doi:10.1017/S1092852912000363

Symptom Dimensional Approach and BDNF in Unmedicated Obsessive-Compulsive Patients: *An Exploratory Study*

Igor Marcanti dos Santos, MD, Leandro Ciulla, MD, Daniela Braga, MD, Keila Maria Ceresér, PharmD, PhD, Clarissa Severino Gama, MD, PhD, Flávio Kapczinski, MD, PhD, and Ygor Arzeno Ferrão, MD, PhD

ABSTRACT

Introduction: The dimensional approach of the obsessive-compulsive symptoms may help to find more homogeneous groups of patients. The brain derived neurotrophic factor (BDNF) may help to identify neurobiological differences between obsessive-compulsive symptom dimensions.

Methods: We compared serum BDNF (pg/µg) levels of 25 unmedicated patients meeting *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for obsessive-compulsive disorder (OCD) and 25 controls, using the Dimensional Yale-Brown Obsessive-Compulsive Scale, the Yale-Brown Obsessive-Compulsive Scale and the Beck's Anxiety and Depression Inventories.

Results: There were no sociodemographic differences between the groups. The standard error of mean serum BDNF levels were reduced in unmedicated OCD patients (0.47+0.038) when compared to healthy controls (0.75+0.060) (P<.001). The patients with the presence of sex/religion obsessive-compulsive symptoms (OCS) dimension (P=.002), with chronic course of OCS (P=.022) and the presence of lifetime major depression (P=.016) and social anxiety (P=.030) presented higher levels of BDNF than

FOCUS POINTS

- Serum brain derived neurotrophic factor (BDNF) may be involved in obsessive-compulsive disorder (OCD) pathophysiology, since it is decreased in OCD patients when compared to healthy subjects.
- There is an association between serum levels of BDNF and the obsessive-compulsive symptoms dimensions, corroborating the heterogeneity of OCD.
- In evaluating the correlation between serum BDNF levels and severity of OCD, special attention is paid to specific obsessive-compulsive symptoms dimensions, especially the sexual/religious dimension.

Dr. dos Santos and Dr. Ciulla are psychiatrists at Porto Alegre Health Sciences Federal University in the Anxiety Disorders Outpatient Program, at Presidente Vargas Maternal-Infantile Hospital. Dr. Braga is a psychologist, Dr. Ceresér is a research assistant, Dr. Gama is a psychiatrist, Dr. Kapczinski is a psychiatrist and professor, all in Department of Psychiatry, Federal University of Rio Grande do Sul, Porto Alegre; Dr. Ferrão is a psychiatrist and pProfessor at Porto Alegre Health Sciences Federal University in the Anxiety Disorders Outpatient Program, Presidente Vargas Maternal-Infantile Hospital; Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders.

Faculty Disclosures: Dr. Santos, Dr. Ciulla and Dr. Braga reported no biomedical financial interests or potential conflicts of interest. Dr. Gama has been a paid speaker for AstraZeneca. Dr. Kapczinski reports research funding from Dr. Ferrão has been a paid speaker for Wieth, Ely Lilly, Solvay Pharma and Roche Laboratories. This work had financial supported from Fundação de Incentivo à Pesquisa of Hospital das Clínicas de Porto Alegre (FIPE-HCPA). Dr. Gama reports grant/research support from Brazilian National Research Council (CNPq) (processes 305967/2008-8 and 477974/2009-0) from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), from FIPE–HCPA, and Endeavour Award. Dr. Ceresér reports research grant from CNPq (process number, 473424/2009-6).

Acknowledgements: Drs. dos Santos and Ciulla contributed equally to the final manuscript. None of the institutions above had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Date Submitted: September 13, 2010; Date Accepted: June 15, 2011; First published online: September 1, 2011.

Correspondence: Ygor Arzeno Ferrão, MD, PhD, Rua Padre Chagas,185/403, Porto Alegre, RS, CEP:90570-080, Brasil; E-mail: ygoraf@terra.com.br

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

OCD patients without those features. The severity of aggression (*P*=.039) and sex/religion (*P*<.001) OCS dimension presented direct (moderate and strong, respectively) correlation with serum BDNF levels in this sample. Serum BDNF levels were decreased in OCD patients when compared to healthy controls.

Discussion/Conclusion: Sexual and religious content of symptoms and aggression and sex/religion dimensions severity should be better explored, since these specific OCS dimensions could be based on neurocircuits diverse from those of the other OCS dimensions.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is classically considered to be constituted by two major syndromes: obsessions, which are intrusive unwanted thoughts, fears or images; and compulsions, which are ritualized behaviors or mental acts, generally performed to relieve the anxiety and/or distress caused by the obsessions.[1,2] It has a lifetime prevalence of 2% to 3%[3] and it is the fourth most common mental disorder, frequently accompanied by dysfunctions in several areas: family, social, school, and occupation.[4] Some efforts of attempting to find OCD subgroups were conducted, including aspects such as: the age of obsessive-compulsive symptoms (OCS) onset[5-7]; subjective experiences preceding OCS (sensory phenomena)[8-10]; comorbidity patterns[11-13]; and clinical course.[14] The results of those several approaches have led the researchers to consider OCD as a clinical and genetically heterogeneous disorder.[15] The heterogeneity makes it difficult to comprehensively understand the varied clinical manifestation of OCD, complicates the search for candidate genes, and reduces the treatment response of conventional therapeutical arsenal. Approximately 40% of OCD patients are partial responders and ~20% seem to be refractory to any of the available therapeutics.[16]

Rosario and colleagues[17] developed the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) to allow the identification of more homogeneous subgroups of OCD patients. It is based on valid and reliable constructs, tested by several factor-analytic studies, involving more than 2,000 patients (to see the complete list, please see Rosario and colleagues[17]). Each of the six factors or dimensions (aggression; sex and religion; symmetry, ordering and arrangement; contamination and washing/cleaning; hoarding; and miscellaneous) includes obsessions and related compulsions.[17] For example, it is possible with it to identify associations between symptom dimensions and treatment response or refractoriness,[16] although the associations are too weak to gudie clinical practice. Attempts to identify the association of biological markers with the OCS dimensional approach (ie, DY-BOCS) has not been conducted yet, except for imaging studies.[18-24]

Recently, Maina and colleagues[25] showed that brain derived neurotrophic factor (BDNF) levels were decreased in drug-naïve OCD patients when compared to controls (36.90±6.42 ng/ml versus 41.59±7.82 ng/ml; *P*=.043). No correlations were evidenced between serum BDNF content and the severity of OCD symptoms as measured by Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores or other clinical variables. They also found no significant correlations with the obsession/compulsion subscale scores, age at onset of OCD and of symptoms, length of illness, family history, Hamilton Anxiety Inventory scores, Clinical Global Inventory, and Short Form (36) total scores. Only a trend (*P*=.09) for a decrease in serum BDNF was observed in patients with a lifetime history of major depression.[25]

BDNF is an essential neurotrophic factor, responsible for cholinergic, dopaminergic, and noradrenergic neuron development, function, plasticity and survival, especially in the central nervous system,[26,27] where it may be found in the cerebellum, mesencephaon, neocortex and hippocampus.[27] It regulates the response to environmental stimulations as stress events during life and studies in human post-mortem brains have shown an involvement of BDNF in the pathophysiology of stress-related human psychopathologies, such as psychotic, depressive, and anxiety disorders.[28-30] BDNF was also reduced in other psychiatric disorders, as major depression,[31-33] bipolar disorder,[34] and schizophrenia.[35,36]

The neurotransmission systems dysregulation (mainly those associated to serotoninergic, dopaminergic and glutamatergic function) of cortical-talamic-striatal-cortical circuits are the patophisiological basis of OCD.[37-39] The fact that some

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

studies suggest that BDNF modulates the serotonin transporter function,[40,41] turns the BDNF gene an attractive OCD candidate gene, from both a brain development and neurotransmitter perspective, as suggested by Katerberg and colleagues.[42] OCD studies have reported inconsistent findings regarding the BDNF Val66Med polymorphism, which is a valine to methionine substitution in the prodomain of BDNF protein.[42-49]

In an attempt to provide further data about the neurotrophin hypothesis in OCD, the objectives of this exploratory paper are to compare serum levels of BDNF in currently unmedicated OCD patients versus healthy controls; to evaluate if there is categorical association between serum levels of BDNF and those DY-BOCS dimensions with enough sample size; to evaluate if there is correlation between serum BDNF levels and severity of OCD and severity of the OCS dimensions according to DY-BOCS, when sample size is enough; to investigate whether serum levels of BDNF are associated to some OCD clinical features, as: chronic course; other axis I psychiatric comorbidities (especially, tics disorders, other anxiety disorders, impulse control disorders and major depression); and OCS age at onset.

METHODS

This exploratory case-control study was composed by 25 OCD patients and 25 healthy controls. OCD patients were recruited from outpatients services from Presidente Vargas Maternal-Infantile Hospital (PVMIH) and from Hospital de Clínicas de Porto Alegre (HCPA), both located in Porto Alegre, Brazil. The inclusion criteria for OCD patients were: diagnosis of OCD according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edtion*, had been unmedicated for at least 60 days, and scoring currently at least 16 points at the Y-BOCS. Forty-two patients included on a waiting list for a group cognitive-behavior therapy program were initially selected, but 15 (35.7%) were using anti-obsessive medication (ie, serotonin reuptake inhibitors) and two (4.8%) refused to participate. Controls were recruited from one of the hospitals volunteers' employees list. The inclusion criteria for healthy controls was not having any axis I psychiatric diagnosis according to the *DSM-IV*. Exclusion criteria for both groups were: current history of alcohol or any other illicit psychoactive use or abuse; history of encephalic/brain trauma followed by posttraumatic amnesia; current history of any other neurological or systemic disorders (ie, epilepsy, Parkinson's disease, or systemic Lupus); current use of medication that could lead to any psychopathological manifestations; current imminent suicide risk; pregnant or breast-feeding women; <18 and >60 years of age; and a cognitive deficit that could turn patient unable to understand the applied instruments and questionnaires. Of the initial 29 pre-selected controls, four (13.8%) were excluded (two for an inconsistent history of epilepsy and two refuse to participate). No OCD patients were excluded because of the above criteria.

Patients were evaluated by the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders Initial Evaluation Protocol, which includes sociodemographic data, socioeconomic status according to Associação Brasileira de Imprensa e Pesquisa de Mercado (ABIPEME), OCD course, history of medication use and psychiatric disorders familial history[50]; the structured clinical interview for axis I diagnosis of *DSM-IV*[51]; the structured clinical interview for axis I diagnosis of *DSM-IV* adapted for impulse control disorders[52]; the Y-BOCS[53]; the DY-BOCS (constituted by 6 symptoms dimensions: aggression, sexual/religious, symmetry/ordering/arrangement, contamination/washing, hoarding and miscellaneous. Each dimension score varies from 0 to 15, and total score, from 0 to 30.[17] For the purpose of this study, Miscellaneous Dimension results will not be shown, due to its heterogeneous composition; Beck Depression[54] and Anxiety[55] inventories.

Five milliliters of human blood were collected without anticoagulant from all patients and healthy controls. Serum was immediately separated within 30 min by centrifuging at 4.000 X g for 10 min at 4° C. The supernatant was stored at -80° C until analyzed. For BDNF measurement, a commercially available BDNF immunoassay enzyme-linked immunosorbent assay kit (Chemikine by Chemicon, Temecula, California) was used according to the manufacturer's instructions. Briefly, a 96-well plate coated with antibody generated against BDNF was incubated for 24 hours with the samples diluted 1:2 in sample diluents. The standard curve concentrations used for the ELISA's kit were 5,000 pg/mL, 2,500 pg/mL, 1,250 pg/mL, 625 pg/mL, 312 pg/mL, 156 pg/mL, and 78 pg/mL of BDNF. The wells were then washed four times with wash buffer and incubated with monoclonal rabbit anti-BDNF diluted 1:1,000 with sample diluents at room temperature for 3 hours. After washing, a second incubation with anti-rabbit antibody conjugated with peroxidase diluted 1:1,000 for 1 hour at

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

room temperature was carried out. After the addition of streptavidin, substrate and stop solution, the amount of BDNF was determined (absorbance at 450 nm). The standard curve and serum samples were assayed in duplicate and demonstrated a direct relationship between optical density and BDNF concentrations. All samples were assayed in the same experiment. The final BDNF levels are expressed as pg/ug of protein. The coefficient of variation between duplicates of samples and standards was <5%. Total protein was measured by the Lowry's method using bovine serum albumin (BSA) as a standard. The blood withdraw and the BDNF measurement were performed at the HCPA.

The study was approved by the two hospital's ethics committees under protocols 31/08 (PVMIH) and 08-609 (HCPA), and written informed consent was obtained from all participants.

Statistical analysis was performed initially by descriptive methods. Continuous and symmetric variables were described by means and standard error of the mean (SE) (SE was used instead of standard deviation, because it considers the sample size. The SE falls as the sample size increases, as the extent of chance variation is reduced—this idea underlies the sample size calculation); continuous and asymmetric variables, by medians and minimum–maximum observed values (min-max); categorical variables, by absolute (n) and relative values (%). Shapiro-Wilk test was proceeded to control normal distribution. To compare the 2 groups, the Student's *t* test was used for means and Mann-Whitney U test for medians. To compare means of plasma BDNF levels between 3 or more categories of clinical features, analysis of variance (ANOVA) was used, with a post-hoc Tukey test, if necessary. Associations between categorical variables were analyzed by the Yates chi-square or by the Pearson chi-square, Pearson correlation test (BDNF levels x continuous symmetric variables) and Spearman correlation test (BDNF levels x continuous non-symmetric or ordinal variables). The chosen level of significance was 5%. Data analysis was performed through the Statistical Package for the Social Sciences for Windows (15.0, SPSS Inc., Chicago, Illinois).

RESULTS

The comparison of the sociodemographic data and plasma BDNF levels between OCD patients and healthy controls are presented on Table 1 and Figure 1. The body mass index (BMI) was the only variable with statistical significance, showing a lower value for OCD patients (P=.042). As can be seen, serum BDNF levels were significantly reduced in patients when compared to the control group (t= -3.92; P<.001).

According to ABIPEME, 1(4%) of the patients was classified in class A, seven (28%) in class B, 16 (64%) in class C and 1 (4%) in class D. Twenty-four (96%) OCD patients were Caucasian. Seven (28%) were working, six (24%) were receiving social security, four (16%) were unemployed, four (16%) were students and four (16%) were homemakers. Eighteen (72%) of the OCD patients have already used SSRI in the past. Table 2 presents clinical descriptive features of the OCD patients.

The main *DSM-IV* Axis I lifetime psychiatric comorbidities were major depression (n=16, 64%); any of the other anxiety disorders (n=11, 44%) [six (24%) with posttraumatic stress disorder, six (24%) with panic disorder, five (20%) with social anxiety, four (16%) with generalized anxiety disorder, and two (8%) with agoraphobia]; two (8%) with skin picking, and one (4%) with body dysmorphic disorder. There were no patients with dysthymia, bipolar disorders, schizophrenia or psychotic features, somatoform, eating or tic disorders.

The analysis of the categorical variables possible influences on plasma BDNF levels in OCD patients are described on Table 3, where it can be observed that the presence of the sex/religion DY-BOCS dimension, the chronic course of the OC symptoms and the comorbidity with lifetime major depression and social anxiety are associated to higher levels of plasma BDNF levels, when compared to OCD patients without those features. Also, OCD patients with previous SSRI treatment (n=18; 72%) seems to have higher levels of BDNF (0.53+0.045) when compared to drug-naïve patients (n=7, 28%) (0.33+0.023) (t= -3.93; P=.001).

Otherwise, the analyses of the influences of the continuous variables on OCD patients' plasma BDNF levels are presented at Table 4. The severity of the DY-BOCS aggression and of the sex/religion dimensions, were directly correlated to the BDNF levels: the aggression dimension moderately, and the sex/religion, strongly correlated. When using the Y-BOCS, only the severity of the compulsions score had a statistical trend to be directly correlated to the BDNF levels.

The plasma BDNF levels are reduced in unmedicated OCD patients when compared to healthy controls. The unmedicated OCD patients with the presence of sex/religion OCS dimension according to the DY-BOCS, with chronic course of OCS

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

and the presence of lifetime major depression and social anxiety presented higher levels than OCD patients without those features. The severity of aggression and sex/religion OCS dimension according to the DY-BOCS presented direct (moderate and strong, respectively) correlation with plasma BDNF levels in this sample. According to the Y-BOCS, there was only a statistical trend to the compulsions score to be directly correlated to the BDNF levels. There was no correlation of the BDNF levels and severity of depression or anxiety according to the Beck's inventories. The number of axis I psychiatric comorbidities had also no association with BDNF levels.

DISCUSSION

To our knowledge, this is the first study evaluating the peripheral BDNF levels in unmedicated OCD patients with a dimensional approach of OCS.

Comparing OCD Patients with Controls

We detected a significant decrease in plasma BDNF levels compared to controls. Maina and colleagues[18] also found reduced levels of BDNF in drug naïve OCD patients, but found no association with clinical aspects. As we found similar plasma BDNF results of Maina and colleagues'[25], some clinical aspects seem not to be confounding variables. For example, their sample was ~40% female patients, while ours had ~85% of females. Trajkovska and colleagues,[56] analyzing 206 healthy subjects, found that female gender is associated with higher whole blood BDNF concentrations. Another aspect could be the current age, since our OCD patients were also older (44.1+14.3 x 37.7+12.2) than Maina and colleagues.[25] Trajkovska and colleagues[56] relates that age was not associated to BDNF levels.

BMI was higher for controls in our sample, what could have lowered the BDNF levels in that group, approximating the values to the OCD patients' results, since lower BDNF levels seems to be associated to overweight and obesity.[57,58] The mean number of studied years (educational level), the marital status and the occupational functioning were similar to the Maina and colleagues'[25] OCD group. The fact that our OCD patients were not all drug-naïve, but unmedicated for at least 60 days, could explain the higher plasma BDNF levels in our sample (0.47x0.37, respectively), since plasma levels of BDNF seems to improve with selective serotonin reuptake inhibitor (SSRI) treatment not only in OCD patients[59] but also in depressed ones.[60,61] Although our sample was constituted by unmedicated patients and 72% of them have been, at least once, medicated with an SSRI, the plasma BDNF levels were still lower for the patients when compared to controls.

ANALYZING CLINICAL FEATURES AND DIMENSIONAL OCS

Comparing the mean plasma levels of BDNF between the DY-BOCS dimensions, we found that the sex/religion dimension had higher lev-

TABLE 1.
Comparison of the Sociodemographic Data Between OCD Patients and Controls

	OCD Group (n=25)	Control Group (n=25)	Statistical Test	*P*
Male gender	4 (16%)	5 (20%)	χ^2_{Yates}=0.14	1.00
Marital status				
Single	13 (52%)	13 (52%)	$\chi^2_{Pearson}$=2.18	.34
Married/stable union	10 (40%)	12 (48%)		
Separated/Divorced	2 (8%)	0 (0%)		
	Mean (SE)	**Mean (SE)**		
Age (years)	44.1 (2.82)	37.44(3.09)	*t*=1.58	.12
Years of education	12.1 (0.74)	12.4 (0.83)	*t*=-0.25	.80
Body Mass Index (kg/m^2)	23.5 (0.7)	26.3 (1.14)	*t*=-2.09	.042

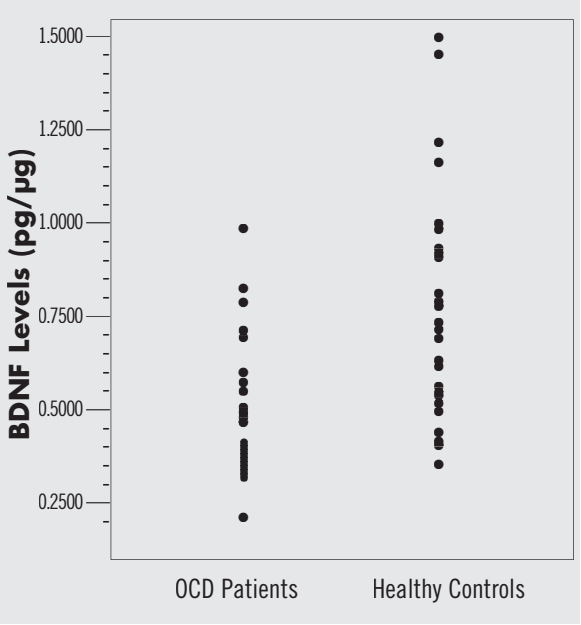
OCD=obsessive-compulsive disorder; tStudent=independent Student t test.

dos Santos IM, Ciulla L, Braga D, Ceresér KM, Gama CS, Kapczinski F, Ferrão YA. *CNS Spectr*. 2011.

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

els of BDNF. One explanation could be the fact that this dimension (which is based on "shameful thoughts") was identified by some authors as one of the most severe[62-64] and non-respondent to conventional OCD treatments.[16] This specific characteristic of the dimension could have led these patients to receive more frequently higher doses of SSRI in the past. Of the 19 patients with sex/religion dimension, 17 (89.5%) have already used an SSRI in the past versus 4 (66.7%) of the patients without sex/religion dimension (χ^2 Yates=0.48; *P*=.49). This result shows that there is no association between having sex/religion dimension and have been medicated with an SSRI. But when analyzed on a continuous way, the dimension mean (SD) score of those whom have used an SSRI was 9.90 (4.72) versus 4.54 (3.75) of those whom have never used any medication before (*t*= -3.04, *P*=.006). This means that the more severe the sex/religion dimension, higher the percentage of patients whom used SSRI before, which could have increased the serum BDNF levels in those sub-group of OCD patients.[59-61] Notwithstanding the exposure to an SSRI sometime in the past (perhaps years in the past) affecting current serum levels of BDNF could be considered as mere speculation, future works may verify it.

FIGURE 1.
Scatter plot showing serum BDNF mean (SE) levels (pg/µg) in healthy controls (0.747 [0.060]) and unmedicated obsessive-compulsive patients (0.470 [0.038]) (*t*=-3.92; *P*<.001)



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Another explanation for that is the fact that sex/religion OCS do not share the same neurobiology or neurocircuitry of the other dimensions, since some authors consider sex/religion dimension as "taboo thoughts" or "taboo symptoms",[65,66] suggesting that this dimension is predominantly based on cognitive processes (more obsessive than compulsive), which means that moral, ethical and cultural aspects may be involved, affecting specific and diverse brain structures when compared to symmetry, ordering, arrangement, contamination, washing/cleaning, and hoarding dimensions. Some functional magnetic resonance imaging studies[18-23] demonstrated that social values, social adaptation and moral behavior emerge from coactivation of stable abstract social conceptual representations in the superior-anterior temporal lobe, and context-dependent moral feelings encoded in fronto-mesolimbic regions, especially the anterior-medial prefrontal cortex,[22,23] which may also be involved in the sex/religion dimension neurocircuitry, as well as the classical fronto-striato-thalamocortical circuitries.[24] Unfortunately, no neuroimaging study with dimensional approach was conducted specifically to sexual or religious symptoms content in OCD patients.

Total scores of Y-BOCS and DY-BOCS were not correlated to the plasma BDNF levels, but the severity of OCS dimensions according do DY-BOCS, showed statistical significance to sex/religion and aggression dimensions. This analysis corroborates the above discussed, since aggression dimension is also classified into the "taboo thoughts."[65] As in sex/religion dimension, aggression dimension is predominantly obsessive and may share similar neurocircuitry.

Contrary to what was expected, higher plasma levels of BDNF were associated to some OCD clinical features, especially chronic course and comorbid major depression and social anxiety. These conditions also turns OCD more severe and may have been responsible for a more frequent prior use of SSRI, resulting in a higher level of BDNF levels when compared with those patients without these features. It could be expected that

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OCD with comorbid depression would have much lower BDNF levels, since both disorders independently have shown it in some studies,[25,60,61] but the opposite have occurred. Unfortunately, serum BDNF levels have not yet been assessed in patients with social anxiety. It was not possible to evaluate comorbid tics because there was no patient with this diagnosis. It was expected that early onset of OCD and/or longer periods of time without adequate treatment could show lower levels of BDNF, but it was not found in this study. It could be due the small sample size or due to a memory bias in the data collection, as the information was retrospectively collected. Longitudinal studies are

TABLE 2.
Clinical Descriptive Aspects of Obsessive-Compulsive Patients Group

	n	%
Dimensional Yale-Brown Obsessive-Compulsive Scale dimensions presence		
Agression	22	88
Sex/religion	19	76
Symmetry, ordering, arrangement	24	96
Contamination, washing/cleaning	24	96
Hoarding	20	80
Chronic Course	16	64
Symptom onset		
Abrupt (<3 months)	6	24
Intermediary	5	20
Insidious (>3 months)	14	56
	Mean	**SE**
Obsessive-compulsive symptoms age at onset (years)	14.6	2.06
Obsessive-compulsive disorder age at onset of the treatment (years)	39.9	3.22
Period of time without treatment (years)	25.9	3.06
Beck Depression Inventory score	20.4	2.05
Beck Anxiety Inventory score	18.4	1.72
Yale-Brown Obsessive-Compulsive Scale		
Total score	27.8	1.40
Obsessions score	13.7	0.84
Compulsions score	14.1	0.73
Dimensional Yale-Brown Obsessive-Compulsive Scale		
Current total score	23.6	0.85
Worse-ever total score	25.0	0.85
	Median	**(Min.-Max.)**
Dimensional Yale-Brown Obsessive-Compulsive Scale		
Agression dimension score	9	(0-15)
Sex/Religion dimension score	6	(0-15)
Symmetry, ordering, arrangement dimension score	10	(0-15)
Contamination, washing/cleaning dimension score	11	(0-15)
Hoarding dimension score	5	(0-12)
Number of *DSM-IV* Axis I psychiatric comorbidities	2	(0-5)

Min.=minimum; Max.=maximum.

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https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

TABLE 3.
Analysis/Comparison of the Plasma BDNF Levels According to Categorical Clinical Variables of OCD Patients

	BDNF (pg/ug)		Statistical Test	*P*
	Mean	SE		
Gender				
Male (n=4)	0.46	0.051	*t*= -0.11	.911
Female (n=21)	0.47	0.044		
Dimensional Yale-Brown Obsessive-Compulsive Scale				
- Agression	0.48	0.042	*t*=0.76	.456
Yes (n=22)	0.39	0.036		
No (n=3)				
- Sex/Religion	0.51	0.014	*t*= -3.52	.002
Yes (n=19)	0.34	0.046		
No (n=6)				
- Symmetry/Ordering/Arrangement	0.48	0.039	*	*
Yes (n=24)	0.33	-		
No (n=1)				
- Contamination/washing	0.48	0.038	*	*
Yes (n=24)	0.30	-		
No (n=1)				
- Hoarding	0.49	0.046	*t*= -1.42	.172
Yes (n=20)	0.40	0.036		
No (n=5)				
Course				
Chronic (n=16)	0.50	0.032	*t*=2.46	.022
Wax/waning (n=9)	0.35	0.022		
Symptoms onset				
Abrupt (<3 months) (n=6)	0.43	0.038		
Intermediary (n=5)	0.33	0.006	F=2.21	.135
Insidious (>3 months) (n=14)	0.52	0.040		
Main psychiatric comorbidities				
Major depression				
Yes (n=16)	0.53	0.040	*t*=2.62	.016
No (n=9)	0.38	0.012		
Posttraumatic stress disorder				
Yes (n=6)	0.53	0.046	*t*=0.61	.550
No (n=19)	0.48	0.034		
Panic disorder				
Yes (n=6)	0.57	0.046	*t*=1.27	.220
No (n=19)	0.46	0.034		
Social anxiety				
Yes (n=5)	0.65	0.036	*t*=2.33	.030
No (n=20)	0.45	0.034		
Generalized anxiety disorder				
Yes (n=4)	0.47	0.038	*t*= -0.25	.810
No (n=21)	0.50	0.038		

* For these variables it was not possible to perform statistical analysis due to small sample size.

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https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

expected to find more trustable results.

Some limitations of the current study should be mentioned. First, differently from Maina and colleagues,[25] the patients were not all drug-naïve, but unmedicated for >60 days. The findings are dependent on small samples that are not likely to be representative of larger samples of OCD subjects (eg, comparing 6 patients without sex/religion symptoms to 19 with these symptoms, and 5 patients with a history of social anxiety disorder to 20 without this history) which could have led to chance findings, peculiar to the particular patients included in this study. Nevertheless, our results were similar to Maina and colleagues,[25] especially when compared to healthy controls. Although the small sample of this study, the statistical power of comparison between groups of the BDNF means was 90.4%, according to the obtained results. The advantage of unmedicated patients' strategy versus drug-naïve is that it resembles the reality of psychiatric clinics and do not exclude the recruitment of patients with more severe symptomatology. Second, the familial history of OCD was not collected, and may be an important aspect to determine the phenotypical expression of BDNF. We suggest that future studies include direct family members interviews to check OCD occurrence. Third, it was not possible to genotype single-nucleotide polymorphisms of BDNF in specific brain structures (as hippocampus, for example), which could evince the nature of protective variation in the BDNF locus and the signaling pathways

TABLE 4.
Pearson Correlations of Plasma BDNF Levels and Continuous Clinical Variables Presented by OCD Patients

	BDNF	
	$r_{Pearson}$	*P*
Age (years)	0.057	.785
Body Mass Index	-0.113	.589
Years of education	0.230	.269
Yale-Brown Obsessive-Compulsive Scale		
Total score	0.269	.194
Obsessions score	0.105	.618
Compulsions score	0.391	.053
Dimensional Yale-Brown Obsessive-Compulsive Scale		
Total Score	0.035	.870
Obsessive-compulsive symptoms age at onset (years)	0.258	.224
Period of time without treatment (years)	- 0.167	.446
Beck Depression Inventory score	0.095	.659
Beck Anxiety Inventory score	- 0.108	.624
	$r_{Spearman}$	*P*
Dimensional Yale-Brown Obsessive-Compulsive Scale		
Agression dimension score	0.415	0.039
Sex/religion dimension score	0.654	<0.001
Symmetry, ordering, arrangement dimension score	0.194	0.354
Contamination, washing/cleaning dimension score	- 0.083	0.693
Hoarding dimension score	0.076	0.718
Number of *DSM-IV* Axis I psychiatric comorbidities	0.234	0.294

BDNF=brain derived neurotrophic factor.

dos Santos IM, Ciulla L, Braga D, et al. *CNS Spectr.* 2011.

https://doi.org/10.1017/S1092852912000363 Published online by Cambridge University Press

affected by it. Recent work, which needs to be replicated, suggests that the Val66Met polymorphism impacts intracellular trafficking and activity-dependent secretion of BDNF, especially serotonin transmission.[44-48]

CONCLUSION

Our findings confirms that serum BDNF levels are decreased in OCD patients when compared to healthy controls and, for the first time, explored the clinical dimensional approach with an adequate instrument. Sexual and religious content of symptoms and aggression and sex/religion dimensions severity should be better explored, since these specific OCS dimensions could be based on neurocircuits diverse from those of the other OCS dimensions. Confirming that each OC dimension has its own neurobiology could reinforce the heterogeneity of the disorder. The multiple symptoms presentation (one patient having more than one dimension), otherwise, may represent a difficulty to better investigate the exact neurobiology of OCS dimensions. As an exploratory study, our results should be described as a fishing expedition, looking for interesting data that could lead to testable hypotheses for future research.

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