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Title: Obsessive beliefs in first-degree relatives of probands with Obsessive-Compulsive Disorder: is the cognitive vulnerability in relatives specific to OCD?

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Abstract

Background: Specific dysfunctional beliefs have been identified as candidate endophenotypes for Obsessive-Compulsive Disorder (OCD). Rector et al. (2009) investigated cognitive vulnerability for OCD and their results support both the notion of familial-based origin of obsessive beliefs, and the hypothesis that inflated responsibility/overestimation of threat, could represent candidate endophenotypes for OCD.

Aims: The primary aim of this study was to replicate previous findings of a familial cognitive vulnerability for OCD. The secondary purpose was to test the hypothesis that obsessive beliefs of patients with OCD and those of their first-degree relatives (FDRs) are correlated, supporting dysfunctional beliefs as candidate endophenotypes for OCD.

Method: 65 patients with DSM-IV-TR (SCID-I) OCD were included together with one healthy FDR. 77 non-affected FDRs of patients with Bipolar Disorder were enrolled as a control group. Obsessive beliefs were measured with the OBQ-44.

Results: First-degree relatives of subjects with OCD scored significantly higher than controls on the total score and on the domain tapping inflated responsibility and overestimation of threat. There was no significant correlation between each obsessive belief in patients with OCD and their non-affected FDRs.

Conclusions: Our study provides evidence of a specific cognitive vulnerability for OCD in FDRs of probands with OCD.

Key Words: Obsessive-compulsive disorder; obsessive beliefs; cognitive vulnerability; inflated responsibility; overestimation of threat; perfectionism; endophenotypes

1. Introduction

Obsessive-compulsive disorder (OCD) is characterized by recurrent unwanted thoughts, images or urges (obsessions) that provoke anxiety, as well as efforts to resist or neutralize the obsessional anxiety through avoidance behaviours and deliberate overt or covert actions (i.e., compulsive rituals; APA, 2013).

The causes of obsessions are unclear, because it is generally acknowledged that “normal” intrusions content is similar to obsessional content. These “normal” although unwanted and unacceptable intrusive thoughts occur in at least 90% of the general population (Abramowitz et al., 2007; Clark et al., 2014; Rachman, 1997; Rachman & De Silva, 1978; Salkovskis and Harrison, 1984; Taylor et al., 2010). While in healthy individuals these symptoms are ignored, they develop to obsessions in patients with OCD and cause impairment in functioning.

According to the cognitive model of OCD (Salkovskis, 1985; Rachman, 1997, 1998; Salkovskis et al., 1999; Frost and Steketee, 2002; Clark, 2004), obsessive-compulsive symptoms arise from particular kinds of dysfunctional beliefs (cognitive vulnerability); subjects who interpret intrusive thoughts through dysfunctional beliefs are at risk for the disorder, with strength of belief influencing severity of obsessive-compulsive symptoms. These beliefs lead some people to appraise otherwise benign intrusive thoughts as harmful and thereby lay the groundwork for OCD. Several dysfunctional beliefs have been reported to be relevant for OCD, concerning appraisal of responsibility (Salkovskis, 1985; Steketee et al., 1998; Arntz et al., 2007), meaning and importance of control of thoughts, (Wells, 1997; Rachman, 1997), perfectionism (Frost and Steketee, 1997), and intolerance of uncertainty (Carr, 1974).

In 1997 the Obsessive-Compulsive Cognitions Working Group (OCCWG) started the development of a questionnaire to assess the beliefs and appraisals considered pivotal in the pathogenesis of OCD (OCCWG, 1997, 2001, 2003). The first final version of the Obsessive Beliefs Questionnaire is an 87-item questionnaire (OBQ-87), entailing six domains of dysfunctional beliefs: inflated responsibility, overestimation of threat, perfectionism, intolerance of uncertainty, overimportance of thoughts, and importance of controlling one's thoughts. However, high correlations between the OBQ-87 sub-scales and factor analysis of this instrument led the OCCWG to develop in 2005 a 44 item version of the questionnaire with sounder psychometric properties, the OBQ-44. Three factors were retained: a) inflated responsibility and overestimation of threat (OBQ-R/T): exaggerated estimates of the probability and consequences of negative events; belief to be personally responsible for causing or preventing any disastrous consequences associated with obsessional thoughts (*even if harm is very unlikely, I should try to prevent it at any cost*); b) perfectionism and intolerance of uncertainty (OBQ-P/U): inability to tolerate mistakes or imperfection, and belief that it is possible to be completely perfect (*In order to be a worthwhile person, I must be perfect at everything I do*); and c) overimportance of thoughts and need to control thoughts (OBQ-I/C): the mere presence of intrusive thoughts means that they are extremely significant. Control of thoughts involves the belief that complete control over one's thoughts is not only possible but also necessary (*I should be able to rid my mind of unwanted thoughts*)(OCCWG, 2005).

Dysfunctional obsessive beliefs as measured by the OBQ are associated with obsessive-compulsive symptoms both in community and clinical samples, with partial evidence of a specificity of some dysfunctional beliefs to OCD (Tolin et al., 2003; Anholt et al., 2004; Faull et al., 2004; OCCWG, 2005; Tolin et al., 2006; Tolin et al., 2008; Wu and Carter, 2008;

Clark, 2004; Frost & Steketee, 2002). Experimental manipulations of responsibility, e.g., affect OC symptoms in OCD patients (Lopatka & Rachman, 1995; Shafran, 1997).

Some studies found that each OCD symptom dimension is predicted by one or more dysfunctional domains/obsessive beliefs (Wheaton et al., 2010). In addition, longitudinal studies showed that obsessive beliefs (OBQ scores) predict the onset of obsessive-compulsive symptoms (Abramowitz et al., 2006; Abramowitz et al., 2007; Coles et al., 2008). Moreover we know that in psychotherapy, through cognitive restructuring it is possible to reduce the strength of dysfunctional beliefs, and this modification leads to a reduction of obsessive-compulsive symptoms (Woody, Whittal, & McLean, 2011).

Taylor and Jang (2011), in a community sample of monozygotic and dizygotic twins, found that dysfunctional beliefs cause obsessive-compulsive symptoms, but also that such beliefs accounted for only a fraction of the phenotypic variance in obsessive-compulsive symptoms, suggesting that aetiological factors other than dysfunctional beliefs need to be taken into consideration. On the whole, dysfunctional beliefs appear at least partially to confer a cognitive vulnerability to the development of obsessive-compulsive symptoms (Abramowitz et al. 2006; Frost and Steketee, 2002; Mancini and Barcaccia, 2014; Salkovskis et al., 1999), although there is no incontrovertible evidence that dysfunctional beliefs as measured by OBQ are specifically and exclusively associated to OCD. Cogle & Lee (2014), e.g., conclude their reconsideration of the cognitive models in OCD, stating that dysfunctional beliefs are relevant for OCD as possible maintenance factors, but they also represent non-specific cognitive vulnerabilities observed in other anxiety problems such as GAD.

Along these lines, it is to be acknowledged that the literature on the relations between dysfunctional beliefs and OCD is not unambiguous. For instance, some research has shown that the associations between beliefs and OCD are attenuated when depression is controlled

for (e.g., Tolin, Worhunsky, & Maltby, 2006) and that the OBQ-44 beliefs domains may not be specific risk factors for OCD relative to other disorders (e.g., Gentes & Ruscio, 2011; Viar, Bilsky, Armstrong, & Olatunji, 2011).

Nevertheless, a large body of literature is now available on the genesis of the cognitive vulnerability to OCD, suggesting that, as a result of prior experience, the individual develops particular dysfunctional beliefs. Specific learning experiences in childhood may give rise to specific dysfunctional beliefs. We shall present here beliefs concerning 1) perfectionism 2) inflated responsibility. Regarding the role of perfectionism, a family atmosphere characterized by parental over-control and criticism, very high expectations and performance standards, and the influence of perfectionistic parents modelling perfectionistic attitudes and behaviours, can contribute to the development of perfectionistic beliefs in offspring (Waters & Barrett, 2000; van Noppen & Steketee, 2009).

Regarding the role of responsibility, Salkovskis et al. (1999) identified early familial experiences contributing to the development of dysfunctional beliefs in children: 1) significant figures promoting an early developed sense of responsibility during childhood, 2) strict codes of conduct, or 3) being shielded from responsibility during childhood and subsequently feeling incompetent to cope with risk/danger. These dysfunctional beliefs may interact later on with a significant life event, particularly those triggering sense of responsibility and the idea of causing harm, giving rise to obsessive-compulsive symptoms.

Perfectionism and inflated responsibility can be learned through the parental rearing style: a child exposed to systematic and continuous criticism experiences high levels of distress and, fearing future criticism, may plan strategies such as checking repeatedly, in order to prevent being newly criticised and reproached. Obsessive beliefs can develop in response to criticism

and compulsive behaviours can work as strategies to prevent future criticism (Pace et al., 2011).

The mediating role of inflated responsibility between childhood experiences and obsessive-compulsive symptoms has been empirically highlighted (Adams, 2012; Smári et al. 2010). Childhood experiences of responsibility correlate with the dimension of responsibility in the OBQ and turn out to be the most powerful predictor of OBQ-R (Responsibility subscale) (Careau et al., 2012). Thus, some dysfunctional beliefs specific to OCD, may be learned through the family environment, where parents set very high performance standards and stably criticise and reproach children.

These maladaptive beliefs may interact later during life with a significant stressor or life event (for example the birth of a child) triggering the onset of OCD or its relapse (Abramowitz, 2006; Salkovskis et al., 1999). Abramowitz et al. (2006), e.g., longitudinally evaluated the influence of obsessive cognitions on OCD symptoms in a non-clinical sample of 75 expecting parents of their first child, administering the OBQ before the birth and after childbirth. The study confirmed that obsessive dysfunctional beliefs predict the development of OCD symptoms at postpartum in checking, washing, and in obsessing, also after controlling for trait anxiety.

However, it is also possible that these cognitive vulnerability factors are, at least partially, genetically transmitted. Taylor and colleagues indicated that dysfunctional beliefs are significantly heritable in a community sample of twin pairs, with genetic variance accounting for 32% to 40% of the variance in OBQ scores (Taylor et al., 2010). It may be that cognitive-behavioural models overemphasize environmental variables, particularly shared environment, to the neglect of genetic factors, while contemporary biological models overemphasize the role of hardwired (inherited) dysregulations in neurobiology circuitry, to the neglect of the

role of environmental factors (Taylor, 2011). Nevertheless, little research examined familial transmission of cognitive dysfunctional beliefs in clinical samples.

Dysfunctional beliefs have been proposed as candidate endophenotypes for OCD (Taylor, 2012). Endophenotypes are conceptualized as measurable intermediary variables lying somewhere in a causal chain linking genes to a given disorder, but the concept has been expanded to include endophenotypes that are intermediary between environmental aetiologic factors and disorders. Endophenotypes could facilitate research into the aetiology of complex disorders such as OCD. According to the Author it is now well established that specific and rigidly held dysfunctional beliefs could be promising candidate endophenotypes, particularly if considering research using the OBQ (Taylor, 2012). As a matter of fact dysfunctional beliefs as measured by the OBQ fulfil several criteria to be candidate endophenotypes (as they are currently conceptualized)(Cannon and Keller, 2006; Gottesman and Gould 2003; Kendler and Neale 2010) for OCD. In fact 1) scores on the OBQ are correlated with the severity of OCD symptoms and are higher in people with OCD compared to clinical and non-clinical controls. 2) Dysfunctional beliefs appear to be causes rather than consequences of OCD symptoms. 3) Twin studies show that dysfunctional beliefs and OCD symptoms arise, in part, from a shared set of environmental and genetic influences. An endophenotype should co-segregate with the disorder; for dysfunctional beliefs to be candidate endophenotypes for OCD, first-degree relatives (FDRs) of probands with OCD should have greater scores on the OBQ scales than controls (Taylor, 2012).

To our knowledge, only the study by Rector and colleagues (2009) investigated cognitive vulnerability for OCD by examining obsessive beliefs in FDRs of probands with OCD: non-affected relatives scored significantly higher than controls on the OBQ domains tapping inflated responsibility and overestimation of threat. Results of this study support the notion of

the origin of obsessive beliefs within a familial-based developmental context and the hypothesis that obsessive beliefs, specifically those of inflated responsibility/overestimation of threat, could represent a candidate endophenotype for OCD.

Rector's study, however, included a small sample consisting of 24 FDRs of probands with OCD. The Authors also noted that their design could be enhanced by including a group of FDRs of control probands for comparison purposes.

Given that the OBQ domain of inflated responsibility/overestimation of threat could be a candidate endophenotype for OCD, we wanted to investigate whether there is a correlation between scores on the OBQ-R/T in patients with OCD and those in their non-affected FDRs. Such a correlation would add strength to the notion of inflated responsibility/overestimation of threat as an endophenotype for OCD.

Thus, the primary aim of this study was to replicate previous findings (Rector et al., 2009) of a familial cognitive vulnerability for OCD in a sample of patients with OCD and their non-affected FDRs using the Obsessive Beliefs Questionnaire (OBQ-44). As a control group, we included a sample of FDRs of probands with Bipolar Disorder (BD). We hypothesized that the obsessive belief scores (OBQ total score) of non-affected relatives of probands with OCD would be significantly higher than those of FDRs of probands with BD. At the sub-factor level, we hypothesized that the same findings would be likely found specifically for the inflated responsibility/overestimation of threat dimension. We also wanted to test the hypothesis that obsessive beliefs of patients with OCD and those of their non-affected first-degree relatives are correlated, supporting that some belief domains could be endophenotypes for OCD.

2. Methods

2.1 Participants

This study enrolled four different groups: 1) Proband with a principal diagnosis of Obsessive-Compulsive Disorder; 2) their non-affected first-degree relatives; 3) probands with a principal diagnosis of Bipolar Disorder; and 4) a control group of their non-affected first-degree relatives. Participants were recruited consecutively from December 2010 to December 2012 among subjects referred to the Psychiatric Section of the Department of Neuroscience, University of Turin (Italy); this is a tertiary referral centre located within the University Hospital and specialized in the treatment of patients with OCD and Mood Disorders.

The aims of the study as well as study procedures were thoroughly explained to potential participants who gave written consent before participation. The study design was approved by the local ethics committee.

2.1.1 Proband with OCD: To be enrolled in the study, probands fulfilled the following inclusion criteria: a) a DSM-IV-TR principal diagnosis of Obsessive-Compulsive Disorder according to the Structured Clinical Interview for Axis I Disorders (SCID-I/P)(First et al., 1996). b) At least 18 years of age. c) A minimum total score of 16 on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)(this cut-off is conventionally considered to identify clinically meaningful OCD)(Goodman et al., 1989a,b). d) OCD duration exceeding 1 year. d) Written informed consent before enrolment in the study. e) Willingness to have a first-degree relative participating. The exclusion criteria included comorbid schizophrenia, bipolar affective disorder, severe personality disorders (such as borderline or antisocial) or alcohol- or

drug addiction, evidence of metabolic or neurological disease, as identified by history and/or laboratory screening, pregnancy or having just gave birth.

Since hoarding is currently better conceptualized as a separate disorder when not secondary to other OCD symptom dimensions (Rachman et al., 2009; American Psychiatric Association, 2013), we deliberately excluded from the present study subjects who had hoarding symptoms as the chief or only concerns.

2.1.2 First-degree relatives of probands with OCD: for each patient, one first-degree relative was recruited. To be enrolled in the study, FDRs fulfilled the following inclusion criteria: a) absence of a current or past diagnosis of mental disorder; b) at least 18 years of age; c) written informed consent before enrolment in the study. They were interviewed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) Axis I Disorders, Non Patient version (SCID-NP) (First et al., 2001) in order to exclude the presence of any current or lifetime mental disorders.

2.1.3 Control group (probands with Bipolar Disorder and their FDRs): A control group of non-affected FDRs of patients with Bipolar Disorder was enrolled. We chose this control group for practical considerations. Patients with a principal diagnosis of BD I or II (SCID-I, DSM-IV-TR) were selected from referrals to our Unit and asked for participation in the study. We deliberately excluded patients with comorbid OCD. Upon acceptance, a first-degree relative of each patient with BD was identified. To be enrolled in the study, FDRs fulfilled the same criteria of FDRs of probands with OCD.

2.2 Assessments and procedures

Data were obtained from each patient by a semi-structured interview with a format that covered the following areas: a) socio-demographic data (age, gender, marital status, years of education and occupational status); b) diagnosis: diagnoses (current and lifetime) were performed by clinicians with at least four years of postgraduate clinical experience by means of the Structured Clinical Interview for DSM Axis I Disorders (SCID-I); c) clinical data (such as age at onset, type of onset, duration of illness, etc. for OCD; type of BD, age at onset of first affective episode, total number of affective episodes, duration of illness for BD). In addition, the following rating scales were included in the assessment, depending on the principal diagnosis: Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)(OCD patients); Young Mania Rating Scale (YMRS)(BD patients), 17-item Hamilton Depression Rating Scale (HAM-D)(both OCD and BD patients), Hamilton Anxiety Rating Scale (HAM-A)(both OCD and BD patients), and the Clinical Global Impression Scale-Severity of Illness (CGI-S)(both OCD and BD patients). Obsessive beliefs were measured in the three groups using the Obsessive Beliefs Questionnaire-44 item (OBQ-44) (OCCWG, 2005; Dorz et al., 2009).

2.2.1. Measures

The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). The Y-BOCS is a semi-structured, clinician-administered interview designed to measure symptom characteristics and severity in OCD patients (Goodman et al., 1989a, 1989b). It entails a checklist of 58 symptoms (Y-BOCS Checklist) evaluating the presence (yes/ no) of current and past symptoms and 10 items measuring the severity of obsessions and compulsions (Y-BOCS Severity). The checklist administered prior to the administration of the severity ratings is used for identifying

relevant obsessions and compulsions: obsessions are classified into 8 types (aggression, contamination, sexual, collection, religious, symmetry, somatic, other), and compulsions into 7 types (cleaning, verification, repetition, counting, ordination, collection, other). In the Y-BOCS Severity scale, five items inquire about obsessions and five about compulsions: each of the ten severity items is rated on a 5-point Likert scale ranging from 0, none, to 4, extreme. Total possible scores range from 0 to 40. The scale has high internal consistency ($\alpha=.89$), good convergent and discriminate validity, and is sensitive to change (Goodman et al., 1989a, 1989b).

The Young Mania Rating Scale (YMRS). This is an 11-item clinician-rated scale that asks about the core symptoms of mania. It has been widely used and is reported to have good validity and reliability (Young et al., 1978). The inter-rater reliability is reported to be between .84–.93 and the internal consistency to be .80 (Dew et al., 2005).

The Hamilton Depression Rating Scale (HAM-D). The HAM-D is a 17-item clinician-rated scale designed to assess the severity of depression. A total score is derived from summation of the 17 items, which vary in their scales from 1–3 to 1–5 (Hamilton, 1960). It has been widely used with good reports of validity and reliability; the inter-rater reliability is reported to be between .70–.96 and the test retest reliability to be between .65–.96 (Kobak, 2003).

The Hamilton Anxiety Rating Scale (HAM-A). The HAM-A is a 14-item clinician-rated scale designed to assess the severity of symptoms of anxiety (Hamilton, 1959). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0–56, where <17

indicates mild severity, 18–24 mild to moderate severity and 25–30 moderate to severe. Validity and reliability are reported to be good (Maier et al., 1988).

The Clinical Global Impression Scale-Severity of Illness (CGI-S). The CGI-S is a 7-point clinician-rated scale that requires the clinician to rate the severity of the patient's illness at the time of assessment, relative to the clinician's past experience with patients who have the same diagnosis. Considering total clinical experience, a patient is assessed on severity of mental illness at the time of rating 1, normal, not at all ill; 2, borderline mentally ill; 3, mildly ill; 4, moderately ill; 5, markedly ill; 6, severely ill; or 7, extremely ill (Guy, 1976).

The Obsessive Beliefs Questionnaire-44 item (OBQ-44). The OBQ-44 item is a self-report questionnaire, designed to assess three empirically derived domains of maladaptive beliefs that are implicated in the development and maintenance of obsessive-compulsive symptoms: a) Inflated Responsibility/Overestimation of Threat (R/T); b) Perfectionism/Intolerance for Uncertainty (P/U); c) Importance/Control of Thoughts (I/C). Each item of the OBQ-44 is rated on a 7-point scale ranging from 1 (disagree very much) to 7 (agree very much), with higher scores indicating greater belief strength. The OBQ-44 gives a total score (OBQ-total) and three sub-scores for each of the obsessive belief (OBQ-R/T, OBQ-P/U, OBQ-I/C). The instrument's good validity, internal consistency, and test-retest reliability are described in OCCWG (2005).

All assessments were conducted in Italian, with the Italian versions of the SCID-I (Mazzi et al., 2000) and of the rating scales (Y-BOCS, YMRS, HAM-D, HAM-A, CGI-S)(Conti, 1999). For the OBQ, we used the Italian version (Dorz et al., 2009) and we operationalized the scale using the three-factor solution (OBQ-44). Another possibility would have been to use the

OBQ-TRIP, Obsessive Beliefs Questionnaire: Threat, Responsibility, Importance and control of thoughts, Perfectionism and Intolerance of uncertainty (Moulding et al., 2011), which is a short-version (38-item), four-factor solution of the OBQ, where threat and responsibility form separate dimensions. We chose to use the three-factor solution in order to have comparable data with the literature.

2.3 Statistical analysis

Subjects' characteristics were summarized as mean and SD for continuous variables and frequency and percentage for categorical variables.

OBQ-44 mean scores across the three groups were compared with the ANOVA with Bonferroni post-hoc comparisons. Moreover, we compared mean scores of probands with OCD and their non-affected FDRs to mean scores of a community sample driven from the OCCWG validation study (OCCWG, 2005) using the one-sample t-test. Finally, correlation analyses between OBQ-44 mean scores of probands with OCD and those of their non-affected FDRs were made by Pearson correlation tests.

3. Results

Sixty-five patients with OCD and 65 non-affected FDRs were enrolled; the control group was composed of 77 FDRs of patients with BD. We excluded 5 patients with OCD, 3 because they presented with hoarding symptoms as the only symptom dimension and 2 because of a Y-BOCS total score at evaluation <16. Other 4 subjects with OCD were excluded after the initial assessment because their first-degree relative had a current or lifetime diagnosis of a mental

disorder. Among subjects with Bipolar Disorder, 6 patients had a comorbid diagnosis of OCD and were excluded from the study.

Patients with OCD had a mean age of 28.6 (± 11.2) years at intake, 37 of them (56.9%) were males, 55 (84.6%) single, only 22 (33.8%) were working at the time of enrolment. Concerning clinical characteristics of the OCD, the mean age at onset was 17.0 (± 5.3) years, the mean duration of the illness 11.5 (± 10.1) years; onset had been for the majority of patients insidious (46, 70.8%) and course of the disorder chronic (62, 95.4%). At study entry, OCD patients had a mean YBOCS total score of 26.8 (± 5.5), obsession score of 13.5 (± 2.8) and compulsion score of 13.9 (± 3.7); the mean HAM-D, HAM-A and CGI-S scores were: 11.9 (± 5.9), 11.6 (± 6.3) and 4.0 (± 1.1), respectively.

The control group of BD patients was older, with a mean age of 48.1 (± 18.5) years at intake, 32 of them (41.6%) were males, 33 only (42.9%) single, only 24 (31.2%) were working at the time of enrolment. Concerning clinical characteristics of the disorder, 46 (59.7%) subjects were diagnosed with BD type I and 31 (40.3%) with BD type II; the mean age at onset (first affective episode) was 27.5 (± 9.7) years, the mean duration of the illness 20.6 (± 14.5) years; the mean total number of affective episodes was 7.5 (± 4.5). At enrolment, BD patients had a mean YMRS total score of 9.5 (± 10.8); the mean HAM-D, HAM-A and CGI-S scores were: 11.7 (± 8.3), 8.9 (± 5.2) and 4.4 (± 1.1), respectively.

Insert table 1 about here

Table 1 reports socio-demographic characteristics of FDRs: a greater proportion of the OCD relatives are parents compared to the BD relatives (81.5% versus 41.6%).

Insert table 2 about here

Table 2 shows mean OBQ scores in patients with OCD, their FDRs and FDRs of probands with BD: probands with OCD scored significantly higher than the other groups on all domains of the OBQ scale (total score, OBQ-R/T, OBQ-P/U and OBQ-I/C). First-degree relatives of patients with OCD scored significantly higher than controls (FDRs of subjects with BD) on the total score and on the domain tapping inflated responsibility and overestimation of threat (OBQ-R/T).

Insert table 3 about here

When we compared our results with mean scores of the community control group from the OCCWG study (2005), both patients with OCD and their FDRs scored significantly higher than the control group on all domains of the OBQ scale (total score, OBQ-R/T, OBQ-P/U and OBQ-I/C)(table 3).

Insert table 4 about here

Contrary to our hypothesis, there was no significant correlation between each obsessive belief in patients with OCD and their non-affected FDRs (table 4).

4. Discussion

Our primary objective was to replicate findings of a cognitive vulnerability for OCD (Rector et al., 2009), as measured with the OBQ-44, in FDRs of probands with OCD.

Patients with OCD, as expected, had significantly greater dysfunctional beliefs as compared to controls (community norms from the original study of the OCCWG, 2005) and this was evident for the total score and all cognitive domains of the OBQ-44.

The cognitive vulnerability for OCD was evident in first-degree relatives of OCD probands only for the dysfunctional belief inflated responsibility/overestimation of threat (OBQ-R/T), while specificity was not found for the other two beliefs types. FDRs of OCD probands scored significantly higher than both controls and FDRs of bipolar probands on the OBQ total score. When examining the three dimensions of the OBQ-44, the same finding was evident for the dysfunctional belief inflated responsibility/overestimation of threat (OBQ-R/T); however, FDRs of OCD probands showed elevations on the other two sub-factors of the OBQ only compared to community controls (but not compared to FRDs of bipolar probands). A possible explanation for the lack of significant difference between the OCD and BD FDRs on the P/U domain is that self-critical perfectionism, characterized by harsh self-scrutiny and judgement, high concern about others' criticism, strive for high achievement and perfection (Dunkley & Kyparissis, 2008), has been conceptualized as a risk and maintenance factor across several disorders (Egan et al., 2011), including bipolar disorder: the cognitive style of individuals with bipolar disorder is typically characterized by perfectionism, self-criticism, and goal striving (Lam et al., 2004; Alloy et al., 2009).

This pattern of associations supports the notion of a cognitive vulnerability (as measured with the OBQ) in families of patients with OCD, suggesting that at least one of the dysfunctional beliefs could be endophenotype for OCD.

We replicated results of the only study to date that examined cognitive vulnerability in first-degree relatives of probands with OCD (Rector et al., 2009), but enrolling a larger sample of patients and relatives and using as a control group FDRs of patients suffering from another disorder (Bipolar Disorder). The inclusion of a control group composed of healthy relatives of patients affected by another disorder is useful, in our opinion, to test for the specificity of the cognitive vulnerability. As a matter of fact our data suggest non-specificity for two of the three dysfunctional beliefs (P/U and I/C), leaving only inflated responsibility and overestimation of threat to account for the significant difference on OBQ total score.

Our results provides support to the notion of familial transmission of beliefs concerning inflated responsibility and overestimation of threat: whether this elevated cognitive vulnerability is due to parental behaviour (shared environment), parent-child reciprocal interactions (which could reflect gene-environment interactions), or whether the effects are simply due to shared genetic factors, it is still argument of debate and our study does not help in answering this question.

Contrary to our hypothesis, we failed to find a correlation between OBQ scores in patients and in their non-affected relatives. However, each domain of the OBQ is composed of several items: it is possible that a shared genetic endophenotype could give rise to elevation on different items within sub-factors between patients and their FDRs. Both groups would then show higher scores (as is the case) although not highly correlated (as is the case).

Our study adds to the existing literature in suggesting that dysfunctional beliefs, in particular those involving inflated responsibility and overestimation of threat, co-segregate in families of patients with OCD. This result seems to supports the notion of dysfunctional beliefs as candidate endophenotypes for OCD.

We believe our results might also have some clinical implications. As noted by Clerkin and Teachman (2011) there is evidence that OC-relevant beliefs can be manipulated, being amenable to therapeutic interventions, thus affecting behaviours and emotions. Cognitive vulnerability to Obsessive-Compulsive Disorder might be attenuated through psycho-educational programs for patients and their family members addressing these specific cognitive beliefs. Along these lines, also prevention programs designed for parents might be developed in order to attenuate cognitive vulnerability to OCD. Prevention programs for parents might be based on two main cornerstones: 1) the identification in parents of dysfunctional beliefs regarding inflated responsibility/overestimation of threat and then their modification/attenuation, sharing the notion of their potential role in contributing to the vulnerability to obsessive-compulsive disorder. 2) The acquisition of a communicative style with the child that is based neither on criticism nor on hyper/hypo responsabilization, where explicitly or implicitly extremely high standards are not set, neither are children stably reproached/criticised. It might be worthwhile noting that those communicative styles, when encountered in the interaction between an individual already affected by OCD and the family members, largely account for the maintenance and exacerbation of the symptomatology (Saliani, Barcaccia & Mancini, 2011).

Our study has also several limitations, first of all the cross-sectional design; secondly, the operationalization of dysfunctional beliefs with a single measure. Additionally, measuring cognitive constructs only with self-report questionnaires is an important limitation in itself. Moreover, the two samples of first-degree relatives of probands presented with some differences, mainly the greater proportion of parents among the FDRs of OC patients, when compared to FDRs of BD patients. This could be a limitation of our study, considering that we hypothesized a familial (parental) transmission of the dysfunctional beliefs relevant to

obsessive-compulsive disorder. For this reason the higher levels of threat/responsibility in the FDRs of obsessive patients might also be due to the difference in the samples' composition. The sample size, moreover, does not allow us to address the question of the heterogeneity of OCD (which can confound the search for candidate endophenotypes). Finally, we did not use a non-clinical control group. We included FDRs of probands with a principal diagnosis of BD as a control group for practical reasons (having such patients available for several studies in our tertiary referral centre); we acknowledge, however, that this may be a limitation of our study. Future researches using relatives of probands with non-OCD anxiety disorders are needed as a more stringent test of specificity. Future studies could also examine cognitive vulnerability to OCD in larger independent samples, including a non-clinical control group, and using multiple measures to assess dysfunctional obsessive beliefs.

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Table 1 - Socio-demographic characteristics of first-degree relatives included

First-degree relatives of	probands with OCD (N=65)	Probands with BD (N=77)	t/ χ^2	p
Actual age (years) (Mean \pm SD)	50.0 \pm 12.6	47.7 \pm 14.5	.999	.320
Gender (males), N (%)	29 (44.6)	33 (42.9)	.044	.833
Kinship, N (%)			28.064	<.001
Parents	53 (81.5)	32 (41.6)		
Offsprings	5 (7.7)	36 (46.8)		
Siblings	7 (10.8)	9 (11.7)		

OCD=Obsessive-Compulsive Disorder; BD=Bipolar Disorder