



Role of stressful and traumatic life events in obsessive–compulsive disorder

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Practice points

- Patients with obsessive–compulsive disorder (OCD) frequently report stressful life events (including trauma) before the onset of illness, although these rates do not seem to be significantly different from those described in other mental disorders.
- The association between OCD and post-traumatic stress disorder (PTSD) may result from symptom overlap, although cases of post-traumatic OCD with obsessive–compulsive symptoms that were unrelated to trauma have been described in the literature rather consistently.
- It is not completely clear whether patients with OCD and a history of stress-related factors (including precipitants, traumatic events or comorbid PTSD) may respond better or worse to the available treatments, including serotonin reuptake inhibitors and different forms of cognitive behavioral treatment.
- Although comorbid PTSD may modify the clinical expression of OCD, controlled studies comparing pre- versus post-PTSD patients with OCD are still unavailable.
- The available data do not allow us to establish whether stress-related factors lead to a distinct subtype of OCD.

SUMMARY Whilst genetic factors are thought to contribute to the development of obsessive–compulsive disorder (OCD), the role of environmental factors in OCD is only beginning to be understood. In this article, we review the influence of stress-related factors in OCD. Overall, studies indicate that: patients with OCD frequently report stressful and traumatic life events before illness onset, although these rates do not seem to be significantly different from those described in other disorders; the association between OCD and post-traumatic stress disorder (PTSD) might result from symptom overlap, although cases of patients developing OCD after PTSD and showing obsessive–compulsive symptoms that were unrelated to trauma have been described fairly consistently; it is unclear whether patients with OCD and a history of stress-related factors (including stressful life events, traumatic life events or comorbid PTSD) may respond better or worse to the available treatments; and comorbid PTSD may modify the clinical expression of OCD – although controlled studies comparing pre- versus post-traumatic OCD patients are still unavailable. In conclusion, there is a growing evidence to suggest a role for stress-related factors in OCD. Although the available literature does not confirm the existence of a post-traumatic subtype of OCD, it does call for further systematic research into this topic.

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Obsessive–compulsive disorder (OCD) is characterized by repetitive and unwanted thoughts (i.e., obsessions) and perseverative and ritualized behaviors (i.e., compulsions) [1]. It often follows a chronic course [2] and is frequently associated with substantial impairment in different aspects of quality of life [3]. Community studies using the Composite International Diagnostic Interview have found that OCD may affect up to 3.1% of the general population [4]. Unfortunately, despite being disabling and relatively common, OCD is still mysterious in its origins and research on the etiology remains in its infancy.

Despite evidence accumulating in support of a genetic basis to OCD (for a review see [5]), there remains an equivalent need to better understand the role of environmental influences, including gene–environment interactions, in shaping the etiology and pathophysiology of this disorder. This follows from early proposals that OCD is highly dependent on external events in the patient's life. Pollitt, for example, thoughtfully described the reactivity of OCD patients to environment factors (e.g., he suggested that the symptoms of OCD become more severe and prominent when anxiety and tension increase and when resistance to symptoms is lowered by fatigue) [6]. Furthermore, he argued that the severity of symptoms improves when tension is reduced or new life circumstances or events take precedence in the patients' lives. In the longitudinal study of Grimshaw [7], a third of patients who improved in the long term attributed their progress to some kind of environmental change leading to a reduction of current life stressors (e.g., relief of pressure of work, residence change, marriage, divorce or acquisition of a secure job).

As for many other psychiatric disorders, the diathesis–stress model is generally invoked to explain the development of OCD, both in regards to the onset and course of the disorder [8,9]. According to recent theories on gene–environment interactions, the consequences of exposure to an environmental pathogen on health is highly conditioned to a person's genotype [10,11]. Thus, it is likely that certain genotypes moderate the risk of expression of OCD in the presence of specific environmental factors. For example, it has been suggested that patients with glutamate transporter gene *SLC1A1* polymorphism may be more prone to atypical antipsychotic-induced OCD [12], while individuals with variations in the promoter region of the *TNFA* gene may be more likely to

show infection-triggered OCD [13]. In pursuing this line of inquiry, it will become increasingly more important to evaluate whether certain genetic variations predispose individuals to develop OCD under different conditions of psychological stress.

Indeed, there is increasing recognition that stressful and/or traumatic life events (SLEs/TLEs) may be important environmental vulnerability factors in OCD, particularly in OCD patients without a family history of the illness [14,15]. For example, Albert *et al.* compared OCD patients with and without a family member diagnosed with OCD and found that SLEs prior to the onset of OCD were more common and more severe in nonfamilial OCD subtypes [14]. Cath *et al.* studied the role of environmental factors in obsessive–compulsive (OC) symptoms using 25 monozygotic (MZ) twin pairs discordant, 17 MZ twin pairs concordant high and 34 MZ pairs concordant low on OC symptoms (according to the Padua Inventory-Revised) from a large longitudinal Dutch sample [15]. The high-scoring MZ twins of the discordant group reported more life events (especially sexual abuse) than their low-scoring twin-siblings. These findings suggest that there may be an interaction between stress-related factors and a genetic predisposition towards OCD. Epigenetics, that is, any change in gene function not associated with sequence variation, typically involving DNA methylation, histone acetylation and noncoding RNAs, may provide one possible mechanism through which traumatic experiences may lead to OCD [16]. Nevertheless, the exact role of life events in OCD remains elusive. It is still unclear, for example, whether trauma leads to a specific subtype of OCD, that is, post-traumatic OCD.

The aim of this article is to provide a brief summary of the relevant literature linking stress-related factors (i.e., SLEs and TLEs) to the onset and development of OCD.

Finally, we discuss the possible existence and plausibility of a trauma-related subtype of OCD. It is necessary to provide a working definition of the terms that will be used in this article: 'stress' refers to diverse factors that tend to alter an existent equilibrium [101]. We understand it as a rather general term including concepts such as SLE and TLE. We will use SLE to refer to changes in the external environment that occur sufficiently rapidly to be approximately dated [17]. Therefore, they are usually abrupt rather than insidious,

external rather than internal and social rather than nonsocial [17]. Finally, a TLE, or simply trauma, will be used as stated in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (i.e., an event that involves actual or threatened death or serious injury or a threat to physical integrity of self or others [18]).

SLEs in OCD

Although SLEs have long been considered to play a role in the development of OCD, few studies have addressed this issue comprehensively. Initial attempts to link SLEs to the onset of OCD were made by means of nonvalidated instruments focusing on different periods of time and including open assessments [19], structured interviews [20], questionnaires covering different types of ‘precipitants’ [21], self-report checklists [6] or even nonspecified methods [22,23]. As a consequence, highly variable rates were reported, ranging from 30% [20] to 56% [22], 58% [24] 60% [19], 62% [6], 69% [23] and 77.6% [21]. Yet, despite these erratic rates, some compelling findings have emerged. For example, in a retrospective study of information contained in the files of patients with OCD (n = 159), agoraphobia (n = 80) and other specific phobias (n = 120), OCD patients reported a significantly higher frequency of ‘sexual problems, occupational or academic difficulties, childbirth and other crisis’ compared with the other groups, while ‘frightening and unavoidable conflicts’ were significantly more common in these groups [21].

More recently, standardized and validated instruments (i.e., Paykel’s Recent Life Events Interview) have been employed to systematically assess the role of SLEs in OCD [9,25–28]. In a handful of studies, patients with OCD described an increased number and severity of SLEs (including arguments, childbirth, serious illness and traumatic brain injury [9]) in the 6 months prior to the onset of illness [9,25], with a peak at 1 month before [9]. Similarly, Gothelf *et al.* found that children with OCD had significantly more total and negative SLEs (particularly major illness or injury of a relative) in the year before onset than normal controls, and perceived them as being more impactful [27]. Although Maina *et al.* were unable to replicate these findings, they reported that female patients with OCD were more likely than normal female subjects to report exposure to postpartum events [26]. In another study, Tolin *et al.* noted that changes in relationships and interpersonal

violence were disproportionately associated with periods of symptom onset or exacerbation of hoarding symptoms in a self-identified sample of 751 hoarders (36.8% of the hoarding sample scored above the Obsessive–Compulsive Inventory-Revised [OCI-R] cutoff of four, which best discriminates individuals with and without OCD) [28]. These findings have been confirmed in community samples. For example, in their two-stage epidemiological study, Valleni-Basile *et al.* found that adolescents who experienced more undesirable and less desirable life-events, according to the Coddington Life Events Scale for Adolescents, were at higher risk for developing OCD in the long term [29].

In sum, although early studies, which adopted nonvalidated and more categorical definitions (i.e., yes or no) of precipitants, were unable to generate reliable results, more recent investigations (including at least one epidemiological study), which employed validated instruments and a continuous approach towards precipitants (including number and severity of life events), have confirmed that SLE may play a significant role in the development of OCD.

TLEs in OCD

While the link between SLEs and OCD is becoming more clearly established in the literature, the role of TLEs is somewhat less clear. Indeed, extreme trauma may have a unique etiological effect on the development of post-traumatic stress disorder (PTSD) in comparison to less dramatic events (SLEs) [30]. For example, different epidemiological studies have reported that a person’s experience of a situation where they feared serious injury or death was associated with increased rates and/or severity of PTSD, major depressive episode, agoraphobia, social anxiety disorder and OCD [31–36]. Curiously, while PTSD acts as a strong mediator between victimization and most axis I disorders, trauma remained a significant and independent predictor of OCD in at least two studies [33,34].

Of note, in the study published in 1957 by Pollitt [6], overt sexual trauma was significantly more common among patients with OCD than in a control group that included patients with ‘neuroses and psychoses’. Nevertheless, modern studies comparing the rates of traumatic events in OCD to those reported in other disorders (e.g., trichotillomania [37,38], social anxiety disorder [39] and panic disorder [40]) or even in healthy controls [41] show that the history of

traumatic events is not higher in OCD, thus suggesting that some other factor (e.g., genetic liability, among others), may explain the development of OCD among trauma survivors [8,42].

The number of patients with OCD and comorbid PTSD is extremely variable, ranging from 1.6 [43] and 7.0% [44] of OCD patients to 4.2 [45] and 22.0% [44] of PTSD samples. These figures suggest that, while patients with OCD may be less inclined to experience traumatic events or trauma-related symptoms, patients who develop PTSD may exhibit OCD as a comorbid condition more consistently. It could be argued, however, that an increased rate of OCD in PTSD samples does not correspond to true comorbidity, but rather to the effects of associated depression, or simply to symptom overlap, since both OCD and PTSD exhibit intrusive thoughts and include avoidant and/or ritualized behaviors to ensure safety [46]. In an attempt to elucidate this issue, Huppert *et al.* examined samples of patients with OCD and PTSD using scales that assessed OC, PTSD, depression and nonoverlapping OCD and PTSD items [47]. They found that the positive correlations between OCD and PTSD symptoms in both groups disappeared after controlling for symptom overlap and depression, thus suggesting that the association between these disorders may also be a phenomenological artifact.

It has also been debated whether some patients who develop OCD after or concurrently with PTSD should be diagnosed with OCD, since the criteria for OCD specify that compulsions cannot be restricted to the context of another axis I diagnosis – in this case, PTSD [48]. Gershuny *et al.* suggest that OC symptoms in PTSD may function as some type of coping or protective response to trauma-related thoughts and emotions that are too psychologically distressing to endure [49]. Nevertheless, it should be stressed that OCD symptoms that are ostensibly unrelated to the content of trauma have been described among patients with post-traumatic OCD [50,51]. Considering that hyperestimation of risks and great need for certainty, security and control are core OCD features, it is understandable that exposure to really dangerous situations may favor OCD development in predisposed persons [51]. For some authors the trauma may act as a learning experience that leads to anxiety, hypervigilance, inference errors and generalization of fears, which are temporarily relieved by compulsive rituals via negative reinforcement [50].

Therefore, OC symptoms could become chronic, a residual effect of the traumatic event. It is noteworthy that some authors described clinical cases in which PTSD and OCD symptoms overlapped for some time and OCD remained as the patients' main or only diagnosis [52].

In sum, while the rates of PTSD among patients with OCD seem to be low, OCD may be more frequently found among PTSD samples. Furthermore, although symptom overlap and associated depression may explain some of these findings, there is still a handful of case reports of patients who develop PTSD and OCD with symptoms that are unrelated to the trauma content and cannot be solely explained by PTSD diagnosis.

SLEs, TLEs & outcome in OCD

The first attempt to evaluate the impact of stress-related factors on the outcome of patients with OCD was performed by Lo [22]. This study reported that the presence of 'precipitants' (defined as significant triggers occurring within 6 months of the onset of the illness, including psychological, physiological or physical events, among others) was significantly associated with a more favorable prognosis. More recently, Bogetto *et al.* established an indirect link between life events and episodic course of the disorder, by describing that, compared with males, females with OCD more frequently reported an acute onset, an episodic course and stressful events in the year preceding OCD [53].

Only one study [54] has attempted to assess the impact of traumatic events on the treatment response of OCD patients to serotonin reuptake inhibitors (SRIs) and cognitive behavioral group therapy in a prospective manner. Shavitt *et al.* found that patients who reported a history of trauma were more frequently rated as an SRI responder (47.4%) compared with patients without a history of trauma (22.2%) [54]. On the other hand, in this same study, patients with and without a history of trauma did not differ in terms of their response to cognitive behavioral group therapy (60 vs 63% response, respectively). When both SRI and cognitive behavioral group therapy were considered as a single outcome and treatment response was considered as a continuous variable (i.e., absolute number of points reduction in baseline Yale–Brown Obsessive–Compulsive Scale [Y-BOCS] scores), patients with OCD and comorbid PTSD exhibited greater treatment response than patients with OCD without

PTSD. Furthermore, OCD treatment resulted in greater reductions for OCD patients with PTSD than for those without PTSD in the washing, hoarding and miscellaneous dimensions, and in the anxiety scores.

The above results are in sharp contrast to some previous single cases [55], case series [50,52] and open studies [56] suggesting that individuals with co-occurring OCD and PTSD may be particularly resistant or refractory to treatment. For example, Gershuny *et al.* reported increased rates of trauma (82%) and PTSD (39%) in a treatment-resistant OCD sample [57]. Indeed, some data suggest that patients with OCD and PTSD who are treatment resistant may also be less likely to respond to intensive therapeutic strategies. Gershuny *et al.* reported that treatment-resistant OCD patients with comorbid PTSD exhibited a worse response to an intensive residential treatment (i.e., coached and self-directed exposure and response prevention as well as in group therapy targeting specific OCD symptoms and related difficulties) than those without PTSD [57]. The authors reported that the symptoms of OCD patients with comorbid PTSD in the best cases abated somewhat or remained the same, or in the worst cases, increased in frequency and intensity [57]. Based on these findings, they argued that the behavioral treatment of OCD may be adversely affected by the presence of comorbid PTSD and indeed may be contraindicated for some patients in order to avoid symptom exacerbation [57]. While it might be too early to avoid exposure and response prevention to treat patients with OCD and PTSD, one should attempt to take trauma into account in the treatment plan. Stress inoculation training, prolonged imaginal exposure to trauma-related memories, SRIs and neuroleptic medications could be added to treatment [56].

In summary, studies on the impact of life events and trauma on treatment response of OCD are heterogeneous in terms of methodology (single cases, case series, open studies, case–control studies and naturalistic follow-ups), sample (regular vs treatment-resistant OCD patients), environmental stressors (milder life events vs severe trauma), comorbid conditions (PTSD vs non-PTSD patients) and types of intervention (SRIs, cognitive behavioral group therapy or residential treatment involving both), which are factors that might explain the seemingly discrepant impact of environmental stress on treatment response.

Towards a trauma-related subtype of OCD

The identification of a trauma-related subtype of OCD is of potential interest, since this condition might be associated with a poor outcome in response to conventional anti-OCD interventions but adequate response to particular therapeutic strategies. In fact, attempts to delineate a subtype of OCD that is precipitated by severe trauma have been performed for more than a century, but mainly in the form of anecdotal case reports. For example, in 1903, Janet described the case of a 59-year-old woman who developed obsessions after seeing the charred body of her daughter who had died in a fire [58]. Pitman described the case of a combat-exposed Vietnam War veteran who developed OCD, along with PTSD, that persisted for two decades [55]. De Silva and Marks reported on eight cases of OCD patients whose symptoms started either in the immediate aftermath, or within a few weeks of experiencing different traumatic events (e.g., plane crashes, sea disasters, industrial accidents, serious road traffic accidents, personal violence, sexual assault and combat exposure) [50]. Sasson *et al.* reported 13 cases of Israeli army veterans diagnosed with both PTSD and OCD [52]. In all but one of the reported cases, the traumatic experiences involved physical contact with elements that evoked disgust (i.e., one's own wounds or the body of other wounded or dead persons). Finally, some have suggested that such post-traumatic cases may be particularly likely in patients who display late-onset OCD [51,59,60], who, in general, are less likely to exhibit a positive family history of the disorder [61].

Few systematic attempts to delineate phenotypical aspects of trauma-related OCD have been made and it is still doubtful whether a traumatic event may determine the pattern of symptoms exhibited by OCD patients [62–65]. For example, Cromer *et al.* reported that, among 256 patients with OCD, those who endorsed at least one lifetime traumatic event (54% of the sample) exhibited increased obsessions/checking, symmetry/ordering and global symptom severity, which were independent of age, age at onset of OCD and comorbidity effects [63]. A subsequent study by the same group included the Saving Inventory-Revised and found that OCD hoarders who reported lifetime trauma (24% of the sample) had greater severity of hoarding, particularly clutter, which was independent of age, age of onset and Y-BOCS scores [64].

Interestingly, some authors [50,52] have pointed out that the content of OC symptoms in individuals previously exposed to trauma may be, at least in part or in the beginning, related to this negative experience. For example, subjects submitted to sexual violence may develop obsessions with dirt, disgust feelings and cleaning rituals; those exposed to road accidents or other violent situations may also present aggressive obsessive thoughts or images, such as fear of hurting other people, guilt feelings and checking compulsions.

Although some of these studies have significant strengths, including a high number of research subjects enrolled, they also display a number of drawbacks that leaves the question regarding the etiological role of trauma in OCD unanswered. For example, the exact age at which each traumatic event took place was not adequately assessed by these studies, making it impossible to draw any conclusions regarding the temporal relationship between traumatic events and the onset of OCD.

Conclusion & future perspective

Patients with OCD frequently report SLEs and TLEs prior to the illness onset, although these rates do not seem to be significantly different from those described in other psychiatric disorders. When OCD and PTSD co-occur, this association might result both from symptom overlap or true comorbidity, as cases of post-traumatic OCD with OC symptoms that were unrelated to trauma have been described in the literature rather consistently. Furthermore, it is not completely clear whether patients with OCD and a history of stress-related factors (including precipitants, traumatic events or comorbid PTSD) may respond better or worse to the available treatments, including SRIs and cognitive behavioral therapy. Finally, although comorbid PTSD may modify the clinical expression of OCD, controlled studies comparing pre- versus post-PTSD patients with OCD are required. Taken together, the available data do not permit one to establish whether stress-related factors lead to a distinct subtype of OCD.

There are a number of general limitations with the research methodologies used to study the influence of stress-related factors in OCD. All early studies employed nonvalidated assessments in an attempt to catalog various risk factors that may precipitate OCD, a strategy that has led to highly variable results. Furthermore, although recent studies on stress-related factors in OCD

have employed valid instruments for the assessment of life events, all of them were retrospective and relied on the ability of patients with OCD to remember significant life events. This approach is obviously not optimal because some patients may be more sensitive to recalling trauma than others and may exaggerate the causal impact of certain life events [63]. This bias may be ascribed to different non-OCD factors among OCD patients, including temperament and personality factors that have already been shown to modify the perceived impact of life events in OCD (e.g., harm-avoidance [27], conscientiousness [36] and even personality disorders [9]).

There are some additional problems. In some circumstances, it can be difficult to disentangle the psychological impact of some forms of trauma, such as the experience of severe illness, from its organic consequences. Another issue that may complicate the field is the lack of agreement on what should be considered age at onset of OCD (i.e., the age at the onset of subclinical OC symptoms, age at which OC symptoms started to lead to distress, or the age at which patients started to fulfil DSM-IV-TR or ICD-10 criteria for OCD) [66,67]. Poorly characterized age at onset might lead to confusion regarding the temporal relationship between OCD and trauma and, as a consequence, regarding post-traumatic OCD. In addition, studies that have compared treatment response between OCD patients with versus without PTSD are hampered by the heterogeneous quality of the former group, which may contain subgroups (pre- vs post-traumatic OCD) that may respond differentially to treatment. Finally, no studies have attempted to compare OCD occurring after trauma/PTSD to OCD occurring before trauma/PTSD or nontraumatic OCD. Further studies addressing this question may be instrumental in clarifying the etiological interplay between OCD and PTSD.

If one intends to investigate whether there is a post-traumatic subtype of OCD, a number of strategies could be adopted. Follow-up studies of community individuals exposed and non-exposed to traumatic events along with comparisons between the phenotypes and natural histories of those who develop OCD would be informative. Longitudinal studies comparing individuals with and without a family history of OCD or PTSD could investigate the effects of stress-related factors on the development of these conditions with valid and reliable instruments.

This analysis would benefit from an assessment of personality and temperament to control for the perceived impact of events and the likelihood of being exposed to trauma. Analyses that take into account whether OCD or OC symptoms onset occurs before, together or after trauma or PTSD should also provide critical information on the etiological factors associated with both disorders. Finally, sociodemographic, clinical, family history and treatment response characteristics related to a post-traumatic, pretraumatic and nontraumatic OCD could be identified. Ideally, these groups would need to be paired by age at onset of OCD, since there would be a natural trend for pretraumatic OCD to represent an early-onset OCD phenotype and post-traumatic OCD to represent a late-onset OCD phenotype.

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