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Exposure and Response Prevention in Virtual Reality for Patients with Contamination-Related Obsessive–Compulsive Disorder: a Case Series

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Abstract

Exposure therapy in virtual reality is successful in treating anxiety disorders. Studies on exposure and response prevention in virtual reality (VERP) in obsessive-compulsive disorder (OCD) are rare, and it is unclear whether distress associated with other emotions than anxiety (e.g., disgust) can be evoked. The present study aimed to investigate whether distress can be induced during VERP in patients with contamination-related OCD (C-OCD) and a primary feeling of disgust. We treated eight female patients with C-OCD with the primary emotion of disgust over six weeks with VERP and assessed their OC symptoms before and after the intervention period with the Y-BOCS. We measured subjective units of distress (SUD), heart rate and skin conductivity (arousal), sense of presence, and simulator sickness during four consecutive exposure sessions. VERP was able to induce distress and arousal. The qualitative feedback was heterogeneous and sense of presence moderate. Patients' OC symptoms reduced over the treatment period with medium to large effect sizes, but only two patients were considered responders; two patients discontinued treatment due to lack of treatment success. Although VERP was able to induce distress and arousal associated with disgust and evoked a moderate sense of presence, the low rate of symptom reduction diminishes the positive results. Possible reasons for the heterogeneous results and implications are discussed. *Trial registration:* German Registry for Clinical Studies (DRKS00016929), 10.04.2019.

Keywords CBT · Psychotherapy · New technologies · Obsessions · Compulsions · Exposure therapy

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Introduction

Disgust is one of the humans "basic emotion" and links together cognitive and bodily responses. The responses related to the emotion disgust (expression, physiology and behaviour) are relatively stable across situations and cultures [1]. Literature on disgust indicates that disgust is – compared to other basic emotions – less responsive to circumstances and consequences, both in intensity and behaviour and resistant to corrective information [2, 3].

More than half of individuals with OCD (56%) have obsessions related to contamination (C-OCD) [4]. When patients with C-OCD are confronted with the feared contaminant (e.g., blood, urine), they will often experience disgust in addition to fear. This is in contrast to many individuals with other subtypes of OCD, particularly checking. Accordingly, studies have shown that individuals with C-OCD experience greater disgust compared to non-clinical controls [5–7]. Moreover, behavioral studies have demonstrated that participants with high contamination obsessions avoid disgust-related stimuli to a larger extent than those with low contamination obsessions [8–10].

Besides playing a major role in C-OCD, disgust is also present in individuals with specific phobias (i.e., spider phobia and blood-injection-injury phobia) [11]. For both OCD and specific phobias, exposure therapy is recommended [12]. However, disgust seems to be a more treatment-resistant emotion than fear [13]. Viar-Paxton and Olatunji [14] argued that the physical consequences of disgust, as for example nausea, may increase the recurrence rate. In line with this, Engelhard et al. [15] demonstrated that learned disgust was resistant to extinction in an undergraduate student sample. Similarly, several studies showed that fear declined to a greater extent than disgust in patients with specific phobias [16, 17] as well as OCD [18] during treatment. A study by McKay [19] compared the decline in anxiety and disgust in patients with C-OCD with the decline in symptoms of other subtypes of OCD (e.g., checking) during exposure and response prevention (ERP) and found that both groups showed a decline in anxiety (in response to an anxiety-evoking stimulus). Yet, patients with C-OCD habituated more slowly and to a lesser degree than patients with other subtypes of OCD, which was confirmed by two subsequent studies [18, 20]. In the treatment of patients with C-OCD it thus is essential to not only target anxiety but also disgust [21].

Exposure Therapy in Virtual Reality in Anxiety Disorders

To successfully target disgust, it is necessary to improve our understanding of its role during exposure therapy. The new technology of virtual reality (VR) is promising in this regard as it allows the exposure environment to be standardized among patients. Moreover, the use of VR in psychotherapy has considerable advantages such as a lower threshold for access to treatment, greater controllability, easier organizational requirements, and efficiency [22, 23]. The implementation of exposure therapy in VR (VRET) has been extensively studied in anxiety disorders [22–32]. A meta-analysis encompassing 30 studies on VRET for specific phobias, social anxiety disorder, post-traumatic stress disorder (PTSD), and panic disorder found a large effect size ($g = 0.90$) in favor of VRET compared to wait list and a medium to large effect size ($g = 0.78$) for VRET compared to psychological placebo conditions [26]. Effect sizes of VRET compared to in vivo exposure did not differ significantly ($g = -0.07$), which indicates noninferiority. A more recent meta-analysis included 16 trials examining the effectiveness of VRET (with or without CBT) in more

severe anxiety disorders and PTSD (excluding specific phobias and subthreshold anxiety disorders) and found a medium significant effect size of $g = -0.49$ in favor of VRET when compared to non-active controls [24]. Compared to CBT, the effect was small and non-significant. Based on the findings in anxiety disorders, it is reasonable to investigate the potential benefits of VR also in the treatment of OCD.

Exposure Therapy in Virtual Reality in OCD

Although a large number of studies have shown that VRET is successful in the treatment of specific phobias, other anxiety disorders, and PTSD, studies on ERP in virtual reality (VERP) for OCD are scarce [29]. The previously mentioned meta-analysis from van Loenen et al. [24] screened for studies on OCD but none did meet the inclusion criteria. It is particularly unclear whether the success generalizes to OCD as this disorder is characterized by high idiosyncrasy and cognitive avoidance, making implementation challenging. Moreover, it may be challenging for patients, in particular for patients with C-OCD, to use a device (i.e., the VR glasses) that has been used by other patients. As triggers are only visual (no smell or touch) during VERP, it is unclear in how far distress can be induced in patients that primary experience disgust. In contrast to this, the "law of similarity" (the image is equally to the object) indicates that distress could be well triggered by VERP in patients with C-OCD with the primary emotion of disgust as it suggests that disgust can be elicited by only the percept of a stimulus even when there is knowledge that the stimulus is not real [2].

Moreover, there is preliminary evidence for the feasibility of VERP in OCD [33–35]. Three studies concluded that it may be possible to induce anxiety and disgust with contamination-related virtual environments and therefore give cause for further research. The study by Belloch et al. [33] investigated the feasibility of four different scenarios in a contaminated virtual environment (COVE) in four women with C-OCD in a one-session intervention. Results indicated that the COVE produced a satisfactory sense of presence (i.e., the illusion that the virtual environment is real; sense of presence is considered a key mechanism of anxiety induction during VRET) [28, 36] and was able to induce both anxiety and disgust. Interestingly, the authors found that anxiety but not disgust, which was rated after each scenario (the patient indicated his/her levels of anxiety and disgust on visual analog scales), correlated with emotional engagement and sense of presence during VERP. Unfortunately, the VERP was not implemented over a long treatment period. Laforest et al. [34] investigated the use of VERP in three patients with C-OCD within a multiple-baseline protocol with baseline periods of either three, four, or five weeks. They provided a therapeutic VR environment that consisted of a virtual public washroom with varying degrees of dirty stimuli and without any cleaning utensils. The intervention period was twelve weeks, with weekly sessions that lasted about 60 min. VERP was conducted in eight of twelve sessions; after four sessions the participants were instructed to practice in vivo ERP as homework (which makes interpretation of the effect of the VERP difficult). All three participants reported a significant reduction in obsessions and compulsions (with a reduction of 7 to 9 points in the Yale-Brown Obsessive Compulsive Scale, Y-BOCS), but the treatment success was not maintained at the 12-month follow-up in two of the three participants. Inozu et al. [35] were the first who included a control condition in a study assessing the use and effectiveness of VERP for treating C-OC symptoms in a non-clinical sample of individuals with high contamiation sensitivity. The

experimental group received a minimum of three VERP sessions with varying disgust-related VR scenarios based on the ones used in the study of Belloch et al. [33]. From their results, the authors concluded that VERP was an effective technique in reducing the severity of C-OC symptoms as they found significant decreases in anxiety, disgust, and urge to wash scores in the experimental group compared to the control group at post-treatment. In contrast, they did not find significant differences in the reduction rates of disgust and anxiety after repeated VERP sessions and also no significant differences on self-reported measures such as the Y-BOCS. As in the previously mentioned studies, group sizes were small ($n = 9$; $n = 12$) and generalizability is limited. Although all three studies represent an important first step, they do not provide physiological data (such as heart rate).

Aim of the Present Study

The aim of the present study was twofold. First, we attempted to explore barriers and facilitating factors for the induction and course of distress and arousal within a case series of eight patients with C-OCD and the primary emotion of disgust who received VERP over a period of six weeks, with four consecutive exposure sessions. In addition to assessing subjective distress, we recorded psychophysiological activity (arousal) during VERP in order to validate the subjective distress ratings by psychophysiological data. Second, we were interested in investigating the feasibility and preliminary effectiveness of VERP. In particular, we expected (1) a decline in patients' OC symptoms from baseline to post intervention, (2) an increase of distress (self-report) and arousal (heart rate, galvanic skin response), (3) a high acceptance of the intervention, (4) no increase in simulator sickness from before to after the session, and (5) a high sense of presence.

Method

Design

The eight cases were derived from an ongoing assessor-blind randomized controlled trial (RCT) with parallel assignment to the intervention group or the control group. The study was comprised of a baseline and a post assessment that were conducted both as personal diagnostic interviews and as online self-assessment questionnaires. The intervention group received VERP over a period of six weeks that included four consecutive exposure sessions. Members of the control group did not receive VERP but were given an established self-help manual for OCD [37, 38] after the last assessment. Both groups had access to regular outpatient care (day or inpatient treatment led to exclusion). For the present case series, we focused on the baseline and post assessments as well as the in-session data of eight participants with C-OCD who were allocated to the intervention group within the RCT and whose data were available at the time of data analyses (see inclusion criteria). The RCT was approved by the local ethics committee of the Center for Psychosocial Medicine of University Medical Center Hamburg-Eppendorf in Germany (Lokale Psychologische Ethikkommission am Zentrum für Psychosoziale Medizin, LPEK-0020). The RCT was registered at 10.04.2019 with the German Registry for Clinical Studies (DRKS00016929).

Participants

Participants were recruited through online advertisements (e.g., related websites/forums, Google AdWords) and by contacting participants from earlier studies whose consent had previously been obtained. The main inclusion criteria for the RCT was the presence of contamination and/or checking obsessions and compulsions based on the Mini International Neuropsychiatric Interview (MINI) [39], written informed consent, age between 18 and 75 years, sufficient command of the German language, and willingness to participate in VERP for six weeks.

For the present case series, patients were included only if they were randomized into the intervention group, had C-OCD (according to the Y-BOCS symptom checklist), participated in the VERP, and reported disgust as their primary emotion in the context of their OCD. Interested individuals who had lifetime symptoms of psychosis, a severe neurological disorder, or were experiencing acute suicidality were excluded from the study.

Procedure

Trained interviewers (master's students) conducted personal diagnostic interviews determining OCD and comorbid disorders using the MINI as well as OC symptom severity using the Y-BOCS. Afterwards, participants were randomized into one of the two conditions (VERP or control group). Throughout the following six weeks, participants in the intervention group received weekly treatment sessions (see "19") that lasted approximately 1.5 h each. During the four consecutive exposure sessions (session 3 to 6), subjective units of distress (SUD) were assessed approximately every three minutes, and heart rate and skin conductivity were measured continuously. Prior to and after each exposure session, simulator sickness was assessed (see "11"). After six weeks, all participants filled out a subjective appraisal rating scale for VERP and rated subjective sense of presence during VERP (Igroup Presence Questionnaire), and the Y-BOCS was conducted once again.

Measures at Baseline and Post Assessments

Yale-Brown Obsessive Compulsive Scale

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [40, 41] is a semi-structured interview that assesses the presence and severity of OC symptoms. The range of the total score is 0 to 40 (subclinical [0–7], small [8–15], medium [16–23] severe [24-31], and extreme [32–40]) [42]. For the German version of the Y-BOCS [43], high inter-rater reliability ($r = .90$) and also good internal consistency (Cronbach's $\alpha = .80$) [44] have been reported.

Measures at Post Assessment

Igroup Presence Questionnaire

The Igroup Presence Questionnaire (IPQ) [45] is a self-rating questionnaire that measures the subjective sense of presence in a virtual environment. It consists of three subscales—(1)

spatial presence (items 2–6), (2) involvement (items 7–10), and (3) experienced realism (items 11–14)—and one additional item measuring the general sense of "being there" (item 1). Except for item 7 and item 12, all items were measured on a 7-point Likert scale ranging from 0 = *fully disagree* to 6 = *fully agree*. Items 7 and 12 were measured on a 3-point Likert scale from 1 = *extremely aware* to 3 = *not aware* and from 1 = *not consistent* to 3 = *very consistent*, respectively. The total possible score ranges from 14 to 94. The internal consistency of the IPQ is good, with Cronbach's α between .85 and .88 [45, 46]. Studies using the IPQ in VRET have found mean scores ranging from 18.3 to 55.4 [47, 48].

Subjective Appraisal Rating Scale

The Subjective Appraisal Rating Scale measures the acceptability of an intervention and has been previously used by Jelinek et al. [49, 50]. We adapted the scale for VERP to assess how patients evaluated and accepted the intervention. The scale consists of 18 items (see Figs. 4 and 5). In total, there are 17 closed questions, which are rated on a 5-point Likert scale ranging from 1 = *completely agree* to 5 = *completely disagree*, and one open question that assesses what the participants liked about VERP.

Measures In-session

Simulator Sickness Questionnaire

The Simulator Sickness Questionnaire (SSQ) [51] is a self-rating questionnaire that assesses symptoms associated with the perception of motion without actual physical motion, known as simulator sickness. The original version consists of 16 items on 3 subscales—(1) oculomotor (items 3–5, 11), (2) disorientation (items 12–14), and (3) nausea (items 6, 8, 15, 16), but a more recent factor analysis revealed a better fit for a two-factor structure with (1) nausea (items 1, 6–8, 12–16) and (2) oculomotor (items 2–5, 9–11) [52]. We used 15 items from the original 16-item scale; due to a technical problem, the item "Dizziness (eyes closed)" was not assessed. All items are rated on a 4-point Likert scale from 0 = *none* to 3 = *severe*. Internal consistency of the SSQ is high (Cronbach's $\alpha = .87$) [52]. This applies also to our study, in which the item "Dizziness (eyes closed)" was not included (Cronbach's $\alpha = 0.88$).

Subjective Units of Distress Scale

The Subjective Units of Distress Scale (SUDS) [53] was used to assess the subjective distress. Patients are asked to self-rate their current perceived intensity of distress on a scale from 0 = *no distress* to 100 = *maximum distress*. SUD ratings were assessed approximately every three minutes (for reasons of practicability for the therapist as well as for the recording of each important event, we decided against a standardized time recording of SUD) as well as immediately before and after the VERP.

Heart Rate

As a physiological indicator of distress, heart rate (HR) was measured during VERP sessions using a NeuLog heart rate and pulse logger sensor NUL-208. The device measures beats per minute (BPM) via an electrode attached to the fingertip, with a possible range

from 0 to 240 BPM and a maximum sampling rate of 100 per second. In addition to the continuous digital recording, the current HR can be read on a connected screen.

Skin Conductivity

To measure galvanic skin response (GSR) during VERP sessions, a NeuLog GSR logger sensor NUL-217 was used. Via electrodes attached to two fingers, the device measures skin conductance level in microsiemens (μS), with a maximum sampling rate of 100 per second.

Exposure Therapy in VR

The therapy sessions lasted 60 to 90 min. All six therapy sessions were highly structured, and the four study therapists were provided with a manual based on emotional processing theory (referencing a CBT manual for OCD by Oelkers and Hautzinger [54]) and detailed instructions in order to achieve high standardization of the sessions. The aim of the first two sessions was to prepare the patient for the VERP (e.g., rationale behind ERP and presentation of the distress-inducing objects that would be included in the VR environment by a video of the VR environment). The third session started with an introduction to the VR equipment in a neutral VR environment in which no OC-triggering stimuli were included (i.e., a virtual room not furnished). Then, the actual VERP started. The therapist instructed the patient with the aim of increasing disgust and preventing the patient from engaging in compulsions and avoidance behavior. The fifth and sixth sessions were conducted using the same procedure as the third session. Based on the previous rating of stimuli (session 2), gradual exposure with medium intensity at the beginning of the VERP progressed to the most distress-provoking stimuli. The therapists were licensed psychological psychotherapists and psychotherapists in training, all with at least a master's degree.

The VERP was conducted using game engine Unity (version 2018.2.9f1) with a head-mounted display (HTC Vive Pro). The participant was tracked with the help of four base stations in each corner, which formed a virtual room of 7.5 m^2. The participant could only walk through the VR to a limited extent but could instead use teleportation with a controller to go to a different location in the VR (StreamVR Teleport); this is recommended to prevent motion sickness [55]. The therapist could see on a monitor what the patient was seeing through the head-mounted display. The virtual environment aimed to elicit contamination obsessions by displaying a filthy (e.g., blood, urine and feces) public restroom with various degrees of filthiness (see Fig. 1 for an illustration of the VR environment). The VR had an area with sinks plus seven separate stalls for the women's restroom and two for the men's. Each stall had a toilet, and the common area provided four sinks and four mirrors for both the women's and men's restrooms. No items for eliminating germs or for cleaning (i.e., cleaning tools or gloves) were visible in the VR.

Statistical Analyses

In order to evaluate the change in OC symptomatology from baseline to post assessment as well as the differences in SUD ratings from baseline (i.e., at the start of the session, when the participants put on the head-mounted display) to peak (i.e., the maximum SUD rating during a session), we performed *t*-tests (assumptions were checked and not violated). For effect size Cohen's *d* were calculated applying Cohen's [56] rules of thumb for

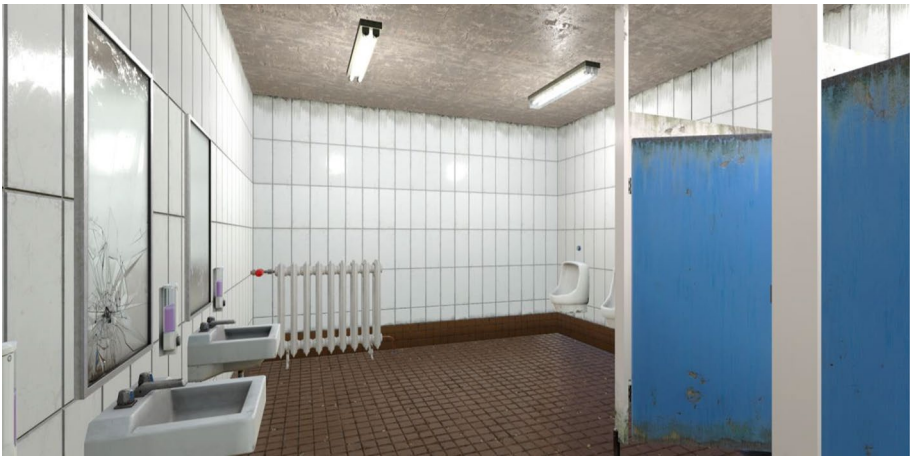

Fig. 1 Screenshot of the virtual environment

evaluation with a Cohen's *d* of ≈ 0.2, ≈ 0.5, and ≈ 0.8, corresponding to small, medium, and large effects. Differences from baseline to peak SUD were only analyzed for session 3, as this was the only session for which data for all eight participants were available. The course of the SUD ratings over the course of all available ERP sessions (sessions three to six) as well as the SSQ, which patients assessed immediately before and after each exposure session, are descriptively displayed. Means of the available ratings on the SSQ were aggregated across the four VR sessions. To evaluate the acceptability of the intervention, the subjective appraisal ratings as well as the IPQ at post assessment were also reported descriptively. Pearson's correlations were calculated for the relationship between sense of presence (IPQ) and the peak SUD rating of session 3 as well as for the relationship between sense of presence and the reduction in OC symptoms (Y-BOCS).

A low-pass Butterworth filter with the cut-off frequency at 1 Hz was used to smooth the GSR and HR signals. In addition, a threshold of 30 Hz to 200 Hz was applied to the HR data as this range approximately covers the HR of human subjects of all ages both at rest and during high-intensity activities [57–59]. Both types of signals were normalized using the following formula [60, 61]:

$$S = \frac{s - \min(\bar{s})}{\max(\bar{s}) - \min(\bar{s})}$$

where S is the normalized signal, s is the smoothed signal, and $\bar{s}$ is the signal taken over the entire session. The average of S over a 5-s window was used for the analysis.

Results

Sample

Eight female patients with C-OCD were included in the present case series (see Table 1 for sociodemographic data), with a mean illness duration of 16 years and an onset at 24 years. The main comorbid diagnoses were depression (25%, $n = 2$ with a current depressive episode; 25%, $n = 2$ with a lifetime episode), binge eating disorder 12.5%

Table 1 Demographic and Treatment-Related Data: Mean (*M*) and Standard Deviation (*SD*) or Frequency (*n*)

	Patients with OCD ($N=8$)
Background	
Gender (female/male)	8/0
Age (years)	40.13 (11.53)
Years of school education	11.75 (1.49)
Treatment-related variables	
Illness duration (years)	16.25 (5.68)
Previous and current treatments	2.81 (1.41)
Age at OCD onset	24.00 (16.35)
Medication	
Antidepressant (AD)	3
Antipsychotic (AP)	0
Combination (AD + AP)	1
Beta blocker	1
None	3

($n=1$), and generalized anxiety disorder 12.5% ($n=1$). Only three patients (37.5%) were not taking any psychopharmacological agents (see Table 1 for specifics). All of the participants had previous experience with psychotherapy; five participants (62.5%) had undergone psychotherapy in the past, and three participants (37%) reported that they were currently receiving outpatient treatment. Six patients (75%) reported that they had previously undertaken exposure therapy, four of those (75%) more than once. One of these six patients (16.7%) indicated that the exposure therapy had not helped at all; three indicated (50%) that it had been very successful.

Table 2 Psychopathological Data at Baseline and Post Assessments: Mean (*M*) and Standard Deviation (*SD*) or Frequency (*n*)

	Patients with OCD ($N=8$)		
	Baseline	Post	Statistics
Y-BOCS total	29.00 (4.87)	25.00 (8.82)	$t(7)=2.30$, $p=.055$, $d=1.82$
Patient 1	27	29	
Patient 2	29	27	
Patient 3	36	36	
Patient 4	37	36	
Patient 5	24	14	
Patient 6	27	21	
Patient 7	27	24	
Patient 8	25	13	
Y-BOCS obsessions	14.00 (3.02)	12.87 (4.67)	$t(7)=0.93$, $p=.386$, $d=0.47$
Y-BOCS compulsions	15.00 (2.39)	12.13 (4.22)	$t(7)=3.75$, $p=.007$, $d=3.31$

Y-BOCS Yale-Brown obsessive compulsive scale

Psychopathology

Table 2 displays OC symptom data of the sample at baseline and post assessments by *t*-tests and effect sizes (Cohen's *d*). The sample showed a reduction in the Y-BOCS subscale compulsions with a large effect size ($d = 3.30$). A large effect size was found for the change in the Y-BOCS total sore ($d = 1.82$) and a medium effect was observed for the subscale obsessions ($d = 0.47$), however, both effects lack of significance in the current sample of eight patients. According to the established response criterion of at least a 35% decrease in the Y-BOCS total score [62], only two of the eight patients were classified as responders over the intervention period.

In-session Data

The difference in the SUD ratings from baseline to peak in session 3 (i.e., the first VERP session) is depicted in Table 3. An induction of subjective disgust-related distress (as measured by the SUD) in the first exposure session was possible in six out of eight patients (75%). On average, the sample showed a significant increase in SUD ratings over the session ($t(7) = 3.23$, $p = .015$) with a large effect size ($d = 1.11$).

The course of the SUD ratings (session 3) for each participant is presented in Fig. 2. These ratings are incomplete for various reasons, such as discontinuation of treatment due to lack of success (patients 2 and 3, $n = 2$, 25% dropout rate), cancellation of a session due to illness (session 6 of patient 1), and technical problems with the VR (session 6 of patient 7).

The differences in the GSR and HR signals from baseline to peak in session 3 are shown in Table 4 and the individual course of GSR over the session in Fig. 3. A significant increase over the session as assessed by the differences from baseline to peak was observed for HR ($d = 2.38$) as well as GSR ($d = 4.84$).

After each session, patients indicated how they evaluated VERP and whether the environment had felt real. Selected qualitative feedback of each patient is provided in Table 5.

Simulator Sickness and Sense of Presence

Responses to questions about the participants' reactions to VR (i.e., simulator sickness and sense of presence) are depicted in Table 4. Ratings of simulator sickness (nausea and

Table 3 Subjective Units of Distress (SUD), Galvanic Skin Response (GSR) and Heart Rate (HR) from Baseline to Peak in Session 3

	M (SD)	Minimum	Maximum	Statistics
SUD baseline*	33.12 (26.31)	0	80	$t(7) = 3.23$, $p = .015$, $d = 1.11$
SUD peak*	67.50 (24.93)	30	100	
HR baseline**	0.38 (0.13)	0.28	0.57	$t(3) = 5.46$, $p = .010$, $d = 2.38$
HR peak**	0.83 (0.09)	0.72	0.94	
GSR baseline**	0.34 (0.18)	0.22	0.6	$t(3) = 7.52$, $p = .005$, $d = 4.84$
GSR peak**	0.99 (0.01)	0.98	0.99	

*$N = 8$; **$n = 4$

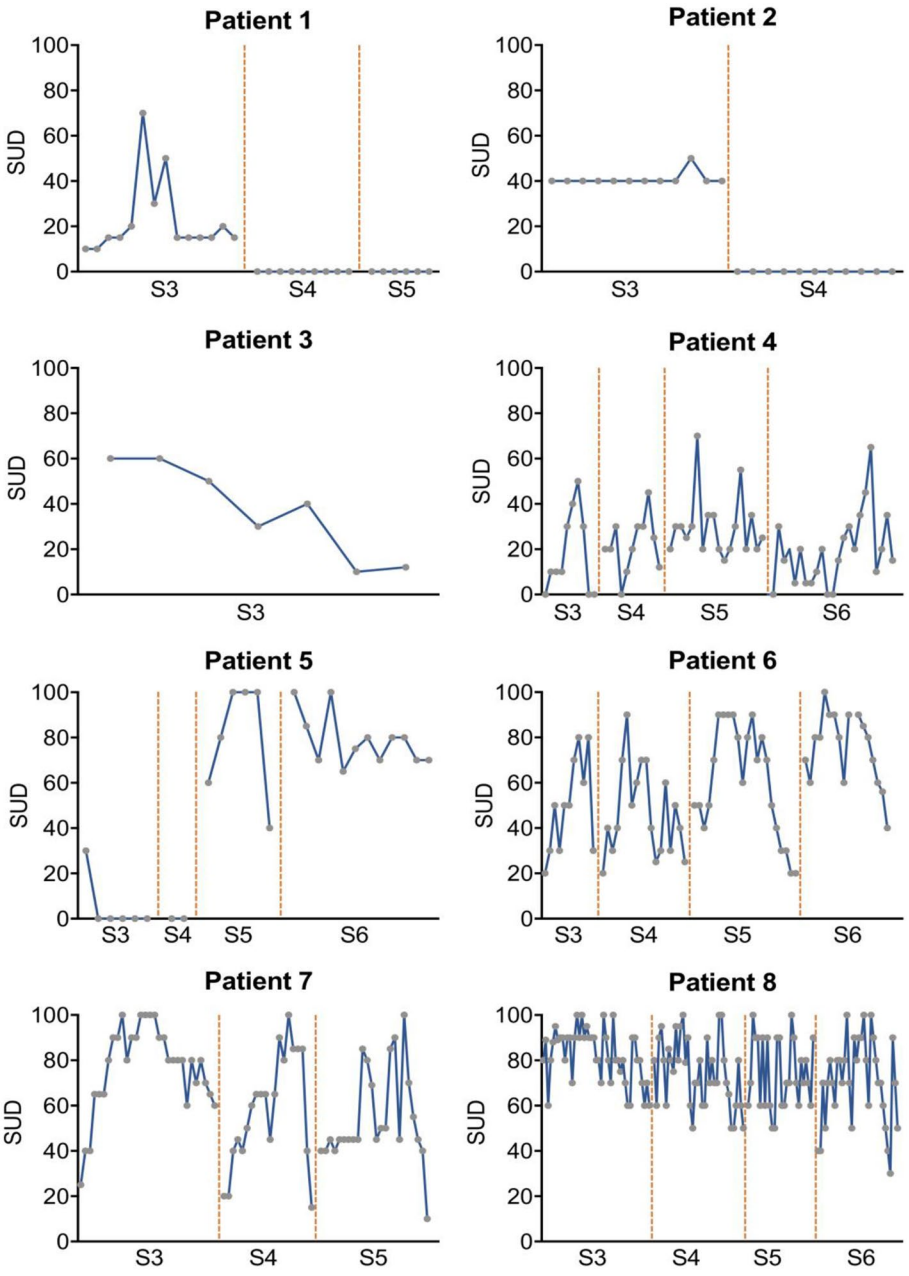

Fig. 2 Subjective units of distress across all exposure and response prevention in virtual reality sessions (sessions 3–6), $N = 8$

Table 4 Means and Standard Deviations for SSQ and IPQ, Wilcoxon test for SSQ; Differences before and after Exposure and Response Prevention in Virtual Reality (VERP)

Subscales	Pre VERP *M (SD)*	Post VERP *M (SD)*	Statistics
SSQ*[a]	8.57 (5.26)	9.71 (5.26)	$t(7) = .74$, $p = .498$, $d = 0.28$
Nausea	3.22 (3.57)	3.89 (2.50)	$t(7) = .91$, $p = .394$, $d = 0.32$
Oculomotor	5.35 (3.17)	5.83 (3.49)	$t(7) = .43$, $p = .681$, $d = 0.16$
		Post assessment *M (SD)*	
IPQ**	-	36.57 (17.52)	-
Spatial presence	-	16.29 (5.65)	-
Involvement	-	11.29 (5.35)	-
Experienced realism	-	6.00 (7.48)	-

SSQ simulator sickness questionnaire, *IPQ* Igroup presence questionnaire

*$N = 8$; ** $n = 7$

[a]all available data from sessions 3–6 were aggregated; the two-factor structure proposed by Bouchard et al. [52] was assumed

oculomotor) before and after the VERP only increased with small effect size (Cohen's $ds < 0.35$). The overall sense of presence was moderately high ($M = 36.57$, $SD = 17.52$). The positive correlation in large magnitude ($r = .746$) of sense of presence with the peak SUD rating of session 3 bordered on statistical significance ($p = .054$). Moreover, sense of presence correlated in moderate magnitude ($r = .558$) with the reduction in the Y-BOCS from baseline to post assessment (difference score), however, in the current sample of eight patients, this correlation was not significant.

Subjective Appraisal

Results on acceptability of VERP are displayed in Fig. 4 for the positively formulated items and Fig. 5 for the inverted items. All patients (100%) agreed that they "felt com-

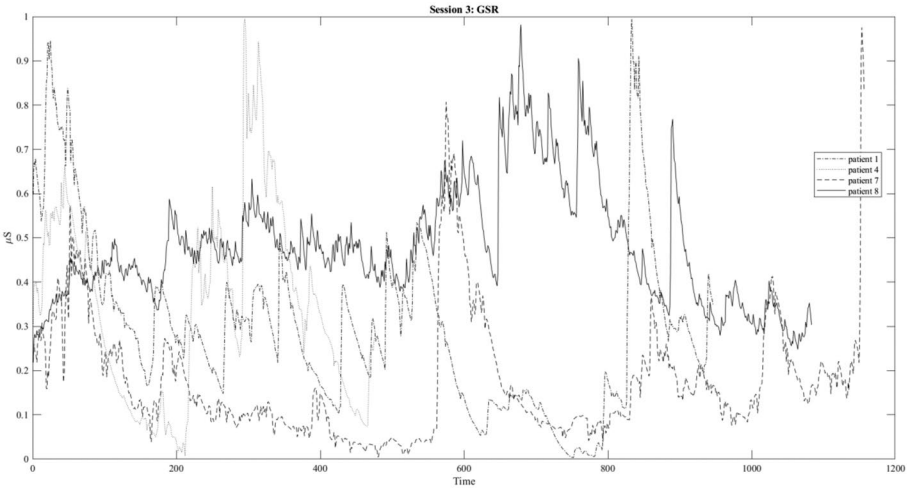

Fig. 3 Galvanic skin response (GSR) for session 3, $n = 4$

Table 5 Selected Qualitative Feedback of each Patient

Patient number	Statement
1	"You feel like you're in the room. Your own feet and hands are missing. Objects are not so realistic, sometimes slightly out of focus or transparent. I feel more disgust than fear. In reality, it is the other way around."
2	"Before the session, I was very excited, even the day before. Within the session, I could not ignore the fact that it was VR, and I was desperate because it was not working for me. I put a lot of pressure on myself."
3	"It seemed very real and disgusting but also like a computer game. The movement was very unrealistic."
4	"It was sometimes blurry, and the excrement did not look real."
5	"First, it did not seem realistic at all; I was rather relaxed and curious. I knew that nothing could happen to me.... However, when the therapist pointed out more strongly that this toilet might already have been used by dirty people who didn't care about hygiene and I no longer was focused on the virtual setting, I felt strong disgust."
6	"It seemed very realistic. I had the thought that it was not real, but it physically felt very real."
7	"Very realistic. But no smells and no insects. However, I had the feeling that the feces would stick to my dress. Several times I had the impulse to tear off the glasses, but I didn't want to undermine the success of the therapy. I noticed my avoidance behavior. For example, I kept my distance from the walls and the toilet seat."
8	"Very realistic. I was able to get fully involved, and I didn't notice any avoidance behavior."

fortable with the therapists" and that the "goals and rationale of VERP were clear" and disagreed that "VERP had negative effects on other interventions." More than half of the participants (57.2%) agreed on most of the positively formulated items (e.g., "VERP was useful and sensible"). Patients' response to the items regarding the reduction in compulsion and obsessions due to the VERP was rather heterogeneous (see Figs. 4 and 5). More than 70% disagreed with almost all negatively formulated items (e.g., "I had to force myself to

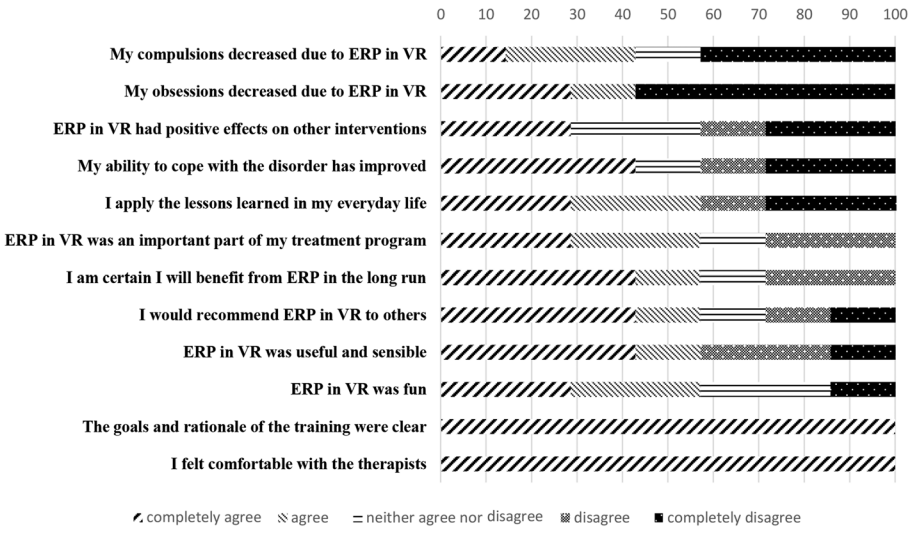

Fig. 4 Subjective appraisal (positive items) of the exposure and response prevention in virtual reality (VERP) for patients with OCD at post assessment ($n = 7$). The scale ranges from 0 to 100%

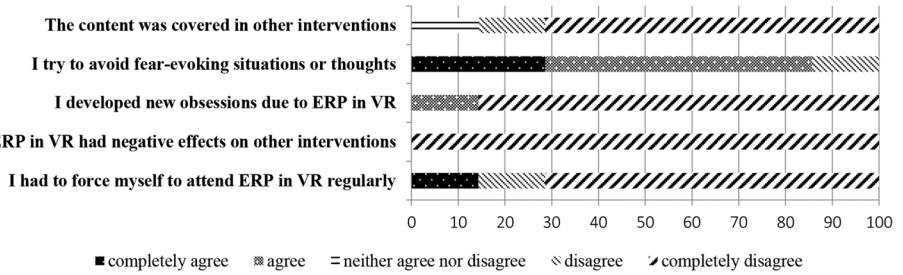

Fig. 5 Subjective appraisal (inverse items) of exposure and response prevention in virtual reality (VERP) for patients with OCD at post assessment ($n=7$). The scale ranges from 0 to 100%

attend VERP regularly"), but 85.7% agreed that they "try to avoid fear-evoking situations or thoughts."

Discussion

The present case series aimed at investigating the feasibility as well as barriers and facilitating factors of VERP in patients with C-OCD and the primary emotion of disgust during exposure and response prevention therapy. Results indicated that the induction of subjective distress (SUD) in the first exposure session occurred in six out of eight patients (75%). Patients' OC symptoms reduced with medium to large effect sizes (Y-BOCS), but only the reduction in compulsion was significant. Sense of presence (assessed by the IPQ) was verified by most patients, and the increase of level of simulator sickness (assessed by the SSQ) over the session was only small. The subjective evaluation of the intervention was heterogeneous.

Induction of Distress

According to the differences in the subjective distress ratings from baseline to peak in session 3 (i.e., the first exposure session) as well as the significant changes in vital parameters, VERP was able to induce subjective distress. For subjective distress, the mean SUD rating at baseline was 34.38 ($SD=27.96$) and increased to a mean peak rating of 67.50 ($SD=24.93$) with a large effect size ($d=1.11$) during the course of the VERP session. On an individual level, subjective distress numerically increased in six out of eight patients in session 3. Moreover, an increase in subjective distress was found later (in sessions 5 and 6) in patient 5, who had not reported an increase in session 3. Effect sizes were large for changes in arousal assessed with GSR ($d=4.84$) and HR ($d=2.38$) measurements and significantly changed over the course of the session (i.e., from baseline to peak). Thus, the subjective and physiological data match, indicating that the present VERP is able to induce distress and arousal in patients with C-OCD and the primary emotion of disgust. Notably, this is not self-evident. In VR, patients are aware that the environment is not "real", that is, that contamination with a potential disease is not possible in a virtual public restroom. One may argue that this is also the case for in sensu exposure, which also works in OCD [63]. However, in in sensu exposure the patient is able to imagine a highly idiosyncratic situa-

tion. In VR, on the other hand, the situation is highly standardized, which might additionally prevent feelings of disgust. Moreover, VR exposure is highly limited in comparison to in vivo exposure because "contamination" by touching things is not possible in VR.

Contrary to the assumption that the highest possible induction of distress and subsequent decline are necessary in exposure therapy, it has been argued that (besides expectancy violation) a sustained level of distress is a prominent predictor of long-term outcome [64, 65] and thus needs to be induced in exposure treatment. In the present VERP, we achieved a sustained level of disgust over the course of the sessions, particularly in patients 6, 7, and 8 (Fig. 3), highlighting the feasibility of VERP in C-OCD.

Sense of Presence and Simulator Sickness

To evaluate VERP, a sufficient sense of presence is considered a key mechanism of success [28, 36]. This may be indicated by the increase in distress during VERP but was additionally measured by the IPQ as well as open questions. Compared to other studies investigating the use of VR in the treatment of anxiety disorders ($M = 18.3–55.4$) [47, 48], the reported sense of presence in the present VR environment was moderate ($M = 36.57$). Moreover, the subjective statements of three patients emphasize the pronounced sense of presence in the current environment (patients 6, 7, and 8; see "24"; e.g., "It seemed very realistic. I had the thought that it was not real, but it physically felt very real"). However, certain features of the current VR environment (e.g., the movement was described as unrealistic; see "24") may have reduced the feeling of presence. The need for a more realistic environment in order to induce distress in all patients was, for example, indicated by patient 5 ("It does not seem realistic at all; I was rather relaxed and curious. I knew that nothing could happen to me"), which was also reflected in the course of the SUD ratings (see Fig. 3; the SUD ratings of this patient were almost all 0 in the first two VR sessions). This patient's distress first emerged in session 5, potentially after mental avoidance was reduced ("However, when the therapist pointed out more strongly that this toilet might already have been used by dirty people who didn't care about hygiene and I no longer focused on the virtual setting, I felt strong disgust"). From this it could be deduced that the instructions of the therapist are of major importance and play a role in controlling the effects of the exposure. This might underline the hypothesis that a high level of sense of presence may not be obligatory when experiencing disgust, since disgust can already be resolved by an image and not by experiencing real objects (see introduction "law of similarity").

Additionally, the correlation of sense of presence with the peak SUD rating in session 3 reached statistical trend level, and we expect the effect to reach significance in a larger sample ($r = .746$, $p = .054$). This is only partly in line with the study by Belloch et al. [33], who found no relationship between sense of presence and disgust but did find a relationship between sense of presence and anxiety. For anxiety, the relationship seems to be well established as a meta-analysis found a medium effect size for the correlation between sense of presence and the peak anxiety during the first exposure session ($r = .28$, 95% CI: 0.18–0.38) with varying effect sizes across different anxiety disorders (high correlations for fear of animals, small correlations for social anxiety disorder) [28]. Our study suggests that this relationship also exists for patients with C-OCD and the primary emotion of disgust, but this needs to be validated in a larger sample and with an explicit rating of the emotion disgust. The same applies to the relationship between sense of presence and reduction in the Y-BOCS, which in our study showed a moderate magnitude (presumably again due to

the small sample size) but did not reach significance. However, correlational analyses need to be interpreted cautiously due to the small sample size.

The results on simulator sickness, as an indicator of acceptability, were satisfactory as they were generally low and the increase between the assessments before and after the VERP session was only small. This indicates that no adverse effects in terms of nausea or oculomotor disturbances occurred in the current study, further highlighting the feasibility of the current VR environment.

Reduction in OC Symptoms

On average, the severity of compulsions (assessed by the Y-BOCS subscale) was reduced after the intervention, with a large effect size ($d = 3.30$). For the improvement of the Y-BOCS total score also a strong effect was found ($d = 1.82$), although it only reached statistical trend. For the decrease of the Y-BOCS subscale obsessions, a medium effect ($d = 0.47$) was found with absence of significance in the current sample of eight patients. The non-significant findings regarding the improvement of symptom severity measured with the Y-BOCS correspond with the results found in Inozu's study [35]. If the established response criterion of at least a 35% decrease in the Y-BOCS [62] was used, only two of the eight patients could be classified as responders over the intervention period (see Table 2).

In general, however, our findings on the decrease in OC symptoms due to VERP have limited informative value due to the small sample size. While these results are partly in line with the finding of Laforest et al. [34] reporting a reduction in both compulsions and obsessions immediately following VERP in three patients with C-OCD, our nonsignificant findings in the Y-BOCS total and compulsions scores may be due to several reasons. First, an effect might have existed but the sample size was too small (the total Y-BOCS score showed a strong effect of $d = 1.82$), so the analyses might have lacked the power to detect it [66], especially with the large variation in the course of OC symptoms (reflected in the standard deviations). Second, the number of responders ($\geq 35\%$ decrease in the Y-BOCS) was very low, which may be explained by the long illness duration and previous treatments in the past or present (see Table 1). More specifically, one patient reported that previous ERP had not helped her, which would reduce the chance of treatment effects in this study [67]. Third, conducting four sessions of VERP is presumably insufficient to evoke a significant decline in obsessions. According to Laforest et al. [34], even twelve sessions of CBT, including eight sessions in VR, may be too short to treat such a chronic and complex disorder. Furthermore, in the study by Laforest et al. [34], homework, including in vivo ERP, was assigned in some sessions, so the symptom improvement may not be due to VERP alone. To conclude, studies with larger samples are needed to demonstrate whether a reliable symptom reduction can be achieved solely by VERP.

Subjective Appraisal of Exposure and Response Prevention in Virtual Reality

The subjective evaluation of VERP was largely positive. However, patient 8 stated that she developed new obsessions (negative-formulated item). As she also stated that her obsessions had improved over the intervention (positive-formulated item), a clear interpretation of the results is challenging. Approximately 57% agreed that "ERP in VR was useful and sensible," which highlights the positive appraisal of the intervention. In view of the high dropout rate in in vivo ERP (18.7%) [68], good acceptance of the intervention likely fosters adherence to the intervention. The noncompletion rate of 25% ($n = 2$)

in the current study was high, which, in combination with the predominantly positive evaluation of the intervention, suggests a heterogeneous appraisal of the VERP. Two patients (patients 2 and 3) discontinued the treatment due to lack of treatment success, which is also reflected in their qualitative feedback. Patient 2, in particular, apparently attributed the lack of success to herself ("Within the session, I could not ignore the fact that it was VR and I was desperate because it was not working for me. I put a lot of pressure on myself."). This result demonstrated again that the sense of presence must be improved so that patients feel more immersed in the VR environment. Furthermore, this is an important finding that underlines that patients' pressure on themselves needs to be more specifically addressed during the sessions. Additionally, in the patient information about this therapy it should be more explicitly stated that VERP does not work for everyone.

Limitations

Several limitations of the present study have to be acknowledged, especially the small sample size and the uncontrolled design that clearly limit the generalizability of our findings. Our study, as with any case series, could be subject to a selection bias as the cases were selected by the researchers (although selection criteria were determined before the selection). In addition, due to technical problems several pieces of data of the vital parameters are missing. Furthermore, the present case series lacks follow-up data, and thus no conclusion can be made with regard to long-term effects. Moreover, our sample only consisted of female participants. Additionally, no reliability indicator existed for the Y-BOCS and data analyses did not adjust for a potential clustering within the four therapists. Moreover, one item of the Simulator Sickness Questionnaire was not asked due to a technical problem, which meant the mean values could not be compared to other studies' results. However, in our study we focused on the changes in simulator sickness from before to after the exposure sessions, making comparisons with other studies not strictly necessary.

Conclusions

To conclude, the present case series offers the first evidence of the feasibility of VERP for C-OCD, as subjective distress and arousal was induced in the majority of patients, patients' compulsions decreased on average, most patients evaluated VERP as useful and sensible, and simulator sickness did not occur. However, the lack of a reduction in obsessions, the moderate sense of presence, and the heterogeneous subjective appraisals indicate that there is still a great need for improvement. It remains unclear whether the heterogeneous results regarding acceptability and OC symptom reduction are due to the resistance of disgust to treatment, a sample selection bias, or the VR environment (e.g., the moderate level of sense of presence is insufficient; the correlation of sense of presence and reduction in the Y-BOCS is expected to reach significance in larger samples). For future research, the course of distress in patients with C-OCD without the primary emotion of disgust might also be worth investigating. However, the results of the present study do provide valuable information that can be used to revise the virtual environments used in the current study (e.g., more realistic movement, higher resolution so that objects look more real, integration of the patients' bodies and hands into the VR

environment) in order to optimize patients' sense of presence and acceptability, which in turn might enhance the efficacy of the intervention.

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Author Contributions FM and LB wrote the draft of the manuscript. SK, SM and LJ designed the study, created the framework conditions (e.g., helping to recruit patients, providing rooms) and edited the manuscript. FM helped with the data analyses of the physiological parameters and edited the manuscript. JB and CG created the VR environments and edited the manuscript. AB and LL helped to collect data, helped with data analyses and edited the manuscript. All authors have contributed to and have approved the final manuscript.

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Availability of Data and Material The data supporting the results and analyses presented in the paper are available upon request from first authors FM and LB.

Declarations

Ethics Approval The study was approved by the local ethics committee of the Center for Psychosocial Medicine of University Medical Center Hamburg-Eppendorf in Germany (Lokale Psychologische Ethikkommission am Zentrum für Psychosoziale Medizin, LPEK-0020).

Consent to Participate All participants gave written informed consent for participation.

Consent for Publication All participants consented to publish their data.

Competing Interest The authors declare that they have no conflict of interest.

References

1. Rozin P, Haidt J, McCauley CR. Disgust: the body and soul emotion. In Handbook of Cognition and Emotion, John Wiley & Sons, Ltd; 2005, p. 429–445.
2. Rozin P, Millman L, Nemeroff C. Operation of the laws of sympathetic magic in disgust and other domains. J Pers Soc Psychol. 1986;50(4):703–12. https://doi.org/10.1037/0022-3514.50.4.703.
3. Russell PS, Giner-Sorolla R. Bodily moral disgust: What it is, how it is different from anger, and why it is an unreasoned emotion. Psychol Bull. 2013;139(2):328–51. https://doi.org/10.1037/a0029319.
4. Mataix-Cols D, Marks IM, Greist JH, Kobak KA, Baer L. Obsessive-compulsive symptom dimensions as predictors of compliance with and response to behaviour therapy: Results from a controlled trial. Psychother Psychosom. 2002;71(5):255–62. https://doi.org/10.1159/000064812.
5. D'Olimpio F, Cosentino T, Basile B, Tenore K, Gragnani A, Mancini F. Obsessive-compulsive disorder and propensity to guilt feelings and to disgust. Clin Neuropsychiatry. 2013;10(3 Suppl 1):20–29.
6. Whitton AE, Henry JD, Grisham JR. Moral rigidity in obsessive-compulsive disorder: Do abnormalities in inhibitory control, cognitive flexibility and disgust play a role? J Behav Ther Exp Psychiatry. 2014;45(1):152–9. https://doi.org/10.1016/j.jbtep.2013.10.001.
7. Whitton AE, Henry JD, Grisham JR. Cognitive and psychophysiological correlates of disgust in obsessive-compulsive disorder. Br J Clin Psychol. 2015;54(1):16–33. https://doi.org/10.1111/bjc.12058.
8. Deacon BJ, Olatunji BO. Specificity of disgust sensitivity in the prediction of behavioral avoidance in contamination fear. Behav Res Ther. 2007;45(9):2110–20. https://doi.org/10.1016/j.brat.2007.03.008.
9. Olatunji BO, Ebesutani C, Haidt J, Sawchuk CN. Specificity of disgust domains in the prediction of contamination anxiety and avoidance: a multimodal examination. Behav Ther. 2014;45(4):469–81. https://doi.org/10.1016/j.beth.2014.02.006.
10. Olatunji BO, Lohr JM, Sawchuk CN, Tolin DF. Multimodal assessment of disgust in contamination-related obsessive-compulsive disorder. Behav Res Ther. 2007;45(2):263–76. https://doi.org/10.1016/j.brat.2006.03.004.

11. Cisler JM, Olatunji BO, Lohr JM. Disgust, fear, and the anxiety disorders: a critical review. Clin Psychol Rev. 2009;29(1):34–46. https://doi.org/10.1016/j.cpr.2008.09.007.
12. Abramowitz JS, Deacon BJ, Whiteside SPH. Exposure therapy for anxiety: Principles and practice. Guilford Press; 2011.
13. Mason EC, Richardson R. Treating disgust in anxiety disorders. Clin Psychol Sci Pract. 2012;19(2):180–94. https://doi.org/10.1111/j.1468-2850.2012.01282.x.
14. Viar-Paxton MA, Olatunji BO. Context effects on habituation to disgust-relevant stimuli. Behav Modif. 2012;36(5):705–22. https://doi.org/10.1177/0145445512446189.
15. Engelhard IM, Leer A, Lange E, Olatunji BO. Shaking that icky feeling: Effects of extinction and counterconditioning on disgust-related evaluative learning. Behav Ther. 2014;45(5):708–19. https://doi.org/10.1016/j.beth.2014.04.003.
16. Smits JAJ, Telch MJ, Randall PK. An examination of the decline in fear and disgust during exposure-based treatment. Behav Res Ther. 2002;40(11):1243–53. https://doi.org/10.1016/S0005-7967(01)00094-8.
17. Olatunji BO, Smits JAJ, Connolly K, Willems J, Lohr JM. Examination of the decline in fear and disgust during exposure to threat-relevant stimuli in blood-injection-injury phobia. J Anxiety Disord. 2007;21(3):445–55. https://doi.org/10.1016/j.janxdis.2006.05.001.
18. Olatunji BO, Wolitzky-Taylor KB, Willems J, Lohr JM, Armstrong T. Differential habituation of fear and disgust during repeated exposure to threat-relevant stimuli in contamination-based OCD: an analogue study. J Anxiety Disord. 2009;23(1):118–23. https://doi.org/10.1016/j.janxdis.2008.04.006.
19. McKay D. Treating disgust reactions in contamination-based obsessive-compulsive disorder. J Behav Ther Exp Psychiatry. 2006;37(1):53–9. https://doi.org/10.1016/j.jbtep.2005.09.005.
20. Adams TG, Willems JL, Bridges AJ. Contamination aversion and repeated exposure to disgusting stimuli. Anxiety Stress Coping. 2011;24(2):157–65. https://doi.org/10.1080/10615806.2010.506953.
21. Ludvik D, Boschen MJ, Neumann DL. Effective behavioural strategies for reducing disgust in contamination-related OCD: a review. Clin Psychol Rev. 2015;42:116–129. Elsevier Inc. https://doi.org/10.1016/j.cpr.2015.07.001.
22. Bush J. Viability of virtual reality exposure therapy as a treatment alternative. Comput Human Behav. 2008;24(3):1032–40. https://doi.org/10.1016/j.chb.2007.03.006.
23. Botella C, Fernández-Álvarez J, Guillén V, García-Palacios A, Baños R. Recent progress in virtual reality exposure therapy for phobias: a systematic review. Curr Psychiatry Rep. 2017;19(7):42. https://doi.org/10.1007/s11920-017-0788-4.
24. van Loenen I, Scholten W, Muntingh A, Smit J, Batelaan N. The effectiveness of virtual reality exposure–based cognitive behavioral therapy for severe anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: Meta-analysis. J Med Internet Res. 2022;24(2): e26736. https://doi.org/10.2196/26736.
25. Benbow AA, Anderson PL. A meta-analytic examination of attrition in virtual reality exposure therapy for anxiety disorders. J Anxiety Disord. 2019;61:18–26. https://doi.org/10.1016/j.janxdis.2018.06.006.
26. Carl E, et al. Virtual reality exposure therapy for anxiety and related disorders: a meta-analysis of randomized controlled trials. J Anxiety Disord. 2019;61:27–36. https://doi.org/10.1016/j.janxdis.2018.08.003.
27. Fodor LA, Coteț CD, Cuijpers P, Szamoskozi Ş, David D, Cristea IA. The effectiveness of virtual reality based interventions for symptoms of anxiety and depression: a meta-Analysis. Sci Rep. 2018;8(1):10323. https://doi.org/10.1038/s41598-018-28113-6.
28. Ling Y, Nefs HT, Morina N, Heynderickx I, Brinkman W-P. A meta-analysis on the relationship between self-reported presence and anxiety in virtual reality exposure therapy for anxiety disorders. PLoS One. 2014;9(5): e96144. https://doi.org/10.1371/journal.pone.0096144.
29. Maples-Keller JL, Bunnell BE, Kim SJ, Rothbaum BO. The use of virtual reality technology in the treatment of anxiety and other psychiatric disorders. Harv Rev Psychiatry. 2017;25(3):103–113. Lippincott Williams and Wilkins. https://doi.org/10.1097/HRP.0000000000000138.
30. Mishkind MC, Norr AM, Katz AC, Reger GM. Review of virtual reality treatment in psychiatry: Evidence versus current diffusion and use. Curr Psychiatry Rep. 2017;19(11):1–8. Current Medicine Group LLC 1. https://doi.org/10.1007/s11920-017-0836-0.
31. Opriş D, Pintea S, García-Palacios A, Botella C, Szamosközi Ş, David D. Virtual reality exposure therapy in anxiety disorders: a quantitative meta-analysis. Depress Anxiety. 2012;29(2):85–93. https://doi.org/10.1002/da.20910.
32. Powers MB, Emmelkamp PMG. Virtual reality exposure therapy for anxiety disorders: a meta-analysis. J Anxiety Disord. 2008;22(3):561–569. https://doi.org/10.1016/j.janxdis.2007.04.006.
33. Belloch A, Cabedo E, Carrió C, Lozano-Quilis JA, Gil-Gómez JA, Gil-Gómez H. Virtual reality exposure for OCD: Is it feasible? Rev Psicopatol y Psicol Clin. 2014;19(1):37–44. https://doi.org/10.5944/rppc.vol.19.num.1.2014.12981.

34. Laforest M, Bouchard S, Bossé J, Mesly O. Effectiveness of in virtuo exposure and response prevention treatment using cognitive-behavioral therapy for obsessive-compulsive disorder: a study based on a single-case study protocol. Front Psychiatry. 2016;7:1–13. https://doi.org/10.3389/fpsyt.2016.00099.
35. Inozu M, Celikcan U, Akin B, Cicek NM. The use of virtual reality (VR) exposure for reducing contamination fear and disgust: Can VR be an effective alternative exposure technique to in vivo? J Obsessive Compuls Relat Disord. 2020;25:100518. https://doi.org/10.1016/j.jocrd.2020.100518.
36. Price M, Anderson PL. The role of presence in virtual reality exposure therapy. J Anxiety Disord. 2007;21(5):742–51. https://doi.org/10.1016/j.janxdis.2006.11.002.
37. Hauschildt M, Schröder J, Moritz S. Randomized-controlled trial on a novel (meta-)cognitive self-help approach for obsessive-compulsive disorder ('myMCT'). J Obsessive Compuls Relat Disord. 2016;10:26–34. https://doi.org/10.1016/j.jocrd.2016.04.010.
38. Moritz S, Jelinek L, Hauschildt M, Naber D. How to treat the untreated: effectiveness of a self-help metacognitive training program (myMCT) for obsessive-compulsive disorder. Dialogues Clin Neurosci. 2010;12(2):209–20 [Online]. Available at http://www.ncbi.nlm.nih.gov/pubmed/20623925. Accessed 7 May 2018.
39. Sheehan DV, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59(Suppl 2):22–33;quiz 34–57 [Online]. Available at http://www.ncbi.nlm.nih.gov/pubmed/9881538. Accessed 24 May 2018.
40. Goodman WK, et al. The Yale-Brown obsessive compulsive scale. I. Development, use, and reliability. Arch Gen Psychiatry. 1989;46(11):1006–11. https://doi.org/10.1001/archpsyc.1989.01810110048007.
41. Hand I, Büttner-Westphal H. Die Yale-Brown Obsessive Compulsive Scale (Y-BOCS): Ein halbstrukturiertes Interview zur Beurteilung des Schweregrades von Denk- und Handlungszwängen. Verhaltenstherapie. 1991;1(3):223–5. https://doi.org/10.1159/000257972.
42. Jänsch P, et al. Der frühe Beginn der Zwangsstörung: Einfluss auf Symptomatik und Schweregrad. Verhaltenstherapie. 2007;17(1). https://doi.org/10.1159/000097878.
43. Hand I, Büttner-Westphal H. Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Verhaltenstherapie. 1991;1(3):226–33. https://doi.org/10.1159/000257973.
44. Jacobsen D, Kloss M, Fricke S, Hand I, Moritz S. Reliabilität der deutschen Version der Yale-Brown Obsessive Compulsive Scale. Verhaltenstherapie. 2003;13(2):111–3. https://doi.org/10.1159/000072184.
45. Schubert T, Friedmann F, Regenbrecht H. The experience of presence: Factor analytic insights. Presence Teleoperators Virtual Environ. 2001;10(3):266–81. https://doi.org/10.1162/105474601300343603.
46. Schuemie MJ, Van der Straaten P, Krijn M, Van der Mast CAPG. Research on presence in virtual reality: a survey. Cyberpsychol Behav. 2001;4(2):183–201. https://doi.org/10.1089/109493101300117884.
47. Morina N, Brinkman WP, Hartanto D, Emmelkamp PMG. Sense of presence and anxiety during virtual social interactions between a human and virtual humans. PeerJ. 2014;1:2014. https://doi.org/10.7717/peerj.337.
48. Da Costa RT, De Carvalho MR, Ribeiro P, Nardi AE. Virtual reality exposure therapy for fear of driving: Analysis of clinical characteristics, physiological response, and sense of presence. Rev Bras Psiquiatr. 2018;40(2):192–9. https://doi.org/10.1590/1516-4446-2017-2270.
49. Jelinek L, Moritz S, Hauschildt M. Patients' perspectives on treatment with Metacognitive Training for Depression (D-MCT): Results on acceptability. J Affect Disord. 2017;221:17–24. https://doi.org/10.1016/J.JAD.2017.06.003.
50. Jelinek L, et al. Patients' perspectives on treatment with metacognitive training for OCD: Feasibility and acceptability. Zeitschrift fur Neuropsychol. 2018;29(1):20–8. https://doi.org/10.1024/1016-264X/a000211.
51. Kennedy RS, Lane NE, Berbaum KS, Lilienthal MG. Simulator sickness questionnaire: an enhanced method for quantifying simulator sickness. Int J Aviat Psychol. 1993;3(3):203–20. https://doi.org/10.1207/s15327108ijap0303_3.
52. Bouchard S, Robillard G, Renaud P. Revising the factor structure of the Simulator Sickness Questionnaire. academia.edu; 2007. p. 128–37.
53. Wolpe J, Lazarus A. Behavior therapy techniques: a guide to the treatment of neuroses. 1966.
54. Oelkers C, Hautzinger M. Zwangsstörungen - Kognitiv-verhaltenstherapeutischen Behandlungsmanual. 2nd ed. BELTZ; 2013.
55. Bozgeyikli E, Raij A, Katkoori S, Dubey R. Point & Teleport locomotion technique for virtual reality. In CHI PLAY 2016 - Proceedings of the 2016 Annual Symposium on Computer-Human Interaction in Play, 2016. p. 205–16. https://doi.org/10.1145/2967934.2968105.
56. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale N.J.: L. Erlbaum Associates; 1988.

57. Gellish RL, Goslin BR, Olson RE, McDonald A, Russi GD, Moudgil VK. Longitudinal modeling of the relationship between age and maximal heart rate. Med Sci Sports Exerc. 2007;39(5):822–9. https://doi.org/10.1097/mss.0b013e31803349c6.
58. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. J Am Coll Cardiol. 2001;37(1):153–6. https://doi.org/10.1016/S0735-1097(00)01054-8.
59. Chung H, Lee H, Lee J. State-dependent Gaussian kernel-based power spectrum modification for accurate instantaneous heart rate estimation. PLoS One. 2019;14(4): e0215014. https://doi.org/10.1371/journal.pone.0215014.
60. Healey JA. Wearable and automotive systems for affect recognition from physiology. Massachusetts Institute of Technology. 2000.
61. Lykken DT, Rose R, Luther B, Maley M. Correcting psychophysiological measures for individual differences in range. Psychol Bull. 1966;66(6):481–4. https://doi.org/10.1037/h0023922.
62. Mataix-Cols D, Fernandez de La Cruz L, Nordsletten AE, Lenhard F, Isomura K, Simpson HB. Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. World Psychiatry. 2016;15(1):80–1. https://doi.org/10.1002/wps.20299.
63. Abramowitz JS, Arch JJ. Strategies for improving long-term outcomes in cognitive behavioral therapy for obsessive-compulsive disorder: Insights from learning theory. Cogn Behav Pract. 2014;21(1):20–31. https://doi.org/10.1016/j.cbpra.2013.06.004.
64. Craske MG. Optimizing exposure therapy for anxiety disorders: an inhibitory learning and inhibitory regulation approach. Verhaltenstherapie. 2015;25(2):134–43. https://doi.org/10.1159/000381574.
65. Culver NC, Stoyanova M, Craske MG. Emotional variability and sustained arousal during exposure. J Behav Ther Exp Psychiatry. 2012;43(2):787–93. https://doi.org/10.1016/j.jbtep.2011.10.009.
66. Button KS, et al. Power failure: Why small sample size undermines the reliability of neuroscience. Nat Rev Neurosci. 2013;14(5):365–76. https://doi.org/10.1038/nrn3475.
67. Keeley ML, Storch EA, Merlo LJ, Geffken GR. Clinical predictors of response to cognitive-behavioral therapy for obsessive-compulsive disorder. Clin Psychol Rev. 2008;28(1):118–30. https://doi.org/10.1016/j.cpr.2007.04.003.
68. Ong CW, Clyde JW, Bluett EJ, Levin ME, Twohig MP. Dropout rates in exposure with response prevention for obsessive-compulsive disorder: What do the data really say? J Anxiety Disord. 2016;40:8–17. https://doi.org/10.1016/J.JANXDIS.2016.03.006.

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