The Temporal Relationship between Premonitory Urges and Covert Compulsions in Patients with Obsessive-Compulsive Disorder

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Abstract

Recent studies in patients with obsessive-compulsive disorder (OCD) have shown that many compulsions are associated with urges rather than obsessions. Premonitory urges are uncomfortable sensory feelings or a rising inner tension, often likened to the urge to scratch, yawn or blink. We studied premonitory urges preceding mental compulsions in 19 patients with OCD and preceding eye blinks in 16 healthy controls. Urge intensity was assessed continuously over 20 min using a real-time urge intensity monitor; compulsions and blinks were measured as discrete events in a free compulsion/blinking and a compulsion/blink suppression condition. Urge intensity showed an inverted U-shaped relationship (increase then decrease) around compulsions within a time-window of approximately 60 s in patients with OCD and within 13 s around blinks in healthy controls. Urge intensity was higher during compulsion / blink suppression and varied more independently of compulsion execution in patients with OCD. There is a close temporal relationship between premonitory sensations and compulsion execution that changes when compulsions are suppressed, indicating that urge intensity might drive the execution of and is then alleviated by compulsions. Suppression weakens the association between urge intensity and compulsion execution.

Keywords: premonitory sensation; sensory urge; exposure with response prevention; real-time urge monitor; OCD-Tourette spectrum; obsession

1. Introduction

Obsessive-compulsive disorder (OCD) is the fourth most common psychiatric disorder with a lifetime prevalence of 1-3% (Karno et al., 1988; Kessler et al., 2012; Ruscio et al., 2010). It is characterized by repetitive, intrusive thoughts or impulses (obsessions), and the repetitive execution of overt or mental (covert) acts (compulsions) aiming at "neutralizing" these distressing thoughts or feelings (DSM-5, 2013). Neutralizations, similar to overt compulsions, are carried out in an attempt to reduce the likelihood of a feared event to occur or to reduce the discomfort caused by intrusive thoughts or impulses, which are often experienced as morally or physically repulsive (Rachman and Shafran, 1998). Neutralization is mainly a covert mechanism and is referred to as a compulsion when the same neutralization is repeatedly used whenever a certain obsessive thought intrudes (Rachman and Shafran, 1998).

While it has long been assumed that obsessions and compulsions are the defining symptoms of this disorder (Fontenelle et al., 2004), more recent studies suggest that patients with OCD display highly heterogeneous symptoms and that existing treatments relieve symptoms only in a proportion of patients (Braga et al., 2010; de Haan, 2006; Farris et al., 2013). This has inspired the question whether treatment response in patients with OCD could be optimized if treatment could be tailored to specific subtypes of OCD (Ferrao et al., 2006; McKay et al., 2004), such as gender (Labad et al., 2008; Mathis et al., 2011), symptom dimensions, e.g. contamination/washing vs. checking (Ferrao et al., 2006; Leckman et al., 2010; Okada et al., 2015), comorbid tic disorders (Conelea et al., 2014; Jaisoorya et al., 2008) or experiencing sensory phenomena (Miguel et al., 2000; Prado et al., 2008).

Sensory phenomena have first been described in patients with Gilles de la Tourette syndrome (GTS) (Bliss, 1980) and typically precede repetitive behavior (Brandt et al., 2016). Researchers have recently defined different premonitory sensory phenomena, although they

are not clearly distinct (Cavanna and Nani, 2013). “Premonitory sensation” refers to any sensation that precedes the onset of tics or compulsions. The temporal order of these sensations in relation to tics was long under debate and it has only recently been experimentally shown that the term “premonitory” is justified (Brandt et al., 2016). The specific premonitory sensation that accompanies tics and compulsions can be further classified into categories (Cavanna and Nani, 2013). An “urge” is a drive to execute repetitive behaviors in the absence of obsessions. “Just-right experience” refers to a feeling of imperfection and the need for things to feel or look a certain way. Patients will repeatedly execute compulsive behaviors until a feeling of completeness is reached. Sensory tics are uncomfortable bodily sensations, experienced, for instance, in muscles or joints that drive repetitive actions until the patient feels relieved (Cavanna and Nani, 2013). “Sensory phenomena” describe bodily sensations, such as pressure-like, warm, cold, or tickling sensations (Banaschewski et al., 2003). While the quality of these subjective sensations may be described in different ways, they are commonly thought to precede a repetitive behavior and subside when the behavior has been executed.

Premonitory sensations were initially assessed in patients with OCD with and without tics to differentiate subgroups of patients on the OCD-TS spectrum (Leckman et al., 1994; Miguel et al., 2000; Prado et al., 2008), but a recent study in a large sample of patients with OCD found that the majority (65%) of patients experienced premonitory sensations rather than obsessions prior to at least one repetitive behavior and that the strongest predictor was symmetry/ordering/arranging, followed by the presence of tics (Ferrao et al., 2012).

Characterizing premonitory sensations in patients with OCD can be helpful in determining which behavioral interventions may be most effective in treating the associated compulsions (Summerfeldt, 2004). Although different types of premonitory sensations have been described in patients with OCD (Ferrao et al., 2012; Miguel et al., 2000), they have so far relied mostly on questionnaire data and self-reports (Ferrao et al., 2012; Sampaio et al., 2014). Little is

known about the temporal relationship between premonitory sensations and compulsions in OCD. Although exposure with response prevention (ERP) relies on the assumptions that premonitory sensations increase before repetitive behaviors are executed, and then subside, this assumption has never been experimentally tested. Furthermore, it is unclear in what time-window clinicians should expect this rise and fall of urges to occur. There is some evidence showing that neutralizing thoughts leads to an immediate temporary relief in anxiety and the urge to neutralize (Rachman et al., 1996) but exact timings have not been assessed. However, knowledge about this relationship is essential in tailoring behavioral interventions to patients with OCD who experience premonitory sensations.

The following study aimed to address several open questions regarding the urge to perform mental compulsions in patients with OCD. First, we hypothesized that urge intensity increases prior to mental compulsions and decreases following the compulsion. We further tested the hypotheses that urge intensity increases overall when compulsions are suppressed and that variation in urge intensity becomes more independent from compulsion execution under suppression. Finally, we were interested in the time-window in which urge intensity increases and decreases around compulsions. The urge to execute compulsions was compared to the urge to blink in healthy controls. A control group was included to assure that the experimental paradigm worked and to compare a physiologically necessary urge (eye blinking) with an urge that has no apparent necessity (premonitory urge).

2. Methods and materials

2.1 Participants and clinical assessment

Nineteen patients with a diagnosis of OCD (aged 30.58 ± 9.68; 5 female), all of whom had mental compulsions, according to DSM-5 (DSM-5, 2013) and 16 healthy controls (aged 33.13 ± 13.59; 10 female) were included in this study. patients with OCD were recruited from the Department of Psychiatry and Psychotherapy at the University Clinic in Lübeck. All

patients had undergone a comprehensive clinical assessment and had been diagnosed by an experienced clinician in a unit specialized for OCD treatment (for comorbidities see supplementary table 1). Patients received a written information sheet about the study in the clinic. If patients were interested, they could agree to be contacted by the experimenter or contact the experimenter. Inclusion criteria encompassed a confirmed OCD diagnosis, experiencing urges and mental compulsions and age > 18. Exclusion criteria encompassed psychosis and most neurological diseases (apart from tics). Exclusion criteria for healthy controls encompassed an OCD, ADHD or tic diagnosis and any neurological disease. All procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All participants gave their written informed consent.

In order to further characterize the sample, OCD symptom severity was assessed using the „Yale-Brown Obsessive Compulsive Scale“ (Y-BOCS; Goodman et al., 1989a; Goodman et al., 1989b) a structured interview with very good reliability (Goodman et al., 1989b) and good convergent but poorer divergent validity (Goodman et al., 1989a; Kim et al., 1990) and the „Obsessive Compulsive Inventory- Revised“ (OCI-R; Foa et al., 2002), a self-report scale with good reliability, convergent and divergent validity (Gonner et al., 2008; Hajcak et al., 2004). Presence and severity of tics was assessed with the „Yale Global Tic Severity Scale“ (YGTSS; Leckman et al., 1989), a clinician-rated tic scale with high internal consistency, stability and convergent as well as discriminant validity (Storch et al., 2005). Likelihood of having (had) a tic disorder was assessed with the „Diagnostic Confidence Index“ (DCI; Robertson et al., 1999). Psychometric properties of the DCI are not well established but it is a useful, structured instrument to assess whether a patient may fulfil criteria for a tic disorder at present or in the past (Robertson et al., 1999).

2.2 Experimental procedure

Participants were seated in front of a laptop displaying the real-time urge monitor (Figure 1A and 1B). The laptop screen showed a coordinate system with an intensity scale on the y-axis, which ranged from 0 - 100; 0 was equivalent to no urge and 100 represented the strongest urge participants typically experience. The x-axis represented time. After pressing the start button, a countdown (3 s – 2 s – 1 s – 0 s) indicated time to start. Then a blue line appeared on the right side of the coordinate system at level 50, moving towards the left, crossing the screen within 10 s. The blue line could be adjusted to the current level of urge intensity by moving a scroll bar on the right side of the screen via a mouse pad. All participants practiced the task for 1 min. The validity of the real-time urge monitor has been assessed and the task has been described in detail in a previous study (Brandt et al., 2016).

Participants were instructed to report changes in urge intensity immediately and continuously (Figure 1A). Patients with OCD were asked to report the intensity of their current urge to execute a mental compulsion, whereas healthy controls reported their urge to blink. Patients with OCD were asked to additionally report the occurrence of mental compulsions by pressing a foot pedal (Figure 1B). Urge intensity was measured a) during a free compulsions/blinking condition and b) during a compulsion/blink suppression condition (instruction: “please suppress the execution of compulsions / eye blinking in the next 10 min for as long as you can”). Each condition was assessed in 2 × 10 min blocks (Figure 2A). Participants were given 2 min breaks between the blocks. The task always started with the free blocks, to avoid after-effects of compulsion/blink suppression on urge intensity or compulsion/blink frequency in the free condition. Blinks were captured by video using a Panasonic HDC-TM700, with a frame rate of 25 frames per second. Patients with OCD were also filmed during the task to detect overt compulsions or tics. None of the patients displayed overt compulsions during the task.

Thereafter, participants completed the clinical questionnaires and an in-house questionnaire assessing whether the real-time urge monitor was able to reflect urges appropriately and whether the foot pedal was suitable for indicating mental compulsions.

2.3 Statistical analysis

2.3.1 Data pre-processing

The continuous real-time urge recording resulted in 12000 data points per participant per 20 min. For analyses investigating the temporal relationship between urge intensity and mental compulsions / blinks, the urge data was down-sampled to 1 data point per second, resulting in 1200 urge data points per condition per participant. The first 10 s of each block were discarded to allow for time until participants had adapted the scroll bar to the correct intensity level of their currently experienced urge, resulting in 1180 data points. Urge intensity was then z-standardized for each participant and condition respectively $z = \frac{\mathrm{xi} - \bar{\mathrm{x}}}{sd}$ and concatenated across participants for each condition. Blinks were rated as absent (0) or present (1) per second, also resulting in 1200 data points. Mental compulsions were aggregated into 1200 data points, showing whether a mental compulsion had been present (1) or not (0).

2.3.2. Average urge intensities and mental compulsion/blink occurrence across conditions and groups

For the group level analysis, the remaining 1180 data points per person were aggregated into mean urge values per participant per condition. Differences in mean urge intensity and differences in the number of mental compulsions / blinks between the free and the suppression condition were analyzed using paired samples *t*-tests.

Only 15 patients with OCD reported mental compulsions in the free compulsion condition. One patient who did not report compulsions in the free condition reported

compulsions in the suppression condition. The three patients who did not report any compulsions did not differ from the other patients regarding age [$t(17) = 0.75$, $p = 0.46$], DCI score [$t(16) = -0.76$, $p = 0.46$] or medication use [$t(17) = -0.79$, $p = 0.44$] but had a significantly lower YBOCS mental compulsions score [$t(17) = 3.40$, $p = 0.003$]; it is therefore likely that our experimental condition was too short to capture compulsions in these patients.

2.3.3. Temporal relationship between urge intensity and single mental compulsions / blinks

The strength of the urge- mental compulsion/blink relationship, i.e., the common variance between urge intensity and mental compulsions / blinks was calculated using binary regression analysis.

Based on the hypothesis that urge intensity increases before the occurrence of a mental compulsion/blink and declines afterwards, we investigated the temporal trajectory of urge intensity around single mental compulsions / blinks by extracting the standardized urge intensity within a 4 min time-window around single mental compulsions and a 40 s time-window around blinks. These mental compulsion/blink-related urge-tracks were aggregated into one average track per person per condition.

To test whether urge intensity followed an inverted U-shaped function, the mental compulsion/blink-related tracks were averaged across patients and healthy participants respectively in each condition, returning one mental compulsion-related track and one blink-related track for the free condition and one each for the suppression condition. A curvilinear regression analysis was computed for each experimental condition and group with time-to-mental compulsion/blink as the independent variable and mean standardized urge intensity as the dependent variable.

2.3.4 Parameters of the urge trajectory

To investigate the characteristics of the temporal development of urge intensity around single mental compulsions / blinks more closely, four parameters were extracted from the aggregated mental compulsion/blink-related urge tracks for each participant: a) *peak latency*, i.e. the time of maximum urge intensity relative to compulsion/blink occurrence, b) *width* was defined as the difference between the first local minimum before the peak and the last local minimum after the peak, c) *skewedness* of the urge trajectory, and d) *excess kurtosis* (for results regarding skewedness and excess kurtosis see supplementary section). The four parameters were tested against a null-hypothesis using one-sample *t*-tests. In addition, the parameters were compared between groups and conditions with repeated measures ANOVAs (see supplementary table 2). N = 2 healthy controls were excluded from analysis of urge trajectory characteristics in the free condition because they reported no change of urge intensity during free eye blinking. Hence, no peak etc. could be extracted around eye blinks.

Results were considered significant if $\alpha < 0.05$. To reduce the risk of false positives, the four *t*-tests per parameter (2 conditions, 2 groups) were Bonferroni-corrected and only considered significant if $\alpha < 0.0125$.

3. Results

3.1 Clinical Assessment

The mean Y-BOCS score (M ± SD) in patients with OCD was (22.58 ± 6.85), indicating moderate or moderate to severe OCD. Healthy controls scored significantly lower on the OCI-R (6.59 ± 3.94) than patients with OCD [29.83 ± 17.30; $t(31) = 5.40$, $p < 0.001$] (for clinical characteristics of the sample according to the OCI-R subscales see table 1). None of the healthy controls had tics but three of the patients with OCD had tics [n = 3; YGTSS: 24.30 ± 11.55; DCI: 38.00 ± 10.54]. Fifteen patients (79%) were taking psychotropic medication at the time of the study (supplementary table 1). All but two (n = 13) were taking

serotonin reuptake inhibitors; n = 9 additionally received an augmentation mostly with aripiprazole (n = 8).

3.2 Assessment of the urge measure

Of the 19 patients with OCD, 89% stated that the urge monitor reflected their urges well and 15 out of 16 patients who reported compulsions (94%) judged the foot pedal as being an appropriate method to capture occurrence of compulsions. Average number of mental compulsions in the free condition correlated with the Y-BOCS score (r = 0.55, p = 0.015), mean urge intensity in the suppression condition correlated with the OCI-R score (r = 0.52, p = 0.026).

3.3 Average urge intensities and mental compulsion/blink occurrence across conditions and groups

First, the average number of mental compulsions and blinks (events), as well as the average urge intensity across conditions were evaluated on the group level. A 2 × 2 [“condition” × “group”] repeated measures ANOVA with events as the dependent variable revealed that mental compulsions (8.89 ± 9.43) and blinks (255.31 ± 154.49) occurred significantly more frequently in the free compulsions / blinking condition than in the suppression condition (5.42 ± 7.45; 159.31 ± 84.98) across both groups [$F(1,33) = 15.36$, $p < 0.001$, $\eta = 0.32$], indicating successful suppression of eye blinks as well as mental compulsions. A significant interaction between “condition” and “group” [$F(1,33) = 13.29$, $p = 0.001$, $\eta = 0.29$] indicated that this effect was significantly larger in healthy controls [$t(15) = 3.46$, $p = 0.004$] than in patients with OCD [$t(18) = 2.45$, $p = 0.025$].

A 2 × 2 [“condition” × “group”] repeated measures ANOVA with urge intensity as the dependent variable showed, as expected, that urge intensity was higher in the suppression condition in patients with OCD (39.12 ± 27.56) and healthy controls (39.38 ± 15.98)

compared to the free condition [OCD: 31.65 ± 22.05; healthy: 5.44 ± 7.75; $F(1,33) = 53.1$, $p < 0.001$, $\eta = 0.62$], and a significant interaction between "condition" and "group" [$F(1,33) = 22.67$, $p < 0.001$, $\eta = 0.41$], indicating that this effect was significantly larger in healthy controls [$t(15) = -7.84$, $p < 0.001$] than in patients (Figure 3). Urge intensity in patients with OCD was only marginally higher in the suppression condition compared to the free condition [$t(18) = -1.94$, $p = 0.07$]. However, excluding patients with tics showed a significant increase in urge intensity in the suppression condition [$t(15) = -2.68$, $p = 0.017$].

3.4 Temporal relationship between urge intensity and single compulsions / blinks

A binary logistic regression showed a significant temporal relationship between urge intensity and mental compulsion occurrence during free compulsions [Cox & Snell $R^2 = 0.004$, $\chi^2(1) = 100.04$, $p < 0.001$; Exp(B) = 2.0, Wald(1) = 113.95, $p < 0.001$], which decreased during suppression [Cox & Snell $R^2 = 0.001$, $\chi^2(1) = 20.01$, $p < 0.001$; Exp(B) = 1.51, Wald(1) = 25.46, $p < 0.001$]. In healthy controls, urge intensity and blink occurrence were significantly associated during free blinking [Cox & Snell $R^2 = 0.001$, $\chi^2(1) = 23.52$, $p < 0.001$; Exp(B) = 1.1, Wald(1) = 24.66, p < 0.001] and slightly stronger during suppression [Cox & Snell $R^2 = 0.025$, $\chi^2(1) = 474.13$, $p < 0.001$; Exp(B) = 1.57, Wald(1) = 474.45, p < 0.001].

In order to determine how urge intensity relates to mental compulsions / blinks over time on average, the "urge intensity trajectory", i.e., the way urges behave around these events, was analyzed. In patients with OCD, the average urge trajectory ranged from - 17 s (± 16) to + 42 s (± 32; average minimum before and after mental compulsion) in the free condition and from - 24 s (± 27) to + 55 s (± 45) in the suppression condition, suggesting that urges built up and subsided over a longer time period when mental compulsions were suppressed (see also width). A curvilinear regression with time-to- mental compulsion as the independent variable and urge intensity as the dependent variable showed that the temporal

pattern of urge intensity followed a highly significant quadratic distribution (increase, then decrease) over time (- 17 to + 42 s) in the free condition [$F(2,57) = 116.07$, $p < 0.001$, $R^2 = 0.8$, b1 = 0.025, b2 = -0.001] and the suppression condition [- 24 to + 55 s; $F(2,77) = 22.68$, $p < 0.001$, $R^2 = 0.37$, b1 = 0.008, b2 = 0.00].

In healthy controls, the urge trajectory ranged from -06 s (± 03) to +07 s (± 08) in the free condition and from – 11 s (± 6) to + 10 s (± 5) in the suppression condition. Urge intensity followed a highly significant quadratic distribution over time (- 6 to + 7 s) in the free condition [$F(2,11) = 16.48$, $p < 0.001$, $R^2 = 0.75$, b1 = 0.003, b2 = - 0.004] and the suppression condition [- 11 to + 10 s; $F(2,19) = 62.06$, $p < 0.001$, $R^2 = 0.87$, b1 = - 0.028, b2 = - 0.005].

3.5 Parameters of the urge trajectory

After determining that urge intensity did significantly increase and decrease around mental compulsions / blinks, the properties of the urge intensity trajectory in relation to mental compulsions / blinks were analyzed.

3.5.1 Peak

In patients, urge intensity peaked approximately 6s after the onset of mental compulsions in the free condition [5.67 s ± 6.55; $t(14) = 3.35$, $p = 0.005$] but did not differ significantly from 0 in the suppression condition [9 s ± 24.72; $t(12) = 1.31$, $p = 0.21$]. In healthy controls, peaks in urge intensity around single blinks did not differ from 0 in the free condition [0.21 s ± 3.45; $t(13) = 0.23$, $p = 0.82$] or the suppression condition [0.94 s ± 3.02; $t(15) = 1.24$, $p = 0.23$] (supplementary table 2).

3.5.2 Width

A repeated measures ANOVA with “width” as the dependent variable showed that the urge trajectory was significantly narrower in the free condition (33.73 ± 33.64) than the suppression condition [48.50 ± 40.71; $F(1,24) = 5.25$, $p = 0.031$, $\eta = 0.18$], there was no significant interaction between condition and group [$F(1,24) = 2.84$, $p = 0.105$, $\eta = 0.11$] and the urge trajectory was significantly wider in patients (69.04 ± 35.66) compared to healthy controls [17.08 ± 10.70; $F(1,24) = 61.41$, $p < 0.001$, $\eta = 0.72$].

4. Discussion

4.1 Temporal relationship between urge intensity and single mental compulsions

The present study showed a strong temporal relationship between the urge to perform mental compulsion and the execution of mental compulsions in patients with OCD. Studies relying on questionnaires have previously suggested that compulsions are frequently associated with premonitory sensations instead of obsession (Ferrao et al., 2012; Leckman et al., 1994; Prado et al., 2008). This study is the first to experimentally confirm that urge intensity increases before mental compulsions and decreases following the compulsion, within approximately 60s when compulsions are not suppressed. The findings suggest that urge intensity increases for 17 s before it has reached a level that motivates the patient to perform a compulsion in order to feel urge relief. After the mental compulsion starts, it takes another 6 seconds before the patient starts to feel relief and 42 seconds until the urge has returned to the baseline level. Although the data are correlational, their relationship over time suggests that urges drive mental compulsions and that compulsion execution leads to a relief in urge intensity. This relationship is congruent with a model suggesting that repetitive behaviors might be maintained by negative reinforcement (see Figure 4) through relief of uncomfortable feelings or urges (Taylor et al., 2007). This is in line with previous studies investigating the relationship between urges and neutralizing behavior, which have shown that neutralizing leads to a temporary relief in anxiety and the urge to neutralize (Rachman et al.,

1996). Delaying neutralization also leads to a decrease in urges, albeit not as much as immediate neutralizing (Rachman et al., 1996). However, experimental data from healthy individuals suggests that neutralizing intrusive thoughts, rather than using a distraction technique, leads to increased anxiety and a higher urge to neutralize when the thoughts are evoked a second time (Salkovskis et al., 1997). Hence, incidental neutralization of intrusive thoughts might increase the urge to neutralize in the long run. Repeated neutralizing has been shown to manifest in meta-beliefs about the importance of thoughts and need to neutralize (as the only way to relieve anxiety) in patients with OCD (Myers et al., 2009).

The urge trajectory associated with eye blinks was flatter than a normal distribution in the free condition but not the suppression condition, indicating that some of the participants did not experience any urge to blink as long as they blinked freely. The results show that the (physiologically necessary) urge to blink is only induced properly once eye blinks are suppressed, contrary to premonitory sensations in patients with OCD.

4.2 Premonitory sensations during compulsion suppression

Patients and healthy controls were able to successfully suppress or postpone mental compulsions and eye blinks respectively. Notably, patients with OCD often postpone compulsions in everyday life. Urges were overall stronger in the suppression condition and urge intensity increased over a longer time period, probably because mental compulsions (and blinks) were postponed. If a compulsion was delayed, patients tolerated urge intensity to increase for another 7 s before executing a compulsion. Compulsions then provided immediate urge relief but urge intensity took another 55 s until it returned to the baseline. This change in the urge-compulsion relationship between conditions provides further proof for a causal relationship between urges and mental compulsions.

At the same time, results from the logistic regression indicate that the urge- mental compulsion relationship becomes partly de-coupled under suppression. In the free condition, a

rise in urge intensity was likely followed by the execution of a compulsion and then a decrease in urge intensity, whereas urge intensity could increase and then decrease in the suppression condition even though no compulsion was executed. Hence, patients could experience that urges will subside without the necessity to perform a compulsion. This finding provides experimental support for the assumption that urges start to fluctuate more independently of compulsion execution in the suppression condition, thereby confirming assumptions about the therapeutic mechanism of ERP. During ERP, patients ideally experience that their obsessive thoughts, images or impulses subside after a time, even if the patient does not perform cognitive or behavioral rituals to relieve them (Foa and Chambless, 1978). This study suggests that similar mechanisms apply to sensory urges. Taken together, the results show that patients can use mental compulsion suppression (even for relatively short time periods) to experience that the urge to perform a mental compulsion can vary and subside without execution of a mental compulsion. However, when a compulsion is executed, it will lead to a quick relief in urge intensity, stressing the necessity to treat urges in this patient group. The evidence indicates that it might be worthwhile to assess whether an OCD patient experiences premonitory urges and if they do, ERP may be particularly suited for the treatment of these compulsions.

Although urge intensity was overall higher when mental compulsions were suppressed, this effect only became significant when patients with tics were excluded from the analysis. This finding suggests that co-morbid tic disorders may have an impact on the experience of urges in relation to mental compulsions, though the sample is too small to draw firm conclusions. It has already been shown that the quality of premonitory urges differs between the majority of patients with GTS and OCD (Ferrao et al., 2012; Kwak et al., 2003) but it remains unclear how the urge to tic and the urge to perform compulsions might interact with each other. A previous study showed that the urge to tic develops over a time-course of approximately 20s (Brandt et al., 2016). While this suggests that urges associated with

different repetitive behaviors can be differentiated regarding the time-course (Brandt et al., 2016), they may also share common features, such as neural correlates (Jackson et al., 2011; Subirà et al., 2015) and sensory quality (e.g. just-right feelings) (Ferrão et al., 2012; Reese et al., 2014).

Several different types of urges, such as the urge to urinate or to swallow have been shown to be associated with activation in overlapping brain areas, predominantly the insula and the cingulate cortex (Jackson et al., 2011). Moreover, the urge to tic has been linked to activation in the supplementary motor area (Ganos et al., 2013). Very little is known about the neural correlates of urges in OCD. Structural abnormalities in the sensorimotor cortex appear to be present in both OCD (Subirà et al., 2015) and GTS (Draper et al., 2016); however, it is unclear whether structural alterations in sensorimotor areas are a cause or a consequence of urges. Using fMRI, modelling hemodynamic functions (regressors) to detect neural correlates of urges preceding mental compulsions in patients with OCD could be informed by the temporal characteristics found in this study.

4.3 Evaluation of the real-time urge monitor and limitations of the current study

Patients' evaluation of the urge monitor indicated good usability of the instrument. Although the urge monitor has a high resolution, it depends on interoceptive awareness, like all subjective measures, and will therefore entail some error variance. The same is true for operating the foot pedal. Furthermore, reaction times are approximately 10ms slower for feet than for hands (Pfister et al., 2014). Therefore, the timing of urge intensity and mental compulsions in the range of seconds should be regarded with some caution and the results should be confirmed in an independent study. However, both the free and the suppression condition are subject to the same limitations; hence, the results concerning the comparison between the two conditions should be robust.

Patients with OCD had to operate a mouse and an additional foot pedal, whereas healthy controls did not have to operate a foot pedal. Hence, patients had a higher cognitive load during the task. Some of the differences between patients and healthy controls may be explained (at least partly) by this difference in cognitive load. However, previous research using the exact same task for patients and healthy controls also found differences between the groups (Brandt et al., 2016). Also, the main findings (increase and decrease of urge intensity around compulsions) and comparisons between conditions are not affected.

Another limitation arises from the homogeneity of the group investigated; i.e. only mental compulsions were studied. Overt compulsions would pose a greater challenge for a continuous urge rating and might have to be provoked. However, it would be interesting to make the urge monitor more flexible so that it could be used in real-life settings, investigating overt compulsive acts, such as washing hands.

Furthermore, this study evaluated the relationship between mental compulsions and the urge to perform mental compulsions, without differentiating between different types of premonitory sensations, which might be interesting to follow up on in future studies. While the control group comprised more females than males, the ratio was reversed in the patient group. We are not aware of studies showing gender-differences in physiological urges but would like to acknowledge this limitation.

Paying attention to urges and mental compulsions may increase the urge overall. However, urges and mental compulsions cannot be reported unless the patient pays attention to them.

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Table 1 Clinical characteristics OCI-R

Subscale	**Checking**	**Ordering**	**Obsessing**	**Hoarding**	**Neutralizing**	**Washing**
(cut-off)	(5)	(7)	(5)	(5)	(3)	(3)
Mean +/- SD (N)	6.6 ± 4.7 (10)	4.9 ± 4.1 (6)	8.2 ± 3.4 (14)	3.8 ± 4.0 (5)	3.7 ± 4.3 (7)	3.7 ± 3.6 (7)

The table displays means ± standard deviations (SD) and total number of patients (N) scoring above the cut-off for each sub-scale of the OCI-R respectively.

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Figures

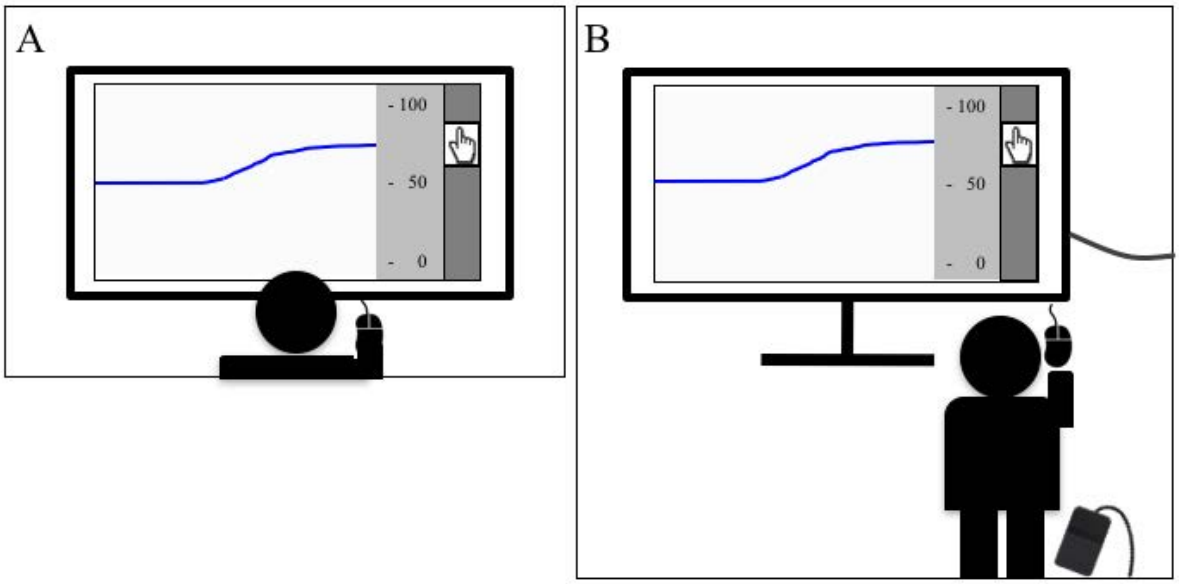

Figure 1.

A. The real-time urge monitor. After a countdown, a blue line started moving across the screen continuously from right to left and always displayed the last 10s of urge ratings. Participants were asked to operate the scroll bar on the right using the mouse pad to continuously indicate the intensity of their current urge to blink on a scale from 0 to 100, displayed on the right of the screen.
B. Patients were asked to report their current urge to perform a mental compulsion and to report mental compulsions via a foot pedal.

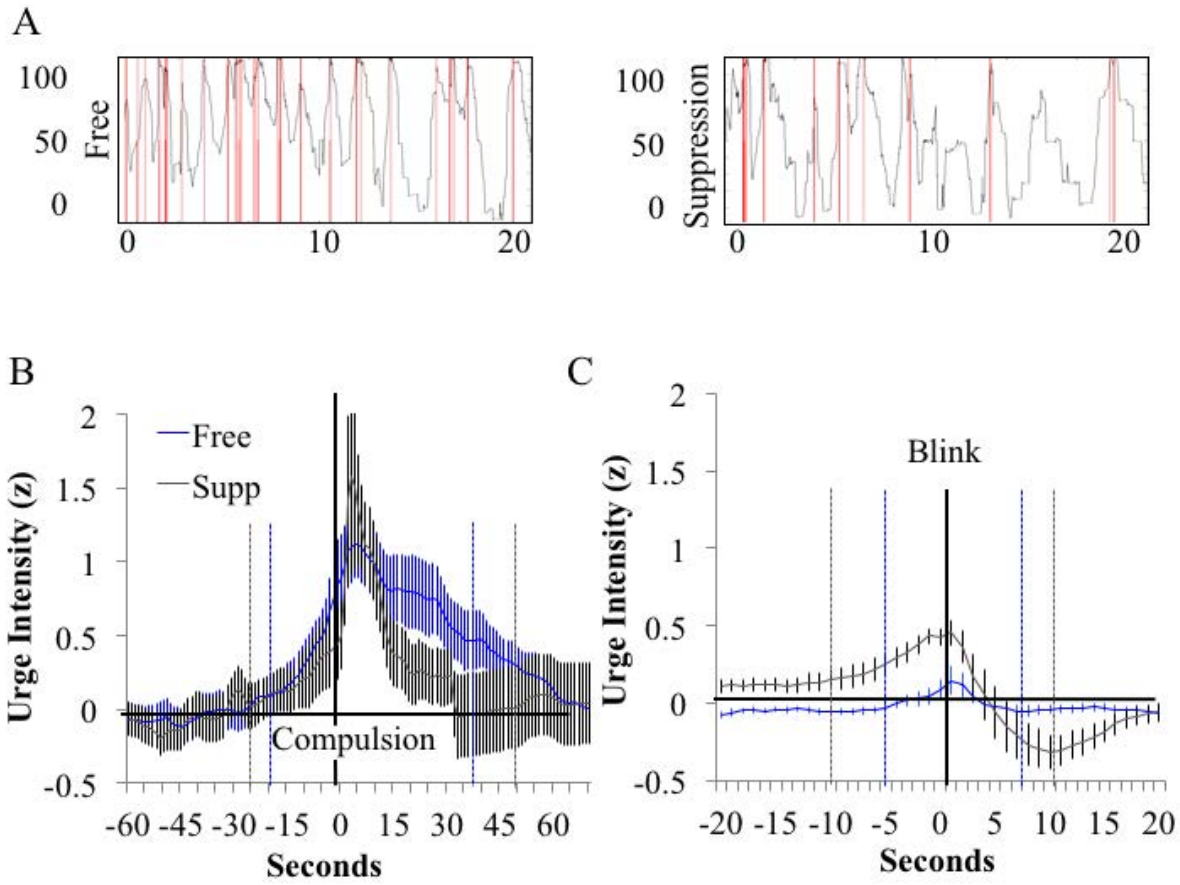

Figure 2.

A. Example of continuous real-time urge intensity data. Self-reported urge intensity (black line) of a representative OCD patient across the 20 min "free" condition and the "suppression" condition. Compulsions are displayed as vertical lines. Please note that the first 10 seconds of each time course were discarded to allow patients to adjust the line to their current urge intensity level.

B. Temporal trajectory of the average z-standardized urge intensity around single compulsions during free compulsions (blue) and suppression (grey). Confidence Intervals (CI) across participants are given for every time-point. Compulsions occurred at time zero. In Patients with OCD, curvilinear regression analyses explained 80% of the variance of average urge intensities in the free compulsions condition and 37% of the variance of average urge intensities in the suppression condition.

C. Average urge intensity trajectory (+/- CI) around single blinks. In healthy controls, curvilinear regression analyses explained 75% of the variance in the urge to blink in the free blinking condition and 87% of the variance in the suppression condition.

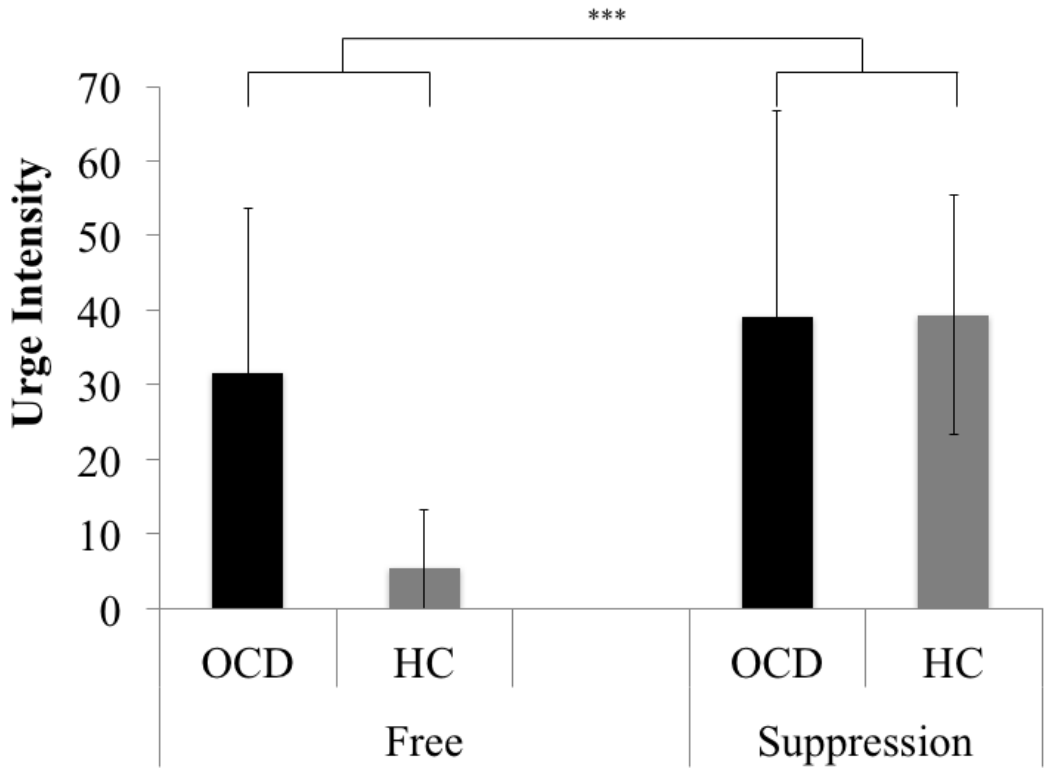

Figure 3.

Mean urge intensity in the free compulsions/blinking and the suppression condition. Urge intensity was overall higher in the suppression condition than in the free condition. Healthy controls indicated a significant increase in urge intensity in the suppression condition, while this increase was only significant in patients with OCD when patients with comorbid tics were excluded.

*** $p < 0.001$

Error bars are standard deviations.

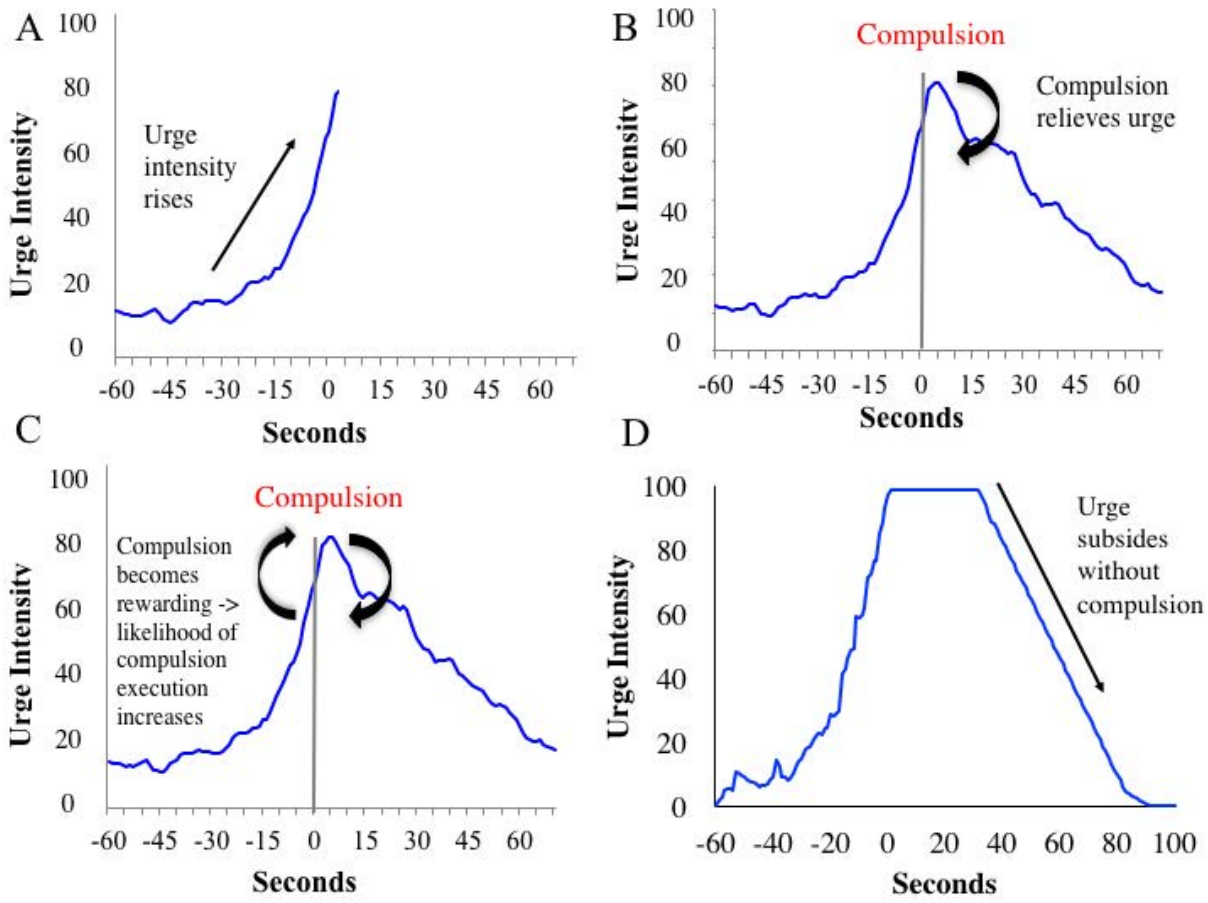

Figure 4. Model of negative reinforcement

A. Patients with OCD feel an increasing urge to execute a compulsion. Our data support this assumption

B. The execution of a compulsion is followed by a relief in urge intensity. This assumption is also supported by the results of this study.

C. The compulsion becomes rewarding because it removes a negative stimulus, the urge (negative reinforcement). Therefore, the likelihood of executing a compulsion increases.

D. Not executing a compulsion in response to an increasing urge enables the patient to experience that urges will subside even when compulsions are not executed. Our data also provides limited support for this assumption. While our data show that this is the case, urge intensity was overall higher in the suppression condition than in the free

condition. During therapy, the urge should decrease overall in the long run (habituation).

Supplementary table 1. Comorbidities and medication

Diagnosed comorbidities (ICD-10)	**% (absolute number)**
Major depressive disorder, single episode, mild (F32.0)	5.26% (1)
Major depressive disorder, single episode, moderate (F32.1)	5.26% (1)
Major depressive disorder, single episode, severe without psychotic features (F32.2)	10.53% (2)
Major depressive disorder, recurrent, moderate (F33.1)	10.53% (2)
Major depressive disorder, recurrent severe without psychotic features (F33.2)	21.05% (4)
Bipolar disorder, current episode depressed, mild or moderate severity (F31.3)	5.26% (1)
Tourette Syndrome (F95.2)	10.53% (2)
Borderline personality disorder (F60.31)	21.05% (4)
Histrionic personality disorder (F60.4)	5.26% (1)
Obsessive-compulsive personality disorder (F60.5)	5.26% (1)
Avoidant personality disorder (F60.6)	5.26% (1)
Dependent personality disorder (F60.7)	10.53% (2)
Pathological gambling (F63.0)	5.26% (1)
Skin Picking Disorder (F63.9)	10.53% (2)
Social phobia (F40.1)	10.53% (2)
Alcohol dependence (F10.2)	10.53% (2)
Attention-deficit hyperactivity disorder (F90.0)	5.26% (1)
Medication	**Absolute number**
Sertraline, Aripiprazole	3
Sertraline, Aripiprazole, Trimipramine	1
Venlafaxine, Risperidone	1
Clomipramine, Aripiprazole	1
Fluoxetine	2
Doxepin, Trimipramine, Lorazepam	1
Venlafaxine, Fluvoxamine	1
Sertraline, Aripiprazole, Lithium	1

Citalopram	1
Escitalopram, Aripiprazole	1
Bupropion	1
Tranylcypromine, Aripiprazole, Promethazine	1

ICD-10 = International Statistical Classification of Diseases and Related Health Problems

Supplementary table 2. Urge intensity distribution parameters

Peak latency	**Mean ± SD**	***F*-value**	***t*-value**	***p*-value**
OCD patients free	5.7s ± 6.6		3.35	**0.005**
OCD patients suppression	9.0s ± 24.7		1.31	0.21
Healthy controls free	0.2s ± 3.5		0.23	0.82
Healthy controls suppression	0.9s ± 3.0		1.24	0.23
Main effect group		2.17		0.15
Main effect condition		0.57		0.46
Group-by-condition interaction		0.17		0.69
Width				
Main effect group	OCD: 69s; HC: 17s	61.41		< **0.001**
Main effect condition	Free: 34s; Supp: 49s	05.25		**0.031**
Group-by-condition interaction		02.84		0.105
Skewedness				
OCD patients free	-0.2 ± 1.0		-0.69	0.50
OCD patients suppression	-0.8 ± 1.7		-1.75	0.11
Healthy controls free	0.3 ± 0.5		1.93	0.075
Healthy controls suppression	-0.5 ± 0.7		-3.08	**0.008**
Main effect group		2.86		0.144
Main effect condition		8.67		**0.007**
Group-by-condition interaction		0.10		0.76
Excess kurtosis				
OCD patients free	-0.14 ± 1.7		-0.33	0.75
OCD patients suppression	3.0 ± 7.1		1.50	0.16
Healthy controls free	-1.0 ± 1.3		-2.91	**0.012**
Healthy controls suppression	-0.4 ± 1.3		-1.17	0.26

Main effect group	4.25	**0.05**
Main effect condition	4.46	**0.045**
Group-by-condition interaction	1.93	0.18

The table displays the results for the characteristics of the urge trajectory across groups and conditions. Comparisons between conditions and groups were made using repeated measures ANOVA (*F*-values). Whether values differed from 0 was tested using one-sample t-tests (*t*-values).

Peak latency = time of the highest point in the urge intensity distribution, negative values show that the centre lies left of point zero. Width = measure of width of the distribution; Skewedness = measure of skewedness of the distribution. Negative values indicate that the decrease is steeper than the increase. Excess kurtosis = roundness/peakedness of peak. Negative values indicate that the peak is flatter than a normal distribution; positive values indicate that the peak is more peaked than a normal distribution. OCD = obsessive-compulsive disorder, HC = healthy controls.