



# “Not Just Right Experiences” as a psychological endophenotype for obsessive-compulsive disorder: Evidence from an Italian family study



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## ABSTRACT

The heart of the obsessional process may be considered the subject's underlying impression that “something is wrong” or “that something is not just as it should be”. This phenomenon, labeled “not just right experiences” (NJREs), has increasingly been receiving attention as a possible marker of obsessive-compulsive disorder (OCD). The present study sought to add to the evidence that NJREs may be a putative endophenotype of obsessional symptoms. To this aim, measures of NJREs, obsessive-compulsive (OC) symptoms and psychological distress were compared in offspring of parents with and without OC symptoms. The offspring of parents with OC symptoms (N=120) reported higher frequency and severity of NJREs compared to offspring of parents without OC symptoms (N=106). Such differences remained significant for NJREs frequency and close to significance for NJREs severity, when general distress (i.e., anxiety and depression) was controlled. The possible role of NJREs as an endophenotype for OCD is discussed in reference to Gottesman and Gould criteria and the National Institute of Mental Health RDoC initiative.

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## 1. Introduction

Obsessive-Compulsive Disorder (OCD) is a serious mental condition characterized by the presence of persistent, intrusive, and distressing obsessions or compulsions, with marked impairment in quality of life (Eisen et al., 2006; Kugler et al., 2013; Parkin, 1997). Obsessions are uncontrolled, unpleasant and unwanted thoughts, impulses or images accompanied by a feeling of urgency or catastrophe, leading to repetitive, time-consuming or ritualistic behaviors (compulsions). OCD represents one of the most incapacitating psychiatric disorders owing to its intensity, the continuous and unchanging or deteriorative course of its symptoms, and the disturbance in psychosocial functioning that they cause (Albert et al., 2010; Mancebo et al., 2008; Visser et al., 2014).

OCD is characterized by a clinical diversity reflected in a wide range of symptoms, and the clinical presentation can vary both within and across patients over time. Actually, many studies have provided strong evidence that OCD is clinically heterogeneous and that this clinical heterogeneity is likely due to etiologic heterogeneity (e.g., Abramowitz and Jacoby, 2015; Bloch et al., 2008;

McKay et al., 2004).

Behavioral genetic (twin) research shows that OCD arises from a mix of genetic and environmental factors, but much remains to be learned about the nature of these etiologic influences (e.g., Pauls et al., 2014). In particular, recent genetic studies demonstrated that OCD is associated with multiple genes, with most having a modest association with OCD, suggesting a polygenic model in which multiple genes make small, incremental contributions to the risk of developing the disorder (e.g., Taylor, 2012; Taylor and Jang, 2011; see also Stewart et al., 2013 on the null results in genome-wide association study of OCD).

Unfortunately, little is known about the predictors and moderators of response to therapies in OCD, despite extensive research on this topic (see review by Knopp et al., 2013).

Like all psychiatric disorders, gaining a complete understanding of what comprises OCD and the underlying etiological mechanisms will probably require a change in how the disorder is conceptualized. In particular, the notion of endophenotype has been proposed as a means of facilitating research into the etiology of complex and heterogeneous disorders such as OCD. Endophenotypes may be considered intermediary between etiologic factors (bottom-level) and phenotypic manifestations (top-level) of a given disorder (see Gottesman and Gould, 2003; Kendler and Neale, 2010). An endophenotype may be a variable from any of a number of levels of organization, including biochemical,

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neurophysiological, neuroanatomical, cognitive, or other variables, including those obtained from self-report measures (Cannon and Keller, 2006; Gottesman and Gould, 2003). Importantly, an endophenotype can be a risk factor for a disorder even if the person is not currently symptomatic; in addition, it should be found in unaffected family members at a higher rate than in the general population (for a broad discussion about the role of endophenotypes in psychopathology, see Hasler et al., 2004).

In the last few years, several scholars have considered the lack of a sense of satisfaction and presence of feelings of doubt as central features of obsessions and associated compulsions. In fact, the heart of the obsessional process seems the subject's underlying impression that "something is wrong". In other words, obsessions may be thought of as the perception of a mistake and/or error in certain behavioral situations (see Sica et al., 2015). Based on various empirical data, the construct of "not just right experiences" (NJREs; Coles et al., 2003) has been proposed as a candidate endophenotype for OCD (see also Miguel et al., 2005).

What evidence supports NJREs as an endophenotype? First, the cross-sectional association between NJREs and OCD or obsessive-compulsive (OC) symptoms appears robust for both in nonclinical and clinical populations (e.g., Ferrão et al., 2012; Ghisi et al., 2010; Ghisi et al., 2013; Taylor et al., 2012). In addition, Coles et al. (2012) investigated patients' reports of various factors that may have played a role in the transition from the presence of obsessions and compulsions to full-blown OCD. Increases in the strength of urges for things to feel 'just right' were commonly viewed as contributing to the onset of OCD. Importantly, associations between sensory phenomena (i.e., NJREs) and OCD were also noted in a pediatric OCD population (Lewin et al., 2015).

Second, experimental studies have demonstrated that NJREs elicited in the laboratory predicted OC symptoms. For instance, in a sample of undergraduate students, affective response to clutter (i.e., NJREs) was uniquely predictive of hand-washing duration when controlling for pre-wash anxiety (Cogle et al., 2011). Moreover, measures of incompleteness predicted urges to check following a stove checking task (Cogle et al., 2013; see also, Summers et al., 2014). Buse et al. (2014) assessed reaction times (RT) to harmonic and disharmonic chord sequences as well as their emotional appraisal in 64 healthy young adults. The participants clearly indicated that disharmonic chord sequences sounded not just right and incomplete and rated them as unpleasant, arousing, and irritating. This effect tended to be greater among participants who reported stronger general experiences of incompleteness as an underlying core dimension of OCD-like symptoms.

Third, in a one-year longitudinal study on undergraduates, NJREs predicted OC symptom variation even when looming style (a specific cognitive mechanism for anxiety, Rachman et al., 2005) was accounted for (Sica et al., 2012).

Lastly, NJREs appear specific to OCD. In several studies, NJREs were significantly more strongly correlated with OC symptoms than other domains of psychopathology (e.g., social anxiety, worry, depression; Coles et al., 2003; Coles et al., 2005; Ecker and Gönner, 2008; Ghisi et al., 2010; Taylor et al., 2012). Sica et al. (2015) who found that a group of OCD patients reported higher levels of NJRE severity than groups of patients with either gambling (GD) or eating disorders (ED) recently corroborated this evidence. In the same study, while a measure of NJREs did not discriminate between OCD patients and patients with hair-pulling disorder, this last group did not have higher scores of NJREs severity than GD and ED counterparts.

It is not surprising therefore that the DSM-5 newly acknowledged NJREs as one of the "affective responses" seen in OCD (American Psychiatric Association, APA, 2013, p. 239). Despite the substantial evidence that indicate NJREs as a possible mechanism

involved in OCD, no published studies have investigated whether NJREs are present in relatives of individuals with OCD or OC symptoms (unaffected family members) at a higher rate than in the general population. Providing data about this important issue would strengthen the evidence for NJREs as a putative endophenotype for OCD and OC symptoms.

### 1.1. The current study

We speculated that the frequency and/or severity of NJREs should be higher in offspring of parents with OC symptoms compared to offspring of parents without OC symptoms. This supposition is in fact coherent with the idea that NJREs might be a liability factor for the OCD. To test our hypothesis, measures of NJREs, OC symptoms, anxiety, and depression were collected from a sample of college students and their parents. Then, we identified two groups of college students: those with at least one parent with some OC symptoms (as measured by the Obsessive-Compulsive Inventory, see below) and those with no parents with OC symptoms. The first group of students was considered an "at-risk group" for OC symptoms whereas the second one was considered not at risk for OC symptoms.

We chose a nonclinical sample because we believe that, in case of OCD, it has certain advantages compared to clinical counterparts. For example, those seeking treatment for OCD represent a minority of the OCD population (Grabe et al., 2000), and likely differ from non-help seekers on social, economic, attitudinal, and personality factors. Confounding factors such as prior treatment types and treatment effects and, above all, comorbidity, also pose challenges for studies of OC phenomena in clinical populations. In addition, OCD is a chronic disorder, especially if not treated in the appropriate way (Sica et al., 2010): we do not know how a chronic OCD affects the psychological (and neurobiological) functions of people in the long-term. Also, since OCD occurs in only 2–3% of the population, it can be time intensive and costly to recruit clinical samples of an adequate size.

On the other hand, OC symptoms do occur in the general population (e.g., Adam et al., 2012; de Bruijn et al., 2010; Grabe et al., 2000), allowing researchers to recruit larger samples with relative convenience. As a matter of fact, researchers have pursued various forms of analogue research in order to study OC phenomena. Let us consider the evidences in favor of such choice.

- 1) Studies of analogue samples (i.e., student and community participants) highlight the prevalence of subclinical OC symptoms. According to surveys, up to 90% of people report that they at least occasionally experience intrusive thoughts that are similar in form and content to clinical obsessions (e.g., Clark, 1992; Freeston et al., 1991). Several studies of student or community samples have reported the prevalence of "caseness" as assessed by the Obsessive Compulsive Inventory-Revised (OCI-R; Foa et al., 2002) (e.g., Cuttler and Taylor, 2012; Kaczurkin, 2013). Therefore, OC symptoms are present to some degree in the non-clinical samples, providing initial evidence for a continuum of severity.
- 2) Distress, impairment, and reduced quality of life are also part of the diagnostic criteria for OCD (APA, 2013). Accordingly, studies also reveal some degree of impairment and treatment seeking even among non-clinical groups, and thus support the dimensional model of OC symptoms (Adam et al., 2012; de Bruijn et al., 2010; Grabe et al., 2000). Even more important, two taxometric studies have found support for a dimensional latent structure for OC symptoms globally (Haslam et al., 2005; Olatunji et al., 2008).
- 3) A large body of research indicates that for the most part, the themes, content, and form of intrusive distressing (obsession-

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