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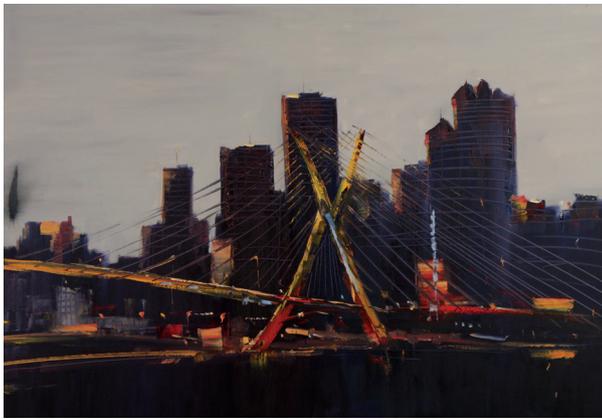
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Review article

Brief report

Letter to the editor

Investigation of distinctive characteristics of children with specific learning disorder and borderline intellectual functioning

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Abstract

Background: Borderline intelligence function (BIF) and specific learning disorder (SLD) are common diagnoses in children who are brought up for learning problems and school failure. **Objective:** The aim of our study was to determine whether there were distinctive aspects of cognitive testing routinely used in evaluating SLD and BIF and investigate emotion regulation skills and minor neurologic symptoms. **Method:** Sixty children (30 SLD and 30 BIF) who are currently attending primary school are selected for study. Visual Aural Digit Span Test – Form B, Gessel Figure Drawing Test, Bender Gestalt Visual Motor Perception Test, WISC-R, Emotion Regulation Scale (ERS) and Neurological Evaluation Scale (NES) was administered. **Results:** There was no statistically significant difference between groups in cognitive tests. The emotional regulation ability measured by the emotional regulation subscale was better in the SLD group than the BIF group (p = 0.014). In the NES, sensory integration (p = 0.008), motor coordination (p = 0.047) and other (p < 0.001) subscales showed higher scores in the BIF group. **Discussion:** It has been shown that cognitive tests don't have distinguishing features in the evaluation of SLD and BIF. Emotion regulation subscale score of ERS and sensory integration, motor coordination, and total scores of NES can be used in both discrimination of groups.

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Keywords: Specific learning disorder, borderline intellectual functioning, cognitive functions, minor neurological symptoms.

Introduction

Learning problems and school failure are common causes of child and adolescent psychiatric outpatient visits, especially in primary school age. Borderline intelligence function (BIF) and specific learning disorder (SLD) are common diagnoses in children who are brought up for this reason.

In a study conducted in Turkey "school failure" was the third most common cause of admission in all children and adolescents, and was the most frequent cause of admission in the age group 6-11[1]. In a study examining the distribution of diagnoses in all children and adolescents who applied to a Child and Adolescent Psychiatry Unit in Turkey between January 2012 and April 2013, 2.2% of the diagnoses were BIF, 1.8% were SLD in boys and 2.9% were BIF and 2.3% were SLD in girls[2]. In another study which was performed in GATA Child and Adolescent Psychiatry Department which was examining the distribution of the diagnosis, the rate of SLD was 8.9% and the rate of BIF was 2.1%[3].

Despite the fact that they are both frequent reasons for referral, there are frequent difficulties in discrimination between these two diagnoses. The common feature of these two groups of diagnoses is that they usually do not have a significant set of symptoms in the pre-school period, so they do not cause problems in the pre-school period, and therefore the reasons for initial admission of families are often reading and writing problems. The existing scales developed to distinguish these diagnoses which have clinically similar symptomatology are inadequate in most cases and may lead to diagnostic confusion. There are no studies in which a comparison of these two diagnoses is made and the differences to be used in differential diagnosis are identified.

The SLD is a relatively more studied diagnosis. There are studies showing that the accompanying problems in SLD are more frequent, especially in neurological and psychological and emotional problems than in normal children. Similar results were obtained by comparing with the control group in studies conducted with BIF even though there are very few. However, when the literature is searched, these two distinctions are unprecedented in these respects.

The BIF is used to describe situations where the IQ score from standard intelligence tests is not low enough to be called mental retardation, but below average intelligence (usually between 70 and 85). BIF is not a disease, syndrome or disorder. It is a neurodevelopmental syndrome and neurodevelopmental syndromes are formed by heterogeneous grouping of disorders and diseases, or they are a variant of normal. They are expected to have limitations according to the normal intelligence group in all areas of functioning, and to be in better condition compared to the group with mental retardation[4]. There are only a few number of studies on BIF. Current studies indicate about 13%-15% incidence rate in the population[5-7].

In the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV-TR), SLD was diagnosed when the individual's (that have normal or above normal level of intelligence) reading, written expression or mathematics levels found below from expected for his or her age and level of intelligence obtained in standardized intelligence tests. In the DSM-IV-TR, SLD was classified as Reading Disorder, Math Disorder, Written Expression Disorder and Learning Disorder, Not Otherwise Specified. In DSM-5, separate classification of SLD diagnosis is abolished and SLD is defined as a single diagnostic category with "specifiers" to characterize the specific manifestations of learning difficulties at the time of assessment in three major academic domains, namely; reading, writing, mathematics (*e.g.*, SLD with impairment in reading)[8,9].

Due to the fact that, SLD does not have clinically defined clear borders and the use of different cut-off points in the studies, the data about the frequency of SLD may be different. Surveys conducted in this area reveal a wide range of prevalence, from 1% to 30%[10]. In an epidemiological study, Lewis et al found that 1.3% of children had arithmetic difficulties, 2.3% had both arithmetic and reading difficulties and 3.9% had reading difficulties[11]. Although different ratios are reported in the studies for gender distribution, the general opinion is that the male/female ratio is between 1.39-3.19 in the SLD[12].

In this study, it was aimed to determine whether there are distinctive aspects of the cognitive tests used in routine evaluation

of these two disease groups in the clinical sample, to investigate emotional competence in patient groups and to compare the presence of minor neurological symptoms (MNS).

Minor neurological symptoms has been described as abnormal performance in motor or sensory neurological examination without a focal lesion[13]. In the literature, MNS have different nomenclature such as minor neurological deficits, soft neurological signs, neurological minor signs.

Minor neurological symptoms include poor motor coordination, sensory perceptual difficulties, difficulties in organizing complex motor tasks[14]. There are many studies that relate MNS with psychiatric diseases, behavioral problems, and academic difficulties. In addition, there are data indicating that neurological symptoms are present in varying proportions in healthy individuals[15,16].

Emotion regulation has been the subject of many different studies in child and adolescent psychiatry. In a study examining the effect of emotion regulation skill on academic achievement, 325 children receiving preschool education were evaluated. The assessment was made after the children's intelligence scores were equalized. It was found that there was a significant positive correlation between academic achievement and emotional regulation skill[17]. In another study, the children with specific speech impairment are reported to have worse emotion regulation skills than those without. In addition, emotion regulation problems were found to be higher in girls than in boys[18].

Materials and methods

This study is a cross-sectional and descriptive study carried out between May 2016 and June 2016 in Gulhane Military Medical Academy, Department of Child and Adolescent Psychiatry. The participants were 30 SLD and 30 BIF children who referred to child and adolescent outpatient clinic. Children who are still in primary school (grades 2, 3 or 4) have been selected for the reason that school failure and/or learning difficulties are being addressed in primary school. Children were included in the study after written confirmation from their parents. Diagnosis was made by a child and adolescent psychiatrist considering DSM-5 criteria. Developmental history, parental report, previous relevant diagnostic data and school information had been gathered. Following DSM-5, when classifying SLD, IQ discrepancy criterion wasn't applied. Those with clear neurological abnormalities such as epilepsy, muscular diseases, cerebral palsy, spina bifida, disabilities such as sight, hearing and major psychiatric diseases were not included in the study.

Sociodemographic data form, Emotion Regulation Scale (ERS) was filled by caregivers. Bender Gestalt Visual Motor Perception Test, Gessell Figure Drawing Test, Visual Aural Digit Span Test – Form B (GISD-B) form were conducted by clinical psychologist. Intelligence scores were obtained by applying Wechsler Intelligence Scale for Children – Revised (WISC-R) on a different day from the planned cognitive tests during the study period. The Neurological Rating Scale was administered by the clinician to the child on the same day or on different days with Cognitive Tests or WISC-R.

Ethics approval has been obtained from Ethics Committee of Gulhane Military Medical Academy (50687469-1491-351-16/1648-1195/06.05.2016).

Sociodemographic form

It is an interview form filled by interviewing the patient face to face, questioning the sociodemographic characteristics (such as age, sex, education status) of the participants and caregivers.

Wechsler Intelligence Scale for Children – Revised form (WISC-R)

WISC-R is a test used to determine the level of intelligence in children. WISC-R was developed in 1949 and revised in 1974, the form was created[19]. Turkish adaptation and standardization work

was carried out in 1995[20]. The result of the test is a score for full Scale IQ (FSIQ) and scores for the verbal scale IQ (VSIQ) and the performance scale IQ (PSIQ). It consists of a total of 12 sub-tests. VSIQ; General Information, Comprehension, Arithmetic, Similarity, Vocabulary, Digit Span sub-tests, PSIQ contains Picture Completion, Picture Arrangement, Block Design, Object Assembly, Coding, Mazes sub-tests.

Neurological Evaluation Scale (NES)

The NES was developed in 1988 to evaluate the minor neurologic symptoms. It was first used in schizophrenic patients and in the family members and relatives of these patients to do the examinations. After the adult and child mental health field has been used in research on the subject is associated with many different diseases[21]. The scale consists of 26 questions. Scores of 0, 1 and 2 are given for each question. High score represents the significance of the neurological symptoms, a zero score indicates that the person has passed through the examination involved in the question and there is not a problem.

Emotion Regulation Scale

It is a scale developed to assess children's emotional regulation features. The scale is filled by the child's parents or other caregivers. It consists of 24 items in total. As the score on the scale increases, the emotions are dysregulated, and as the score decreases, the emotions are well-regulated. It consists of two subscales. One of these is emotion Regulation Subscale and the other is the Lability-Negativity subscale. Emotions subscale set of 9 items, the lability-negative subscale consists of 15 items[22]. Turkish validity and reliability study of the scale was made in 2009[23].

Visual Aural Digit Span Test – Form B (GISD-B)

GISD-B is administered to children individually. Auditory Verbal, Visual Verbal, Auditory Written and Visual Written subtests. The sum of the scores obtained from the sub-tests constitutes the test score.

Koppitz[24] developed Visual Aural Digit Span Test but it has the limitation and reduction of errors, to eliminate these GISD-B form was developed. It is a commonly used measurement tool in patient groups with academic difficulties. This test measures short-term memory capacity, sensory-motor integration and complex attention skills[25,26].

Bender Gestalt Visual Motor Perception Test

It measures perceptual motor skills, perceptual motor development, and gives an indication of neurological intactness. Stimulus cards containing a specific figure are given to the child one at a time, and the child is asked to copy the figure on a blank sheet of paper. Copying figures requires fine motor skills, the ability to discriminate between visual stimuli, the capacity to integrate visual skills with motor skills, and the ability to shift attention from the original design to what is being drawn[27].

Gessel Figure Drawing Test

It is a test consisting of 8 geometric shapes in total. It gives an idea about visual perceptual development and mental development. Children are asked to copy these figures drawn on A4 size paper. The figures are arranged from easy to difficult. The use of an eraser is not allowed during drawing. Evaluation is done as "successful, considered successful, considered unsuccessful, unsuccessful".

Statistical analysis

The research data were presented in computerized mean, frequency distribution and percentages via SPSS (Statistical Package for Social Sciences). Pearson Chi-square test was used to evaluate categorical

variables. The normal distribution of the variables was examined using the Shapiro-Wilk test. In statistical significance between two independent groups, Student T test was used for those with normal distribution, and Mann-Whitney U Test was used for those who did not. The relationship between the variables was assessed by the Spearman Correlation Test. Statistical significance level was accepted as $p < 0.05$.

Results

A total of 60 children with 30 SLD and 30 BIF were included in the study. There was no statistically significant difference between the groups in terms of age, gender, class, parental age, parental education status. Sociodemographic characteristics of the groups are given in Table 1.

There were no statistically significant differences between the SLD and BIF groups in terms of test performances of the Bender Gestalt and Gessell Figure Drawing Test (Table 2). The results of the WISC-R, Gessell Figure Drawing Test and Bender Gestalt test of the groups are shown in Table 2.

No statistically significant difference was found between the groups when the performances of the Visual Aural Digit Span Test – Form B (GISD-B) were evaluated. The auditory verbal and audio-written subscale scores were not considered statistically significant [$p < 0.05$ and for auditory verbal: 4 cells (66,7%) and for auditory written: 6 cells (75,0%) have expected count less than 5, the number of cells count less than 5 should be less than 20%] (Table 3).

There was no statistically significant difference between the scores of emotional adjustment scale total score and variability/negativity subscale scores among the groups. The emotional regulation ability measured by the emotion regulation subscale was found to be significantly better (lower score) in the SLD group. The ERS scores of the groups are given in Table 4.

We assessed whether there is a correlation between the emotion regulation scores and intelligence scores in the diagnostic groups. A statistically significant negative correlation was found between the emotion regulation subscale and PSIQ and FSIQ in the SLD group. There was no correlation between variability/negativity subscale and intelligence scores. In addition, there was no correlation between intelligence scores and Emotional Regulation Scale and its subscales in the BIF group (Table 5).

There was a statistically significant difference in sensory integration, motor coordination and other subscales between the SLD and BIF groups in the NES. Children with BIF were found to have more minor neurological symptom scores than those with SLD. No statistically significant difference was found between the groups for the complex motor movements subscale (Table 6).

We also assessed whether there is a correlation between MNS and intelligence scores. When the diagnostic groups were evaluated within themselves, a statistically significant negative correlation was found between the sensory integration subscale of NES and FSIQ. There were no correlations between subscales and FSIQ in the BIF cases (Table 7).

Table 1. Socio-demographic characteristics

		SLD (n = 30)	BIF (n = 30)		p
Age		8.73 ± 1.08	8.63 ± 1.03	0.366**	0.75
Gender (n/%)	Male	19 (63%)	22 (73%)	1.631*	0.20
	Girl	11 (36%)	8 (26%)		
Class (n/%)	2nd class	8 (26%)	10 (33%)	0.682*	0.71
	3th class	7 (23%)	8 (26%)		
	4th class	15 (50%)	12 (40%)		
Father's age		41.00 ± 6.77	39.93 ± 6.82	0.369**	0.62
Mother's age		35.26 ± 4.97	34.70 ± 6.78	0.588**	0.43
Father's educational status (n)	No education	-	-	2.379*	0.52
	Primary school	10 (33%)	7 (23%)		
	Middle school	4 (13%)	8 (26%)		
	High school	12 (40%)	13 (43%)		
	University	2 (6%)	1 (3%)		
Mother's educational status (n)	No education	2 (6%)	5 (16%)	6.618*	0.17
	Primary school	13 (43%)	14 (46%)		
	Middle school	3 (10%)	-		
	High school	10 (33%)	11 (36%)		
	University	2 (6%)	-		

SLD: specific learning disorder; BIF: borderline intellectual functioning; ±: values are given as means and standard deviation. * x^2: Chi Square test. ** t: t test.

Table 2. WISC-R, Gessell Figure Drawing Test and Bender Gestalt test results of the groups

	SLD (n = 30)	BIF (n = 30)		p
WISC-R				
VSIQ	84.76 ± 7.74	72.80 ± 4.85		
PSIQ	101.83 ± 7.87	81.90 ± 7.04		
FSIQ	92.53 ± 5.41	75.40 ± 3.45		
Gessell Figure Drawing Test				
Successful	8 (26%)	4 (13%)	1.833*	0.68
Considered successful	5 (16%)	5 (15%)		
Considered unsuccessful	3 (10%)	3 (10%)		
Unsuccessful	14 (46%)	18 (60%)		
Bender-Gestalt Test	6 (1-10)	7 (2-14)	-2.124**	0.05

WISC-R: Wechsler Intelligence Scale for Children – Revised; SLD: specific learning disorder; BIF: borderline intellectual functioning. Gessell Figure Drawing Test results are given as categorical values and Bender Gestalt test results as median, minimum and maximum. * x^2: Chi Square test. ** Z: Mann Whitney U.

Table 3. GISD-B scores

GISD-B subtests	SLD (N = 30)	BIF (N = 30)	X^2	P
Auditory Verbal				
Below age and class level	24 (80%)	30 (100%)	6,667	0.03
At age level	2 (6%)	-		
At class level	-	-		
At age and class level	4 (13%)	-		
Visual Verbal				
Below age and class level	25 (83%)	30 (100%)	5,455	0.06
At age level	4 (13%)	-		
At class level	1 (3%)	-		
At age and class level	-	-		
Auditory Written				
Below age and class level	15 (50%)	28 (93%)	14,264	0.003
At age level	1 (3%)	-		
At class level	4 (13%)	-		
At age and class level	10 (33%)	2 (6%)		
Visual Written				
Below age and class level	20 (66%)	26 (86%)	3,836	0.14
At age level	4 (13%)	1 (3%)		
At class level	2 (6%)	1 (3%)		
At age and class level	4 (13%)	2 (6%)		

GISD-B: Visual Auditory Digit Test – Form B; SLD: specific learning disorder; BIF: borderline intellectual functioning.

Table 4. Emotion Regulation Scores and comparison

	SLD (n = 30)	BIF (n = 30)	t	P
Lability/Negativity Subscale	30.26 ± 7.05	29.66 ± 7.44	-0.321	0.75
Emotion Regulation Subscale	18.13 ± 4.28	20.93 ± 4.30	-2.523	0.01
ERS total	48.30 ± 9.61	50.60 ± 10.13	-0.902	0.37

SLD: specific learning disorder; BIF: borderline intellectual functioning.
Values are given as mean and standard deviation.

Table 5. The relationship between ERS subscale scores and intelligence for those with SLD

Intelligence Quotient	Lability/Negativity Subscale (Correlation coefficient)	P	Emotion Regulation Subscale (Correlation coefficient)	P
VSIQ	-0.095	0.47	-0.217	0.11
PSIQ	-0.102	0.43	-0.405	0.004
FSIQ	-0.099	0.46	-0.352	0.005

SLD: specific learning disorder; BIF: borderline intellectual functioning; VSIQ, PSIQ, FSIQ: Verbal, Performance, Full scale intelligence quotient.

Table 6. Neurological Evaluation Scale scores

	SLD (n = 30)	BIF (n = 30)	Z	P
The sensory integration	1.66 ± 1.20	2.82 ± 1.65	-2.633	0.008
Motor coordination	0.62 ± 0.71	1.21 ± 1.10	-1.985	0.047
Complex motor movements	1.66 ± 1.37	2.28 ± 1.51	-1.602	0.109
Other	0.75 ± 0.67	2.75 ± 1.50	-4.921	< 0.001
NES total	4.70 ± 2.52	9.0 ± 4.09	-3.824	< 0.001

SLD: specific learning disorder; BIF: borderline intellectual functioning.
Values are given as mean and standard deviation.

Table 7. Relationship between NES scores and FSIQ

NES subscales	FSIQ(SLD) (Corr. Coefficient)	P	FSIQ (BIF) (Corr. Coefficient)	P
Sensory integration	-0.399	0.029	-0.336	-0.700
Motor coordination	-0.194	0.303	-0.188	0.320
Complex motor movements	-0.013	0.947	-0.036	0.848
Other	-0.122	0.522	-0.082	0.667
NES total	-0.160	0.399	-0.211	0.263

NES: Neurological Evaluation Scale; FSIQ: Full Scale Intelligence Quotient.

Discussion

In this study, cognitive test performances, minor neurological symptom presence and emotion regulation difficulties of children with SLD and BIF were compared. According to the findings of the study, there was no significant difference between the two groups in the Gessell Figure Drawing Test, the Bender Gestalt visual motor integration test and the GISD-B form test. ERS emotional regulation subscale scores of the SLD group were found to be better. In NES, statistically significant difference was found between the groups except for the complex motor movements subscale, and the performance of the SLD group was shown to be better.

It has been reported that children with SLD have worse performance in tests of visual perceptual development (such as the Gessell test) than healthy children. In our study, 26.6% of the SLD group and 13.3% of the BIF group were found successful in the test of the child Gessell Figure Drawing Test. Identified in this study to SLD 73.4% failure rate is consistent with literature[28,29]. No statistically significant difference was found between the two groups. In this respect, it is estimated that the distinction between the two diagnoses cannot be made. However, no literature information was available for testing Gessell Figure Drawing Test for BIF.

The Bender Gestalt test was applied to compare visual motor integration skills between the two groups. Previous studies have found a relationship between intelligence level and Bender Gestalt test scores[27]. Similarly, children with SLD have been shown to have worse test performance than non-SLD children[30]. There was no statistically significant difference in Bender Gestalt test performances between two diagnostic groups in our study. The groups showed similar performance in terms of visual motor integration.

Another area in which two groups are compared is the GISD-B form results. In previous studies, GISD-B test performance of children with SLD was found to be lower than that of healthy children[28,29]. There is no study done with GISD-B test in BIF ones. A statistically significant difference was not found, although we found that the SLD group had better performance in our study. Significant results can be obtained with this test battery in further studies with more cases.

There are no studies investigating the relationship between ERS and SLD or BIF. In our study, there was a difference in the emotion regulation subscale scores between the two groups. The SLD group has lower (better) subscale scores than the BIF group. No statistical difference was found for ERS total score and for the lability/negative subscale scores. In addition, in other analyzes of subscales, there was a negative correlation between PSIQ and FSIQ and emotion regulation subscale scores in SLD cases. When these two findings are combined, it can be considered that the emotion regulation skill is directly related to the FSIQ, and the negative correlation with the PSIQ decreases in the SLD patients, resulting in a statistical difference between the two diagnoses. One of the main aims of this study is the search for an additional evaluation method that can be used in the differential diagnosis of SLD and BIF. We can say that the emotion regulation subscale of the ERS can be used for this purpose.

There was no significant difference between the two groups in terms of variability-negativity subscale. McClure et al.[31] reported that, emotional adjustment is directly related to the level of intelligence, while other areas of emotion (such as understanding their own feelings, recognizing others' emotions, facial expressions) are not clearly associated with intelligence. The similarity of lability/negativity subscale scores between the two groups in our study is consistent with this review.

In the literature MNS is associated with many psychiatric disorders, academic and behavioral problems. There are no studies investigating the frequency of MNS in BIF cases or the relationship between MNS and intelligence. In a study comparing the SLD, ADHD, and SLD + ADHD groups with the controls, it was reported that MNS frequency was higher than healthy group[32]. In our study, NES was used to reveal the frequency of MNS in BIF and SLD cases. Sensory integration, motor coordination and NES total scores were found significantly higher in the BIF group than in the SLD group. There was no correlation between the subscales and the FSIQ in the BIF group, while there was a negative correlation between the sensory integration and the FSIQ in the SLD group. There was no correlation between NES scores and VSIQ and PSIQ.

As with the ERS, it means that the SLD group which have higher FSIQ scores has better performance in NES than BIF. In other words, it turns out that the NES scale can be predictive of the distinction between these two identities. Perhaps even more meaningful than this finding is that the NES scores are also valuable for prognostic evaluation in cases of complex diagnosis. The basis of this statement is that the presence of minor neurologic symptoms in psychiatric illnesses is associated with a worse neuropsychological profile in these patients. As MNS increase, executive functions, visual and verbal memory performance have been shown to decrease[32-34].

The main limitation of our study is that assessors are not blind to the diagnosis of patients. At the same time, even if they are evaluated free from psychotropic or similar medical treatment, it is a limitation of not excluding ADHD in both SLD and BIF groups. Another limitation of this study was the selection of consecutive patients who applied to the outpatient clinic and the randomization procedure was not performed and lack of a control group.

In summary, there is frequent diagnostic confusion due to the fact that they have very few studies and very few diagnostic tools related to SLD and BIF which are the frequently diagnosed identities in child and adolescent psychiatry outpatient clinics. Symptoms of BIF and SLD occur with formal education and the similarity of the pre-markers in retrospective questionnaires related to the pre-school period may lead to diagnostic confusion. Among the scales used in this study, it was found that the emotion regulation subscale scores of the ERS and sensory integration, motor coordination, and total scores of the NES can be used for both discrimination and prognostic evaluation of these two diagnoses.

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Borderline personality disorder and bias in the recognition of facial expressions of emotion: a pathway to understand the psychopathology

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Abstract

Background: The identification of facial emotions is a key skill as it promotes rapid and accurate recognition of emotions and enables better communication and greater social adaptation. More recent studies have suggested that impaired social interactions may be related to deficits in social cognition and therefore in the recognition of facial expressions, contributing to social disturbance among individuals with borderline personality disorder (BPD). **Objective:** To present the results of an empirical study assessing the recognition of facial emotion expressions in women with BPD, having as reference a group of healthy women from the general population. **Methods:** The subjects (40 female with BPD and 40 controls) were assessed with a dynamic task on a computer screen for recognition of facial expressions of emotion. **Results:** The BPD group had a lower accuracy in perceiving emotions of fear and surprise and slowness in recognising happiness. Logistic regression analyses also identified an association between BPD and higher sensitivity in the recognition of anger. **Discussion:** Women with BPD made more mistakes in the recognition of negative emotions, which can bias the behaviour and regulation of affective states, favouring in turn the emergence of some typical symptoms associated with BPD.

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Introduction

Borderline personality disorder (BPD) is characterised by experiences of great affective intensity and distinct impairment of emotion regulation, thus resulting in affective instability, especially within the social context[1,2]. Studies have recently suggested that this impairment in social interactions may be related to social cognition deficits, which consequently affects the recognition of facial expressions of emotion and contributes to social problems among individuals with BPD[3-5].

Some studies report minor impairments in BPD patients. Von Ceumern-Lindenstjerna[6] showed images of facial expressions to female adolescents diagnosed with BPD and to health ones, including those with other psychiatric diagnoses. The subjects were asked to name the emotion shown on each image and estimate the intensity of negativity and pleasantness in the face. The adolescents with BPD showed no deficit in naming the emotions, not differing from the other groups. Nevertheless, the adolescents with BPD perceived positive facial expressions of emotion with less intensity and pleasantness, but perceived negative facial expressions with more intensity and negativity.

A literature review conducted by Domes *et al.*[4] showed that individuals with BPD who performed emotion recognition tasks presented alterations, such as subtle deficits in recognising basic emotions and response bias (i.e. attributing negativity or anger to the face), including increased sensitivity in detecting negative feelings. In this sense, the authors hypothesised that there must be an emotional hyper-activity in these patients which interferes with their cognitive processing of facial emotions.

Similarly, a study conducted by Unoka *et al.*[7] demonstrated that BPD patients were less accurate than controls in the emotional recognition tasks, mainly in discriminating negative emotions. These patients also attributed excessive feelings of disgust, fear and surprise to the faces. On the other hand, these patients presented no impairment in the recognition of happiness facial expressions.

Corroborating these data, a meta-analysis on the issue showed that subjects with BPD had a lower rate of hits in the recognition

of negative emotions compared to controls, mainly regarding anger and disgust. However, they poorly performed in the identification of neutral faces as they attributed erroneously emotions to them[8].

Another interesting aspect regarding studies on facial recognition and BPD has to do with changes observed in neuroimaging examinations. Within this context, it was found that patients with BPD had an increase in the activation of amygdala when they were shown images inducing adverse emotions or with human faces expressing feelings. It should be highlighted that amygdala is known to be the main structure involved in the processing of anxiety and other emotional states, in addition to being associated with BPD because of specific alterations[9,10].

These findings indicate that deficits in facial recognition of emotional expressions can favour biases in behaviour and regulation of affective states, favouring in turn the emergence of some typical symptoms associated with BPD, such as impulsivity, self-aggression and hetero-aggression, and contributing to unstable social relationships[4]. Therefore, it is clinically relevant to know this dimension regarding mainly control and treatment of the picture.

Considering this whole context, the results of an empirical study carried out in Brazil will be presented with the objective of assessing the recognition of facial expressions of emotion in BPD women, having as reference a group of healthy women from the general population.

Methods

Subjects

The sample consisted of two distinct groups consisting each of 40 adult women matched by socio-demographic characteristics. The subjects of BPD group were recruited from private and public psychiatric outpatient clinics and met DSM-IV criteria for BPD[1]. The control group consisted of students and staff of an education institution and of a primary healthcare program, and users of a non-governmental organisation, with no history of previous diagnosis

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or psychiatric treatment. The psychiatric condition assessment was performed by using the Structured Clinical Interview based on the DSM-IV (SCID-IV)[11,12]. Exclusion criteria for both groups were the following: lack of signature of the informed consent form and incomplete filling-up of the questionnaire.

Instruments

The following instruments were used to characterise the sample:
A. Clinical and sociodemographic questionnaire;
B. Structured and Clinical Interview for DSM-IV[11,12];
C. Beck Anxiety Inventory (BAI) – developed by Beck *et al.*[13], translated into Brazilian Portuguese, adapted, and validated for the Brazilian population by Cunha[14];
D. Patient Health Questionnaire (PHQ-9) – developed by Spitzer *et al.*[15], translated into Brazilian Portuguese and validated for the Brazilian population by de Lima Osório *et al.*[16];
E. Fast Alcohol Screening Test (FAST) – developed by Hodgson *et al.*[17], translated into Brazilian Portuguese and validated for the Brazilian population by Menezes-Gaya *et al.*[18];
F. Fagerström's Nicotine Dependence (FTND) – developed by Heatherton *et al.*[19], translated into Brazilian Portuguese and validated for the Brazilian population by Carmo and Pueyo[20];
G. Facial expression recognition task – computerised task consisting in a series of 24 photos of actors expressing typical characteristics of six basic emotions (i.e. happiness, sadness, fear, disgust, anger and surprise) are presented to the subjects for recognition. The stimuli used were those described by Ekman and Friesen[21] and the procedure was that standardised by Arrais *et al.*[22]. In such a procedure, photographs with four white actors (i.e. two men and two women) representing the six basic emotions were selected. Images of each emotion were submitted to the morphing technique and then grouped, resulting in a video clip starting with a neutral face (no emotion) and ending with a typical representation of the emotion in question (full emotion). The video clips were shown on a touch screen by using the Superlad 4.0 software (Cedrus Corporation®). For analysis, accuracy was regarded as primary variable (1 = hit; 0 = error) and response time (seconds) and emotional intensity for recognition (0%-100%) were regarded as secondary variables.

Data collection and analysis

The present study was conducted according to the ethical human research code and approved by the Local Ethics Committee (HCRP Process n. 2316/2011).

Data were individually collected and inserted in a database. To analyze the data, we used: a) descriptive statistics: analysis of the sociodemographic and clinical features of the sample; b) Z-score test for two population proportions (Bonferroni's correction, Chi-square test, Student's t-test and covariance analyses: comparison groups;) Multivariate logistic regression (backward method) in which the outcome variable was BPD. The variables whose p value was below 0.20 in the univariate analyses were included in the initial logistic regression model[23].

It was adopted a significance level of $p < 0.05$.

Results

Socio-demographic and clinical characterisation of the groups can be seen in Table 1.

According to Table 1, the groups are homogeneous regarding age and education level, but differing in the clinical characteristics, with BPD group presenting more indicators of psychopathology (comorbidity) and greater functional impairment (72.5% unemployed). In the BPD group, 100% were undergoing psychiatric treatment, 50% had at least one lifetime psychiatric hospitalization, and 85% reported at least one suicide attempt. With regard to medications used, the main ones were: selective serotonin re-uptake inhibitors, mood stabilisers, benzodiazepines, neuroleptics and tricyclic antidepressants, most of them used jointly.

The rates of hits/accuracy in facial emotion recognition are listed in Table 2, with only differences being found in the emotions of fear and surprise. The BPD group had significantly more mistakes in recognising such feelings compared to the control group. When indicators of depression, anxiety and substance abuse (confounding variables) were included as co-variables, the significant differences between the groups were maintained ($p < 0.05$). By analysing the incorrect responses, no specific bias was observed between the groups ($p > 0.05$).

Table 3 shows data regarding the response time in the task of facial emotion recognition in which the only statistically significant difference between the groups was found for emotion of happiness, although the response time was longer for all emotions in the BPD group.

Table 4 shows the results regarding the emotional intensity required in the task of facial emotion recognition by using the morphing technique. BPD group required more emotional intensity to identify all the basic emotions, regardless of the face gender. However, there was statistically significant difference only in the emotion of happiness.

Table 5 shows data regarding the final model of logistic regression analysis for identification of the most significant associations between BPD and recognition of facial expressions of emotions.

Table 1. Socio-demographic and clinical characteristics of the sample

Variables		BPD (N = 40) N%		C (N = 40) N%		Statistics
Education level	≤ 9 years	22	55.5	22	55.5	$p = 1.00$
	> 9 years	18	45.0	18	45.0	
Marital status	Single/divorced	25	62.5	22	55.0	$p = 0.49$
	Married	15	37.5	18	45.0	
Employment status	Unemployed	29	72.5	9	22.5	$p < 0.001$*
	Employed	11	27.5	31	77.5	
Children	Mean (SD)	1.0	(1.3)	1.1	(1.6)	$p = 0.88$
Age	Mean (SD)	35.7	(10.5)	35.4	(11.0)	$p = 0.91$
Depression Score	Mean (SD)	19.22	(6.4)	7.77	(6.76)	$p < 0.001$*
Anxiety Score	Mean (SD)	33.35	(14.19)	9.92	(10.73)	$p < 0.001$*
Alcohol Score	Mean (SD)	2.27	(3.48)	1.76	(2.5)	$p < 0.001$*
Tobacco Score	Mean (SD)	4.42	(3.05)	0.58	(1.6)	$p < 0.001$*

SD: standard deviation; *p*: significance level; BPD: group of borderline personality disorder; C: control group; Children: average number of children of the participants. * Statistic significance.

Table 2. Accuracy in the facial emotion recognition task

Emotion	BPD (N = 40) Mean (SD)/Rate Hits	C (N = 40) Mean (SD)/Rate Hits	Statistics
Happiness	3.72 (0.78)/93.0%	3.90 (0.30)/97.5%	$p = 0.19$
Sadness	3.07 (0.91)/76.8%	2.95 (1.06)/73.8%	$p = 0.57$
Fear	1.85 (1.07)/46.3%	2.32 (1.02)/58.0%	$p = 0.04$*
Disgust	2.77 (1.07)/69.3%	2.85 (0.89)/71.3%	$p = 0.73$
Anger	2.85 (1.14)/71.3%	2.52 (0.90)/63.0%	$p = 0.16$
Surprise	2,67 (1.24)/66.8%	3.30 (0.88)/82.5%	$p = 0.01$*
Female face	8.10 (2.51)/67.50%	8.67 (1.50)/72.25%	$p = 0.21$
Male face	8.85 (2.31)/73.8%	9.17 (1.41)/76.4%	$p = 0.24$
Total	16.95 (4.29)/70.6%	17.85 (2.20)/74.4%	$p = 0.45$

SD: standard deviation; *p*: significance level; BPD: group of borderline personality disorder; C: control group. * Statistic significance.

Table 3. Response time (seconds) in the facial emotion recognition task

Emotion	BPD (N = 40) Mean (SD)	C (N = 40)	Statistics
Happiness	9.89 (3.81)	8.86 (5.38)	$p = 0.03$*
Sadness	12.44 (4.82)	11.06 (3.78)	$p = 0.16$
Fear	11.59 (4.30)	10.78 (3.61)	$p = 0.37$
Disgust	12.54 (4.57)	10.87 (3.63)	$p = 0.07$
Anger	12.66 (3.68)	12.27 (5.16)	$p = 0.70$
Surprise	12.26 (5.20)	10.59 (3.07)	$p = 0.08$
Female	11.43 (3.70)	10.46 (3.65)	$p = 0.24$
Male	11.16 (3.79)	10.01 (3.28)	$p = 0.15$
Total	11.77 (3.96)	10.65 (3.47)	$p = 0.18$

SD: standard deviation; *p*: significance level; BPD: group of borderline personality disorder subjects; C: control group. * Statistic significance.

Table 4. Emotional intensity (percentage) required in the task of facial emotion recognition

Emotion	BPD (N = 40) Mean (SD)	C (N = 40)	Statistics
Happiness	85.96 (17.92)	73.98 (22.0)	$p = 0.01$*
Sadness	95.10 (14.66)	89.72 (13.13)	$p = 0.88$
Fear	93.14 (14.23)	89.09 (15.90)	$p = 0.23$
Disgust	95.12 (14.86)	90.58 (13.23)	$p = 0.15$
Anger	96.29 (13.78)	92.74 (12.88)	$p = 0.23$
Surprise	91.05 (18.06)	90.14 (14.98)	$p = 0.80$
Female	93.93 (14.66)	87.89 (16.41)	$p = 0.08$
Male	93.15 (15.18)	87.01 (15.67)	$p = 0.07$
Total	94.83 (14.13)	89.18 (14.94)	$p = 0.08$

SD: standard deviation; *p*: significance level; BPD: group of borderline personality disorder subjects; C: control group. * Statistic significance.

Table 5. Final model of multivariate logistic regression analysis

Variables	B	SD	P	OR	95% CI	
					Lower	Upper
Fear (rate of hits)	-0.48	0.25	0.05	0.61	0.38	1.00
Anger (rate of hits)	0.58	0.27	0.03	1.79	1.06	3.02
Surprise (rate of hits)	-0.73	0.26	0.01	0.48	0.28	0.80

B: beta value; SE: standard error; *P*: significance level; OR: odds ratio; CI: confidence interval.

The logistic regression analysis identified an association between BPD and higher sensitivity in the recognition of anger and low accuracy in the recognition of fear and surprise.

Discussion

Nowadays, it is considered that processing, recognition and expression of emotions are not just innate phenomena which invoke genetic memories in order to allow humans to react to the environment on an adaptive basis, as proposed by Darwin[24]. With the development of cerebral cortex over the evolution of the human species, it is suggested that this phenomenon also occurs at some level with mediation of learning, cognitive resources and cultural values[25]. In view of this, several studies have been investigating particularities of the facial emotion recognition in a variety of contexts to understand this complex phenomenon[26,27].

In the field of mental health, alterations in the facial emotion recognition were evidenced in several psychopathologies characterised by impairments in both recognition tasks and emotion processing, with abnormal activation of various cerebral areas[28,29]. Specifically in relation to BPD, changes in the emotional recognition can be attributed to the deregulation of emotions, personality traits,

cognitive impulsivity, aggressiveness, alterations in specific brain structures, among other damages, which can impact the social-cognitive functioning[4].

Previous studies on the issue showed evidence on some of the main impairments in BPD, such as presence of negative bias to ambiguous and neutral stimuli, increase in the sensitivity on recognising emotions of fear and anger, impairment in the recognition of basic emotions, emotional hyper-activity, and functional and structural changes in the brain[4,30,31].

With regard to the alterations demonstrated in the present study, one of them was the recognition of fear (low rate of hits). The adaptive value of this emotion is in the anticipation of the danger as the feeling of fear activates protective and avoidant behaviours to any person, animal, idea or event seeming dangerous and which may cause physical and psychological damage. Fear may occur in response to immediate or upcoming situations, and experiencing it may be sometimes as bad as the real damage itself. Therefore, identifying the emotion of fear in the people's face may indicate the presence of threats nearby, thus mobilising the individual to prompt action to couple with danger[27,32].

The poor recognition of fear is corroborated by previous studies, and a possible hypothesis explaining this deficit has to do with functional changes in limbic structures and anterior regions of the brain. These regions are related to, respectively, degree of subjectively experienced negative events and regulation of emotions[33]. In the limbic system, amygdala plays an important role in fear conditioning, control of aggressiveness, emotional memory and fight-or-flight response.

Another hypothesis explaining the deficit in fear recognition can be supported by Wagner and Linehan[34], who stated that the emotional dysregulation observed in BPD patients can also be evidenced in terms of deficits (hyper-activity), which facilitates the lack of emotional reaction in view of some environmental stimuli with affective valence. On the other hand, according to the same authors, the perception of fear in the other can increase the one's own experience of fear as there is an association between perceiving emotions in the other and activation of the one's own physiological arousal. This would compromise the individual's ability to handle with the other's feelings (empathy) and to fit to the environmental stressors and dangers, thus making them vulnerable.

Similar changes were found in the recognition of the emotion of surprise. This feeling is characterised for being the briefest of all emotions, lasting only a few seconds at the most. Almost everything can provoke surprise because of the fact that this emotion is elicited by unexpected situations, comments, opinions, gestures and events. Nevertheless, as soon as what had surprised us is identified, this emotion transforms into another feeling, such as fear, happiness or anger. Fear is the most commonly emotion following a surprise, perhaps because unexpected events are often interpreted as a threat. In this sense, fear and surprise are frequently misunderstood in the recognition of these emotions, since there are even facial similarities in their expressions[27,32].

In the recognition of surprise, the BPD group also made significantly more mistakes compared to the control group. The greatest difficulty in recognising such an emotion is partially corroborated by related studies as it is not specifically a negative feeling and whose recognition is reportedly impaired in BPD patients.

Among the six basic emotions, anger is perhaps the most highlighted in the BPD as such a feeling is one of the most experienced by individuals with the disorder and has been mostly reported in studies using facial emotion recognition tasks, thus being frequently related to biases, less or more hits and hyper-reactivity in its detection[4,31,34,35].

Anger may be one of the most dangerous emotions. There are several causes for this feeling, such as being rejected, cheated or expectations not met. Depending on the individual's personal history, even small frustrations can elicit anger. Experiencing anger, in part, involves the risk of losing control and thus it is important to recognise

this emotion, mainly in the other person by predicting aggression, insult or rejection so that one can defend against them[26,32].

Although our study has not found any statistical difference between the groups regarding anger-related variables, it should be emphasised that the logistic regression analysis showed that this emotion was one of the strongest factors associated with BPD. Hypothetically, these patients are more skilled in detecting anger as a way of predicting rejection or threat, which can be reflected by an increase in the emotional response involving limbic system and amygdala. This response pattern can contribute to the conflicting relationships often reported by BPD patients[4].

With regard to the emotion of happiness, it was possible to identify two changes during the facial emotion recognition task. Happiness is considered the only positive emotion among the six basic ones, being characterised by a feeling which the majority of people want to experience. The emotion of happiness not only involves the sensation of physical pleasure, but also other more global domains, such as excitement, achievement, relief and positive self-concept. In this sense, the recognition of happiness is adaptively important for tightening social and family bonds as well as for receiving gratitude, appreciation and motivation[26,32].

The present study has found statistical difference between BPD and control groups for detection of happiness, with the BPD subjects being less sensitive and more hyper-reactive. Veague and Hooley[36] also used dynamic faces with increasing emotional intensity and found that BPD subjects had a longer response time than the controls in the recognition of a happy face, despite the lack of difference between the groups regarding the total hits for this emotion.

Thome *et al.*[37] also reported evidence that BPD patients rated the intensity of happiness in happy faces lower than controls. In this study, the lower rating of happiness was linked to a high-anger state. Such findings can be supported by the hypothesis that the emotion recognition of facial expressions may be a trait-dependent ability[34].

It is still worth citing some studies which detected specific response biases for BPD regarding negative facial emotions, with highlight to the emotions of anger and fear[30,36]. In the present study, no type of specific response bias was found in the BPD group. The biases found in both groups were for the emotions of fear and surprise, which are common and clinically less significant[26,32].

In view of the discussion raised about the facial emotion recognition task in BPD subjects and about the diversity of findings, one can observe that there still exists an area to be explored because of the methodological variability regarding the tasks of facial emotion recognition used by the different studies, which makes it difficult to compare and generalise the results[38]. In addition, further studies are necessary to assess the recognition of emotions in more complex and dynamic situations, that is, which are as close as the daily-life interactions, thus integrating more complex auditory, corporal and visual stimuli with mixed and ambiguous emotions[4,10].

We emphasise that the present findings should be interpreted with caution as our sample consisted of women only and whose statistical power was not estimated, which does not allow direct generalisations to males and makes it difficult to determine whether the negative findings are due to the limited number of subjects. Another limitation is the fact that the use of different medications was not controlled in the outcome analyses, since some studies pointed to the influence of psychotropic substances on the recognition of emotional expressions[39].

Regardless of the methodological gap and inconsistencies in this area, it is possible to state that individuals diagnosed with BPD in general tend to have deficits in the facial emotion recognition task compared to healthy ones[8,33,40]. In this sense, the results of the present study suggest that the BPD group had a poorer performance compared to the control group, a finding also corroborated by the literature.

Disclosure

The authors report no conflicts of interest.

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Original article

Changes in thyroid function status of suicidal patients

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Abstract

Background: This study was carried out at Punjab Institute of Mental Health and Centre for Nuclear Medicine Mayo Hospital, Lahore. It is aimed at the possible association of thyroid malfunctioning with suicide attempts of patients. **Objective:** Determination of thyroid function status of suicidal psychiatric patients and their comparison with psychiatric patients without suicide attempt or ideation. **Methods:** Total 54 patients with either past history of suicide attempt or current suicidal ideation were selected for analysis of their thyroid function status (age 15-55 years). Age matched 50 non-suicide psychiatric patients were included for comparison. **Results:** Two patients with suicide attempt had overt thyroid dysfunction. Remaining patients had serum FT_4, FT_3 and TSH level within normal range. Suicide attempter patients had lower FT_4 but increased FT_3 and TSH levels compared to suicidal ideation patients. Serum FT_4 and TSH levels in suicidal patients were not different from psychiatric patients. Serum FT_3 in suicidal patients was lower than psychiatric patients (3.7 ± 0.8 *vs.* 4.3 ± 0.5; $p < 0.05$). Female suicidal patients had lower FT_3 levels compared to male patients (3.4 ± 0.6 *vs.* 3.9 ± 0.8 pmol/L; $p < 0.05$). **Discussion:** Local suicidal patients have higher incidence of overt thyroid disorder and lower FT_3 levels compared to non-suicidal psychiatric patients.

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Keywords: Suicide, thyroid hormone, psychiatric patients, depression.

Introduction

Death is a bitter reality of human life everyone is scared of. Mentally healthy persons never want to die. Still, there are present such individuals in our society who really want to leave this world by committing suicide. Such individuals are considered as mentally unhealthy and require immediate medical treatment. Suicide is a complex issue which involves a number of social, cultural, biological as well as psychological factors. In the last 45 years, the world has seen 60% increase in the suicide attempts with a prediction that global suicide figures will potentially reach to 1.5 million mark by the year 2020[1,2]. This shocking act of uncivilized behavior is now attributed to the presence of a psychiatric disorder. This disorder is among the most consistently reported risk factors associated with the suicidal attempts. It is now known that more than 90% of people who either attempt a suicide or die as a result of attempting suicide are psychiatrically ill[3]. This fact is further supported by the recent studies which proves that the depressed individuals attempting suicide constitute a particular subgroup of depressed subjects with a higher severity of depressive disorder and higher social impairment[4].

This psychiatric illness may arise as a result of abnormalities originating within the human body, particularly hormonal disturbances. The thyroid hormones are known to have profound effects on mood swings as well as human behavior. In the recent attempts to investigate the relationship between suicidal behavior and thyroid hormonal activity in depressed patients, it was reported that various degrees of hypothalamic-pituitary-thyroid (HPT) axis dysregulation are associated with the history of suicide[5,6].

The activity of thyroid is considerably regulated by iodine and, unfortunately, Pakistan is considered one of the severely iodine deficient countries in the region[7]. About 70% of Pakistani population is reported to be at risk of iodine deficiency disorder[8]. In this context, it is expected that a number of psychiatric patients may have underlying thyroid abnormalities which can lead towards suicide attempts. So far, the data from Pakistan, on prevalence of abnormal thyroid hormones among psychiatric patients, has not been reported[9,10]. Therefore, present study is a part of a large study exploring the role of thyroid hormone in psychiatric patients. The current study focuses on determination of serum levels of free thyroxin (FT_4), free triiodothyronine (FT_3) and thyroid stimulating hormone (TSH) in the patients who undergo suicide attempts (SA) as well as suicide ideation (SI) and the obtained results are compared with psychiatric patients without suicide attempts or ideation.

Material and methods

The details of patients for this study and the methods adopted has been provided.

Patients

Consecutive patients with past history of SA or SI were recruited from outpatient department of Institute of Mental Health, Lahore during June to September 2013. A careful Psychiatric history of each patient was taken and noted on a proforma by the qualified psychiatrist. For each patient, the physical examination of thyroid gland as well as signs and symptoms associated with thyroid dysfunction were also carried out. The patients already diagnosed with thyroid diseases and were either taking thyroid medications or underwent a thyroid surgery, the pregnant women and patients suffering from cardiac diseases and hepatitis were excluded from this study.

Methods

A 5.0 mL blood sample was taken from each patient in the study. The serum was separated from each sample by low-speed centrifugation (2000×g) for 5 minutes at room temperature and stored at minus 20 °C until analysis. All collected serum samples were analyzed for FT_4, FT_3 and TSH at CENUM, Mayo Hospital, Lahore. The serum FT_4 and FT_3 were determined by radioimmunoassay (RIA) and TSH was determined by IRMA techniques using commercial kits of Immunotech Inc. (Beckman, Czech Republic). The RIA & IRMA batches were tested with commercially derived control sera at low, medium and high concentrations. Measurement of radioactivity, fitting of the standard curve and analysis of samples was carried out using a computerized gamma counter (Cap-RIA 16, Capintec Inc.

USA). Assay reliability was determined by the use of commercially derived control sera of low, medium and high concentrations which were included in every test. All assays were carried out in duplicate. The RIA and IRMA results were expressed at less than 10% CV of imprecision profile. Normal ranges for FT_4, FT_3 and TSH, as standardized in CENUM RIA laboratory, are 11.0-22.0 pmol/L, 2.5-5.8 pmol/L and 0.3-5.0 mIU/L, respectively. The diagnosis of hyperthyroidism was marked as positive if serum TSH was found to be < 0.3 mIU/L and FT_4 > 22 pmol/L. Hypothyroidism was considered if serum TSH was > 5.0 mIU/L and FT_4 < 11.0 pmol/L.

The analysis of data was carried out using Microsoft Excel program on a personal computer. Mean values were compared by Student t-test in order to test the significance of difference between two arbitrary groups. A value of $p < 0.05$ was considered as significant.

Results

A total number of 54 consecutive psychiatric patients (21 females and 33 males) presenting with SA (n = 39) or SI (n = 15) were selected for this study. Their mean (± SD) age was 30.5 ± 10.1 years with age ranging from 15 to 55 years. Among them 24 (44.4%) were residents of Lahore city. As controls, age matched 50 patients (22 females and 28 males) with psychiatric disorder but no history of either past suicide attempts or current suicidal ideation were included in this study. Analysis of thyroid function tests showed that among 39 SA patients, one female and one male had severe hypothyroidism and hyperthyroidism, respectively (prevalence: 5.1%). The remaining 52 patients were found to have serum FT_4, FT_3 and TSH levels within the normal range. Among them a comparison of mean concentration of serum FT_4, FT_3 and TSH levels between SA and SI patients is shown in Table 1. The SA patients were found to have lower FT_4 and increased FT_3 and TSH levels as compared to those of SI patients. However, difference was slight and did not reach significant level. Thus, thyroid function tests were not different in patients who have attempted suicide compared to those who have current suicidal ideation.

Table 1. Mean concentration of FT_4, FT_3 and TSH in different groups of suicidal patients

Thyroid hormone (n = 37)	Suicidal attempter (n = 15)	Suicidal ideation	P-value
FT4 (pmol/L)	14.8 ± 3.2	16.0 ± 3.2	0.79
FT3 (pmol/L)	3.7 ± 0.8	3.6 ± 0.6	0.38
TSH (IU/L)	2.3 ± 1.0	1.7 ± 0.9	0.66

All control patients also had normal levels of thyroid related hormones. A comparison of mean concentration of serum FT_4, FT_3 and TSH in suicidal and control patients is shown in Table 2. Results showed that mean FT_4 and TSH levels in suicidal patients were not different from psychiatric patients. However, serum FT_3 in suicidal patients was significantly lower than psychiatric patients.

Table 2. Mean concentration of serum FT_4, FT_3 and TSH in different groups of patients

Thyroid hormone (n = 52)	Suicidal	Psychiatric (n = 50)	P-value
FT4 (pmol/L)	15.1 ± 3.2	15.0 ± 2.2	
FT3 (pmol/L)	3.7 ± 0.8	4.3 ± 0.5	0.335
TSH (IU/L)	2.1 ± 1.0	2.3 ± 1.1	

We further explored the effect of different patient's variables on serum FT_3 levels in suicidal patients; results are shown in Table 3. In female suicidal patients, the FT_3 levels were significantly reduced as compared to the male patients. However, patient's education level as well as place of residence has no effect on serum FT_3 levels in suicidal patients.

Table 3. Effect of different variables on mean serum FT_3 levels in suicidal patients

Variable	FT$_3$ levels (pmol/L)	P-value
Gender		
Male	3.9 ± 0.8	0.01
Female	3.4 ± 0.6	
Educational level		
Matriculation and above	3.8 ± 0.7	0.69
Below matriculation	3.7 ± 0.8	
Place of residence		
Inside Lahore	3.5 ± 0.6	0.15
Outside Lahore	4.2 ± 0.9	

Discussion

The aim of this study was to determine thyroid function status of suicidal psychiatric patients and their comparison with those of non-suicidal psychiatric patients. The results of this study showed that the thyroid function tests were not significantly different among suicidal patients who had either attempted suicide in the past or were currently idealizing it. Compared to psychiatric patients without suicide history or idealization, suicidal patients had significantly decreased serum FT_3 levels. This decrease in FT_3 levels was comparatively more pronounced in female suicidal patients as compared to male suicidal patients. A noteworthy result was that more than 5.0% patients with past history of suicide attempt had severe thyroid dysfunction. This points towards the speculation that before a patient attempts suicide, his or her thyroid hormones may get dis regulated[6].

Mann and Currier have reviewed the prospective studies of suicidal behavior and serotonergic, noradrenergic, dopaminergic and hypothalamic-pituitary adrenocortical (HPA) as well as HPT axis in mood disorders[11]. The relationship between suicide and the HPT activity has been previously described in the literature[6,12-15]. Most of these studies have focused on the change in serum TSH levels among the suicidal patients as compared to the depressive patients. These studies report conflicting results regarding serum TSH. Although most of the investigators have found that depressed patients with either a suicidal behavior or intent exhibited a reduced TSH response to morning administration of thyrotropin releasing hormone (TRH)[6,12,13] while others did not agree to this generalization[13,14]. In these reports, the serum FT_4 and FT_3 levels were not studied extensively in suicidal patients due to preoccupation with serum TSH. Recently, Duval et al.[6] carried out a study on 95 medication-free DSM-IV euthyroid major depressed inpatients along with 44 healthy hospitalized controls; they found that control patients with a positive suicide history (n = 53) showed lower basal FT_4 (at 0800 h: p < 0.005; at 2300 h: p < 0.03) and normal FT_3 levels, whereas patients with a negative suicide history (n = 42) showed normal FT_4 and FT_3 levels[6]. In contrast to this finding, Pompili conducted a study on 439 patients suffering from major depression disorder, bipolar disorder and psychotic disorders (schizophrenia, schizoaffective disorder and psychosis not otherwise specified). They found that suicide attempters and non-attempters differ regarding their FT_3 values only. A multinomial logistic regression model revealed that suicidal attempters were 2.27 times (odds ratio = 0.44; 95% confidence interval: 0.23/0.82; p = 0.01) less likely to have higher FT_3 values than non-attempters. Earlier Jokinen et al. have shown that suicide patients' plasma T_3 had a negative correlation with the Beck Suicide Intent Scale and the Montgomery Asberg Depression rating scale[16]. Thus, these few studies on FT_4 and FT_3 are not consistent regarding serum FT_4 and FT_3 levels in suicidal patients. The results of this study are in accordance to Pompili showing that serum FT_3 levels were significantly lower in suicidal patients as compared to non-suicidal patients.

Disturbances in the serotonin (5-hydroxytryptamine, 5-HT) system constitute the most common biochemical abnormality

associated with suicide[17]. It is proposed that thyroid hormones are involved in a complex compensatory mechanism to correct reduced central 5-HT activity with existence of either of the two situations[12]. The compensatory mechanisms are effective: in this situation decrease in 5-HT function leads to an increase in thyroid axis activity. This may be understood as a repairing process aiming to restore an efficient 5-HT functioning and the compensatory mechanisms are not effective: in this case the 5-HT deficiency remains. In depressed patients with a history of suicidal behavior, 5-HT dysfunction may be understood as a failure of the compensatory mechanisms. If thyroid hormones might be involved in a complex compensatory mechanism to correct reduced central serotonin activity, then the lower FT_3 levels in our patients mean the failure of thyroid compensation of serotonin secretion. In the past studies regarding TSH, the TRH hyper secretion has been considered a compensatory mechanism to maintain normal thyroid hormone secretion and to normalize serotonin activity in depressed patients[12,13].

The strength of the present study is the enrollment of consecutive suicidal patients constituting a measure of homogeneousness. Similarly, control group of patients was suffering from psychiatric disorders which made it suitable for differentiation between the effect of the psychiatric illness and the effect of suicidal behavior. However, there are some limitations to the generalization of the present results. First, the relatively small sample size may affect the replicability of results. Second, the sample of patients taken was not free of medication which might have affected thyroid hormone values.

Further, large studies should confirm this generated data regarding higher prevalence of overt thyroid diseases and lower FT_3 levels in local suicidal patients. Moreover, studies should be conducted to ascertain whether thyroid hormonal patterns found in suicide attempts can be ameliorated with T_3 supplementation before starting anti-depressive treatment. In the past, most of such acceleration studies have yielded favorable results before the use of tricyclic antidepressants[18]. Recently, it has been suggested that hyperactive HPT axis is associated with better antidepressant response and T_3 due to its short half-life may reduce the antidepressant response time[19]. This necessitates the trial of T_3 as acceleration agent before start of selective serotonin reuptake inhibitors (SSRIs). Such studies are of great importance because use of SSRIs alone have not completely eliminated the risk of future suicide attempt in admitted depressive patients[20], particularly the bipolar disorder patients[21].

Conclusion

It has been observed from the present study that suicide attempting patients do not differ significantly in the levels of their FT_4, FT_3 and TSH when compared to those with suicidal ideation. Also, Serum FT_4 and TSH levels in suicidal and psychiatric patients were almost the same. However, serum FT_3 in suicidal patients was significantly lower than psychiatric patients as far as females are concerned. Female suicidal patients had lower FT_3 levels compared to male patients. It has also been noted that local suicidal patients have higher incidence of overt thyroid disorder as well as significantly lower FT_3 levels as compared to non-suicidal psychiatric patients.

Declaration of interest statement

The authors declare no conflict of interest in this article.

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The delusional dimension of anorexia nervosa: phenomenological, neurobiological and clinical perspectives

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Abstract

Background: Delusional characteristics have been largely ignored in patients suffering from anorexia nervosa (AN). **Objectives:** To review the literature on delusional features in AN from phenomenological, neurobiological, and clinical viewpoints. **Methods:** Data were obtained through searches of Medline, PubMed, SciELO and Cochrane Library. **Results:** Distorted beliefs in AN may range from an overvalued idea to an overt delusion, involving affective, personality and/or psychotic disorders. Studies confirm alterations in monoaminergic systems. It has also been seen a decreased integration of visual/proprioceptive information, and alterations in neural networks involved in body processing. It is known that body image distortion may present "delusional proportions" as a consequence of great concern about body. Concomitantly, "embodied defence hypothesis" has been proposed. Restrictive AN exhibits higher levels of delusionality, and a particular delusional type of AN has been suggested, associated with a worse long-term outcome. Low doses of atypical antipsychotics are recommended combined with cognitive techniques. **Discussion:** Delusional thinking in AN is likely a dynamic and dimensional phenomenon that can vary, both in nature and/or severity, whereas high insight levels, before and after refeeding, result in positive outcomes. Neurobiological research on this topic must be encouraged, since clinical and phenomenological approaches are comparatively more frequently reported.

Behar R et al. / Arch Clin Psychiatry. 2018;45(1):15-21

Keywords: Anorexia nervosa, delusions, body image, neurobiology, phenomenology.

Introduction

Body image and weight concern are the most important features of eating disorders (EDs), particularly in anorexia nervosa (AN), but the knowledge of underlying thoughts, attitudes, behaviours and related neural mechanisms is still scarce[1]. Diagnostic criteria of AN highlight strongly held beliefs related to eating, shape and body weight, but they do not specify the range of its intensity, which sometimes is so severe as near of delusionality[2], which can also be viewed dimensionally, ranging from completely delusional, to having overvalued ideas, and to being with no insight at all[3]. The occurrence of a delusional or "near delusional" reality testing has been largely ignored in anorectic patients, and their belief systems have not been systematically explored[2].

According to Bruch[4], the anorectic patient behaviour is addressed to produce and/or maintain a remarkable weight loss associated to a perceptual overestimation of the subject's body weight or shape, as a consequence of body dissatisfaction. Due to this misperception, patients usually deny the seriousness of weight loss. Nowadays, it is well known that restrictive-type anorectics are more susceptible to exhibit psychotic features. Rigidity, high levels of alexithymia and introversion would be eliciting factors acting as pre-psychotic conditions, while concrete, dichotomous and ruminative thinking style, aided by fasting and emaciation, would make them more prone to dissociative experiences and therefore to psychosis. In this line, depersonalisation and derealisation episodes are often found as dissociative warning signals ready to evolve to a psychotic disclosure. Extreme malnutrition, a highly obsessive state, simultaneous mood disorders, electrolytic and/or hormonal misbalances, substance abuse and iatrogenic effects are possible mechanisms leading to psychosis through hyperactivation of the dopaminergic system, whose most prevalent manifestations are delusions with somatic and paranoid contents and hallucinations[5].

The aim of this article is to conduct a comprehensive review of the literature on delusional features displayed by some patients suffering from AN, emphasizing a holistic view of its psychotic features from phenomenological, neurobiological and clinical dimensions.

Methods

A literature search was carried out using the electronic databases Medline/PubMed, SciELO, Cochrane Library and six specialised handbooks, since 1950 up to 2018, in order to perform a comprehensive literature review about the delusional phenomenon in AN. Keywords included anorexia nervosa, eating disorders, delusions, body image, phenomenology and neurobiology. A total of 452 references were found. After excluding duplicates, title and abstract screening and full-text assessment for eligibility, forty five articles were considered the most relevant because of their contribution to the subject, according to the common agreement of the authors. All of them were critically studied. Considering the design of this review, no ethical approval was required due to the nature of this type of research. The whole process of studies eligibility is detailed in Figure 1.

Results

In this review, we included 3 systematic reviews, 19 research articles, 19 review articles and 4 case reports. We also include 6 specialised handbooks.

The delusional spectrum

Distorted beliefs in AN may range from an overvalued idea to an overt delusion, that may imply affective and/or personality components and even a psychotic disorder[6]. In some cases, delusional

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│ Records identified through       │
│ database searching MEDLINE/      │
│ PubMed, ScieLO, Cochrane Library │
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│ Articles after removing duplicates│
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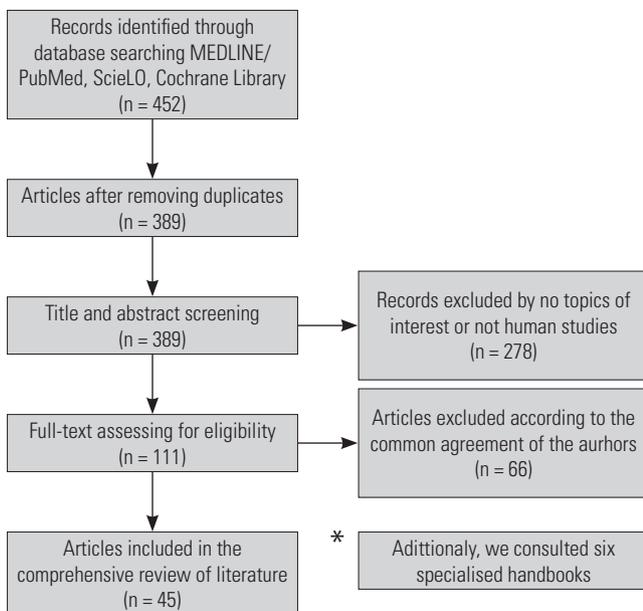
Figure 1. Flowchart of studies included in the review.

conviction occurs with no clear division between delusional and nondelusional thinking. It is often difficult to distinguish between a delusion and an overvalued idea, which is an unreasonable and isolated sustained belief, not as inflexible or as idiosyncratic as a delusion, and more likely to be a passionate religious, fanatical or political conception and typically does not hinder the individual from remaining functional[7]. Jaspers[6] defined a primary delusion as a belief, impossible with regards to its content and contextual implausibility[6], unlikely and often fantastic, with lack of evidence, held with extraordinary deep subjective certainty, incapable of being modified by other experiences, and convincing and/or reasonable counter-arguments. Hypothetically, a disease process in the brain could cause it and therefore it is unsusceptible to psychological inquiry. Nevertheless, the evidence has suggested that sociocultural influences impact the content of delusions rather than on their form, but usually the false belief has a great personal significance and is not always shared by others from a similar socio-cultural-economic group. Secondary delusion can be understandable within the patient's mood circumstances and/or life events, in relation to peer group beliefs or as a long-term development of personality traits, displaying different degrees of insight[8]. It seems to be a key aspect of AN[1], being a dimensional rather than categorical construct, and ranging from a more general insight into having a disorder at all, to a more disorder-specific belief (*e.g.*, body image distortion in AN)[3]. Konstantakopoulos *et al.*[1] have stated that there is a wide range of illness denial rates in EDs, fluctuating from 15% to 80%, probably related to divergent criteria used to categorise patients as delusional or insightful (*e.g.*, clinical judgement, low scores on self-report symptom questionnaires).

Diagnostic criteria

Bruch[4] introduced the concept of "delusional denial of thinness" as a core of the disorder, distinguishing primary AN from an atypical subtype in which patients may not express this "delusion." However, the Fifth Version of the Diagnostical and Statistical Manual of Mental Disorders (DSM-V) does not refer to patients' thoughts about their bodies as delusional, instead using the term "intense" beliefs. This nomenclature reflects that reality testing in anorectics, besides eating-related issues, is generally unimpaired, usually recognising their beliefs as unshared by others[2]. Descriptions of body image disturbances in DSM-IV represent a wide range of intensity of body image beliefs as well[9], whereas the term "intrusive overvalued idea" is

used in the International Classification of Diseases, Tenth Revision[10]. Additionally, DSM-IV-TR criterion C (body image disturbance) for AN is reported as: (I) a "disturbance in the way in which one's body weight or shape is experienced", or (II) "undue influence of body weight and shape", or (III) "denial of the seriousness of the current low body weight"[2].

Body image beliefs in AN according to DSM-IV-TR are "unreasonable and sustained" judgements "maintained with less than delusional intensity"[9]. A specifier meaning delusionality and conveying the broad range of insight from good to absent has already been included in DSM-V for obsessive-compulsive disorder, body dysmorphic disorder, hoarding disorder, and olfactory reference syndrome, but not for AN[1]. Nevertheless, a coherent systematisation of appearance beliefs in AN has been proposed including good or poor insight, or with delusional (psychotic) features, but not in the DSM schema[11].

Neurobiological basis of body image distortion

Evidence that directly associates psychotic symptoms in AN with a neurobiological substratum is limited. On one hand, specialised literature has extrapolated findings from psychotic disorders to AN. On the other, some authors have guessed about possible correlations among other features of the disorder more biologically based with delusional spectrum in AN (*e.g.*, obsessionality, perfectionism). A major issue in research on the neurobiological basis of AN, is the fact that anorectics are food deprived[12]. Hence, neural alterations might correspond to consequences rather than causes in these patients[13] (*e.g.*, appetitive conditioning using food as a reward increases dopamine levels in mesolimbic neurons[14], and also hunger related hormones act on them[15]. Some authors have consistently stated that individuals with AN have anxious, inhibited, and inflexible premorbid traits, probably due to altered monoamine neuronal modulation, or an impaired dorsal caudate function, that predates the onset of the disorder. Some other factors might exacerbate these vulnerabilities during the adolescence. Puberty-related female gonadal steroids might provoke dysregulation of serotoninergic and dopaminergic systems and brain changes might further promote these processes. Increased activity of orbital and dorsolateral prefrontal cortex regions during and after puberty might contribute to excessive worry, perfectionism, and strategising in AN patients. Finally, stress and/or sociocultural pressures may contribute by increasing anxious and obsessional temperament[16].

Neurotransmitter systems

Research has mainly focused on the serotoninergic system. It is involved in regulatory feeding behaviour such as playing an inhibitory role in eating patterns, regulating meal size and controlling eating rate. Moreover, the system is the cornerstone in several symptoms and behaviours associated with AN, such as obsessional features, anxiety, impulse control, inhibition, attention and mood. Some serotonin deficits reported in AN are: increased 1A and a decreased 2A serotonin receptors binding in ill and weight-recovered patients. Thus, after recovery from AN[17], studies have confirmed persistence in altered serotonin activity, anxiety symptoms, perfectionism and obsessive behaviour as well. Therefore, serotonin dysfunction may be a characteristic independent of the illness state. Some investigations suggest perfectionism as a possible endophenotype in EDs, associated with polymorphisms in the dopamine D4 receptor[18].

As stated, dopamine also plays an important role in behaviours, which are found to be disturbed in AN, such as eating patterns, motivation, reinforcement and reward. Deficits in dopamine function have been reported in AN, specifically, reduced levels of cerebrospinal fluid homovanilic acid and altered dopamine receptor functioning[19]. While there are fewer studies, alterations of dopamine in recovered individuals may persist[20], as has been found in serotoninergic system. It has been suggested that reduced food intake increases the

risk for AN by engaging mesolimbic dopamine neurons (involved in psychotic manifestations), causing an initial reward to dieting. Additionally, functional magnetic resonance studies have confirmed that dopamine neurons are activated in AN, but it is unclear whether this response is due to the disorder or to its resulting nutritional deficit[13]. As with psychotic disorders, the amphetamine model of psychosis would explain some symptoms characteristically observed in AN, namely, image distortions and stereotyped behaviors[21].

Genetic studies

Linkage studies have detected an association between *loci* in chromosome 1p34.2 in the restrictive subtype of AN and serotonin 1D and opioid delta 1 receptor *locus*. Other studies have determined signals in chromosome 2 for obsessionality, chromosome 13 for drive for thinness and chromosome 1 for the two traits[22]. These findings have not been followed up through rigorous replication studies, but they encompass relevant aspects of AN associated to these core features of EDs, involving distorted attitudes, behaviours and thoughts.

Published AN genome-wide association studies have yet to show significant findings for AN. A lack of sufficient sample size likely explains the disappointment of the AN genome-wide research efforts to date, as typically thousands of subjects are needed to yield significant *loci*. Another reason is the complexity of gene interaction and regulatory effects to other genomic factors. For instance, perturbation of the serotonergic and noradrenergic system is likely a result of complex interactions and compensatory mechanisms with other neurobiological systems and brain regions[23].

Structural and functional studies

Relatively little is known about the mechanisms underlying body image distortion in AN. A potential deficit in visual and tactile integration has been proposed. A study compared the size-weight illusion in individuals with AN and healthy controls. The size-weight illusion arises when two objects of equal weight but different sizes are held. Controls should experience a strong and robust illusion that the smaller object feels much heavier than the larger one because of an implicit assumption that weight scales with size. Individuals with AN exhibited a markedly reduced size-weight illusion relative to controls, even though their ability to discriminate weight was unaffected. These findings suggest a decreased integration of visual and proprioceptive information in AN, which may reflect a dysfunction in interactions between sensory integration in the inferior parietal lobule (concerned with body image), affective processing of bodily states in the insula and regulation of appetite through the hypothalamus[24]. Also, there is evidence for different networks in AN and healthy controls during visual processing of human bodies. It has been reported that a left sided effective connectivity in the occipital cortex of women with AN is negatively correlated with body size misjudgment. The altered networks for body processing would explain body size misjudgment, a key feature in AN[25]. Another study has investigated self-other body-shape comparison, concluding that AN patients displayed greater anxiety to the self-other body-shape comparison, and they were less satisfied with their current body shape. The self-other body-shape comparison induced more activation of the right sensorimotor brain regions (i.e., insula, premotor cortex) and less function of the rostral anterior cingulate cortex. These findings may be critical for altered interoceptive awareness to body self-comparison and/or for impaired implicit motivation to thin-idealised body images in AN patients[26]. Concerning body image distortion in AN, it has been considered such feature as a multidimensional construct. Analyses of their components, revealed that: 1) the perceptive component is mainly related to alterations of the precuneus and the inferior parietal lobes; 2) the affective component is mainly linked to changes of prefrontal cortex, insula and amygdala; 3) the cognitive component has been weakly explored and requires further investigations[27].

Phenomenology of delusions in anorexia nervosa

Phenomenological research has distinguished four main domains to describe belief intensity: action (linked with some behaviours), distress (related to negative affects such as depression or anxiety), preoccupation (how often the belief is focused on) and conviction (how strongly the belief is held). The latter, has probably received the greater attention due to its usefulness in distinguishing an overvalued idea from a delusion[28]. For instance, delusions in AN would be dissimilar to those in schizophrenia because AN patients would show higher levels of preoccupation and distress explained by a greater degree of insight[29].

Body image disturbance: delusion or defence mechanism?

Schilder[30] defined the concept of body image as "the picture of our own body, which we form in our own mind, that is to say, the way in which the body appears to ourselves." This first definition has supported the idea that body image could be more or less "objectively" captured. In agreement with Gaete and Fuchs[31], it is questionable that an objective body image is attainable at all, both for patients and normal individuals[32]. Furthermore, Schilder[30] described the "libidinous aspect" of body image, meaning with it that every mental image or perception has emotional and affective aspects, deeply related to the own personality. Nevertheless, mostly the representational facet of the body image concept has prevailed through the time. Body image distortion in AN was characterised by Bruch[4] as a feature with delusional proportions. Meanwhile, Roa[33] conceptualised AN symptoms as the expression of a "delusion of beauty." Both authors, in different ways, highlight the denial implied in the emaciation state and the strong force to uphold both their nutritional state and their eating behaviours as normal. Bruch[4] described the denial of starvation as the expression of the fear of fatness or of being haunted by the fear of ugliness. In fact, it is this dramatic denial of the illness as a delusional self-concept, including body image, what justifies for Bruch[4] to consider AN as a specific mental disorder[4]. She also distinguished between the external (mirror) and internal image of the body; the former appears to be distorted in anorectic patients and the latter is related to affective, sensorimotor and emotional aspects, which in turn are always participating in the external body image. Roa explains the body image disturbance driven by the "delusion of beauty" and the searching for perfection. What Bruch and Roa[33] describe differently as a fear of ugliness or "delusion of beauty," entrap patients into an extreme attentional concern with their bodies. The puzzling matter is that they do not seem interested in following fashion trends, but to hide their bodies under floating and big clothes, frequently of dark colours, with rather a monotonous and stereotyped style, and without any joyful attention to their images. Both perspectives are thought as two sides of the same coin: patients seeking for perfection as the result of their extreme insecurity and lack of self-esteem that leads to an almost persistent paranoid attitude on avoiding any "mistake," both in daily life and towards their bodies. Thus, the "delusional proportion" of Bruch[4], is understood from the phenomenological perspective as a consequence of great concern: the more fear of fatness, the more delusional degree of body image disturbance. In some cases, it seems that patients are protecting themselves from becoming fat by the irrational idea of being already fat. From this point of view, a delusional thinking is characterised by the lack of logical reasoning and the resistant nature to any argumentation or experience. However, there is no consensus yet whether the beliefs about body image in anorectic patients can be classified as overvalued or obsessive ideas, delusions or a combination of them[34]. Furthermore, Mountjoy *et al.*[34] explore the nature and the intensity of body image beliefs in anorexia nervosa, especially with regard to the so-called overvalued ideas. They propose a *continuum* through normal and delusional thinking, where AN can be placed in between. However, only a minority of anorectic patients have been categorised within compatible ranges for both pathological kinds of thinking. With regard to delusional beliefs, Roa[33] highlights the desperate searching

for individuation, which can be linked with the conceptualisation of a defence mechanism against the threat to self-organisation. This is in agreement with the "embodied defence hypothesis"[31], which refers to the body experience as an object expressed on the extreme attentional concern, leading patients to no longer perceive their bodies as the way for experiencing the world, but becoming the primary attentional focus. This viewpoint states that the emotional bodily experiences represent highly threatening experiences that patients are unable to cope with, due to their vulnerable self-organisation. Therefore, they recover the sense of security and control by retreating their bodies as objects, relieving them of coping with daily life affective and emotional stimuli. Consequently, they feel protected but isolated, replacing their self-others relationship by a self-body as "the other" relationship. So, delusional ideas about their bodies are part of the extreme attentional focus on them as "objects," which necessarily leads to a lack of perspective and to a loss of the emotional bodily resonance[31], a core feature of the subjective emotional bodily experience. The weaknesses that impede patients to cope with affective and emotional stimuli would favour a vicious circle, in which objectification of the body leaves patients without the basic resource to accomplish adaptive responses to daily life events as "somatic markers" of emotions[35]. Thus, they are unable to take emotionally based decisions for adjustment responses, reinforcing the suppression of the bodily resonance of emotions through the body objectification, which at the same time strengthen the deficits of self-organisation as well. It has been suggested that these vulnerabilities are triggered by early attachment experiences, if the child did not experience sensitive responses to its bodily expressions[36-38]. Hence, if there is a conflict with someone affectively relevant, it becomes an extremely unbearable situation for anorectics, suppressing the bodily resonance as a consequence of such an uncomfortable emotion, representing an efficient defence mechanism. This suppression of bodily resonance implies that patients might experience feelings like "nothing is happening with my life, everything is fine; but my only problem is with my body," as object.

Clinical features

There is consistent evidence that restrictive AN exhibits higher levels of delusionality (a less impulsive and less insightful pole), lending support to their significance and major role in the development and the maintenance of EDs, particularly during the early phase of the illness, reflecting a link between cognitive and emotional aspects of body image disturbances in AN[1]. However, ED patients who develop a stable psychosis would preserve psychopathological phenomena of the feeding syndrome[39]. Additionally, emaciation is associated both with serious medical morbidity and firmly held beliefs, which are impressively stereotyped, reporting the most of anorectics as a dominant belief that if they eat, they get fat or change shape in some way immediately after eating[2]. Poor illness insight is a predictor of worse long-term outcome, and vice-versa, decreasing in delusional beliefs or enhancement in disorder awareness constitute an important marker of patients' improvement[1].

A particular phenomenon known as "anorectic voice" has been described. It is often experienced as a second or third person commentary about actions related to eating, weight and shape. It is possible to distinguish it from auditory hallucinations because they are recognised as internally generated. At the early disease stages they would be supportive, but then they become controller and hostile. The importance of the understanding of this phenomenon has been pointed out in cognitive models of psychosis, which stress the relevance of the power and nature of the voice[40].

Differential diagnosis

Psychotic disorders

A close relationship between a previous psychotic structure and AN symptomatology has been observed, with weight loss contributing to

exacerbate both delusions and hallucinations[39]. Psychotic episodes are found in 10% to 15% in ED patients. Most of them are transient, although 1% to 3% will obtain a schizophrenia diagnosis[5].

Classification of anorectic patients according to the degree of delusionality of body image beliefs could facilitate further research on the role of insight deficits. In this sense, Konstantakopoulos *et al.*[1] have recognised a psychotic form of AN with poor insight correlated with restrictive eating and early beginning of the symptomatology.

Schizophrenia

The prevalence of diagnosable schizophrenia in patients with EDs is estimated as below 10%. Males would have a higher risk than females, particularly for the hebephrenic type[41]. Those who suffer from restrictive AN share neurocognitive deficits with schizophrenics: diminishing in shifting attention, overestimation of detail and reduced central coherence (i.e., a difficulty to understand the general context)[5]. Although they could display marked body image disturbances, their content does not seem to be specifically related to weight and appearance[4]. Thus, the diagnosis of schizophrenia should preferably be made and is only valid after re-nutrition has been achieved[39]. It is important to take into account the possibility of developing ED behaviours induced by antipsychotic medications as well[42].

Affective and schizoaffective disorders

Psychotic symptoms in EDs also co-occur in patients with co-morbid schizoaffective and/or bipolar disorder, although the latter display greater levels of comorbidity for full and partial EDs. Indeed, eating disturbances in childhood often precede affective psychosis in adulthood, while patients who develop psychotic symptoms after the onset of AN may show schizothymic personality traits[43]. On the other hand, anorectics seem to show higher preoccupation and distress levels for their beliefs in comparison to patients with schizophrenia/ schizoaffective disorder[34].

Furthermore, Cotard syndrome comprises a delusion in which the subject believes he is dead or does not exist; a denial of self-existence within a severe melancholic depression. It may also be observed in schizophrenia or bipolar disorder, which could be related to temporo-parietal lesions of the non-dominant brain hemisphere[44].

Obsessive-compulsive disorder

Perfectionism has been considered a transdiagnostic process within the obsessive-compulsive spectrum and AN[45]. Higher levels of it have been correlated with poorer degrees of insight and delusional symptomatology. Obsessive-compulsive patients feel compelled to carry out rituals to compulsively relieve the associated upheaval as a consequence of their intrusive thoughts associated to several contents (*e.g.*, fears of contamination, a need for symmetry or orderliness, fears of harming others by mistake, cleaning, checking, thinking "neutralising" thoughts, etc.) with an understandable and coherent link between both, in contrast to AN where perfectionism, obsessive thoughts and compulsive rituals are focused mainly on body image, weight gaining, some kind of foods and feeding, *versus* schizophreniform psychosis, where a primary core delusional belief emerges characterised by an incoherent behaviour with no related rituals[1].

Body dysmorphic disorder

Delusionality of appearance beliefs is present in individuals with AN, but is less pronounced than in body dysmorphic disorder. In AN, delusionality is related to shape concerns and drive for thinness, whereas delusionality in dysmorphophobia would be associated to the severity of symptoms[3,46]. In this line, Grant *et al.* found that 39%

of anorectic patients exhibited a comorbid body dysmorphic disorder, displaying significantly lower global functioning and higher levels of delusionality[47].

Risk factors

Overvalued ideas appear to be frequent in both anorexia and bulimia nervosa. Nevertheless, Konstantakopoulos *et al.*[1] observed that only anorectics (28.8%) had delusional body image beliefs associated with restrictive behaviours, early onset of the condition and body dissatisfaction, but these were not related to the duration of illness (insight would remain stable through time)[1]. Neither age nor educational level were found to affect the degree of delusionality, which would constitute an independent phenomenon of weight loss or eating behaviour, a different psychopathological component of AN, perhaps contributing to therapeutic resistance and illness chronicity[1]. These findings point out that a delusional type of AN represent the end of a *continuum* in patients with EDs[1].

Treatment

Irrational eating-related thinking may contribute to avoidance of therapy, difficulties to be engaged in treatment and high rates of dropout and relapse[1]. Mental rigidity, body distortion and magical thinking play an essential role in resistance to therapies, in particular as seen in chronic patients with complex developmental histories[39,42].

Delusional thinking in AN, mainly related to body image distortion and drive for thinness to which pursues changes in beliefs and/or cognitive patterns, seems to be underlying the emphasis that cognitive techniques have received along the development of diverse EDs treatments[31].

Pharmacotherapy

An important aspect to consider is that a group of patients exhibit a good symptomatic response with antipsychotics. This would support that a subgroup in AN requires distinct pharmacological treatment, with special attention to structural deficits for long-term maintenance.

First generation antipsychotics have been considered, but given their side effects, poorer efficacy in changing eating behaviour and body image distortion, their usage is not recommended. Low doses of haloperidol have been found to be effective in the AN restricting subtype[48]. On the other hand, atypical antipsychotics can diminish anxiety, agitation, aggressiveness and obsessive thoughts linked to food control and body image distortion[49], by modulating both serotoninergic and dopaminergic systems[39]. Administration at the minimal effective dosage has been suggested[5]. Some agents like olanzapine and quetiapine can be a desirable choice due to their orexigen and sedative effects[5], in decreasing inner tensions and phobia regarding food intake, related to paranoid ideation on body image and/or weight gain. Particularly, olanzapine, recommended from 2.5 to 15 mg daily[50], might be considered in patients with long-term history of AN, several hospitalisations, poor insight, rejection of therapy, delusional thinking and risk of dropout with life-threatening consequences, by improving the compliance to treatment[39] with refeeding and weight gain as well as postdischarge weight maintenance. In Table 1 the main findings of the review are summarised.

Discussion

Dimensionally, delusional spectrum in AN goes from an overvalued idea to a categorical psychotic picture, although in many cases, clinical differences between nondelusional and delusional states are not so clear. Consequently, evidence shows that illness denial is so variable, depending on diverse degrees of individual self-awareness. Certainly, emaciation and somatic disturbances due to malnourishment

Table 1. Main findings summary

Perspective	Findings
Clinical perspective	– Restrictive AN exhibits higher levels of delusionality. – Alexithymia and introversion would facilitate pre-psychotic conditions. – Concrete, dichotomous and ruminative thinking style would foster dissociative experiences and therefore psychotic manifestations. – Poor illness insight is a predictor of worse long-term outcome. – The "anorectic voice" has been described as a second/third person commentary about actions related to eating behaviours, recognised as internally generated. – The presence of overvalued ideas has been proposed as a risk factor in delusional phenomena. – The main differential diagnoses in delusional AN are psychotic disorders, schizophrenia, affective and schizoaffective disorders, obsessive-compulsive disorder and body dysmorphic disorder. – The treatment of delusional aspects in AN considers cognitive techniques, pharmacotherapy (haloperidol, quetiapine and particularly olanzapine), among others.
Neurobiological perspective	– Altered monoamine neuronal modulation (*e.g.*, altered metabolism of serotonin and dopamine receptors). – Impaired dorsal caudate, amygdala and precuneus functioning. – Increased orbital and dorsolateral prefrontal cortex activity. – Dysfunction in sensory integration of inferior parietal lobule, insula and hypothalamus. – Decreased cingulate cortex activity.
Phenomenological perspective	– In AN, body image distortion may present "delusional proportions" as a consequence of great concern about body. – The phenomenon of "denial" is deeply implied in emaciation state. – "Delusion of beauty": extreme attentional concern to the body, seeking for perfection. – Searching for individuation: conceptualisation of a defence mechanism against the threat to self-organisation. – "Embodied defence hypothesis": emotional bodily experiences represent threatening experiences that patients are unable to cope with; therefore, the sense of security and control is recovered by retreating the body as an object.

contribute to a lack of reality judgement. Additionally, some pre-morbid psychological traits have been identified (*e.g.*, dichotomous and ruminative thinking, alexithymia, rigidity and perfectionism), which interact with the Western sociocultural, historical and economic context, that emphasises the drive for thinness to achieve an ideal feminine slim body shape. Nonetheless, some authors state that sometimes delusionality is independent of weight loss or eating pathology and therefore a manifestation of a different AN subtype, related to treatment resistance and a chronic illness course[1]. In this sense, classification of AN patients based on the level of delusionality beliefs could facilitate further research on the role of insight deficits in these disorders[1], which was not included in the DSM-V as a specifier[9]. Hence, a systematic assessment of the irrational thinking in AN would contribute by identifying cognitive processes underlying the clinical picture[2]. Besides, some researchers have verified that if self-perception is altered, it is often mildly, unsatisfactory to explain the tremendous delusional denial of reality seen in severe cases of AN. Thus, Gardner and Bokenkamp propose that perceptual distortion is

due mainly to comorbid affective disorders usually observed during AN evolution[51]. Conversely, recent studies[13] have documented that alterations in dopamine system found in AN patients, are more likely to be physiological responses to starvation than signs of mental pathology. Nevertheless, as stated above, neurobiological aspects of psychotic features in AN have been scarcely explored, and due to the permanent malnourishment state of these patients, it is difficult to distinguish causal and consequent mechanisms,

McElroy *et al.*[45] stated that, although EDs show differences from obsessive-compulsive disorder they also display some similarities (obsessive thinking and/or compulsive behaviours, course, comorbidity, family patterns, biological abnormalities and treatment responses) which allow to include them in the obsessive-compulsive spectrum among other disorders. Moreover, they hypothesised that some differences may be partly explained by variation along a dimension of compulsivity *versus* impulsivity, and, because most of these conditions appear to be related to mood disorders, the obsessive-compulsive spectrum may belong to the larger family of affective spectrum.

Delusional thinking in AN, seems undeniable, but it is likely a dynamic and dimensional phenomenon that can vary both in nature and in severity. This means that not all patients show a delusional thinking, and in some good insight levels are preserved. However, the presence of delusional thinking probably means an outcome index that must be taken into account from a therapeutic point of view. Thus, this feature can be understood as a part of a broader phenomenon described by Gaete and Fuchs[31] and named "disturbance of the emotional bodily experience," where the embodied defence mechanism is involved. Hence, cognitive or perceptual approaching techniques for body image disturbance may disregard the severe difficulties of patients related to the bodily resonance of emotions, that permit adaptive responses to daily life, which can explain the high risk of relapse and complexity in modifying cognitive patterns and "perceptual distortions." It seems relevant to develop new psychotherapeutic techniques, which offer patients a safe way of recovering their living bodies as subjects.

Delusional features in AN have been reported from multidimensional perspectives along the history of psychiatry (i.e., phenomenological, neurobiological, psychodynamic clinical). However, current versions of mental diseases guidelines often do not include them. It is therefore of utmost importance to encourage neurobiological research on this topic, since clinical and phenomenological approaches are more developed and have contributed to a comprehensive understanding of the delusional dimension of AN. Insight assessment before and after refeeding, as a marker of the nature and severity of the disorder, should be systematically performed in order to provide an optimal treatment option.

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Long-term effects of ayahuasca in patients with recurrent depression: a 5-year qualitative follow-up

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Abstract

Background: Ayahuasca is a botanical hallucinogenic preparation traditionally used by indigenous populations of Northwestern Amazonian countries for ritual and therapeutic purposes. It is rich in β-carboline alkaloids and *N,N*-dimethyltryptamine (DMT). Preclinical, observational, and experimental studies suggest that ayahuasca and its alkaloids have anxiolytic and antidepressive effects. We recently reported in an open-label trial that ayahuasca administration was associated with significant decreases in depression symptoms for 2-3 weeks after the experimental session in 17 patients with treatment-resistant major depressive disorder. **Objectives:** To investigate if the experiment had any long-lasting effects on patients **Methods:** Eight patients were interviewed 4 to 7 years after ayahuasca intake. **Results:** Our results suggest that ayahuasca was well tolerated and that symptom reductions were limited to a few weeks. Importantly, most patients believed that the experience was among the most important of their lives, even 4-7 years later. **Discussion:** To the best of our knowledge, this is the first long-term follow-up of a clinical sample that participated in an ayahuasca trial. Further studies with different and repeated dosing should be designed to further explore the antidepressive and anxiolytic effects of ayahuasca.

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Keywords: Hallucinogens, psychedelics, ayahuasca, depression, safety.

Introduction

Ayahuasca is a botanical hallucinogenic preparation traditionally used by indigenous populations of Northwestern Amazonian countries for ritual and therapeutic purposes[1], and also as a sacrament and therapeutic tool by Brazilian syncretic religions such as the *Santo Daime*, *Barquinha* and *União do Vegetal*[2,3]. It is usually prepared by the prolonged concoction of the bark of the vine *Banisteriopsis caapi* together with the leaves of the shrub *Psychotria viridis*. The vine is rich in β-carboline alkaloids such as harmine, tetrahydroharmine (THH), and harmaline, and *P. viridis* contains *N,N*-dimethyltryptamine (DMT). The β-carbolines act as reversible inhibitors of monoamine oxidase (MAO)-A, and DMT act as a $5-HT_{1A/2A/2C}$ agonist[4]. DMT by itself is not orally active due to degradation by peripheral MAO-A, but MAO-A inhibition by the β-carbolines renders DMT active by allowing it to reach the brain[4-6]. The neural basis of the effects of ayahuasca seem to involve modulation of frontal and midline brain structures, such as the default mode network (DMN)[5-9].

Preclinical, observational, and experimental studies suggest that ayahuasca and its alkaloids have anxiolytic, antidepressive, and antiaddictive effects[2,3,10-14], and studies with healthy volunteers[2-8] and psychiatric patients[10,11] show that it is well tolerated. Previous observational studies assessing the mental health of members of Brazilian ayahuasca churches described the potential effects of regular ayahuasca use on anxiety, depression and dependence symptoms[2,14]. Moreover, the first double-blind, controlled study showing that a single ayahuasca dose induced significant reductions on panic-like and depressive symptoms was conducted among *Santo Daime* members[3].

We recently reported that administration of a single oral dose of ayahuasca (dose: 2.2 mL/kg; alkaloid content in the sample: 0.8 mg/mL DMT, 0.21 mg/mL harmine, no harmaline was detected, and THH was not analyzed due to a lack of analytical requirements) in an open-label trial to 17 patients with treatment-resistant major depressive disorder (MDD) was associated with significant decreases in depression symptoms assessed with the Hamilton Rating Scale for Depression (HAM-D) and the Montgomery-Åsberg Depression Rating Scale (MADRS) from 80 minutes to day 21[10,11]. Average baseline score in the HAM-D scale was 19.24 (SD = 5.52), and at day 21 the average score was 7.56 (SD = 4.7). We recently replicated these results in a parallel arm, double-blind, randomised, placebo-controlled trial with 35 patients with treatment-resistant MDD[15]. Compared to placebo, HAM-D scores at day 7 were significantly lower in patients treated with ayahuasca (Cohen's d = 0.98), and MADRS scores were significantly reduced in the ayahuasca group at days 1, 2 and 7.

After the publication of the open-label study[10,11]; we were interested in interviewing the volunteers after a long-time period to ask if the experiment had any long-lasting effects on them. To the best of our knowledge, this is the first long-term follow-up of a clinical sample that participated in an ayahuasca trial.

Methods

An experienced psychiatrist that was closely involved with the volunteers during the study (RFS) tried to contact the volunteers by telephone. At least three attempts, in three different times of the day, were made to try to contact the volunteers. The contacted volunteers were then asked the following questions by a telephone interview:

#1. *Do you classify your experience with ayahuasca as negative, neutral, or positive?*

#2. *Did the experience bring any significant changes (positive or negative) to your life in general?*

#3. *Did the experience bring any significant changes (positive or negative) to your daily life?*

#4. *Did the experience bring any significant changes (positive or negative) to your relationship with other people (friends, family, or in your work)?*

#5. *Did the experience bring any significant changes (positive or negative) to your spirituality/religiosity or in your way to see the world and nature?*

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#6. *Did the experience bring any significant changes (positive or negative) in the way you perceive music or art in general?*

#7. *After the experiment, did you have desire to drink ayahuasca again?*

#8. *After the experience, have you used ayahuasca? If yes, how many times? Briefly describe the experience.*

#9. *How did your symptoms evolved since the experience? They improved, got worse, or remained stable?*

#10. *Have you changed your medications after the experience? Did you stop taking your medications, returned to the same medications, or increased the dose or number of medications?*

#11. *Did you observe any kind of changes in your behavior or symptoms during or after the experience that you believe is important to mention?*

#12. *Would you classify the experience among the 10 most important experiences of your life? In which position, from 1 to 10?*

#13. *If you passed for a difficult and challenging experience during the study, do you think it was positive anyway?*

#14. *Did you observe something negative or positive during the experience that you think is important to mention?*

Questions #1 to #13 could be answered as positive (+), negative (-), or neutral/stable (=). Question #14 could be answered more freely.

Results

The results of the interview are described in Table 1.

Of the 17 patients that participated in the study, we could contact only eight (seven women; mean age 39.87 years; range 28-54). The other nine patients could not be contacted after several attempts. All the non-participant subjects were not able to be located, thus, there were no subjects that refused to participate in the study.

The contacted patients had a mean baseline HAM-D score of 20.37 (range 17-24) and a mean baseline MADRS score of 27.12 (range 21-32). Means HAM-D and MADRS scores on D21 were 6.75 (range 2-15) and 8.75 (range 1-19), respectively. Patients have participated in the experiment from October 2010 (patient #1) to January 2013 (patient #8), and the follow-up interviews were conducted from January to May 2017. Therefore, patients were interviewed after a mean of 56.37 months (range 49-76), or 4.7 years.

As can be observed in Table 1, although volunteers had difficult experiences, most of them reported that participation on the study was positive and had a positive impact on their general and daily lives, and that they would like to experiment ayahuasca again (although none did). Furthermore, six patients reported that the experience was among the 10 most important experiences of their lives, with four patients reporting that the experience was among the five most important experiences of their lives.

However, four patients reported neutral effects or that their symptoms remained stable, nine reported that their medications were unchanged (one reported that the medication was changed, and none have stopped the medication), and almost all patients that reported positive effects also noted that they were short-lived. Furthermore, only three patients reported improvements in their relationships with friends, family, or at work, and only one described a positive effect of the experiment on music and art perception and on spirituality/religiosity or in the way one sees the world and nature. Negative effects included mostly nausea and vomiting.

Discussion

Previous observational studies in members of the Brazilian ayahuasca churches reported the potential effects of ayahuasca on anxiety and mood regulation[3,14]. Moreover, a controlled study in members of these groups also reported anxiolytic and antidepressive effects[3], which were corroborated in recent open-label and controlled studies with depressed patients[10,11,15]. In the present work, the first long-term follow-up of those depressed volunteers[11], we found that ayahuasca was well tolerated and associated with antidepressive effects.

The main limitations of this follow-up are the long time that passed since the experimental session was conducted and that not all volunteers were contacted. The first limitation could have increased the chances of recollection bias in the sample, and the second makes it impossible to know if the other volunteers had the same kind of responses, thus limiting the extrapolation of the results for the whole sample. Nevertheless, to the best of our knowledge, this is the first study long-term follow-up of depressed patients that have ingested ayahuasca.

Even considering the above-cited limitations, our results suggest that ayahuasca was well tolerated by these patients and that the reductions in depressive symptoms attributed to ayahuasca intake were limited to a few weeks. Moreover, most patients that participated in the interview believed that the experience was among the most important of their lives, even 4-7 years later. This last observation could be related to the fact the patients had been suffering with their depressive symptoms for a long time, and a significant (although limited in time) improvement in their symptoms could have a great significance for them.

The results and limitations of this qualitative study suggest that future studies involving administration of ayahuasca should try to perform follow-ups after shorter periods of time to try to observe any effects that could appear a few months of the experiments and to try to avoid losing contact with the volunteers, so that a clearer image of the results can be achieved. Furthermore, the present results and the data from our open-label and controlled studies suggest that

Table 1. Depressive symptoms assessed with the Hamilton Depression Rating Scale (HAM-D) and the Montgomery-Åsberg Depression Rating Scale (MADRS) and results from the follow-up questions

	Age at the time of the experiment	Time since the experiment (months)	HAM-D / MADRS (baseline)	HAM-D / MADRS (D1)	HAM-D / MADRS (D7)	HAM-D / MADRS (D14)	HAM-D / MADRS (D21)	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13
Patient 1	31	76	20 / 27	14 / 12	3 / 6	3 / 3	2 / 1	=	=	=	=	=	=	-	-	=	=	×	-	=
Patient 2	36	67	20 / 32	9 / 17	11 / 7	4 / 2	2 / 3	+	+	+	+	+	+	+	-	+	≠	+	+ (6)	+
Patient 3	38	52	20 / 32	3 / 1	7 / 11	2 / 2	4 / 2	=	=	+	+	=	=	-	-	+	=	+	+ (4)	+
Patient 4	46	55	17 / 21	10 / 12	8 / 15	10 / 15¹	13 / 15	=/-	+	=	=	=	=	-	-	=	=	+/=	-	+
Patient 5	39	51	20 / 28	17 / 20	18 / 22	15 / 18	15 / 19	+	+	+	=	=	=	+	-	+	=	=	+ (8)	+
Patient 6	54	51	19 / 23	6 / 3	10 / 9	16 / 14	5 / 8	+	+	+	=	=	=	-	-	=	=	=	+ (5)	+
Patient 7	28	50	23 / 25	5 / 7	5 / 5	6 / 6	5 / 5	=	+	=	+	=	=	-	-	=	=	=	+ (3)	+
Patient 8	47	49	24 / 29	13 / 17	20 / 23	16 / 19	10 / 17	+	=	=	=	=	=	+	-	+	=	=	+ (4)	+

Ayahuasca intake for these eight patients occurred between October 2010 and January 2013. Interviews were conducted between January and May 2017.
+: positive, -: negative, =: neutral/stable; ≠: changed medication; ×: do not remember.
The numbers in parenthesis on question #12 are the position from 1 to 10 reported by those volunteers that had a positive answer to that question.
¹ Missing data: mean of D7 and D21.

ayahuasca holds some promise as a viable treatment for refractory depression. Nevertheless, future studies designed to further explore the antidepressive and anxiolytic effects of ayahuasca should be performed with more volunteers, different doses and also with repeated dosing for longer periods of time.

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Hypochondriasis as a distinct phenomenological presentation of complicated grief

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Almeida B, Santos G / Arch Clin Psychiatry. 2018;45(1):25

Dear Editor,

Grief is a psychobiological response with emotional, cognitive and behavioural components[1]. The experience of grief in reaction to loss is universal, yet there is lack of an integrative theory of bereavement which could merge neurobiological, psychological and sociocultural factors[2]. Unsurprisingly, during the last decades, grief has posed a nosological challenge, in which the border between normal and pathological reactions may not always be clear[3].

Through the presentation of the following clinical vignette, we aim to attract more attention to highly heterogeneous phenomenology of grief reaction. We report a 20-years old female, farmer, single (and lived with her parents). She had no relevant past medical and psychiatric history. She attended our outpatient department for panic disorder that started after her grandfather's death (a very important figure in her life), two years prior, in the context of a rapid progressive colon cancer. She consulted previously a psychiatrist and took escitalopram, but she abandoned after four months, without improvement. Apart from the panic attacks, she also presented feelings of acute grief – intense sadness, crying, feelings of guilt about his death, the sensation of his presence around her and vivid dreams – and hypochondriac symptoms: the belief that there was something wrong with her body and something bad could be happening with her (not related with the panic attacks) despite the normal medical exams done by her general practitioner (echocardiogram, electrocardiogram and several blood tests). She missed her work, got isolated from social contacts and visited many times her general practitioner asking for repeatedly medical examinations. Given the severity of the symptoms, we started Sertraline (50 mg/day) and supportive psychotherapy. The symptoms resolved after six months. We conceptualized this clinical case as a complicated grief with secondary panic attacks and hypochondriasis. In the setting provided, patient was able to do her grief work and adapt/cope with her lost, with the subsequent resolution of the symptoms.

Hypochondriacal symptoms could be found in a wide range of mental disorders. Interestingly, hypochondriasis was seen psychodynamically as a defence against guilt or low self-esteem[4], which bears obvious resemblances with the role of self-blame in bereavement[5]. One could say: "Why should I be healthy now that my grandfather is dead from a disease I couldn't help?".

Focusing on the phenomenological account of the patient, the misinterpretation of otherwise normal bodily sensations could be triggered or aggravated by the emotional state (due to grief)[6]. The overvalued ideas firmly held by the patient refer to a fear of illness, which could mediate a deeper fear of death.

We also suggest that the first trial of SSRI (escitalopram) failed, at least in part because the psychosocial aspects of grief were underlooked. Supportive psychotherapy promoted emotional repair and cognitive restructuring with new coping strategies.

As far as we know this is the first report in the literature of hypochondriasis as a phenomenological presentation of complicate grief. This article outlines the need to recognize hypochondriasis in times of distress, avoiding unnecessary exams and investigation, and prompting supportive psychotherapy, tailored to the singularity of the grief process.

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