative to those in a control condition. While accounting for potential confounding variables, we found that the relationship between alexithymia and interoceptive accuracy in the current sample was best described as quadratic; elevated alexithymia was associated with having either relatively high or relatively low interoceptive accuracy. With regards to group differences in performance on interoceptive and emotional awareness tasks, we found that both the meditation and control groups showed significant increases in interoceptive accuracy from baseline to follow-up, with moderate effect sizes. Contrary to hypotheses, there were no group differences in degree of improvement. Also contrary to hypotheses, there were no group (meditation vs. control) differences in performance on affect labeling or emotional granularity.

We found a statistically significant quadratic relationship between interoceptive accuracy and total alexithymia, an effect which was moderate in magnitude. This effect was statistically significant for all alexithymia subscales, and strongest in effect for difficulty identifying feelings and difficulty describing feelings. Some existing research suggests that alexithymia may relate to reduced interoceptive accuracy (10). While this account is intuitive and supported by some empirical evidence, a negative relationship between alexithymia and interoceptive accuracy is not consistently reported (16, 19). The current findings highlight one potential source of inconsistency for these disparate findings in suggesting that the relationship between alexithymia and interoceptive accuracy may not be best categorized by a negative linear association, and rather, may be quadratic. In addition to individuals with elevated alexithymia that is associated with reduced interoceptive accuracy, a subset of individuals with heightened alexithymia may be characterized by increased interoceptive accuracy, which could also be maladaptive. Evidence from various clinical populations—briefly discussed in our introduction—supports this conjecture. This pattern may characterize other clinical populations as well. For example, hypervigilance toward pain is related to the development and maintenance of chronic pain conditions (41); however, chronic pain is also associated with elevated alexithymia (40). Likewise, negative outcomes may be associated with increased interoceptive accuracy in the case of panic disorders, where hypervigilance toward sensations of anxiety is thought to promote catastrophic interpretations, resulting in symptoms of panic (24).

To summarize, our findings indicate that greater interoceptive accuracy is not necessarily associated with better outcomes (e.g., emotional awareness); rather, a specific degree of interoceptive accuracy paired with neutral (vs. catastrophic) interpretations of interoceptive signals may be most adaptive. This is an empirical question for future research studies, which should continue investigating the relationship between alexithymia and interoceptive accuracy, as well as possible cognitive, clinical, and personality moderators of this relationship. This line of research has potential to shed light on developing and delivering targeted and personalized interventions to ameliorate the broad range of affective deficits associated with alexithymia. It is also important that future research replicate the findings presented in the current study, and using varied assessment approaches. As we discuss in more detail in the limitations section, there are limitations to the assessment approach adopted in this particular study. Replication and variety of methodological approach will help shed more light on the preliminary findings of a quadratic relationships between alexithymia and interoceptive accuracy reported in this study. In particular, recent guidelines have been published that will be helpful in guiding future research in this area (35).

The relationship between interoceptive sensibility and total alexithymia in the current study was best characterized as linear, although this was a considerably weaker effect, particularly for alexithymia subscales. A significant negative relationship between interoceptive sensibility and alexithymia has been reported in some (15, 16), but not all (18), empirical investigations of the linear relationship between these two variables. In the current study, interoceptive sensibility was quantified as participants' self-rated confidence in their accuracy detecting heart beats, which was impacted by self-report biases. Alexithymia is strongly related to psychological distress (42) and negative affect (43), which can result in a negative bias of one's abilities. Individuals with elevated alexithymia may be more likely to rate their abilities as poor, regardless of objective accuracy (42) and this may be particularly prominent when they are asked about confidence in areas concerning emotional and bodily awareness. We did not find a statistically significant relationship between externally oriented thinking and interoceptive sensibility. Although we cannot assess this in the current study, one possible explanation for these findings is that externally oriented thinking is less tightly linked to psychological distress compared to other alexithymia subscales (44), and thus less likely to be impacted by a negative self-bias. Moreover, other studies have failed to find a significant relationship between interoceptive sensibility and externally oriented thinking (16, 18), and the theoretical basis and psychometric properties of this construct have been questioned (45). Overall, there remains inconsistency in the relationship between alexithymia subscales and interoceptive sensibility. Future research is needed to more rigorously examine relationships between interoceptive sensibility and alexithymia (total and subscales), the potentially mediating role of negative affect, and using other indices of interoceptive sensibility—particularly those that minimize the confounds associated with self-report.

Contrary to our hypothesis, the mindfulness-based body scan intervention did not result in improvements in interoceptive accuracy above and beyond that of a control condition: both groups showed improvements in interoceptive accuracy, which were large in magnitude. These improvements are consistent with other studies that show a single, brief, mindfulness meditation can result in improved sensory awareness (36) and meaningful clinical change (37). These findings are inconsistent with several studies of small sample sizes (ns <41), which reported no statistically significant improvements in interoceptive accuracy among individuals in a meditation vs. control condition (46, 47). A recent study with a large sample size ($n = 300$) showed that adults enrolled in a 9-month mindfulness training program showed improvements in interoceptive accuracy, and that these improvements corresponded with reductions in alexithymia (6). Interestingly, the adults in that trial showed steady improvement in interoceptive accuracy over the duration of the 9-month training program, and the authors noted that long-term mindfulness training may be required for clinically meaningful and lasting improvements in interoceptive accuracy. Thus, the brief meditation intervention in the present study may have been insufficient in dose to cause measurable benefits in interoceptive accuracy, interoceptive sensibility or emotional awareness. With consideration to the quadratic relationship observed between interoceptive accuracy and alexithymia, additional research is needed to determine how to promote an adaptive degree of interoceptive accuracy using efficient intervention design, and with consideration to potential clinical moderators. Thus, ideally, treatment delivery might be best customized to individuals based on specific diagnoses or symptom profiles.

There were no overall changes in interoceptive sensibility from baseline to follow-up. However, we found a statistically significant interaction of time by group for interoceptive sensibility, which was moderate in effect. *Post-hoc* tests revealed that whereas those in the mindfulness intervention group showed small and statistically non-significant reduction in interoceptive sensibility from baseline to follow-up, those in the control group showed small and statistically non-significant improvement in interoceptive sensibility. These findings are inconsistent with some others, which show, for example, that mindfulness meditation training can result in improvements in interoceptive sensibility but not interoceptive accuracy (47), a pattern also found in expert meditators (48). These current findings should be interpreted with caution, as *post-hoc* comparisons were statistically non-significant, and these and other reported findings are certainly in need of replication; larger sample sizes are often required for adequate statistical power to accurately detect interactions, compared to main effects. Nonetheless, one possible explanation for the aforementioned significant interaction is that the body scan meditation led to increased awareness of the challenge of accurately perceiving interoceptive cues, resulting in decreased perceived accuracy on the heartbeat tracking task, relative to those in a control condition: Experts in the field of mindfulness meditation have argued that initially, such practices may increase awareness of one's deficits (49).

Contrary to our hypotheses, there were no significant group differences (meditation intervention vs. control) in affect labeling or emotional granularity. A brief mindfulness-based body scan meditation may be insufficient to increase emotional awareness, at least as assessed using the current paradigm. More interactive approaches might prove more useful for targetting specific alexithymia-related deficits in emotional awareness. For example, a recent study developed a novel body mapping intervention program, in which participants received education about affect and physiology, underwent guided emotion-focused body scan meditations, and completed digital mapping exersizes, visually depicting experienced emotions. When compared to a control condition of a body scan meditation alone, body mapping resulted in more precise and complex affect labeling, even in individuals with heightened alexithymia (34). Interactive and educational interventions may be superior to more passive, body scan meditations, such as that used in the current study, in improving affective labeling. Prior literature demonstrates the malleability of affect labeling and emotional granularity (31, 34), and additional research is needed to continue investigating effective methods of improving emotional awareness in the context of elevated alexithymia.

A number of methodological limitations are necessary to consider when interpreting the findings of this study. To account

for the potential covariance of depression and anxiety on the relationship between alexithymia and interoceptive accuracy and sensibility, we excluded participants with a current or historical diagnosis of depression, anxiety or substance abuse. However, it is possible that sub-clinical symptoms impacted study findings. Future studies should control for these variables more rigorously. Further, as participants in the current study were healthy young adults, screened to ensure the absence of current or past psychopathology, variability in our constructs of interest (e.g., alexithymia, emotion granularity, and interoceptive awareness) was potentially limited. Participants completed a single practice trial of the heartbeat detection task prior to baseline assessment of interoceptive accuracy and sensibility; practice effects from baseline to follow-up may account in part for improved interoceptive accuracy in both the meditation and control groups. Future studies should administer a greater number of practice trials to better account for the potential confound of practice effects. The sample size for this study was informed by a power analysis of a single study examining the relationship between interoceptive accuracy and alexithymia, which reported a moderate negative association; this was likely to overestimate the expected effect size, and we were underpowered to detect statistically signficant smaller effects, particularly at the alexithymia subscale level.

It is important to note that heartbeat tracking tasks like Schandry's (14) have been criticized and their validity questioned (50). For example, participants can estimate their heartbeat in the absence of sensation. When participants are explicitly instructed to count only felt (and not estimated) heartbeats, interoceptive accuracy is reduced by 50% (35). While we took steps in the current study to remove non-interoceptive heartbeat detection cues (e.g., removing watches and clocks from room; instructing participants to rest with palms faced up on the table), participants were not explicitly instructed to report only felt heartbeats or to avoid using non-interoceptive signals (e.g., pulse) as information. Other covariates, including beliefs about heart rate and time estimation, were not assessed and could not be controlled for. Based on the conclusions of Desmedt et al. (35), interoceptive accuracy was likely overestimated in the current study. In the absence of such explicit instructions, heartbeat detection scores in the current study likely reflect a combination of actual detection, past knowledge of heartrate, or time estimation. A benefit of this paradigm is that it facilitates comparison with prior research done in this area, which has utilized a similar approach to assessing heartbeat detection. However, this has also likely contributed to the inconsistency of findings in this field. Considering this limitation, the current finding of a quadratic relationship between interoceptive accuracy and alexithymia must be considered preliminary. Future studies should examine this relationship using more rigorous methods, in line with recently published guidelines [cf. (35)], and assessing other domains of interoceptive accuracy.

Recent years have seen an explosion of research on alexithymia, a promising transdiagnostic construct with the potential shed light on socioemotional deficits across a variety of clinical phenomena and diagnostic groups. Our current work provides new insights on a particularly promising branch of this field, the relation between alexithymia and interoceptive accuracy and sensibility. These findings provide preliminary evidence that there may be more to the interplay of these two constructs than a simple negative, linear relationship. Specifically, in addition to the purported mechanism whereby interoceptive deficits contribute to elevated alexithymia, for some individuals, high levels of interoceptive accuracy might be associated with higher levels of alexithymia. These findings are preliminary and require replication in larger samples using recently published guidelines for assessing interoceptive accuracy (35). In addition, possible moderators, mediators, and direction of causality remain undetermined. We consider these important avenue for future research, particularly as findings carry implications for delivering targeted and personalized intervention to ameliorate affective deficits associated with alexithymia. Indeed, a "one size fits all" approach to ameliorating affective deficits associated with alexithymia may be inappropriate, given potential variability in interoceptive accuracy among those with elevated alexithymia. The current findings take steps toward providing a nuanced elucidation of the relationship between alexithymia and interoceptive accuracy and sensibility, while also setting forth a useful framework for future investigations.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Vanderbilt University IRB Review Board. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

RA and SP contributed conception and design of the study. RA, MS, and SB performed statistical analysis. RA wrote the first draft of the manuscript. MS and SB wrote sections of this manuscript. All authors contributed to the manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2020.00132/full#supplementary-material

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BRIEF RESEARCH REPORT
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Emotional Awareness Correlated With Number of Awakenings From Polysomnography in Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome—A Pilot Study

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Introduction: Unrefreshing sleep is one of the diagnostic criteria in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), which could be explained by sleep disorders, for example obstructive sleep apnea, reported in our previous study with polysomnography. Our previous findings also indicate difficulties in emotional regulation when measuring alexithymia by TAS-20 (Toronto Alexithymia Scale) and level of emotional awareness by LEAS (Level of Emotional Awareness Scale) in ME/CFS patients. However, the reasons for this are unknown. The purpose of this study was to investigate correlations between data from subjective emotional regulation and polysomnography.

Methods: Twenty-three ME/CFS patients (5 men and 18 women) of mean age 43, and 30 matched healthy controls (9 males and 21 women) of mean age 45, filled in TAS-20, LEAS, and Hospital Depression and Anxiety Scale (HADS). A polysomnography was performed on patients but not on healthy controls. Thus, values of normal population were used for sleep evaluation in ME/CFS patients.

Result: There were significant differences between patients and controls in several aspects of emotional regulation, for example LEAS-self and LEAS-total. Seventy percent of the patients had increased numbers of awakenings (shifts from any sleep stage to awake), 22% had obstructive sleep apneas, and 27% had periodic limb movements. Correlation analysis showed that number of awakenings significantly correlated with LEAS-self and LEAS-total, $p < 0.01$, respectively. There were no other significant correlations.

Conclusion: This pilot study demonstrated significant correlations between reduced emotional awareness and number of awakenings in polysomnography. Future studies with larger cohorts need to be conducted.

Keywords: myalgic encephalomyelitis/chronic fatigue syndrome, sleep, awakenings, alexithymia, emotional awareness

INTRODUCTION

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is characterized by pathological fatigue and fatigability and a number of symptoms, presented over a 6 months period. Patients also report pain, gastrointestinal symptoms, and cognitive difficulties (1). They also complain about the feeling of malaise and fever, both worsening with effort, as well as sore throat and/or lymph nodes (1). The prevalence varies from 1.2%, when the stricter Canadian criteria are applied, to 2.6%, when the broad Oxford criteria are used (2, 3). Sleep disturbances is another important criterion of ME/CFS. However, the exact definition of sleep disturbances in case definition guidelines for ME/CFS is not clear (4). Subjectively reported "non-restorative sleep" or "waking non-rested in the morning" is good enough to classify the presence of sleep disturbances. Our recent study of a total of 381 patients referred for ME/CFS showed that 20.5% (n = 78) of patients fulfilled the criteria for further investigation with full-night polysomnography (5). Thus, patients had increased excessive daytime sleepiness and/or tiredness. Among them, 31 (40.3%) patients were diagnosed with obstructive sleep apnea (OSA), 7 (8.9%) patients with periodic limb movement disorder, and 32 (41.0%) patients with restless legs syndrome. Taken together, among those reporting pathological sleep symptoms, 69.3% of patients had one or more sleep disorders. Further, a majority (84%) had an increased "number of arousals" per sleep hour (mean 8.7, SD 5.1). However, these arousals were actually a shift from any sleep stage to waking, and are in the present study called "number of awakenings". A majority of these awakenings were probably caused by the sleep disorders. Other authors have speculated that sleep disorders in general contribute not only to fatigue (6) and cognition failure (7), the key symptoms in ME/CFS, but also to emotional regulation (8). Since emotional regulation starts with identification of emotions and situations related to these emotions (8), the emotional awareness seems to be crucial in the process of emotional regulation. Our recent study indicated that ME/CFS patients had increased alexithymia by scoring in Toronto Alexithymia Scale (TAS-20) and lower levels of emotional awareness by scoring in Level of Emotional Awareness Scale (LEAS), as compared to healthy controls (9).

Alexithymia can be described as a reduced capacity to conceptualize emotional information, related to both verbal and non-verbal stimuli (10). This leads to disturbances of affect regulation (11). For example, alexithymic individuals have difficulties identifying and describing their own or others' feelings (10) and have an externally-oriented thinking style with a scarcity of fantasy life (12, 13). Alexithymia might be considered as an original personality trait (14) or may develop as a result of a stressful situation as well as medical/psychiatric illness (15). Emotional awareness is another construct related to alexithymia but does not include externally-oriented thinking (16). Both measures show a significant but weak negative correlation (17).

Sleep disorders such as obstructive sleep apnoea (OSA) and periodic limb movement disease are well-known causes of sleep fragmentation, with awakenings and arousals, noted during polysomnography (18).

The aim of this study was to investigate correlations between the alexithymia (TAS-20) and the level of emotional awareness (LEAS), as well as depression and anxiety [Hospital Anxiety and Depression Scale (HADS)], with objective sleep parameters from polysomnography in patients with ME/CFS.

METHODS

Participants

Twenty of the 23 ME/CFS patients were included from our recently published cohorts (5, 9). Three additional patients who underwent polysomnography, but whose results from questionnaires had not previously been analyzed, were also included. The inclusion criteria for the present study was diagnosis of ME/CFS given by a multidisciplinary team, completed TAS-20 and LEAS, and a full-night polysomnography. Our criteria for performing polysomnography (PSG) were excessive daytime sleepiness, evaluated by Epworth Sleepiness Scale (ESS) ≥ 10, and/or often or always tired during mornings and/or daytime. A full-night polysomnography was performed at the Department of Otorhinolaryngology (ORL), Karolinska University Hospital. Afterwards, the results of the manual polysomnography-scorings were analyzed by a specialist in sleep medicine (Danielle Friberg).

All 23 patients had entered a clinical ME/CFS project at Danderyd University Hospital, Stockholm during the period from 2011 to 2013. During 2011–2016, the unit at the Danderyd University Hospital served as a public healthcare tertiary clinic for patients with chronic fatigue. The majority of patients were referred from primary healthcare clinics, psychiatry, and neurology departments within Stockholm County. The majority of patients were already thoroughly investigated and had a long history of fatigue. Their fatigue was not explained by other primary diseases and they were refereed to ME/CFS clinic for further investigation.

The diagnosis of ME/CFS was made in accordance with the Centers for Disease Control (19) and/or Canadian criteria (1), summarized in **Table 1**. During 2011–2012, patients were evaluated by a team: a clinician, who was a specialist in rehabilitation medicine or neurology; a psychologist, who performed a standardized psychiatric interview and neuropsychological testing; a physiotherapist, an ergotherapist, a social worker, and a nurse. The laboratory tests were performed for all patients in order to exclude other pathological conditions, since ME/CFS is considered to be an exclusionary diagnosis. The majority of patients were also referred to brain magnetic resonance imaging to exclude brain disorders. Due to administrative changes, the complete team-based evaluation was terminated 2013. Thus, the physician and psychologist performed clinical evaluation during a 90-minutes visit.

The group of healthy controls (n = 30) had previously participated in studies on emotional awareness (5) and health-related life quality (20). The healthy control group was recruited by using a convenience sample of family, friends, and co-workers. Healthy controls should not have had current or previous diagnosis of ME/CFS and other comorbidities such as

TABLE 1 | Comparison of set of criteria for ME/CFS according to CDC/Fukuda (19) and Canada (1), both coded as G93.3 in ICD-10.

Symptoms	Chronic fatigue syndrome (19).	Myalgic encephalomylitis (1) G93.3. Abridged.
Exhaustion	No required symptom but included as an additional symptom.	A) Post-exertional malaise, with hallmark features: 1. Physical and/ or cognitive fatigability; 2. Post-exertional symptom exacerbation; 3. Recovery period is prolonged, usually taking 24 h or longer.
Fatigue	A) Severe chronic fatigue.	B) Physical and mental fatigue.
Additional symptoms	B) At least four of the following symptoms: B1) substantial impairment in short-term memory or concentration; B2) headaches of a new type, pattern, or severity; B3) tender lymph nodes; B4) unrefreshing sleep; B5) post-exertional malaise lasting more than 24 hours; B6) muscle pain; B7) pain in the joints without swelling or redness; B8) a sore throat that is frequent or recurring.	C) Sleep dysfunction. D) Pain. E) Neurological/cognitive manifestations: Two or more (i.e., impairment of concentration and short-term memory consolidation, difficulty with information processing, overload phenomena: cognitive, sensory—e.g., photophobia and hypersensitivity to noise etc.) F) At least one symptom from two of the following categories: F1) Autonomic manifestations (i.e., orthostatic intolerance—NMH, POTS etc.; F2) Neuroendocrine manifestations (i.e., loss of thermostatic instability—subnormal body temperature and marked diurnal fluctuation, sweating episodes, recurrent feelings of feverishness and cold extremities; worsening of symptoms with stress etc.); F3) Immune manifestations (i.e., tender lymph nodes, recurrent sore throat, recurrent flu-like symptoms, etc.)
Functional impairment	Significantly interferes with daily activities and work.	Substantially reduced activity level as compared to premorbid level.
Duration	Symptoms should have existed for at least 6 months.	Symptoms should have existed for at least 6 months.
Exclusion	Medical disorders primarily explaining the fatigue. Several psychiatric disorders.	Medical disorders primarily explaining the symptoms. Primary psychiatric disorders.
Precipitating factor	Infection in up to 75%	Infection in up to 75%

ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; NMH, neurally mediated hypotension; POTS, postural orthostatic tachycardia syndrome.

psychiatric disorders, chronic pain, allergies/asthma, sleep disorders, hypothyreosis, heart disorders, or be on the sick-leave. They also scored high for health-related quality of life (20).

Questionnaires

- The ESS—a self-administered questionnaire measures daytime sleepiness, the maximum score is 24 points (21). The patients also responded to a non-validated questionnaire, confirming the clinical symptoms for further indication to PSG.
- The HADS screens the levels of anxiety and depression, the maximum score is 21 point for each measure (22).
- The TAS-20 is a self-reported questionnaire measuring alexithymic traits. Twenty items are rated using a 5-point Likert scale. The items are divided into three subscales: 1) Difficulty Identifying Feelings (DIF); 2) Difficulty Describing Feelings (DDF); and 3) Externally Oriented Thinking (EOT). The TAS-20 has demonstrated good internal consistency with test–retest reliability in the Swedish population (23). In the present study, the Cronbach´s alpha coefficient for TAS-20 subscales was 0.8.

LEAS is an observer-rated measure of emotional awareness (24). The shortened 10-item version of the LEAS (LEAS-A) was applied. The test consists of 10 descriptions of emotion-provoking interactions between two people. Participants were asked to describe how they would feel as a protagonist in each scene and how "the other person" would feel. Answers were quantified according a manual of scoring rules. Scores from 0–5 were assigned for the categories "self," "other," and "total," with lower scores reflecting a lower level of emotional awareness. Maximum "total" scores of 50 and "self" or "other" scores of 40 were possible. A score of 0 was given when the subject either gave no answer or did not describe thoughts (i.e., *I feel that it is expensive.*). A score of 1 was given when bodily sensations were described (i.e., *I would feel fatigued.*). A score of 2 was given to an action tendency or an undifferentiated affect state (i.e., *I would like to run away. My friend would feel good.)*. A score of 3 was given when a single emotion was described (i.e., *I would feel happy.*). A score of 4 was given to blends of emotions (i.e., *I would feel angry and a bit of sadness.*). A score of 5 was given to multiple blends of emotions (i.e., *I would feel disappointed. But if someone else won, I would be happy that it was my friend. My friend will be proud and happy, but also concerned about me.*). The Cronbach´s alpha coefficient for LEAS subscales was 0.94.

Polysomnography

A full-night polysomnography was performed using the Embla technology (Flaga Medical; Reykjavik, Iceland) in a sleep laboratory. PSG recordings were interpreted manually by registered technicians, later on also checked by a specialist in sleep medicine (Danielle Friberg). Due to the fact that a sleep laboratory was used in a day-care unit, the patients were woken at 6 am. Totally, 16 channels were recorded: electroencephalography (EEG) (sensors C3-A2, O1-A2, O2-A1, C4-A1), electrooculography (EOG) (left and right), electromyography (EMG) chin and tibialis (left and right), oronasal flowmetry, respiratory movements (abdomen and thorax), snoring, electrocardiography (ECG), pulse, and body position. PSG parameters of American Academy of Sleep Medicine 2007 for normal values were used for comparisons (25).

The use of clinical data for scientific analysis was considered by the regional ethical review board in Stockholm (Ref. no. 2014/300-31) and approved by Danderyd University Hospital (DS2014-0447).

Statistical Analysis

Descriptive statistics were presented by percentage, medium (minimum-maximum), and by mean with standard deviation as well as 95% confidence interval, when appropriated due to the qualitative *vs*. quantitative parameters measured. Nonparametric tests (Mann-Whitney U) were used for group comparisons of ordinal data from questionnaires, and parametric independent two-tailed t-tests were used for age. A p-value <0.05 was considered significant for these tests. A non-parametric Spearman correlation test was used to analyze correlations between emotional questionnaires (TAS-20, LEAS, and HADS) and sleep parameters, respectively. Due to multiple analysis, a stricter criterion for statistical significance was used, a p-value less than 0.01 was considered a significant correlation, and p-value less than 0.05 was considered a weak correlation. Cronbach´s alpha was used for internal consistency of TAS-20 and LEAS.

The statistical package SPSS 25.0 was used for coding and analyzing the data.

RESULTS

Emotional Status in ME/CFS Patients and Healthy Controls

Twenty-three patients (5 men and 18 women) with a mean age of 43 (SD 12) years, and a mean body mass index (BMI) of 24 (SD 3) were included in the study. Their mean ESS score was 7.6 points and there were 7 (30%) patients with a pathological ESS ≥ 10.

Healthy controls (9 males and 21 women) were 45 years old (SD 12) and there was no difference between the groups concerning age and gender (BMI of controls not measured). Comparisons between ME/CFS patients and healthy controls showed that ME/CFS patients had significantly higher scores in TAS-DIF and total TAS-20, as well as significantly lower values in LEAS-self and LEAS total (**Table 2**).

The clinical emotional status was also scored using the HADS (**Table 2**). Six (26%) patients scored ≥ 10 in HADS depression and 4 (17%) ≥ 10 in HADS anxiety. Among the controls, only 1 (3%) participant scored 11 in HADS depression and no-one scored ≥ 10 in HADS anxiety. The HADS depression index was also significantly higher in ME/CFS patients as compared to controls (**Table 2**).

HADS depression correlated significantly with TAS-20 (r = 0.47, p = 0.000; r = 0.37, p = 0.008 and r = 0.49, p = 0.000; DIF, DDF, and TAS-total, respectively) and LEAS (r = −0.44, p = 0.001; r = −0.36, p = 0.008, and r = −0.51, p = 0.000; LEAS-self, LEAS-other, and LEAS-total, respectively). HADS anxiety had a weak correlation with DDF (r = 0.3, p = 0.02) but with no other TAS/LEAS parameters.

Objective Sleep Measures in ME/CFS Patients From Polysomnography

Table 3 summarizes sleep measures from the polysomnography. The majority of patients had reduced total sleep (100%) and increased sleep latency (78%). For more than half of the patients, the percentage of N1 stage was higher (61%) and REM was lower (57%). The number of awakenings was higher in 16 patients (70%), though the total arousal index was impaired only in 5 (22%) of patients. Their mean apnoea-hypopnoea index (AHI) was 2.9 (SD 3.2), and 22% had an AHI > 5, which is the definition of OSA, and 27% had a periodic limb movements index (PLMI) above 5, but only one had a PLM arousal index above 5.

Correlation Analysis

Table 4 summarizes correlation analysis between polysomnography and emotional parameters TAS-20, LEAS, and HADS. A negative significant correlation was found between LEAS-self and LEAS total with number of awakenings registered by polysomnography (r = −0.6, p = 0.005–0.001). Weak correlations (p < 0.05) were found between DIF TAS-20 and total TAS-20 with percentage of deep sleep (r = −05, p = −0.02) as well as between LEAS-self and LEAS-total with percentage of N1 (r = −0.5, p = 0.02–0.03), respectively.

There were two weak negative correlations between sleep efficiency and HADS depression (r = −0.44, p = 0.04) and anxiety (r = −0.43, p = 0.04), respectively, **Table 4**.

DISCUSSION

The focus of this study was the correlation analysis between parameters of sleep from polysomnograhy and emotional regulation evaluated with validated questionnaires TAS-20, LEAS, and HADS, respectively. The main results were the

TABLE 2 | Results from three questionnaires concerning alexithymia (TAS-20), emotional awareness (LEAS) and mood (HADS) from ME/CFS patients and healthy controls.

Group	TAS-20 DIF N=21–30	TAS-20 DDF N=21–30	TAS-20 EOT N=21–30	TAS Total N=21–30	LEAS-Self N=23–30	LEAS-Other N=22–30	LEAS-Total N=23–30	HADS Depression N=23–30	HADS Anxiety N=23–30
ME/CFS	16 ***	9	16	39*	28**	24	29**	5 ***	5
	[9–31]	[5–17]	[9–29]	[27–68]	[13–33]	[11–32]	[11–36]	[1–15]	[0–16]
Controls	10.5	8	13	33.5	32	28.5	36	1	4
	[7–19]	[5–14]	[8–25]	[20–44]	[13–39]	[11–38]	[22 -45]	[0–11]	[0–9]

DIF, difficulty in identifying feelings; DDF, difficulty in describing feelings; EOT, externally orientated thinking; HADS, Hospital Anxiety and Depression Scale; LEAS, Level of Emotional Awareness Scale; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; TAS-20, Toronto Alexithymia Scale.

*Values are presented as median, with minimum and maximum values. Comparison between the groups was performed by using Mann-Whitney test and significance is indicated as following: *p < 0.05, **p < 0.01 and ***p < 0.000.*

TABLE 3 | The results from polysomnography of ME/CFS patients and compared to normal values according to the AASM 2007 (25).

Polysomnography measures	Polysomnography values	Abnormal values according AASM	Number of patients with abnormal values
Total sleep time (min)	291.7 (75.6)	<7 h (420 min)	23 (100%)
N=23	[259.0–324.4]	>9 h (540 min)	0
Sleep efficiency (SE) (%)	75.9 (16.2)	85%—decreased	14 (61%)
N=23	[68.9–82.9]		
Sleep latency (min)	36.0 (26.2)	<5 min	1 (4.3%)
N=23	[24.7–47.3]	>20 min	18 (78%)
N3 sleep latency (min)	85.9 (53.7)	NA	NA
N=16	[57.3–114.6]		
REM stage latency (min)†	141.0 (73.3)	≤8 min	0
N=20	[106.6–175.3]		
Number of awakenings	4.9 (7.3)		16 (70%) had more than 5
N=23	[1.7–8.0]		
Respiratory Arousal Index	2.3 (3.1)	>5	4 (17%)
N=23	[1.0–3.7]		
Spontaneous Arousal Index	2.0 (1.9)	>15	0
N=22	[1.1–2.8]		
Total Arousal Index	10.5 (10.2)	>15	5 (22%)
N=23	[6.1–14.9]		
N1 duration (%)	15.0 (8.7)	<5%	1 (4.3%)
N=23	[11.2–18.7]	>10%	14 (61%)
N2 duration (%)	51.3 (17.6)	<45%	9 (39%)
N=23	[43.7–58.9]	>55%	7 (30%)
N3 duration (%)	18.2 (9.1)	<5%	1 (4.3%)
N=23	[14.2–22.2]	>25%	5 (22%)
REM duration (%)	12.4 (8.0)	<15%	13 (57%)
N=23	[9.0–15.9]	>25%	1 (4.3%)
AHI	2.9 (3.2)	≥5	5 (22%)
N=23	[1.5–4.3]		
Supine position-related AHI	4.2 (9.1)	≥5	5 (22%)
N=20	[-0.1–8.5]		
Central AHI	7.2 (9.4)	≥5	9 (39%)
N=23	[3.1–11.2]		
RERA index	4.9 (7.3)	≥5	6 (26%)
N=23	[1.7–8.0]		
ODI	2.3 (3.7)	≥5	1 (4.3%)
N=22	[0.7–3.9]		
PLMI	5.8 (11.8)	>5	6 (27%)
N=22	[0.6–11.0]		
PLMAI	1.3 (3.9)	≥5	1 (4.5%)
N=22	[–0.5–3.0]		

AASM, American Academy of Sleep Medicine; AHI, apnoea-hypopnoea index; AI, arousal index; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; N1, N2, N3, respectively sleep stage 1, 2, 3; NA, not applicable; ODI, oxygen desaturation index; PLMAI, periodic limb movements arousal index; PLMI, periodic limb movements index; REM, rapid eye movements; RERA, respiratory effort related arousals.

†The cut-off of 8 min for REM stage latency is chosen according to the diagnostic criteria for narcolepsy.

Values are presented as mean with standard deviation in the parenthesis (first row) and 95% confidence interval (second row). The numbers of patients with abnormal values are presented as a total number and a percentage.

significant negative correlations between LEAS-self and LEAS-total and number of awakenings in polysomnography. This indicate that the awakenings and sleep fragmentation might be an important sleep disturbance, affecting emotional awareness. The awakenings could to some extent be explained by the fact that several patients had milder forms of other sleep disorders, for example OSA, periodic limb movement, and or restless legs. Interestingly, another study has shown that the severity of the OSA does not directly correlate with the severity of mood symptoms. Using the becks depression inventory (BDI) and State-Trait Anxiety Inventory Lee and colleagues investigated anxiety and depression in association with OSA severity (26). Interestingly, anxiety and depressive symptoms were more prevalent in patients with mild OSA than those with severe OSA. However, there were no other significant correlations between TAS-20 or HADS and polysomnography parameters, but this is only a pilot study with a small study sample, therefore no conclusions can be drawn. In a previous study, alexithymia measured by TAS-20 was associated with shorter pre-REM sleep stages (N1 and N3) in normal healthy participants (27). At the same time an increase in REM episodes but not in REM duration was associated with alexithymia (27).

In the present study, the different correlation results between polysomnography measures and TAS-20 vs. LEAS, indicate that alexithymia and emotional awareness could have different associations with sleep, and probably are regulated in different ways, though overlapping each other. This is also in line with our previously published meta-analytic review on correlation patterns between TAS-20 and LEAS in different psychiatric, psychosomatic, and somatic disorders (17). It is known that

TABLE 4 | Results from Spearman correlation analysis with r-values between sleep parameters from polysomnography and questionnaires TAS-20, LEAS and HADS, respectively, in ME/CFS patients.

	TAS-20 DIF	TAS-20 DDF	TAS-20 EOT	TAS Total	LEAS-Self	LEAS-Other	LEAS-Total	HADS Depression	HADS Anxiety
Total sleep time	0.03	–0.13	–0.22	–0.16	0.12	0.28	0.16	–0.38	–0.36
Sleep efficiency	–0.254	–0.263	–0.318	–0.390	0.07	0.25	0.15	–0.44	–0.43
Sleep latency	–0.18	–0.09	0.17	0.01	0.10	–0.23	0.001	0.30	0.37
REM latency	–0.07	0.01	0.14	0.01	–0.045	–0.19	–0.04	0.32	0.37
N3 latency	–0.05	–0.35	0.04	–0.12	–0.09	–0.43	–0.10	0.47	0.25
N1 %	0.06	0.10	0.39	0.21	–0.49	–0.33	–0.4	0.35	0.16
N2 %	0.44	0.18	0.27	0.39	–0.05	0.17	0.00	–0.26	–0.11
N3 %	–0.44	–0.33	–0.43	–0.51	0.18	0.09	0.26	–0.03	–0.17
REM %	–0.076	–0.140	–0.216	–0.192	0.37	0.24	0.31	–0.27	–0.23
Number of awakenings	0.23	0.26	0.46	0.40	**–0.62***	–0.38	**–0.56***	0.18	0.24
Respiratory AI	–0.07	0.09	0.23	0.08	–0.36	–0.25	–0.30	0.33	0.28
Spontaneous AI	–0.11	–0.02	–0.30	–0.20	–0.27	–0.08	–0.21	–0.07	0.00
Total AI	–0.07	0.05	0.09	0.01	–0.18	–0.08	–0.19	0.06	–0.07
AHI	–0.18	–0.5	0.17	–0.06	–0.01	0.05	0.04	0.30	0.24
Supine AHI	–0.18	–0.05	0.17	–0.06	0.13	0.09	0.09	0.09	0.07
Central AHI	–0.22	0.14	–0.09	–0.13	0.04	0.05	0.04	0.27	0.27
RERA index	–0.14	–0.06	0.03	–0.10	–0.04	0.08	–0.04	0.03	–0.14
ODI	0.11	–0.01	0.310	0.183	–0.14	–0.19	–0.12	0.40	0.31
PLMI	–0.20	–0.07	0.12	–0.11	–0.03	–000	–0.05	–0.09	–0.15
PLMAI	–0.11	–0.01	0.12	–0.03	–0.10	–0.04	–0.11	–0.14	–0.21

AHI, apnea-hypopnoea index; AI, arousal index; HADS, Hospital Anxiety and Depression Scale; LEAS, Level of Emotional Awareness Scale; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; N1, N2, N3, respectively sleep stage 1, 2, 3; ODI, oxygen desaturation index; PLMAI, periodic limb movements arousal index; PLMI, periodic limb movements index; PSG, polysomnography; REM, rapid eye movements; RERA, respiratory effort related arousals; Toronto Alexithymia Scale (TAS-20) (DIF, difficulty in identifying feelings; DDF, difficulty in describing feelings; EOT, externally orientated thinking).

Correlations with p-values <0.001 are marked in bold.

arousals and awakenings contribute to daytime sleepiness (18). However, the research on the role of arousals and awakenings is not so easy to perform since most of the studies are carried out on sleep deprivation in healthy subjects or animals, which is not the same as pathological arousals due to long-term disease status (28). The experiments with sleep deprivation in healthy subjects have demonstrated negative effects on mainly facial expression (29). As suggested, sleep deprivation amplifies amygdala reactivity in response to negative emotional stimuli, triggers emotional sensitivity, increases central sympathetic tonus, and disrupts peripheral autonomic nervous system feedback to visceral body information (29). Sleep is crucial in normalizing central adrenergic signaling, which usually occurs during REM sleep (30). In other words, there is a connection between long-term sleep disturbances, impaired emotional regulation and psychosomatic symptoms through several regulatory mechanisms. This connection might be in part applicable to ME/CFS patients, since clinically there is a broad panorama of both mental and somatic symptoms as well as increased tonus in the sympathetic nervous system.

In general, emotional regulation is described by identification of an emotion to be regulated; selection of emotion regulation strategy and implementation of this strategy (31). Emotional awareness and alexithymia are, therefore, crucial for identification of an emotion as well as placing it in a conscious context before applying the regulatory strategies. Research on sleep disorders and emotional awareness is scarce, but one study has indeed reported that mindfulness promotes better emotional regulation and improves sleep (32). Evaluation of healthy controls is also important since both insomnia (33) and alexithymia (34) are found in the normal population.

Limitations and Strengths of the Study

Limitations of this study are the absence of sleep recordings in healthy controls, and a small study sample with no previous power analysis. The correlation analysis with a strict limit for significant p values might result in false negative results, and also multiple correlations might create positive false results randomly.

There are also several strengths: namely, the use of gold standard polysomnography, validated questionnaires, well-defined and thoroughly investigated ME/CFS patients.

CONCLUSION

Our pilot study could indicate a biological mechanism such as sleep fragmentation, affecting emotional awareness. Further studies on emotional regulation should include both healthy participants and patient populations, even those with other psychosomatic and neurological conditions known to have symptomatology of sleep disorders. Furthermore, there is a need of more objective evaluation of emotional regulation, since TAS-20 and LEAS carry a risk of learning moment when applied several times. Altogether, future research is important to explore our preliminary results, including treatment strategies on both sleep disorders and emotional regulation in order to understand the connection between sleep and emotions.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the regional ethical review board in Stockholm (Ref. no. 2014/300-31) and approved by Danderyd University Hospital (DS2014-0447). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

IB-L has put together and analyzed the results of sleep parameters and emotional regulation. She wrote the main draft of the manuscript and created the tables. DF performed the major job in analyzing the sleep protocols and reviewing the manuscript with tables.

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Interoceptive Abilities in Inflammatory Bowel Diseases and Irritable Bowel Syndrome

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Alexithymia is usually described by three main dimensions difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking (EOT). The most commonly used questionnaire investigating alexithymia, the Toronto Alexithymia Scale (TAS-20), supports this three-factor structure. One important assumption is that alexithymia severity is associated to vulnerability to somatic diseases, among them gastrointestinal disorders. However, the association between alexithymia and gastrointestinal disorders is not systematic, thus questioning the role of alexithymia as a vulnerability factor for those illnesses. A recent factor analysis suggested another four-factor structure for the TAS-20: difficulties in awareness of feelings (DAF), difficulties in interoceptive abilities (DIA), externally oriented thinking (EOT), and poor affective sharing (PAS). We assume that DIA and DAF might be more relevant to investigate the association between alexithymia and gastrointestinal disorders. The rationale is that DIA and DAF reflect impairments in emotion regulation that could contribute to an inappropriate autonomic and HPA axis homeostasis in irritable bowel syndrome (IBS), ulcerative colitis (UC), or Crohn's disease (CD). The aim of this study was to investigate whether DIA and DAF are associated with the presence of IBS, UC or CD, while checking for anxiety, depression, parasympathetic (vagus nerve) activity and cortisol levels. We recruited control participants (n=26), and patients in remission who were diagnosed with IBS (n=24), UC (n=18), or CD (n=21). Participants completed questionnaires to assess anxiety, depression, and alexithymia. A blood sample and an electrocardiogram were used to measure the level of cortisol and parasympathetic activity, respectively. Logistic regressions with the four-factor structure of the TAS-20 revealed that DIA was a significant predictor of IBS ($W(1)=6.27$, $p=.01$). Conversely, DIA and DAF were not significant predictors in CD and UC patients. However, low cortisol level was a

significant predictor of UC ($W(1)=4.67$, $p=.035$). Additional logistic regressions based on the original 3-factor structure of TAS-20 (DIF, DDF, and EOT) showed that only DDF was a significant predictor of CD [$W(1)=6.16$, $p < .001$]. The present study suggests that DIA is an important dimension for assessing potential risk for gastrointestinal diseases, in particular for IBS.

Keywords: inflammatory bowel disease, irritable bowel syndrome, alexithymia, interoceptive abilities, hypothalamic-pituitary adrenal axis

INTRODUCTION

Among gastrointestinal pathologies, the most common diagnoses in gastroenterology are irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD). Although these are common pathologies that affect the intestine and are characterised by alternating periods of remission and relapse, only the intestinal symptoms (e.g., abdominal pain and chronic diarrhoea) are similar. The main difference is that IBS is a functional disorder (i.e., without structural abnormalities) (1) while IBD are structural diseases where digestive and extra-digestive manifestations are caused by chronic inflammation (2). IBD include ulcerative colitis (UC) and Crohn's disease (CD). Patients with UC have inflammation confined to the rectum and colon, while patients with CD have inflammation that can affect the entire gastrointestinal tract.

Although the aetiology is multifactorial, numerous studies have agreed that among environmental factors, stress has a major impact on the development and/or relapse of IBS and, more recently, IBD. This is due to the existence of bidirectional communication between the brain and the gut through the autonomic nervous system (ANS), the hypothalamo-pituitary-adrenal (HPA) axis, and the gastrointestinal tract (gastrointestinal immune system, intestinal barrier, enteric nervous system and microbiota) (i.e., brain-gut-microbiota axis) (3, 4). Another explanation for the relapse of functional gastrointestinal disorders is the important role of psychological status and physiological stimuli (5). In IBS and IBD patients, the presence of adverse symptoms, anxiety, depression (6, 7), as well as individual visceral hypersensitivity (8) is critical for the regulation of psychological mood, which in turn may influence the perception and generation of regulatory physiological signals (9).

Depending on the studies, IBS patients have an increase of sympathetic activity at rest (10) or under stress (11), or a decrease of vagal tone (12, 13). Moreover, IBS patients with low vagal tone are reported to have high levels of blood epinephrine at rest (14). Among IBD patients, UC patients exhibit high sympathetic (15–17) and low vagal tone related to negative affects compared to healthy individuals (18). CD patients also present higher sympathetic-parasympathetic ratio compared to control individuals, which can be explained by an increase in sympathetic activity (19). However, the overactivity of the HPA axis in patients with gastrointestinal pathologies remains controversial. IBS patients facing a psychological stressor exhibit an overactivity of the HPA axis (20, 21). Compared to healthy individuals, IBS patients at rest have salivary cortisol levels higher in the morning and lower in the evening (22), a difference not always observed (23) except in patients with low vagal tone (14). Conversely, IBD patients exhibit hypocortisolism rather than a hypercortisolism profile (24, 25). The communication between the brain and the gastrointestinal tract (i.e., brain-gut-microbiota axis) is mediated by the HPA axis, the ANS and the immune system. As a result, alterations in the functioning of these systems can lead to impaired motor, sensory, secretory, and immune functions of the gastrointestinal tract, the development of inflammatory-related or immunosuppressed medical conditions, leading to depression and anxiety that could accelerate a relapse (4).

Besides differences in stress mediator regulation, IBS and IBD also present an impairment in interoception (26, 27) and high levels of alexithymia (28, 29). Interoception refers to the ability to accurately detect internal body changes. Interoceptive abilities are composed of different facets: (i) interoceptive accuracy (objective ability to perceive internal body changes), (ii) interoceptive sensibility (subjective ability to report on body states), (iii) interoceptive awareness (degree of overlap between interoceptive accuracy and sensibility), and (iv) interoceptive emotional evaluation (emotional degree attributed to body sensations that are expressed or paid attention to in a specific situation) (30). Interoception is considered a necessary component of the emotional experience (31, 32). It implies that the evaluation and perception of one's own emotional states cannot be separated from the processes of evaluating one's own body experiences (33). This connection is illustrated by a majority of studies looking at self-reported interoception that find a link with alexithymia (34–39). Alexithymia is a personality construct that implies difficulties identifying and describing one's own feelings, limited imaginative processes, an externally oriented cognitive style, and difficulties in distinguishing between feelings and bodily sensations (40–42). This construct is associated with many disorders, such as gastrointestinal pathologies (28, 29). This association can be explained by deficits in the strategies used in emotion regulation (43). In this perspective, a recent study suggests that only the difficulties identifying and describing one's own feelings and an externally oriented cognitive style dimensions define the alexithymia construct. Difficulties identifying and describing one's own feelings dimensions would correspond to difficulties in the *appraisal* stage of emotion valuation system and externally oriented cognitive style dimension would correspond to difficulties in the *attention* stage of emotion valuation system (44). Emotion regulation involves mechanisms that allow individuals to modulate their emotions during environmental demands (45). This ability is an essential component for the

general well-being of individuals. If the emotion regulation mechanisms are not sufficiently efficient, individuals are more vulnerable to developing a chronic stress state and in the long term psychological and somatic diseases (46). For example, an individual with difficulties in detecting, processing or becoming aware of internal body changes (interoception) is also likely to have difficulties identifying and describing feelings (alexithymia). When faced with challenging emotional situations, he/she could exhibit difficulties regulating his/her emotions and autonomous functioning.

In patients in remission, we tested a vulnerability model in which difficulties in interoceptive abilities (DIA) and in awareness of feelings (DAF) could potentially represent vulnerability factors, while checking for psychological (anxiety, depression) and physiological (activity of the parasympathetic ANS and the HPA axis) factors. We hypothesize that DIA and DAF could predict the presence of IBS or IBD (both CD and UC). We focused on DIA and DAF because these dimensions could explain difficulties in emotion regulation and, consequently, explain physiological and psychological alterations that could contribute to an increase in and/or inappropriate stress response and the recurrence or aggravation of gastrointestinal pathologies. Although the EOT dimension appears to assess difficulties in emotion regulation (44), we decided not to use this dimension for two reasons. Firstly, its internal reliability is usually poor (47–50). Secondly, the dimension might better reflect the social norms that guide emotional behaviors rather than a cognitive style of thinking (51). Identifying factors that affect the well-being of patients with IBS or IBD in remission renders possible an intervention to modify some of these factors or promote a better understanding of patients with IBS or IBD who experience alternate periods of remission and relapse.

METHOD

Participants and Ethics Statement

Patients in remission and clinically diagnosed with IBS (mean age: 38.21 ± 11.26 years; 7 men, 17 women), UC (mean age: 40.94 ± 10.78 years; 9 men, 9 women), or CD (mean age: 40.29 ± 11.17 years; 9 men, 12 women) were recruited from the Gastroenterology Department of Grenoble University Hospital (CHU) between September 2009 and October 2011. Patients with IBS were selected according to the Rome II criteria (52). Patients with UC and CD were recruited according to their pathology activity index, respectively UC activity index (UCAI) (53) and Harvey-Bradshaw index (HBI) (54). UC patients with a UCAI ≤ 10 and CD patients with an HBI < 4 on inclusion were considered in clinical remission. In addition, we recruited healthy control (HC) participants (mean age: 36.23 ± 10.06 years; 8 men, 18 women), with no chronic medication intake for any disease, from a list of healthy volunteers from the Grenoble INSERM Clinical Investigation Centre.

The study was conducted according to the Declaration of Helsinki and in accordance with the guidelines of Good Clinical Practice. The Ethical Committee of the CHU approved the study (ref: CPP 08-CHUG-23; ClinicalTrials.gov Identifier: NCT010950421). Some of the results of this protocol have already been published twice (14, 29).

Criteria for Exclusion

Patients were excluded from the study if they (*i*) had past or present severe disorders (e.g., diabetes, heart failure, dysthyroidism, renal or liver insufficiency, malignant condition, alcoholism, psychiatric disorders, and amyloidosis); (*ii*) had autonomic dysfunction (e.g., peripheral neuropathy, vagotomy, and asthma); (*iii*) were taking medication that could alter ANS functioning (e.g., anticholinergics, antiarrhythmics, clonidine, and β-blocking agents); (*iv*) were pregnant or breast-feeding; and/or (*v*) had past abdominal surgery except for appendectomy and/or cholecystectomy.

Materials

Psychological Assessments

Interoceptive abilities and awareness of feelings were assessed using a part ofthe French version of the Toronto Alexithymia Scale (TAS-20) (55, 56). The TAS-20 allows the assessment of three dimensions: difficulty identifying feelings (DIF; items 1, 3, 6, 7, 9, 13, 14; α=.83), difficulty describing feelings (DDF; items 2, 4, 11, 12, 17; α=.65), and EOT (items 5, 8, 10, 15, 16, 18, 19, 20; α=.60). However, based on literature highlighting interoceptive alteration in alexithymic individuals, Fournier and colleagues (2019) propose a new structure for this scale without items 16 and 20. This new structure is composed of four dimensions: DIA (tems 1, 2, 4, 6, 9, 11, 13, 14; α=.81), difficulty in interoceptive abilities (DIA; items 3[1], 7[2]; α=.77), externally oriented thinking (EOT; items 5, 8, 10, 18, 19; α=.48), and poor affective sharing (PAS; items 4, 11, 12, 15, 17; α=.63). For this study, we decided to use the factor structure proposed by Fournier and colleagues, because the DIA and DAF dimensions were predominantly associated with a deficit in emotion regulation (i.e., depression, anxiety, emotional instability, high level of perceived stress, use of dysfunctional coping strategies) and DIA dimension was specifically associated with health disorders (i.e., somatic disorders, eating disorders, medication intake, cardiovascular disease) (57). A high score of DIA indicates a high level of DIA and a high score of DAF indicates a high level of difficulty in awareness of feelings.

Depressive symptomatology was assessed using the French version of the Center for Epidemiologic Studies–Depression scale (CES-D) (58, 59). This brief scale of 20 items assesses symptoms and behaviors often associated with depression. A high score means a high level of depressive symptomatology (α=.87).

Anxiety trait was assessed using the French version of the State–Trait Anxiety Inventory (STAI-Y) (60, 61). This scale consists of 20 items. A high score indicates high anxiety (α=.91).

HRV for Parasympathetic Activity Assessment

Parasympathetic activity was evaluated by investigating heart rate variability. We performed an electrocardiogram (ECG) using electrodes placed on each wrist. Heart rate variability analysis was performed using the Heart Rhythm Scanner software (Biocom Technologies, USA). QRS complexes were automatically classified, and then visually checked to detect

[1] Item 3: *"I have physical sensations that even doctors don't understand".*
[2] Item 7: *"I am often puzzled by sensations in my body".*

and remove abnormal complexes. A standard spectral analysis was applied to inter-beat intervals using a Fast Fourier Transformation (FFT) according to the standards of measurement of the task force on heart rate variability (62). We considered the high frequency (HF) spectrum (from 0.15 to 0.40 Hz.ms^2) that reflects 90% parasympathetic tone fluctuations caused by respiratory sinus arrhythmia at rest in a sitting position (63). We computed normalized scores [HFnu = HF/(TP–VLF)] to minimise the effect of changes in very low frequency power on HF power and emphasised the changes in parasympathetic regulation.

Blood Samples for Neuroendocrine Assessment

Blood samples were collected between 8:30 am and 9:00 am. Cortisol levels were measured in serum by means of a competitive immunoassay using direct chemiluminescent technology on ADVIA Centaur® XP (Siemens Health Care Diagnostics, Saint Denis, France).

Procedure

Upon arrival in the Gastroenterology Department of Grenoble University Hospital, participants were welcomed in a quiet room. The experimenter verified the inclusion/exclusion conditions in each group. The nature and potential risks of the study were fully explained, and written informed consent was obtained from each participant.

After this short interview, the participant started the experimental protocol. All sessions took place between 8:00 am to 10:00 am, after a light breakfast to avoid strong influences of circadian and postprandial variations. At the beginning of the protocol, participants completed psychological questionnaires (i.e., STAI-Y, CES-D, TAS-20). Then, a nurse placed electrodes on the wrists (ECG recording) and an intravenous catheter in the arm vein (blood sample). A standardized interview with questions mainly related to the symptomatology and history of the pathology) was then carried out for 30 min. This interview also allowed participants to recover from the stress of the prick. After this resting period, participants rated the intensity of their current visceral pain using a visual analogue scale (0: no perceived pain; 10: maximum perceived pain). Finally, a 10-min ECG was recorded, and a 30-ml blood sample was taken immediately after the ECG recording. The overall study design consisted of two parts. The analyses presented here concern only the first part of the study [for a complete description of the study see Fournier and colleagues (29)].

Statistical Analysis

Statistical analyses were carried out with SPSS v.24.0 (IBM Corp., USA). Data are expressed as means (± standard deviation, SD). The *p*-value for statistical significance was set at $p \leq .05$, and the trend for significance was set at $p \leq .07$.

ANOVAs were used to evaluate the main effects of groups on visceral pain, and psychological, biological, and physiological measures. When a significant effect was observed, a Bonferroni *post hoc* test was applied to determine the differences between each group. If the homoscedasticity was not respected, we used adjusted *Welch's F*. For two-by-two comparisons, we used a Bonferroni *post hoc* test to determine the differences between each group.

Then, to examine the predictive value of the DAF and DIA dimensions on the presence of gastrointestinal pathologies, we performed hierarchical logistic regressions with the patient group as the dependent variable (considering separately IBS, UC, and CD). The presence of gastrointestinal pathologies was coded 1 and the absence of disorder (HC group) was coded 0. It is known that anxiety, depression and cortisol levels are associated with gastrointestinal disorders (64). In addition, autonomic dysfunction can be a confused factor between digestive disorders and alexithymia. In order to examine the specific contribution of DAF and DIA dimensions and avoid cooccurrences, we checked for any possible effects of anxiety and depression by entering STAI-Y and CES-D at Step 1. Then, we checked cortisol levels and autonomic activity by entering cortisol and HFnu at Step 2 and we entered our dimensions of interest, DAF and DIA dimensions, at Step 3. A significant improvement of the χ^2 (observed from the $\Delta\chi^2=\chi^2_{\text{new model}}-\chi^2_{\text{previous model}}$) means that the new model is better than the previous model. Despite the fact that the DIA dimension had good internal reliability, this dimension includes only two items (57). For this reason, we carried out additional analyses by including, instead of DAF and DIA dimensions, the theoretical DIF and DDF dimensions of the TAS-20 as predictors. We decided to keep only these two dimensions because they included all the items distributed in the DAF and DIA dimensions.

Given the restricted sample size, we used bootstrapping to perform hierarchical logistic regressions. The level of confidence was 95% and we used a bootstrap percentile method for 5,000 bootstrap replications. The odds ratio was used to compare the relative odds of the occurrence of the outcome of interest (i.e., IBS, UC, CD), given exposure to the variable of interest (i.e., anxiety, depression, HFnu, cortisol, DAF/DIF, DIA/DDF). An odds ratio equal to one means that exposure to the variable of interest (anxiety, depression, HFnu, cortisol, DAF/DIF, or DIA/DDF) does not affect the odds of the occurrence of a gastrointestinal pathology (IBS, UC, or CD); an odds ratio greater than one means that exposure to the variable of interest is associated with higher odds of the occurrence of a gastrointestinal pathology; and an odds ratio less than one means that exposure to the variable of interest is associated with lower odds of the occurrence of a gastrointestinal pathology (65). An absence of multicollinearity between predictor variables was verified before performing hierarchical logistic regressions. Only results with a confidence interval not including zero were retained and interpreted.

RESULTS

Differences between groups. The groups did not differ in age or on EOT, PAS scores of the TAS without items 16 and 20, EOT of the TAS-20 and HFnu index (*ps* > .07*)*. However, there was a significant effect of the disease on the level of perceived visceral pain [*Welch F*(3,43.82)=5.11, *p*=.004]. IBS had the highest score

of perceived visceral pain compared to controls (p=.001). There was also a significant effect of the disease on the scores of anxiety ($F(3, 85)=6.69$, $p < .001$)] and depressive symptomatology [*Welch* $F(3,42.88)=9.75$, $p < .001$]. IBS and CD patients had higher scores of anxiety than HC participants ($p < .001$ and p=.021 respectively), and IBS patients had the highest scores of depressive symptomatology in comparison to HC participants and CD and UC patients ($p < .001$, p=.031, $p < .001$ respectively).

There was a significant effect of the disease on the total alexithymia (TAS-20 without items 16 and 20) scores [$F(3, 78)=4.02$, p=.01], DAF scores [$F(3, 83)=3.43$, p=.021], DIA scores [*Welch* $F(3,41.63)=9.18$, $p < .001$], PAS scores [*Welch* $F(3,41.71)=3.54$, p=.023], on the total TAS-20 scores [$F(3, 77)=3.56$, p=.018], DIF scores [*Welch* $F(3,45.14)=4.93$, p=.005)] and DDF scores [*Welch* $F(3,44.09)=3.14$, p=.035]. CD patients were more alexithymic overall (TAS-20 without items 16 and 20: p=.018; TAS-20: p=.041) and had more difficulties in awareness of feelings, in interoceptive abilities and in identifying feelings than HC participants (p=.019, p=.015, p=.030 respectively). Also, IBS patients were more alexithymic (TAS-20 without items 16 and 20: p=.035; TAS-20: p=.052) and tended to have more DIF (p=.061) than HC participants, and had more DIA than HC participants ($p < .001$) and UC patients (p=.004). In addition, there was a significant effect of the disease on the cortisol levels [*Welch* $F(3,43.90)=4.45$, p=.008]. UC patients had the lowest cortisol levels compared to CD patients (p=.032) (see details in **Table 1**).

Contribution of DAF and DIA dimensions in predicting the presence of IBS. When entering anxiety in addition to depression as a predictor of the presence of IBS into Step 1, the full regression equation was significant, $\chi^2(2)=22.45$, $p < .001$; R^2 *Nagelkerke*=.51. The model correctly classified 85.1% of cases. Only depression was a significant predictor of the presence of IBS, *W(1)*=8.01, p=.004. The introduction of the HFnu index and cortisol levels in the model (Step 2) also led to a significant equation, $\chi^2(4)=22.52$, $p < .001$; R^2 *Nagelkerke*=.51. However, the introduction of physiological parameters did not add a significant explanation for the presence of IBS ($\Delta\chi^2(2)=.07$, p=.968) contrary to the introduction of the interest variables, DAF and DIA dimensions in Step 3 ($\Delta\chi^2(2)=10.94$, p=.004). At this last step, the full regression equation was significant ($\chi^2(6)=33.46$, $p < .001$; R^2 *Nagelkerke*=.68) and correctly classified 87.2% of cases. Only DIA was a significant predictor of the presence of IBS, *W(1)*=6.27, p=.01. DAF and depression were not significant, as evidenced by confidence intervals including zero. This model was better than the first model [$\Delta\chi^2(4)=11.01$, p=.026]. In summary, in the best model, only DIA factor was a significant predictor of IBS presence. Results are reported in **Table 2**.

Contribution of DAF and DIA dimensions in predicting the presence of UC. When entering anxiety in addition to depression as a predictor of UC, the result of the full regression equation was not significant, $\chi^2(2)=1.07$, p=.587; R^2 *Nagelkerke*=.03. However, at Step 2, when introducing HFnu index and cortisol levels in the model, the full regression equation was significant [$\chi^2(4)=9.81$, p=.044; R^2 *Nagelkerke*=.28] and correctly classified 71.4% of cases. The difference from Step 1 revealed that the introduction of physiological parameters added an explanation of the prediction of the presence of UC, $\Delta\chi^2(2)=8.74$, p=.013. However, only cortisol levels were a significant predictor of UC, *W(1)*=4.67, p=.035. At Step 3, the introduction of the interest variables, DAF and DIA dimensions, did not improve the model. Model 3 explained less well the presence of UC than model 2 [$\Delta\chi^2(2)=0.04$, p=.982] and the full regression model was not significant, $\chi^2(6)=9.85$, p=.131; R^2 *Nagelkerke*=.28. In summary, in the best model (Step 2), only cortisol levels were a significant predictor of UC presence. Results are reported in **Table 3**.

TABLE 1 | Socio-demographic, medical, and psychological data.

	HC (n=26)	IBS (n=24)	UC (n=18)	CD (n=21)	Group comparisons
Mean age (years)	36.23 ± 10.07	38.21 ± 11.26	40.94 ± 10.78	40.29 ± 11.17	_
Visceral pain (/10)	0.31 ± 1.19	2.25 ± 2.31***	0.94 ± 1.55	1.29 ± 1.62	IBS > HC
Anxiety (/80)	31.38 ± 7.62	41.5 ± 10.8***	33.5 ± 6.10	39.26 ± 10.03*	IBS;CD > HC
Depression (/60)	8.88 ± 4.48***	19.63 ± 9.37	10.17 ± 7.01***	13.67 ± 6.09*	IBS > HC;UC;CD
Alexithymia (TAS-20 without items 16 and 20)	30.12 ± 6.06	36.19 ± 9*	34.56 ± 8.5	36.75 ± 5.12*	IBS;CD > HC
DAF (/32)	12.96 ± 3.61	15.78 ± 5.68	14.59 ± 4.58	16.86 ± 3.32*	CD > HC
DIA (/8)	2.5 ± 1.03	4.82 ± 2.08***	3.06 ± 1.21**	3.95 ± 1.76*	IBS;CD > HC IBS > UC
EOT without items 15,16,20 (/20)	9.27 ± 2.51	9.64 ± 1.99	10.29 ± 2.91	9.71 ± 2.45	_
PAS (/20)	9.04 ± 2.3	10.23 ± 3.75	11.18 ± 3.11	11.33 ± 2.99	_
Alexithymia (TAS-20)	34.04 ± 6.51	40.20 ± 9.11^t	39.00 ± 9.40	40.40 ± 5.37*	IBS;CD > HC
DIF (/28)	10.19 ± 3.24	13.33 ± 5.85 ^{t}	10.94 ± 3.46	13.76 ± 3.60*	IBS;CD > HC
DF (/20)	9.15 ± 2.46	9.92 ± 4.14	10.33 ± 3.38	11.57 ± 2.82	_
EOT (/32)	14.88 ± 3.82	14.75 ± 4.08	17.22 ± 4.29	15.57 ± 3.41	_
HFnu	44.32 ± 17.72	42.74 ± 17.01	37.74 ± 17.82	33.98 ± 19.86	_
Cortisol (nmol/l)	369.04 ± 143.23	338.38 ± 184.36	251.11 ± 103.76*	445.55 ± 337.46	CD > UC

****≤.001; **≤.01; *≤.05; ^{t} ≤.07. Data are expressed as means ± SD. TAS-20, Toronto Alexithymia Scale; DAF, Difficulty in awareness of feelings; EOT, Externally oriented thinking; DIA, Difficulty in interoceptive abilities dimension; PAS, Poor affective sharing; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings; HFnu, High Frequency Normalized unit.*

TABLE 2 | Summary of hierarchical logistical regression analysis predicting the presence of irritable bowel syndrome (IBS) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−4.48	.003**	−11.38	−1.88			
Anxiety	0.05	.225	−0.03	0.23	0.96	1.05	1.15
Depression	0.19	.004**	0.06	0.46	1.06	1.21	1.37
Step 2							
Constant	−4.53	.006**	−16.71	−0.92			
Anxiety	0.05	.243	−0.03	0.41	0.96	1.05	1.16
Depression	0.19	.002**	0.07	0.75	1.06	1.21	1.38
HFnu	−0.004	.860	−0.12	0.09	0.95	1	1.04
Cortisol	<0.001	.906	−0.02	0.01	1	1	1.01
Step 3							
Constant	−2.43	.223	−401.51	646.37			
Anxiety	0.05	.258	−2.43	15.01	0.94	1.05	1.18
Depression	0.24	.024	−0.06	80.25	1.03	1.28	1.58
HFnu	−0.04	.327	−21.73	2.17	0.90	0.96	1.03
Cortisol	0.001	.492	−0.53	0.43	1	1	1.01
DAF	−0.42	.033	−146.99	0.23	0.42	0.65	1.01
DIA	1.25	.010**	0.35	367.91	1.31	3.48	9.21

***≤.01. HFnu, High Frequency Normalized unit; DAF, Difficulty in awareness of feelings; DIA, Difficulty in interoceptive abilities dimension of the Toronto Alexithymia Scale; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings.*

Contribution of DAF and DIA dimensions in predicting the presence of CD. When entering anxiety in addition to depression as a predictor of CD, the full regression equation was significant, $\chi^2(2)=11.21$, $p=.004$; R^2 *Nagelkerke*=.30. The model correctly classified 68.9% of cases. Only depression was a predictor of CD, $W(1)=3.51$, $p=.027$. The introduction of the HFnu index and cortisol levels in the model did not add an explanation ($\Delta\chi^2(2)=4.35$, $p=.113$) despite the fact that the full regression equation was significant, $\chi^2(4)=15.56$, $p=.004$; R^2 *Nagelkerke*=.39. Finally, the introduction of the interest variables, DAF and DIA dimensions, improved the model, $\chi^2(6)=25.67$, $p < .001$; R^2 *Nagelkerke*=.58. Model 3 better explained the presence of CD than model 2 ($\Delta\chi^2(2)=10.10$, $p=.006$) or model 1 ($\Delta\chi^2(4)= 14.46$, $p=.006$), and correctly classified 80% of cases. However, neither the psychological nor the physiological parameters predicted the presence of CD. Although anxiety and DIA tended to be significant in the model, the confidence intervals included zero, revealing unreliable results. In summary, the best model was Step 3 and no factor was a significant predictor of CD, even if the introduction of DIA and DAF factors significantly improved the model. Results are reported in **Table 4**.

Additional Analysis

Despite the fact that the DIA dimension had good internal reliability, this dimension includes only two items (57). For this reason, we have carried out additional analyses by including, instead of the DAF and DIA dimensions, the theoretical DIF and DDF dimensions of the TAS-20 as predictors. We decided to keep only these two dimensions because they included all the items distributed in the DAF and DIA dimensions.

Contribution of DDF and DIF dimensions in predicting the presence of IBS. When entering anxiety in addition to depression as a predictor of IBS, the full regression equation was significant, $\chi^2(2)=23.10$, $p < .001$; R^2 *Nagelkerke*=.50. The model correctly

TABLE 3 | Summary of hierarchical logistical regression analysis predicting the presence of ulcerative colitis (UC) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−1.64	.309	−6.60	1.45			
Anxiety	0.03	.621	−0.07	0.19	0.94	1.03	1.13
Depression	0.04	.472	−0.12	0.19	0.93	1.04	1.17
Step 2							
Constant	2.04	.384	−3.64	12.01			
Anxiety	0.04	.52	−0.1	0.24	0.93	1.04	1.15
Depression	0.004	.961	−0.24	0.25	0.88	1	1.15
HFnu	−0.02	.315	−0.11	0.03	0.94	0.98	1.02
Cortisol	−0.01	.035*	−0.04	−0.002	0.98	0.99	1
Step 3							
Constant	2.36	.469	−8.13	18.58			
Anxiety	0.04	.515	−0.15	0.35	0.93	1.04	1.16
Depression	0.01	.906	−0.50	0.33	0.86	1.01	1.19
HFnu	−0.02	.361	−0.15	0.06	0.93	0.98	1.02
Cortisol	−0.01	.029*	−0.07	−0.002	0.98	0.99	1
DAF	−0.02	.869	−0.54	0.82	0.76	0.98	1.26
DIA	0.01	.968	−1.31	2.17	0.47	1.01	2.19

**≤.05. HFnu, High Frequency Normalized unit; DAF, Difficulty in awareness of feelings; DIA, Difficulty in interoceptive abilities dimension of the Toronto Alexithymia Scale; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings.*

TABLE 4 | Summary of hierarchical logistical regression analysis the presence of Crohn's disease (CD) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−4.29	.001***	−9.20	−1.76			
Anxiety	.07	.072	−0.01	.23	0.99	1.08	1.18
Depression	.13	.027*	0.02	.35	0.99	1.14	1.31
Step 2							
Constant	−4.23	.008**	−14.31	−1.15			
Anxiety	.09	.028	0.001	0.37	0.99	1.09	1.20
Depression	.15	.066	−0.02	0.61	0.99	1.16	1.36
HFnu	−.04	.071	−0.19	−0.001	0.92	0.96	1
Cortisol	.002	.408	−0.004	0.01	1	1	1.01
Step 3							
Constant	−9.52	.001***	−1365.01	−4.51			
Anxiety	.11	.051	−0.26	19.76	0.98	1.11	1.26
Depression	.06	.553	−6.65	22.64	0.87	1.06	1.29
HFnu	−.05	.074	−12.58	0.002	0.90	0.95	1
Cortisol	.01	.077	−0.01	0.95	1	1.01	1.01
DAF	.20	.260	−5.1	18.93	0.88	1.22	1.68
DIA	.73	.058	−0.71	170.57	0.97	2.08	4.49

****≤.001; **≤.01; *≤.05. HFnu, High Frequency Normalized unit; DAF, Difficulty in awareness of feelings; DIA, Difficulty in interoceptive abilities dimension of the Toronto Alexithymia Scale.*

classified 83.7% of cases. Only depression was a predictor of IBS, *W(1)*=7.71, *p*=.005. The introduction of HFnu index and cortisol levels in the model did not add an explanation ($\Delta\chi^2(2)$=0.34, *p*=.844) despite the fact that the full regression equation was significant, $\chi^2(4)$=23.44, $p < .001$; R^2 *Nagelkerke*=.51. Finally, the introduction of the interest variables, the DDF and DIF dimensions, did not improve model, $\Delta\chi^2(2)$=.04, *p*=.98, $\chi^2(6)$ =23.48, *p*=.001; R^2 *Nagelkerke*=.51. Model 1 better explained the presence of IBS than model 3 ($\Delta\chi^2(4)$=.38, *p*=.984). In summary, the best model was Step 1 and only depression scores were a significant predictor of IBS. Results are reported in **Table 5**.

Contribution of DDF and DIF dimensions in predicting the presence of UC. When entering anxiety in addition to depression as a predictor of UC, the result of the full regression equation was not significant, $\chi^2(2)$=0.98, *p*=.613; R^2 *Nagelkerke*=.03. However, at Step 2, when introducing HFnu index and cortisol levels in the model, the full regression equation was significant ($\chi^2(4)$=10.87, *p*=.028; R^2 *Nagelkerke*=.30) and correctly classified 72.1% of cases. The difference from Step 1 revealed that the introduction of physiological parameters added an explanation of the prediction of the presence of UC, $\Delta\chi^2(2)$=9.89, *p*=.007. However, only cortisol levels were a significant predictor of UC, *W(1)*=5.11, *p*=.026. At Step 3, the introduction of the interest variables, the DDF and DIF dimensions, did not improve the model ($\Delta\chi^2(2)$=2.14, *p*=.344), but the full regression model was significant, $\chi^2(6)$=13, *p*=.043; R^2 *Nagelkerke*=.35. Therefore, the best model was Step 2 and only cortisol levels were a significant predictor of UC. Results are reported in **Table 6**.

Contribution of DDF and DIF dimensions in predicting the presence of CD. When entering anxiety in addition to depression as a predictor of CD, the full regression equation was significant, $\chi^2(2)$=11.21, *p*=.004; R^2 *Nagelkerke*=.30. The model correctly classified 68.9% of cases. Only depression was a predictor of the presence of CD, *W(1)*=3.51, *p*=.025. The introduction of the HFnu index and cortisol levels in the model did not add an explanation ($\Delta\chi^2(2)$=4.35, *p*=.113) despite the fact that the full regression equation was significant, $\chi^2(4)$=15.56, *p*=.004; R^2 *Nagelkerke*=.39. Finally, the introduction of the interest variables, the DDF and DIF dimensions, improved the model, $\chi^2(6)$=28.19, $p < .001$; R^2 *Nagelkerke*=.62. Model 3 better explained the presence of CD than model 2 ($\Delta\chi^2(2)$=12.62, *p*=.002) or model 1 ($\Delta\chi^2(4)$= 16.98, *p*=.002), and correctly classified 82.2% of cases. Only DDF predicted CD, *W(1)*=6.16, $p < .001$. Although anxiety and cortisol levels tended to be significant in the model, the confidence intervals included zero, revealing unreliable results. In summary, the best model was Step 3 and only DDF was a significant predictor of CD. Results are reported in **Table 7**.

DISCUSSION

The aim of this paper was to explore the contribution of DIA and DAF in predicting the presence of gastrointestinal pathologies which could be considered vulnerabilities. After checking for the effects of psychological (i.e., anxiety, depression) and physiological (i.e., ANS and HPA axis activities at rest) factors, the results showed that DIA was a significant predictor only for IBS patients. In IBD patients, despite the fact that UC and CD are usually grouped in the same category (i.e., IBD), the factors

TABLE 5 | Summary of hierarchical logistical regression analysis predicting the presence of irritable bowel syndrome (IBS) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−4.35	.003**	−11.08	−1.80			
Anxiety	0.053	.226	−0.03	0.23	0.96	1.05	1.16
Depression	0.18	.005**	0.07	0.42	1.05	1.20	1.36
Step 2							
Constant	−4.44	.006**	−14.70	−0.97			
Anxiety	0.06	.223	−0.03	0.36	0.96	1.06	1.16
Depression	0.19	.003**	0.07	0.61	1.05	1.20	1.37
HFnu	−0.01	.713	−0.12	0.06	0.95	0.99	1.04
Cortisol	0.001	.778	−0.01	0.01	1	1	1.01
Step 3							
Constant	−4.74	.055[t]	−291.88	6.43			
Anxiety	0.06	.260	−.09	7.20	0.96	1.06	1.17
Depression	0.18	.014*	.04	29.74	1.02	1.19	1.4
HFnu	−0.01	.726	−3.82	.12	0.95	0.99	1.04
Cortisol	0.001	.737	−.23	.02	1	1	1.01
DIF	0.02	.858	−5.35	3.23	0.79	1.02	1.31
DDF	0.01	.897	−18.69	2.01	0.75	1.01	1.36

***≤.01; *≤.05; [t] ≤.07. HFnu, High Frequency Normalized unit; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings on the Toronto Alexithymia Scale.*

TABLE 6 | Summary of hierarchical logistical regression analysis predicting the presence of ulcerative colitis (UC) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−1.67	.308	−6.66	1.57			
Anxiety	.03	.534	−0.07	0.20	0.94	1.03	1.13
Depression	.03	.583	−0.15	0.17	0.92	1.03	1.16
Step 2							
Constant	2.22	.347	−3.30	13.39			
Anxiety	.04	.471	−0.10	0.25	0.93	1.04	1.16
Depression	−.004	.959	−0.24	0.22	0.87	1	1.14
HFnu	−.02	0.3	−0.11	0.03	0.94	0.98	1.02
Cortisol	−.01	.026*	−0.04	−0.003	0.98	0.99	1
Step 3							
Constant	2.88	.431	−12.37	19.99			
Anxiety	.07	.218	−0.10	0.66	0.95	1.08	1.21
Depression	.09	.442	−0.51	0.59	0.89	1.09	1.33
HFnu	−.04	.147	−0.21	0.06	0.91	0.96	1.01
Cortisol	−.01	.011*	−0.11	−0.003	0.98	0.99	1
DIF	−.27	.148	−1.57	0.36	0.51	0.76	1.14
DDF	.12	.514	−0.37	1.76	0.84	1.12	1.51

**≤.05. HFnu, High Frequency Normalized unit; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings on the Toronto Alexithymia Scale.*

TABLE 7 | Summary of hierarchical logistical regression analysis predicting the presence of Crohn's disease (CD) (95% BCa bootstrap confidence intervals based on 5,000 samples).

	b	p	95% Confidence Interval		95% Confidence Interval for Odds Ratio		
			Lower	Upper	Lower	Odds	Upper
Step 1							
Constant	−4.29	.002**	−9.38	−1.87			
Anxiety	.08	.076	−0.01	0.23	0.99	1.08	1.18
Depression	.13	.025*	0.01	0.35	0.99	1.14	1.31
Step 2							
Constant	−4.23	.008**	−14.87	−1.02			
Anxiety	.09	.033*	.001	.38	0.99	1.09	1.2
Depression	.15	.067	−.01	.61	0.99	1.16	1.36
HFnu	−.04	.074	−.17	.001	0.92	0.96	1
Cortisol	.002	.401	−.004	.01	1	1	1.01
Step 3							
Constant	−15.13	.001***	−1605.15	−8.86			
Anxiety	.16	.015	−.10	18.32	1.01	1.17	1.36
Depression	.11	.331	−1.19	23.91	0.87	1.11	1.43
HFnu	−.03	.193	−5.14	.07	0.92	0.97	1.01
Cortisol	.01	.016	−.003	.61	1	1.01	1.01
DIF	.13	.438	−1.12	25.65	0.8	1.14	1.63
DDF	.56	< .001***	.15	53.73	1.12	1.74	2.71

****≤.001; **≤.01; *≤.05. HFnu, High Frequency Normalized unit; DIF, Difficulty identifying feelings; DDF, Difficulty describing feelings on the Toronto Alexithymia Scale.*

predicting the presence of these pathologies are different. UC was predicted by biological parameters (i.e., cortisol level), while CD was not predicted by any factors, although some psychological factors (i.e., depression and DIA scores) tended to explain the presence of this disease. Analyses with the original TAS-20 dimensions (i.e., DIF and DDF) showed that the lack of consideration of interoceptive abilities (i.e., DIA dimension) in IBS or IBD patients led to different predictions. Indeed, in IBS patients, depression scores were a significant predictor of the presence of the pathology, while in CD patients it was the DDF scores. Cortisol remained the predictor of the presence of UC disease.

In this study, IBS patients exhibited an alteration of interoceptive abilities that might reflect increased attention to their visceral sensations and an intense concern for their own health (26). All internal stimuli, including visceral sensations, are monitored by interoceptive mechanisms, closely associated with pain (66). An alteration in interoceptive abilities could thus explain the high levels of visceral pain as observed in the IBS group, but also could explain the presence of high levels of alexithymia. Indeed, interoceptive abilities are difficult to separate from the ability to identify and describe feelings. Being aware of one's internal bodily changes necessarily implies being able to identify them. As a consequence, poor discrimination and sensitivity of body states would lead to difficulties in regulating one's own emotional states in an adaptive way, and thus to the use of more somatic patterns to describe emotions (67, 68), which can, in turn, contribute to the development of psychological and physical disorders. In addition, interoceptive dysfunctions are associated with psychopathology (69) such as panic disorders, anxiety syndromes, depression, schizophrenia (34), addictions, eating disorders and somatic symptom disorders (70). One of the major components of interoception is the immune communication between the periphery and the brain. Through various channels of communication, including the interoceptive pathway, the peripheral inflammatory state is transmitted to the brain. These signals are then integrated and translated into experiential feeling states and can lead to changes in reward/punishment motivational behaviors, mood, cognition, and visceral pain perception. When inflammation is severe or chronic, these changes may be comparable to those observed in major depressive disorders (71). Consistent with this theory, a review of the literature mentions a link between inflammation and depression and suicidal behaviors (72). Similarly, high levels of C-reactive protein in schizophrenia suggest a role of inflammation in the pathogenesis of this psychopathology (73). The potential roles of interoception and inflammation in the aetiology and/or symptomatology of a number of psychiatric conditions makes understanding these relationships a central goal for clinical psychology. Understanding these relationships could be instructive about how the brain perceives the body and could help identify the mechanisms by which interoception and inflammation lead to a risk of developing or relapsing into pathology. Therefore, DIA could be the aetiology of a greater vulnerability to develop or relapse into IBS when faced with stressful situations. This study could provide new targets for effective treatment.

Since pharmacotherapy has limited effects on IBS (74), physicians are increasingly using psychological interventions such as cognitive behavioral therapies (CBT) or interpersonal psychotherapy (IPT), (75) and hypnotherapy (76). Among these therapies, CBT seems to be the most effective practice for alleviating IBS symptoms compared to hypnosis, psychodynamics and relaxation (77). This practice involves a combination of different techniques (i.e., psycho-education, relaxation strategies, cognitive restructuring, problem-solving techniques or coping skills, interoceptive, and situational exposure techniques) (78). Its aim is to modify dysfunctional behaviors and thoughts, but also to promote awareness of the body's sensations as felt in the gastrointestinal tract and during breathing. In particular, the integration of interoceptive exposure exercises in CBT has shown their effectiveness in comparison to stress management intervention and an attention control group (79). Therefore, Craske and colleagues (79) and Kinsinger (78) showed the need to focus on interoceptive abilities when treating IBS patients. IBS patients present a hypersensitivity to and a hypervigilance of gastrointestinal symptoms that may contribute to visceral anxiety. In addition, IBS patients avoid many situations (e.g., situations without access to restrooms) and adopt safe behaviors (e.g., taking medication during a trip) which also contributes to maintaining symptom-related anxiety. The incorporation of interoceptive exposure in a CBT programme would thus reduce visceral anxiety by acting on the fear of gastrointestinal sensations. The practice of these exposure exercises could lead to increased self-efficacy and change the misperception about the nociception of gastrointestinal

sensations and the urgency of symptoms. The results of this study therefore support the need to improve the interoceptive capacities of patients with IBS for alleviating symptoms and ideally preventing relapses. New longitudinal studies in which the intervention's target is the improvement of interoceptive abilities must therefore be conducted.

For UC patients in remission, low cortisol levels predicted the presence of this pathology. Cortisol has an antiinflammatory action and reduces visceral pain. Low cortisol levels are associated with an increase in pain perception (80) and may reflect dysfunction of the HPA axis (81). This axis inhibits the sympathetic (adrenergic) nervous system (82, 83). An alteration of these feedback loops could favor overactivity of the sympathetic axis during rest and when faced with a stressful situation. It therefore makes UC patients more vulnerable to stress. In addition, low cortisol levels could reflect habituation to an environment considered as hostile (84, 85). This could result in the body's inability to maintain a state of homeostasis. In the long term, this could lead to the development of many pathologies related to chronic stress (86, 87), or to a greater vulnerability to relapse into the disease. Another explanation is that low cortisol levels could reflect a previous trauma in early life. Repeated and prolonged exposure to one or more adverse situations in childhood (e.g., physical trauma, loss of a parent, physical/sexual abuse) increases an individual's susceptibility to somatic and psychiatric diseases (88). An explanation of this link is based on brain-gut-microbiota axis, involving the ANS, the HPA axis, and the gastrointestinal tract (89). In a review article, Agorastos and colleagues detail the various mechanisms involved in early-life stress and trauma (90). They mentioned that early-life trauma is associated with insufficient glucocorticoid signalling that may have negative effects on the regulation of the immune system and ANS functioning. In addition, a repeated activation of the stress system may result in increased or decreased peripheral cortisol levels due to an alteration of the HPA axis. The HPA axis is closely interconnected with the ANS. An alteration of the HPA axis may deregulate the central autonomic network, thereby altering peripheral ANS activity and overall stress responsiveness. This can then lead to a dysregulation of inflammatory feedback mechanisms, which promotes the development of inflammatory-related or immunosuppressed medical conditions. Even years later (91, 92), these alterations may persist. Thus, this assumption of repeated or chronic stress in early life in UC patients would not be surprising given that the prevalence of early adversities (i.e., exposure to parental domestic violence, childhood physical abuse, childhood sexual abuse) is high in these patients (93).

Despite the inclusion of DIA and DAF assessment in the best model, no factors predicted CD. A 1-year longitudinal study found that psychosocial factors associated with chronic disease (i.e., stress induced by the physical symptoms of the disease, the use of emotion-focused coping, loss of resources and the quality of life related to chronic diseases) were the best predictors of vulnerability to relapse in CD (94). Due to their longitudinal dimension, the quantitative and qualitative data in this paper provided a comprehensive assessment of the stressors and quality of life associated with relapse. However, psychosocial stressors act through complex neuroendocrine immune pathways. Thus, biological factors underpinned psychosocial factors when considering a relapse in CD. A study integrating physiological and psychological factors revealed that physiological factors were independent predictors of relapse (higher CRP, fistulizing behavior, and colon-confined disease) and psychological factors were protectors of relapse (patients living in low stress conditions and with low avoidance rates) (95). Moreover, among CD patients, some have an overlap between their symptoms and IBS symptoms (96). CD patients suffering IBS-like symptoms present visceral hypersensitivity (97) while patients with CD alone have instead visceral hyposensitivity (64). Here, we do not differentiate between CD with IBS-like symptoms and CD-like symptoms. It may be that the DIA factor can predict the presence of CD with concomitant features of IBS. Further studies should be carried out to further develop this hypothesis.

For IBD patients, treatment typically focuses on the prevention of disease symptoms and inflammatory episodes, addressed through medications and/or surgery (2, 98). Yet, a White Paper from the American Gastroenterological Association provided evidence-based recommendations from health centres for the integration of psychosocial management in IBD care (99). Moreover, the results of this study and the literature highlight the importance of considering psychological factors in the vulnerability of IBD to develop chronic stress, which could lead to the recurrence or aggravation of gastrointestinal pathologies. However, the integration of psychosocial care seems to be more important for CD than UC patients. However, studies on the effectiveness of CBT in the treatment of HPA axis dysfunction in UC have shown that this practice increases cortisol levels by reversing some of the effects induced by low physical activity levels, depression and stress in early life (81). CBT may therefore influence the management of UC. However, recent research has reported better outcomes for CD patients than UC patients after CBT therapy, but these data were self-reported, were not from a standardized measure, and thus have to be interpreted with caution (100).

In Fournier and colleagues (57) and in this study, the DIA dimension had good internal reliability. However, this dimension includes only two items. For this reason, we carried out additional analyses by including the theoretical DIF and DDF dimensions of the TAS-20 as predictors. For UC patients, the introduction of the DDF and DIF dimensions instead of the DIA and DAF dimensions did not change the results. The best model was the model at Step 2 and only cortisol levels predicted the presence of an UC. However, for IBS patients, the best model became the one at Step 1 and only depression scores could predict the presence of this disorder. Without considering the DIA and DAF dimensions, we would have made wrong conclusions about the targets of action. Indeed, we could have concluded that the target of action must be depression when in fact it would be interoception involving other types of therapeutic interventions. Regarding CD patients, the best model reported that DDF scores predicted the presence of this

disease. Yet, in the first analysis, the DAF dimension, that included items from the DDF (item 2, 4, 11) and DIF (item 1, 6, 9, 13, 14) dimensions, was not a significant predictor of CD. This suggests that the main difficulty of CD patients is in describing feelings to others and not a global difficulty in awareness of feelings. CD patients could be able to identify their feelings but might be unable to find the right words to describe them to others. CD patients would have more semantic difficulties (revealed by the original structure of the TAS) while IBS patients would have more visceral difficulties (revealed by items 3 and 7 of the new TAS structure). Thus, both forms of the TAS (traditional and new structures) are interesting because they reveal the weak point of each of the pathologies with regard to the identification and description of one's body sensations or feelings. The new factorial structure can be helpful for predicting some diseases like IBS, but not for predicting others like CD where DDF is the strongest predictor. Therefore, the traditional factor structure is still relevant for predicting diseases other than IBS. However, for IBS, there is a need to use the new subscales of alexithymia. These data lead us to believe that it would be useful to keep, in alexithymia assessment, a dimension that allows the evaluation of the difficulty in describing feelings to others, but also to include a new dimension of interoception based on a factor for which new items need to be developed.

This study had various limitations. First, the number of participants included in the study was small and the number of predictors high. However, all validity criteria for statistical analyses were verified and met, making the results reliable. Second, patients with IBS were diagnosed from Rome II criteria (52). Now, we are in Rome IV criteria (101). The main differences between these two criteria concern the frequency and duration of symptoms (at least 12 weeks out of the preceding 12 months for the Rome II criteria and at least 1 day/week in the last 3 months for the Rome IV criteria), the addition of a classification of IBS by subtypes based on predominant bowel habits on days with abnormal bowel movements, and the term "discomfort" was removed from the current definition and diagnostic criteria to keep only the notion of abdominal pain. Another significant change was that the symptom of bloating as a primary symptom was eliminated from the definition. It is therefore possible that some IBS patients may have been misdiagnosed. Third, the DIA measurement was obtained from only two items of the TAS-20. Despite good internal consistency for this dimension, it is necessary to develop a new alexithymia scale that would contain an interoceptive dimension. Current studies highlight the importance of considering interoceptive abilities when studying alexithymia and the results of this study support the interest of including this dimension in alexithymic individuals with chronic pathologies. In addition, it would be interesting to conduct new studies with validated interoceptive measures such as the Multidimensional Assessment of Interoceptive Consciousness (MAIA) (102) to measure subjective interoceptive abilities, and a heartbeat-counting task to measure objective interoceptive abilities, different from Schandry's task (103) which seems controversial (104, 105). Fourth, our study does not consider all the alterations in the biopsychosocial sphere mentioned in the literature such as inflammatory markers. It may be interesting to conduct another study that takes more predictors into consideration.

In summary, this paper highlights the importance of considering interoceptive abilities in gastrointestinal disorders as a vulnerability factor when patients are faced with stress situations, especially in IBS patients. In the IBS group, the DIA dimension was predictive of the presence of IBS, suggesting that when faced with a new stressful situation, patients in remission would have difficulty in perceiving their own internal body changes and thus would have difficulty properly regulating their emotions. Faced with intense and/or repetitive stress, this could contribute to a relapse into the disease. In the CD group, difficulties describing feelings to others would be a predictor of the presence of this disorder. In light of the literature and our results, the contribution of factors such as the DIA and DDF dimensions and cortisol levels could be significant. Further studies are needed to deepen or improve knowledge. In the UC group, predictors seem to belong more to the physiological sphere. Even if CD and UC are grouped under the term "IBD," it seems that their psychophysiological functioning is completely different. Genetic susceptibility, environmental factors, and altered gut microbiota, leading to dysregulated innate and adaptive immune responses, are the core issue of IBD (106, 107). Despite some common aetiological factors between UC and CD, some differences exist at the macroscopic level since the digestive expression of the disease restricted to the rectum and colon in UC is generalised to the all tract in the CD, but also at the autonomic level and psychologic level. For instance, the autonomic balance between UC and CD has been shown to be different depending on affects and psychological adjustment (18). Moreover CD patients generally report more anxiety and depression than UC patients (108, 109). However, few studies compare the functioning of the HPA axis between UC and CD, which does not allow us to conclude on the role of cortisol in UC. It is therefore of great importance to distinguish UC from CD when studying IBD. The model presented in this paper must now be tested under experimental conditions in patients with regards to relapse. These results are promising and open new perspectives for the healthcare of patients with gastrointestinal diseases, such as CBT.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethical Committee of the CHU (ref: CPP 08-CHUG-23; ClinicalTrials.gov Identifier: NCT010950421). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SP, CD, FC, LM, and BB designed the study. BB and NM recruited the patients. SP and BB raised funds to finance the protocol. SP recruited the healthy controls for inclusion. SP and CD performed the experiments and collected psychological and physiological data. AG performed the biochemical assays. AF analysed the data. OL and AF interpreted the data. AF, OL, LM, and SP drafted the manuscript. FC, NM, AG, CD, and BB undertook a critical revision of the manuscript. All the authors approved the final version submitted for publication.

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Using the Body When There Are No Words for Feelings: Alexithymia and Somatization in Self-Harming Adolescents

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The present case-control study aimed to investigate the relationship between alexithymia and somatic complaints in the psychopathological setting of non-suicidal self-injury (NSSI). A clinical sample of 134 adolescents (115 females; 85.5%) from 12 to 18 years old engaging in NSSI was compared with a control group of 243 high-school students (157 females; 64.6%) from 13 to 18 years old. Data were collected using two questionnaires: The Youth Self-Report 11–18 and the 20 Toronto Alexithymia Scale. In both cases and controls, the presence of somatization and alexithymia was associated with more severe psychopathological problems. Analyses were conducted to explore the association between somatic disorders and alexithymia. In the clinical group, somatic complaints were reported by 95.9% of alexithymic individuals, whereas only 44.3% of alexithymic adolescents reported somatic complaints. A one-way relationship emerged between somatization and alexithymia: while alexithymia would seem to be a factor associated with self-injury, somatic disorders were strongly associated with alexithymia, but not necessarily with self-injury. Among the self-harming adolescents, those with both alexithymia and somatization had a more severe psychopathological picture than the individuals with alexithymia but no somatization. This would suggest that, in the setting of NSSI, greater difficulty with identifying feelings is associated with somatization, and alexithymia would be an attribute common to self-harming behavior and somatization, both of which are characterized by the body being used to express psychological and emotional problems. Future research could further investigate alexithymia in self-harming individuals, in relation to any presence or absence of somatic disorders, with longitudinal assessments on any differences in their manifestation of self-injury and its psychopathological correlates.

Keywords: somatic complaints, somatization, non-suicidal self-injury, alexithymia, adolescence, developmental psychopathology, self-harming

INTRODUCTION

"Nonsuicidal self-harming, or self-injury" (NSSI) was defined by Nock and Favazza (1) as the voluntary destruction or alteration of body tissue without any suicidal intent, for purposes that are not socially approved. This category includes behavior such as self-cutting, head banging, burning, self-hitting, scratching to the point of bleeding, and interfering with the healing of a wound (1–6).

Research on NSSI has been increasing, particularly in the last two decades (7). Published empirical studies report that hospitals have been seeing rising numbers of people who engage in self-harming behavior, with or without suicidal intent, over the past 10 to 20 years (3, 8, 9). Self-harming can generally be considered a growing health problem worldwide (10), and the individuals engaging in this behavior are at high risk of subsequent suicide (4, 11), so it is important to identify them and take preventive action. While some empirical evidence shows that people tend to contact the healthcare services before a self-harming episode or suicide attempt, they often complain of physical rather than psychological problems. In a study by Idenfors et al. (12) it emerged that children and adolescents beginning to engage in self-harming behavior had more contact with healthcare services and more hospitalizations for non-psychiatric causes before any episodes of self-injury than their peers not engaging in such behavior. In a subsequent study, the same authors found that individuals who had complained of somatic disorders in the 12 months before an episode of self-injury were also at a higher risk of suicide. The authors concluded that it is important to check for a possible self-injuring or suicidal risk in adolescents who access healthcare for somatic symptoms (13). Another study by Houston et al. (14) found that two in three patients arriving at a hospital in Oxford for NSSI had been seen by a general practitioner in the month preceding the self-harming episode, and one in three had done so in the previous week. In particular, 36.1% of those who had been seen by a general practitioner within a month before the episode of NSSI had physical ailments. Approximately one in three patients had suicidal ideation during the medical examination, but only 13.3% reported such thoughts to the specialist in hospital (14).

In light of such findings, some authors have claimed that self-harming patients show their malaise through somatic rather than psychical symptoms (15). On the other hand, several studies highlighted the association between self-harming and difficulty with regulating emotions regulation, and with identifying and communicating feelings. Specifically, in adolescent age, moreover, the motives behind self-harming are mainly linked to dealing with negative emotions.

In both psychosomatic patients and self-harming individuals, the body serves as a means to cope with psychological pain. While psychosomatic patients express their psychological distress in the shape of physical disorders (e.g., headache, stomachache, nausea, sleep problems, dizziness, rashes, or other skin problems), self-harming individuals hurt the surface of their body to contain their psychological pain. Neither psychosomatic nor self-harming individuals can mentalize and express their negative feelings in words, so they use their body to show their psychological pain (16).

Empirical studies found that alexithymia, i.e., difficulty in identifying and describing feelings and modulating states of emotional arousal (17, 18), is associated with both self-harming (19–21) and psychosomatic behavior (16–18).

A limited ability to identify, understand, and express an emotional state may increase the risk of NSSI (22). An Italian study on a non-clinical adolescent population found a positive association between difficulty in identifying and describing one's feelings and NSSI behavior. It also found that dysfunctional relationships with peers and parents can raise the risk of NSSI and suicidal ideation, consequently impairing an adolescent's ability to identify their emotions (23).

In a longitudinal study conducted in New Zealand, alexithymia emerged as a predictive and proximal factor for NSSI. In the presence of mood disorders, alexithymia determined an individual's vulnerability to the use of NSSI as an avoidance coping strategy, or an alternative way to express emotions (24).

The association between alexithymia and NSSI has been analyzed in neuroimaging studies, too, using functional magnetic resonance imaging. Different patterns of activation of the supramarginal gyrus, angular gyrus, and mid-temporal gyrus emerged as a result of individuals viewing different images of facial expressions. These areas appear to be involved in identifying and understanding emotions from others' facial expressions, in empathy, and the assimilation of multisensory information. In particular, a more outward-oriented way of thinking, or a lesser tendency for introspection seem to relate to a lack of activation in response to seeing facial expressions of happiness. Functional tests on NSSI patients who reported not caring about their feelings showed lower levels of neuron activation at the sight of images of happy expressions and higher levels of activation for frightening images (25).

As mentioned earlier, difficulties with identifying and communicating feelings (i.e., alexithymia) could also be a factor common to both somatic symptoms and self-injury. In both clinical pictures, the body is used to express psychological and emotional aspects that are otherwise impossible to communicate (16). Besides, in the case of self-harming behavior in people with somatic symptoms, several authors found a strong association between their latter symptoms and signs of anxiety and depressed mood (26, 27). Bohman et al. (28) reported that adolescents with depressive disorders had more somatic symptoms (e.g., headache, abdominal pain, dizziness, nausea, tired eyes) than healthy controls. They also found that the duration and severity of their depression correlated with the number of their somatic symptoms. A strong correlation emerged between their depression, the number of somatic symptoms they experienced, and their suicidal plans, thoughts, or attempts as well. Ginsburg, Riddle, and Davies (29) made the point that children and adolescents with anxiety disorders have significantly more somatic symptoms, and their reported somatic symptoms are more severe the higher the severity of their anxiety. Studies in the literature have emphasized how depressive symptoms and anxiety coincide with NSSI (30–32),

as well as with suicide (33). This gives the impression that the presence of NSSI in individuals with somatic symptoms might be mediated by comorbidity with internalizing disorders (34).

More research is needed to elucidate the relationship between somatic complaints and self-harm in young people. Some studies exploring the relationship between alexithymia and somatic symptoms (35–38)—also in clinical samples, such as patients with depression (39)—have identified an association between these two conditions, especially for difficulty in identifying feelings, however, this link is sometimes unclear or can be mediated by psychological distress (40). These features of alexithymia could represent itself, indeed, a high risk of psychological distress (41).

Parolin and colleagues (42) investigate the levels of alexithymia in young adults with substance use disorders compared to a young adolescent with psychiatric disorders and healthy individuals. In this study, the authors found higher levels of alexithymia in both clinical groups as compared to control groups, but they did not differ from each other. This study highlights that alexithymia is not associated with specific clinical disorders but is correlated with depressive symptoms.

At the same time, some authors find the strong association between psychological factors and medical condition, as fibromyalgia, psoriasis, diabetes, where psychological distress and poor quality of life correlate with higher severity of the pathology (43, 44). However, no work has been done on the combination of alexithymia and somatic symptoms with NSSI.

Hence the present study, which aimed: i) to test whether self-harming adolescents have significantly more somatic complaints (with no known medical cause) than their peers who do not engage in NSSI; and ii) to clarify the relationship between somatization and alexithymia in the setting of NSSI, and the related clinical characteristics.

MATERIALS AND METHODS

Subjects

We enrolled self-harming young people attending two neuropsychiatry units for children and adolescents in Northern Italy from January 2015 to December 2018. Participants and their parents gave their informed consent to the study (the two services have an institutionally approved protocol based on the use of standardized forms for obtaining informed consent to the administration of questionnaires and the collection of data for clinical and research purposes). Our final clinical sample consisted of 134 self-harming adolescents, 19 males (14.2% of the sample), and 115 females (85.8%), from 12 to 19 years old (mean 15.4 years, SD=1.36).

The experimental group has been enrolled with the following inclusion and exclusion criteria: a) aged between 12 and 19 years; b) presenting almost 1 episode of self-harming; c) that does not exhibit an intellectual disability [tested with the Wechsler Intelligence Scale)(45)]; d) parents signed the informed consent.

A control group was recruited from among students attending five regional high schools. The non-experimental group sees the following inclusion and exclusion criteria: a) aged between 12 and 19 years; b) have had a formal consent signed by parents (or legal ward/caregiver). After an informative interview with the headmaster, parents were sent a letter describing the research project, providing details of the test methods, and requesting that they sign a form to authorize their child's participation. The questionnaires administered to the controls were the same as those administered to the cases. They were completed anonymously in class during regular school hours, in compliance with current legislation on privacy, and the presence of an operator from our service. After ruling out respondents who admitted in the questionnaire to having taken some self-harming action, the group of controls considered in the statistical analysis amounted to 243 students: 86 males (35.4% of the sample) and 157 females (64.6%), aged from 13 to 19 years (mean 15.8, SD=1.35).

Procedures

Patients completed the questionnaires used in the study (see list below) at the time of clinical interviews for their diagnostic assessment. During these interviews with patients, we recorded their clinical history, their reason for coming to our service, clinical aspects of their self-harming behavior.

The clinical sample was classified with certain characteristics: reason for accessing our service (patients presenting with NSSI, or with a history of such behavior; patients presenting with problems other than NSSI, who subsequently experienced NSSI episodes); frequency of self-harming episodes (occasionally or habitually, i.e., patients with fewer or more than five episodes a year, respectively); psychopathological features from administration tests' results.

Study Protocol and Materials

Case-control study design was adopted. The cases and controls were administered two questionnaires: the 11-18 Youth Self-Report (YSR) (46); and the 20 Toronto Alexithymia Scale (TAS-20) (17). The scores obtained were first compared between cases and controls. Then comparisons were drawn between the groups into which the clinical sample was further divided.

The Achenbach questionnaires are among the scales most often used internationally for juvenile rating behavior, in the clinical setting, and research. We used the version for adolescents (YSR 11-18), which yields two profiles: one concerning competences (activities, social functioning, school performance), then how well the adolescent performs in sports, hobbies, autonomy, and socialization, and at school; the other covers behavioral and emotional problems, which can be classified as "normal," "borderline," or "clinical" on eight specific syndrome scales. These syndrome scales relate to various psychopathological pictures: anxiety/depression; withdrawal; somatization; social problems; thought-related problems, attention problems; aggressive and rule-breaking behavior. Problems are grouped into internalizing problems (anxiety, depression, withdrawal, somatization); externalizing problems (aggressive and rule-breaking behavior); and other problems (social problems, thought-related problems, attention problems).

The 20 Toronto Alexithymia Scale (TAS 20) is 20 items self-report questionnaire that measures the three factors defining alexithymia: "difficulty in identifying feelings," "difficulty in communicating feelings to others," and "externally-oriented thinking." Respondents were classified as non-alexithymic (scores <51), borderline (scores 51–60), or alexithymic (scores >61). We used the Italian validated version of the TAS-20.

Statistics

The statistical analyses were all conducted with the "Jamovi" statistical software. Univariate analysis of variance (ANOVA) was run to identify possible similarities or differences between the clinical and control groups as regards their psycho-behavioral profile and the alexithymia dimension. A bivariate parametric correlation analysis (Pearson's r coefficient) was conducted to investigate the relationships between clinical features and groups. Within the clinical group, analyses were run to examine the relationship between alexithymia, somatic disorders and psychopathological characteristics. The statistical tests used in this study were bidirectional, and the threshold for statistical significance was set at $p < 0.05$.

RESULTS

Frequency and percentage statistics are shown for the categorical variables corresponding to the clinical group's characteristics. We obtained information on the frequency of self-harming for 84 subjects: 30 of them (35.7%) did so occasionally, and 54 (64.3%) habitually. Information on the reasons for accessing our services was only available for 77 subjects: it was NSSI in 37 cases (48.1%); NSSI in association with attempted suicide in 4 (5.2%); affective disorders in 12 (15.6%); and problems at school in 5 (6.5%); and other reasons—including eating disorder, depression and NSSI, behavioral disorder, phobia, and social closure—in one case each (1.3%).

Psychopathological Characteristics

ANOVA revealed statistically significant differences between the clinical group and the control group regarding emotional-behavioral problems. There were no statistically significant differences within the clinical group based on the frequency of self-injury. The descriptive statistics are shown in **Table 1**. The clinical group had more severe problems than the control group on all the scales investigated:

- *YSR 11-18*: "internalizing problems" (F=132.89, p<.001), "externalizing problems" (F=71.53, p<.001), "total problems" (F=163.73, p<.001), "social problems" (F=85.59, p<.001), "anxious/depressed" (F=85.11, p<.001), "withdrawn/depressed" (F=78.64, p<.001), "somatic complaints" (F=82.35, p<.001), and "aggressive behavior" (F= 41.73, p<.001).

To be more specific, 74% of our patients with NSSI had clinically-relevant scores for internalizing problems, as opposed to 41.2% in the control group. The situation was similar for clinically-relevant externalizing problems (identified in 28.6% of the patients and 8.2% of the controls). As for somatic problems, 22.8% of the NSSI group obtained a borderline score, and 18.1% were in the clinical range, whereas 90.5% of the control group presented no such problems. In short, our clinical group had more psychopathological issues than controls, including internalizing and externalizing problems, depression, anxiety, social difficulties, and aggressive behavior.

Pearson's correlation analysis revealed statistically significant correlations between the clinical group and all test scores (**Table 2**). Statistically significant negative correlations emerged on the Competence scales (NSSI individuals scored lower), while

TABLE 1 | Average scores on the Youth Self-Report (YSR) scales for cases and controls.

CBCL	Group	M (SD)		Group	M (SD)
Anxious/depressed	Case control	70.3 (12.30)	Affective problems	Case control	72.3 (12.15)
		59.1 (8.59)			56.6 (7.09)
Withdrawn depressed	Case control	69.5 (12.1)	Anxiety problems	Case control	64.4 (8.58)
		58.5 (9.61)			58.5 (7.68)
Somatic complaints	Case control	63.9 (9.26)	Somatic problems	Case control	62.4 (9 .70)
		55.6 (6.40)			55.1 (6.52)
Social problems	Case control	66.0 (9.68)	Oppositional defiant problems	Case control	58.6 (7.63)
		56.6 (8.41)			53.8 (5.50)
Thought problems	Case control	64.6 (10.22)	Attention deficit/hyperactivity problems	Case control	58.1 (6.72)
		54.2 (5.43)			53.6 (5.02)
Attention problems	Case control	63.4 (9.66)	Conduct problems	Case control	58 (8.70)
		55.4 (7.30)			52.1 (4.62)
Rule-breaking behavior	Case control	59.2 (8.42)	Internalizing problems	Case control	69.7 (10.72)
		53.9 (5.40)			56.1 (11.01)
Aggressive behavior	Case control	59.3 (8.53)	Externalizing problems	Case control	58.6 (9.66)
		53.8 (5.72)			49.9 (8.84)
Activities	Case control	37.4 (9.39)	Total problems	Case control	66.2 (9.31)
		39.8 (8.76)			53.0 (9.63)
Social	Case control	39.2 (9.74)			
		45.6 (8.97)			
Total competence	Case control	35.1 (9.71)			
		40.4 (9.27)			

TABLE 2 | Correlations of the Youth Self-Report (YSR) global problems scales.

	Group	Conduct	Internalizing	Externalizing	Total problems	Somatic problems	Anxiety depression	Thought problems	Affective problems
Gender	.228**	.063	.242**	.048	.173**	.204**	.204**	.102	.202**
Group	1	.410**	.512**	.413**	.551**	.409**	.473**	.556**	.631**
Conduct		1	.359**	.777**	.598**	.301**	.349**	.532**	.473**
Internalizing			1	.513**	.879**	.622**	.855**	.687**	.829**
Externalizing				1	.799**	.416**	.481**	.601**	.567**
Total problems					1	.603**	.802**	.793**	.839**
Somatic problems						1	.482**	.530**	.550**
Anxiety depression							1	.672**	798**
Thought problems								1	.783**

$^{**}p < 0.01$.

statistically positive correlations were seen for all the other YSR scales; that means that the clinical group has less competences and more problems. All psychopathological characteristics investigated were significantly associated with NSSI. In qualitative terms, there were stronger correlations between the clinical group and affective disorders, and specifically for thought problems in the cluster of affective problems. As for differences by gender, female sex was associated with more psychopathological problems.

The Alexithymia Dimension

Our assessment of alexithymia showed statistically significant differences between the clinical and control groups.

- *TAS-20*: "difficulties identifying feelings" (F=92.69, p<.001), "difficulties describing feelings" (F=35.64, p<.001), "externally-oriented thinking" (F=40.44, p<.001), "total alexithymia" (F=99.17 p<.001).

The mean score for total alexithymia in the clinical sample was M= 63.8 (SD=12.01), while in the control sample, it was M= 51 (SD=11.27). Adopting a score of 61 as a cut-off for alexithymia, the clinical group scored higher (i.e., had alexithymia), and the control group lower. In detail, 64.1% of the NSSI individuals showed clinically-relevant levels of alexithymia, while 23.4% obtained borderline scores. In the control group, 21.1% had clinical scores, and 24.8% were in the borderline range. As reported elsewhere in the literature, alexithymia is a common characteristic of self-harming individuals (**Table 3**).

Pearson's correlation analyses revealed statistically significant positive correlations between the clinical group and the TAS-20 sub-scales. Individuals engaging in NSSI were associated with a higher degree of alexithymia. TAS-20 factors also showed a statistically significant positive correlation with all the YSR problem scales except for social competence, with which they correlated negatively. The higher the difficulties in identifying and describing feelings, and in externally oriented thinking, the higher the scores on the psychopathological scales for internalizing and externalizing disorders (**Table 4**).

TABLE 3 | Average Toronto Alexithymia Scale (TAS)-20 scores for cases and controls.

TAS-20	Group	Mean (SD)
Difficulties identifying feelings	Case control	23.4 (6.54)
		16.6 (6.16)
Difficulties describing feelings	Case control	17.5 (4.64)
		14.4 (4.95)
Externally oriented thinking	Case control	23.0 (4.49)
		20.0 (4.04)
Total alexithymia	Case control	63.8 (12.01)
		51.0 (11.27)

Relationship Between Alexithymia and Somatic Disorders in the Clinical Group

To investigate the link between alexithymia, somatic disorders and psychopathological characteristics, we ran analyses on the clinical group and compared it with the control group. Subjects were subgrouped by the presence of alexithymia and the presence of somatic disorders. Analysis of variance in the clinical group revealed statistically significant differences within these subgroups: NSSI patients with alexithymia had more severe emotional-behavioral problems. The same pattern emerged when these subjects were grouped by the presence or absence of somatic disorders. Alexithymia and somatization were both associated with more severe psychopathological issues. The analyses conducted on the control group produced the same results. To explore possible associations between alexithymia and somatization, a statistical analysis was carried out with the x^2 test. We obtained statistically significant results in both the NSSI

TABLE 4 | Correlations between condition, gender, Youth Self-Report (YSR) scores, and Toronto Alexithymia Scale (TAS)-20 subscales.

	Difficulties describing feelings	Difficulties identifying feelings	Externally-oriented thinking	Total alexithymia
Gender	.238**	.142**	–.034	.186**
Condition	.455**	.297**	.324**	.470**
Internalizing	.630**	.591**	.347**	.701**
Externalizing	.457**	.226**	.309**	.447**
Total problems	.669**	.533**	.387**	.714**
Somatic complaints	.536**	.402**	.226**	.527**
Affective problems	.632**	.469**	.339**	.643**
Somatic problems	.453***	.359**	.224**	.463**

$^{**}p < 0.01$.

group (x^2=5.24; p=0.02), and the control group (x^2=10.7; p=0.001); see **Table 5**.

The presence of somatic disorders is strongly associated with the alexithymia dimension. Only two individuals in the NSSI group had somatic disorders but no alexithymia, while 95.9% of those reporting clinically-relevant somatic complaints had alexithymia. That said, alexithymia was not necessarily associated with somatic disorders: 55.7% of the NSSI subjects with alexithymia did not report any clinically-relevant somatic complaints. Within the NSSI group, 38.8% had somatic complaints concomitantly with alexithymia. When the same analyses were run on the control group, the same one-way relationship between somatic disorders and alexithymia came to light: 78.3% of the individuals presenting somatic disorders had clinical alexithymia. The controls differed from the group of NSSI patients in that alexithymia was less strongly associated with somatization: only 16.2% of the controls had clinical levels of alexithymia concomitantly with somatic complaints. No statistically significant differences were found when we checked for possible associations between frequency of NSSI, alexithymia and somatic disorders.

Since alexithymia was not necessarily associated with the presence of somatic disorders in the group with NSSI, we run an ANOVA on this group to seek any differences between the alexithymic cases based on the presence or absence of concomitant somatization. The results showed statistically significant differences between these two subgroups.

- *YSR 11-18*: "internalizing problems" (F=18.46, p<.001), "externalizing problems" (F=5.54, p=0.021), "total problems" (F=19.34, p<.001), "anxious/depressed" (F=6.13, p=0.016), "withdrawn depressed" (F=4.01, p=0.04), "social problems" (F=5.30, p=0.023), "thought problem" (F=7.34, p=0.008), "aggressive behavior" (F=5.22, p=0.025), "affective problems" (F=12.26, p<.001), "oppositional defiant problems" (F=5.46, p=0.022)
- *TAS-20:* "difficulties identifying feelings" (F=8.98, p=0.003), "difficulties describing feelings" (F=5.89, p=0.017), "total alexithymia" (F=10.23, p=0.002)

The association between alexithymia and somatization correlated with a clinically more severe psychopathological condition. This association was more common in the group of NSSI patients than in the control group.

We conducted further analyses to clarify what distinguishes a self-harming individual among those revealing a combination of alexithymia and somatization. We considered only the subgroups with clinically-relevant levels of both alexithymia and somatization within each of the two groups (cases and controls). The results of our ANOVA showed statistically significant differences between them.

- *YSR 11-18*: "internalizing problems" (F=9.23, p=0.005), "externalizing problems" (F=13.81, p<.001), "total problems" (F=20.36, p<.001), "anxious/depressed" (F=9.70, p=0.003), "withdrawn depressed" (F=8.83, p=0.006), "social problems" (F=10.52, p=0.003), "thought problem" (F=26.33, p=<.001), "attention problems" (F=10.73, p=0.002), "rule-breaking behavior" (F=8.73, p=0.005), "aggressive behavior" (F=14.58, p<.001), "affective problems" (F=36.27, p<.001), "anxiety problems" (F=7.34, p=0.01), "oppositional defiant problems" (F=7.56, p=0.009), "attention deficit/hyperactivity problems" (F=11.01, p=0.002), "conduct problems" (F=14.37, p<.001).
- *TAS-20* "difficulties identifying feelings" (F=10.43, p=0.003), "externally oriented thinking" (F=6.32, p=0.016), "total alexithymia" (F=11.23, p=0.002).

The subgroup of NSSI cases with both alexithymia and somatization differed from the controls with these two concomitant conditions in that the former had more severe degrees of psychopathology, and higher difficulties with identifying feelings, and outward-oriented thinking.

TABLE 5 | Relationship between alexithymia and somatic disorders.

Somatization	Alexithymia			
	Absent		Present	
	Case	Control	Case	Control
Absent	13 (10.7%)	126 (52.1%)	59 (48.8%)	93 (38.4%)
Present	2 (1.7%)	5 (2.1%)	47 (38.8%)	18 (7.4%)
Total	15 (12.4%)	131 (54.1%)	106 (87.6%)	111 (45.9%)

DISCUSSION

As in the literature, which points to females engaging in self-injury more than males, both in clinical samples (47, 48), and in the general population (19, 48–51), our clinical group consisted mainly of girls, with a male to female ratio of one to six.

This study aimed to investigate the relationship between psychopathological traits, alexithymia, and somatic disorders in a sample of self-harming adolescents. More than half of our sample (64.3%) engaged habitually in self-injury (more than five episodes a year). This is a higher proportion than the figures reported in non-clinical populations (52), but similar to the rate seen in clinical populations considered in other Italian studies (20), and lower than the percentage recorded by Washburn (53) in a clinical population of adolescent inpatients and outpatients.

Regarding the reasons why our NSSI patients came to our neuropsychiatric service, about half of the sample mentioned not NSSI, but affective disorders, problems at school, phobias, social problems, behavioral issues, or eating disorders. Such disorders are often associated with self-harming behavior, and the latter might be investigated as part of the clinical assessment of patients presenting with these kinds of psychopathological issues. Much the same picture emerged in other clinical studies (19). We can also assume that most adolescents revealing self-harming behavior tend to underestimate it, and even their parents—when they are aware of it—may minimize the problem (54). Parents are frequently unaware of their children's self-harming behavior. However, a meta-analysis recently revealed that only 49% of adolescents engaging in NSSI ask for help, and only 25% of them talk to members of their family about the problem (55).

General practitioners or pediatricians (who can request a neuropsychiatric examination) might have difficulty in diagnosing NSSI, especially when it is not associated with behavioral or affective disorders or suicidal behavior. A recent review found that about one in two pediatricians did not feel able to deal with a patient engaging in self-harming, and less than one in three routinely assessed their patients for NSSI (6).

The results of the present study generally show more severe psychopathological traits in the clinical population of adolescents engaging in NSSI. This confirms other clinical reports (3, 48, 51, 56–61) of several psychopathological disorders being related to self-injury, an aspect that underscores the nosographic transversality of NSSI. We hypotheses that self-harming adolescents could have significantly more somatic complaints (with no known medical cause) than their peers who do not engage in NSSI. There was a statistically significant correlation in our sample with all the scales in the YSR questionnaire, including somatic complaints. The same picture emerged in other studies using the same instrument (YSR): in a case-control study, Laukkanen et al. (62) found more pathological scores in self-injuring adolescents than controls on all the syndrome scales considered (anxiety and depression, depression and social withdrawal, somatic complaints, social problems, thought problems, attention problems, rule-breaking and aggressive behavior). Baetens et al. (63) found their NSSI group scored higher on the following DSM-oriented scales: affective problems, anxiety problems, somatic problems, attention and hyperactivity problems, oppositional-defiant problems, and conduct problems. The same differences emerged in another Italian case-control study too (20), with self-harming patients showing more severe psychopathological issues than controls in all subscales of the YSR.

It is important to emphasize, however, that internalizing disorders were qualitatively the most represented in our clinical sample, and stronger correlations were apparent between the NSSI group and the presence of affective disorders. This finding seems to be in line with other studies (19, 51, 64, 65). Some authors have concluded that the presence of a mood disorder can be a predictor of NSSI (65), as seen in other works on non-clinical adolescent populations (24, 66, 67). One hypothesis is that adolescents with mood disorders find comfort in the act of self-injury (68), as a strategy for coping with their depressive symptoms, like brooding (or rumination), to escape negative emotional and cognitive states (69–71). Among the mood disorders, bipolar disorder is characterized by strong emotional lability, and patients may be more vulnerable to acts of NSSI (72). Young people with severe depressive symptoms may use NSSI to obtain positive emotions, and as behavior that gives them social reinforcement (73).

The literature shows that the female gender is associated with more significant psychopathological problems (74). Studies on clinical samples and general populations report to a higher prevalence of females with a history of NSSI (47, 48, 50, 51). Some authors even consider female sex a risk factor for NSSI (75, 76), as well as for a range of feelings of distress, such as anxiety and depression (51, 77). Compared to their peers of the opposite sex, females tend to have a higher prevalence of psychopathological issues, especially internalizing problems, and they are associated with a higher risk of developing more severe forms of self-injury, such as suicidal behavior (78, 79).

Alexithymia appears to be a specific feature associated with self-harming behavior. In fact, a significant correlation emerged between our NSSI group and all subscales of the TAS-20 questionnaire. The risk of NSSI developing in alexithymic subjects was highlighted in a study by Norman and Borril, too (22). These findings also confirm a previous report from Gatta et al. (19) on a non-clinical population of adolescents: those engaging in self-harming had considerably more difficulty in recognizing and expressing their own and others' emotional states, suggesting a fundamental role for alexithymia in the onset of NSSI (19). Similar evidence comes from other research in Italy and New Zealand (23, 24), suggesting that alexithymia is a risk factor for NSSI as a dysfunctional coping mode, as well as by neuroimaging studies using functional magnetic resonance imaging (25).

In our results, the correlation between the YSR and TAS-20 scales goes to show how a higher difficulty with identifying and communicating feelings, and with outward-oriented thinking is associated with more serious mental issues. It is also important to emphasize that, inasmuch as a self-report questionnaire can measure psychopathological issues, the presence of alexithymic traits could just impact this.

This study aimed to clarify the relationship between somatization and alexithymia in the setting of NSSI and the related clinical characteristics. To investigate the relationship between alexithymia, somatization, and emotional-behavioral psychopathological issues, in the NSSI group, we divided the sample by the presence or absence of somatic complaints and alexithymia. Our results showed a one-way relationship between the presence of somatic disorders and alexithymia: while 95.9% of the adolescents reporting clinically-relevant somatic complaints had alexithymia, 55.7% of those with alexithymia reported no somatic complaints. There was a statistically significant association between alexithymia and somatization in the control group too, consistently with the literature (35, 36, 39), but this association was weaker in qualitative terms.

Difficulties in identifying and communicating feelings thus seem to be a factor common to both somatization and self-harming. In both cases, the body is used to express psychological and emotional issues that an individual finds impossible to communicate verbally (16).

Further analyses conducted on our sample of clinical cases aimed to look for differences between individuals with alexithymia based on whether or not they had concomitant somatization. Our results showed more severe psychopathological issues in the adolescents in our NSSI group who had clinical levels of alexithymia and somatization than in those with clinically-relevant alexithymia alone. Although we cannot identify a cause-effect relationship, we can say that concomitant somatization in self-harming individuals with clinical levels of alexithymia is associated with a more severe psychopathological picture. We, therefore, surmise that alexithymic individuals' expressions of psycho-

emotional distress in the form of somatic complaints constitute a risk factor for their engaging in self-harming.

The concomitant presence of alexithymia and somatization was seen mainly in our self-harming group, and to a lesser degree in the control group. We sought to identify what distinguished the individuals who engaged in self-harming, after accounting for the association between somatization and alexithymia, in our sample of adolescents as a whole. To answer this research question, we analyzed only the individuals with both alexithymia and somatic complaints, divided by the presence or absence of NSSI. We found that the adolescents who engaged in self-harming had higher scores for psychopathological problems, and for difficulties in identifying feelings, and in outward-oriented thinking.

CONCLUSION

This study aimed to explore the relationship between alexithymia, somatic disorders, and psychopathological traits in a group of self-harming adolescents, as compared with a control group. Our results indicated that individuals who engaged in NSSI had more problems in the internalizing and externalizing domains than the control group. There was evidence of the nosographic transversality of self-injury. In qualitative terms, internalizing disorders (and affective disorders in particular) were the factor that most strongly characterized the clinical group. This finding has important implications for clinical practice, and for primary and secondary prevention.

Self-harming individuals had more severe somatic disorders and alexithymia. Our results showed a one-way relationship between somatization and alexithymia (with somatic complaints reported by 95.9% of our alexithymic adolescents, while only 44.3% of alexithymic adolescents reported somatic complaints). Alexithymia would thus seem to be a factor associated with self-injury, whereas somatization would be closely associated with alexithymia, but not necessarily with self-injury. It may be that an alexithymic trait is like a common denominator in the use of the body instead of words to express emotion in the case of psychological disease: through somatization when the psychic conflict is displaced inside the body; or through NSSI when the emotional dysregulation and negative feelings prevail.

In our NSSI sample, the combination of alexithymia with somatization was associated with a more severe psychological picture than alexithymia alone. It could be that, in the context of NSSI, higher difficulty with identifying is associated with somatization. This leads us to suggest, once again, that alexithymia is an attribute shared by self-harming and somatization, both of which are characterized by the use of the body to express an emotional problem. Somatic complaints also appeared to be associated with more severe psychopathological issues in our sample, however, so it may be that the former was a manifestation of the latter.

Further longitudinal research is needed on alexithymia in NSSI, vis-à-vis the presence or absence of associated somatic disorders, to identify any differences in the manifestation of self-injury and its psychopathological correlates. Moreover, further researches should consider causal relationships. As regards methodology, the main limitation of the present study lies in our use of self-report tools and the lack of any clinical assessment. Since alexithymia can hinder individuals' proper identification and description of feelings, future research could include multiple informants, also considering the clinician's opinion.

DATA AVAILABILITY STATEMENT

The datasets analyzed for this study will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by "Comitato Etico per la Ricerca Clinica" Aulss 16 Euganea. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

AR: wrote the first draft of this paper, literature review, and discussion of results. CA: wrote the first draft of this paper, data analysis, and discussion of results. PV: database and discussion of results. MM: discussion of results, and wrote revisions. MG: study design, discussion of results, and conclusion.

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SYSTEMATIC REVIEW
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The Impact of Alexithymia on Treatment Response in Psychiatric Disorders: A Systematic Review

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Treatment of psychiatric disorders relies heavily on a trial and error approach, often prolonging the time required to obtain symptomatic improvements. The identification of reliable predictors of treatment response is instrumental to enact an individualized approach. Alexithymia represents a personality trait reflecting an intrinsic difficulty in recognizing the emotional components of subjective experiences. Thus, its modulating role on treatment outcome has gathered substantial attention during the past years. In the present paper, we aimed at exploring the available evidence for Alexithymia role in influencing the treatment outcome on a wide range of psychiatric conditions by means of a systematic review.

Data Source: We performed a systematic review in Medline and Scopus, augmented by tracking the reference list of the pertinent articles.

Inclusion Criteria: To be included in this review, research studies had to assess alexithymia impact on a treatment intervention delivered to manage a primary psychiatric disorder.

Study Evaluation and Data Synthesis: After removing duplicates, titles were screened first, then abstracts, and last full texts were read, eventually leading to the inclusion or exclusion of the papers according to the criteria established before the online search. Then results of the search were downloaded in.xml format and uploaded in Rayyan, a free web software, that helps expedite the initial screening of abstracts and titles using a process of semi-automation while incorporating a high level of usability. After uploading, screening of the literature was performed in blind by two investigators. Disagreement between reviewers was resolved by joint discussion with a third senior investigator. The quality of evidence was assessed using the Newcastle Ottawa Scale. Thereafter, the data considered relevant was extracted and synthetized in this paper.

Results: Our search yielded a total of 30 articles dealing with a wide range of psychiatric conditions and exploring both pharmacological and psychotherapeutic interventions. Several lines of evidence suggest a complex role for alexithymia in influencing the

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psychiatric treatment outcome, further underscoring the need for additional research in this area to better address the existing knowledge gaps.

Keywords: depression, longitudinal, personality disorders, systematic review, eating disorders

INTRODUCTION

Psychiatric disorders exact a large toll on society at a global level (1, 2). The epidemiological figure in 2016 showed that more than one billion people worldwide were affected by mental or addictive disorders making up about 16% of the world's population (2). This determines the very high levels of disability exemplified by the 162.5 million Disability-Adjusted Life Years lost in 2016 (2). In turn, this substantial burden of illness is responsible for the enormous socio-economic costs associated with psychiatric disorders (3).

In this context, reducing the burden of psychiatric illness is vital. Several approaches, including those at large scale, have shown their effectiveness in decreasing the impact of these severe chronic disorders (4, 5). These include interventions that can be implemented in parenting, at schools, at the workplace, in older age, and that focus, among the others, on the innovative use of technological platforms to enhance access, cut costs, and reduce stigma (5). However, direct interventions on psychopathological symptoms, either pharmacological or non-pharmacological, remain the backbone in the clinical management of psychiatric disorders. For instance, historical trends showed that the advent of antipsychotic treatment improved significantly the clinical outcome of patients affected by schizophrenia (6). Yet, the prevalence of common psychiatric disorders has remained unchanged in the last decades (7), suggesting that, even if psychological and pharmacological treatment are effective, several factors might reduce their capacity of decreasing their burden.

In this context, the search for moderators of treatment response has received much attention in the past years. The identification of these factors (clinical and/or biological) might ideally lead to accurate predictive models of response to treatment. Indeed, machine learning algorithms were able to identify relatively accurate predictive models of resistance to antidepressant treatments relying solely on patient self-reported measures (8). Of interest, some clinical factors, such as low energy or presence of psychosis, were among the contributors to the risk of treatment resistance (8). Acting on factors that might limit the effectiveness of treatments, either with primary or secondary/tertiary preventive strategies, might decrease the burden of these severe chronic disorders.

In this context, alexithymia represents a promising candidate. Since its introduction as a psychological construct (9), research has focused on the delineation of its clinical (phenotypic), neurophysiological, neurobiological, and genetic underpinnings (10, 11). These investigation have helped in delineating the developmental trajectory of alexithymia, with the recognition that there might be an etiological heterogeneity leading to the manifestation of alexithymia (12). Indeed, Messina et al. have postulated that at least three forms, primary, secondary, and organic, might characterize alexithymia (12). The presence of contributing factors to the development of alexithymia acquires importance in light of the possibility of reducing its detrimental impact on the effectiveness of treatments. Indeed, the literature shows that alexithymia is a potent predictor of resistance to treatment, and this effect extends beyond the area of psychiatric disorders as testified by the evidence gathered in somatic disorders such as gastrointestinal (13) and dermatologic (14) conditions, among the others. Furthermore, alexithymia can be a precipitating factor of suicidal behavior in patients affected by psychiatric disorders (15–17).

In this manuscript, we aim to perform a qualitative assessment of the literature on the moderating role of alexithymia on psychological and pharmacological interventions in common psychiatric disorders.

Our group has previously investigated the impact of alexithymia on the treatment of eating disorders (18), highlighting: 1) its significant role in modulating the effectiveness of interventions, and 2) that alexithymia levels remain often elevated even in the presence of symptomatologic relief in other dimensions. Building on this work, we expanded the systematic search updating the results on eating disorders and summarizing findings for each diagnostic category.

Aim

As summarized above, there is consistent evidence pointing to a role of alexithymia in moderating treatment response. It is conceivable that higher levels of alexithymia before treatment initiation might reduce the response to the intervention. In addition, the impact of alexithymia could be more prominent in specific diagnostic categories (for instance, anxiety or eating disorders, than in others, such as psychosis). In this context, we performed a systematic review of the available literature with the aim of clarifying to what extent alexithymia exerts its moderating role on treatment response.

METHODS

Systematic Assessment of the Literature

We performed a systematic review in Medline and Scopus according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (19) (**Figure 1**) using the following search string: "Alexithymia" AND ("treatment" OR "drug" OR "pharmacotherapy"). The search was performed on October 28, 2019. This search strategy was augmented by identifying additional original reports by tracking citations from reference lists of included articles. After removing duplicates, titles were screened first, and those clearly not in line with the purpose of

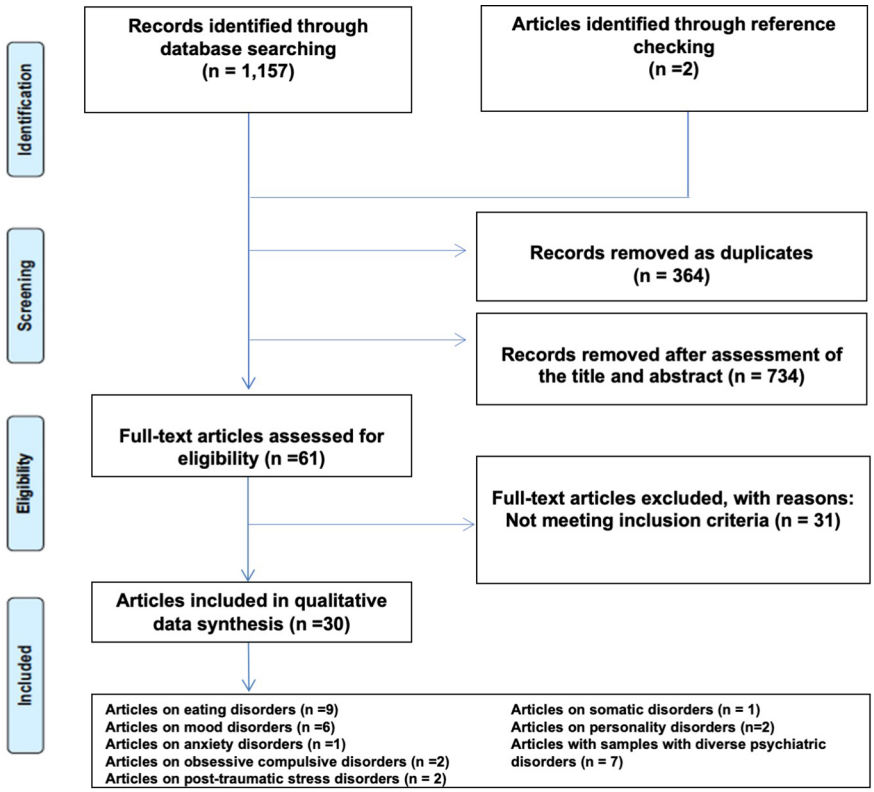

FIGURE 1 | PRISMA flowchart of the study selection.

the review were excluded. Then abstracts were assessed, and last full texts were read, eventually leading to the inclusion or exclusion of the papers, according to the criteria established before the online search. The systematic review of the literature was performed on Medline and Scopus. Then results of the search were downloaded in.xml format and uploaded in Rayyan, a free web software, that helps expedite the initial screening of abstracts and titles using a process of semi-automation while incorporating a high level of usability (20). After uploading, screening of the literature was performed in blind by two investigators (MM and PP). Disagreement between reviewers was resolved by joint discussion with a third senior investigator (FP). The quality of evidence was assessed using the Newcastle Ottawa Scale (NOS) (21).

Inclusion and Exclusion Criteria

To be included in the review, research studies had to: (a) deal with patients affected by a primary psychiatric disorder (excluding substance use disorders), without limits of age; (b) involve the application of any kind of pharmacological or non-pharmacological treatment; (c) assess alexithymia and the impact of alexithymia on a treatment intervention using a validated standardized assessment tool; (d) be written in English. We excluded reviews and meta-analyses of the literature, case reports, and case series from the systematic appraisal.

Data Extraction

The following data considered relevant for the systematic search were extracted from each study and tabulated in a data management software: authors, year of publication, study objectives, study design, clinical methodology, assessment tool of alexithymia, type of treatment, diagnostic assessment tools, diagnosis, findings.

RESULTS

Literature Search and Selection of Papers

Our systematic search identified 1,157 papers (440 from Medline and 717 from Scopus). 2 papers were added through accurate check of reference lists. After removing 364 duplicates, 795 papers were screened for an initial assessment. We then excluded 734 papers through the assessment of the title and abstract content. The PRISMA selection process is illustrated in **Figure 1**.

Quality Assessment

The NOS scale average score for the included studies was 3.7 (standard deviation, ± 1.3). The assessment scores are available in the **Supplementary Table**.

Assessment Tools of Alexithymia

The majority of studies employed the Toronto Alexithymia Scale 20 items (TAS-20) (22, 23) and its older 26-item version (24). One study applied the Alexithymia Provoked Response Questionnaire APRQ (25).

Included Studies

Thirty studies were included in the final systematic assessment. Extracted data are presented according to the main diagnostic outcome as detailed below. We created a miscellaneous disorders category for studies where multiple diagnoses were reported.

Alexithymia in the Treatment of Mood Disorders

Our systematic search identified six studies examining the role of alexithymia in the treatment of mood disorders. Ozsahin et al. (26) conducted the first follow-up study to assess the impact of alexithymia on response to antidepressant treatment and the impact of antidepressant treatment on alexithymia levels in patients affected by major depression (MD). The working hypothesis was to investigate the influence of alexithymia on the short-term outcome of treatment. The study sample included 65 outpatients with MD, 32 with alexithymia, and 33 devoid of alexithymia, who were treated with paroxetine, 20 mg/day for 10 weeks. Over the course of treatment, changes in HAM-D scores were found to correlate significantly with baseline alexithymia levels measured using TAS-20. Conversely, changes in TAS-20 scores failed to correlate with baseline levels of depression. The percentage of responders, defined by a 50% decrease in total HAM-D scores versus baseline, was 21.9% in the alexithymia group and 54.5% in the group without alexithymia. Following treatment, 31.2% of basal alexithymia patients had returned to the category of non-alexithymia patients, obtaining a cut-off score at TAS-20 below the threshold for alexithymia, while alexithymia persisted in 68.8% of cases. Response to antidepressant treatment was observed in 50% of patients who were no longer alexithymic compared to baseline, and in only 9.1% of patients with persistently stable alexithymia. Based on these findings, the authors highlighted the potential of alexithymic features and stability of alexithymia to produce a negative influence on short-term response to antidepressant treatment in patients with MD. Subsequently, Ogrodniczuk et al. (27) conducted a retrospective study to assess the potential role of alexithymia in predicting the persistence of residual symptoms following short-term individual psychotherapy. A sample of 33 outpatients with a diagnosis of unipolar MD was studied. Data relating to all patients selected were extrapolated from a randomized controlled study of two forms of short-term individual psychotherapy (interpretative and supportive); patients all responded positively to psychotherapy, as attested by scores obtained at the Beck Depressive Inventory (BDI) (50% reduction in scores obtained at BDI rating scale and a post-treatment BDI score equal to or lower than 8). Concomitant to psychotherapy, 52% of patients received antidepressant treatment (tricyclics or selective serotonin reuptake inhibitors) for a period of at least 6 weeks. Residual depressive symptoms were observed in 82% of recruited patients. No significant correlations were revealed between baseline levels of depression and levels of alexithymia and individual factors at TAS-20, thus underlining a scarce association between alexithymia and severity of depressive symptoms at baseline. Scores obtained for DIF factor at TAS-20 were predictive of the severity of residual symptoms (measured using BDI) to a considerably higher extent than initial levels of depression and anxiety, type of psychotherapy, and use of antidepressants. The authors concluded that difficulty in identifying feelings may impact on the subject's ability to effectively benefit from psychotherapy and might consequently be considered a factor underlying the persistence of residual symptoms. The results obtained also support the notion according to which alexithymia and depression are separate constructs, particularly bearing in mind the scarce correlation between baseline levels of depression and scores relating to alexithymia factors. Even when giving due consideration to the effect of initial levels of depression and anxiety, to the form of psychotherapy received and to the use of antidepressants, scores relating to the "Difficulties Identifying Feelings" (DIF) factor of TAS continued to act as a predictor of the severity of residual symptoms. A possible explanation for the association between DIF and residual symptoms might lie in the patient's inability to identify his or her feelings, thus potentially compromising the ability to effectively share these feelings and emotional problems with the therapist who, faced with a series of vague complaints may not be able to develop an effective treatment plan for the patient. Moreover, the ability of the patient to understand the measures implemented by the therapist relating to his or her feelings may be compromised. Given the importance in psychotherapy of working with feelings and bearing in mind the difficulty of alexithymic patients of sharing their feelings, treatment may not achieve the desired efficacy. Based on the hypothesis of a series of authors who considered alexithymia a stable characteristic capable of hindering a favorable outcome to psychotherapy, Spek et al. (28) conducted a study to assess whether alexithymia was a stable or changeable trait when associated with a change in depressive symptoms, and whether the pre-treatment presence of alexithymia prevented the patient from benefitting from psychotherapeutic treatment. A sample of 129 subjects affected by sub-threshold depression (presence of significant depressive symptoms although not sufficient to meet DSM-IV criteria for a diagnosis of major depression) underwent cognitive behavioral therapy. The type of outcome was defined according to the change in depressive symptoms as measured by BDI, from the pre-treatment to the post-treatment stage and at 1-year follow-up. Changes in depressive symptoms correlated significantly with changes in alexithymia, measured using TAS-20, thus demonstrating how alexithymia is actually a less stable trait than frequently maintained. Baseline alexithymia levels were not indeed correlated with treatment outcome. The authors hypothesized that this finding, at variance with other studies using different forms of psychotherapy, may be related to the possibility that CBT represents a less problematic treatment option in alexithymia patients. Gunther et al. (29) carried out a prospective study to evaluate the association between pre-

treatment alexithymia levels (TAS-20) and depressive symptoms at follow-up (7 weeks) following multimodal inpatient treatment. Forty-five patients admitted for acute MD who had taken part in a multimodal treatment program comprising both individual therapy and psychodynamic-interactional oriented group therapy were studied. The majority of patients were also prescribed antidepressant treatment. Of all TAS-20 factors, only scores obtained for the "Externally Oriented Thinking" EOT factor were predictive of the severity of depressive symptoms at follow-up, when measured using both self-administered questionnaires (BDI-II) or clinician-administered scales (HAM-D). A higher baseline score for the EOT factor correlated with more severe depressive symptoms, even following evaluation of potential confounding factors, such as baseline levels of anxiety and depression. Total baseline scores at TAS-20 were predictive for severity of depressive symptoms measured by means of BDI, but not HAM-D. A moderate correlation was moreover revealed between alexithymia (DIF and "difficulties describing feelings" DDF factors) and self-reported depressive symptoms at baseline, in accordance with previous studies reporting a moderate correlation between DIF and DDF, but not EOT, with depression (30). Furthermore, alexithymia was found to be a stable trait, as a significant reduction in scores at BDI-II and HAM-D failed to correspond to a significant change over time in scores obtained at total TAS-20 and factors DIF, DDF, and EOT. The impact of alexithymia in terms of outcome was demonstrated for the EOT factor, but not for DIF and DDF. Several authors maintain that the EOT factor is a fundamental characteristic of alexithymia and emotional ability (31). DIF and DDF factors have been subject to debate due to their sensitivity to a series of biases in assessing the emotional ability of an individual (self-critical response biases, perfectionism, mood-congruent memory biases). The finding of elevated scores for DIF and DDF in depressed patients may indeed correlate not only with a more marked level of alexithymia, but also with a singular predisposition to provide specific answers induced by the state of depression. Conversely, the EOT factor may well be less susceptible to this type of response bias, focusing tendentially on the subject's preferences and habits, and may result in a more precise indicator of the alexithymic construct in clinical populations. The authors suggest that patients affected by MD with a more externally oriented cognition and lower interest in intrapsychic conflicts may derive less benefit from a multimodal therapeutic approach (including psychodynamic interactional therapy, antidepressant medication, and complementary therapies). Bearing in mind that the program used envisaged a series of therapeutic approaches, it is unclear which aspect of the treatment (group or individual psychotherapy, antidepressant drugs or complementary therapies) may prove less effective in the presence of an externally oriented cognition. In a study conducted by Bressi et al. (32), the authors evaluated the efficacy of Short-Term Psychodynamic Psychotherapy (STPP) using Mentalization-Based Techniques (STMBP) on the clinical outcome of 274 patients affected by MD, focusing on the impact of Reflective Functioning (RF) and baseline alexithymia on treatment outcome. The duration of treatment was 40 weeks, and patients were assessed at T0, T1 (after 40 weeks) and T2 (after 1-year follow-up). All patients recruited to the study were receiving antidepressants (SSRIs or SNRIs). Treatment proved effective on both depressive symptoms (HAM-D) and levels of alexithymia. A significant reduction of scores for the EOT factor and, to a lesser extent DIF, was observed between T0 and T1. A further improvement of alexithymia, limited to EOT, was subsequently observed at follow-up. Higher levels of depression at HAM-D and higher levels RF at T0 were predictive of a worse treatment outcome. Alexithymia levels (TAS-20) at T0 displayed no significant impact in terms of outcome. Quilty et al. (33) investigated the role of alexithymia in predicting the therapist- and patient-rated therapeutic alliance and response to psychotherapy (CBT and IPT) in a sample of patients with MD. Seventy-five adults affected by MD were randomized to two treatment arms comprised of weekly individual sessions of CBT or IPT over a period of 16 weeks. Scores obtained at TAS-20 and factor DIF correlated with a negative impact on the patient-rated therapeutic alliance at week 13; at week 13, DIF factor alone displayed a negative impact on therapist-rated therapeutic alliance. Path models supported the hypothesis of a direct negative effect of alexithymia on response to treatment by means of a negative association with therapeutic alliance. More specifically, alexithymia was negatively associated with the alliance which, in turn, was positively associated with the change in depression registered during treatment. Contrary to expectations, scores for the EOT factor negatively correlated with the severity of depression at week 13 (pre-treatment, a rise in EOT corresponded to a decrease in severity of depression) and correlated positively with the change in depression (pre-treatment, a rise in EOT was associated with a more marked change in levels of depression from week 1 to week 13). Data present in literature in line with the hypothesis whereby therapists were negatively influenced by the alexithymic features of their patients were further confirmed by the findings of the present study that highlighted the impact of alexithymia on patient-rated perception of therapeutic alliance, including perception of the understanding and involvement of the therapist. Moreover, the results of the study invite us to reflect on the impacts produced by the different facets of the alexithymic construct in terms of clinical outcome. The study conducted by Quilty et al. (33) revealed a negative prognostic role of alexithymia in general, and of the DIF factor on patient-rated therapeutic alliance, and a positive prognostic role of the EOT factor on depression. The authors underlined the possibility that the DIF factor might impact on fundamental psychotherapeutic activities such as cognitive restructuring, which may be limited to those patients unable to adequately express their feelings. On the other hand, it may be the case that the EOT factor in depressed patients correlates with a decrease in ruminative thinking and, hypothetically, with more adequate adaptive and problem-focused coping strategies. The therapeutic strategies used for the purpose of the study (CBT and IPT), in view of their characteristics as active and objective-oriented treatments, may explain the reduced impact of alexithymia in

negatively affecting outcome of the study treatment, at variance with other studies conducted using a different approach (27). All these findings are summarized in **Table 1**.

Alexithymia in the Treatment of Eating Disorders

Nine studies investigating the role of alexithymia in eating disorders were identified by our systematic search. Schmidt et al. (34) were the first to analyze the impact of alexithymia on response to short-term pharmacological treatment of bulimia nervosa (BN). Forty-one female outpatients with a diagnosis of BN according to DSM-III-R were recruited to a 10-week prospective study of patients receiving fluvoxamine treatment. Alexithymia levels failed to correlate with any of the other variables investigated at either baseline or T1. On completion of treatment, higher TAS scores registered at T1 correlated with a persistently higher number of episodes of binge eating. Overall, post-treatment, no significant change in total TAS scores was registered versus baseline, although the eating pathology displayed a marked improvement. The authors hypothesized that the persistence of eating symptoms and a failure to achieve recovery during treatment might correlate with the presence and persistence of elevated TAS scores. The concomitant absence of a significant change in TAS following treatment, albeit in the presence of an improvement of the eating disorder (ED), appeared to suggest that alexithymia should not be seen as a dimension that correlates exclusively with the ED trend, but rather as an independent feature. Subsequently, de Groot et al. (35) assessed the impact of alexithymia on response to a 9.6-week intensive group psychotherapy program focused on nutrition, body image, management of symptoms, relationships, and family interactions (Toronto Hospital Day Hospital Program for ED). The sample was comprised of 31 women with severe BN according to DSM-III-R, and a control group of 20 healthy subjects (all nurses) was set up. On completion of treatment, patients who were more alexithymic at T1 were also found to be those most affected by both ED symptoms and depression. Although on completion of treatment patients' mean alexithymia levels remained high - considerably higher than those of healthy controls, overall treatment had produced a positive impact not only on eating symptomatology, but also on alexithymia levels, particularly in a subgroup of patients who had been devoid of binge episodes and vomiting (abstinent) over the 28 days prior to discharge. The authors linked the partial reversibility of alexithymia to a series of factors, including a direct effect of treatment, reduction of associated depressive symptoms, and reduction of eating symptomatology. A cross-sectional study conducted by Beales et al. (36) studied a total of 79 women affected by severe, chronic ED treated with a range of therapeutic options, who were divided into 3 groups — anorexic, bulimic, and recovered — according to EDI-2. Scores obtained at TAS-20 revealed that 65% anorexic, 83% bulimic, and 33% recovered patients were alexithymic, with a significant difference between those presenting with ongoing ED and the group of recovering patients. This led the authors to hypothesize that lower levels of alexithymia may have a potentially relevant impact on the recovery of ED patients. The specific study design prevented assessment of the impact of treatment on alexithymia levels.

Becker-Stoll et al. (37) evaluated 47 female patients with ED diagnosed according to DSM-IV criteria, who attended the Treatment Center for Eating Disorders of the Max Planck Institute of Psychiatry in Munich. A three-phase treatment plan was envisaged: a 4-week outpatient motivation phase, a 4-month day-hospital phase, and a 4-month outpatient follow-up treatment phase. Treatment options included Cognitive Behavioural Therapy (CBT), Interpersonal Therapy (IPT) and Psycho-educational Therapy (PET). During group psychotherapy sessions, art therapy, among others, was used to stimulate the identification and expression of feelings. Post-treatment, both eating symptomatology and alexithymia improved irrespective of diagnosis. The most significant impact produced related to the factor DIF, while EOT was impacted only marginally. Despite evidence of an improvement of alexithymia, patients displayed an ongoing tendency towards alexithymia. No correlation was detected in the study between baseline TAS and outcome variables. Conversely, high TAS scores registered post-treatment, indicating persistent alexithymia, correlated with an increased severity of eating symptoms and a less favorable prognosis. In a subsequent study, Shiina et al. (38) investigated the effectiveness and predictors of drop-out in a treatment program comprised of 10-week outpatient group therapy combining CBT with assertiveness training and self-esteem building therapy (combined group CBT). The final stages of treatment envisaged two role-play sessions during which patients were expected to identify and try to express their feelings. Treatment produced a positive effect on both eating pathology and alexithymia, self-esteem, and social functioning. Baseline alexithymia levels were not predictive of drop-out. In 2007, bearing in mind the limitations of the previous studies, Speranza et al. (39) carried out a long-term naturalistic prospective study with 3-year follow-up to evaluate the impact of alexithymia on the outcome of an outpatient sample of ED patients who underwent a range of therapeutic interventions available in routine clinical practice. The sample was made up of 102 young women affected by severe, chronic ED, 39 of whom with BN and 63 with AN. Exclusion criteria included major depressive episode or ongoing substance or alcohol addiction. Two categories of clinical outcome were envisaged: "favorable outcome" with full remission of eating symptoms at follow-up, and an "intermediate/unfavorable outcome" with persistence of a subsyndromal pattern or full ED diagnosis at follow-up. At 3-year assessment 75% of patients displayed an "intermediate/unfavorable outcome" and 25% "favorable outcome". The majority of patients had undergone at least one form of therapeutic intervention over the three-year period, mainly psychotherapy (57%) or treatment for depression (40%). DIF factor of TAS-20 was found to be a significant predictor of unfavorable outcome. The predictive power of this factor persisted, although to a lesser extent, in a second predictive model taking into account depressive symptoms, clinical severity of the disorder, and treatment prescribed. Patients experiencing

TABLE 1 | Studies investigating the impact of alexithymia on treatment outcome in mood disorders.

Reference	Objectives	Study design	Sample size	Standardized assessment of alexithymia	Treatment	Assessment tools	Diagnosis	Results
Ozsahin et al., (26)	To investigate the influence of alexithymic features on depression treatment outcome, along with the eventual change in alexithymia burden over the course of treatment.	Prospective design with patients evaluated before beginning treatment (T0), and post-treatment (T1) after 10 weeks.	65 (32 alexithymic and 33 non-alexithymic)	TAS-20	Antidepressant (i.e. Paroxetine)	SCID for DSM-IV, HAM-D	MDD	At T1 a positive correlation was described between HAM-D and TAS-20, with a significantly greater HAM-D score reduction among non-alexithymic individuals.
Ogrodniczuk et al. (27)	To investigate the association between alexithymia and residual symptoms among short-term psychotherapy responders in the outpatient setting.	A 20-week RCT including individuals randomly assigned to receive either interpretative or supportive psychotherapy	33	TAS-20 DIF, DDF, EOT	20 weekly sessions of either interpretative or supportive psychotherapy (17/33 concomitantly received antidepressant medication, either a SSRI or a tricyclic; these individuals were equally distributed between the 2 study groups)	Computer assisted SCID I and II for DSM-III R, BID assessed pre- and post-treatment, STAI	MDD	No association was found between baseline alexithymia and baseline depression severity; DIF was significantly associated with residual depressive symptoms.
Spek et al. (28)	To investigate the interplay between alexithymia and CBT outcome at 12 months follow-up	Prospective design with 1-year follow-up	119	TAS-20	CBT psychotherapy	BDI	Subthreshold MDD	Changes in alexithymia were significantly correlated with BDI changes, however no significant association was found between pre-treatment alexithymia and treatment outcome.
Gunther et al. (29)	To study the relationship between alexithymia and symptom severity after a course of	Prospective design with assessments performed after an average of 2 weeks from admission (T0) and at 7 weeks after starting therapy (T1)	45	TAS-20 DIF, DDF, EOT	Psychodynamic interactional psychotherapy (at T1 33/45 individuals were also taking antidepressants)	BDI-II, HAM-D, SCID for DSM-IV, STAI	MDD	Baseline EOT (T0) predicted depressive symptom burden at T1.
Bressi et al. (32)	A 12-month follow-up study exploring the effectiveness of STMBP in MDD (1), the possible correlation among alexithymia and reflective functioning (2), the correlation among clinical variables and their eventual impact on TAS-20 and HAM-D	Prospective design with assessments (GAF, HAM-D, TAS-20) at baseline (T0), after 40 weeks (T1) and at 12 months follow-up (T2)	24	TAS-20	40 weekly session of STMBP; all study participants were taking antidepressant medications (SSRI, SNRI); during the follow-up no medication allowed except for occasional BDZs administration	AAI-RF, GAF, HAM-D	MDD	A reduction in HAM-D and TAS-20 scores was described, along with a negative correlation between RF and TAS-20 score.
Quilty et al. (33)	To test the role of alexithymia in influencing CBT and IPT treatment	An 16-week RCT with patients randomized	75	TAS-20 DIF, DDF, EOT at baseline	16 weekly sessions of either IPT or CBT (no antidepressant	BDI-II and CALPAS at 3-8 and 13 weeks; SCID	MDD	A negative correlation was described for EOT and 13-

(Continued)

TABLE 1 | Continued

Reference	Objectives	Study design	Sample size	Standardized assessment of alexithymia	Treatment	Assessment tools	Diagnosis	Results
	outcome in MDD affected individuals.	either to IPT or CBT (38 to IPT, 37 to CBT)			medication was allowed during the trial)	for DSM-IV, HAM-D		week depression burden; an increased alexithymia level was also associated with lower alliance score

AAI-RF, Adult Attachment Interview-RF; BDZ, benzodiazepine; BID, Beck Depression Inventory; CALPAS, California Psychotherapy Alliance Scale; CBT, cognitive behavioral therapy; DIF, TAS-20 factor 1 Difficulty Describing Feelings; DDF, TAS-20 factor 2 Difficulty Identifying Feelings; DSM-III, Diagnostic and Statistical Manual of Mental Disorders III edition; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders IV-edition; HAM-D, Hamilton Depression Rating Scale; IPT, Interpersonal Therapy; MDD, major depressive disorder; RCT, randomized controlled trial; RF, reflective functioning; SCID, Structured Clinical Interview for DSM-IV; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; STAI, Spielberger State Trait Anxiety Inventory; STMBP, Short-Term Psychodynamic Psychotherapy with Mentalization-Based Techniques; TAS-20, Toronto Alexithymia Scale 20 items.

more difficulty in identifying their feelings at baseline were more frequently symptomatic at follow-up, displaying a substantially less favorable clinical course. Tchanturia et al. (40) conducted a cross-sectional study to evaluate a sample of 148 subjects, 105 of whom with either ongoing ED or recovered meeting DSM-IV criteria, in comparison with a group of healthy controls (n = 43) with no family or personal history of mental disorders. Patients with ongoing ED displayed higher levels of alexithymia and social anhedonia versus recovered patients, collocated on an intermediate level, and healthy controls who registered the lowest levels of alexithymia at TAS-20. A significant correlation was revealed between persistence and severity of ED symptoms and higher levels of alexithymia and social anhedonia. This correlation remained even when depression was taken into account in analysis. A study by Balestrieri and colleagues (41) analyzed the factors underlying response to a short-term (10 weeks) psychoeducational outpatient group treatment. The study was conducted on a sample of 98 patients (91% women) with a diagnosis of BED (n=54) and EDNOS (n=44) according to DSM-IV. Each treatment session included nutritional counselling, analysis of thoughts and behaviors correlated with ED, and assertiveness training. On completion of treatment patients displayed an improvement, although of negligible clinical significance, in total TAS scores. Lower levels of alexithymia at baseline were predictive of a higher probability of patients achieving recovery from ED following treatment. Finally, Ohmann et al. (42) studied 29 adolescent girls with AN in a 10-month multimodal group CBT study conducted in an outpatient setting. Treatment provided for nine modules (therapeutic motivation, psychoeducation, individual problem analysis, teaching of problem-solving strategies, soft and communication skills, hedonistic training, elements of awareness, body, and schema psychotherapy) and monthly family sessions. On request, individual CBT sessions were arranged. Three separate patient groups were subsequently obtained on the basis of outcome: good outcome (n=16), bad outcome (n=5), drop-out (n=8). Evaluations made throughout the different treatment stages (3, 6, 9, and 12 months after onset and 1 year after completion of treatment) revealed lower levels of alexithymia in the good outcome group of patients compared to the bad outcome and drop-out groups. Alexithymia was shown to be a factor resistant to change, particularly in patients with a bad outcome, even in the presence of improvement of other clinical variables including BMI, eating habits, mood, social anxiety, personal care, and self-efficacy. These findings are summarized in **Table 2**.

Alexithymia in the Treatment of Anxiety Disorders

A study carried out by Rufer et al. (43) is the sole study to have specifically investigated the role of alexithymia as a predictor of outcome in the treatment of anxiety disorders. In the context of a naturalistic study, the authors assessed the impact of alexithymia on the outcome of a short-term cognitive-behavioral group therapy (CBGT) lasting 5 weeks. Fifty-five consecutive outpatients with panic disorder (PD), 58% of whom without agoraphobia and 42% with agoraphobia, were enrolled. Forty percent of patients presented with comorbidity of one or two Axis I disorders, mainly major depression. Patients underwent CBGT and were assessed at baseline, post-treatment, and at follow-up 6 months after completion of treatment. Thirty-five percent of patients were on concomitant antidepressant treatment. Baseline alexithymia levels were not predictive of the outcome of CBGT either post-treatment or at 6-month follow-up. Conversely, the presence of comorbidity with Axis I disorders was predictive of outcome post-treatment but not at follow-up. A comparison between treatment completers and non-completers and follow-up completers and non-completers failed to reveal any significant differences in alexithymia levels. Over the course of treatment, a reduction in scores obtained for total TAS-20 and factors DIF and DDF of TAS was observed, but not for factor EOT, which remained substantially stable. A tendency towards improvement of alexithymia during treatment persisted even after verifying the potential influence of depression which strongly correlated with alexithymia pre-treatment. The authors suggest that failure to detect a negative impact of alexithymia on outcome of CBGT treatment may be attributable to the efficacy of this psychotherapeutic approach on the type of patient studied, not focused specifically on the degree

TABLE 2 | Studies investigating the impact of alexithymia on treatment outcome in eating disorders.

Reference	Objectives	Study design	Sample size	Standardized assessments of alexithymia	Treatment	Assessment tools	Diagnosis	Results
Schmidt et al. (34)	To investigate alexithymia prevalence among individuals affected by DSM-III defined eating disorders as compared with healthy controls (1), eventual differences in alexithymia prevalence among the included nosological categories (2), alexithymia persistence in these conditions (3), the predicting value of alexithymia for short-term treatment outcome (4)	Combination of cross-sectional study and of a 10-week double blind placebo-controlled trial	(a)173 F cases (93 BN, 55 AN/R, 25 AN/BN); 95 healthy controls (48 F, 47 M). (b)41 F individuals affected by BN	a. TAS-26 b. TAS-26	(b) Fluoxetine vs placebo	a. BITE, BSQ b. BITE, BSQ, HAM-D	AN/RN, AN/BN, BN	(a)Cases had a significantly higher alexithymia prevalence than controls. TAS did not correlate with BMI, BITE, BSQ. (b)TAS at t0 correlated with TAS at t1 but did not correlate to any other variable. TAS at t1 positively correlated with rater-assessed binge.
de Groot et al. (35)	To estimate alexithymia prevalence among women affected by DSM-III defined BN treated in a DH (1), alexithymia relationship with somatic symptoms and depression (2), efficacy of group psychotherapy in reducing alexithymia burden	Prospective study with assessments pre- and post-treatment; case control analysis with a comparison group assessed at 1 point only	31 cases, 20 controls	TAS-26	Psychotherapeutic group focusing on body image, nutrition, family interactions and symptoms management (average duration of treatment 9.6 weeks)	BDI, EDE, EDI	BN	A greater proportion of BN affected individuals presented alexithymia as compared with healthy controls before treatment (t0); post-treatment (t1) there was a significant reduction in alexithymia proportion among BN individuals, but it persisted at a higher level than the comparison group
Beales et al. (36)	To explore the presence of alexithymic features in a selected group of individuals affected by ED and the potential implications of the said features for the primary care setting	Survey	79	TAS-20		EDI-2, 16-PF5,	AN/R, BN and RV	A higher prevalence of alexithymia was found among AN/R and BN groups as compared with the R group; 16PF5 social skills domain negatively correlated with alexithymia
Becker-Stoll et al. (37)	To investigate the potential efficacy of an intensive 4-month intervention program on alexithymia in ED (DSM-IV defined) and the possible alexithymia role in predicting treatment outcome	Prospective design with assessments performed before (t0) and after treatment (t1)	47	TAS-20	A 4-month psychotherapeutic program employing interpersonal, cognitive-behavioral and psychoeducational methods.	EDI	AN, BN, EDNOS	There was a significant reduction in both EDI-2 and TAS-20 (especially DIF) at T1. TAS-20 score at T1 correlated with EDI2 at T1 and with a worse prognostic outlook; there was no significant correlation between TAS at t1 and the recovery state
Shiina et al. (38)	To study the efficacy of a CGCBT for BN affected individuals in the outpatient setting, further exploring the characteristic of individuals failing to respond under such treatment	Prospective design with assessments at the beginning (T0) and at the end of the treatment course (T1)	25	TAS-20	1-h weekly sessions of CGCBT over a 10-week period, including diet psychoeducation, social skill training, self-esteem enhancement, coping training for interpersonal problems	BITE, CGI-C, CGI-S, EDI-2, GAF, HAM-D, RSES	BNP, ANBP, BNNP, EDNOS	Among the 16 individuals that completed the treatment course, at T1 there was a significant reduction in BITE, GAF, EDI-2, RSES scores as compared with T0; mean TAS-20 scores showed a non-significant reduction ($p = 0.06$). No significant association was found

(Continued)

TABLE 2 | Continued

Reference	Objectives	Study design	Sample size	Standardized assessments of alexithymia	Treatment	Assessment tools	Diagnosis	Results
								between TAS-20 and treatment outcome.
Speranza et al. (39)	To investigate the influence of alexithymia on treatment outcome in a large sample of ED affected individuals	3-year longitudinal study	102	TAS-20 DIF, DDF, EOT	Due to the naturalistic study design no treatment was specifically recommended; of the total sample 57% was undergoing psychotherapy, 40% was on antidepressants	MINI, BDI-13, CGI-S, PSRS	ED	At the 3-year follow-up assessment 76 patients were judged to have an unfavourable prognosis with DIF being a significant predictor of a negative outcome
Tchanturia et al. (40)	To explore the complex interplay between ED, social anhedonia and alexithymia	Observational study	148	TAS-20 DIF, DDF, EOT	Due to the observational nature of the study, no specific treatment was recommended	SCID for DSM-IV, DASS, EDE-Q, RSAS	AN, BN	A positive correlation was described between social anhedonia and alexithymia
Balestrieri et al. (41)	To explore the efficacy of a 10-week psychoeducational group program among BED and EDNOS affected individuals, and the persistence of its eventual benefits	A 1-year follow-up study with assessments before treatment (T0), after treatment (t1) and at 1-year follow up (T2)	98	TAS-20	10-week psychoeducational group including nutritional interventions and thoughts related to eating disorder along with assertiveness training. After the first 10-weeks, those individuals still satisfying ED criteria were involved in a further extension protocol comprising 8 additional monthly sessions	EDI-2, EDI-SC, HADS	BED, EDNOS	A lower or absent alexithymia level was associated with a higher likelihood of responding to treatment
Ohmann et al. (42)	To explore emotional problems of young individuals affected by AN and undergoing GCBT	A 12-month follow-up study with assessments before treatment (T0), during treatment (at 3 and 6 months, T1 and T2, respectively), and post-treatment (T3) after 12 months	29	TAS-26	GCBT focusing on psychoeducation, schema psychotherapy, communication skill training, problem analysis, therapeutic motivation, hedonistic training, problem solving (5 individuals were concomitantly treated with antidepressants)	ASW, BDI, JTCI, MDI, YSR	AN	Only two patients described themselves as not alexithymic. Alexithymia presented a non-significant trend toward improvement in responding individuals.

16PF5, Sixteen Personality Factor Questionnaire 5th Edition; AN/RN, Anorexia Nervosa/Restrictive subtype; AN/BN, Anorexia Nervosa/Bulimic subtype; NBP, Anorexia Nervosa Binge-eating/Purging type; ASW, Assessment of Self-Efficacy; BDI-13, Beck Depression Inventory 13 items version; BITE, Bulimic Investigatory Test; BMI, Body Mass Index; BNNP, Bulimia Nervosa Non-Purging type; BNP, Bulimia Nervosa Purging type; BSQ, Body Shape Questionnaire; CGCBT, Combined Group Cognitive Behavioral Therapy; CGI-C, Clinical Global Impression Change; CGI-S, Clinical Global Impression Severity; DIF, TAS-20 factor 1 Difficulty Describing Feelings; DDF, TAS-20 factor 2 Difficulty Identifying Feelings; DSM-III, Diagnostic and Statistical Manual of Mental Disorders III-edition; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders IV-edition; ED, eating disorders; EDE-Q, Eating Disorder Examination Questionnaire; EDI-2, Eating Disorder Inventory-2; EDI-SC, Eating Disorder Inventory-Symptom Checklist; EDNOS, eating disorder not otherwise specified; EOT, TAS-20 factor 3 Externally Oriented Thinking; GCBT, Group Cognitive Behavioral Therapy; HADS, Hospital Anxiety and Depression Scale; HAM-D, Hamilton Depression Rating Scale; HC, healthy control; JTCI, Junior Temperament and Character Inventory; MDI, Marburg Diagnostic Inventory; MINI, Mini International Neuropsychiatric Interview; PSRS, Psychiatric Status Rating Scale; RAN, recovered anorexia nervosa; RSAS, Revised Social Anhedonia Scale; RSES, Rosenberg Self-Esteem Scale; RV, recovered; SPS, Social Phobia Scale; SIAS, Social Interaction Anxiety Scale; TAS-20, Toronto Alexithymia Scale-20; YSR, Youth Self Report.

of insight nor on verbal interventions, but rather on behavioral "experiments" such as exposure (43). The opportunity for alexithymic patients with PD to experience new emotional events during exposure sessions might motivate patients to modify a series of dysfunctional beliefs and behaviors, in turn capable of impacting positively on their anxiety symptoms. These studies are listed in **Table 3**.

Alexithymia in the Treatment of Post-Traumatic Stress Disorders

Two studies on Post-Traumatic Stress Disorder (PTSD) were identified in our systematic review. The first study to investigate the role of alexithymia as predictor of treatment response in PTSD dates back to 1992 (44). The authors analyzed a sample of 57 Vietnam veterans affected by PTSD according to DSM-III. The impact of alexithymia on response to treatment was evaluated in the context of an 8-week randomized controlled double-blind trial with two treatment arms (imipramine and phenelzine) and 1 placebo arm. All participants underwent concomitant individual psychotherapy based on a short-term psychodynamic approach. Alexithymia levels were assessed using the APRQ. Lower levels of alexithymia were predictive of a better outcome for avoidance items (emotional numbing, distance from others, and efforts to avoid thinking about the traumatic event) on the Impact of Events Scale (IES), irrespective of the severity of trauma. This finding was only relevant for placebo-treated subjects receiving psychotherapy. No impact was observed for on intrusion items of the IES or in pharmacologically-subjects receiving psychotherapy. As all three treatment groups received psychotherapy in addition to the pharmacological agent, the results of the study suggest that psychotherapy alone may not be effective in reducing avoidance symptoms in alexithymic patients with PTSD. More recently, Zorzella et al. (56) examined the role of alexithymia in terms of improvement of trauma-specific difficulties experienced before and after trauma therapy in women with a history of childhood abuse. Date were collected from 167 women enrolled in the Women Recovering from Abuse Program (WRAP), an 8-week multimodal treatment program comprising a series of therapeutic options, both group and individual, specifically devised for women with a history of severe childhood trauma. Contrary to expectations, baseline alexithymia levels were not predictive of the magnitude of change registered post-treatment in PTSD symptoms, dissociation, and interpersonal issues. Higher baseline levels of alexithymia (TAS-20) prior to any form of treatment were found to be predictive of increased severity of PTSD, higher degree of dissociation, and additional interpersonal difficulties. At the same time, improvement in alexithymia levels over the course of treatment correlated significantly with better treatment response in terms of symptoms of PTSD, levels of dissociation, and interpersonal difficulties. The methodology applied in the study does not enable a causal relationship to be established between these variables. These studies are summarized in **Table 3**.

Alexithymia in the Treatment of Personality Disorders

Two studies analyzed the impact of alexithymia on the treatment of personality disorders. The first study to analyze the implications of alexithymia on treatment outcome in personality disorders (PD) was carried out by McMain et al. (51). The authors conducted an exploratory study aimed at investigating the relationship between specific emotional processes and cognitive problem-solving processes and treatment outcome in subjects with borderline personality disorder (BPD). Patients were recruited from an extended sample of subjects enrolled in a randomized controlled study to compare the clinical effectiveness and cost-effectiveness of a yearly program of Dialectical Behavior Therapy (DBT) or General Psychiatric Management (GPM), a multimodal outpatient treatment comprised of individual psychodynamic therapy, case management, and symptom-targeted medication management. The sample selected for the study was made up of 80 subjects, mainly women, all of whom treatment completers, in line with the specific aims of the study. The majority of participants presented with one or more comorbidities with other Axis I and/or Axis II mental disorders (major depressive disorder, anxiety disorders, and substance use disorders). Assessments were carried out at baseline (pre-treatment) and then every 4 months during the course of active treatment. An analysis was conducted to ascertain whether changes observed during treatment (identification of emotions, ability to describe emotions, externalizing, verbalization of positive emotions, affect balance, perceived cognitive problem solving) impacted on treatment outcome. Assessments were made bearing in mind the working alliance, a consolidated outcome predictor. Improvements observed over the course of treatment relating to the ability to identify, describe, and fully experience emotions were associated with a more favorable treatment outcome (symptom distress and interpersonal functioning). Löf et al. (51) conducted a longitudinal naturalistic study aimed at assessing the effectiveness of Mentalization-based treatment (MBT) and psychiatric and psychological moderators of outcome in a sample of 75 patients with BPD. Evaluations were made at baseline and 6, 12, and 18 months after start of treatment. Treatment proved effective on borderline symptoms and on general psychiatric symptoms, suicidality, self-harm, alexithymia, particularly difficult in identifying feelings, and self-image. Alexithymia, similarly to severity of BPD and, in general, to psychological moderators, revealed no predictive effect in terms of outcome. These studies are summarized in **Table 3**.

Alexithymia in the Treatment of Obsessive-Compulsive Disorders

Our systematic review identified two studies assessing the role of alexithymia in obsessive compulsive disorder (OCD) treatment. Rufer et al. (47) evaluated absolute and relative stability of alexithymia in response to treatment and the predictive power of alexithymia on treatment outcome in patients with OCD.

TABLE 3 | Studies investigating the impact of alexithymia on treatment outcome in diverse psychiatric disorders.

Reference	Objectives	Study design	Sample size	Standardized assessments of alexithymia	Treatment	Assessment tools	Diagnosis	Results
Kosten et al. (44)	To explore the complex interplay between alexithymia and treatment outcome in PTSD	An 8-week double blind RCT with randomization to either imipramine, phenelzine or placebo	57	APRQ	8-week course of either imipramine, phenelzine or placebo	IES	PTSD	Alexithymia level was significantly associated with a worse treatment outcome
Bach and Bach (45)	To evaluate pre-treatment alexithymia as a potential outcome predicting factor among individuals affected by SD, along with the assessment of alexithymia level heterogeneity among different diagnostic categories	Prospective design with assessments performed at baseline and at 2-years follow-up	30	TAS-26	Integrated behavioral therapy over a minimum of 8 weeks including exposure, group cognitive therapy, muscle relaxation and assertiveness training	WI, SCID, SCL-90R	SD, PD, HY, USD	A non-significant correlation between higher pre-treatment TAS-26 score and USD persistence at follow-up was described
McCallum et al. (46)	To explore the predicting value of alexithymia and PM	Reanalysis of two previously published clinical trials	251	TAS-20 DIF, DDF, EOT	Either 12 weeks of weekly STGT or 20 weeks of STIT	PMAP	CG, MDD, AVO, DEP, BPD, DST, OCD, PAR	A modest portion of improvement variance was linked to alexithymia and PM in both treatment group.
Rufer et al. (47)	To test the predicting value of alexithymia among OCD patients undergoing CBT	Prospective design with assessment before and after treatment	39	TAS-20 DIF, DDF, EOT	Multimodal CBT (25 individuals received concomitant antidepressant)	Y-BOCS, HAM-D	OCD	Alexithymia level did not predict treatment outcome
Rufer et al. (48)	To investigate alexithymia outcome predicting value for OCD in the long term	A 6-year prospective design with assessments before, after treatment and at 6 years follow-up	34	TAS-20 DIF, DDF, EOT	Multimodal CBT (25 individuals received concomitant antidepressant)	Y-BOCS, HAM-D	OCD	Alexithymia level did not predict treatment outcome at follow-up
Grabe et al. (49)	To explore alexithymia persistence in the inpatient setting and its influence on the outcome	Prospective analysis with assessments at T0 at baseline, T1 at 4 weeks and at discharge T2	297	TAS-20	Treatment duration varied from 8 up to 12 weeks administered in the inpatient setting and included: 3 weekly sessions of psychodynamic STGT and 1 weekly session of individual psychotherapy; daily art, sport, movement and relaxation therapy (medications were administered as needed)	SCL-90R, GSI	AUD, MDD, ADD, SFD, DIS, ED, PED	Higher levels of psychological stress were described among alexithymic individuals as compared with non-alexithymic individuals; alexithymia was not associated with a higher likelihood of early withdrawal from therapy, nor with a higher degree of treatment resistance. Nonetheless, a higher post-treatment GSI was described among alexithymic
Leweke et al. (50)	To investigate baseline alexithymia influence on treatment outcome in an inpatient setting	Prospective design with a 4 or an 8-week treatment course depending on	480	TAS-26 DIF, DDF, EOT, RD	Multimodal treatment including psychodynamic oriented individual psychotherapy, associated with art, group body and music	SCL-90R, GSI	DD, ADS, ASD, PTSD, ADJ, SFD, ED	Alexithymia was associated with a small risk for worse outcome as compared with non-alexithymic.

(Continued)

TABLE 3 | Continued

Reference	Objectives	Study design	Sample size	Standardized assessments of alexithymia	Treatment	Assessment tools	Diagnosis	Results
		the underlying condition			therapy; pharmacotherapy was offered as needed			
Löf et al., (51)	To investigate the complex interplay between alexithymia, self-image and treatment outcome among BPD undergoing MBT.	Prospective design with a 12-month treatment course; assessments were performed at baseline, at 6, 12, and 18 months.	75	TAS-20 DIF, DDF, EOT, RD	Multimodal treatment comprising individual and group MBT; pharmacotherapy was administered as needed.	DSHI-9, KABOSS-S, MINI, RQ, SASB, SCID-II, SCL-90-R, ZAN-BPD	BPD	No correlation was described between treatment outcome and alexithymia.
Rufer et al. (43)	To test alexithymia predictive value on treatment outcome among PD individuals receiving a course of CBT (1), and the eventual change of alexithymia over time (2).	Prospective	55	TAS-20 total score, DIF, DDF, EOT	5 sessions of GCBT (19 patients received concomitant pharmacotherapy)	MINI, BDI, PAS-20	PD with and without agoraphobia	Alexithymia level decreased over time, but it did not predict GCBT outcome. The EOT factor remained more stable over time.
Ogrodniczuk et al. (45)	To test the potential efficacy of a group therapy among outpatient psychiatric users, and the impact eventual alexithymia changes in interpersonal functioning	Prospective 2-year observational study with assessments at baseline, post-therapy and at 3 months follow-up	68	TAS-20 DIF, DDF, EOT	5 weekly sessions of group therapy for 3 months	BDI, IIP-28	AD, DD, PED	Alexithymia level was associated with greater interpersonal difficulties at follow-up, with higher alexithymia changes corresponding to greater improvement in interpersonal functioning
McMain et al. (52)	To test the relationship between treatment outcome and specific changes in emotion processes and problem-solving	A subset analysis of an RCT	80	TAS-20 DIF, DDF, EOT	Either multiple weekly sessions of DBT (individual and group therapy) or GPM (combined psychodynamic and pharmacotherapy)	DABS, SCID-I, SCL-90-R, IIP-64, LIWC	BPD	No significant correlation was described between alexithymia level and treatment outcome; changes on the DDF significantly predicted IIP improvements
Terock et al. (53)	To study the relationship between alexithymia, SD and their eventual influence on the outcome	Prospective analysis with assessments at admission and discharge	716	TAS-20 DIF, DDF, EOT	6-8 weeks of psychodynamic oriented therapy with cognitive behavioral elements (pharmacotherapy was offered as needed)	SCL-90R, GSI, TCI	AD, AUD, ED, PED, SFD	The DIF was the only factor in the TAS-20 predicting treatment outcome.
Probst et al. (54)	To explore the complex interplay between alexithymia, therapeutic alliance and	Reanalysis of a 12-week RCT	83	TAS-20 DIF, DDF, EOT	12 sessions of weekly PIT	SCID for DSM-IV, HAQ, PHQ-9, PCS	MSD	No significant relationship was described between alexithymia, therapist alliance and treatment outcome when controlling for depression burden

(Continued)

TABLE 3 | Continued

Reference	Objectives	Study design	Sample size	Standardized assessments of alexithymia	Treatment	Assessment tools	Diagnosis	Results
	treatment outcome in MSD							
McGillivray (55)	To study the potential influence of alexithymia on treatment outcome	Prospective study with assessments performed at the beginning and at the end of the treatment course	61	TAS-20 DIF, DDF, EOT	Integrated group therapy CBT-based	DASS-42	AD, MD, SFD, PED	No significant correlation was described between alexithymia and treatment outcome either at baseline or after treatment
Zorzella et al. (56)	To test the influence of alexithymia on treatment outcome among women with a history of sexual abuse	Prospective study with assessments were performed at baseline (T0), post BRG (T1), post WRAP (T2)	51	TAS-20 DIF, DDF, EOT	4-6 weekly sessions of a group therapy (BRG) followed by a further 8-week course of multimodal trauma therapy WRAP (e.g. CBT, Psychoeducation, IPT)	CTQSF, PTSDC, DES, IIP, MMPI, PSI, WAI-S	PTSD	A significant correlation was described between alexithymia improvements at T1 and T2 and changes in dissociation, PTSD and IP at the same timepoints

AD, anxiety disorders; ADD, adjustment disorder; ADJ, adjustment disorder; APRQ, Alexithymia Provoked Response Questionnaire; ASD, acute stress disorders; AUD, alcohol use disorder; BDI, Beck Depression Inventory; BPD, borderline personality disorder; BRG, Building Resources Group; CBT, cognitive behavioral therapy; CG, complicated grief; CTSFQ, Childhood Trauma Questionnaire Short Form; DABS, Derogatis Affects Balance Scale; DASS, Depression Anxiety Stress Scale; DD, depressive disorders; DIF, TAS-20 factor 1 Difficulty Identifying Feelings; DDF, TAS-20 factor 2 Difficulty Describing Feelings; DIS, dissociative disorders; DSHI, Deliberate Self-Harm Inventory-9; DSM-III, Diagnostic and Statistical Manual of Mental Disorders III; DST, dysthymia; ED, eating disorders; EOT, TAS-20 factor 3 Externally Oriented Thinking; GSI, Global Severity Index; GPM, general psychiatric management; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; HAQ, Helping Alliance Questionnaire; HC, healthy control; HY, hypochondria; IES, Impact of Events Scale; IIP-64, Inventory of Interpersonal Problems-64 items; IIP-28, Inventory of Interpersonal Problems-28; IPT, Interpersonal Therapy; KABOSS-S, Karolinska Borderline and Symptoms Scales; LIWC, Linguistic Inquiry and Word Count; MBT, Mentalisation-based Therapy; MD, mood disorders; MDD, major depressive disorder; MINI, Mini-International Neuropsychiatric Interview for DSM-IV; MMPI, Minnesota Multiphasic Personality Inventory; MSD, Multisomatoform Disorder; PCS, Physical Component Summary from the SF-36; PD, panic disorder; PED, personality disorders; PHQ-9, Patient Health Questionnaire; PIT, Psychodynamic-Interpersonal Psychotherapy; PM, psychological mindedness; PMAP, Psychological Mindedness Assessment Procedure; PSI, Problem-Solving Inventory; PTSD, posttraumatic stress disorders; PTSDC, Post-Traumatic Stress Disorder Checklist; RD, reduced daydream; RQ, Relationship Questionnaire; SASB, Structural Analysis of Social Behavior; SCID-II, Structured Clinical Interview for DSM-IV Axis-II disorders; SCL-90, Symptoms Checklist 90R; SD, somatization disorder; SED, self-directedness; SFD, somatoform disorder; STGT, Short-Term Group Therapy; STIT, Short-Term Individual Therapy; STP, short-term psychotherapy; TAS-20, Toronto Alexithymia Scale 20 items; TCI, Temperament and Character Inventory; USD, Undifferentiated Somatoform Disorder; WAI-S, Working Alliance Inventory, short form; WI, Whiteley Index; WRAP, Women Recovering From Abuse Program; Y-BOCS, Yale-Brown Obsessive-Compulsive Scale; ZAN-BPD, Zanarini Rating Scale for Borderline Personality Disorder.

Forty-two patients affected by OCD were recruited to the study, hospitalized, and subjected to intensive multimodal CBT for a mean period of 70 days. Treatment provided for both individual and groups sessions, as well as pharmacological treatment with antidepressants, largely fluvoxamine, for some of the patients. Although treatment proved effective on obsessive compulsive symptoms and associated depressive symptoms, no significant changes were observed from pre- to post-treatment for total TAS-20 or factors DIF and EOT. A decrease in levels of factor DDF alone was registered during treatment, and a relative stability of alexithymia emerged as a personality trait rather than a state-dependent phenomenon in obsessive-compulsive patients. Neither alexithymia pre-treatment nor other variables examined (depression and pharmacological treatment) appeared to significantly predict response to multimodal CBT in OCD. Bearing in mind the limitations of the previous study which, being devoid of a follow-up period, had not enabled the long-term course of alexithymia or its predictive power on the long-term outcome of treatment to be established, Rufer et al. (48), followed on from this work to conduct a long-term study with a 6-year follow-up period. Thirty-four of the 42 patients enrolled in the previous study (47) were recruited and, thus, reassessed 6 years after their hospitalization. In addition to confirming the relative long-term stability of alexithymia, the study also confirmed the absence of a predictive power of alexithymia levels, both pre- and post-treatment, on the long-term outcome of OCD. On the other hand, the decrease in alexithymia levels observed at follow-up (total TAS-20, DIF, and DDF) may have been implicated in protecting some patients against a worsening of obsessive-compulsive symptoms during the follow-up period. These findings are illustrated in **Table 3**.

Alexithymia in the Treatment of Somatoform Disorders

The only study to date to have specifically investigated the role of alexithymia as predictor of treatment outcome in somatoform disorders (SD) was carried out by Probst et al. (54). In reanalyzing data from a multicenter randomized, controlled trial on brief psychodynamic-interpersonal therapy (PIT) for patients with multisomatoform disorders, the authors addressed the issue of whether alexithymia moderated the association

between therapeutic alliance and outcome of PIT and the implications of the depression variable on these potential effects. 107 patients affected by multisomatoform disorder with pain as predominant symptom were randomized to PIT (duration 12 weeks) and 104 patients to the control condition (enhanced medical care, EMC). Only the subsample randomized to PIT was considered for the purpose of analysis, based on the singular relevance of the therapeutic alliance in PIT compared to the control condition. All patients met the criteria for a somatic disorder according to DSM-5. The outcome was based on self-reported physical quality of life 9 months after completion of treatment. Pre-treatment alexithymia and therapeutic alliance post-treatment and at 9-month follow-up were rated by both patients and therapists. Neither alexithymia nor therapeutic alliance correlated with PIT outcome. On considering patient-rated therapeutic alliance, alexithymia was not found to moderate the associations between alliance and outcome. Conversely, when considering therapist-rated therapeutic alliance, alexithymia was found to significantly moderate the relationship between alliance and treatment outcome. A stronger alliance in the therapists' perspective was beneficial for the outcome only in patients with very high scores at TAS-20, and therefore with very high levels of alexithymia. The importance of the therapist's perception of a good alliance with the patient is underlined, also in view of an improved outcome when treating patients with alexithymia. As demonstration of the complex interaction between alexithymia and depression, the significance of alexithymia as a moderator of the alliance-outcome link was lost when pre-treatment levels of depression as covariate to the moderation model. These results are presented in **Table 3**.

Alexithymia and Its Impact on Treatment in Samples With Diverse Psychiatric Disorders

A series of studies assessed the impact of alexithymia on treatment response analysis samples with diverse diagnoses. Bach & Bach (57) investigated the potential role of alexithymia in predicting long-term treatment outcome in 30 patients admitted to hospital for somatoform (36.7%) and panic disorders (63.3%). Thirteen of the 19 patients affected by panic disorder presented with an additional diagnosis of somatoform disorder. In all subjects, the presence of functional somatic symptoms, mainly cardiorespiratory, gastrointestinal, and neurological symptoms constituted the main reason underlying request for treatment. All patients underwent integrative behavior therapy with both group and individual sessions over a period of hospitalization of no less than 8 weeks. The study envisaged diagnostic assessment prior to hospitalization and 2 years after discharge. Assessment at 2-year follow-up revealed how patients who met the criteria for undifferentiated somatoform disorder had presented with higher baseline levels of alexithymia (TAS-26) versus patients who had gone into remission from the somatoform disorder and those who had never met the criteria for somatoform disorder. No other baseline or follow-up diagnosis was found to correlate significantly with baseline levels of alexithymia. Higher levels of alexithymia at baseline were therefore predictive of a persistent somatization, irrespective of other variables relating to psychopathology, socio-demographics or severity of the disorder, thus demonstrating the potential role of alexithymia in predicting relapse in the long-term and a less favorable response to treatment in somatizing patients. The presence of alexithymic characteristics, and therefore, a difficulty for patients to identify and share their feelings, might make these subjects more susceptible to communicating through use of bodily sensations, an aspect that could complicate the process of recovery from their illness. Several years later, McCallum et al. (46) explored the impact of alexithymia and psychological mindedness (PM) as predictors of outcome in 4 forms of short-term psychotherapy. Data were extrapolated from two comparative trials of interpretive therapy versus supportive therapy. The first trial provided for a once-weekly session of short-term group therapy over a period of 12 weeks in 107 outpatients with complicated grief. The second trial involved 144 psychiatric outpatients with a mixed diagnosis, who underwent once-weekly short-term individual therapy for a total of 20 weeks. Seventy-one percent of patients met the criteria for an Axis I diagnosis, with a higher prevalence of major depressive disorder; fifty-five percent of patients were affected by an Axis II disorder; 38% of patients received a diagnosis of both Axis I and Axis II disorders. In the two trials, both alexithymia (TAS-20) and PM were found to be predictive of outcome. Higher levels of PM and lower levels of alexithymia were associated with a more favorable response to the four forms of therapy, with the additive effect of the two variables on outcome. In supportive individual therapy, the DDF factor of TAS-20 was inversely associated with an improvement on General Symptoms. In the short-term individual therapy trial, the DIF factor was found to be inversely associated with improvement on General Symptoms and Social-Sexual Maladjustment; the EOT factor was inversely associated with improvement on Social-Sexual Maladjustment. One clinical implication of these findings may lie in the hypothesis whereby, generally speaking, patients with lower levels of alexithymia and a higher PM may prove better suited to psychotherapy, both of an interpretative and supportive nature. Likewise, patients displaying high levels of alexithymia and low levels of PM pre-treatment may experience an improvement of these characteristics following psychotherapy, and thus benefit from treatment in the same way as subjects who approach therapy with low levels of alexithymia and high levels of PM. With regard to the impact of alexithymia of the different forms of interpretative and supportive therapy, non-alexithymic patients were generally found to benefit from both supportive and interpretative treatment. Contrary to expectations, and bearing in mind the specific deficits of subjects with alexithymia, although alexithymia was not found to interfere with the ability of patients to gain benefit from individual interpretative therapy, it was however seen to interfere with their ability to benefit from individual supportive treatment, at least in terms of improvement of symptoms. The authors suggested that this finding might be explained by the attitude of the therapist during supportive therapy; indeed, by avoiding

the exploration and interpretation of an association between symptoms and underlying feelings, the therapist could further exacerbate the initial difficulty of the alexithymic subject to identify and share his or her feelings. Although the findings of the study underline the predictive value of alexithymia on treatment outcome, they however fail to provide sufficient elements to allow this variable to be considered of use in opting for one specific therapeutic approach over another.

Grabe et al. (49) assessed a total of 414 consecutive psychiatric patients admitted for hospital treatment, 297 of whom had been followed up at 4 weeks (T1) and 8-12 weeks (T2) after discharge. Patients underwent psychodynamic group therapy in a naturalistic setting over a period of 8-12 weeks. Pharmacological treatment was offered when clinically indicated. Art therapy, sport therapy, relaxation therapy, body, and movement therapy were available on a daily basis. Patients admitted to psychotherapy were affected by depressive disorders, anxiety and adjustment disorders, somatoform disorders, eating disorders, and comorbid alcohol-related disorders and personality disorders. Subjects with alexithymia at T0 displayed a higher Global Severity Index at Symptom Checklist-90, and consequently increased psychopathological distress at T0, T1, and T2. Over the course of treatment, the group with alexithymia displayed a significant improvement over time of alexithymia levels and at individual factors at TAS-20, at variance with the very slight reduction in TAS scores manifested by the patients without alexithymia. Levels of alexithymia in patients who had suspended treatment within the first 4 weeks were no higher than those of patients who had continued treatment, thus highlighting a lack of interference of the alexithymia variable on treatment compliance. Alexithymic features were therefore found predictive of a worse long-term outcome in this study. In the context of an extended study conducted on 480 psychiatric patients from a series of diagnostic categories (eating disorder, depressive disorder, anxiety disorder, acute or post-traumatic stress disorder, somatoform disorder), Leweke et al. (50) assessed alexithymia as outcome predictor of psychodynamic-oriented multimodal inpatient therapy. The treatment program included both individual and group psychodynamic-oriented therapy, art and music therapy, and pharmacological treatment as indicated. Both short-term and long-term treatments were envisaged, with duration ranging from 4 to 8-12 weeks. A high baseline level of alexithymia (TAS-26) was found to be a significant predictor of treatment outcome only in patients with somatoform disorder, with a marked association with the DDF factor, whereby subjects registering higher scores at factor DDF displayed a less favorable evolution of symptoms.

Ogrodniczuk et al. (45) evaluated 68 psychiatric outpatients with heterogeneous psychopathological issues who were enrolled in a comprehensive group therapy program organized in group sessions 5 days a week for a total of 12 weeks. Patients were assessed at baseline, post-therapy, and at 3-month follow-up. Alexithymia levels, in particular factor DIF at TAS-20, were found to improve significantly during treatment. A reduction in alexithymia levels during treatment and throughout the follow-up period were significantly associated with an improvement in interpersonal issues both during treatment and the follow-up period, i.e. in the long-term. The findings of the study confirmed the hypothesis according to which a positive change in alexithymia levels may contribute towards an improved treatment outcome, particularly with regard to interpersonal functioning. In the light of this evidence, the authors highlighted the feasibility of considering alexithymic traits as changeable features, thus focusing treatment come on the optimal management of the same with the aim of producing a positive impact on treatment outcome. In 2015, Terock et al. (53) investigated the impact of alexithymia and self-directedness (SD) on general psychopathology and on treatment outcome in a sample of 716 consecutively admitted day-clinic outpatients with alcohol/drug dependence and abuse (8.7%), depressive disorders (84.4%), anxiety and somatoform disorders (18.3%), eating disorders (0.6%), and personality disorders (20,5%). Routine treatment provided for psychodynamic-oriented psychotherapy with the inclusion of elements of CBT. Duration of the treatment program ranged from 6 to 8 weeks according to patients' individual needs. The program included sessions of art therapy, group therapies, and individual psychotherapy, in addition to pharmacological treatment when clinically indicated. Both baseline alexithymia levels (TAS-20) and SD levels were found to be significant predictors of psychopathological stress at baseline at the Global Severity Index of SCL-90 (GSIT0). SD, but not alexithymia levels, proved to be a significant predictor of treatment outcome as measured by GSI at T1. The DIF factor of TAS was the only strong predictor of GSI both at T0 and T1, thus constituting the sole alexithymic factor capable of predicting treatment outcome. Changes in levels at TAS-20, together with changes in SD were predictive of GSI at T1. The results obtained highlight the higher impact of the SD variable on treatment outcome compared to alexithymia. More recently, McGillivray et al. (55) evaluated the role of alexithymia on treatment outcome in a naturalistic group therapy setting. Sixty-one psychiatric outpatients affected by mood disorders (54.1%), neurotic, stress-related, and somatoform disorders (19.7%), disorders of adult personality and behavior (14.8%), schizophrenia, schizotypal, and delusional disorders (9.8%) and behavioral syndromes associated with physiological disturbances and physiological factors (1.6%) were enrolled in the study and assessed both pre- and post-treatment. Treatment lasted for approximately 8 weeks and was based on a CBT approach. Baseline alexithymia levels, in relation to both total scores obtained at TAS-20 and to individual factors, was not found to be a significant predictor of treatment outcome (change in psychological distress) once baseline psychological distress was controlled for. In the course of treatment, a small, albeit significant, reduction in mean alexithymia scores at TAS-20, and reduction in alexithymia levels during treatment, proved to be a significant predictor of a decrease in psychological distress during treatment. The authors hypothesized that absence of a correlation between baseline alexithymia levels and treatment outcome might be associated with the efficacy of the

implemented group cognitive behavioral therapy on the alexithymia dimension, as demonstrated by the findings of the study. All these findings are summarized in **Table 3**.

DISCUSSION

Over the years increasing debate has been focused on the issue of whether, and if so to what extent, alexithymia should be considered a stable personality trait or a phenomenon linked to psychopathological status, and whether it is capable of predicting treatment outcome. However, in spite of the increasingly frequent findings confirming the clinical significance of alexithymia and its correlation with a wide range of physical complaints and mental disorders, studies conducted to investigate, in the context of psychiatric disorders, the implications of alexithymia as a predictor of treatment outcome are still numerically scarce and methodologically limited. More and more frequently in the field of psychiatry, the finding of sub-optimal responses to treatment requires an increasingly personalized treatment plan focused on the individual and his or her characteristics, problems, and specific needs, rather than merely on his or her illness. The need to improve treatment outcome in the case of mental disorders implies a growing urgency to identify outcome predictors, both generally and in specific categories of patients and for specific therapeutic approaches. The reasons underlying the hypothesis whereby alexithymia is purported to be significantly implicated in terms of impact on the outcome of mental disorders are numerous and include a negative influence of alexithymia on clinical expression of the disorder and on response to therapeutic intervention, its correlation with other disorders and pathological behaviors, in addition to treatment choices made by the clinician and the clinical setting. Of note, a recent study showed that distinct clinical and sociodemographic characteristics, such as lower educational level, high rates of psychiatric comorbidity as well as of cardiological comorbid disorder, were associated with alexithymia in mood disorder patients (16). These findings point to alexithymia as a relevant determinant of adverse outcomes in psychiatric disorders, underlying its potential in the implementation of personalized care. For the purpose of the present review, a total of 30 studies were selected and analyzed. Eating disorders represented the mental disorders in which alexithymia fostered increasing interest as a predictor of outcome. These were followed by mood disorders (depressive disorders), personality disorders (borderline personality disorders), post-traumatic and obsessive-compulsive disorders, and lastly, somatoform (multisomatoform disorders) and anxiety disorders (panic disorder). Overall, seven studies focused on the analysis of mixed patient samples with a series of psychiatric diagnoses. Almost all studies selected featured a longitudinal prospective design, 1 study had a retrospective design (27), and 2 studies a cross-sectional design (36, 40). The studies invariably focused on evaluation of the predictive impact of alexithymia on the outcome of different forms of group or individual psychotherapy (cognitive behavioral therapy, psychodynamic therapy, interpersonal therapy, psychodynamic-interpersonal therapy, psychoeducational therapy, mentalization-based treatment, rhythmic movement therapy, dialectical behavior therapy) conducted in a series of treatment settings (doctor's surgery, day-hospital, hospital). Three studies alone assessed the impact of alexithymia primarily on the outcome of pharmacological treatment (imipramine and phenelzine versus placebo; fluvoxamine; paroxetine) (26, 34, 44). It should however be highlighted that even when the primary treatment was psychotherapy, a percentage of patients also received concomitant pharmacological treatment. In many cases the treatment program provided for an integrated approach comprising both individual and group psychotherapeutic and pharmacological measures, in addition to the use of a series of psychotherapeutic techniques. This prevented the identification of the degree of impact of specific approaches or measures on alexithymia levels and insight into the type of interventions impacted to a greater extent by alexithymia, particularly in terms of outcome. In the majority of cases, samples recruited were relatively small, scarcely representative, and featured a marked heterogeneity with regard to patient characteristics (outpatients, inpatients, acute or chronic, with varying degrees of severity and alexithymia levels), diagnostic groups considered, and psychiatric comorbidities. Moreover, in view of the scarce number of patients assessed in the majority of studies selected, the additional impact of missing data both post-treatment and during the follow-up period, if envisaged, should be taken into account. A short longitudinal observation period was implemented in numerous studies, limiting assessment of alexithymia levels to pre- and post-treatment. Only a few studies implemented a medium to long-term follow-up (28, 32, 37, 39, 42, 43, 45, 48, 49, 51, 54, 57), the presence of a control group of healthy individuals (34, 35, 40) or comparison between the different therapeutic approaches used (27, 33, 44, 46, 52, 54). Moreover, in the studies selected, the alexithymia dimension was detected solely by means of self-reported assessments which, in view of the issues addressed and the high risk of confounding by other pathological variables, may not be sufficiently reliable in measuring the true entity of alexithymic involvement. Finally, certain studies Overall, although the results obtained should be read and interpreted bearing in mind the numerous limitations of studies available to date, the data provided largely correlate lower baseline and/or post-treatment levels of alexithymia and/or improvement in alexithymia levels over the course of treatment, with a less favorable treatment outcome on the mental disorders considered.

A smaller number of studies, although substantial (8 out of 30 studies), failed to acknowledge a predictive role for alexithymia in terms of treatment outcome (28, 32, 38, 43, 47, 48, 51, 54). In the study by Kosten et al. (44), a double-blind, randomized controlled trial of patients with PTSD, higher levels of alexithymia were found to be predictive of a worse outcome with regard to avoidance symptoms, although only in subjects treated with placebo and psychotherapy. This finding led the authors to hypothesize that when given alone, psychotherapy

may not be effective in reducing avoidance symptoms in PTSD patients with alexithymia. In the study conducted by Leweke et al. (50) higher baseline levels of alexithymia were a significant predictor of treatment outcome only in individuals affected by somatoform disorder, showing a particularly strong correlation with the DDF factor, with higher scores indicating a less favorable evolution of symptoms in these subjects.

When the studies included did not report correlations between levels of alexithymia and treatment outcome, to justify this lack of confirmation the authors mentioned: efficacy of treatment on alexithymia, and therefore improvement of alexithymia in the course of treatment; increased feasibility and adaptability of a series of therapeutic approaches in patients with alexithymia; a different impact of alexithymia in relation to the diagnostic group considered. In the context of the naturalistic study conducted by Rufer et al. (43) the authors attributed failure to detect a negative impact of alexithymia on treatment outcome to the type of psychotherapy approach based on behavioral "experiments" used in the study, maintaining that this approach may have elicited a change in alexithymic features, thus impacting positively on symptoms of anxiety.

Throughout the majority of studies analyzed, the impact of alexithymia on treatment outcome was assessed on the basis of the association between baseline alexithymia levels and outcome variables post-treatment and, where relevant, at follow up. In other cases, the correlation between improvement in alexithymia levels during treatment and outcome variables was analyzed (45). In yet others, both aspects were taken into account, at times yielding discordant findings (55, 56). In the study carried out by Zorzella et al. (56) in a sample of patients with PTSD, an improvement in alexithymia levels over the course of treatment was found to correlate significantly with a better response to treatment, in relation to both PTSD symptoms and levels of dissociation and interpersonal difficulties. This was in line with the findings of McGillivray et al. (55) who investigated a sample of psychiatric outpatients with different diagnoses, all of whom treated with CBT. In some studies, the evaluation was limited to alexithymia levels post-treatment and outcome variables (36, 40). Despite a failure to detect a correlation between correlation between baseline alexithymia levels and treatment outcome, other studies highlighted how higher levels of alexithymia post-treatment, indicating persistent alexithymia, correlated with an increased severity of the disorder post-treatment, and accordingly, with a lower response to treatment (34, 37).

Most of the studies examined confined their evaluation to the global alexithymia construct, implying that total baseline or post-treatment TAS scores or improvements in total TAS over the course of treatment correlated with outcome variables. A smaller number of studies investigated the different facets of alexithymia and assessed their impact as predictor of outcome. The study conducted by Speranza et al. (39) found the DIF factor to be the best predictor of an unfavorable outcome, being negatively correlated in particular with clinical improvement of patients with severe or chronic eating disorders. This was in line with the findings of Ogrodniczuk et al. (27) and Terock et al. (53). Accordingly, a difficulty in identifying feelings may, hypothetically, impinge on the ability of the individual to gain effective benefit from psychotherapy. Conversely, in a study in hospital inpatients affected by major depression, Gunther et al. (29) detected a predictive role for the severity of depressive symptoms at follow-up solely for the EOT factor. Indeed, higher EOT scores at baseline correlated with more severe depressive symptoms, even once the potential influence of confounding factors, such as baseline levels of anxiety and depression had been accounted for. The authors suggested that such a multimodal therapeutic approach might not be effective in depressed patients with a more marked externally oriented cognition and decreased interest in intrapsychic issues.

At variance with the observations made by these authors, Quilty et al. (33) reported a positive prognostic role for the EOT factor. The authors underlined the possibility that in depressed patients the EOT factor might be associated with a decrease in ruminative thinking, and therefore, with a more adaptive and problem-focused coping strategy. In addition, McCallum et al. (46) revealed how higher levels of psychological mindedness and lower levels of alexithymia at DIF and EOT factors were associated with a more generally positive response to treatment, with an additive effect of the two variables on outcome. Based on the above findings, and despite the current paucity of available data, the observation of a varying predictive impact across the different dimensions of alexithymia, in addition to the diverse impacts of treatment on the various factors, suggests that in future studies it may prove more informative and useful to implement a multidimensional approach to alexithymia. A further fundamental aspect, in the light of which the results obtained in the studies examined should be construed and interpreted, relates to the role of confounding factors. Only a few of the studies examined took into consideration the impact of variables, such as depression, clinical severity of the disorder, psychiatric comorbidities, and treatments received. In some cases, significance of the predictive power of TAS and related factors persisted, although to a lesser extent, even when the impact of depression, clinical severity of the disorder, and treatments received had been taken into account (39). In yet others, the correlation of results obtained for the confounding variables resulted in a loss of significance for the association alexithymia and treatment outcome (54). In the study by Probst et al. (54), the sole study to have specifically assessed the role of alexithymia as outcome predictor in the treatment of somatoform disorders, alexithymia was initially found to significantly moderate the correlation between therapist-rated therapeutic alliance and treatment outcome, although this significance was subsequently lost on accounting for the levels of depression present pre-treatment. With regard to the effect of specific treatments on alexithymia levels, although this aspect was not included among the specific aims of this review, it may be helpful to briefly refer to these. Indeed, several authors assessed the impact of an improvement of alexithymia in the course of treatment on the outcome of the same treatment. Moreover, in some cases failure to detect a predictive power of alexithymia on treatment outcome was attributed by the authors to the particular efficacy of the treatment options adopted on

alexithymia. It should however be highlighted that even when a decrease in alexithymia levels was observed post-treatment, the finding that levels frequently continued to be elevated, invites us to reflect on the actual clinical effectiveness of these changes, underlining the need to identify types of treatment capable of producing a significant impact on the alexithymia dimension (35, 37). Furthermore, although the finding that an improvement in alexithymia levels over the course of treatment was largely correlated with a better treatment outcome is certainly of interest, it should be viewed as a preliminary finding which, particularly in view of the methodological limitations of the studies, does not allow any conclusions to be drawn as to possible causality. An additional limitation concern the use, in some studies, of the older 26-item version of the TAS, which might have impacted the reliability in the assessment of alexithymia. Undoubtedly, the increasingly frequent findings reporting alexithymia as a trait which is, at least in part, modifiable, appear encouraging, and should motivate us to undertake more extensive and methodologically valid studies aimed at identifying the forms of treatment capable of impinging more effectively on the alexithymia dimension, thus resulting in an increased probability of impacting on treatment outcome. A considerable number of studies examined observed over the course of treatment an improvement of varying significance at TAS, with a tendentially greater efficacy of treatments providing for specific intervention on feelings (37, 38). At the same time, the marked heterogeneity of treatment strategies adopted and the methodological limitations of the studies are such as to prevent the generalization and comparison of available data.

Crucially, therefore, particular focus should be placed on identifying which types of treatment and elements involved may prove of greater efficacy in patients with alexithymia. Treatment options encouraging the identification, sharing, and understanding of feelings would appear to be more effective in reducing alexithymia (58). Additionally, these patients appear to prefer, and obtain greater benefit from, a group therapeutic setting (58). A group context provides these patients with an opportunity to observe and copy other members of the group who are able to express their feelings more effectively, to gather feedback on their method of communication, to be encouraged to share their feelings with the others in the group, to witness the watering down of their "emotional arousal" with a lower risk of somatic expression, or to be, as needed, mere observers (58). Several authors have highlighted how patients with alexithymia may be poorer responders to classic medical treatments and to psychotherapy, particularly psychodynamic psychotherapy (27). Indeed, in patients with high levels of alexithymia their emotional experiences may prevent the formulation of a fully aware symbolic and verbal elaboration in the course of treatment. This aspect, together with a scarce interest for introspection, might prevent patients with alexithymia from benefitting from psychotherapeutic interventions based on the above activities (48). In a study by McCallum et al. (46), contrary to expectations, while alexithymia was not found to interfere with patients' ability to benefit from individual interpretative therapy, it did however interfere with their ability to benefit from individual supportive therapy, at least in terms of improvement of symptoms. The authors suggest that this finding could be explained by the attitude of the therapist during supportive therapy who, by avoiding the exploration and interpretation of an association between symptoms and the underlying feelings, might contribute toward maintaining the initial deficit of the alexithymic subject in identifying and describing his or her feelings to the therapist. It would not therefore seem to be appropriate to maintain that patients with alexithymia are necessarily reluctant to undergo psychotherapeutic treatment (59). Likewise, the opinion according to which patients with alexithymia are poorly suited to psychodynamic approaches has to date found little support, although it is assumed that individuals with high levels of alexithymia may gain greater benefit from psychodynamic approaches involving a more active and empathetic role of the therapist, elements of supportive therapy, and a good therapeutic alliance (58). In the study conducted by Speranza et al. (60) patients were found to have been treated differently by their therapists, both on a quantitative and qualitative levels, based on their alexithymic profile. Accordingly, the authors hypothesize that the clinician might incorrectly view this type of subject as being less suited to psychotherapy (60). It has moreover been demonstrated how high levels of alexithymia may elicit negative reactions in the therapist, as well as negative interpersonal processes with controtransferal feelings of frustration or boredom, which might hinder the achievement of a good therapeutic alliance, and thus contribute to a less favorable outcome of treatment (59).

CONCLUSIONS

To conclude, although the results obtained should be scrutinized and interpreted bearing in mind, the marked limitations of the studies published to date, the available data tend largely to correlate low baseline, and/or post-treatment levels of alexithymia and/or an improvement in levels of alexithymia over the course of treatment, with a more favorable outcome of the treatment of the mental disorders considered. However, the presence of numerous discordant findings prevents us from drawing any firm conclusions as to the actual impact produced by alexithymia on the treatment of psychiatric disorders both in general and in specific diagnostic groups. Likewise, at the current state of the art, we are still far from being able to draw conclusions in favor of specific treatment protocols demonstrating a greater efficacy in this type of patients. It is conceivable, however, that the analysis of large datasets containing longitudinally collected information on measures of alexithymia, with innovative analytical methods, including machine learning, could lead to more accurate estimates of the predictive power of this construct in terms of response to treatments. Further studies should be undertaken on more extensive and homogeneous patient populations, including controlled studies and a comparison between different forms of

treatment. Moreover, in analyzing the observations made, due consideration should be given to potential confounding factors, and to a multidimensional analysis of alexithymia and an objective assessment of the alexithymic construct performed.

AUTHOR CONTRIBUTIONS

FP drafted the first version of the manuscript, performed the assessment of the included manuscripts, and oversaw the systematic search. MM contributed to the writing of the first draft, performed the systematic search, and designed the study. PP performed the systematic search and contributed to the writing. BC critically revised the paper, designed, and oversaw the study. All authors have seen and approved the submitted version of this paper.

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Rates of Alexithymia and Its Association With Smartphone Addiction Among a Sample of University Students in Egypt

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Introduction: Alexithymia is characterized by difficulties in describing feelings. Many studies have shown that there is a relation between alexithymia and different types of addictions. Nowadays, smartphone addiction is proposed to be a global problem. The current study focuses on the rates of alexithymia and its association with smartphone addiction in an Egyptian university.

Materials and Methods: This is a cross-sectional study that was conducted in Ain Shams University. A sample of 200 university students was surveyed using Toronto Alexithymia Scale (TAS) and Smartphone Addiction Scale–Short Version (SAS-SV).

Results: The results showed that 44 students (22%) had alexithymia. It was also found that around one third of the sample (N=65, 32.5%) met the criteria of smartphone addiction. There was a strong association between alexithymia and smartphone addiction (OR=4.33, 95% CI 2.15–8.74, p= < 0.001).

Conclusion: This study supports existing literature indicating the strong association between alexithymia and smartphone addiction.

Keywords: alexithymia, smartphone addiction, university students, behavioral addiction, Smartphone Addiction Scale–Short Version (SAS-SV), Toronto Alexithymia Scale (TAS)

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INTRODUCTION

Alexithymia is characterized by difficulties describing feelings and a decreased ability to differentiate between emotions and physical sensations (1). It was first studied in patients with psychosomatic disorders (2). Those suffering from alexithymia are unable to verbalize their own emotions and/or the emotions of others. Alexithymia has been linked to difficulties in facing and dealing with stressful conditions (3), anxiety and depression (4), lower self-esteem, dissociative experiences (5), low relationship satisfaction (6), and difficulties in building and maintaining healthy interpersonal relationships (7).

Moreover, many studies have shown that there is a relation between alexithymia and different types of addictions; including opioid use disorder (8), alcohol use disorder (9), and behavioral addictions like internet addiction (10).

On the other hand, smartphones are devices capable of processing information that include access to Internet and social networks, messaging, and multimedia besides their main function as a

tool for communication (11). As individuals almost always have their smartphones with them, and they can use their smartphones multiple times during the day, smartphone use may become an automatic behavior that is performed with little thinking (12). Therefore, a great concern has emerged that high frequency smartphone use may suggest that smartphones could become a behavioral addiction. However, the fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) does not recognize smartphone addiction as a disorder (13).

Individuals with symptoms of smartphone addiction tend to bring their phone with them wherever they are and think about their phone even if they cannot use it, which ultimately influences daily tasks. The proposed criteria to determine whether an individual suffer from smartphone dependence consists of four main components: compulsive phone use, tolerance witnessed by longer and more intense use, withdrawal symptoms, and functional impairment by interfering with other life activities (14).

Despite the advantages of providing information and communication opportunities (15) and not yet being officially recognized as a disorder (13), smartphone overuse or addiction is proposed to have negative impacts on health. Physical health problems such as visual impairment, musculoskeletal problems (16, 17), ear pain, headache, and sleep disorders, (18, 19) have been suggested to be related to it. Moreover, some mental health problems have also been linked to smartphones addiction such as depression and anxiety (20).

On the other hand, as individuals with alexithymia complain of having difficulties in identifying and describing their feelings, thus, they may resort to internet use to manage them (21). With the rapid development of smartphones, internet use became easier and more accessible (22). Thus, the use of smartphone and even dependence on it might be higher among this group. Few previous studies have investigated the relation between alexithymia and smartphone addiction and the results were interesting. Alexithymia was positively correlated with mental health problems and smartphone addiction (23–25). Yet, to our knowledge, no studies have explored such relation in Arab countries.

Furthermore, many smartphone addiction studies were focused on college students. They may spend much time on "interaction" with the mobile phone which may affect their daily life. Moreover, researchers suggest that the higher the degree of mobile phone addiction, the greater the likelihood that college students' academic performance will be affected (26). Hence, the current study focuses on alexithymia and its relation to smartphone addiction in students at an Egyptian university.

MATERIALS AND METHODS

This is a cross-sectional study that was conducted in Ain Shams University, which is in Cairo, Egypt, from April to August 2019. The study obtained the approval of the Research Ethics Committee (REC) of Faculty of Medicine (approval no. FMASU: R 45/2019). The sample size was calculated to be 200 students setting alpha error at 5% and confidence interval width at 0.1 (margin of error at 5%). Prevalence of alexithymia among university students was shown to be 12.5% in a previous study (27). The sample size was calculated taking in account 10% drop out rate. Students were recruited from campus and asked to complete a questionnaire including some demographic data and two scales. A total of 200 students participated in the study. The participants were requested to fill in a traditional paper-and-pencil questionnaire. They were informed about the aim of the study and that by filling in the questionnaire they consent to take part. It took the respondents approximately 15 min to complete the questionnaire.

Measures

Demographic information collected includes age, sex, faculty, and academic year. The questionnaire included two scales: Toronto Alexithymia Scale and Smartphone Addiction Scale–Short Version.

Toronto Alexithymia Scale (TAS-20), Arabic Version

Toronto Alexithymia Scale, (28) Arabic Version (29) was used to measure alexithymia. TAS is the most used and extensively validated measure for alexithymia (30). TAS consists of 20 items that is divided into three subscales: difficulty identifying feelings (DIF) with seven items, difficulty describing feelings (DDF) with five items, and externally oriented thinking (EOT) with eight items. TAS is five-point Likert scale ranging from 1 "strongly disagree" to 5 "strongly agree," with five items negatively keyed. The total score is calculated by summing the responses of all the items with a range of 20–100. The cutoff point is 60 and people with score of more than 60 are considered as having alexithymia. People with scores between 52 and 60 are considered to have possible alexithymia. People with a score of 51 or below are considered free of alexithymia. This tool has been translated to Arabic and back translated to the original language by a panel of experts following the World Health Organization (WHO) guidelines for translation of instruments. The scale showed good internal consistency reliability, test–retest reliability, convergent, discriminant, and concurrent validity. In this study, we arranged the sample into two groups using the score of 60 as a cutoff point for having alexithymia or not.

The Smartphone Addiction Scale–Short Version (SAS-SV), Arabic Version

The SAS-SV is a validated scale which was originally designed in South Korea but published in English (31, 32). This scale is a shortened version of the original 40 itemed scale. It is a ten itemed questionnaire used to assess levels of smartphone addiction. Participants are asked to rate on a dimensional scale how much each statement relates to them. The total score ranges from 10 to 60. This scale has been used in various research across different cultures including (33, 34). The scale is very quick and easy to use, there are no reverse scores involved. Smartphone addiction cut-off values of ≥ 31 and ≥ 33 for male and female participants, respectively, were applied as suggested by Kwon et al. (31, 32). Arabic version of SAS-SV used in this study was translated and validated by Sfendla et al. (35) and showed excellent reliability based on Cronbach's alpha ($\alpha = 0.94$).

Data Analysis

The SPSS 22.0 was used in our study for statistical analyses. The significance level was set at 0.05. Chi square and T-test were used to check the differences regarding alexithymia and smartphone addiction among the demographic features. Odds ratio was used to express the magnitude of the association between alexithymia and smartphone addiction.

RESULTS

Demographic Features of the Participants

Data were collected from 85 males (42.5%) and 115 females (57.5%). The age of the participants ranged from 17 to 27 years with a mean age of 21.225 ± 1.986. Eighty-four students (42%) were enrolled in practical faculties (i.e. medicine, engineering, etc.) and 116 (58%) students were enrolled in theoretical faculties (i.e. law, commerce, etc.). Regarding academic years, 21 students (10.5%) were enrolled in the first year, 38 students (19%) were enrolled in second year, 48 students were enrolled in third year (24%), 72 students (36%) were enrolled in fourth year, 17 students (8.5%) were enrolled in fifth year, and only 4 students (2%) were enrolled in sixth year.

Alexithymia According to TAS-20 Scores

Alexithymia was measured by TAS-20. In this study the cutoff score of 60 was used to differentiate those with and without alexithymia. The results showed that 44 students (22%) had alexithymia, while the remaining 78% were considered negative for it. There was no significant difference between males and females (p=0.917), between practical and theoretical faculties (p=0.391), nor academic year (p= 0.520) regarding alexithymia rates as shown in **Table 1**. There were also no significant differences between males and females (p=0.790), type of faculties (p=0.795), nor different academic years regarding (p=0.750) the scores of TAS as shown in **Table 2**.

Smartphone Addiction According to SAS-SV Scores

Smartphone addiction was measured by SAS-SV scale and results showed that around one third of the sample (N=65, 32.5%) met the criteria of smartphone addiction. There was no significant difference between males and females (p=0.086) nor practical and theoretical faculties (p=0.691) regarding smartphone addiction rate as shown in **Table 1**. No significant differences in SAS-SV scores were found between faculties (p=0.293) nor different academic years (p=0.125), however,

TABLE 1 | Comparing rates of smartphone addiction and alexithymia according to sex and type of faculty.

		Sex					
		Female		Male		Chi square test	
		N	%	N	%	p value	sig.
Smartphone Addiction (SAS-SV)	Negative	72	62.6%	63	74.1%	0.086	NS
	Positive	43	37.4%	22	25.9%		
Alexithymia (TAS)	No Alexithymia	90	78.3%	66	77.6%	0.917	NS
	Alexithymia	25	21.7%	19	22.4%		
		Faculty					
		Practical		Theoretical		Chi square test	
		N	%	N	%	p value	Sig.
Smartphone Addiction (SAS-SV)	Negative	58	69.0%	77	66.4%	0.691	NS
	Positive	26	31.0%	39	33.6%		
Alexithymia (TAS)	No Alexithymia	68	81.0%	88	75.9%	0.391	NS
	Alexithymia	16	19.0%	28	24.1%		

		Academic Year													
		One		Two		Three		Four		Five		Six		Chi Square test	
		N	%	N	%	N	%	N	%	N	%	N	%	p value	Sig.
Smartphone Addiction (SAS-SV)	Negative	17	81.0%	27	71.1%	32	66.7%	44	61.1%	12	70.6%	3	75.0%	0.626	NS
	Positive	4	19.0%	11	28.9%	16	33.3%	28	38.9%	5	29.4%	1	25.0%		
Alexithymia (TAS)	No Alexithymia	15	71.4%	33	86.8%	36	75.0%	54	75.0%	14	82.4%	4	100%	0.520	NS
	Alexithymia	6	28.6%	5	13.2%	12	25.0%	18	25.0%	3	17.6%	0	0.0%		

SAS-SV, Smartphone Addiction Scale–Short Version; TAS, Toronto Alexithymia Scale.

females had significantly higher scores on SAS-SV (p=0.003) as shown in **Table 2**.

Relation Between Alexithymia and Smartphone Addiction

There was a strong association between alexithymia and smartphone addiction (OR=4.33, 95% CI: 2.15–8.74, p= < 0.001) as shown in **Table 3**. Also, logistic regression analysis for predictors of smartphone addiction only showed presence of alexithymia as a significant factor as shown in **Table 4**.

TABLE 4 | Logistic regression analysis for predictors of smartphone addiction.

Dependent SAS-SV	OR	95% C.I. for OR	p value	Sig.
Sex (ref. Male)	1.85	0.96–3.58	0.067	NS
Faculty (ref. Theoretical)	1.04	0.55–1.99	0.898	NS
Age	1.11	0.95–1.3	0.197	NS
TAS (ref. negative)	4.72	2.29–9.73	<0.001	S

SAS-SV, Smartphone Addiction Scale–Short Version; TAS, Toronto Alexithymia Scale.

DISCUSSION

The term alexithymia was introduced by Peter Sifneos in 1972 (1) and was originally described in patients with psychosomatic complaints (36). The present study addressed the rates of alexithymia and its relation with smartphone addiction among a sample of university students. To our knowledge this is the first study to address the topic in Arab countries and one of the few worldwide.

This study showed that the rate of alexithymia for the whole sample was 22%, and almost the same in both sexes (21.7% of males and 22.4% of females). This rate is comparable to alexithymia rate (24.6%) among Jordanian university students (37). However, this rate is higher than rates found in western countries; 16.7% among Italian high school students (21) and 17.92% among British undergraduate students (38). This discrepancy may be explained by the cultural belief in Arab countries that emotional expression is

TABLE 2 | Relation between scores of SAS-SV and TAS and different factors.

		Sex		T Test	
		Females (N=115)	Males (N=85)	P value	Sig.
SAS-SV	Mean ± SD	31.504 ± 11.716	26.871 ± 9.723	0.003	S
TAS	Mean ± SD	55.948 ± 14.063	56.565 ± 18.694	0.790	NS

		Faculty		T test	
		Practical (N=84)	Theoretical (N=116)	P value	Sig.
SAS-SV	Mean ± SD	28.560 ± 11.555	30.241 ± 10.802	0.293	NS
TAS	Mean ± SD	56.560 ± 17.831	55.957 ± 14.894	0.795	NS

		Academic Year						ANOVA	
		One (N=21)	Two (N=38)	Three (N=48)	Four (N=72)	Five (N=17)	Six (N=4)	P value	Sig.
SAS-SV	Mean ± SD	23.381 ± 8.891	29.632 ± 12.314	29.042 ± 10.244	31.361 ± 11.493	30.529 ± 9.049	29.750 ± 15.945	0.125	NS
TAS	Mean ± SD	61.048 ± 30.556	54.316 ± 11.414	55.292 ± 14.265	56.667 ± 14.900	55.059 ± 12.060	56.500 ± 4.726	0.750	NS

SAS-SV, Smartphone Addiction Scale–Short Version; TAS, Toronto Alexithymia Scale.

TABLE 3 | Relation between alexithymia and smartphone addiction.

			Smartphone addiction (SAS-SV)		OR (95% CI)	P value	Sig.
			Negative	Positive			
Alexithymia (TAS)	No alexithymia	N	117	39	4.33 (2.15–8.74)	<0.001	S
		% of TAS	75.0%	25.0%			
		% of SAS	86.7%	60.0%			
	Alexithymia	N	18	26			
		% of TAS	40.9%	59.1%			
		% of SAS	13.3%	40.0%			

SAS-SV, Smartphone Addiction Scale–Short Version; TAS, Toronto Alexithymia Scale.

a sign of personal weakness (39). Another explanation might be that previous research has found psychosomatic complaints to be higher in Arabic cultures (40).

On the other hand, smartphone addiction is a global problem with multiple complications that have been addressed in multiple research. This study showed smartphone addiction to be present among 32.5% of the sample. Moreover, despite being a not statistically significant difference, rate among females (37.45) was higher than males (25.9%). This rate is comparable to those found in some other studies as 28.7% in the Netherlands (41) and 25% in the United States (42). However other studies reported lesser rates as low as 6% in Italy (43) and 18.8% in Japan (44). On the other hand, the non-statistically significant gender difference of smartphone addiction is consistent with previous studies (44, 45). Yet, some studies have reported that female participants indeed have higher rates of smartphone addiction than males (46, 47).

Regarding the relationship between alexithymia and smartphone addiction, our study results showed that there is a strong association between both. This was consistent with most of previous literature (23, 24). One possible explanation of such relation is that people with alexithymia tend to regulate their emotions by various types of addictive behaviors (48). However, one study showed that individuals with alexithymia had less frequent mobile phone use (49)

Several limitations are present in this study. The cross-sectional study design could not provide the causal relationship between alexithymia and smartphone addiction so longitudinal studies are needed to address this problem. Secondly the study is based on a self-reported questionnaire, which may result in several confounding factors. Thus, a more objective data collection methods should be used to improve credibility in the future. Finally, the small sample size and the collection of data from one university could affect the generalizability of the findings. Despite that the sample size was calculated to be enough, we would recommend larger samples and recruitments from more than one university in future studies.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Research Ethics Committee (REC) of Ain Shams University Faculty of Medicine (approval no. FMASU: R 45/ 2019). Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

All authors contributed to the conceptualization and design of the study. II was responsible for the field work. All authors were responsible for data revision. HE and II drafted the first version. HE and ME critically revised and finalized it for publication. All authors approved and contributed to the final version.

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Alexithymic Traits and Hair Cortisol Concentrations in Pregnant Women

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Introduction: Alexithymia, a personality construct characterized by difficulties in identifying and expressing emotions, and an externally oriented thinking style, has been associated with a number of stress-related disorders, and physiological markers of stress. We examined the relationships of alexithymia and hair cortisol concentrations (HCC), a measure of long-term cortisol levels, in pregnant women.

Methods: Participants were 130 women from the FinnBrain Birth Cohort study. Alexithymia was measured with the Toronto Alexithymia Scale (TAS-20). Analysis of covariance and regression analyses were used to assess the associations between alexithymia and HCC. Educational level, current depressive symptoms, and body mass index (BMI) were applied as covariates.

Results: In the adjusted analyses, individuals with moderate to high alexithymic traits had significantly higher HCC (F = 5.11, partial η^2 = 0.040 , p = 0.026) compared to non-alexithymics. Regression analyses in the whole sample revealed that, of the individual dimensions of alexithymia, Difficulty Identifying Feelings (DIF) was associated with HCC (β = 0.187, t = 2.064, p = 0.041).

Conclusions: Alexithymia, and especially its dimension DIF, were associated with higher HCC and, therefore, may be linked to increased chronic physiological stress. Implications for pregnancy outcomes and infant development are discussed.

Keywords: alexithymia, stress, cortisol, prenatal, emotional regulation, psychosomatic medicine

INTRODUCTION

Alexithymia is a personality construct characterized by difficulties in identifying and expressing emotions, and an externally oriented thinking style, lacking tendencies for fantasy and imagination (1). Although it is not considered a psychiatric disorder in itself, alexithymia has been linked with a number of stress-related disorders, such as depression, anxiety, pain syndromes, and an increased

risk of cardiovascular disease and mortality (2–6). According to the stress-alexithymia hypothesis, alexithymic individuals, due to a lack of emotional awareness, may fail to identify and respond to stressful events adequately, thus leading to increased levels of chronic stress (7). This chronic stress in turn could explain the higher psychiatric and somatic morbidity associated with alexithymia.

Previous studies have provided support for the stress-alexithymia hypothesis, showing increased cortisol responses in alexithymic individuals following a social stress test (8, 9). As for chronic stress measures, alexithymia has been linked to increased cortisol secretion in the dexamethasone suppression test, as well as an aberrant cortisol awakening response (10, 11). Furthermore, several studies have associated alexithymia to altered immune responses and tissue inflammation, possibly reflecting physiological effects of prolonged stress (12–14). Interestingly, alexithymia seems also to be more prevalent in patients with immune-related disorders, such as rheumatoid arthritis, multiple sclerosis, and systemic lupus erythematosus (15–17). Existing studies on alexithymia and stress have largely focused on acute stress markers in experimental settings and have rarely controlled for the effects of depressive symptoms, which are highly prevalent in alexithymic individuals (3).

To our knowledge, only two studies have investigated alexithymia during pregnancy (18, 19). In both studies alexithymia was related to psychiatric symptoms during pregnancy. Le et al. (18) additionally concluded that alexithymia was a stable phenomenon during pregnancy and the postnatal period. No studies have investigated the association of alexithymia and objective stress measures during pregnancy. Elucidating psychological factors associated with physiological stress is especially relevant in the prenatal context, as psychosocial stress during the gestational period can have long-term consequences for offspring development and future health outcomes (20). Glucocorticoids are able to partially pass the placental barrier and play an important role in fetal development. However, excessive exposure to glucocorticoids may have adverse consequences for the developing brain. Animal models have indicated that prenatal stress or glucocorticoid treatment induces permanent changes in offspring physiology that increase the risk for later somatic and neuropsychiatric disease (21–23). Similarly, in humans, elevated maternal glucocorticoid levels may disrupt fetal brain development and harmfully affect child socioemotional functioning (20, 24).

The aim of this study was to test the stress-alexithymia hypothesis by analyzing the association of alexithymia, depressive symptoms, and physiological stress in the prenatal period. We examined alexithymia levels and hair cortisol concentrations (HCC) in a birth cohort sample of pregnant women. Hair cortisol is an emerging potential biomarker for chronic stress (25, 26) and is thought to reflect cumulative cortisol concentrations over the previous months (27). According to the stress-alexithymia hypothesis, we expected higher alexithymia levels to be associated with higher HCC.

METHODS

Study Details and Participants

This study is based on the FinnBrain Birth Cohort study (www.finnbrain.fi), a prospective cohort established to study the effects of prenatal and early life stress exposure on child brain development and health (28). Participants were recruited between December 2011 and April 2015 from maternal welfare clinics in the South-Western Hospital District and the Åland Islands in Finland. After recruitment, the participants filled in a set of self-report questionnaires three times during pregnancy, at gestational weeks (gwk) 14, 24, and 34. After birth, the families are followed up at 3- to 6-month intervals (the first 30 months) or 12-to 36-month intervals (from 36 months onward), and the study is planned to continue for decades. The parents gave written informed consent on their own and on their child's behalf. The children will be asked for personal consent at an appropriate age. The ethics committee of the Hospital District of Southwest Finland has approved the study protocol (number of ethical approval ETMK-57/180/2011). The participants for this study consist of those mothers who provided hair samples (collection began at the end of the cohort recruitment) and filled in all relevant questionnaires concerning alexithymia levels and depressive symptoms (N = 130). Depressive symptoms were assessed in the 3rd trimester of pregnancy (at gwk 34), and hair samples were collected at the maternity ward 1 to 3 days after childbirth.

Educational level and BMI were considered as potential confounders as they have previously been associated with both alexithymia (29, 30), as well as HCC levels (31, 32). Depressive symptoms were also initially controlled for because the measurement of alexithymia may show some overlap with negative affect (33). However, consistently with previous research (31), depressive symptoms were not associated with HCC levels, and were therefore removed from the final analyses. Regarding possible substance abuse problems, our protocol was to refer participants with substance abuse to treatment. However, as discussed below, no participants reported problematic substance use during pregnancy.

QUESTIONNAIRE DATA

Questionnaire data included a variety of background information on the participants. For this study, we included age, body mass index (BMI), previous, and/or current substance use (including alcohol, tobacco, and illicit drugs), and the level of education divided into five classes: 1) high school or lower; 2) vocational degree; 3) upper secondary school; 4) applied sciences or bachelor's degree; 5) graduate school or PhD degree. Current medication use during pregnancy was inquired including antidepressant (SSRI or SNRI), non-steroidal anti-inflammatory (NSAID), and glucocorticoid and thyroid medication use. Background information was collected in the

1st trimester of pregnancy, substance use was additionally assessed in the 3rd trimester. Participants were also asked to report any diagnosed medical or psychiatric conditions.

Toronto Alexithymia Scale (TAS-20) (34, 35) is one of the most commonly used self-report scales used to measure alexithymic features. It consists of 20 items divided into three subscales: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking style (EOT). Items are rated with a five-point Likert scale (1, strongly disagree; 5, strongly agree). Thus, the total score ranges from 20 to 100. An individual is considered highly alexithymic if the TAS-20 total score exceeds 60 points, and moderately alexithymic if the total score is between 52 and 60 points (36). The TAS-20 was administered 6 months after the baby was born. Alexithymia levels were assessed both continuously as well as categorically. As the prevalence of high alexithymia was very low (3.1%, N = 4), the cutoff score of moderate to high alexithymia (TAS-20 overall score > 52) was used. Individuals scoring under 52 points were classified as non-alexithymic.

The Edinburgh Postnatal Depression Scale (EPDS) (37) is a widely used questionnaire for screening prenatal and postnatal depression. It is a 10-item self-report scale that asks respondents to rate their mood and other depressive symptoms in the previous 7 days. Questions are scored from 0 to 3, and thus, the total score ranges from 0 to 30 points. Depressive symptoms were measured at gwk 34 and used as a continuous variable.

Hair Cortisol Assessment

Maternal hair samples were collected from a random population of the FinnBrain Cohort participant mothers at the maternity ward 1 to 3 days after delivery between December 2014 and November 2015. A strand of hair was cut from a standardized area of the posterior vertex region of the head as close to the scalp as possible. Hair samples were stored in foil in a dry place protected from light according to good research practice, Finnish legislation, and data protection until the analyses. The analyses were performed at Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal. For the analysis, a 5-cm segment was used. As hair grows approximately 1 cm per month (38), a 5-cm segment was estimated to reflect the cortisol concentrations of the previous 5 months.

The hair segments were washed in isopropanol for 3 min three times and finely minced using surgical scissors. For extraction of cortisol, 1.5 ml of methanol was added to each sample, and the samples were incubated at 55°C for 24 h. After centrifuging at 10,000 rpm for 2 min, the supernatant was transferred to a new vial. Methanol was evaporated at 60°C under a constant stream of nitrogen until the samples were dried completely. Finally, 0.15 ml of phosphate buffer was added, and 50 µl of each sample was analyzed with ELISA (IBL International Cortisol Saliva ELISA) following the manufacturer's procedure. All samples were analyzed in duplicates with coefficients of variation below 15%.

The HCC data were examined for outliers, and values >3 standard deviations (SD) above the mean were excluded from the final analyses (HCC > 190.5 pg/mg, N = 5) (31). Hair samples weighing < 5 mg (N = 0) or > 15 mg (N = 7) were excluded.

Statistical Methods

All statistical analyses were conducted using the IBM SPSS (version 24.0). Normality of distribution within variables was assessed with the Shapiro-Wilk test. Associations between categorical variables were analyzed with Chi Square test. Student's t-test was used to examine differences in HCC between groups. As BMI was non-normally distributed, Mann Whitney U-test was used. An analysis of covariance (ANCOVA) was conducted to examine group differences in HCC between alexithymic individuals and non-alexithymics while controlling for the selected covariates. Multiple regression analyses were conducted to examine the associations between alexithymia dimensions, overall alexithymia scores, and HCC, controlling for the effects of educational level, BMI, and current depressive symptoms (EPDS) at gwk 34. As substance use levels were negligible, they were not used as covariates. Maternal age was unrelated to both alexithymia levels and HCC, and was thus also left out of the final analyses. Natural logarithmic transformations were performed on the HCC data to reduce skewness according to common practice (26, 39). After transformation, HCC was normally distributed (Shapiro-Wilk test, $p > 0.4$ for both groups).

RESULTS

Basic information on the study sample is provided in **Table 1**. Only one participant in each group reported tobacco use after the 1st trimester of pregnancy. Nine individuals (7.7%) in the non-

TABLE 1 | Basic information and comparison of hair cortisol concentrations between alexithymia groups.

	No alexithymia (N = 118)	Moderate to high alexithymia (N = 12)	Test statistic	*p*
Level of education*				
1.	0%	16.7%		
2.	9.6%	25.0%	–2.257[b]	**0.024**
3.	9.6%	8.3%		
4.	37.4%	25.0%		
5.	43.5%	25.0%		
Age	Mean (SD)	Mean (SD)		
	31.6 (3.7)	30.2 (4.6)	1.24[a]	0.217
Depressive symptoms	4.3 (3.9)	7.3 (3.9)	–2.55[b]	**0.011**
BMI	24.2 (27.6)	27.6 (7.2)	–1.68[b]	0.094
HCC (pg/ml)	17.8 (19.3)	35.1 (31.5)	–2.73[a]	**0.007**
DIF	11.2 (3.6)	20.8 (4.3)	–5.22[b]	**<0.001**
DDF	9.2 (3.0)	16.4 (3.4)	–5.12[b]	**<0.001**
EOT	17.7 (4.3)	22.0 (3.4)	–3.21[b]	**<0.001**
TAS-20 total	38.0 (7.2)	59.2 (5.8)	–5.67[b]	**<0.001**

[a]*Student's t-test.*
[b]*Mann Whitney U test.*
**Level of education: 1, high school or lower; 2, vocational degree; 3, upper secondary school; 4, applied sciences or bachelor's degree; 5, graduate school or PhD degree.*
HCC, hair cortisol concentrations; BMI, body mass index; DIF, difficulty identifying feelings; DDF, difficulty describing feelings; EOT, externally oriented thinking.
No alexithymia = TAS-20 score ≤ 52.
Moderate to high alexithymia = TAS-20 score > 52.

alexithymia group, and one (8.3%) in the moderate to high alexithymia group reported alcohol use after the 1st trimester. Frequency of use in all cases was less than once a month, and ≤ 1 standard dose of alcohol per occasion. No participants reported current illicit drug use. Three participants reported SSRI/SNRI use during pregnancy, eight participants reported thyroid medication (levothyroxine) use during pregnancy, and five participants reported glucocorticoid use during pregnancy. None of the participants reported NSAID use. Regarding somatic diseases and disorders potentially affecting the immune system or causing inflammation, one participant reported a diagnosed cancer and two reported a diagnosis of an autoimmune disorder (not further specified). No one reported current bacterial or viral infections. Mean duration of pregnancy was 280 days (min, 254 days; max, 296 days). Duration of pregnancy had no correlation with HCC (Spearman's rho = 0.032, $p = 0.714$), TAS-20 scores (rho = 0.117, $p = 0.185$), or DIF (rho = 0.116, $p = 0.189$).

Figure 1 shows the distributions of HCC and alexithymia levels. The moderate/high alexithymia group showed higher HCC levels compared to those with low alexithymia levels ($t = 2.75$, $p = 0.007$). Results of the ANCOVA showed that the difference in HCC between alexithymia groups stayed significant after controlling for the selected covariates ($F = 5.11$, partial $\eta^2 = 0.040$, $p = 0.026$). One participant in each group reported SSRI/SNRI use during late pregnancy. Removing these participants from the analyses slightly strengthened the group difference ($F = 6.12$, partial $\eta^2 = 0.049$, $p = 0.015$). Additionally, one participant in the moderate/high alexithymia group reported SSRI/SNRI use only in the first trimester of pregnancy. Removing all three SSRI/SNRI users did not affect the results. Five participants in the low alexithymia group reported current glucocorticoid use, and removing these did not affect the results. Removing those with thyroid conditions/medications, cancer, and autoimmune disorders did not affect the results either.

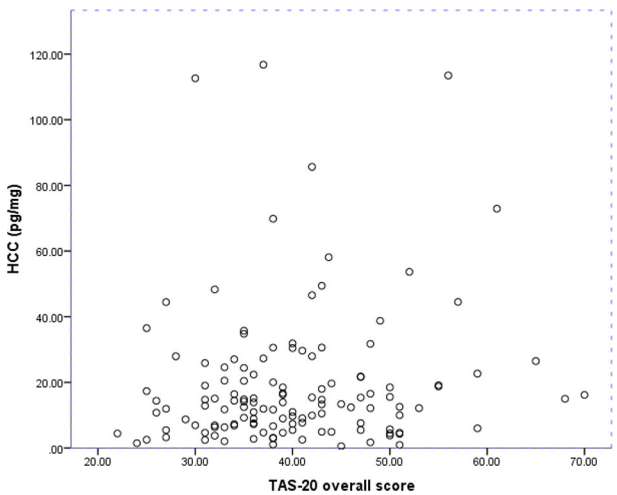

FIGURE 1 | Hair cortisol concentrations and overall alexithymia levels in the whole sample. HCC, Hair cortisol concentrations. TAS-20, Toronto Alexithymia Scale.

TABLE 2 | Summary of multiple regression analysis of variables predicting hair cortisol concentration.

	B	Standard error	β	t	p
Body mass index	−0.045	0.017	−0.243	−2.668	0.009
Level of education	−0.213	0.080	−0.234	−2.667	0.009
DIF	0.039	0.019	0.187	2.064	0.041

DIF, difficulty identifying feelings.

Separate regression analyses were conducted for TAS-20 and its individual dimensions in the whole sample. As the EPDS score was not associated with the outcome variable HCC (Spearman's rho = 0.092, $p = 0.298$), it was excluded from the covariates in the regression analyses.

After controlling for confounders, DIF remained a significant predictor of HCC (**Table 2**). The associations between HCC and TAS-20 total score, as well as the two other (DDF and EOT) alexithymia dimensions were non-significant ($p > 0.1$ for all comparisons). Of the covariates, educational level and BMI were negatively associated with HCC (**Table 2**).

DISCUSSION

Our results suggest that, among pregnant women, moderate to high alexithymia is associated with elevated HCC levels, compared to the non-alexithymic group. This association was driven by subjective difficulty in identifying feelings (DIF), as it was the only dimension of alexithymia that was associated with HCC in the whole sample, after controlling for potential confounders. While educational level and BMI were both negatively associated with HCC, depressive symptom scores in late pregnancy (gwk 34) were unrelated to HCC.

Our results are in line with previous research that has associated alexithymia with altered HPA axis functioning, inflammatory markers, and immune responses (8–14, 39). A review article by De Berardis et al. (40) summarized findings showing that alexithymia has been consistently linked to higher circulating levels of acute phase proteins, as well as proinflammatory cytokines. They argued that alexithymia may involve a chronic hyperreactivity of the HPA axis to stressful situations, increasing cortisol levels, which in turn affect immune responses and cytokine production. As hair cortisol is considered a marker of long-term HPA axis activity, our findings lend support to these ideas. Chronically heightened cortisol concentrations as a result of prolonged psychosocial stress may at least partially explain the altered immune system functioning, as well as the higher prevalence of alexithymia in individuals suffering from stress- and immune-related disorders.

Several psychological mechanisms could explain the apparent link between alexithymia and physiological stress. Martin & Pihl (7), in their stress-alexithymia hypothesis, proposed that alexithymia could directly increase long-term stress levels due to an impaired ability to identify and downregulate stress responses. The fact that only DIF was related to increased hair

cortisol levels is partially in line with previous research: In a study by Hua et al. (9), only the DIF dimension of alexithymia was associated with increased salivary cortisol secretion before, during, and after a social stress test. They suggested that DIF may impede emotional appraisal and may, therefore, increase anticipatory reactions to stressful situations and hinder recovery from them. A recent study by De Berardis et al. (41) found that DIF together with low resilience was associated with suicide ideation. They hypothesized that alexithymia, and particularly the DIF dimension may contribute to low resilience *via* maladaptive coping strategies. In sum, from the different facets of alexithymia, DIF may be particularly relevant for stress vulnerability and resilience.

However, other mediating factors for the association of alexithymia and stress are also possible. Alexithymic individuals tend to suffer from social anhedonia and interpersonal difficulties, possibly making everyday social situations more stressful. Alexithymic individuals are also more prone to substance use, and more often engage in a sedentary lifestyle and unhealthier diets (42–44), all of which may increase physiological stress levels. As our study was cross-sectional and did not assess potential mediating factors for chronic stress, future studies will need to address specific causal pathways between alexithymia and stress. Furthermore, as prenatal stress in mothers may have programming effects for fetal development, increasing the likelihood of future somatic and psychiatric morbidity in the offspring, future studies should examine the effects of maternal alexithymia on child development.

Some limitations of this study should be considered. The prevalence of alexithymia in this sample, as well as in the whole birth cohort, was low compared to the prevalence of alexithymia in the general population (45, 46), and the distribution of HCC was substantially wide. The low prevalence of alexithymia may be explained by the fact that the FinnBrain study sample is relatively highly educated and consists of young adults, thus the results may not be generalizable to all populations and other countries. Therefore, the results should be replicated in a larger and more representative sample of alexithymic individuals, and with more diverse measures of stress. Furthermore, HPA axis metabolism as measured by HCC in the context of alexithymia should be investigated among non-pregnant females and males, to gain more generalizable knowledge on the associations between long-term HPA axis homeostasis and alexithymia. Another limitation was that alexithymia was measured postnatally, whereas HCC was measured during late pregnancy. Cortisol levels are generally known to rise toward the end of pregnancy, and little longitudinal data exists on postnatal alterations off HCC (47). However, this is a minor limitation as several studies have concluded that alexithymia is a relatively stable trait (48), including in the course of pregnancy and the postnatal period (18). Finally, we did not assess traumatic experiences in adult life, adjustment disorders or post-traumatic stress disorder, and therefore we cannot speculate whether the alexithymic features in our study sample were attributable to developmental factors, traumatic experiences in adulthood or some other predisposing factor.

CONCLUSIONS

Alexithymia in pregnant women was associated with higher hair cortisol concentrations during the third trimester, possibly indicating chronic prenatal stress. The association was driven by subjective difficulty in identifying feelings, and was independent of current depressive symptoms. Further research is warranted to examine if alexithymia plays a causal role in prenatal physiological stress, and whether maternal alexithymia may affect offspring development.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee, Hospital District of Southwest Finland. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

All authors have been involved in the writing process of the article. JK, MK, NS, LK, and HK were involved in planning the research. JK has conducted the statistical analyses and most of the planning and writing.

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Panic Disorder as Unthinkable Emotions: Alexithymia in Panic Disorder, a Croatian Cross-Sectional Study

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Objectives: Previous research on alexithymia has led to controversy over its prevalence in panic disorder. The aim of this study was to assess the difference in the prevalence of alexithymia in panic disorder and other anxiety disorders.

Design and Methods: We performed a cross-sectional study on a sample of 71 patients diagnosed with panic disorder and 113 patients diagnosed with other anxiety disorders; both groups were 18–50 years old. Primary outcome was the 20-item Toronto Alexithymia Scale (TAS) score. Secondary outcome was the prevalence of alexithymia defined as a TAS score ≥61.

Results: Patients diagnosed with panic disorder had a 25% higher score on the TAS subscale of difficulty identifying feelings than patients diagnosed with other anxiety disorders. The prevalence of alexithymia was 27% in patients with panic disorder and 13% in patients with other anxiety disorders. Patients diagnosed with panic disorder had significantly higher odds for alexithymia.

Conclusions: The results of our study support the hypothesis of higher prevalence of alexithymia in individuals with panic disorder than in individuals with other anxiety disorders. In addition, difficulty identifying feelings as a salient feature of alexithymia is higher in panic disorder than in other anxiety disorders.

Keywords: alexithymia, anxiety disorders, mentalizing, panic disorder, psychoanalytical interpretation

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INTRODUCTION

The construct of alexithymia refers to a cluster of features, comprising difficulty identifying and describing subjective feelings, an impoverished fantasy life, and preoccupation with external events rather than to inner mental processes (1–3). Initially, alexithymia was described in psychosomatic patients (4–7). As alexithymia theory advanced, the construct progressed beyond the psychosomatic field. For almost half a century, researchers and clinicians argued whether alexithymia is specific to certain groups of patients or not specific and theoretically accessible to all of us, a prerequisite of

symptom formation or itself a symptom, primary or secondary, innate or acquired, a state or trait, a defense mechanism, or a structure deficit (3, 8). Nowadays, alexithymia as unique personality trait is considered to reflect deficits in cognitive-emotional processing and regulation of affect (9, 10). While the accurate meaning of the term alexithymia suggests a type of anomia instead of agnosia, for most clinicians and researchers inspired by Sifneos and Nemiah, it is the name of a multifaceted construct that encompasses more than a difficulty finding words for emotional feelings, rather words denuded of their affective significance (11, 12). Alexithymia is also viewed as a massive defense against intolerable emotions as well as a deficit in the mental representation of emotions (9, 12). Alexithymia is in neither the Diagnostic and Statistical Manual of Mental Disorders (DSM) nor the International Classification of Diseases (ICD) diagnostic category. Prevalence of alexithymia is around 10% in the general population (13–17).

Panic disorder (PD) is characterized by recurrent and unexpected panic attacks (18, 19). The lifetime prevalence of PD is approximately 4% (20). PD has high rates of relapse, which suggests a gap in our understanding of the maintain factors behind PD symptoms and that improving our understanding of the psychological processes underlying PD may enhance the efficacy of treatment (21). "Other anxiety disorders" (AODs; ICD-10 F41), including PD, are disorders in which manifestation of anxiety is the major symptom manifested by the somatic and affective component. Somatic arousal activates psychic elaboration whereby metabolize emotions into feelings (22, 23). Analogous to PD, alexithymic persons are prone to misinterpret somatic sensation as signs of physical illness and focus on the somatic manifestation of emotional arousal while minimizing the affective components of emotion (24, 25).

Nemiah was the first author who highlighted the connection between alexithymia and PD (26). In 1993, the first empirical studies were published to confirm this theoretical assumption (27, 28). Subsequently, using the Toronto Alexithymia Scale with 26 item (TAS-26), Bach et al. found no significant association between alexithymia and personality disorders (29). Since 1995, the 20-item Toronto Alexithymia Scale (TAS-20) has been used predominantly for research. The most researchers investigated the prevalence of alexithymia in PD, or in comparison with its prevalence in social phobia, affective disorders, obsessive compulsive disorder, suicidality, personality traits, eating disorders, substance use disorders, and childhood trauma (19, 30–36). De Berardis made a major contribution in this area by studying the impact of alexithymia on anxiety disorders (37, 38). At the same time, theories of pathophysiological mechanisms underlying PD have been developed. Nevertheless, the treatment of PD is still unsatisfactory (39–42). Moreover, alexithymic persons are thought to have poor response to treatment (43, 44). Consequently, there are still many questions to be answered.

In individuals with a normally functioning affective system, somatic arousal activates psychic elaboration (45). Panic can be understood as a core basic signal that is not adequately processed in its significance as a signal function and is not clearly defined or mentalized (46). Elaboration of affect includes identification of the meaning of panic, converting it to an anxiety signal that does not overwhelm the cognitive system (46). It is to be assumed that patients with PD are typically unable to identify bodily experiences and symptoms as representations or symbols of affective states. Somatic symptoms of the PD apparently have neither biological sense nor symbolic significance. The threat is experienced as if it is occurring in the body rather than in the mind, and as if it is a catastrophic danger to the body. This subjective experience indicates a deficit in symbolizing, a sub-symbolic state that has not been represented (46). Bypassing the psyche, anxiety directly affects the soma (47).

We assume that intense anxiety in PD and alexithymia due to insufficient psychological elaboration precipitate into fear and relocates to a somatic symptom (19). This implies that the degree of anxiety is more pronounced in PD than in OAD, leading to a breakdown of the mentalization process. Panic attack as alexithymia is an inability to master bodily arousal and a failure to metabolize primary somatic and affective experiences: a failure to metabolize emotions into feelings (23, 48). PD provides a useful model for exploring maladaptive alarm systems (46). This motivated us to deepen our research on alexithymia in PD.

Contemporary conceptualization of alexithymia inclined toward a dimensional rather than a categorical approach as well as it often included trait and state components (49–53). Nevertheless, the largest number of studies used a categorical model. In line with different methodology, sample size, version of the TAS scale, history of illness, comorbidity, and pharmacological treatment, a diverse range, from 16% to 67%, of alexithymia in individuals with PD was obtained (27, 28, 30, 31, 34, 36, 54–56).

So far researchers have studied alexithymia in Neurotic, stress-related and somatoform disorders. Regarding anxiety disorders, most researches compared alexithymia in PD and phobic disorders where anxiety is evoked only in certain well-defined situations. Since the emotion of anxiety in phobic disorder can be identified and mentalized and is oriented toward external object, it is questionable whether it can be named anxiety or fear.

Considering the above mentioned, our intention was to focus on insufficiently researched diagnostic category, "Other anxiety disorders" (F41). Although this category might seem heterogeneous, the disorders encompassed in it have a common core symptom—a free-floating, unrepresented, unmentalized anxiety directed toward own bodily sensations rather than an external object (like in phobias), which is especially seen in PD and generalized anxiety disorder. While the label "Other anxiety disorders" might imply all anxiety disorders, actually it doesn't encompass F40 codes, under the label of "Phobic anxiety disorders."

The aim of our study was to assess the prevalence of alexithymia in PD, the difference in alexithymia prevalence in PD and OAD, and correlation between alexithymia and the severity of PD. We hypothesized that the prevalence of alexithymia is higher in patients with PD (F41.0) than in patients with OAD (F41.1, F41.2, F41.3, F41.8, and F41.9).

According to our knowledge, this is the first study comparing these diagnostic categories. We also bring into focus the qualitative assessment between PD and alexithymia, using the Panic Disorder Severity Scale (PDSS).

METHODS

Study Design

Cross-sectional study was performed during three years in Mental Health Center Zagreb, Croatia. The study protocol was approved by the Ethics Committee of the Mental Health Center Zagreb. All participants provided written informed consent for participation, and their identities were concealed by assigning them a numerical code. We kept the signed informed consent forms and completed questionnaires separate. Informed consent included the aim and the purpose of the research. The study was performed in accordance with the World Medical Association Declaration of Helsinki 2013 (57).

Subjects

Our targeted population was outpatients newly diagnosed with PD (ICD-10 F41.0). The control population was patients newly diagnosed with OAD (ICD-10 F41.1–F41.9). We selected a consecutive sample, enrolling the patients by the order of their arrival to the first psychiatric evaluation. Inclusion criteria included both genders, age 18–50 years, and ability to complete the questionnaires by themselves. Exclusion criteria consisted of presence of other psychiatric or somatic disorders, previous PD or OAD, psychotherapy or pharmacotherapy, and acute suicidality. Of the 192 respondents, two did not give their consent to participate in the study, five had psychiatric or somatic comorbidity, and one had a previous psychotherapy so they were excluded from the sample. Therefore, 71 patients with PD and 113 with OAD were included in the study.

The diagnosis was made by an experienced psychiatrist during a clinical interview according to the ICD-10 criteria verified by the PDSS for patients with PD. The PDSS was administered by the same psychiatrist. Participants were screened for exclusion criteria during the clinical interview, and in the self-report questionnaire (made for the purpose of this research) that included items regarding comorbidities and previous pharmacological and psychotherapy treatment. We performed the power analysis before the enrollment. We obtained the expected TAS-20 values from the Cucchi et al. study (35), set the needed power at 80%, the significance at $p < 0.05$, and the minimal difference at least as large as the one found in the Cucchi et al. study. The largest sample size was needed for the externally oriented thinking (EOT) TAS-20 subscale, n = 58 in each group. We expected up to 10% of incorrectly collected data and determined the initially needed sample size to be 65 in each group. The needed sample size was calculated using PASS 13 Power Analysis and Sample Size Software (2014) (NCSS, LLC; Kaysville, Utah, USA, ncss.com/software/pass).

Outcomes

Our primary outcome was the 20-item TAS-20 score (58, 59). Each item was rated on a five-point Likert-type scale, ranging from "strongly disagree" (scored 1) to "strongly agree" (scored 5), with scores ranging from 20 to 100. Higher total scores indicated more alexithymia. TAS-20 has three subscales that assess difficulty identifying feelings (DIF), difficulty describing feelings (DDF) to others, and EOT. The scale has been translated into numerous languages, and its three-factor structure, has been cross-validated by confirmatory factor analysis across many countries and cultures (60–65). These findings support the view that alexithymia is a common trait rather than a culture-specific construct (3). Our secondary outcome was the prevalence of alexithymia. TAS-20 at the same time provides continuous assessment of alexithymia characteristics to identify persons with high and low alexithymia as well as empirically derived cutoff scores (58). Subjects with a total score of ≤51 are considered non-alexithymic, those scoring 52 to 60 possibly alexithymic, and subjects scoring ≥61 considered alexithymic (66). As a tertiary, exploratory outcome, we analyzed the association of the TAS-20 score with the severity of PD measured by the PDSS (67, 68).

The PDSS was developed to provide a simple method of measuring the overall severity of PD (68). It consists of seven items, each rated on a five-point Likert scale. The items consider panic frequency, distress during panic, anticipatory anxiety, phobic avoidance of situations, phobic avoidance of physical sensations, impairment in work functioning, and impairment in social functioning (68). A total score is calculated by summing the scores for all seven items. Individual responses are scored on a scale of 0–4, and total scores range from 0 to 28.

Possible Confounders

Possible confounders of our primary and secondary outcomes whose effects we tried to control by the multivariable statistical analysis were: age in years, gender, education, partnership, having children, work status, and number of household members. All this data was collected by participants' self-reports by answering the questionnaires. We did not independently check the validity of any of this data.

Statistical Analysis

In the analysis of our primary outcome, we calculated the absolute difference between medians of the TAS-20 and its three subscales in PD and OAD patients with Bonett–Price 95% confidence intervals (CI), the difference relative to the median in the OAD group; the statistical significance of the difference, using quantile regression; and Cliff's delta as the standardized effect size in the crude, unadjusted, and in the analysis adjusted for all preplanned possible confounding factors. We used the sequential Holm–Bonferroni correction to control the false-positive rate caused by multiple testing. In the analysis of our secondary outcome, we analyzed the difference in the prevalence of alexithymia in PD and OAD by multivariable, adjusted, binary logistic regression. Finally, we analyzed the unadjusted correlation between the TAS-20 score and the

TABLE 1 | Participants' sociodemographic characteristics.

	Panic disorder (n = 71)		Other anxiety disorder (n = 113)	
Sociodemographic characteristics				
Gender				
Men	29	(40.8)	45	(39.8)
Women	42	(59.2)	68	(60.2)
Age (years), median (IQR)	29	(24–36)	32	(23–36)
Education				
High school	49	(69.0)	70	(61.9)
University	22	(31.0)	43	(38.1)
Partnership				
Single	18	(25.4)	30	(26.5)
In a steady partnership	13	(18.3)	26	(23.0)
Married	40	(56.3)	57	(50.4)
Having children				
Yes	40	(56.3)	61	(54.5)
No	31	(43.7)	51	(45.5)
Work status				
Employed or student	47	(66.2)	82	(73.2)
Unemployed or retired	24	(33.8)	30	(26.8)
Number of household members, median (IQR)	3	(3–4)	4	(3–4)
Number of household members				
≤2	17	(23.9)	24	(21.2)
3	20	(28.2)	31	(27.4)
4	27	(38.0)	35	(31.0)
≥5	7	(9.9)	23	(20.4)

Data is presented as number (percentage) of participants if not stated otherwise.
IQR, interquartile range.
Data was missing for working status for one (0.9%) patient; with other anxiety disorder in one (1.4%) patients with panic disorder.

severity of PD measured by the PDSS in the PD group, using Kendall's tau b coefficient, and the independent correlation after the adjustment for preplanned possible confounding factors, using a quantile regression. We set the level of significance at two-tailed p <0.05 and all CIs at 95%. We performed statistical data analysis by using the R Core Team (2018). R is a language and environment for statistical computing (R Foundation for Statistical Computing; Vienna, Austria; URL https://www.R-project.org).

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

RESULTS

We enrolled 71 patients diagnosed with PD and 113 patients diagnosed with OAD. Two study groups were balanced regarding the gender, age, education, partnership status, having children, work status, and number of household members (**Table 1**).

After the adjustment for preplanned possible confounding factors and sequential Holm–Bonferroni correction for multiple testing, patients diagnosed with PD had significantly higher scores on the DIF subscale (**Table 2**). The difference in adjusted medians was Δ = 4 (95% CI: 3.1–5.6), which was 25% relative to the score in the OAD group. This was a moderately high standardized effect size of Cliff's δ = 0.61 (95% CI: 0.48–0.70). The differences between PD and OAD patients regarding the other two TAS-20 subscales, DDF and EOT, as well as the total TAS-20 score, were not significant.

In PD, the unadjusted prevalence of alexithymia was 19/71 (27; 95% CI: 17%–39%) and 15/113 (13%, 95% CI: 8%–21%) in OAD. Patients diagnosed with PD had unadjusted odds for alexithymia odds ratio (OR) = 2.39 (95% CI: 1.05–2.28) compared to patients diagnosed with OAD. PD patients had

TABLE 2 | Toronto Alexithymia Scale (TAS-20) results in two study groups.

	Panic disorder (n = 71)		Other anxiety disorder (n = 113)		Δ	(95% CI)	Δ%	δ	(95% CI)	p	p_{corr}
	Median	(IQR)	Median	(IQR)							
Crude, unadjusted											
TAS total score	53	(43–63)	46	(37–54)	7	(2.0–12.0)	15%	0.25	(0.08–0.41)	0.004	0.024
TAS subscales											
DDF	13	(10–16)	12	(9–15)	1	(–0.8–2.8)	8%	0.17	(–0.01–0.33)	0.261	0.522
DIF	20	(14–26)	15	(12–21)	5	(2.9–7.1)	33%	0.27	(0.10–0.43)	0.002	0.016
EOT	20	(16–22)	19	(15–21)	1	(–0.8–2.8)	5%	0.09	(0.08–0.25)	0.213	0.639
Adjusted*											
TAS total score (20-100)	52	(51–57)	45	(42–48)	7	(5.9–8.0)	16%	0.66	(0.55–0.74)	0.012	0.060
TAS subscales											
DDF	14	(12–15)	12	(11–13)	2	(1.6–2.4)	17%	0.56	(0.42–0.67)	0.065	0.260
DIF	20	(17–23)	16	(13–18)	4	(3.1–5.6)	25%	0.61	(0.48–0.70)	0.003	0.021
EOT	19	(18–20)	18	(17–20)	1	(0.4–1.7)	6%	0.15	(–0.01–0.30)	0.680	0.680

DDF, difficulty describing feelings; DIF, difficulty identifying feelings; EOT, externally oriented thinking; Δ, absolute median difference; CI, Bonett-Price confidence interval; Δ% median difference relative to the value in other anxiety disorder group; δ, Cliff's delta given as the standardized effect size of the difference in medians; p, statistical significance of the difference between the panic disorder and other anxiety-disorder groups calculated by quantile regression; p_{corr}, statistical significance corrected by the sequential Holm–Bonferroni correction for multiple testing.
** Medians were adjusted for age, gender, education, working and partnership status, having children, and number of household members.*

61% higher relative risk for alexithymia than OAD patients, relative risk (RR) = 1.61 (95% CI: 1.03–2.28). After the adjustment for preplanned possible confounding factors by multivariable binary logistic regression, patients diagnosed with PD had significantly and more than two times higher odds for alexithymia, defined as TAS-20 score ≥61, than patients diagnosed with OAD (OR = 2.75; 95% CI: 1.19–6.36; p = 0.018).

In unadjusted analysis in the PD group, the severity of PD measured by the PDSS was significantly correlated with the total TAS-20 score (Kendall's tau b, $\tau = 0.16$, p = 0.011) (**Figure 1**), subscales: DIF (Kendall's tau b, $\tau = 0.14$, p = 0.030), and DDF (Kendall's tau b, $\tau = 0.17$, p = 0.010), but not with the EOT subscale (Kendall's tau b, $\tau = 0.09$, p = 0.186). After the adjustment for preplanned covariates by quantile regression, the total TAS-20 score and none of its subscales were significant independent predictors of the severity of PD (total TAS-20, p = 0.065; DIF, p = 0.187; DDF, p = 0.159; EOT, p = 0.060).

DISCUSSION

The results of this study are limited and only partially confirm our hypothesis. In this study, TAS-20 DIF subscale scores were significantly higher in the PD group than in the OAD. This is consistent with the results of previous similar research (27, 28, 36, 69). This result supports the hypothesis of a higher rate of alexithymia in patients with PD than in those with OAD, as well as understanding alexithymia as the difficulty to identify emotions. Capacity to communicate and name one's emotion, in other words DIF subscale, is a central aspect in alexithymia (19, 70).

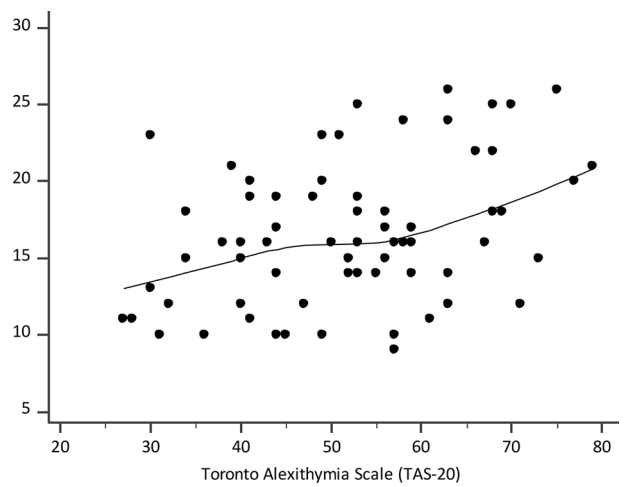

FIGURE 1 | Scatter diagram of correlation between the Toronto Alexithymia Scale (TAS-20) and the Panic Disorder Severity Scale (PDSS); the line is a locally estimated scatterplot smoothing (LOESS) trend-line with the smoothing span of 80%.

In this survey, the prevalence rate of alexithymia in PD was 27%. The first two studies of alexithymia and PD that used the TAS-26 suggested that alexithymia may constitute one of the psychological characteristics of PD, with a prevalence of 67% and 46.7%, respectively (27, 28). The first and highest prevalence rate of alexithymia in PD could be explained due to the relatively small sample of 27 patients (28). Successively, Iancu and colleagues (56) reported a prevalence of alexithymia of 39% by use of the TAS–26, whereas Cox and colleagues (30) found a prevalence of 34.0% with the TAS-20. In a more recent and well-conducted follow-up study on 52 adult patients with PD, Marchesi et al. (32) reported a prevalence for alexithymia of 44.2%. Contrary to De Berardis and colleagues (34), many studies examined PD patients with a relatively long history of illness, and this could lead to potential biases due to actual or previous psychological and pharmacological treatments that may, on their own, influence psychological characteristics, such as alexithymia. We used very selective inclusion criteria and restricted the observation to outpatients with recent-onset PD only, and without a history of previous regular treatment in an attempt to avoid potential biases as secondary alexithymia or somatic symptoms secondary to a psychiatric disorder (34, 71).

The differences between PD and OAD patients regarding DDF and EOT, the other two TAS-20 subscales, and the total TAS-20 score, as well as PDSS were not significant.

Most researchers agree that DIF and DDF are salient features of alexithymia, although some researchers have suggested that the EOT subscale is substantially different from the DIF and DDF subscales (72, 73). In our study, the EOT subscale appears to be a quite independent variable from PD, and this finding resonates with those of previous studies. Many authors emphasize the difference and caution interpreting of the EOT subscale scores (74, 75). The EOT dimension corresponds closely to a concept of pensée opératoire (operative thinking) introduced by French researchers Marty and de M'Uzan. An operative or utilitarian style of thinking includes the absence of fantasy and other manifestations of the depleted inner mental world of feelings and ideas about intentions, needs, and attitudes and focused on external events (3, 6). Whereas healthy individual integrate dreams, fantasies, or symbolic interactions in symbolic representations, the alexithymic individual fills his or her inner world with external details, a fact that can be particularly well observed (6, 8). The origin of alexithymia can be located at a stage prior to the formation of representations (8). The failure in the mother–child symbiosis prevents the development of symbolic thinking (8). Emptiness instead of good object, actions instead of language direct person from inside to outside reality, to concrete presence of external objects instead of fantasy and internalization (8, 47). The disturbances of the mother's alfa function do not signalize so much of separation anxiety, but rather an unspecified fear of annihilation (8, 46, 76). No good object representations are accessible, and such individuals remain reliant on on the concrete presence of external objects (8, 47). Object loss represents one of two dangerous extremes of "oneness to

none-ness" and precipitates the formation of somatic symptoms (8).

In terms of affective states, panic patients have particular difficulty identifying, verbalizing, and representing certain affects, although this capacity can vary depending on the context (46). The experience of certain emotions, including anger, dependent feelings, and separation fears, as dangerous is relevant to this difficulty, but identification of these feelings is necessary to identify the danger. In fact, understanding that emotions can trigger anxiety can be seen as part of the process of representing affects. Mentalization as capacity to understand ourselves and others could enhance alexithymic characteristics particularly items in DIF subscale which were negatively correlated with bias in emotion perception, especially in social relation (77). Exploration and interpretation of avoided emotions improve reflective function and mentalization in PD (78).

We suppose that patients with PD, unlike OAD, suffer from the lack of an integrated representational system that links affective, somatic, and verbal realms, adding to the vulnerability to panic and severe anxiety onset and persistence. These bodily and emotional experiences are dissociated from meaningful conscious links and the verbal symbolic realm. Psychoanalytical interpretation enables us to understand alexithymia and PD as an insufficiency in the process of mentalization and, consequently, a deficiency in the regulation of affect.

Limitations of the Study

This study has several limitations. Among the major one is quite dispersive and heterogeneous OAD as a comparison group. In addition to "Generalized Anxiety Disorder" (F41.1), "Other specified anxiety disorders" (F41.8), and "Anxiety disorder, unspecified" (F41.9), other diagnoses such as "Mixed anxiety and depressive disorder" (F41. 2), and "Other mixed anxiety disorders" (F41.3) may contain other symptoms, in particular depressive symptoms, that may affect the results.

The data were collected at one site and by only one rater, experienced psychiatrist. The advantage of such approach is homogeneity, but it could also lead to reduced possibility of generalization as well as lead to systematic error.

The data were mostly based on self-report. This method has some inherent flaws such as poor self-awareness, an increased risk for socially desirable answers, and various response styles (79, 80). Measuring alexithymia by TAS-20 has some shortcomings even though captures an impairment in feeling and describing emotions and is a valid measure of the alexithymia construct (12). The concurrent use of the Toronto Structured Interview for Alexithymia (TSIA) with TAS-20 may overcome some of these limitation (81).

We used a cross-sectional design that is limited in terms of causality.

Concerning theoretical part, there is an additional significant limitation. Psychodynamic theory did not emerge as a result of this study, even though it makes it easier to understand that anxiety in PD is overwhelming and different from anxiety in OAD. Considering the global scientific literature the biological theory of PD are well-researched yet poorly understood while psychodynamic thought is scarcely validated by empirical evidence-based research (82–85). Fostering a multi-perspective approach to PD affords distinctive glimpses into psychopathology and enhances our understanding of PD (86).

CONCLUSIONS

Even though anxiety is the core symptom of the ICD-10 F41 (F41.0–F41.9) diagnostic category, there is a difference between PD (F41.0) and OAD (F41.1–F41.9). The construct of alexithymia enable us to think of PD as an unthinkable emotion. Alexithymia and the "unmentalized" psychosomatic mind in some way distinguish PD from OAD. Alexithymia represents difficulties in affective and cognitive differentiation of emotions characterized by poor verbalization, resomatization, and dedifferentiation of mental and somatic affective experience; similarly, PD is a perfect example of such dedifferentiation and resomatization of affects in undifferentiated form.

Elevated rates of alexithymia in PD may reflect patients' inclination to constrict their emotional experience to avoid affect-based psychological sensation (56). Individuals with alexithymic features, as well as individuals with PD, are unable to use bodily perceptions as a helpful signal for themselves. Enhancing or improving symbolic thinking or mentalizing might be beneficial for these individuals.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Health Center Zagreb. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors contributed substantially to the conception and design, reviewed the manuscript, and approved the submitted version.

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More Than Words Can Say: A Multi-Disciplinary Consideration of the Psychotherapeutic Evaluation and Treatment of Alexithymia

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Alexithymia is a disorder that stands at the border of mind and body, with psychological/affective and physiological/experiential disturbances. The purpose of this article is to propose a new clinical access point for the evaluation and treatment of the deficits in emotional awareness demonstrated in alexithymia. This will be based on insights from recent neuroscientific research, which is adding to the psychodynamic understanding of alexithymia, regarding clinical presentation and etiology. Following a brief review of definitions, forms of measurement, and potential etiologic elements of alexithymia, current neuroscientific theory and research into "predictive processing" approaches to brain function will be outlined, including how "interoception" and "interoceptive inference" underpins emotion and emotional awareness. From this synergistic perspective, I will outline how interoceptive inference provides a key to the link between: problems in early life relational experiences and the patient's long held, but suboptimal models of their inner and outer world. This is reflected in the deficits in affective experiencing and emotional awareness described in alexithymia. Three clinical cases will be presented to illustrate this nuanced consideration of alexithymic etiology and treatment. The implications of the historical, psychological, and somatic aspects of experience will be considered, regarding the patients' diminished ability to: experience and represent emotional experience as distinct feeling states; signify the relevant meaning of affective experience; and incorporate such with cognitions to adaptively guide behavior. These will be addressed using psychometric, psychological, neuro-cognitive, and neurocomputational approaches. Elements from current theory, research, and treatment of alexithymia, will be highlighted that are salient to the clinician, in order to support their understanding of patients against the backdrop of current psychodynamic and neuroscientific research, which will thereby increase treatment options and benefits. The focus, and conclusion, of this article is the role that attention to interoception can play (within the safety of the therapeutic relationship and within any therapeutic process) in allowing updating of the patient's strongly held but dysfunctional beliefs.

Keywords: alexithymia, psychotherapy, interoception, interoceptive inference, mentalization, levels of emotional awareness, TAS-20, predictive processing

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INTRODUCTION

The construct of alexithymia has been studied from many different clinical and neuroscientific perspectives. It was originally organized around common clinical characteristics that psychosomatic patients present, notably their difficulty in verbalizing their emotions as feelings. The word *alexithymia*'s Greek roots describes this lack of the language for feelings (1, 2). Subsequently, the concept has taken on more depth and meaning, now denoting a disturbance in: the individual's affective experience; level of emotional awareness; and, ultimately, verbalizations of emotions as feeling states. There has, however, been persistent difficulty across disciplines in creating a comprehensive clinical and neurobiological account of the disturbance and in representing this in adequately descriptive language that is understandable by all disciplines and which takes account of the inherent variability in clinical presentations of alexithymic patients. As a clinician, it is my intention here to introduce therapists to research and theoretical propositions that are relevant to psychological and neuroscientific perspectives regarding alexithymia.

Following a brief review of the history of the concept of "alexithymia," I will address measurement constructs and review proposals regarding psychological approaches to etiology, focusing on what part early-life development may play in the emotional, relational and bodily-oriented aspects of the disturbance. Neurobiologic theory and processes, that provide insight into both etiological and clinical considerations, will be presented in some detail, to facilitate the clinician's understanding. The relevant neuroscientific terms and theory will be explained, where required.

As a clinician, it is my intention to present a unique perspective of alexithymia, bringing together new information from clinical and scientific disciplines. This will involve contextualizing current psychometric measurement and psychological theories of alexithymia within current neuroscientific theory of how "predictive processes" create emotional experience. These processes rely on: physiological necessities, prior beliefs, and sensory evidence from the environment (in this paper, the focus is on bodily experience). I will link psychological and neuroscientific proposals to explain how an alexithymic patient's unique symptomatic presentation is generated and how this may be best comprehended and responded to in their treatment.

HISTORY OF THE DEFINITION AND MEASUREMENT OF THE ALEXITHYMIA CONSTRUCT

The concept of alexithymia arose from the clinical presentation of symptoms, noticed by a small number of clinicians, who were impressed by distinct similarities in how these patients expressed their emotional state as feelings[1], or, more accurately, could not describe their emotional states. Focus was initially on patients with psychosomatic illnesses, whose thought processes were seen as *"utilitarian"* and concrete, with apparent minimal ability to fantasize or abstract. This form of thought was labeled *"pensee operatoire"* (4) because patients' vocabulary for their emotional states often utilized only somatic descriptions, focusing on external events as causative for internal experiences. However, patients also exhibited behaviors that were disorganized and appeared to be affectively charged, such as poor impulse control and chaotic relationships—expressing no recognition of the affect evidenced in their behaviors (2). Clinicians proposed that such patients did not recognize their emotions through symbolic representation, nor perceive them as signals regarding their needs or wants (5), but rather enacted their feelings in behavior, or referenced affective experience through somatic sensations or somatization.

A consensus was reached on the definition of alexithymia at a 1977 conference on psychosomatic research in Heidelberg, Germany. The definition was organized around the clinically salient features: 1.) difficulty identifying feelings and in distinguishing between feelings and bodily sensations that reference emotions; 2.) difficulty describing feelings to others; 3.) restricted imagination and lack of fantasy; and 4.) an externally oriented thinking style (6–8). Subsequent research has proven alexithymia to be a multi-faceted dimensional personality trait, with varying degrees of expression in individuals (9–11), including individuals who have diagnosable psychiatric illness but also healthy individuals (12). Clinically relevant alexithymia is thought to affect 10% of the general population (13, 14).

Alexithymia is a complex construct that involves both cognitive and affective disturbances. It is considered a deficit in experiencing, describing, and regulating emotion (8), evidenced as a more global deficit in emotional awareness, involving an inability to bring emotional experiences to the level of conceptualizing feelings regarding oneself or others (15). Although there is consensus on the factors comprising alexithymia, there is much disagreement over how to test and quantify these. The most common measurement approaches will be addressed below. (For a more extensive review the reader is directed to Lumley et al. (16) and Maroti et al. (17).

The Toronto Alexithymia Scale (TAS), which is the most commonly used self-report measure, was originally developed as 26 items and then pared down to a 20-item questionnaire (TAS-20). The TAS-20 provides individual sub-scores for the three factors from the Heidelberg consensus i.e.: 1.) Difficulty Describing Feelings (DDF); 2.) Difficulty Identifying Feelings (DIF); and 3.) Externally Oriented Thinking (EOT).

[1] Within this paper, a distinction is made between the terms *emotion* and *feelings*. This is in accord with Damasio's assertion that emotions are embodied experiences, while feelings are the awareness of having emotions (3). The term *affect* is used here to include both emotion and feeling (6).

Daydreaming, as a potential factor, was eliminated from the TAS-20, as it was considered subject to social responsivity bias and insufficiently reflective of the subject's capacity for imagination (8). The overall score generated by the TAS-20 is intended to indicate severity of alexithymia generally. This is widely used within research settings, with cutoff scores indicating the presence (greater than 61) or absence (under 51) of clinical levels of alexithymia. Advantages of the TAS-20 are that it easy to use, brief and has good construct validity (9) and reliability (17).

By contrast, the Levels of Emotional Awareness Scale (LEAS), developed by Lane and co-workers, reflects their conceptualization of alexithymia as a global impairment in affective processing, resulting in deficits in emotion generation, description and awareness (18). The LEAS requires written answers to questions that are intended to elicit feelings—within the subject and in their relation to others. The test rubric allots points for the degree of differentiation in the emotional words used, as well as in the differentiation of the self from other. Therefore, if the individual uses more specifically affectively laden language, and/or describes blends of feelings, and language that differentiates self from other, they will receive a higher score. The LEAS has good inter-rater reliability, internal consistency, and criterion validity (17). A strength is that only the structure of experience is addressed, not the content, which limits the subject's ability to falsely enhance their scores in order to make a desirable impression. The LEAS is linked to the construct of Emotional Awareness (15, 19, 20) as well as to the Three Process Model (TPM) of emotional experience (21–24).

The TAS-20 and the LEAS are both commonly used throughout research and in clinical literature and practice. Importantly, the creators of both measurement tools agree that a disturbance in emotional processing is salient to alexithymia (9, 16). However, both measures have been criticized. It is now recognized that they potentially measure different aspects of alexithymia.

Furthermore, as Lumley notes, the TAS-20 was the first readily reproducible test and has been very commonly used because it is simple to administer. As a result, it has become, by default, improperly considered actually to *define* alexithymia. However, *"the measure one is using, (e.g., TAS-20, OAS, BVAQ, LEAS, etc.) is not itself alexithymia but only an approximation of it"* [(25), p. 241]. We must be mindful, when considering the results of any particular measurement instrument, that alexithymia is *not* a measured score on any given test but, is the affective and cognitive difficulties that characteristically present in some patients. In this article, I will, therefore, treat the TAS-20 as a descriptive measure of predominant deficits that present clinically in an alexithymic patient. I will also address the construct of Emotional Awareness but again as a descriptive measure, not as an empirically measured value.

PSYCHODYNAMIC CONSIDERATION OF ALEXITHYMIA

Psychoanalytic theorists have discussed alexithymia from different perspectives for decades [e.g., (5, 7, 26)]. Krystal (5) hypothesizes that alexithymia could result from: developmental disruptions in affect development related to infantile psychic trauma; post-traumatic disturbances due to trauma experienced later in life (particularly if anhedonia is a significant component of the presentation); and/or neurobiologic dysfunction. In his clinical opinion, alexithymic symptoms are most often associated with *"impairment in the capacity for self-care"* [(5), p. 243)]. Moreover, he posits that patients are fundamentally unable to recognize and utilize emotions as signals to themselves. They can't realize their emotions as feelings, nor can they recognize them as vital and necessary reaction to their lived experience. He elegantly describes this underlying difficulty.

> *"Only when one experiences the cognitive aspect of an emotion—the meaning of the affect and some indication of the "story behind it"—and simultaneously has the expressive reaction and an adequate capacity for reflective selfawareness [sic], can one observe that one is experiencing a 'feeling' and identify it." [(5), p. 243*]

According to Krystal's interpretation, the cognitive disturbances of alexithymia represent a lack of affective vitality, as evidenced in the content of verbalizations, which are externally oriented and monotonous. They may seem well adjusted to reality, *"superadjusted"* in fact (5). However, this present-minded focus overlies a severe paucity of imaginative capacity. Thought is stimulus-bound, with utilitarian attachments and a significant lack of relational involvement with others.

Other theorists highlight that the results of this outward focus is to leave the individual with bodily sensations that are confusing and can trigger somatic disturbance which increase somatization, without the means to break out of this cycle through language and relationship (8). Such a lack of resonance and cohesion between bodily sensation and awareness of their emotional implications leaves alexithymic patients with a distinct inability to symbolize and therefore to regulate their emotional states, leaving them vulnerable to dysregulation, both somatically and psychologically. The functional capacity of *"mentalized affectivity"* (27) is lacking, such that they are unable to: identify; regulate; or communicate their emotional state to themselves or others; and therefore unable to utilize relationships to emotionally regulate (28). As we shall discuss below, reigniting emotional experience and awareness is an important element of psychotherapy with alexithymic patients, within any theoretical formulation.

Regarding patients with both alexithymia *and* anhedonia, Krystal (5) asserts that this combination is reflective of *later* (rather than early) life trauma that can create an experience in which the trauma continues to be subjectively experienced, as if it were punishment for the patient's transgression in seeking their own goals. Thus, reaching for any goal generates distress, with the trauma implicitly acting as a command to the individual not to experience positivity or vitality. McDougall's (26) noted that anhedonic alexithymic patients have a significant distortion in their self-representation, which does not allow them to even *"be"*

themselves, much less to take care of their needs (26). They have diminished access to all affective experience, so as not to touch any pleasurable emotion, with the anhedonia resulting from an inability to play, to demonstrate pleasure, or to seek well-being.

Using Piaget's theory of cognitive development as a template, Lane and Schwartz (15) developed a concept they refer to as Emotional Awareness, which is directly applicable to the deficits in alexithymia. This construct provides a means to: consider the experiential aspect of emotion; provide support to clinical exploration of individual differences in emotional experience: determine, and potentially measure, how this might change over time (15). In their formulation, Emotional Awareness is a trait that represents a cognitive *ability*, or skill, developing in a step-wise progression over time. Thus, an individual's ability to detect and describe their emotional experience, and that of others, undergoes structural transformation, with increasing differentiation. There is a progression from (implicit) bodily-based sensory experience through levels of cognitive awareness that are increasingly more explicitly and consciously recognized. Alexithymia represents dysfunction, with the patient operating at a Level of Emotional Awareness that is limited by specific developmental disturbances that have created deficiency in some of the elements necessary for emotional awareness at higher levels. For example, there may be deficits in awareness of bodily sensation or in recognition of emotions as feeling states. Although this progress represents a continuum of a trait-level ability, Emotional Awareness is conceived as having five levels. (For further information the reader is directed to (15, 19).

Level 1: Awareness of bodily sensations: the individual's experience of emotion will only be reflected in a report of the sensations from their body

Level 2: Awareness of the body in action: emotional experience is through action tendencies and sensation; the ability to experience emotion does not reach the level of feeling

Level 3: Awareness of feeling states: the quality of emotional experience changes to include somatic experience as well as psychologic experience

Level 4: Awareness of blends of feelings: there is an increased range of emotional awareness and this is more coherent and can be recognized to change over time; yet the recognition of other's emotional states is still unidimensional

Level 5: Awareness of blends of blends of feelings: there is greater capacity to recognize and make distinctions in emotions, with descriptions more nuanced and linguistically complex; and the ability to differentiate self from other is most available

Lane and colleagues have incorporated into their model of Emotional Awareness current neuro-cognitive and neuro-computational theories to proposes how different elements of affective processing *"interact to produce self-reportable emotional experience"* [(29), p. 474]. They call this the Three Process Model (24, 30, 31) and assert that disturbances in the elements of affective experience, described within this model (which may be created by various mechanisms that are dependent on the individual's life history), are reflected in lower Levels of Emotional Awareness. First, however, in order to allow deeper insight and understanding by clinicians, it is necessary to review the recent neuroscientific concepts and theories that underpin such models.

OVERVIEW OF RELATED NEUROSCIENTIFIC CONCEPTS AND RESEARCH FINDINGS

Interoception, Homeostasis, and Allostasis

Neuroscience is generating increasing research into how the synthesis of bodily sensation with other sensory input (as well as top-down influences) creates emotion and feelings. Fundamental to this is "interoception," which is the set of senses that sends information from all the tissues of the body to the brain, through neural and blood-borne pathways (32), being formally defined as the *"the process by which the nervous system senses, interprets, and integrates signals originating from within the body, providing a moment-by-moment mapping of the body's internal landscape across conscious and unconscious levels"* (33).

The insular cortex is an area that has widespread importance regarding interoception and emotional experience (34, 35), with interoceptive signals primarily entering the posterior aspect, and the anterior aspect more important relative to the multitude of connections that support subjective experience. The anterior insula cortex (AIC) and the Anterior Cingulate Cortex (ACC) play important complementary roles regarding experience and behavior, serving as interdependent arms of a coordinated system (32). The anterior insula is functionally important towards the generation of feeling states and subjective awareness, while the anterior cingulate is related more to motivation and behavior (34, 36).

In addition to the coordinated activity between the AIC and the ACC, each is also involved in activity with other areas that function together more generally as networks. The resulting connectivity of these networks generates specific functional activities which are dependent on activity within and between linked areas. It has been proposed that the Default Mode Network[2] (DMN), *"is in charge of processing self-related content"* [(38), p. 55]. This network is most active when the brain is "idling." Fluctuation in its activity are thought to be related to the degree to which individuals are thinking introspectively (39). Utilizing fMRI, Liemburg and colleagues (40) found different levels of activity in alexithymic subjects when compared to healthy control subjects. Notably, there was lower connectivity in the anterior area of the DMN that is thought to be most active in emotional processing. They attribute this to the decreased emotional awareness in alexithymia (40, 41).

Crucially for our discussion, it is now understood that the subjective experience and awareness of emotion relies on interoceptive signals from visceral, autonomic, hormonal, and immunological systems that indicate bodily changes [e.g.,

[2]Brain regions identified as DMN include medial prefrontal cortex, posterior cingulate cortex, ventrolateral prefrontal cortex, lateral temporal lobe 37.

(32–34, 42–44)]. It is generally accepted that emotion involves the integration of interoceptive sensations (which provide information about the current state of the body) together with exteroceptive information from the external world (which contextualizes how the state of the world is likely to impact on the state of the body). This integration is performed by top-down brain processes that involve information (i.e. what is known or understood) about the person's past expectations and their understanding of the probable affordances, or possibilities for action within the present environment (45). We will consider the aspects of physiological process for which interoception forms the foundation, before addressing how the deficits noted in alexithymia can be considered in this light.

The continuous flow of interoceptive signal from the body to the brain necessarily provides information about the homeostatic state of the body (which is mostly unconscious). Homeostasis is conceived as a reactive process that is constantly countering an inherent biologic instability within the organism (46).

A more useful characterization of bodily stability is allostasis [(47), p. 1192], which is the process by which the organism prospectively avoids disruptions to homeostatic set points (47–50). Interoceptive information is utilized by allostatic processes to control bodily states by anticipating perturbations (such as energy demands) and implementing allostatic mechanisms within the internal milieu, through ANS reaction or motoric actions within the environment, heading off potential homeostatic changes *before* they actually occur (51). Interoceptive sensations, therefore, are signals to the brain regarding the motivational state of the individual, with ANS activity acting as the effector arm of this processing (32). Thus, the interoceptive signals that underpin homeostasis and allostasis play an essential role in motivated behavior (34, 52, 53). For example, interoceptive signals that indicate falling body temperature will motivate an organism to search for warmth and shelter *before* any vital homeostatic set point is breached. Importantly for this paper, significant allostatic needs are always present, in some form, in a person's social environment, and must be responded to (50)[3].

To better comprehend how sensations interact with top-down influences to create emotional experience and awareness in healthy individuals, as well as those with alexithymia, we must follow a path through neuroscientific theory and research that appears complex at first. However, if the reader contextualizes this information with some personal reflection from their daily experience, it will become increasingly understandable.

[3]While most interoceptive activity occurs outside of conscious awareness, some sensation rises above the brainstem, such that most people are more or less aware of sensation from at least four interoceptive channels which are: cardiovascular; respiratory; visceral (the gut); and urogenital. The research findings that have looked for a relationship between sensitivity to, or awareness of, interoceptive signals and alexithymia unfortunately have failed to reach a consensus. This is due to significant methodological differences and different measurement instruments. The interested reader is directed to the literature for more detail, for example: (13, 16, 54–56).

COMPUTATIONAL NEUROSCIENCE: PREDICTION, PROBABILITY, AND INFERENCE

Recently, computational neuroscience and the use of mathematical modelling has suggested a radical way to understand brain processes. The utility of this approach has great potential in psychiatry and psychosomatic medicine (57, 58, 59).

Crucially, we start from the fact that the human brain does not have direct access to the world. Therefore, in order to make sense of its internal environment (its own body) and the external environment (the world it inhabits), it has to *infer* the causes of the sensory signals it receives from the inner and outer world, in order to decide how best to react, in order to enhance the organism's chances of survival. Predictive processing theory starts from this point and asserts that our brains use our previous experience as the basis for "predicting" (i.e. inferring or hypothesizing) what is the most likely cause (i.e., meaning) of incoming sensations from both our internal and external worlds (60–62). This inferential activity produces what are called "generative models," *"which attempts to predict each wave of sensory input before it arrives"* [(24), p. 30]. Our brain builds these models, throughout our lives, and continuously modifies them in the light of incoming sensory signals, hopefully so that they provide increasingly accurate approximations of the reality in which the individual finds themselves, at any given moment in time, in order to guide behavior. In other words, we learn and adapt by continually updating our generative models for what are the most likely causes of any particular set of incoming sensory information.

Predictive processing describes this model-building in the brain by using Bayes' Theorem, to illustrate how our generative models (also sometimes—confusingly—called hypotheses, predictions, priors, expectations, or beliefs) are built and then tested against the incoming interoceptive and exteroceptive sensory streams. Frith (63) explains Bayes' Theorem thus: *"Given some phenomenon (A) that we want to know about, and an observation (X) that is evidence relating to A, Bayes' Theorem tells how much we should update our knowledge of A, given the new evidence X"* [(63), p. 121]. If we assume that the brain behaves as a "Bayesian observer," we can assume that it is constantly attempting to "*know about*" the hidden causes of its internal and external sensations (i.e. phenomenon A, using incoming sensory data X). Previously learned predictions (or priors) are thus continually being evaluated against the incoming flow of sensation (i.e. observation X) and being potentially updated. Prediction, in this context, is a technical term, not the cognitive "act" of predicting. It is a, generally unconscious, quantitative, and probabilistic attempt to match best examples from previous learning to what the sensory organs are currently receiving. Bayesian inference thus allows the brain to predict (i.e. hypothesize) what is the mostly likely cause of a given (set of) sensation (whether coming from within the body or from the outside world).

This Bayesian process occurs throughout the brain, in a stepwise manner. Thus, the generative models it creates are termed hierarchical. Predictions (i.e. our prior beliefs or expectations) essentially flow down the hierarchy, meeting upcoming sensation from interoceptive, exteroceptive, and proprioceptive sources. When any given prior prediction (the likelihood that sensory inputs would be observed under a given model) is compared against sensory data, further activity in the hierarchical processes determines whether to update that prediction in the light of this new, incoming evidence. To do so it utilizes the difference between the prediction and the sensory evidence. This difference is referred to as "prediction error"—i.e., how wrong the prediction appears to be, when compared to the current sensory data. This hierarchical activity is occurring across multiple levels of the brain at any given instant. Whether any prediction error will update a prior prediction, or whether actions will be generated, following the sensory evidence, depends on the relative salience/reliability of the prior prediction compared with that of the sensation.

To understand this, it is important to reiterate that the words expectation, prior, or belief, do not denote consciously held beliefs, but refer to activity occurring in neurons in the brain. Referring back to our Bayes' example above: all priors (beliefs regarding phenomenon A); incoming sensory information (observation X); prediction errors generated (if phenomenon A doesn't match X); and resulting posterior beliefs (updated beliefs about phenomenon A), are assumed to be held in the form of probability distributions. There is, necessarily, uncertainty associated with each of these probability distributions, reflected mathematically by its relative spread. The inverse of this spread is known as its "precision," which denotes the salience (confidence or reliability) associated with a particular prior or prediction error (64). The precision (salience) imparted to the prior/prediction and also to the incoming sensation is modulated by many factors (e.g., neurochemical, motivational, strength of sensory signal). Crucially, this salience is used by the brain to weight the priors *vs.* prediction errors. The relative weight (i.e. precision) of the prior belief *vs.* the incoming interoceptive sensory information, determines whether the prior gets updated (or not). If the prior is precise, it will tend not to update in the light of imprecise prediction error. By contrast, highly precise incoming sensation can update an imprecise prior. Updating results in a new (hopefully more accurate) belief known as the "posterior" belief. Such updating of beliefs/predictions occurs across all biopsychological domains, including: perception; motor control; emotion; and decision-making.

Predictive processing has been applied within a wider theory of adaptive functioning known as the "Free Energy Principle" (61, 64). This principle asserts that organisms' adaptive changes are *always* in the service of minimizing unexpected (or unpredicted) sensations. Failure to do so will tend to lead to dis-homeostasis, with increasing disorder (entropy) that is dangerous to the organism, ultimately likely to cause death. Through the process of Bayesian updating, therefore, the organism is constantly improving its ongoing modeling of its inner and outer sensory world. By minimizing unexpected sensations, it maintains the body in stable homeostatic/physiologic states. Human beings thus form and update predictions (beliefs or expectations), throughout our lives, about all aspects of our inner and outer worlds. For example, we have prior beliefs/predictions about: homeostatic set points; the meaning of a pain in our body; and our social experience regarding the intentions of another person in the world.

It is important to note that our beliefs (priors), and thus our (generative) models of the world and ourselves in it, can never be veridical but they must be good enough to allow us to survive.

The power of the Free Energy Principal is that it goes beyond providing an account of how the brain adjusts its perceptions (61). This Principal also explains how actions are generated by a process known as active inference (61, 65, 66). In this perspective, motor reflexes are enslaved by predictions about the results of the movement. For example, a generative model of movement involves a prediction that a particular set of muscles will contract in a particular way to produce a particular set of sensations from interoceptive, proprioceptive, and exteroceptive sources, with the prediction errors resolved only if the muscles comply with these predictions to bring the actual sensations in line with the predicted sensations. It is important to note that an "action" taken for the purpose of minimizing prediction error in a generative model can be from: the major muscle groups of the body; the viscera or internal organs of the body; and also through actions of the autonomic nervous system.

Significantly for our purposes, active inference processes are thus also relevant to interoception, homeostasis, and allostasis. The homeostatic set point is itself a prediction. If one considers that allostatic stability is an absolute necessity for the human organism, the brain must constantly be one step ahead of what the incoming sensation implies regarding *future* homeostasis, using its prior predictions based on our past experience to do so. Any deviation from such homeostatic set points produce prediction errors will actively engage allostatic responses to maintain energy regulation (49). Some examples are, visceromotor reactions such as autonomic reflexes (e.g., heart rate, vasodilation, release of hormones), or behavioral actions (reaching for food or water), thus creating a new posterior prediction and continuing the generative process [e.g., (67)]. The hierarchical belief updating that refers specifically to interoceptive signals from the body is known as interoceptive inference (68).[4]

A further aspect of this process is that, ideally, the individual should regularly be seeking further evidence for its models, through its own action or perception, in order to check that its models of the world (and body) are reasonably fit for purpose, thus resolving present and future uncertainty. This seeking is termed "*epistemic foraging*" (61). An important corollary is that epistemic foraging actions will only occur during times when the individual perceives the environment as safe; otherwise its energy will be directed entirely toward protective activity, with no remaining energy available for seeking out new data.

[4]For the purposes of this paper active inference will be considered synonymous with interoceptive inference.

THE BODY IN INTEROCEPTIVE INFERENCE

In light of the theories outlined above, we can now bring together the theoretical perspectives that indicate the crucial importance of the body in the interoceptive inference process that is responsible for generating elemental aspects of experience, such as emotional experience, emotional awareness, and a sense of self.

As described above, interoceptive inference processes occur through a constant hierarchical monitoring of changes in bodily state. Their effect on interoceptive predictions, and subsequent adjustment of homeostatic and allostatic processes, is what engenders emotional content (49, 68, 69). The insular cortex is a vital hub regarding emotion, because interoceptive sensations from the body and predictions about the world, as well as from "higher" brain areas are integrated here. This *"primary interoceptive cortex"* (67) is thus a clearing house, comparing predictions against afferent interoceptive information. As beliefs, or priors, are updated, emotions are consequently generated (49, 69). Further iterations of interoceptive inference of emotional state will ultimately lead to emotional awareness (70).

Moreover, the Free Energy Principle implies that the highest priority will be given to the self-regulating mechanisms of the body, i.e. to homeostatic and allostatic processes that maintain survival (71). Allen and Tsakiris claim that this privileged status, which is a function of the necessity for the body to maintain stability, dictates that the homeostatic functions of the body are, in their words, the *"first prior."* In other words, the salience of any sensory stimulus will always first be evaluated in relation to the impact it will have on regulatory survival processes.

Finally, the result of this high precision afforded to visceral sensations allows visceral sensations to become a consistent *"'anchor' on which to lodge a more permanent feeling of bodily self"* [(71), p. 41]. Thus, visceral sensations provide an implicit sense of self-awareness that may not always be available to conscious access but, pertinently, may still be an important influence in the hierarchical modeling process. Notably, for our patients with alexithymia, the balance between the relative strength (the precision) of prior beliefs *vs.* interoceptive information is elemental to aspects of health and psychopathology regarding emotional experience and awareness.

FACTORS IN THE EARLY ORIGINS OF THE INTEROCEPTIVE INFERENCE PROCESS

Infancy is recognized as a vital time in the formation of links between interoceptive processes and experience. Attuned caretakers are an absolute necessity to maximize the emerging capabilities of the infant. How the child's and adult's emotional life will unfold depends on how this early vital inference process occurs (72). Close repetitive embodied interactions act as homeostatic regulators for the infant, and the quality of that interaction amidst the origins of inferential processing is the basis for the development of early expectations, or priors, about the causes of our sensory states. Furthermore, these early interactive physical activities stimulate the development of *"embodied mentalization"* in the infant which is the basis for an early sense of self and directly impacts the ability of the growing child to develop their own models of their interoceptive states and subsequent adaptive strategies for free energy minimization (72).

The import of relationships in infancy in developing beliefs about our body and sense of self is highly applicable to alexithymia. For example, if there is a sudden unexpected change in an infant's somatic sensation and this is not resolved within the consistent presence of a caretaker, the effect of the "surprising" interoceptive sensations in the resulting hierarchical inference processes is magnified, and may be negatively compounded over time. If cognition is as much affected through embodied experience as Allen and Tsakiris (71) assert, then these unsupported changes in the infant's embodied perception of the world will also have important effects on future cognitions. With very limited resources available to the infant who is experiencing emotion (and who has no ability to comprehend cause and effect), life is a constant surprise. One can see how important the original caretaking relationship is for an individual's tendency to expect safety in the world and thus for their ability and willingness to engage in epistemic foraging. Attuned caretakers are an absolute necessity to maximize the emerging capabilities of the infant. How the child's and adult's emotional life will unfold depends on how this early vital inference process occurs (72).

The power of such experiences can be imagined in the example of an individual who suddenly experiences a strong sense of danger to their bodily state. This is often experienced as a change in visceral sensation (muscles tensing quickly, a sense of distress in the gut), which gives rise to sudden highly precise interoceptive prediction errors, which then impact on generative models, activating priors unique to each individual in that present moment experience. Exteroceptive contextual elements, embedded in this experience, may also stimulate highly precise visceral predictions about what these sensations mean, generalizing to the whole body's response. While in adult life an individual may be able to have cognitive/verbal associations to such physical sensations, and comprehend/express that they feel fear, there are innumerable events in infancy that are experienced as immediately unsafe, *per se*, suddenly overwhelming the infant's physiologic homeostatic processes, with such sensory experience entirely pre-verbal. Such experiences, and the infant's caretakers response to such experiences, as interactions between the body and the world (and other bodies), are the origins of the generative models (predictions/priors/beliefs) and access to interoceptive information (sensation/awareness), that we carry throughout life, about the safety of our body/ourselves in the world.

As noted in psychological theories, it follows that if the alexithymic individual cannot generally recognize bodily signals (for whatever initial reason in early life or through later trauma), bodily sensations that do manage to breach the level of

conscious sensation and are experienced, are more likely to be felt as surprising than by those people who are not alexithymic. The effect on cognitive processes is likely be evidenced in the symptoms described as Difficulty Identifying Feelings (DIF), and Difficulty Differentiating Feelings (DDF), as such "surprise" will readily disrupt the coherence of a narrative focus of experience, and therefore any verbal ability to express emotion as feeling states, affecting the individual's level of emotional awareness. Moreover, if this surprising sensation is hierarchically evaluated by a prior for physical illness or frailty, that happens to have high precision, the expression of the experience would be somatically oriented. Indeed, the lack of embodied sensation as an *"anchor"* would support the alexithymic individual's tendency to focus on the external world, in order to create an external anchor, leading to externally oriented thinking.

EMOTIONAL AWARENESS AND THE THREE PROCESS MODEL

Crucial to alexithymia is the question of how best to characterize emotional awareness. Smith, Lane, and colleagues' solution is their Three Process Model (TPM) (24, 31, 45) which incorporates interoceptive inference, learning and brain processes, to propose how *"an emotion episode is initiated"* within the individual, in response to events that are *"real, remembered, or imagined"* [(24), p. 35]. The Three Process Model breaks down the elements of emotional experience into three factors (see below), which depend on predictive processing, neural network, and global workspace theories of brain functioning (24, 31). The authors create a cohesive model of how different aspects of: the initial response to the event; the bodily sensation; cognitions; motivated behavior; and the recognition of the response that fits an emotion-concept category (e.g., fear, sadness, etc.) may all ultimately become available to conscious awareness. The three processes (steps) designated by the model are (24, 31, 45):

1. Affect Response Generation (ARG): somatovisceral and cognitive processes are modulated through interoceptive inference, in a context-dependent appraisal of the salience of a real or imagined stimulus (which is often implicit), based on for example: the metabolic and behavioral demands; goal-achievement needs regarding elements such as the expectedness/novelty, or a sense of agency related to the event.
2. Affect Response Representation (ARR): the somatovisceral component of the affective response that has been generated is *"perceived via afferent sensory processing"* [(45), p. 5] and is then updated and conceptualized as a certain feeling category that describes the current emotional experience (e.g. fear, anger, etc.).
3. Conscious Access (CA): a process that grants access to domain general cognition for somatovisceral perceptions and emotion concepts, and are thus available for verbal expression and voluntary emotional regulation strategies.

The TPM allows a thorough evaluation of each patient's symptoms and their individualistic expression of alexithymia. In their computationally modeled clinical presentations, Lane and colleagues are able to account for the differences in symptomatology evidenced in alexithymic patients, with a view to improving individualized treatment approaches (24, 29, 30, 45). There is a strong emphasis on the importance of prior experience (and thus on predictions/expectations regarding internal and external states) and also on the inferential process of any emotional experience (24). If there is disturbance in any element of the TPM, the resulting Level of Emotional Awareness will be affected. For example, if a person is limited in their ability to appraise a situation, due to strong priors that quickly "cement" their expectations, the ARG would be circumscribed and they would have a limited range of emotional experience. If there were meager sensory signals available, for reasons associated with trauma and associated somatic disturbance that persists, then emotion concept labeling would result in emotion not being represented (ARR). Finally, a paucity of emotional language could be an indicator that other domain-general processes have created disturbances in how the networks necessary for conscious access (CA) co-operate. (The interested reader is directed to their research that models the influence of the multitude of interactive components of internal state and contextual processes [e.g., 22, 24, 30, 68]).

THE INTERSECTION OF THEORY AND CLINICAL PRESENTATION

As the Three Process Model assumes, each individual has a personal history that is vital to the expression of their symptoms and their available health. Nemiah (73) stresses that we must allow the individual to tell us their life story and their illness in their words, as they inevitably will put their illness within the context of that story, thus, *"The proper study of psychiatry, is biography"* [(73), p. 460]. While the collection of data and neurobiological etiology is fundamental to psychiatric research and practice, we should always address the patient as a unique individual who develops within relationships (73).

By way of illustration, I now present several clinical vignettes in order to consider alexithymia through an examination of how the theories presented above intersect at the clinical level. Each clinical example will be outlined regarding how the individual's history, symptomatic presentation, and clinical interaction best evidences: 1.) psychometric evaluation, 2.) psychological dynamics, 3.) Level of Emotional Awareness, and 4.) the Three Process Model.

The patients described here were treated in psychodynamically-oriented psychotherapy, comprising one individual and one group session per week. Attention in the sessions is paid to the patient's feeling states, with every attempt made to allow full expression while maintaining a self-observant posture. The patient is encouraged to contextualize their emotional experience within the relationships they have had in their past and those that they are currently involved in. The therapeutic

alliance is considered to anchor the patient within the process, through real relationship aspects associated with the therapists. Among other relevant goals, therapeutic intentions are to improve: the emotional awareness of the patient; their functional cognitive abilities; and the effective contribution of prior beliefs and feelings to their perspective of themselves and their relationships in the present moment.

There is an initial psychiatric diagnostic evaluation by the therapist/psychiatrist (PD), with an absolute exclusionary diagnosis for treatment, which includes psychosis. The focus of the therapist is directed toward the psychodynamic presentation of the patient, and the links to early relationships and events. The patient is told at the outset of therapy that there is a commitment required of them during the therapy that they not act on feelings, but rather make every attempt to explore, experience, and verbalize them in the therapeutic process. Their individual therapist (PD) is in the weekly group session, together with a co-therapist. The groups are on-going and process oriented, with the members remaining in the same groups throughout their treatment. Treatment length varies.

Each patient gave informed, written consent to be included in this paper. Various aspects of patients' history and experience have been changed, to protect their identities.

BOX 1 | Clinical Case Presentation.

The most common topic of conversation in Jill's therapy is the state of her body. She has descriptive words for the most minute change in its physical sensations but very few for her feeling states. When Jill speaks, her eyes dart around the room evaluating everyone's response. She will hesitate and change course, in reaction to perceived annoyance or disapproval from others, often making self-deprecating comments. When asked how she feels emotionally, she responds in physical description terms, focusing on her heart rate, fullness in her abdomen, fatigue, and feeling like her thoughts are *"cloudy,"* before concluding that she feels anxious. She believes that her body's strong sensations are indicative of a stress response which will take a physical toll, and that as a result she will get a severe illness or die young. When she began therapy she was encouraged to get a thorough medical evaluation. She was identified as having Irritable Bowel Syndrome and put on a simple regimen by her gastroenterologist. She regularly follows up with her primary care doctor and has been found to have no organic findings in any organ system on multiple screening exams.

Jill has two siblings, one younger by 17 months and the other by 3 years. A prominent memory that Jill reported was of being in a double stroller at about the age of 3 or 4, sitting behind her younger sibling, her mother talking to the sibling and handing him something. This was one of the only early memories she reported originally in her therapy. She didn't recall saying anything but she was able to associate this memory with a sense of her body being drained of energy, as she watched her mother and sibling interact. She reported that her mother was kind and *"tried to help me,"* but she remembers her mother as very anxious and just *"smoothing over"* the worries that Jill voiced about her friendships at school with simple responses that didn't feel comforting. If Jill did complain of feeling sick, she remembers her mother would let her stay home from any event.

In one group session, after the therapist had been engaged with another patient, Jill spoke with insight, noting compassionately to the patient that while she could empathize with her feeling response, she thought the therapist was making an important point that she would do well to consider. Jill spoke with clarity, then blushed and ended her response with, *"Oh, I just don't know, I'm just all confused and feel more nauseated."* When her therapist asked how she felt emotionally at that moment, Jill blushed and claimed loudly, *"I can't feel anything else, especially when I get like this."* When asked what *"like this"* means, she fluttered her hands in front of her abdomen, as if to describe motion moving up her abdomen towards her neck, and said that her heart *"is racing and feels flippy."* She then became quiet and didn't speak for the rest of the group session.

In her next individual session, Jill was asked about the interaction, and why she had become so quiet in the group after that interaction. She claimed that she didn't know why, but it seemed like *"my body just flared up and that was all I could think of and I didn't want to keep on going on about that."* She then began listing other stressors in her life, claiming that she *"just makes everything a mess."* Her therapist remarked that she had heard her speak clearly and kindly to the other patient in the group, and that didn't sound like a *"mess."* She blushed and said, *"you're just trying to reassure me, like it was in my family, just reassurance, but I was always the one who was treated like the 'sickly one.'"* The therapist asked her how it was that she would have been "the sickly one." Jill then reported memories in detail that she had only alluded to in the past.

Jill described a trip when she was 12 to visit family in another state. Her father was dropping them off and returning back home to work. The families were in a restaurant, all the adults talking, and Jill remembered feeling like she was going to choke and maybe die, since because everyone was busy talking they wouldn't see her choking. She did stop choking, and didn't say anything at the table. A few days later, Jill felt light-headed, nauseous, and as if *"my heart was just racing out of my chest."* She told her mother, who took her to the emergency room, where there were nothing physical found to explain her symptoms. Her father was called to return early and take the family home. She could only describe feeling *"just upset"* and notes that this was her earliest memory of experiencing strong physical symptoms in the presence of others and withdrawing from them and ruminating on her fears.

The therapist was aware that Jill had spoken for some time without stopping herself to make some self-denigrating comment or to focus on her bodily sensations. She offered this observation to Jill, who looked at her and then quickly looked away.

"Why did you look away so quickly?" the therapist asked.

Jill glanced back and said, *"It seems 'icky.'"*

The therapist paused a minute, then asked *"What does 'icky' mean, is that a thought or a feeling?"*

"Sort of both, maybe I'm afraid you're going to leave because I am "icky"?"

"Well, I am still here, but I realize when you look away, it is as if I am gone to you because you can't see me."

"That's true," Jill said, and slowly but then purposely brought her eye contact to meet the therapist's eyes.

"What do you make of telling me these stories now? I don't remember you ever telling me them before."

"Something that was said in the group, about how I always imagine the negative. I remember those times as the first times I felt all this in my body, and how much I was focused on how all those sensations felt so bad, but nobody asked me how I was feeling really, not feelings, and all I had was how my body felt to tell me anything, and that left me just feeling 'icky,'" Jill said this pensively while keeping eye contact.

"And how do you feel now?"

"Scared, I think." Her eyes began to water with tears.

"Do you also feel a bit hurt? You have tears in your eyes?"

"Maybe." Jill then described further her deep concern about her elderly mother and how she would be so *"upset if she dies."* When asked what upset meant to her, she first said, *"Oh, upset like anyone is when their parent dies."* When pressed to try and use more words specific to her, she paused. She said, *"I know that I have always lived as if my parents are always going to be here, sometimes that seems like it's absolutely necessary—that I just can't lose them, but other times, like right now, I know that I would feel sad if I didn't have them, but I would keep on going."* Her tears welled up as she said this, and rolled down her face, but she didn't make any movement to wipe them away. The therapist commented that Jill had made a very clear statement describing her strong feelings without defaulting to her usual bodily focus. Jill replied, *"I know, and they seem true, and for once I am just saying them and not looking back in to see how my body is reacting as I say them."*

The session was nearly over, but Jill recounted a few more times when she had been pre-occupied with her bodily sensations and missed out on experiences in life. Her voice was not harsh and she appeared to be reflecting with some compassion for herself.

In clinical case presentation #1 (**Box 1**), Jill's history and symptoms appear to match the TAS-20 factor Difficulty Identifying Feelings (DIF). She uses bodily-based sensations as descriptors of her emotional state, such as that her heart is racing, or makes body movements to indicate the nature and experience of her feelings (e.g. fluttering her hands). She struggles to differentiate her bodily sensations from emotions, and frequently does not identify distinct feelings. Jill also persistently voices complaints of bodily-based symptoms that have been medical evaluated, with no pathology determined, such as her nausea and cardiac complaints. However, she does have a diagnosis of Irritable Bowel Syndrome (IBS) with no detectable organic pathology noted during screening evaluations.

Addressing Jill's presentation from a psychological perspective, one relevant aspect is the difficulty that she has in using the signals from her body effectively regarding emotions—especially in relation to any organized storyline that could create narrative cohesion for her experience. Jill represents her mother as kind but minimally able to engage in any verbal consideration of her child's affective or bodily state: only *"smoothing over"* Jill's physical and social concerns with vague reassurance. Jill recalls the early memory of watching her mother tend to her sibling, while she sat nearby anxious with desire then deflated in resignation. Notably she remembers it in a manner that highlights her bodily experience. Her description of the family trip and her distress focuses on the physical experience, to the exclusion of the relational.

Jill's descriptive style for her somatic experience, especially when she is trying to express an emotion, has been described by researchers as indicative of an inability to recognize how certain physical states are likely to indicate distinct feeling states (6). McDougall (74) has claimed that this form of speech is *"an act, rather than a symbolic means of communication of ideas or affect"* (p. 178). The therapist must recognize this style of communication as a signal reflecting the depth of the patient's alarm, as she comprehends that the therapist is asking for words to describe feelings, yet she has no words available for these but only somatic experience. The therapist must not only tolerate the expressed alarm but also work to discern and comprehend the layers underneath the changing somatic symptoms expressed. It is often necessary for the therapist to utilize their countertransferential experience to discern the actual affective experience of the patient (5, 74).

It is worth noting that Jill has been diagnosed with IBS, a Functional Somatic Disorder (FSD) considered to result from a complex interaction between the individual and their environment (75). Psychodynamic considerations of such syndromes propose that patients use, "*so-called secondary attachment strategies (i.e., attachment deactivating and attachment hyperactivating strategies)*" [(75), p. 252], in reaction to experienced stressors. This decreases their ability to mentalize feeling states, thereby increasing the sense of both somatic and experiential distress, heightening attachment distress (28, 76). Jill expresses such by persistently wanting reassurance yet certain that her *"icky"* feelings will cause others important to her to leave her.

The Level of Emotional Awareness at which Jill operates is often between Levels 1 and 2 (15). Her focus on her bodily feelings is prominent, with a significant discordance between her above-average intelligence and her diminished vocabulary for feelings. Her level of emotional awareness is low because her affective states are not adequately attended to, in the context of her focus on the somatic. However, as she progressed through the period described in the vignette, she did have periods of Level 3 ability, as she was able to engage relationally with the therapist and to direct her attention more purposefully. When encouraged to seek different descriptive language rather than rely on habitual word choices, Jill moved further into Level 4, acknowledging blends of feelings. She was able to reference the somatic sense of *"icky"* to the expectation that the therapist would leave. Furthermore, she was able to verbalize awareness that she often imagines the negative, with her body as a focus, as *"nobody had asked how I was feeling really."* She then verbalized a specific feeling state of sadness, regarding the potential loss of her mother, and noted that she was aware that she was then intentionally stating emotional feelings, and not referencing somatic experience, which she found encouraging.

Using the Three Process Model (24, 29, 31) to designate which processes related to emotional awareness might be disrupted the Affect Response Representation (ARR) process seems to be a significant limiting factor for her. Considering that *"the body is the first prior"* (71), it is notable, in Jill's historical retelling of her life, that her sense that visceral reactions are sudden and portend something negative is prominent in each memory. The hierarchical processing in situations like this, suggests that there is a salient prior, with all new incoming interoceptive sensation interpreted according to this highly precise belief (prior), thus not allowing for alternative possibilities. There are disturbances in her attention regarding the social connections to which Jill has access. Therefore, incoming sensation from these connections that could lead to comforting emotional states is accorded very low precision, limiting her experiential response to her body only. This persists in Jill's reaction in her group and is furthermore reified by her diminished effort to forage for new sensation, as evidenced by her speaking clearly in group and then not interacting further, later claiming that her body *"flared up"* and that was all she could think of at that moment. She also originally dismissed the therapist reaching toward her compassionately in the individual session—specifically, she looked away from her—again decreasing any new socially conveyed sensory information that might alter the high precision of her belief.

BOX 2 | Clinical Case Presentation.

Anna is a woman in her mid-50's, unmarried with no children, who works as an executive in a large insurance company. She presented for therapy with complaints of *"things just aren't going right."*

Originally Anna reported she had no on-going illnesses, but when she was uncharacteristically late for a session she explained that she had *"one of those headaches."* As her therapist probed for the symptoms of this recurring headache, it was clear that she probably suffered from migraines which had not been evaluated or treated. The patient was referred to a neurologist and was

diagnosed with recurrent migraine. She has found relief from them with medication to preempt them, although she often does not take the medication in a timely manner. Anna paid close attention to her personal finances, was highly responsible with her bills, and didn't buy herself very much beyond necessities. She remembered events in people's lives very clearly, and she was always the first person in the waiting room before her weekly group session. She participated in a woman's golf league every summer, keeping close watch on her score from week to week and very frustrated with her play if she does not score well.

While Anna is considered to be very kind and giving by those in her life, at work and by her friends, she has often felt as if she *"were on the outside looking in"* during social encounters. In therapy Anna often appears highly reserved, sitting stiffly in either group or individual sessions, often with her eyebrows knitted in thought and her mouth forming the shadow of a smile. When asked to describe her feelings, she usually first speaks in simple generalities. *"Meh"* is a common descriptor, which she claims is *"not good, not bad, and just not much of anything."*

Anna's mother figured prominently from the beginning in the telling of her history. She described her mother as chronically anxious, likely depressed, and emotionally unavailable to Anna from a young age. There were other significant familial issues. Her father abused alcohol and although he worked regularly, he would drink daily, often ending up on the couch, asleep and drunk. Her younger sibling, born 1 year after Anna, had behavioral disturbances from a young age and Anna was held responsible for managing this, whether they were in the home or out in the neighborhood. Anna's memories of her mother centered on demands that she be compliant, that she control her sibling's behavior and not ask questions.

Her mother resented any attempt by Anna to act independently and was constantly critical, when she might have felt pleasure or pride. Anna often references her mother's severely disapproving look and being told in a harsh voice *"Who do you think you are?"* She commonly hears this phrase echoing in her head: when she is involved in her therapy; when she is describing an experience that was pleasurable; when she is describing anything she wants in her life; or when she is experiencing strong feelings in an intimate relational interaction.

If Anna announces that she can't discern any feelings during an event that would seem to have associated affect, she has been encouraged to describe any feelings she is aware of in her body. At first, she would frown more deeply and then conclude she could feel no sensations beyond some tension in her shoulders. Over time, Anna has begun to describe feelings of anxiety and hurt. Associated with such feelings she also describes a *"feeling like I have this empty space in my chest and there is strong pressure over my shoulders pressing me down into the chair, almost like there are hands on my shoulders."* She has verbalized how these sensations seem like a physical expression of the frequent harsh admonishments from her mother and her earlier necessary response to limit any expression of her emotions.

In a session a few weeks after Anna had helped to land a big contract at her office, an event that had been both exciting and pleasing to her, she was asked in her group session how she was feeling and replied, *"Oh, I am just back at 'Meh.' I don't have any friends, don't do anything but go to work and home, there is just nothing to my life."*

A group member pleasantly said that she remembered a few sessions back Anna had been visibly pleased with her work and the compliments that she had received. Her current expression seemed discordant to the observing patient compared to that recent session. She described several qualities Anna had, that make her a good friend, and several interests she knew Anna had, such as politics and history. Other patients in the group concurred verbally, remembering interactions they had with her. Anna responded with a self-deprecating comment and went silent.

She was asked by her therapist to describe any bodily sensations that she felt. She described the space in her chest as before, and then she stopped. Encouraged to imagine if there was anything surrounding the space, she paused and then replied, *"It's like there is rubber around it, just pushing and compressing everything into a smaller space inside."* She made a crushing movement with her hands.

The therapist asked Anna how she felt regarding the other patient's compliments to her. She said, *"I just hear her like she is just telling facts, I don't feel anything."*

Anna nodded, and then she appeared to tense more and her frown deepened.

"What's going on?" asked the therapist.

"I don't know, maybe like I am frozen still, like I just shouldn't say or do anything?"

"Hmmm, what might happen if you did?"

"It's like I would be found out."

"Found out how?"

"Like I'm not good enough." Anna said this with a severe frown, then plopped her hands into her lap and looked down.

The other patient spoke to Anna again, *"That sure would leave me feeling 'meh' Anna, but it does sound like you are kinda stuck in a 'Who do you think you are?' moment."* Anna listened with a frown on her face and when asked what she felt she said, *"I don't know what I feel, but it seems like there is just a force field around me. I can make an argument how each of my group members is wrong compared to what I see of my life, and could give them concrete examples. They just see snippets of it, not all of it."*

Her therapist decided to take a tack that might elicit an experience of pleasurable sensation in Anna, which might then allow Anna to develop some awareness of associated affect, and then move on from there to other affect. She asked Anna if she ever reached out and felt the clothes in a store when she goes shopping *"to get a feel of the material?"*

Anna grinned slightly and said she did.

"Can you describe the sensation that you might feel as you touch the clothes? Is there a sensation that you prefer?" the therapist asked.

Anna paused and said, "I do like the sensation of soft cotton, or really soft wool, but I don't have money to spend on things that aren't necessary, so I don't usually go through the stores just looking at things." Anna was looking up, with a frown on her face, her hands pressed tightly against the arms of the chair.

"But you do have some sense of the sensation of the material and you do like the feeling of some materials more than others. You're imagining that now, aren't you—how these clothes feel good as you walk by and touch them?"

Anna smiled briefly and then returned to frowning. Another patient noticed the brief smile and asked her, *"What was that?"* Anna looked back at him and said, *"I* was *in a 'Who do you think you are?' place, and when she asked me to imagine that, how the clothes feel good, I then heard even more loudly in my feelings, "Don't you even think of going there!"* She said this with a smile and then quickly quieted and frowned. Her therapist said, *"Wow, so not only 'Who do you think you are?' but you had better not move towards anything good or there will be hell to pay—but you can hear it so clearly, so how about you say it again, see what might happen?"* Anna repeated the phrase, *"Don't you even think of going there!"* and was encouraged to do so several more times. Her group members looked on supportively, at times encouraging her verbally by accenting different parts of the sentence in between her statements. By the fifth time that she said it, she was speaking very directly to her therapist and loudly pronouncing the words, accenting the end of the sentence threateningly. At the end of the repetitions her posture was less tense, arms not braced, shoulders back, and her voice louder. She was smiling broadly.

"How does that tight feeling inside seem now?"

"It is different inside. It's more like a container, softer plastic almost."

"What might you feel?"

"Scared I think, it seems like that would be what I feel, I can feel it as tension, and I think that is scared."

The group member who spoke to her originally said, *"It's as if you are more open to us, as if your eyes are seeing us here in the room, and I can see your feelings in your eyes, so much more after you were so clear in your speaking."* Anna then looked directly at the other patient and thanked her. Over the group she was interactive and commented on other's experiences readily. At the end of the group her therapist returned to how, in repeating a phrase that seemingly told her not to go towards something that was good, Anna was more able to let go of that stance, and let herself be more open. Her therapist asked if she could further describe and express what she had experienced emotionally earlier. Anna paused for quite some time, and then said, *"It must have been fear*

because it is really easier now to "be on the inside of the group" and I can even imagine other things that I want to go toward. And that force field doesn't seem to be here at all right now. I can say I feel kind of like 'Meh' plus, plus, now and that is actually pretty good."

Anna appears to experience the cognitive difficulty described by the TAS-20 facet, Externally Oriented Thinking (EOT). Her cognitive style matches Marty and de M'Uzan's (4), *pensee operatoire*, as elaborated by Nemiah and Sifneos (6). Her thoughts are presented in a pragmatic manner, such as focusing more on her golf score than the pleasure of the game. She can be concrete in her interpretation, focused on the external, (only hearing *"facts"* when people are emotionally expressive towards her). "*Meh*" is her experiential description, describing a lack of affective vitality (8).

From a psychological perspective, Anna's uber-focus on reality is underlain by a paucity of imagination, notably about herself. Krystal (5) notes the importance of the mother's consistent presence in early life. The mother must seem to the infant to exist as an *"invisible holding environment,"* "just" long enough. This relational experience is described by Fotopoulou and Tsakiris (72) as if the caregiver's body "*provide[s] sensory data that can plausibly be experienced by infants as their own."* If this mother-infant body-to-body exchange changes too abruptly, and the mother is not available to the infant, the infant is suddenly left only with deprivation and unmet needs, and does not develop their ability to contextualize such. In other words, the ability to mentalize bodily sensations does not develop (72) and the patient is then unable to imagine that bodily sensations might reflect a need or a desire. This seems applicable to Anna, both regarding her presentation of her history (only 1 year between her and younger sibling—who is also noted as requiring more of the mother's attention), and her description of her mother's persistent critical responses to Anna's expression of self-efficacy and emotional distance. Anna cannot be readily pleased with her accomplishments and has great difficulty in accepting other's encouraging perspectives to seek what she needs or desires. She degrades each interaction by insisting she is not what the person says of her, she is *"just not good enough,"* thereby creating a barrier to her inner experience which (unconsciously) seems fraught with the danger of seeming abandonment.

In the household, Anna experienced her mother as persistently demanding that Anna take responsibility for minimizing disturbance in the house (e.g., limiting her active younger sibling). Experiencing ongoing admonishments as her mother's efforts to limit her affective independence, Anna was presented with the option of repudiating fantasy or repudiating reality [(5); citing (77), p. 283]. Anna's alexithymic presentation makes clear how this forced choice unfolded in her life; she had to repudiate fantasy, she cannot use her imagination, or express wants and desires, even to herself. She can't even let herself imagine the pleasurable feeling of clothing she might buy and she immediately applies a possible reality-based reason as to why she doesn't allow herself to shop, and therefore does not encounter any possible opportunity to imagine pleasure at such sensation.

The Level of Emotional Awareness (15) at which Anna generally operates is Level 2. Her over-focus on attending to reality, all diminish her emotional range. She does move towards Level 3 Emotional Awareness, expressing a muted experience of desire, when she is encouraged to imagine the feel of cloth against her skin. She then returns quickly to the place she knows well, vividly feeling her mother as present and that if she were even to imagine something pleasant to her senses she would be in great danger. So much so, that in Anna's experience of the moment she spoke, as if a prohibition to herself, that she must *"not even think of going there."* She has introjected her mother's forbidding demand, leaving herself unable to formulate her own experience. She cannot just overcome, or let go of the fear, she must repeatedly, "inch by inch," formulate her own experience. Yet, after interventions that specifically increase her body's engagement and active support to take a more self-reflective stance, she is able to label the experienced bodily tension as fear, maintaining Level 3 emotional awareness.

With regard to the TPM (22, 24, 45), Anna has difficulty with the process of Affective Response Generation (ARG). The constriction of affect commonly seen in alexithymia is readily evident in her facial expression. However, as the session unfolds, deeper embodied roots regarding ARG become clear. As Anna describes her experience of the severely limited quality of her life, when an observant group member comments on the discordance between those statements and her very positive experience of Anna as a person who is kind and friendly, Anna first denigrates herself and then falls silent. Subsequently when asked about her bodily experience she can express the sensations, but she continues to remain withdrawn and without affective response, invoking the image of a seemingly physical *"force field"* that limits any view of herself as having positive qualities. She experiences again her mother's statement, *"Who do you think you are?"* as a strong prior injunction against evaluating such interactions as available to her, i.e., not safe to explore. For example, during the interaction with her group member, Anna is unable to attend to novel stimuli and to be curious about what the other person is saying to her, sharply stopping the generation of positive affect and returning her to a self-deprecating and dismissive state regarding herself.[5]

BOX 3 | Clinical Case Presentation.

Susan is in her early 40's, married, with a son. She has a college degree, and works as a librarian, after having tried several other professions. Recently she became a certified yoga instructor. She entered therapy complaining of feeling *"rudderless"* and as if she *"just couldn't make a decision about anything"* and was stumbling around.

Her father was the more emotionally available of her parents, her mother prone to withdrawal. Susan described her mother with, *"her head in a book if*

[5]One could make the case for fear being generated and causative in this interaction. However, this would be a confound within the Affective Generation Response process, as fear is an affect and is also the most common denominator in any situation in which an individual does not feel safe.

she wasn't cooking or cleaning." If Susan wanted her attention, it was hard to get. She describes her mother as *"self -involved, my whole life."* Her father was congenial and pleasant. She remembers him taking her to softball practice regularly, following up on her school work, letting her wash his car, and taking her with him as he ran errands. Susan felt as if he took real interest in her and her activities.

A highly significant event in her early life was her father's death when she was age 12. On the day of his death, Susan was home alone with her mother, her siblings were elsewhere. Her father was at an event in another city. The patient describes the event in the following exchange between the patient and her therapist.

This sense of waiting while something bad is about to happen, something over which she feels a sense of powerlessness, has been a prominent theme in Susan's therapy. She has had periods when she was very quiet, with notable anhedonia. She complained that nothing made her happy, not her job, not her relationships. Group sessions were especially difficult for her, she felt as if no one was interested in what she had to say if they didn't ask her directly, and she would remain quiet throughout. On leaving she would cry in her car all the way home. Arriving at her house she would inevitably start a fight with her husband, who would at times remain calm and at other times said that she was acting crazy and clearly her therapy wasn't helping.

As an individual session began, Susan immediately began tensing up, and crying, harshly wiping the tears off her face, she said, *"I'm in that place again, that same damn place, all wound up tight and can't feel anything, but my body is feeling something because my neck on the left side is starting to tighten."* Her face contorts into a characteristic expression, with her mouth tightened, her pupils appearing almost fixed and not really seeing the therapist. She sobs in short bursts, holds her breath and has very deep horizontal furrows across her forehead. She says at these times, *"I can't feel my forehead. It just feels like there is a blob over the front and top of my head, like I am just a blob."*

Susan continued to cry and speak angrily about how she was *"back in that place"* and that she should *"not have to go there anymore."* Stan (her husband) takes the brunt of it, *"last night I was just yelling again, I just lost it and kept on yelling about everything and nothing."*

Her therapists asked Susan if she was *"willing to try something with me?"* She agreed. The therapist then asked *"What sensations do you feel in your body?"*

Nothing really … something at my throat, tightness in my throat.

Yeah? Tightness there, tightness how?

I don't know … like someone is trying to strangle me. Really tight at my throat and my neck, and I feel that blob over my forehead, that is all I can feel.

Can you feel your feet on the floor?

(Moves her feet) *A little, I can feel the soles of my feet a little.*

Can you feel your bottom in the chair?

(Squirms a little) *Yeah, I can feel my bottom in the chair.*

How about you feel what else you can feel as sensations, just sensations, in your body.

(She begins to become tearful, her mouth grimacing, her breath is limited as she is holding her breath, body tense.) *I don't know if I want to feel my body.*

No? It's just sensations, what could happen?

I don't know … It just feels like I am this blob and I just want to run away. I can feel like my legs just want to run. And if I feel my body more there is just going to be more feelings like this and it is already really bad. I know that I have felt my body before and it even gets me out of this place, but I hate this place, everything seems so impossible.

Ok. There is all that, the blob can take over if you let it. But how about you try to see what you can sense in your body, just see if anything comes to the fore?

(Silent for a bit) *Maybe something in my chest, maybe a tightness. Yes, a tightness here*. (Motioning over the middle of her chest.)

How is that tightness, is it keeping something in, or keeping something out? Keeping something in.

Yeah? How about you look at me as you try to feel any kind of sensation. (Her eyes look at the therapist and then look away just over her shoulder, a habitual kind of eye movement for her.) *Are you here with me, or in there with you?* (The therapist points to her head.)

(She chuckles, and also tears come to her eyes*.) More in here with myself … The feeling in my throat is changing a little. A little less tight. And that feeling in my chest, it is moving a bit now. Like swirling.* (Motions with her hand*.) I can feel my shoulders and how tight they are. And my neck, you know how the left side of my neck always freezes up after my mother does her stuff. It feels like it is stiffening.* (Holding breath and squirming in her chair as she grimaces and cries.) *It is like no one is there, out there!!*

Breathe. Just breathe. (Susan lets out short sharp breaths.) *Breathe deeper, and try to keep your eyes on me.* (Therapist keeps direct eye contact and she looks back a bit more steadily but still looking away a bit, then she starts to weep and tears fall down her face). *Can you see me?*

Yes.

Can you see my eyes, what color are my eyes?

Brown? Yeah brown with a little lightness.

What else is your body saying now?

It is fighting to shut down but I can feel my legs a little more, and my hands, my shoulders. (Moves them around.)

(Her breath is less constrained and she is looking out of her eyes more, not inside to herself.) *How is the blob right now?*

More on my forehead, not all over my head. I can feel it as if it is just up here now, not all over my body as it was when I got here, just stuck there alone, like I am in a bubble and everything feels meaningless. Then I can feel like there is something at the back of my neck pulling all the muscles of my head. (She puts her hand to the back of her neck as if pulling on a scarf, and she points to the prominent creases in her neck.) *It is as if all the muscles get so tight and I can't think at all, about anything. The left side of my neck gets so tight, I can feel it now, but it is different than last night, it is softer now.*

What feeling would you describe that experience as, are there words for it?

It's scared, but no, no, it's hurt too. A lot of hurt, and I can feel some anger. There are flashes of images moving through my mind.

(She cries as she is looking at the therapist, her breath sometimes shallow, and then deepening. Her eyes look inside and then outside at the therapist.)

What are the images?

Some have to do with that day that my dad died. Some are just colors, and then an image pops out.

seems not so scary, your breathing and eyes look less scared, the therapist said compassionately.

It isn't, it's more interesting now. I can look at it, and not just keep on fighting against the looking and pulling away.

How did it happen again? That day, when your dad died. The phone call you always remember when you get upset and pull inside like this?

The phone rang and my mom answered it. The look on her face just changed so quickly. She dropped the phone back so quickly and I said, "What happened?" She stared straight ahead and said, "Dad had a heart attack, they are taking him to the hospital." I yelled, "What, what?" But she just said "They said to wait to hear something." She just sat there staring straight ahead, we both just sat at the table for so long. Then the phone rang again. It was ringing and ringing, she wouldn't pick it up. I yelled at her to pick up the phone!! She wouldn't. Finally I picked it up and Grandpa said, "Your dad died, they couldn't save him." My mom still wouldn't take the phone! She just said "what are we going to do" over and over again. I remember that I was on the floor crying and pounding and she said, "Stop that, just stop that." She sat there at the table, just saying over and over, "What are we going to do?" but she wouldn't talk to me.

So you just shut down. But you have images in your mind today?

Now I can see the phone ringing on the counter, and me screaming at her to answer the phone, and seeing myself answer it and then nothing. I couldn't see or hear anything after that, seems like for so long. It was like after that I had to be squashed, just squashed, nothing could go out.

And nothing could come in.

(Cries heavily.) *Yeah. I didn't know what to do, how to be, I just had to put my head down and read in school, but I didn't learn anything. I went to school but I just went through the motions. I was so scared all the time, and just did exactly as I was told. I studied and gave it back to them how they wanted it but didn't know what I wanted. I did everything by rote, I didn't know what I was doing, and there was no one to ask. And then that day, she didn't say anything for all that time. It just seems to get like that kind of quiet in my head and then I*

get all bound up and I just get all tight and fuss and keep people out, like I am squashed again in all this silence, and I won't let anyone in. Do you remember when I came to therapy and I didn't know what I wanted to do, I was just wandering. I thought I would be a teacher, or maybe a doctor, or maybe just stay at home and take care of our son.

Yes, I do, and I also remember how you would find something you really liked then suddenly leave it.

It was like I couldn't let anything just "be," I would be lost in this silence. I couldn't make any choices, and if I did make a choice when it was good I would have to just quickly leave it. But I can see now that I was just waiting, waiting for something to pass, or something to happen I don't know, I couldn't stand the feeling of waiting but the idea of moving towards something was just overwhelming.

Without your dad with you?

It must have been, I know that my feelings seemed so muted for such a long time. I couldn't feel anything a lot of the time, or I knew there was something but didn't know what. At least last night when I got in a fight with Stan, at least then I could say, wait a minute, and I told Stan that I was just going to take a walk, I would be back. I took a walk down the street, smelled the fall air, and came back, and apologized for the yelling. Stan said ok, and he even said that he had "fallen into it too."

"Today you were able to come out of the squashed place and tell me what was happening inside. And even have some images to see, not just silence. And the blob that seems to take over your thinking and feelings isn't doing that now. Your eyes are clearly looking at me. You were able to move through the feelings, even call them something, and that tightness in your muscles seems a lot less, the lines in your forehead are even less. How is that for you?"

"It is good. I do feel movement in my muscles, my breathing, as if I have some say in things and can say it, and even feel too. Breathing does help. I know I say it in my yoga classes a lot, sometimes I hear it too, even!"

The TAS-20 factor that fits Susan's symptoms is Difficulty Describing Feelings (DDF). She initially describes her emotional experience only as a sense that she "*just a blob.*" There are long periods during which she experiences severely restricted affect, interspersed with intense sudden periods of dysregulated action, which have been noted to occur in alexithymic patients. For example, Taylor, Bagby, and Parker (8) state that when such outbursts occur, if patients are asked what they feel, they are often unable to link such activity with feelings. Affect is expressed only as action. In the midst of strong feeling states, Susan can comment that agitated activity is likely related to feeling experience, but she cannot label what the feelings might be, even when there are clear antecedents that can be tied to memories of earlier events.

From a psychological perspective, her father's death and the events she remembers surrounding that event, echoed through Susan's life in many different ways. Susan describes this affective regression in clear terms: she *"did everything by rote*"; she used action instead of words to describe her distress; and *"I would just be lost in the silence."* She could not gain conscious awareness of her feelings due to this anhedonia, which was self-reinforcing. Significant anhedonia associated with alexithymia is noted by Krystal (5) as likely to result from a trauma occurring later in life and is a *"regression of affect,"* resulting in a severe disruption of subjective experience due to the "*dedifferentiation, deverbalization, and desomatization of affects*" [(9), p. 1010]. Susan describes every aspect of this experientially: dedifferentiation—she feels as if *"I am just a blob"* unable to describe individual feelings; deverbalization—*"I was just lost in the silence"*; desomatization—when asked what sensations she feels in her body she claims *"Nothing really."* Susan's Level of Emotional Awareness (15) appears to have variability functionally. She can be stuck at Level 1, where she is only aware of the tension in her body and her anhedonia, and is quiet in her group only to cry in the car, without identifying any associated feelings. At times, she also reaches Level 3 and then Level 4, expressing awareness of feeling angry, scared, and hurt, which are blends of feelings, and blends and blends of feelings.

Regarding the Three Process Model (TPM) (22, 24, 73), Susan struggles with allowing affective experience into conscious awareness (CA). She initially can only describe her experience with somatic description and she readily berates herself, *"I'm in that place again, that same damn place, all wound up tight and can't feel anything."* While in conversation, Susan can readily remember the events surrounding her father's death and will then describe how she experienced her mother's refusal to answer the phone and her leaving Susan to be told the news. Susan repeatedly re-enacts this event with her family and outside the group (periods of waiting silently and then behavioral disruption)—without placing her state or the actions she undertakes within the context of this event—although she ultimately does so in the safety of the individual therapy session described. This again highlights the necessity of the therapeutic relationship as an anchoring presence for patients who are in the throes of strong feelings, in order to allow feelings into awareness and pursue emotional regulation strategies (78). We will consider in the next section how important this process is for the patient, to encourage attentional shifts and allow for deepening mentalization processes to support change in the patient.

THERAPEUTIC CONSIDERATIONS

There are, of course, many psychotherapeutic treatments for the disturbances in alexithymia. My specific focus in this paper, however, has been on how comprehending of recent advances in the understanding of the neurobiological processes, when applied within the context of the therapeutic relationship, can enhance the clinician's treatment of the alexithymic patient, within any psychotherapeutic protocol. I hope that clinicians will be interested in these elements and adapt them appropriately, in accordance with their personal theoretical standpoint and psychotherapeutic treatment process.

The core of the insights from the theory presented in this paper is that the relative precision of prior beliefs or sensory evidence is vital to the accuracy of the interoceptive inference processes that are continuously unfolding in all individuals at all times. It is my contention that patients with alexithymia function with suboptimal interoceptive inference processes, because their priors (predictions/beliefs) are resistant to change. These patients' attention to their current sensations (and to use these to refine their beliefs) is hampered by their heavily entrenched,

habitual interoceptive inference processes. There are distinct reasons for this, unique to each individual and developing from infancy onward.

While we may not be privy to the direct causes of our patients' suboptimal predictions that are so resistant to change, there are entry points available within the therapeutic relationship that can help the patient to increase their sampling of the evidence currently available to their senses, and thus improve their inference processes, and increase their emotional awareness. One important purpose in this paper is to propose that improving the flexibility of patients' attentional control is a key entry point.

Attention can be regarded as a volitional *"direction of consciousness"* (79, 80). For our purposes, we start with the premise that the Bayesian brain is attempting to *"optimize the evidence for its model of the world"* [(81), p. 16]. Within this framework, attention is activity that infers the precision of the sensory input relative to the predicted state of the world (i.e. to the prior belief). Feldman and Friston (81) also note that attention highlights information from a certain source and that this will increase the precision of that sensory information relative to the top-down prior. To this end, directed attention to sensation vs prior belief will affect the weight of prediction errors as they move up the hierarchy, thus affecting the precision of that stream of sensory stimuli relative to the prior prediction (81).[6]

Patients' models of the world rest on the relative precision that their prior beliefs have relative to the precision of incoming sensation. As described above, in alexithymia, there are various ways in which the precision of over-learned priors may gain excessive strength throughout development, which is later expressed in adulthood. Linson et al. (82), for example, describe instances in which an *"over-fitting"* of sensations occurs, with over-weighted (over-precise) interoceptive sensory experience driving the predicted state, such as in somatic preoccupation (as for Jill, in case study #1). By contrast, in states dominated by precise predictions that stem from prior trauma, there is likely an *"under-fitting"* of sensory information relative to the prediction (70), with a lack of sensory sampling resulting in low precision of sensory information and a predicted state that is highly uncoupled from the actual environment [as for Susan, in case study #3 (**Box 3**)]. Within each of these examples, it is the flexible application of attention between interoceptive and exteroceptive signals and between the sensory information and the patient's habitual priors that can generate changes in precision and allow updating. This flexibility is a skill vital to develop in patients, supporting active changes in the generative models of interoceptive inference, and allowing emotional experience to reach awareness. Important aspects of the therapeutic relationship are essential to provide a much needed, felt sense of safety in our patients, in order to allow this flexible deployment of attention. We will now consider application of these ideas and principles utilizing the case studies described above.

Addressing Jill's (case #1) symptomatic presentation from a predictive processing perspective, her persistent attention to bodily sensations (as well as her interpretation of them) reinforces the precision (the salience) of a high level prior for illness. It also diminishes Jill's ability to infer and identify feeling states (79, 81). Her attention being largely directed toward priors that are illness-related beliefs has the effect of increasing the precision of these priors, thereby further magnifying Jill's attention to her body (that she expects to exhibit symptoms of illness). An initially weak (imprecise) interoceptive signal indicating any kind of illness in her body will therefore become more precise (by the attention she focuses on it), thereby increasing the salience (precision) of the original prior prediction for illness. This results in a "*self-perpetuating cycle*" (83), where worrying about potential illnesses increases the precision of the associated prior and thus the person's belief that they have an illness becomes stronger. Van den Bergh et al. (83), propose that *"symptoms are experienced when the generative model with the lowest overall prediction error represents an interoceptive event with an abnormal (typically disease) cause"* [(83), p. 194]. Conversely, interoceptive signals that may simply signify affect are ignored, or are misinterpreted as sickness. In Jill's case, even with negative objective test results, somatic sensations are insistently expressed as a subjective belief that she is still probably sick.

Meditative practices could support Jill's efforts at de-centering from her bodily experience. They promote a *"disciplined attention"* (84), increasing compassionate and non-judgmental approach to bodily sensation that can support stability in the homeostatic range of the individual. This could be important for Jill, who experiences any change in physiological sensation as threatening. Meditation enhances an individual's ability to manage such processes, thereby decreasing the expected position (the prior) that they are powerless to control the efforts of their mind or, at a more direct level, their thinking (as Jill insisted at first). Such changes in modulation of interceptive information, and subsequently in self-experience, can also affect the compassion and regard the individual holds for themselves and that they are able to accept from others—important features of change (85). Jill could eventually speak more kindly about her sadness, regarding the experiences she had missed while preoccupied with her bodily experience, expressing an increased level of emotional awareness.

The purposeful direction of attention (with relational support) to physical sensation described in Susan's case (case #3) supports epistemic foraging. The purposeful shifting of her attention from exteroceptive to interoceptive sensation greatly increases the flow of sensory information, allowing her to use more personally relevant and descriptive language regarding her somatic experience. There is increased conscious access to old priors that she is reacting to, with expressed insight into those priors, and increasing levels of emotional awareness. As Smith (24) asserts, this attentional process promotes a reappraisal of her situation (such as is intended in therapies such as Cognitive

[6] Such activity as described here actually occurs within the brain through changing levels of cellular activity, with individual cells and networks of the brain activated or inhibited.

Behavioral Therapy), which affords Susan the opportunity to explore new priors or alternative explanations for these (now attended) bodily sensations, producing *"a different and more adaptive affective response"* [(24), p. 45]. Furthermore, this could lead to such old memories (or habitual priors) becoming linked predictively with the new and healthier affective responses, altogether changing how they are stored and recalled (24, 29, 45).

The focus on the interoceptive sensation of breathing, and compassionate body interest promoted by her yoga practice, invokes a new experience of self-care for Susan. It alters the old prior, established with her mother, that there is no available care for her, which stimulates her to dismiss all interoceptive sensations. She reports that yoga has been a meaningful place for her to gain a sense of agency, expressed as her purposeful breath focus, which reminds her that she has *"some say in things."* She describes using such self-calming practices at home, albeit sometimes after she has been too reactive to her prior beliefs regarding others, such as her husband. This increase in agency is accompanied by increasing emotional awareness, with blends of feelings being verbalized. As this shift in bodily experience allows a loosening of the hold that the generative model of an absent mother has on her physical reactions, Susan can now also describe a generalization of such change in cognitions.

The effect of highly precise priors on cognitive style and bodily state are evidenced in Anna's presentation [clinical case #2 (**Box 2**)]. Her strong prior for interpreting most interactions as involving her mother's exhortations (the strongly prohibitive *"who do you think you are?"*) limits any attention to interoceptive sensation, keeping her attentional focus on the external, which greatly limits awareness of her emotional state and that of others. Her limited seeking of new experiences, of any kind that might instigate emotional response, does not allow for the mentalization of affect, leaving her only with the sense that life is *"not good, not bad,"* or with the vague descriptor *"meh,"* with which to express her feeling state.

Nevertheless, as Anna responds to the invitation to loudly express the prohibition that she constantly experiences, the attention this affords to her bodily sensations increases the precision of these sensations relative to the precision of the habitual prior. As a result, alternative priors that she would not previously have entertained, can now "get a hearing," for example, that it is safe for her to actively move and express herself loudly, without the expected rejection. Having alternative priors to select between induces conscious awareness and enables interoception to be mentalized; thereby providing therapeutic access (51). Anna's group members support her expression of her own power. They are encouraging as they describe meaningful changes in her physical presentation and emotional availability, thus further increasing attention to (i.e. the precision of) this new conscious prior, while challenging her habitual reactions as no longer fitting. As prediction errors are resolved between this new high level prior for safety, which now matches the low level sensory data in the present moment, Anna steadily calms down and even smiles. She concludes with an increase in emotional awareness, elevating her experienced sense of feelings from *"meh"* to *"meh, plus, plus,"* and that is pleasing to her.

Importantly, as the therapist endeavors to help the patient direct attention to current experience, in order to affect change in habitual priors that are overly precise, increasing uncertainty is generated. This therapeutic activity therefore requires vital experiential anchoring over time, actively promoted within the therapeutic relationship. This is provided by readily available aspects in the relationship—such as the authentic and genuine qualities of the therapist, which can be described as elements of the *"real relationship"* (78). Morgan et al. (86) notes that the interactional elements based in the real relationship, available to the patient, increases their experienced sense of safety. Thus, the real relationship allows *"a space for departure from past experiences with other people"* [(86), p. 327]. For the alexithymic patient, a therapist's honest expression of curiosity, emotional availability, and reflective stance are powerful resources with which to change overlearned suboptimal priors. The therapist's use of emotionally-valenced language also increases the patient's lexicon for such language. The real presence of the therapist is fundamental to patients' efforts to effect change in their process of living, with themselves and others, regardless of which element is disturbed in the initiation of an emotional episode (or in awareness of emotional experience), or what habitual reaction stifles emotional expression.

CONCLUSION

The disturbance in emotional awareness in alexithymia can be described in many ways. Ongoing research is throwing light on the processes that underpin this disruption and likely means to remediate the difficulties of alexithymic patients. In this article I have described how our patients' unique presentations of alexithymia, and their limitations in emotional expression and awareness, are the result of the hierarchical interoceptive inference processes, by which the brain actively attempts to discern the cause of incoming sensory stimuli. In alexithymia, this process takes place under the ongoing influence of: strongly held suboptimal prior beliefs; dysfunctional attentional control; and diminished ability to seek alternative evidence (known as epistemic foraging). In the light of recent innovations in neuroscientific theory and its application to psychotherapy, I have argued in this article for the vital importance of enhancing our alexithymic patients' ability to flexibly switch their attention between: their incoming interoceptive sensations; exteroceptive sensory signals from the world, in the current moment (i.e. the context); and their own habitual and deeply held prior beliefs about the causes or meanings of sensations. Among other therapeutic benefits, the patient will exhibit increased emotional awareness, affective expression, and mentalization, and improve their relational experiences on many levels. I hope that this characterization, and the recommendations that follow from it, will be of values to therapists of all persuasions, in their attempts to alleviate the difficulties that bring such patients to us.

DATA AVAILABILITY STATEMENT

The datasets for this manuscript are not publicly available because: The information was attained in psychotherapy sessions that are confidential. The author received express written consent from each individual(s) regarding the clinical material that is disguised as to the individual's identity.

ETHICS STATEMENT

Ethical approval was not provided for this study on human participants because the paper involves case studies of patients in private treatment. Written, informed consent was gained from each patient, and all identifiable material was changed to protect their identity.

AUTHOR CONTRIBUTIONS

PD contributed solely to this work.

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