



MONASH University

Virtual Reality in Psychology: Development and Validation of an Exposure Therapy System

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BPsych (Hons)

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GENERAL DECLARATION

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes two original papers submitted for publication in peer reviewed journals. The core theme of the thesis is psychology, specifically the development and validation of a novel Virtual Reality system for psychological research and practice. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the School of Psychological Sciences under the supervision of Professor Murat Yücel.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of Chapters Three and Five my contribution to the work involved the following:

| Thesis Chapter | Publication Title | Status | Nature and % of student contribution | Co-author name(s) Nature of Co-author's contribution* |
|-----------------------|--|---------------|---|--|
| Three | Considerations and Practical Protocols for Using Virtual Reality in Psychological Research and Practice, as Evidenced Through Exposure-Based Therapy | Under review | 85% Literature review. Conceptualisation of virtual environments including equipment selection, engaging end-user feedback processes for development, iterative design of VR environments, overseeing and managing collaborative development of VR system and psychophysiology system integration. Manuscript conceptualisation, write-up and final editing. | All co-authors provided critical feedback on the manuscript to varying extents. James Morrow provided secondary technology support and Nathan Dowling provided clinical consultation. <ol style="list-style-type: none"> 1. Nathan Dowling 5% 2. Rebecca Segrave * 3. James Morrow * 4. Adrian Carter * 5. Murat Yücel 5% *5% collectively |

| | | | | |
|------|--|--------------|---|--|
| Five | Exposure Therapy in a Virtual Environment: Validation in Obsessive Compulsive Disorder | Under review | 85% Literature review, hypothesis conception, selection of research materials and systems, recruitment, participant testing and data collection, data analysis, manuscript write-up and final editing. | <p>All co-authors provided critical feedback on the manuscript to varying extents. Nathan Dowling also provided clinical consultation and recruitment support.</p> <ol style="list-style-type: none"> 1. Murat Yücel 5% 2. Adrian Carter 2.5% 3. Rebecca Segrave 2.5% 4. Nathan Dowling 5% |
|------|--|--------------|---|--|

*No co-authors were Monash students.

I have renumbered sections of submitted papers in order to generate a consistent presentation within the thesis.

Student signature: [REDACTED]

Date: 13th July 2020

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author, I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor signature: [REDACTED]

Date: 13th July 2020

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ABSTRACT

Understanding and treating psychological conditions is often impeded by the disconnect between clients' everyday experiences, and those available in clinical or research environments. Replicating the complexity of the real-world is challenging, diminishing the relevance of treatment experiences and ecological validity. Virtual Reality (VR) offers an avenue for overcoming these limitations by creating immersive, tailored three-dimensional environments. Through this, VR could bridge the gap between the real-world and controlled psychological settings.

Consistent with traditional therapeutic approaches, VR exposure-based therapy enables patients to engage with graded hierarchies of anxiety provoking tasks to learn new associations with feared stimuli. Utilising VR allows for careful control of the timing, duration, and severity of exposure tasks that are more realistic than traditional imaginal approaches. While there is growing evidence of the effectiveness of VR exposure-based therapy in treating post-traumatic stress disorder and phobias, other conditions with common mechanisms that underlie treatment methods—such as Obsessive-Compulsive Disorder (OCD)—remain relatively unexplored.

In light of these opportunities and gaps, this thesis outlines the development and validation of a novel VR system that I have created for OCD treatment and research. An immersive and customisable suite of virtual environments were generated using the latest in VR technology. Through a novel integration of psychophysiology recording equipment, it was possible to collect objective participant responses that were synchronised in real-time during exposure sessions.

Clinical implementations of VR exposure-based therapy have been hindered by a paucity of methodological design and development publications. To address this, the first manuscript of this thesis provides a framework to make VR design approachable for clinicians

and researchers in psychology and neuroscience. By making VR more accessible, this work will directly facilitate the ongoing creation of novel tools to treat mental illness.

The developed VR system was subsequently validated in a sample of patients diagnosed with contamination-based OCD, through comparison of responses to virtual and real-world *in vivo* exposures. This validation utilised both subjective and objective measures of emotional arousal, as well as clinical indicators of engagement and alliance, to comprehensively understand the opportunities and limitations of VR-based Exposure and Response Prevention for OCD. By implementing a repeated-measures, counterbalanced design, participant responses in VR were able to be compared to the traditional, first-line approach in psychotherapeutic treatment of OCD. Critically, I found that virtual and traditional *in vivo* exposures elicit comparable and increasing levels of subjective anxiety across an exposure hierarchy. Psychophysiological responses across the two exposure paradigms were also comparable. Virtual exposure increased both engagement and adherence to exposure tasks. In contrast to what had been hypothesised in the literature, the therapeutic alliance was not adversely affected in VR. This is a particularly important finding, as it suggests the technology does not pose a therapeutic barrier when engagement is factored into design.

Collectively, this thesis provides the frameworks required to support VR becoming applicable within both clinical and research communities. The experimental work contained within also demonstrates that VR holds validity as a potential treatment tool for OCD that can overcome limitations of traditional techniques, while eliciting relevant emotions and upholding clinical factors.

LIST OF ACRONYMS

| | |
|--------------|---|
| AR | Augmented Reality |
| CBT | Cognitive Behavioural Therapy |
| CAVE | CAVE Automatic Virtual Environment |
| ECG | Electrocardiogram |
| ERP | Exposure and Response Prevention (a.k.a. Ritual Prevention) |
| ETVE | Exposure Therapy in a Virtual Environment |
| HMDs | Head Mounted Displays |
| IT | Information Technology |
| MINI | Mini International Neuropsychiatric Inventory |
| OCD | Obsessive Compulsive Disorder |
| PTSD | Post-Traumatic Stress Disorder |
| STAI | State Trait Anxiety Inventory |
| SUDs | Subjective Units of Distress |
| VE | Virtual Environment |
| VR | Virtual Reality |
| YBOCS | Yale Brown Obsessive Compulsive Scale |

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SUMMARY OF RESEARCH OUTPUTS

The following publications and presentations arose from research conducted during the course of my doctoral candidature.

Publications

1. **Cullen, A. J.**, Dowling, N. L., Segrave, R., Morrow, J., Carter, A., & Yücel, M. (under review). Considerations and Practical Protocols for Using Virtual Reality in Psychological Research and Practice, as Evidenced Through Exposure-Based Therapy.
2. **Cullen, A. J.**, Dowling, N. L., Segrave, R., Carter, A., & Yücel, M. (under review). Exposure Therapy in a Virtual Environment: Validation in Obsessive Compulsive Disorder.

Conference Proceedings

Oral Presentations

1. **Cullen, A. J.** (July 2019). Exposure Therapy in a Virtual Environment: Development and Preliminary Findings. *9th World Congress of Behavioural and Cognitive Therapies*, Berlin, Germany.
2. **Cullen, A. J.** (November 2019). Exposure Therapy in a Virtual Environment: Designing Novel Approaches to Psychological Research and Treatment. *College of Clinical Neuropsychologists*, Barossa Valley, South Australia.
3. **Cullen, A. J.** (November 2019) Exposure Therapy in a Virtual Environment: Development and Validation Findings of a Specialised Obsessive-Compulsive Disorder System. *Society for Mental Health Research*, Melbourne, Victoria, Australia.

Symposium

1. **Cullen, A. J., & Yücel, M.** (July 2019). The Potential of Using Virtual Reality to Detect, Overcome and Avoid Addictive and Compulsive Conditions. In Wiers, R. & Yücel, M. (Chairs), *Augmenting Cognitive Behaviour Therapy for Appetitive Disorders with Brain-Based Technological Developments at 9th World Congress of Behavioural and Cognitive Therapies*, Berlin, Germany.

Scientific Communications: End-user Engagement and Knowledge Dissemination

1. **Cullen, A. J., & Yücel, M.** (June 2017). Monash University Research Champions Video.
2. **Cullen, A. J.** (March 2019). Development and Methodology for a Virtual Reality in Obsessive Compulsive Disorder Study. *Royal Melbourne Hospital Neuropsychiatry Unit Research Forum*, Melbourne, Victoria, Australia.
3. **Cullen, A. J.** (November 2019). Virtual Reality for Obsessive Compulsive Disorder Research and Treatment: Virtual Exposure Development and Validation Findings. *The Melbourne Clinic Academic Forum*, Melbourne, Victoria, Australia.

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This work was supported by the establishment of industry, research, and clinical collaborations. Developing the novel VR system relied upon the contributions of software developers from SensiLab, Monash Immersive Visualisation Platform, and Torus Games. I greatly appreciate your patience in carrying out design iterations, ensuring precise requirements were met, and bringing my designs to virtual life! I would also like to express my gratitude to The Melbourne Clinic staff within both the OCD program and professorial unit. Your engagement and genuine interest in this research are much appreciated. Thank you for making me feel welcome and allowing me to learn firsthand within your inpatient program.

To the research participants, I am sincerely appreciative not only of your kindness in volunteering your time, but also your dedication to finding a successful treatment. Thank you for sharing your insights, allowing me a glimpse of the impacts of OCD upon your lives, and your courage and willingness to work through exposure sessions. I sincerely hope these findings fuel further work to improve how we can better support you.

I am immensely grateful for the opportunity to complete this Doctor of Psychology, and the passion for Clinical Neuropsychology shared by the staff and students in this program I will carry throughout my career.

To my wonderful friends, you've brought balance and laughter throughout the highs and lows of this doctorate. Thank you for the overseas escapes, finding the humour in absolutely everything, and being there with patient encouragement and kindness. A few of you have been quite literally by my side since day one, and our friendship is what colours this entire experience with joy. We've supported each other through the biggest challenges (thanks for making sure I never gave up, even forcing me back to the office) and we've celebrated any and all achievements - I can't wait for the next chapter of life with you all.

To my family, you are the foundation for everything. You've listened to every challenge and been there to offer support at any moment - including reading every word of this thesis! Mum, your unwavering belief is what keeps me going, and your incredible strength and attitude to life are a source of endless inspiration. Andrew, there are no words to express my gratitude – your patience, practical support, but most of all your ability to make me laugh, how lucky I am to have you! Completing this course would not have been possible without you both. There is truly no better cheer-squad in the world.

The achievements from my candidature, and the person I have become over the last five years, are a reflection of this range of truly amazing friends and family that I have been surrounded by, and I hope to have made you all proud. Thank you.

DOCTORAL PROGRAM OVERVIEW

This thesis forms the major research component of the Doctor of Psychology (Clinical Neuropsychology). I undertook this degree at Monash University, Melbourne, Australia, continuously across February 2016 to July 2020. The course is a combined clinical training and research program. Therefore, in addition to the research contained within this thesis, I also completed coursework and four clinical placements, including an advanced specialisation internship, across a two-year period.

Regarding the research context specifically, this work was supported by a partnership which was established between The Melbourne Clinic in Richmond, Australia, and the BrainPark Research Laboratory at the Turner Institute for Brain and Mental Health, Monash University. Collaboration with The Melbourne Clinic aided the clinical facets of the work, such as facilitating end-user feedback from patients and clinicians, and recruitment opportunities. The development of the virtual environments was assisted by interdisciplinary partnerships with a range of software development teams including SensiLab and Monash Immersive Visualisation Platform, both at Monash University, as well as an industry partnership with Torus Games in Victoria, Australia.

This thesis is presented in a ‘thesis by publication’ format, prepared in keeping with Monash University guidelines. As such, parts of this thesis are written manuscripts which have been submitted for publication in peer-reviewed journals, thereby differing from more traditional thesis formats. Due to this formatting, there are some instances of repetition of information across chapters. I have edited formatting of the manuscripts to ensure there is consistent presentation across the entire thesis.

INTRODUCTION AND THESIS OVERVIEW

Therapeutic clinical environments and research laboratories struggle to replicate the complexities of the real world. As a result, they can feel dissociated from the symptom provoking experiences of daily life. This inability to realistically elicit symptoms undermines treatment efficacy and diminishes precise measurement, and therefore understanding, of patient responses to anxiety-provoking stimuli. These obstacles to therapeutic effectiveness and ecological validity could be overcome through the use of Virtual Reality (VR) technologies that imitate real-world experiences within supportive, controlled psychological contexts. VR systems create immersive, computer-generated, three-dimensional, multisensory environments that offer the potential for endless experiences, with a flexibility that can be tailored to suit individual patient needs. Throughout the following work, VR will be used broadly to refer to both the hardware and software systems that together provide immersive sensory input and allow user-driven interactions.

Developments in VR technologies have reached a point where there are now exciting opportunities for the assessment and treatment of psychological conditions, with VR exposure-based therapy being an area of growing interest. This approach allows for the precise grading of exposure tasks, that are perceived to be more realistic than traditional imaginal approaches. As such, in the current thesis the term VR exposure-based therapy will be used to refer broadly to this field of exposure-based therapy techniques that may be tailored for a range of disorders, and are delivered in part using VR technologies. The terminology VR-based Exposure and Response Prevention (ERP) will be used to refer to the specific therapeutic technique for Obsessive-Compulsive Disorder (OCD) that can be delivered via VR, and may be included as part of a comprehensive treatment approach, such as Cognitive Behaviour Therapy (CBT).

Empirical evidence is mounting that VR exposure-based therapy is an effective treatment approach for several psychological conditions, including post-traumatic stress

disorder and phobias. Conditions with similar underlying mechanisms, and therefore shared treatment approaches that involve exposure to feared stimuli, may therefore also benefit from VR exposure-based therapy. My research, as outlined in this thesis, extends upon the current VR exposure-based therapy literature and clinical practise into a new area, by designing and creating a VR-based ERP system purpose-built for OCD, and incorporating real-time subjective and objective measurement of response to immersion. In the chapters that follow, I describe the development and validation of this VR-based ERP system for OCD. Such novel approaches to ERP are urgently needed for people with OCD, given their relatively high refusal and attrition rates, and the inadequate symptom management from currently available treatment options (Ong et al., 2016; Öst et al., 2015).

Research Aim and Hypotheses

The overarching aims of this thesis were to i) develop and ii) validate a novel VR system specialised for OCD research and treatment. Specifically, I aimed to create an immersive, customisable series of virtual environments that could be integrated with psychophysiological measurements. Once developed, the system was validated with a sample of people with moderate–severe OCD. Participants engaged in both virtual and traditional real-world *in vivo* ERP sessions. Graded exposure hierarchies were carefully matched across the virtual and *in vivo* sessions. VR would be considered a valid ERP tool for OCD uses if participant responses in our study were comparable to the existing gold-standard therapeutic benchmark of *in vivo* ERP. In order to examine this comparability, it was hypothesised that the two exposure methods would not significantly differ on provocation of subjective and objective indicators of emotional arousal including psychophysiological response, as well as clinical engagement as indicated by measures of adherence to exposure tasks and therapeutic alliance.

Overview of Thesis

In Chapters One and Two, I critically review the pertinent VR and OCD literature, with particular focus on challenges and opportunities at the clinical and research interface. This evidentiary basis provides the foundation for my subsequent empirical work. To address the first stated aim, I describe in detail the process of designing and developing the unique VR system for OCD. This manuscript (currently under peer-review) is presented in Chapter Three. Using our VR-based ERP for OCD system as an applied case study, the manuscript comprises a set of considerations and practical protocols for clinicians and researchers to follow in guiding the creation and application of VR-based ERP systems. This framework of considerations for VR design in psychology is the first of their kind, to comprehensively outline the process of developing a VR-based ERP system.

The VR-based ERP system was then empirically tested in a clinical sample. In Chapter Four, I describe the methodological approach for the empirical validation study, including the establishment of a clinical partnership, end-user design processes, and procedural information for the experiment. The findings from the validation study are outlined in the second manuscript (also currently under peer-review) and presented here in Chapter Five. Through the use of a repeated-measures, counterbalanced design, OCD patient responses in VR were contrasted to those from *in vivo* exposure therapy. A diverse range of subjective, objective, and clinical factors measures are examined, in order to comprehensively evaluate the equivalency of this novel VR approach to existing therapeutic methods. Through this, the research contained herein is the first to validate truly immersive, flexible VR ERP sessions in an OCD sample through direct comparisons to the current first-line treatment in evidence-based psychological therapy. In contrast to previous literature, this work fully utilises and assesses the optimal functionalities of both VR hardware and software to create a system that directly meets clinical and research needs. These novel contributions to the literature, big picture

implications and future research directions generated by this work are outlined in the general discussion of Chapter Six.

CHAPTER ONE: VIRTUAL REALITY

Virtual Reality (VR) describes a heterogeneous group of technologies, whose form and utility has evolved over time. These systems create realistic, immersive virtual environments that hold the potential to significantly enhance research and clinical endeavours. In this chapter I review the current state of the literature in this emerging field, to provide a conceptual basis for the application of VR in psychological practice. Each of the varying forms of VR technology offer unique capabilities and challenges that impact on their use in the treatment clinic or research laboratory. I will focus on the most promising avenue of research using systems with Head Mounted Displays (HMDs), although alternate technologies will also be discussed to explore the broader scope of prospective applications.

Considerable research attention has been devoted to VR exposure-based therapy, in which patients face increasingly anxiety provoking situations in a graded manner, with the aim being to learn new associations to these feared stimuli and to regulate their emotions more adaptively. As with current therapeutic techniques, approaches such as VR exposure-based therapy must be considered as a tool to enhance therapy (Rothbaum, 2005), existing within a broader framework such as Cognitive Behaviour Therapy (CBT). VR exposure-based therapy should therefore be considered to occur in parallel with other CBT components, such as psycho-education and cognitive restructuring, rather than as a standalone technique. In contrast to the limitations of traditional Exposure and Response Prevention (ERP) therapy, VR systems offer opportunities to precisely control the timing and nature of exposure tasks and customise them to clients' everyday experiences. By more closely matching therapy experiences to specific fear structures it would be anticipated to enhance patient engagement, acceptability, and ecological validity, thereby overcoming key limitations of traditional ERP approaches.

Preliminary empirical evidence indicates VR exposure-based therapy is comparable to traditional approaches in several anxiety and related disorders (Carl et al., 2019). This suggests

the potential validity and efficacy of VR exposure-based therapy for other similar conditions, including Obsessive-Compulsive and related disorders. However, further research is required to establish the ability of VR exposure-based therapy to elicit relevant emotions to a clinically significant degree and generate meaningful improvements in symptomatology over time. Notably, the novelty of VR exposure also requires that technological developments are matched with a rigorous framework of ethical and safety considerations. Furthermore, the clinical acceptability and usability of systems must also be considered, if VR techniques are to be used in such treatment settings.

An exploration of these opportunities and considerations will be provided alongside a discussion of the current state of VR applications to both research and therapeutic settings. Due to their common underlying theoretical and treatment mechanisms, particular focus will be placed upon post-traumatic stress disorder, specific phobias, social anxiety disorder, and panic disorder. Within these disorders, shared exposure-based treatment modalities exhibit successful symptom management, but are hindered by high refusal and attrition rates, for which VR exposure-based therapy may provide solutions.

1.1 Overview of VR Systems

VR systems use computer generation to create highly immersive environments, synthesised using a combination of visual, audio, and tactile sensory features (Bohil et al., 2011; Foreman, 2010; Tarr & Warren, 2002). In VR, users may interact with a simulated environment by sharing information between themselves and the computer system (hardware and software) using interfaces (Schuemie, 2003). While technologically broad, the remainder of this work will focus upon VR systems that at a minimum provide: visual input; allow user-driven interactions; and generate three-dimensional environments that can be engaged with dynamically. The term *user* will refer to any individual immersed in VR as the primary agent

of change, and both *patient/client* and *participant* will refer specifically to clinical or research applications respectively.

Detailed sensory simulations that respond to user inputs create convincing virtual environments that are referred to as immersive. Through their design, VR environments can be reactive to user actions and are modifiable in real-time; however, each possible outcome needs to be pre-programmed as an option. A virtual environment could permit a user to move freely through a supermarket, though the ability to pick up and drop a grocery item, then hear and see it break on the virtual floor, needs to be programmed in advance as a capability.

While the VR environment is planned beforehand, the user is able to flexibly choose their own adventure in real-time. This distinguishes VR from more passive experiences like watching a movie. Virtual presence is achieved when the user fails to recognise the contribution of technology to their current mental experiences (Ling et al., 2014). Such creation of an immersive, realistic experience is more likely to generalise back to users' everyday lives, in a manner that is critical for successful VR psychological treatments.

The virtual environments are generated by the hardware and software, that are embedded within real-world spaces, such as a research laboratory or treatment clinic. Through the virtual immersion, challenging experiences of the real-world can be brought into the supportive environment of a clinician's office (hereafter *clinician* will be used to refer to qualified mental health professionals, including psychologists and psychiatrists). However, creating these immersions requires considerable financial, time and skill investments. Each virtual object, interaction, and capability needs to be designed and carefully considered, including whether changes are flexibly user-driven or largely predetermined, and dynamically connected to one another. In order for virtual environments to be perceived as realistic, a user's action needs to be reflected by changes in audio-visual stimuli, such as an engine noise commencing when the user turns the virtual key in a car ignition. Greater system capabilities

create greater design complexities. Balancing these competing demands is a crucial decision-making process at the outset of design and development.

The VR software can generate virtual environments that are larger and more diverse than the real-world space in which they exist. Creative design solutions allow systems to exploit the limitless possibilities of VR within the physical boundaries of the real-world. Both hardware and software design features can allow access to virtual environments that are physically larger than the real-world space available for the user. Software solutions include re-directed walking, in which the system guides the user to change their orientation; and teleporting, in which the user is virtually transported and relocated; while multi-directional treadmills offer a physical mechanism for expanding mobility.

While immersed in these virtual environments, system features can also enable bi-directional interactions between the user and virtual stimuli. Hardware such as joysticks and handheld controllers allow users to manipulate objects, while haptic feedback provides responses of the environment back to the user that increases the immersive experience. For example, a shaking handheld controller may be used to mimic tension and resistance in an archer's bowstring. Greater immersion will be created by hardware that is experienced as naturalistic, imitating the manner in which someone would use their hands in the real-world as much as feasible. These physical sensory simulations contribute to the creation of an environment that is optimally immersive and perceived by the user to be more convincing (Sanchez-Vives & Slater, 2005).

1.1.1 Current Options and Capabilities of VR Systems

Immersion and presence vary according to hardware and software features of systems that are typically made commercially available by manufacturers such as HTC, Google, and Oculus. Systems range from: leveraging smartphones into VR, HMDs that block out real-world input, high-resolution projection-based displays known as CAVE Automatic Virtual

Environments (CAVE), and Augmented Reality (AR) approaches in which the real-world is overlaid or supplemented to allow both as simultaneous experiences.

Many people already own entry-grade VR compatible smartphone devices, presenting an opportunity for widespread dissemination and accessibility of software with minimal financial investment, such as the Google Cardboard. Implementations include chronic pain management (Amin et al., 2017), providing biofeedback in anxiety disorders (Repetto et al., 2013), and these systems are well suited to self-directed therapeutic programs. Drawbacks of these smartphone-based systems are lower visual display resolutions which impede immersion, and limitations in the range of modifications users can make to their virtual experience in real-time.

While HMDs are currently less commonplace and more expensive than smartphones, they provide substantially advanced technical capabilities. The primary distinguishing feature of HMD systems is the headset, which simulates depth perception through two offset stereoscopic images that create binocular disparity and block out visual aspects of the real-world. Some HMD systems are a stationary experience, where the user may be seated and passively experiences an environment or enacts some degree of control using hardware, such as a joystick. An unpleasant sensorimotor discrepancy, termed ‘simulator sickness’, is more likely to occur in these stationary systems that have moving visual inputs in the absence of body movements (Davis et al., 2015; Sharples et al., 2008). This experience may be exacerbated by the use of a low-resolution HMD, or a morphological mismatch between the device and the user’s face. An experience of simulator sickness generally limits users’ ongoing engagement with VR systems, therefore minimising these incidences is an important consideration for system designers.

By matching users’ body movements to virtual simulations, sensorimotor discrepancies can be reduced. HMD systems that translate users’ movements within their physical

environment into modifications of the virtual environment reduce simulator sickness, while also enhancing the immersive experience. Through this capability the virtual experience is more realistically matched to natural body movements. Users may walk within a predefined area, or in some cases utilise infinite walking systems such as 360-degree treadmills. Sensors track the user's body and provide this information to the software program, which updates the simulated visual features in the user's virtual display. A user in a virtual kitchen could physically walk to the left, creating virtual movement and seeing a virtual sink, then turn their body to the right and see a virtual refrigerator. The coordination of movement and visual display heightens the sense of first person perspective and presence (Riva, 2009). Empirical investigations of HMD systems have shown validity in the ability to elicit relevant emotional and physiological responses in users, such as increased heart rate in anxiety provoking scenarios (Chessa et al., 2019).

CAVEs are projection-based systems where images are simultaneously displayed on the blank walls, ceiling, and floor of a space in which the user stands. As they are not wearing a headset, the user can see their own body movements while also experiencing the audio-visual simulations (Cruz-Neira et al., 1993). Research trials using CAVE VR have been conducted in contamination-based OCD (Laforest, Bouchard, Bossé, et al., 2016). Advantages for the user include the ability to share the environment with a clinician or researcher, and greater accessibility for people with physical limitations such as poor balance or gait abnormalities who may be unsafe to use ambulant HMDs. However, CAVE systems are highly expensive, require a large-scale, dedicated space, and are extremely difficult to physically move and re-setup between locations. This would prevent their use in most homes or rapid relocation across clinic sites, undermining uptake and accessibility of VR services.

AR also capitalises upon projection-based displays; however, unlike CAVE systems, elements of the real-world are deliberately incorporated into the experience. AR can utilise

multiple sensory modalities that add to, or modify, the real-world in some manner, and has been investigated as a potential treatment tool for animal phobias (Juan et al., 2005).

1.2 Opportunities for Psychology: VR Exposure-Based Therapies

VR has applications across the gamut of medicine and health science practice, including assessment and diagnosis (Cherniack, 2011; Egger et al., 2017; Morganti et al., 2013; Parsons & McMahan, 2017), training and teaching (Pelargos et al., 2017; Zhao et al., 2011), and treatment, rehabilitation, and self-directed therapy (Krijn, Emmelkamp, Olafsson, et al., 2004; Meyerbröker, 2014; Repetto et al., 2013; Riva, 2005). From a psychological treatment perspective, research has primarily focused on disorders typically treated using exposure-based techniques, including ERP (Botella et al., 2007; Rizzo et al., 2014; Rothbaum et al., 2006; Wallach et al., 2009), a technique classified under CBT that is the first-line psychological treatment indicated for OCD (American Psychiatric Association, 2007; National Institute for Health and Care Excellence, 2005, 2018; The Australian Psychological Society, 2010, 2018). Typically, ERP involves presenting anxiety-provoking stimuli in a hierarchical manner of increasing symptom elicitation, using a combination of *in vivo* (real-world) and imaginal exposure tasks. Through ERP processes, clients learn that therapeutic ‘success’ is not the escape from nor the removal of anxiety, but rather tolerating distress and establishing disconfirming beliefs. In confronting these stimuli while withholding compulsions, clients learn that anticipated consequences remain unlikely to occur (Foa, 2010; Gillihan et al., 2012), and replace their fears with new, adaptive associations with obsessional phenomena (Abramowitz, 1996; Craske et al., 2008; Hodgson & Rachman, 1972). Given optimal treatment outcomes are obtained using an uniquely targeted combination of both *in vivo* and imaginal approaches (Abramowitz, 1996; Foa et al., 1980, 1985), it is anticipated that by expanding opportunities to address each client’s unique fear model, VR would offer an adjunct approach to enhance therapy, and potentially serve as an intermediary between the clinician’s office and

everyday experiences (Riva, 2005; Rothbaum, 2005). A summary of the key opportunities, areas for ongoing research investigation, considerations for ethical and clinical practice, and potential challenges, that will be explored in the subsequent sections of this chapter are outlined in Table 1.

Table 1

Opportunities, Key Considerations, Future Research Directions, and Potential Challenges for Virtual Reality Exposure-Based Therapy

| Opportunities | Ongoing Research | Considerations | Potential Challenges and Limitations |
|--|---|---|--|
| Carefully Controlled Experiences Environments highly specialised to each patient. Controlled task onset. Precise response measurement. | Validation of ERP Processes Replicated evidence of arousal and extinction. Need for multifaceted evidence across objective and clinical measures. | Ethical and Clinical Presently lacking tools to assess client safety and suitability. Guidelines and training protocols needed for specialists. Strategies to maintain multi-disciplinary collaboration. | Practice-based Challenges Robust evidence-base required, limitations of ecological validity of human behavior and actions in VR, and clinical implementation factors. |
| Ecological Validity Improved relevancy. Explore impractical stimuli. | Treatment Delivery Identify factors for transfer of therapeutic gains. Determine predictors of response to identify patient suitability. Tailor protocols such as frequency and duration of sessions. | Uptake and Engagement Improving clinician awareness of the opportunities. Require further empirical investigation of techniques for therapeutic communication, relationship, and engagement within VR exposure-based therapy. | Specific VR-based ERP Challenges Some clients may perceive lower potential for harm. Hardware will create complete ritual prevention in some cases, making VR potentially unsuitable in certain circumstances. |
| Client Engagement Enhanced trust in process and therapeutic alliance. Self-directed therapy to improve service accessibility. | | | |

1.2.1 Carefully Controlled and Customised Exposures

VR systems offer seemingly endless options of audio-visual stimuli, which in psychological practice have the potential to create highly specialised environments that can be matched to each patients' unique presenting concerns (Emmelkamp, 2005; Oprea et al., 2012).

Within these environments, virtual stimuli can be precisely controlled in terms of onset, duration, and nature. These features have already been used to closely replicate client's complicated everyday experiences within VR for assessment and rehabilitation purposes (Adamovich et al., 2009; Cushman et al., 2008; Foerster et al., 2016; Foreman et al., 2005; Gramann et al., 2005; Pani et al., 2005; Rose et al., 2005). The high degree of customisation made possible by VR would enable treatment protocols to precisely match patients' needs, such as their specific fear model for cue exposures. The ability to carefully control the onset of stimuli in VR also enables researchers to record participants' responses to these experimental events. In this manner, participant experiences can be precisely observed and measured in a defined environment (Foreman, 2010). Uniquely to VR, this includes settings that otherwise would be highly challenging to access, including during driving or flying in a plane (Walshe et al., 2003).

Closer similarities between exposure task stimuli and the client's specific fear model will produce greater treatment efficacy (Lang, 1977). This theory underpins the traditional practice of combining imaginal and real-world *in vivo* exposures. Using VR systems to conduct ERP could make these therapeutic sessions more realistic and closely connected to patient symptoms. For clients who have difficulty visualising stimuli in an imaginal exposure, or find real-world exposure too challenging or difficult to replicate, virtual exposures may present a suitable middle ground (Foreman, 2010).

Consistent with traditional ERP procedures, through VR-based approaches clients would learn new associations with feared stimuli in a graded manner. As a product of these progressive learnings, clients self-perceived ability to cope typically increases within and between successful traditional treatment sessions. This speaks to the importance of carefully graded increases in the degree of exposure task severity, which could be more precisely achieved in VR than traditional measures. In turn, such improvements in task grading would

be anticipated to improve both uptake and engagement. This is supported by research indicating that patients with specific phobias consistently opt for VR over *in vivo* exposure with starkly lower refusal rates (Garcia-Palacios et al., 2001, 2007).

Clients' knowledge that exposure hierarchy tasks can be precisely controlled and graded within a virtual environment may increase a sense of control and subsequently their sustained partaking in therapy (Riva, 2005). This enhanced self-efficacy, and the ensuing decreased ambivalence towards behaviour change, may also facilitate OCD symptom improvements and engagement within ERP (Merlo et al., 2010; Simpson, Zuckoff, et al., 2008). Moreover, by removing the barrier of self-managing the grading of tasks, VR may enhance participation in therapeutic homework tasks by diminishing the intense anxiety and doubt associated with acting without clinician support (Lind et al., 2013). By carefully customising and controlling self-help style VR ERP tasks in-home, patients sense of mastery and self-efficacy would be anticipated to improve, with beneficial flow on effects for ERP compliance more broadly (Lind et al., 2013).

1.2.2 Ecological Validity

VR may improve the generalisability of experiences between research or clinical settings and the objective, physical real-world, typically referred to as ecological validity. When considered from an assessment or diagnostic perspective, virtual environments could overcome the discrepancy between clients' performances on traditional 'pen and paper' assessment measures and self-reported concerns. For example, by objectively measuring performance on everyday tasks, such as finding one's car in virtual parking lot or remembering to buy milk in a virtual supermarket, clinicians would be able to observe patients' objective real-world cognitive functioning. As such, this could overcome the major limitations of standard neuropsychological assessment tools (Parsons & McMahan, 2017; Pearman, 2009; Reid & MacLulich, 2006; Yamaguchi et al., 2012). It is important to note that a potential

limitation in the ecological validity of VR is that human actions are not directly replicated within virtual environments. Computer interfaces provide an analogous parallel, and thereby the ecological validity of VR will depend in part upon the capability of design features to naturalistically match those of the objective real-world.

Virtual exposures would also enable the presentation of specific stimuli and events that would otherwise be unable to be generated in a clinician's or researcher's office, such as facing obsessive fears of causing physical harm to another person. Through the use of virtual environments, clients could engage with stimuli or triggers and explore the outcomes of interactions. Performing this in a controlled virtual manner overcomes the difficulty of spontaneously eliciting such symptoms within sessions (Lind et al., 2013), and allows for exploring scenarios that would otherwise be impossible or impractical to bring into the setting (Kim et al., 2009). Conventional exposures may feel detached from patients' everyday experiences, due to inability to replicate an ecologically valid scenario in a clinician's office, and imaginal exposures may not feel sufficiently symptom provoking, due to relying upon a patients mental imagery that may not generate convincing disconfirmation (Gillihan et al., 2012), which are crucial limitations to treatment efficacy, according to the theoretical underpinnings of ERP therapy (Foa & Kozak, 1986; Lang, 1977; Lind et al., 2013). Virtual treatments that are targeted in their design towards patients' everyday experiences would provide opportunities for exposure-based tasks to feel more relevant and customised to their individual needs. Furthermore, the potentially diverse environments available via VR enhance opportunities for inhibitory learning across multiple contexts, producing generalisable safety learning (Craske et al., 2014). Patients may also have difficulty implementing traditional ERP practices in the manner recommended by their clinician. Specifically, compliance with therapeutic homework tasks has been identified as a major contributor to treatment OCD (Lind et al., 2013; Wheaton & Chen, 2020). In these situations, VR could offer a more acceptable

and carefully graded training opportunity, which may in turn enhance motivation to engage in real-world situations in the longer-term.

1.2.3 Client Engagement

The relatively high levels of clients declining to commence, and attrition from, traditional ERP (Ong et al., 2016; Öst et al., 2015) may in part explain the high burden of disease and morbidity for disorders such as OCD (James et al., 2018; Murray et al., 2004; Slade et al., 2009; World Health Organization, 2008). Additionally, despite the evidenced benefits of ERP treatment for people with OCD, many remain symptomatic post treatment (Eddy et al., 2004), with only 25 percent achieving full asymptomatic status (Fisher & Wells, 2005). These factors emphasise the pressing need for new therapeutic techniques that are more likely to be accepted by patients. It has been theorised that features of VR technology may increase clients' sense of control over their own treatment. Furthermore, patients being aware that VR systems are being carefully monitored by the supervising clinician could heighten their trust that exposures will be appropriately matched to their needs and subsequently enhance the therapeutic relationship, which is a known predictor of treatment outcome (Abramowitz et al., 2002; Martin et al., 2000). A traditional, *in vivo* exposure within a public bathroom could be impacted by uncontrolled factors, such as a stranger entering the space, creating uncertainty that may be insurmountable for a patient new to ERP, leading to drop-out from therapy. Within VR, the client and clinician would share an understanding that the virtual bathroom is precisely controlled and exposures appropriately targeted. In addition, the option to grade back the exposure task or switch off the VR at any time could be a benefit above real-world experiences which cannot be ended in such a rapid manner. In these ways, capitalising on the potential benefits of VR over traditional techniques may improve patients' engagement and sense of self-efficacy, which could in turn reduce the aforementioned typically high refusal and attrition rates from therapy (Kim et al., 2009; Ong et al., 2016; Öst et al., 2015).

As VR systems become increasingly commercially available, they also offer unique opportunities for patient-directed therapy engagement within their own homes. Clinicians would be able to more carefully and precisely grade the in-home ERP practice tasks that patients are completing, providing greater standardisation (Cloos, 2005). Doing so would be beneficial for patients completing therapy homework tasks, as well as those who may be unwilling or unable to physically attend a clinic, due to barriers such as geographical location and symptom severity. Through this, psychological services would be able to reach more patients in an efficient manner, including those living in rural or remote areas. This style of therapeutic engagement aligns with telehealth offerings which now offer considerable improvements in service accessibility (Bradford et al., 2016).

1.3 Ongoing Research Investigation

Despite the unique benefits presented by VR, rigorous scientific evidence is still required to properly demonstrate its safety and efficacy. Beyond this, the nature and breadth of specific evidence required will differ across clinical and research applications. Specific to VR exposure-based therapy systems, this includes a demonstrated ability to elicit disorder specific emotions, then in turn extinction processes, and treatment gains that are maintained and transferred to client's everyday lives. It will also be necessary to compare VR to existing best-practices in the field and identify whether VR offers any identifiable advantages. These findings must be replicated across representative, generalisable samples, rather than the currently common utilisation of small samples that do not meet clinical diagnostic criteria (Carl et al., 2019; Inozu et al., 2020; Matthews et al., 2017). As such, the following sections will expand upon these key challenges, with a particular focus upon those that are crucial to OCD interventions with VR exposure-based therapy applications.

1.3.1 Validation: Evidence of Emotional Arousal and Extinction

With clinician guidance, clients being treated with ERP face stimuli that provoke an increasing arousal response across a series of personalised, graded tasks (Brauer et al., 2011; Jenike, 2004), with the goal being to learn new associations with feared stimuli, thereby extinguishing their previous maladaptive fear models. These new learnings are intended to generalise from the therapeutic setting back to their everyday lives, as described by emotional processing theory. Theoretically, each client's fear structure should be activated, and paired with corrective information in order to modify the memory structures underlying such emotions (Foa & Kozak, 1986). Over time, clients learn that they can tolerate arousal, the distress elicited will subside, and they are capable of managing anxiety without compulsions (American Psychiatric Association, 2007; Gillihan et al., 2012). Therapeutic success is not framed as the escape of emotional arousal, nor as habituation, rather the establishment of new associative learnings, disconfirming beliefs, and tolerance of distress (Abramowitz, 1996; Craske et al., 2008). Therefore, in order to achieve these new associative learnings with clients' experiences of distress, novel therapeutic approaches must be justified by reliable evidence that anxiety responses can be elicited in patient groups and guided by the theoretical foundations of traditional ERP therapy. The evidence base for VR exposure-based therapy will need to be established across the domains of traditional exposure, namely, arousal and extinction. Treatment gains are most likely to translate from the clinical setting into clients' everyday experiences when the stimuli closely match those faced in daily life (Lang, 1977). As such, virtual environments that are immersive and realistic would theoretically be more likely to generate habituation and extinction. To realise this potential, VR environments used in ERP need to be perceived and accepted as realistic by each client.

To date, VR exposure-based therapy research has provided evidence of emotional arousal and extinction primarily using subjective symptom distress measures (Carl et al., 2019;

Wiederhold & Wiederhold, 2000). However, a wider range of convergent findings across outcome measures, such as psychophysiology signals that provide indirect indicators of emotional arousal and habituation, are required to strengthen this evidentiary basis (Freire et al., 2010; Moore et al., 2002; Mühlberger et al., 2007; Notzon et al., 2015; Wiederhold et al., 2002). Such a task is not trivial, as the integration of traditional research measures with VR hardware poses logistical challenges due to the difficulties of concurrently operating electroencephalography or other mobile neurobiological assessments with an HMD. This places the onus upon clinician-researchers and their technology collaborators to design novel workarounds to obtain reliable data.

1.3.2 Treatment Delivery and Efficacy

Once research has provided evidence that VR exposure-based therapy can generate arousal and extinction that would enable symptom improvement, then the optimal factors required for treatment will still need to be determined, such as patient symptom severity or personality traits. An understanding of these factors is important as presently the variables that would enhance or impede VR exposure-based therapy effectiveness remain unknown. As with many other forms of treatment, identifying suitable patients relies upon understanding the factors that underlie individual variability in therapeutic responsiveness. The current lack of understanding of ideal treatment conditions that will translate symptom improvements into the real-world is a notable limitation of the research to date (Farrell et al., 2003; Optale et al., 2010; Teo et al., 2016). Assessment tools that can predict prospective patients who are most likely to respond to VR exposure-based therapy on the basis of demographic, symptom, cognitive, or personality profiles are needed.

Moreover, the manner in which sessions should be tailored and delivered, such as the frequency and duration of sessions required to generate clinically meaningful improvements in the target symptomatology, must be unravelled. Eight sessions of VR exposure-based therapy

in a small sample of OCD patients resulted in symptom change; however, these were insufficient to generate clinically satisfactory improvements and a greater number were recommended (Laforest, Bouchard, Bossé, et al., 2016). This represents an important research question for ongoing consideration: do VR exposure-based therapy sessions hold any advantage compared to traditional approaches regarding the speed of treatment improvements, or maintenance at follow-up?

1.4 Considerations for VR Exposure-Based Therapy Design and Implementation

There is a lack of readily available guidelines for the ethical practice of VR in psychology at several levels including: hardware and software safety, specialised risk identification and management at the disorder and individual levels, and professional responsibilities. VR exposure-based therapy implementations also need to consider clinician and health service acceptability, perceived usability and uptake. In order to sustain the therapeutic relationship—a cornerstone of clinical practice (Martin et al., 2000)—examination must also be directed to patient to clinician communication which will need to be maintained throughout VR immersions. Addressing these challenges will require considerations of the unique interactions between the technology and established standards of practice (Yellowlees et al., 2012).

1.4.1 Ethical and Clinical Practice

To ensure patient safety when engaging with hardware and software, all potential VR exposure-based therapy users should be assessed for suitability prior to immersion, and complete consent procedures that include explanations of risks unique to VR (Yellowlees et al., 2012). It is important that patients are carefully informed about what to expect within the virtual therapy session, and how it will differ from other uses of VR like recreational games. Also at the individual patient level, technology should be re-calibrated and trialled with each patient, before commencing any therapeutic processes, to ensure safety using hardware and general software (Behr et al., 2005).

Ethical guidelines are required for patient groups with psychiatric diagnoses, but these standards must be applied on an individual case-by-case level. Certain psychiatric and neurological conditions may predispose individuals to being more susceptible to adverse effects. These may include vulnerability to conflating virtual and real experiences, causing difficulties transitioning back to the real-world post-VR immersion, and being less equipped to cope than people without such diagnoses (Behr et al., 2005; Kellmeyer, 2018). Interestingly, populations that may be considered vulnerable in VR due to poor differentiation between reality and imagination, such as psychosis, have engaged with virtual environment co-design (Realpe et al., 2020) and have demonstrated safe, acceptable use in research settings (Botella et al., 2009; Freeman, 2008). This emphasises the need for screening of suitability on a patient-by-patient basis, and not solely by the diagnostic category. On this background, procedures should be in place to provide support within VR ERP sessions, such as the ability for patients and clinicians to communicate easily, both verbally and non-verbally. While these are standard requirements of ethical practice, the unique interactions between user and technology have the potential to raise novel practical challenges that will need to be addressed. One prominent example is that HMDs may impede nonverbal communication, and through this interfere with building and maintaining rapport. It may also be challenging to provide immediate support according to clinical need, without the adverse effects of rapid immersion cessation.

As a consequence of the aforementioned concerns, it is imperative that appropriately trained specialists oversee the design, use, and accessibility of these systems. Due to the broad range of professional skills required for such systems, doing so will likely require interdisciplinary collaboration between medical specialists, VR developers, implementation researchers, ethicists, and people with lived experience. User-centred, co-design approaches should occur from the outset and throughout development and roll-out, to ensure that systems are purpose-built with the primary goal of addressing patient needs (Kellmeyer, 2018;

Kellmeyer et al., 2019; Realpe et al., 2020). Input from VR competent clinicians will be required to ensure that systems minimise any risks of cognitive or emotional overload, as this would have negative flow on effects for the psychological wellbeing of patients (Behr et al., 2005). Without taking a collaborative design approach, software developers may not understand the unique risks of VR for vulnerable populations, potentially inadvertently heightening exposure severity or triggering symptoms with design features without a clinical purpose.

1.4.2 Maximising Clinical Uptake and Patient Engagement

To date, the clinical uptake of VR systems has been impeded by clinicians believing that such systems would require more training, as well as a reluctance to make costly investments in equipment, and limited understanding of the benefits and opportunities offered (Schwartzman et al., 2012). Greater awareness of the utility of VR amongst clinicians may help to increase uptake, as ‘perceived usefulness’ has shown to predict VR adoption (Bertrand & Bouchard, 2008). Streamlining the simplicity of design features is also likely to facilitate clinical uptake. As such, system designers will need to consult available guidelines to develop user-friendly interfaces specialised for psychological uses (Brinkman et al., 2010).

Clinical implementation will also require empirical evidence of therapeutic factors, such as rapport and alliance, being maintained in VR systems. The quality of a therapeutic relationship is a known predictor of treatment outcome (Martin et al., 2000), and strategies to measure and maintain this alliance must be purposely incorporated into designs. Attention to this is of particular importance, as some hardware choices (like HMDs) create physical barriers to non-verbal communication. It remains unclear whether client’s sense of security and engagement can be maintained while using the technology (Riva, 2005), or the therapeutic relationship will be detrimentally affected. Circumventing these challenges will be important to uphold rapport and keep technology as a tool, rather than an all-encompassing feature of

therapy (Rizzo et al., 2003). Thus far, many studies have not reported the manner of therapeutic communication, nor incorporated measurement of the users' experiences of alliance (Lindner et al., 2017; Repetto et al., 2013), which hinders the current understanding of the impact of such technologies on human to human relationships within the therapeutic space.

1.4.3 Potential Challenges and Limitations of VR Exposure-Based Therapy

From a psychological practice perspective, concerns currently exist about the extent of VR's ecological validity and empirical evidence. Although promising opportunities do exist for ecologically valid VR, available systems are limited by the inability to directly replicate human actions and behaviours. As each user's degree of immersion and cognitive suspension of disbelief will impact the transferability of treatment gains, this has implications for the validity of their VR experience. Clients engaging in VR exposure-based therapy will require systems to offer varied contexts for learning, in order for learned safety to be retained, transferred, and generalised (Carmin et al., 2005; Kozak & Coles, 2005). Achieving this will require greater investments in systems to enable the creation of variable, immersive environments. These constraints are an important consideration, as VR therapy would only be justifiable if the practicalities of cost, accessibility, and side effects (Wilson et al., 2015) are outweighed by benefits above both existing therapeutic modalities and less immersive technologies (Pallavicini et al., 2013). Additionally, translating responsive clinical skills into a therapeutic VR context may present challenges (Riva, 2005), such as headsets impeding non-verbal communication. Such adaptations to the process of the therapeutic relationship will require empirical evaluation to determine whether the rapport and alliance can be upheld.

When considering VR-based ERP, considerations regarding the generalisability of experience are particularly important. It is known that ERP can be fundamentally undermined by inappropriate fear confrontation (Gillihan et al., 2012), which raises concerns given the possibility that some clients may perceive a lower potential for harm in virtual environments.

This introduces the need for careful assessment of whether clients are perhaps more inclined to engage with VR-based ERP due to relatively lower fear than *in vivo*, in which case the potential value of the virtual ERP itself may be challenged. Assessment tools will be required to determine the ability of clients to cognitively suspend disbelief and experience sufficient fears of harm, in order to predict which of either VR-based or traditional *in vivo* and/or imaginal ERP is most likely to yield therapeutic improvements. It must also be noted that VR hardware may force complete ritual prevention, such as the inability for clients to complete a hand washing compulsion in the objective real-world during a virtual immersion. This would impede the opportunity for clients to practice enacting control over their own compulsions, which is an important component of new associative learnings to impede fear (Craske et al., 2008; Foa, 2010). Clinical judgement and formal screening tools will be required to determine client suitability on an individual basis, considering these factors.

At an institution-setting level, creating customisable, ecologically valid systems has significant cost implications that may be insurmountable for clinicians or researchers outside large institutions, limiting implementation (Rothbaum et al., 2006). These challenges and limitations reinforce the importance of VR-based ERP being positioned as a potential adjunct tool within therapy, rather than as a standalone treatment approach. Consideration will be required to weigh up the increased resource costs of VR against the novel advantages offered by this potential therapeutic modality.

1.5 Empirical Evidence of VR Exposure-Based Therapy across Disorders

As explored, clients unique fear structures may be targeted more effectively by VR through carefully customised exposures (Krijn, Emmelkamp, Olafsson, et al., 2004). When contrasted against imaginal techniques, virtual exposures have the potential to be more realistic, ecologically valid, and immersive. In the same manner as standard therapy, in VR exposure-based therapy participants elect to face stimuli that gradually increase in the level of

anxiety provocation. VR exposure-based therapy evaluations report medium to large overall effect sizes compared to control conditions, and no significant differences when compared to traditional therapy, with applicability across an increasing range of disorders (Carl et al., 2019; Parsons & Rizzo, 2008; Powers & Emmelkamp, 2008).

Empirical examination of VR exposure-based therapy systems for Post-Traumatic Stress Disorder (PTSD) reveals large effect sizes, that are superior to waitlist control groups, as well a non-inferiority of therapeutic gains compared to traditional exposure-based techniques (Difede et al., 2006; Gonçalves et al., 2012; McLay et al., 2014). Treatment studies within this patient cohort have repeatedly indicated clinically and statistically significant symptom improvements across multiple sessions (Difede et al., 2006; McLay et al., 2011; Reger et al., 2011; Rizzo et al., 2010, 2014). This may be due to VR exposure-based therapy for PTSD providing the opportunity to more closely match each client's specific traumatic memories to create more successful targeted fear extinction, and thereby holding particular promise for patients who are show ambivalence or treatment resistance to traditional ERP. However, further studies are required that incorporate rigorously controlled samples, longer term follow-ups, and assessment of attrition rates compared to traditional therapy (Gonçalves et al., 2012). It has also not yet been established if decreases in PTSD symptoms are clinically equivalent to those achieved using traditional treatment approaches, a necessary step to justifying VR exposure-based therapy within clinical practice.

Consistent with PTSD research, studies of VR exposure-based therapy systems for specific phobias have reported large, significant declines in symptoms of anxiety across arachnophobia, agoraphobia, and acrophobia (Parsons & Rizzo, 2008). These are maintained at one-month post-treatment, to a comparable degree to psychological treatment, and superior to waitlist control conditions (Carl et al., 2019). At longer-term follow-up, there are no differences between VR exposure-based therapy and traditional *in vivo* (real-world) exposure

therapy outcomes for specific phobias (Morina et al., 2015), with improvements that are broadly equivalent to CBT in the case of social phobias (Klinger & Bouchard, 2005). As such, VR exposure-based therapy has empirical evidence as an efficacious therapy in some phobias including fear of flight, heights, and animal phobias (Carl et al., 2019), which is a promising indicator that other similar disorders—which also use exposure-based approaches to therapy—may exhibit similar results. Ongoing comparisons to active control conditions, involving existing best practices in ERP, and longer term treatment follow-ups are required as the next step across a range of phobic disorders (Gujjar et al., 2019; Minns et al., 2019).

For social anxiety disorder and performance anxiety, VR exposure-based therapy has shown superior outcomes compared to placebo or waitlist conditions (Bouchard et al., 2017), with a large pooled effect size reported across studies (Carl et al., 2019). Initial studies conducted with university students showed public speaking anxiety reductions across four VR exposure-based therapy sessions, evidenced by self-report and psychophysiological measures (Harris et al., 2002). Subsequent investigation in clinical samples showed VR exposure-based therapy was analogous to group-based therapies in symptom reductions across eight sessions (Anderson et al., 2013). These improvements from VR exposure-based therapy may be maintained at up to 12-month follow ups (Anderson et al., 2013), especially when combined with traditional CBT (Bouchard et al., 2017). Beyond symptom improvements, therapists considered VR exposure to be more practical than *in vivo* approaches, a promising finding for future uptake (Bouchard et al., 2017). However, some limitations exist in VR exposure-based therapy relative to *in vivo*. Further rigorous investigation is required to determine the potential secondary beneficial effects on comorbid symptoms and quality of life, and whether inferiority at follow-up occurs (Bouchard et al., 2017; Kampmann et al., 2016).

While a relatively small number of studies have investigated responses to VR exposure-based therapy in panic disorder with or without agoraphobia, large effects sizes have been

demonstrated in comparison to waitlist or placebo controls (Carl et al., 2019). Clinically meaningful improvements have been reported from nine weekly sessions (Botella et al., 2007) and maintained at both short- and long-term follow ups (Pelissolo et al., 2012). Tempered consideration of VR exposure-based therapy for panic disorders is recommended presently, given *in vivo* outcomes appear relatively superior to date (Carl et al., 2019) and longer-term outcomes remain to be determined (Meyerbroeker et al., 2013).

1.6 VR Exposure-Based Therapy for Obsessive Compulsive Disorder

On the basis of the aforementioned evidence, other conditions that also benefit from exposure-based approaches to therapy, such as Obsessive-Compulsive Disorder (OCD) are also excellent candidates for VR exposure-based therapy. Virtual environments designed for OCD populations have shown preliminary validity, evidenced by the ability to elicit disorder specific emotions and behaviours, including increased anxiety and disgust, as well as to trigger compulsions (Belloch et al., 2014; Van Bennekom et al., 2017). These responses to virtual stimuli occur to a greater degree than non-OCD comparison groups (Kim et al., 2008; Laforest, Bouchard, Crétu, et al., 2016), showing specificity of relevant emotions being appropriately targeted. In addition to these studies of emotional arousal, research has investigated opportunities for treatment in OCD. VR exposure-based therapy has generated reductions in the intensity and severity of obsessions and compulsions (Laforest, Bouchard, Bossé, et al., 2016). Symptom improvements have been maintained post-treatment at one-month follow up (Matthews et al., 2017).

However, the evidence base for VR exposure-based therapy in OCD is at a relatively earlier stage when compared to the aforementioned disorders. Limitations include sample sizes of twelve or fewer participants (Belloch et al., 2014; Laforest, Bouchard, Bossé, et al., 2016; Laforest, Bouchard, Crétu, et al., 2016; Van Bennekom et al., 2017) that in some cases do not meet clinical diagnostic criteria (Inozu et al., 2020; Matthews et al., 2017). Many OCD

specialised VR systems have not utilised hardware that is sufficiently immersive to generate presence. By using only rudimentary joysticks for seated ‘movement’ through virtual environments, non-immersive representations of the self on a television, or a proxy character on a computer screen, opportunities for enhanced immersion have been overlooked (Belloch et al., 2014; C. H. Kim et al., 2008; K. Kim et al., 2008; Matthews et al., 2017). Although it is promising that these relatively low-grade immersions designed for OCD can elicit symptoms, they do not utilise naturalistic interactions between the user and virtual environment. This is notably problematic given that making contact with stimuli is often central to OCD symptoms, such as contamination or harm related concerns. In order for this field of research to progress, symptom provocation and improvements should be compared to traditional best-practice methods, as shown in other disorders (Carl et al., 2019). Without this, clinicians would be unlikely to identify the benefits of supplementing therapy with virtual methods beyond imaginal techniques, given the substantial time and financial investments required to create customised systems.

1.7 Concluding Remarks

Evidently, VR exposure-based therapy shows value as a treatment mechanism for several anxiety and stress-related disorders, including potentially Obsessive Compulsive and Related Disorders. This suggests conditions with similar theorised mechanisms and approaches to treatment—such as OCD—may offer an exciting new area to continue examining the beneficial opportunities of VR exposure-based therapy. In light of these outlined opportunities, considerations, and challenges for VR exposure-based therapy implementation, in the following chapter I will provide a critical review of the literature relevant to OCD, which will serve as the applied context for my validation of a novel VR system.

CHAPTER TWO: OBSESSIVE COMPULSIVE DISORDER

Any consideration of the opportunities for OCD using VR must begin with an understanding of the cognitive and behavioural features of this disorder. Of particular importance are commonalities in thinking styles and behaviours exhibited in OCD patient cohorts, as they serve as the theoretical foundation for current psychological treatments. Particular focus will be placed upon Exposure and Response/Ritual Prevention (ERP), due to the conceptual similarities it shares with VR exposure-based therapy. I will review the existing techniques of *in vivo* and imaginal exposure, as well as the clinical importance of response prevention, in order to understand the potential utility of VR-based ERP as a treatment modality. By also providing a brief review of current adjunct treatments, the chapter explores the potential space for VR technology within the existing therapeutic framework. I examine the limitations of ERP and identify opportunities to improve upon current treatments using VR-based ERP, including overcoming traditionally high refusal, attrition, and inadequate symptom improvements.

2.1 Core Diagnostic Features of OCD

OCD is a psychological condition characterised by the presence of obsessions, compulsions, or commonly a combination of the two. Obsessions are persistent and intrusive thoughts, urges, or images that provoke anxiety and distress for the individual. In an attempt to manage this emotional distress, an individual typically feels compelled to perform repetitive mental and behavioural acts in accordance with specific rules, referred to as compulsions. The majority of diagnosed individuals present with both mental and behavioural compulsions (Foa & Kozak, 1995). These symptoms significantly interfere with daily functioning, and are clearly excessive or not realistically connected to what the individual is attempting to prevent (American Psychiatric Association, 2013a). Performing compulsions does not yield enjoyment, nor outcomes that are perceived as inherently useful to the person. Instead, individuals

commonly recognise the behaviours as excessive and ineffective; however, have failed attempts to cease performing them on their own. Unfortunately, the resistance of compulsions usually heightens distress in the short-term, and when compulsions are subsequently performed, this perpetuates a cycle of distress exacerbation over the longer-term.

Diagnostic criteria for OCD stipulate that the individual recognises that the thoughts and images are their own (International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders, 2011; Kogan et al., 2020; World Health Organization, 2019), even if they are involuntary or repugnant, in order to distinguish these thought patterns from those exhibited in some other psychiatric conditions. People with OCD often place high personal significance on unwanted and upsetting thoughts and actions, and this thought-fusion generally explains why an intrusive thought about harm can feel equally as distressing as intentionally harming someone (Gillihan et al., 2012; Salkovskis, 1985).

A diagnosis of OCD is associated with an increased likelihood of a co-morbid psychiatric disorder, reinforcing the importance of accurate diagnosis to disentangle symptoms and ensure appropriate clinical management (Crino et al., 2005; Karno et al., 1988). Most commonly these comorbidities are anxiety disorders such as panic, social anxiety, and generalised anxiety (American Psychiatric Association, 2013a; Ruscio et al., 2010). These high co-occurrence rates can make OCD diagnosis somewhat challenging, as clinicians making differential diagnoses may misclassify obsessions as depressive ruminations, psychotic symptoms, or the racing thoughts typical in mania. Successful treatment of OCD symptoms often also provides some secondary alleviation of co-morbid psychiatric conditions (Dougherty et al., 2004).

Symptom profiles in OCD patients are highly heterogeneous, with each individual likely to present differently from another (Gillan et al., 2017), though over time general symptom themes have been identified and it is highly common for patients to present with

multiple themes simultaneously (Mataix-Cols et al., 2005; Ruscio et al., 2010; van den Heuvel et al., 2009). These themes, also referred to as clusters or dimensions, are used to classify the general content of each patient's obsessive or compulsive content, such as the behaviour of excessive handwashing being clinically classified under contamination concerns. Prevalence rates of commonly recognised themes are checking (79.3%), hoarding (62.3%), ordering (57%), moral concerns (43%), sexual or religious obsessive content (30.2%), contamination (25.7%), harming (24.2%), and concerns about illness (14.3%) (Ruscio et al., 2010). These themes are relatively stable in prevalence across time and place, and have been proposed to correspond with specific neural systems (Leckman et al., 2010). Irrespective of content themes, commonalities in behavioural and thought processes exist across patients. These include inflated sense of responsibility, threat overestimation, intolerance of uncertainty, over-importance and control of thoughts (American Psychiatric Association, 2013a), and feeling the need to be 'absolutely sure' regarding a wide range of situations, motivated by perfectionism or fear of potential negative outcomes (Calamari et al., 1999).

Conjecture remains regarding whether the symptom theme classifications are optimal. Diagnostic criteria continue to be re-adjusted, as has been seen with the re-categorisation of hoarding disorder and shift of the disorder class for OCD in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (American Psychiatric Association, 2013a; Gillan et al., 2017). Distinctions within current themes (heterogeneity), and the overlap of compulsivity and treatments across disorders (homogeneity), indicates that current criteria are insufficient to understand, categorise, diagnose and effectively treat such compulsive disorders (Gillan et al., 2017).

The contamination theme of OCD is characterised by excessive concern regarding the threat of illness to oneself or others and feeling physically and/or mentally unclean. It often presents greater treatment challenges than other themes and has therefore received significant

attention. Patients with contamination concerns are typically more treatment resistant and both exposure and response prevention elements of ERP therapy are particularly important to address this subtype (Foa et al., 1984). Patients with contamination-based OCD may experience exacerbation of anxiety symptoms from stimuli such as dirt, germs, viruses, blood, household chemicals, sticky substances or residues, people who appear unclean or unkempt, and various types of insects or animals (Williams et al., 2013). Contact with these stimuli tends to cause excessive fear, disgust, discomfort, and even guilt if the patient holds concerns about being responsible for spreading contamination to others (Feinstein et al., 2003). To avoid these feelings, patients may enact avoidance behaviours and protective rituals, like disinfection, throwing away objects deemed contaminated, frequently changing clothes, or even designating areas of their home others are not allowed to enter. Should contact be unavoidable, subsequent compulsive behaviours often include excessive hand and body washing, and cleaning their environment in attempt to decontaminate possessions (Williams et al., 2013).

2.1.1 Cognitive and Behavioural Models of OCD

Intrusive thoughts are a normal phenomenon in the general population, though patients with OCD are differentiated by the appraisals that they make towards these thoughts (Salkovskis & Kirk, 1999). Typical thought processes are characterised by initial anticipatory appraisals that focus on stimuli threat, including patient's expectations about danger, harm, or disgust, with secondary appraisals considering consequences – if the primary appraisal holds true, whether they self-perceive an ability to cope (Woody & Teachman, 2000). Commonly, these appraisals consider intrusive content to be threatening or significant, irrespective of the objective level of danger or potential for negative outcomes. Strategies to manage the associated distress are maladaptive, such as avoidance and reassurance seeking. Such behaviours prevent disconfirmation of the initial appraisal through experience, and therefore serve to escalate anxiety. This framework of erroneous appraisals driving heightened

obsessions is agreed upon across cognitive-behavioural models (Foa, 2010; Rachman, 1998; Salkovskis, 1985; Shafran, 2005; Sookman & Pinard, 2002).

In addition to heightened perceptions of threat, patients with OCD often have other characteristic dysfunctional beliefs and information processing biases (Sookman & Pinard, 2002). These common thought processes can be categorised as either cognitive or metacognitive, referring to general beliefs and the control of one's own thoughts respectively (Myers et al., 2008). In OCD these include an inflated sense of responsibility (Salkovskis, 1985), importance of thoughts (Rachman, 1997), perfectionism (Frost & Steketee, 1997), and intolerance of uncertainty (Carr, 1974), each of which can underpin behavioural acts. A patient could experience pathological doubt regarding whether compulsions were performed sufficiently or satisfactorily, and attempt to escape this state of uncertainty by completing ritualised behaviours such as checking (Ladouceur et al., 2000; Mcevoy & Mahoney, 2012; Tolin et al., 2003). Many of these thought styles are common across OCD symptom themes, though perfectionism is especially predictive of washing behaviours (Myers et al., 2008).

Distress can be exacerbated by conflicts between these thought processes, such as the heightened importance of thoughts and co-occurring uncertainty regarding their accuracy. In addition to placing heightened importance upon thought content, OCD patients also yearn for accuracy and vividness in their cognitive processes. The associated mistrust in their recall of events can drive repeated performance of ritualised behaviours until they subjectively feel 'just right' (Constans et al., 1995). These cognitive styles and their associations with overt behavioural patterns are important considerations when designing and implementing treatment programs for people with OCD, with metacognitive beliefs being a significant predictor of recovery post-treatment (Grøtte et al., 2014).

OCD patients may present with overt compulsions and avoidance behaviours, often performed to provide some relief from distress (Roper et al., 1973). This short-term reduction

of obsessional anxiety serves as negative reinforcement for these behaviours, increasing their likelihood of continued use. Unfortunately, this is a maladaptive strategy in the longer-term, as it impedes opportunities for patients to disconfirm faulty appraisals, including that anxiety and obsessions are tolerable and feared consequences unlikely.

There is a tendency for patients with OCD to excessively form habits which can be conditioned to become highly ingrained compulsions that are aversive to change (Cushman & Morris, 2015). According to the 'habit hypothesis' this process may result from deficiency in goal-directed control, as mediated by the caudate and medial orbitofrontal cortex (Dolan & Dayan, 2013; Graybiel & Rauch, 2000), and a higher tendency for avoidance habits. Experimental findings suggest that compulsions may be habits that develop irrespective of the desirability of the outcome (Gillan et al., 2011, 2014).

An alternative suggestion is that compulsive behaviours are stimulus-driven, irrespective of goals (Dickinson, 1985). Under such a framework, a compulsive urge occurs first, accompanied by the 'not quite right' experience (Coles et al., 2005; Ecker & Gonner, 2008), the feeling that something is incomplete and needs to be righted. Obsessive thoughts may follow learned behaviours or vice versa (Salkovskis, 1985). Mowrer's two-stage theory proposes that fear, anxiety, and distress become associated with a conditioned stimulus, and as such avoidance behaviours develop to reduce the anxiety. These manifest as compulsions and rituals, which are maintained because the individual believes they reduce the associated distress (Foa, 2010). A functional association builds over time between obsessions that increase distress and compulsions that feel as though they reduce this distress.

A maladaptive belief about the threat of a stimulus can lead to biased attention and information processing, followed by avoidance or safety behaviours that prevent disconfirmation of the initial belief. Safety behaviours are covert and overt actions that are performed as intentional efforts to prevent an outcome. These include excessive escape and

avoidance of stimuli in an attempt to prevent the patient's feared consequence (Salkovskis, 1991). In actuality, such behaviours are unable to remove the risk of feared outcomes. While encouraging patients to abandon their safety behaviours is commonly integrated into psychological treatment, conjecture remains whether completely withholding these behaviours is therapeutically necessary, and that partial response prevention may be sufficient (Van Den Hout et al., 2011). OCD patients feel unable to abandon their safety behaviours because they attribute the absence of disaster as being the result of their actions (Gillihan et al., 2012). An example of such behaviour would be considering one's own good health as being due to the avoidance of hospitals. Thereby, a learned association is established between their behaviour and an outcome, although the likelihood of the feared consequence was low regardless.

2.1.2 Burden of Disease

Treating OCD is of considerable importance given that anxiety and related disorders are considered by the World Health Organisation as one of the top ten causes of non-fatal disease burden (James et al., 2018). OCD is a chronic condition characterised by periods of remission and relapse. Globally, the 12-month prevalence of OCD is around 2 percent (Crino et al., 2005; Slade et al., 2009; Weissman, 1998), with lifetime rates of up to 3 percent positioning OCD as one of the most common psychiatric disorders (Crino et al., 2005; Karno et al., 1988).

The average age of OCD diagnosis is between 22 and 36 years, with men generally experiencing symptom onset earlier than women (Jenike, 2004; Veldhuis et al., 2012). However, these averages may mask a bimodal onset pattern, covering an average early-onset of 12.8 years old and late-onset of 24.9 years old (Anholt et al., 2014; Heyman et al., 2001). Diagnosed patients are generally young, single, and unemployed (Karno et al., 1988). Typically, from the time of symptom onset it takes 9 years to receive an accurate diagnosis and 17 years to receive clinically appropriate treatment (Ayuso-Mateos, 2006; Jenike, 2004; Ruscio

et al., 2010). As the condition progresses for individuals, the age of initial symptom onset relates to the severity of psychosocial and health outcomes in the longer-term. Patients with an earlier onset of symptoms typically have higher life-long rates of comorbid ADHD symptoms, more compulsions, and more severe OCD symptoms than later-onset patients (Anholt et al., 2014).

Due, in part, to the highly time-consuming nature of obsessive and compulsive symptoms, individuals diagnosed with OCD will experience significant reductions in quality of life and functional impairments (American Psychiatric Association, 2013a; Gava et al., 2007). In Australia, a quarter of OCD patients experience a severe degree of functional impairment, and only half will receive healthcare services for their OCD symptoms (Slade et al., 2009). Despite receiving some form of treatment, a quarter of these patients will continue to experience severe functional impairment, with each person having 6.3 days per month, on average, of being unable to perform their normal activities (Slade et al., 2009). These considerable individual, social, and economic burdens highlight the value and importance of developing a greater understanding of the cognitive and behavioural underpinnings of OCD, and the need to develop treatments that can achieve clinically meaningful symptom improvements.

2.2 Current Treatments for OCD

The present approaches to treatment of OCD have developed from earlier unsuccessful techniques, such as systematic desensitisation, thought stopping, and aversive approaches to operant conditioning—such as the rubber-band technique. Through graded exposures to a hierarchy of feared stimuli that were paired with relaxation or unpleasant consequences, these approaches attempted to extinguish the obsession or compulsion. These techniques have poor effectiveness in improving symptoms of OCD and are not considered to be evidenced-based practices (Foa, 2010; Lam & Steketee, 2008).

Current cognitive therapeutic approaches aim to assist patients in identifying their unrealistic thinking patterns and obsessional worries, then changing the meaning ascribed to these thoughts. In these treatments, the clinician provides psychoeducation and supports the client to challenge their unrealistic beliefs, identify cognitive distortions, and re-evaluate the predicted consequences of not engaging with compulsions (Brauer et al., 2011; Foa, 2010). Symptom improvements attained from cognitive techniques increase in effectiveness when combined with behavioural components, such as ERP approaches (Cottraux et al., 2001; Eddy et al., 2004; Rosa-Alcázar et al., 2008).

Strong evidence of ERP treatment effectiveness has led to it being widely accepted as the recommended first line non-pharmacological treatment for OCD (Abramowitz et al., 2001; American Psychiatric Association, 2007, 2013b; Dougherty et al., 2015; National Institute for Health and Care Excellence, 2005; The Australian Psychological Society, 2010, 2018). ERP is an efficacious therapeutic approach, supported by a strong, replicated evidence base showing successful and significant reductions in symptom frequency and severity that can be maintained post-treatment, and is superior to a range of control conditions (Abramowitz, 1996; Foa, 2010; Foa et al., 2005; Franklin et al., 2000; Gava et al., 2007; Jenike, 2004; Olatunji et al., 2013; Stanley & Turner, 1995; Valderhaug et al., 2007).

2.2.1 Exposure and Response Prevention

The overarching goal of ERP is for clients to acquire new learnings that compete with their existing maladaptive fear structures, through carefully designed behavioural experiments. Working collaboratively with the clinician, clients practice facing anxiety-provoking scenarios and withholding compulsive behaviours. Exposures may take the form of *in vivo* (also referred to as ‘real world’), and/or imaginal exposure (in which the client visualises feared stimuli, or dwells on thoughts and mental images).

Given that performing compulsions impedes learning that anxiety is manageable and temporary (Rachman et al., 1976), patients need to practice and learn skills to choose not to perform the associated compulsive behaviour, referred to as Response Prevention. Through this withholding of compulsions, patients are supported to develop new, helpful learnings that override their existing beliefs to achieve lasting symptom reduction. From this, clients can learn that anxiety and urges to ritualise after facing an anxiety-provoking stimulus will subside over time, without performing compulsions. Incorporating both Exposure and Response Prevention into therapy sessions leads to greatest symptom reductions at post-treatment follow-up (American Psychiatric Association, 2007; Foa et al., 1984). With repeated ERP sessions, the client replaces unhelpful frameworks with new associations to the feared stimuli, which generate declines in both anxiety responses and the urge to ritualise.

Exposure tasks involve clients confronting internal and external anxiety eliciting stimuli, such as thoughts, images, objects, and situations, that bring about obsessions and anxiety. Before treatment, clients' fears are independent of context; any bathroom is feared unconditionally to be contaminated, yet therapeutic learnings are usually context dependent; this one bathroom didn't produce the feared consequence, but what if another still does. Therefore, novel exposure situations aim to establish context-independent learned safety. Exposure tasks are designed purposefully for clients to test out the accuracy of their feared beliefs. A series of tasks would be organised into a set of planned, systematic behavioural experiments, that are faced in multiple contexts. Tasks are often arranged in a graded manner into an exposure hierarchy that increases in anxiety-provocation, which clients progress upwards through until even the most challenging stimuli produce little anxiety (Brauer et al., 2011; Jenike, 2004). Within the ERP framework the patient and clinician work collaboratively, deciding as a team whether and when to increase the level of the exposure. Specifically, the

patient takes an active role in planning the strategy for treatment and the content of the exposures in the hierarchy (Abramowitz, 1996).

In order for therapeutic learnings to be generalised to the client's everyday lives, sessions should include variability in exposure formats (Kircanski & Peris, 2014). Specifically, they should incorporate a range of situations, emotions, times of day, and the presence or absence of other people including the clinician. In doing so, the likelihood of retention, transfer and generalisation are improved (Carmin et al., 2005; Kozak & Coles, 2005). A patient learning that touching 10 toilets in different locations did not result in their feared consequences is more likely to achieve stronger new learnings than one who had touched a single toilet, even if it was repeatedly touching the one toilet. As they undergo these experiences, clients are supported to learn that the distress associated with obsessions does and will subside, and that they can tolerate anxiety, including at higher levels than they may predict. Over time, these experiences reinforce that clients are capable of managing anxiety while with-holding compulsions (American Psychiatric Association, 2007; Gillihan et al., 2012).

Exposures conducted *in vivo* refer to patients confronting their feared stimuli in the real-world environment, for example people with contamination fears using a public bathroom (Foa, 2010). Imaginal techniques can be used to confront feared mental stimuli, including those that may otherwise be impossible *in vivo*, due to fearing they will change in some fundamental way, such as dying from AIDS or hitting a pedestrian with their car (Foa, 2010; Gillihan et al., 2012). Typically, imaginal exposures are written or spoken narratives that include detailed sensory descriptions of stimuli and the patient's worst feared outcomes. Audio recordings may be used for patients to practise outside of session (Freeston et al., 1997; Salkovskis, 1985). These narratives are confronted repeatedly and require the patient to vividly imagine the details to sufficiently elicit anxiety (Gillihan et al., 2012). Repeated presentations of the imaginal narrative aim to teach patients that pondering or dwelling on thoughts does not make them

more likely to occur, and as such learn to believe the outcome is decreasingly likely. Over time, the patient is able to recognise that the distress provoked is manageable and tolerable (Gillihan et al., 2012).

The choice between *in vivo* and imaginal, or a combination, can challenge clinicians and patients, as the incorrect choice of exposure technique may prevent the patient from confronting the core feared stimulus and learning the anticipated consequences do not occur (Gillihan et al., 2012). *In vivo* exposures tend to create stronger improvements than imaginal alone, though the combination of both produces greatest treatment gains (Abramowitz, 1996; Gillihan et al., 2012), and should be customised on a patient by patient basis to most effectively target core fears (Foa et al., 1985). Optimal treatment outcomes will depend upon clinicians designing a targeted combination of *in vivo* and imaginal, and encouraging response prevention to maintain improvements and minimise relapse (Abramowitz, 1996; Foa et al., 1980, 1985). Imaginal and *in vivo* therapy may occur in a synchronised manner within the same session, making contact with stimuli while also actively imagining the potential feared outcomes.

At the outset of an ERP session, a collaborative understanding is established that clients should expect their anxiety to heighten, and that therapeutic success is not defined by the suppression, removal or escape of this feeling. The transient anxiety is provoked in a supportive, therapeutic environment to learn that anticipated outcome is unlikely to occur, thereby over time reducing the associated fear and anxiety from obsessional phenomena (Abramowitz, 1996; Hodgson & Rachman, 1972). While habituation is a likely result, it is not the central goal of ERP—rather clients should work towards tolerance of distress and establishing disconfirming beliefs.

Once the anxiety-provoking stimulus is confronted during an exposure, the accompanying component is the withholding of compulsions. This is central to learning that rituals are unnecessary, and that in their absence the feared consequences remain unlikely to

occur (Foa, 2010), and new associative learnings which inhibit fear are established (Craske et al., 2008). It is therefore important that clients should re-expose themselves if a safety behaviour or compulsion is performed after an exposure. This is a challenging expectation of patients and likely to require clinician support to appropriately grade response prevention. It may be appropriate to start with 'not quite right' or 'imperfect' compulsions, such as patients washing their hands for a shorter duration or delaying beginning such compulsions, with the longer-term goal of refraining from all ritualising. Partial or incomplete performance of rituals or safety behaviours may not hinder the beneficial outcomes of exposure entirely (Rachman et al., 2011; Van Den Hout et al., 2011).

Incorporating some degree of response prevention into therapy is crucial, as many patients would willingly engage in exposure with the knowledge they could subsequently perform a ritual, effectively undermining the goals of ERP (Huppert & Roth, 2003). Mentally neutralising an exposure by thinking about performing a washing compulsion immediately afterwards negates the intended learning experience. Although rituals manage discomfort in the short-term (Huppert & Roth, 2003), they perpetuate the cycle of relying upon compulsions to mitigate experiences of anxiety. Therefore, prevention of these neutralising responses during therapy, such as rituals, requires patients to tolerate immediate discomfort for longer term beneficial outcomes (American Psychiatric Association, 2007).

The effectiveness of ERP may also be detrimentally impacted by clinicians being reluctant to encourage patients to approach distressing situations and to directly address avoidance and ritual behaviours. A balance between supportive acceptance of the client and emphasising the importance of fully engaging with the exposure tasks can be difficult to establish (Abramowitz et al., 2002; Pence et al., 2010). Clinicians can also undermine ERP effectiveness by providing reassurance, failing to address the client's core fear, not confronting mental compulsions, and encouraging distraction during exposure (Gillihan et al., 2012). Strict

exposure guidelines will need to be created and adhered to with each patient so that they are relieved of the burden of deciding which situations are acceptable or unacceptable for them to perform a compulsion (Abramowitz, 1996).

2.2.2 Adjunct and Alternate Treatments

While ERP is the first-line psychotherapeutic approach, it may also be performed in tandem with pharmacological approaches that target abnormalities in serotonergic and dopaminergic neurotransmission (Dougherty et al., 2004; Eddy et al., 2004; Vaswani et al., 2003). Specifically, psychological treatment is often delivered in combination with selective serotonin reuptake inhibitor medication (Bandelow et al., 2008; Dougherty et al., 2004; Foa et al., 2005; Kobak et al., 1998; Simpson, Foa, et al., 2008). Symptom reductions from medications alone are evidenced in 40 to 60 percent of patients (Ackerman & Greenland, 2002; Bandelow et al., 2008), typically decreasing symptoms by 20 to 40 percent (Greist et al., 1995). Tricyclic antidepressants—such as clomipramine—have also shown effectiveness (Ackerman & Greenland, 2002), however they result in the most side effects (Abramowitz, 1997) and the greatest overdose risk (Grunebaum et al., 2004). As such, it is important to consider the relative benefits of behavioural therapies, that are more robust to individual differences than pharmacotherapies and from which patients also exhibit less side effects (Kobak et al., 1998). Despite their combined use, the addition of psychoactive medications to therapeutic treatment may not generate improvements above CBT or ERP alone, and such antidepressant medications are independently less effective than CBT (Öst et al., 2015). Additional weaknesses of pharmacological approaches include typically requiring high dosages and long latencies for effects to emerge (Bandelow et al., 2008), which in turn induces complications in the treatment process, especially when patients exhibit high relapse rates following discontinuation of use (Dougherty et al., 2004).

Surgical approaches have also been proposed for patients who are refractory to both psychological, including ERP, and pharmacological approaches. Preliminary reports suggest deep brain stimulation can be effective (Abelson et al., 2005; Denys et al., 2010; Farrand et al., 2018; Gabriëls et al., 2003; Greenberg et al., 2010), however these are based on highly selective small patient samples and insufficient randomised controlled data (Alonso et al., 2001; Naesström et al., 2016). This evidence should therefore be interpreted with caution, given considerable methodological limitations including sample generalisability. Neurosurgical approaches, such as anterior cingulotomy, limbic leucotomy and anterior capsulotomy, are hypothesised to enact symptom improvements via disruption to the dysfunctional circuitry associated with OCD. Trials of these approaches report beneficial responses in up to 45 percent of cases, which is clinically significant as patients must be refractory to all other types of treatment to be eligible for neurosurgery (Dougherty et al., 2002). It must be emphasised that surgical procedures are also highly invasive and carry considerable risks and ethical considerations, as seen in other psychiatric conditions using similar approaches (Saleh & Fontaine, 2015; Thomson et al., 2018) which limits their general applicability.

2.3 Limitations of OCD Exposure and Response Prevention Using VR

While the current suite of treatment approaches has strong evidentiary support, there remains high variability in response rates across patients. Of the patients who show improvements from treatments, many still remain symptomatic, with only the minority reaching full recovery (Brauer et al., 2011). Of those patients who do commence psychological and/or pharmacological therapy, approximately half respond with some degree of symptom reduction. However, only 33% demonstrate treatment response to achieve minimal symptoms, defined by Yale-Brown Obsessive Compulsive Scale scores below 12 (Simpson et al., 2006; Simpson, Foa, et al., 2008). Achieving symptom improvement often requires multiple commencements of therapy across time, with many patients reporting a long history of

unsuccessful intervention attempts. Even where effective treatment is able to be achieved, symptoms persist at moderate levels (Eddy et al., 2004) and patients remain more symptomatic than the general public (Abramowitz, 1996).

These issues highlight the considerable challenges in achieving clinically meaningful symptom reduction in a majority of patients who present for traditional treatment. In part, this stems from the impracticalities of simulating situations and associated intrusive thoughts during therapy (Lind et al., 2013). Such impracticalities include the low feasibility of clinicians accompanying patients to an *in vivo* exposure within the time and geographical constraints of a therapeutic session, and challenges eliciting sufficient anxiety to achieve new learnings with imaginal narratives alone. Herein lies an important opportunity for VR. Given that virtual environments can be programmed to include an almost endless range of stimuli (notwithstanding big picture economic and time constraints), VR-based ERP holds the potential of being able to customise and target sessions precisely to a client's presenting needs. In this manner, the complex and detailed fears of the real-world can be replicated within the supportive environment of a clinician's office, improving the relevance of exposure sessions to the client's needs. These opportunities also extend to research perspectives, whereby VR offers the ability to precisely control the environment and cue exposure onset that can be synchronised precisely with data collection to record and examine participant responses.

Despite a strong basis of empirical evidence, another key limitation to current ERP treatment is the rates of patient refusal and drop-out, which VR could overcome by enhancing engagement and efficacy. At the outset, refusal rates for engaging in ERP are between 15 to 25 percent and a similar percentage of up to 25 drop out prematurely (Abramowitz, 2006; Jenike, 2004; Ong et al., 2016; Öst et al., 2015; Schruers et al., 2005). Evidently, patients need therapies that are more approachable and acceptable from their own perspectives. VR has been proposed as a mechanism to enhance client's empowerment over treatment, due to the sense of control

over exposure grading and onset. This in turn may heighten the therapeutic alliance and engagement in exposure tasks (Meyerbröker & Emmelkamp, 2008; Riva, 2005).

Of the patients who do engage in therapy, a relatively large number of sessions is often required to achieve any favourable response. Typically at least 10 to 14 sessions supplemented by self-directed homework tasks are needed (Foa, 2010; Stanley & Turner, 1995) with some subtypes such as contamination requiring longer treatment duration than others (Williams et al., 2013). This reinforces the possible advantages of in-home self-directed or semi-supervised VR-based ERP, whereby a clinician could set up a range of exposure tasks that a client could practice in a controlled, targeted manner between therapy sessions (Cloos, 2005). The customisability of VR exposures also enhances the opportunities for patients to practice exposures regularly across a range of virtual settings or contexts, potentially maximising generalisation, as well as to overcome the typically low compliance with ERP between sessions which is necessary to consolidate learning (Lind et al., 2013). More broadly, the protracted nature of current therapeutic engagements causes secondary detrimental effects of long waitlists for therapy services. The greater opportunities for treatment accessibility offered by VR-based ERP evidently could therefore enhance service delivery at a multitude of levels.

New treatment options are needed that are more acceptable to patients, can supplement clinician-guided approaches to hasten rates of symptom improvement, and support clinicians to appropriately grade exposures in an individualised manner. VR methods could make ERP more accessible, approachable, and precisely customisable, thereby potentially maximising symptom management for OCD patients. Crucially, VR-based ERP could be truly individualised to account for the heterogeneity inherent in OCD patient presentations (Brauer et al., 2011). The endless opportunities of virtual stimuli that can be generated would enable exposures that are truly targeted to patient's unique fear structure. VR technology is clearly on

the precipice of being leveraged to overcome common drawbacks of current treatment and offer maximal beneficial outcomes for patients.

2.4 Concluding Remarks

By reviewing the state of the literature for the treatment of OCD, and the opportunities for VR in clinical and research practice, these first two chapters have laid the foundation for the development and validation of a novel VR system specialised for OCD. From this basis, my work focuses upon advancing the VR exposure-based therapy field, with the aim of creating an immersive, customisable series of virtual environments that would be integrated with subjective, objective, and clinical measures. I aimed to maximally capitalise upon the aforementioned opportunities for VR, with due consideration to addressing the limitations of the current research and clinical evidence. As such, based upon the review of the literature contained within these chapters it was hypothesised that in a sample of OCD patients, multifaceted subjective and objective responses to VR and real-world *in vivo* ERP sessions would not significantly differ, and that the validity of VR would be further evidenced by similar clinical engagement.

CHAPTER THREE: DEVELOPMENT MANUSCRIPT

Here I present the results of the first manuscript of the thesis, namely, the development of a VR exposure system for OCD. As was discussed throughout the literature review, this was previously a relatively unaddressed area of clinical and research interest. The potential opportunities of VR applications had been scientifically reviewed in several highly cited articles, and more recently included a shift from theoretical considerations of VR-based therapy, into providing design considerations to leverage upon commercially available systems (Lindner et al., 2017). Although a noteworthy progression, translation into implementation to date remains hindered by a paucity of practical, clinician-friendly protocols, which is an important gap that this manuscript seeks to address.

In order to achieve this, I led an interdisciplinary team that completed the development of the VR components, and designed the integration with accompanying research measurement technologies. I designed a suite of virtual environments, based on both comparable studies and upon consultation with OCD clinicians and patients. All design decisions were informed by a comprehensive knowledge of the capabilities of VR hardware and software solutions. The ultimate choice of these features and components was the guided by a patient centred approach. Furthermore, I was responsible for project management of the work, which involved leading a multidisciplinary team including software design, in order to create the final product.

It is my intent that this chapter serves to highlight the extensive and meticulous design process undertaken. A considerable component of the research output is this customised system. Therefore, this chapter is crucial to representing the learnings and practical achievements of the overall candidature. This chapter presents the manuscript '*Considerations and Practical Protocols for Using Virtual Reality in Psychological Research and Practice, as Evidenced Through Exposure-Based Therapy*' which is currently under review with a peer-review journal.

The manuscript outlines a set of methodological considerations for clinical and research implementations of Virtual Reality (VR), including practical recommendations and an applied case-study for OCD. This paper addresses a notable gap in the literature by providing a framework to make VR accessible for a range of disciplines, including clinicians and researchers in psychology and neuroscience. Making VR more approachable in this field will encourage development of tools that capitalise upon theorised opportunities, as well as encourage rigorous scientific examination of the validity, efficacy, and ethical considerations of such systems.

Given the highly interdisciplinary nature of creating VR systems for human behaviour research and intervention, the lack of methodological considerations is inherently an impediment to the development of a replicated empirical evidence base. Formulating the article as a framework ensures the work has broad applicability across scientific disciplines. The protocols can be applied by researchers who attempt to precisely measure and understand human behaviour, as well as clinicians who intend to improve the relevance of treatments to specific population groups. More broadly, this work will provide a novel way to explore the exciting new frontier of human behaviour research and address the pressing challenge of ecologically valid research and intra-individual efficacy of treatment approaches.

TITLE PAGE

**Considerations and Practical Protocols for Using Virtual Reality in
Psychological Research and Practice, as Evidenced Through Exposure-
Based Therapy**

Authors and Affiliations

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Abstract

Everyday client stressors are often challenging to replicate in clinical and research environments, which hinders the ability to reliably reproduce clinical outcomes. To overcome this obstacle, tools that can bridge the inherent disconnect between these settings and the real-world experiences of clients are urgently needed. Virtual Reality (VR) promises to provide immersive experiences within controlled laboratory or clinical settings. While the potential opportunities and challenges of VR applications have been scientifically reviewed, clinical adoptions into psychology are hampered by a paucity of practical and methodological publications. This paper intends to address that gap, by providing a four-step process for decision-making considerations, including practical recommendations and an applied case-study of developing an exposure-based system for Obsessive Compulsive Disorder. We provide a framework to make VR accessible for clinician-researchers to create similar systems that realise the promise while encouraging ongoing scientific rigour.

Keywords: Virtual Reality, Obsessive Compulsive Disorder, Exposure Therapy, Ethics

Abbreviations: Exposure Therapy in a Virtual Environment (ETVE), Head Mounted Displays (HMDs), Information Technology (IT), Obsessive Compulsive Disorder (OCD), Virtual Environments (VEs), Virtual Reality (VR)

3.1 Introduction

Psychological treatment can lead to beneficial outcomes; however, why, for whom, and under which circumstances, remain to be understood (Lipsey & Wilson, 1993). Research findings frequently do not translate from laboratories into clinically meaningful changes in clients' lives. This may be due to the challenges of replicating real-world experiences in a clinician's office or a research laboratory, causing poor generalisability of findings and relevance of treatment experiences. Subsequently, clinicians, researchers, and clients face issues with substantial inter-individual variability in therapeutic response, ecological validity of research instruments, and a lack of accessible therapeutic tools. As such, the ability to replicate the complexities of real-worlds in a controlled psychological setting is needed. Virtual Reality (VR) is a technology that offers this opportunity, facilitating comprehensive investigation of psychological, cognitive, and physiological experiences.

VR is a computer-generated system that creates immersive three-dimensional environments by incorporating a range of sensory modalities typically including; visual, audio, and touch (see Table 2). Integrating these elements creates specialised Virtual Environments (VEs) that can mimic and extend reality (from a house, to a house on the moon). These endless customisable opportunities could be harnessed to solve real-world problems, particularly in neuroscience and psychology (Bohil et al., 2011). Proposed opportunities include improving diagnostic assessments and treatment outcomes in clinical settings or gathering precise research data in ecologically valid, controlled environments (Foerster et al., 2016, 2019; Foreman, 2010; Oprea et al., 2012; Parsons & McMahan, 2017; Yamaguchi et al., 2012). In anxiety disorders, such as fear of flying, VR could bring an airport into the clinician's office in a realistic manner, overcoming traditional treatment barriers, such as time and cost of *in vivo* exposure, and insufficient symptom provocation from imaginal exposure via mental imagery).

Table 2

Glossary of Key Terms for the Present Article

| Term | Definition |
|----------------------|---|
| Avatar | A virtual representation of a person (Wiederhold & Bouchard, 2014). For example, a computer-generated three-dimensional virtual clinician embedded in a VE. |
| Clinician-researcher | An appropriately qualified individual who will run the session. This may include modifying and monitoring the interactions between the user and software, with consideration to rapport. |
| Creators | Team that oversees the conceptualisation, development, and delivery of a VR system. |
| Developers | Team that uses VR software platforms to create applications, such as specialised VEs. |
| End-users | Individuals or groups who will utilise the VR system once completed. |
| Future-proofed | VR systems that are designed and developed to be highly adaptable, across both immediate (client-by-client customisation) and longer-term (evolving technology capabilities) timeframes. |
| Hardware | Physical components of the VR system, such as headsets and handheld controllers, which the user utilises to engage with the VEs. |
| Immersion | The by-product of technological capabilities, specifically the level of VE detail that can be rendered by sensory inputs to the user (Wiederhold & Bouchard, 2014; Wilson et al., 2015). Heightened participant immersion could be the experience of being fully engaged in the VE, achieved by the degree of sensory input being cognitively accepted as convincing. |
| Presence | The user's psychological response to the VE, characterised as the degree of consciously perceiving that one exists within the VE (Wiederhold & Bouchard, 2014; Wilson et al., 2015). |
| Simulator sickness | Unwanted potential side effects resulting from mismatch between visual information and sensorimotor information (i.e. user's body movements not precisely matched to the VE). |
| Software | Programs and operating systems on the computer. |
| User | Refers in this article to the individual who is using the VR system, typically immersed and engaging with VEs. |

| | |
|-------------------------------|--|
| Platform (a.k.a. game engine) | In this article refers to software that developers use to create VEs. May permit customisation for different target hardware systems. Open platforms permit flexibility to tailor the code to repurpose the software for purposes it was not originally intended. Closed platforms do not permit such modifications. |
| User Interface | Part of a system where information is shared bi-directionally. This may encompass both hardware and software, for example interactions between a handheld controller button press and the user's hand, or software responsively changing virtual stimuli secondary to user input. |
| Virtual Environments (VEs) | The combination of interactive, immersive, three-dimensional graphics (Pratt et al., 1995; Wiederhold & Bouchard, 2014) to create an alternate reality. These may be modified by inputs from a user, or in some cases also an external agent, such as a clinician-researcher. |
| Virtual Reality (VR) | Computer-generated system, creates three-dimensional environments that users can interact with in real-time (Pratt et al., 1995). |

There is growing evidence of the efficacy of VEs across a range of conditions, especially in anxiety disorder treatment (Carl et al., 2019; C. H. Kim et al., 2008; Parsons & Rizzo, 2008). Meta-analyses comparing VR exposure-based therapy both to control conditions and to traditional evidence-based treatments for several anxiety-related disorders (e.g. phobias, panic disorder) exhibit medium-to-large mean overall effect sizes (Carl et al., 2019; Powers & Emmelkamp, 2008), with large effect sizes reported in specific disorders such as post-traumatic stress disorder (Difede et al., 2006; Gonçalves et al., 2012; McLay et al., 2014). Limitations in the VR exposure-based therapy field include insufficient validation against existing gold-standard treatments, particularly in clinically diagnosed samples (Inozu et al., 2020; Krijn, Emmelkamp, Olafsson, et al., 2004; Matthews et al., 2017; Minns et al., 2018), undetermined longer-term outcomes (Kampmann et al., 2016), unquantified attrition rates (Gonçalves et al., 2012), insufficient evidence of treatment effects transferring into the real-world (Morina et al., 2015), and a paucity of detailed published methodologies for employing VR in psychological practice.

Challenges remain in the adoption of potential VR exposure-based therapy opportunities into practical clinical and research applications. VR implementation is at a relatively early phase, meaning factors of acceptability, appropriateness, and feasibility will be crucial to initial research (Proctor et al., 2011). Preliminarily, clinicians' perceptions of VR usefulness and performance expectation are facilitators for intent to use (Bertrand & Bouchard, 2008; Liu et al., 2015), and as such involving end-users in design processes will likely enhance longer-term adoption (Graham et al., 2006). At an institutional level, VR implementation should be supported by addressing resource barriers, such as time and training (Liu et al., 2015; Ogourtsova et al., 2019). Although the applied case-study in the present article was not positioned as an implementation study, consideration to early implementation factors was made. Further implementation research is required in the VR Exposure-Based Therapy field. This article will provide considerations and practical decision-making protocols for VR design and development in psychological contexts. The four key stages of this article are provided in Figure 1 and overviewed in the following text.

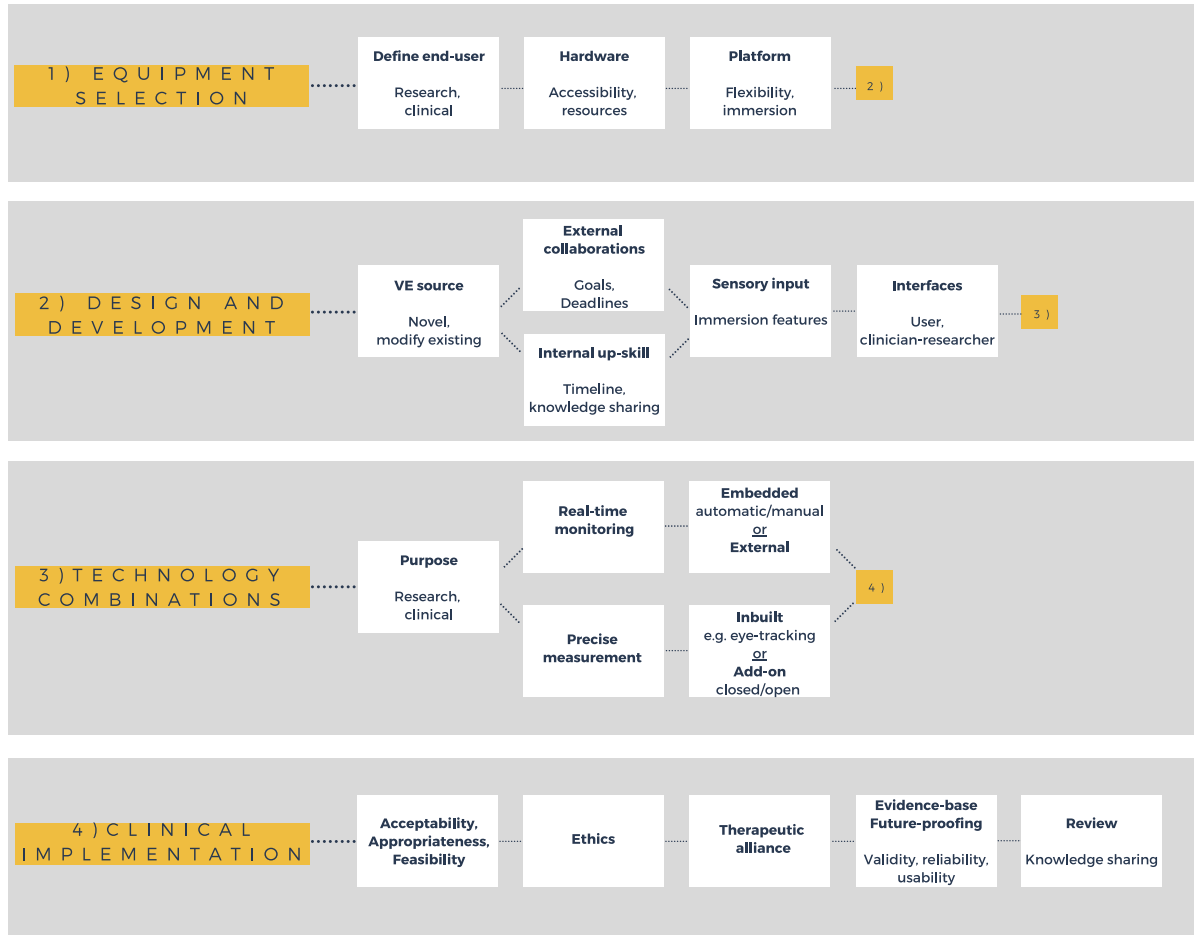


Figure 1. Four-Step Considerations Flowchart.

Firstly, regarding *Equipment Selection*, VR-naïve clinicians and researchers may lack familiarity and confidence with available technology options and capabilities. When selecting equipment they may hold preconceptions and scepticism of systems typically utilised for gameplay rather than scientific endeavours. The range of technologies available in VR with unique capabilities could seem overwhelming when selecting for their client groups. Overcoming this will require knowledge of the varied immersion capabilities, space limitations, resource demands, and options to integrate with other hardware, as outlined herein.

Secondly, the *Design and Development* of VEs needs investment in collaborations across disciplines, skill development, and resources. Expertise in the capabilities of software and sensory input for the creators chosen VR hardware and the associated suitability for psychological population groups is necessary. Collaboration should extend beyond creators

and developers to also include end-user feedback throughout development (Glegg & Levac, 2015). The relatively rapid pace of technology advancements can conflict with the slower establishment of a replicated empirical evidence-base of reliability, validity, and usability, likely necessitating long-term collaborations between these key stakeholders.

Regarding *Technology Combinations*, as clinicians and researchers prioritise precise measurement and real-time flexibility to varying degrees, the intended use of the VR system will create unique design challenges. For example, many clinician-researchers are eager to integrate VR with other technologies (e.g. physiology recording, EEG, MRI). Although some companies are manufacturing VR systems with in-built research features, such as eye-tracking, many are not designed with multi-technology combinations in mind. Therefore, creative solutions with expertise from software developers will be required, in ongoing knowledge exchange (Graham et al., 2006). Clinical VR researchers will also need to appreciate the limitations of open versus closed platforms (refer to Table 2), particularly relating to the greater degree of customisation afforded by the former.

Finally, the developed VR product will need to achieve successful *Clinical Implementation* into clinical healthcare systems, from sole practitioners, to community clinics, hospital wards, and at home self-directed care. Successful implementation depends initially upon appropriateness, acceptability, and feasibility (Proctor et al., 2011). In the longer-term, implementation strategies for settings including end-user training tools for amenable adoption will also be required (Glegg & Levac, 2015; Proctor et al., 2009). Known clinical factors such as the therapeutic alliance, should continue to be considered. For example, developing techniques for VR users and clinicians to interact during immersion, particularly when hardware such as headsets can obscure real-world verbal and non-verbal communication. An evidence-base must identify key attributes of systems considered as important by stakeholders, such as exposure therapy task grading and flexibility. System creators should provide ongoing

training opportunities and troubleshooting guidelines to end-users to enhance clinical practice (Graham et al., 2006), and developers should consider how acceptable and feasible the VEs are within the clinical or research system for which they are being built. Developers and users of emerging therapeutic technologies will also need to consider the unique ethical issues that are raised by its use, such as potential for misuse, risk management including during in-home VR with geographically remote clinicians, and adaptation of consent protocols (Kellmeyer et al., 2019). An evidence-base for the validity, reliability, and usability of a system must be established prior to dissemination. Adoption of VR into clinical therapeutic practice will be enhanced by replicated research of usefulness of systems above currently available treatments, and overcoming barriers to uptake that include clinician time and knowledge (Bertrand & Bouchard, 2008; Glegg et al., 2013).

Developments in these areas are hindered by a lack of published practical considerations and protocols on how to develop VR applications that overcome these challenges. This in turn impedes scientific rigor (reliability, efficiency, credibility) and replication, currently a major topic of debate in the academic literature (Munafò et al., 2017). This article aims to address these challenges by providing practical considerations and protocols that can be applied to the development of VR systems for neuroscience and psychology (see Figure 1 for overview). We examine a case study of our Exposure Therapy in a Virtual Environment (ETVE) system designed for the treatment of Obsessive Compulsive Disorder (OCD) (Cullen, Dowling, Segrave, Carter, et al., n.d.) to illustrate how these processes work in practice. The decision-making considerations are divided into four-parts: (1) Equipment selection, (2) Design and Development, (3) Technology Integrations and (4) Clinical Implementation, each of which includes an introductory overview, practical recommendations, and the applied case study.

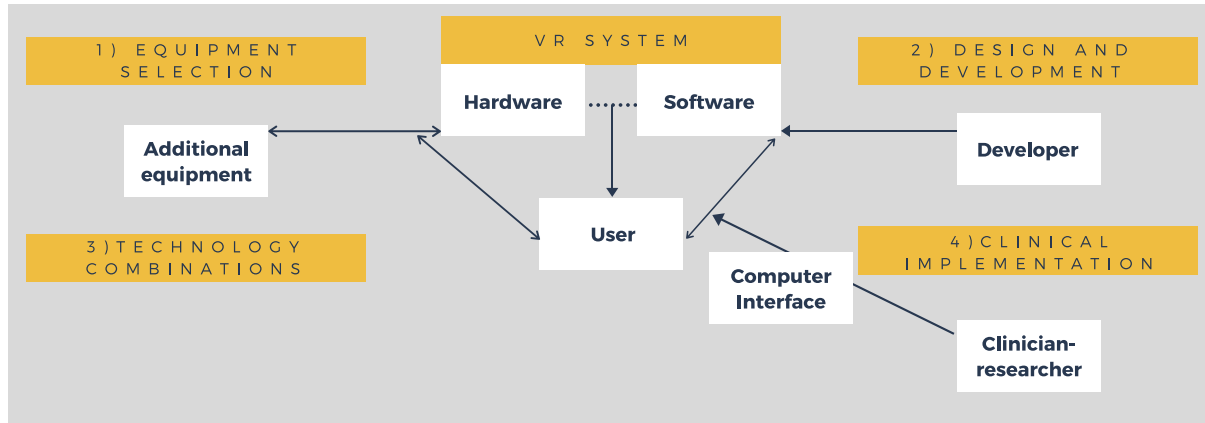


Figure 2. Schematic of a VR System with Associated Four-Part Consideration Sections.

3.2 Equipment Selection

VR encompasses a range of technology forms including Head Mounted Displays (HMDs) and projection displays. Companies (e.g. HTC™, Oculus™) produce and market these products, creating systems with varied technical specifications and purposes, such as gameplay. Software developers create VEs using a VR development platform. The client/participant (hereafter ‘user’) uses the hardware to be immersed in the VEs and engages with the user interface. In therapeutic applications, a clinician may be able to influence the interactions between software and the user using a computer interface (see Figure 2). Specific considerations will vary across purposes and clinical populations, meaning an all-encompassing list would be beyond the scope of a single article. As such, Table 3 outlines equipment selection considerations by drawing from available published descriptions of systems, as well as the authors first-hand VR-design experiences, with an illustrative example of how these would be applied in selecting hardware for VR exposure-based therapy.

Table 3**Equipment Selection: General Considerations and Specific Decision-Making**

| Consideration | Illustrative descriptions of relevant considerations | | | |
|---|---|--|---|--|
| <i>Accessibility and availability</i> | Ease of commercial availability for systems will have secondary impacts on the likelihood of manufacturer technical updates and support, and opportunities to replicate systems across geographically diverse sites. Complexity and demands in set-up processes will influence selection (portable versus fixed hardware), as will the location of end-users and associated physical space limitations (clinic, in-home). | | | |
| <i>Resources</i> | Financial cost (initial investment, longer-term maintenance and upgrades); interdisciplinary knowledge requirements (VE design feature complexity); human specific resources (reliance upon clinician-researcher to set-up and run, or independent user-driven immersion); training (skill sharing, formal knowledge dissemination); sustainability factors (institutional resources to uphold implementation over time). | | | |
| <i>Immersion and presence</i> | Visual resolution (capabilities of the system); the range, diversity and convincingness of sensory inputs; degree of integrating and overlaying the real-world or blocking-out any external real-world inputs. | | | |
| <i>User control</i> | Degree of user-driven action during immersion (flexible versus pre-determined like a movie); associated likelihoods of sensorimotor discrepancies and simulator sickness. | | | |
| <i>Hardware suitability</i> | Safety of the clinical group with consideration to symptomatology (e.g. neurological gait disturbance would make tethered-HMD unsuitable) and treatment needs. | | | |
| Hardware | Pros | Cons | Psychological implementations | |
| Handheld: <i>Headset for mobile device (e.g. Google Cardboard™)</i> | Suited to in-home tasks (e.g. therapy homework). Minimal cost investment for clinician and client. | Technical specifications limited to that of the device (e.g. resolution, refresh rate), limiting immersion. Low ability to interact with VE. | Chronic pain management (Amin et al., 2017), biofeedback in anxiety (Repetto et al., 2013). | |
| Portable headsets: <i>Mobile all-in-one</i> | Greater technical specifications than mobiles (display resolution, audio) and more affordable than higher level | Do not have the same high-resolution visual resolution as generated | Commercially available only relatively recently, | |

| | | | |
|---|---|---|---|
| <i>(e.g. Oculus Quest™)</i> | systems, allowing easy at-home use with simple set-up ('inside-out tracking' requires no base stations). | on headsets connected to a PC. | limiting research applications. |
| <i>Tethered HMD: User headset with binocularly disparate images presented (e.g. original Oculus Rift™).</i> | User embedded within environment, heightening immersion and presence (Moreno & Mayer, 2004). Ease of commercial availability (Bohil et al., 2011). | Stationary causes sensorimotor discrepancy and possible simulator sickness (Sharples et al., 2008). | Treatment of panic disorder (Botella et al., 2007), public speaking anxiety (Wallach et al., 2009), and fear of flying (Rothbaum et al., 2006). |
| <i>Wireless HMD with body sensors (movement tracking): Sensors track user movements within a defined area, providing feedback for the system to adapt sensory simulations (e.g. HTC Vive™).</i> | User has greater control over movement and objects, increasing presence (Sharples et al., 2008; Tarr & Warren, 2002), reducing simulator sickness (Rolnick & Lubow, 1991). Active manipulation of environments more immersive than passive reviewing of a recorded scene. Higher resolution, larger field of view, better visual refresh rates (Niehorster et al., 2017). Typically includes tactile elements (e.g. handheld controllers). Consumer availability. | Greater technical specifications require more powerful and expensive computer processor. Room-scale technology varies across models (e.g. Rift™ requires sensors in front of the individual, Vive™ does not). | Post-traumatic stress disorder exposure therapy (Rizzo et al., 2014). |
| <i>Projection displays: Images projected onto walls, ceiling, floor. Tracks user movement to modify images (e.g. CAVE)</i> | Allows movements to be naturalistic (Cruz-Neira et al., 1993). Option for multiple simultaneous users; however, limitations of movement (e.g. standing between projector and screen). | High resource demands (setup space, costs, computing) and limited research regarding side effects (Sharples et al., 2008). Typically lacks additional sensory input (e.g. tactile). | Acrophobia treatment (Krijn, Emmelkamp, Biemond, et al., 2004). |
| <i>Augmented reality: Superimposes virtual over real</i> | Combines real-world, increasing naturalistic sense. | Integrating virtual and real requires rigorous design process. | Phobia treatment (Juan et al., 2005). |

3.2.1 Recommendations

The system's purpose must be clearly defined at the outset as this determines equipment and design decisions. Clinical implementations with the goal of self-directed therapy homework may consider affordable handheld or portable systems with the trade-off of lower quality immersion, while researchers may invest in a single VR set up with enhanced graphics and precise control over immersion and event recording, at a fixed site where users will attend.

The hardware selections, such as HMD versus projection-based displays, will be driven by considerations summarised in Table 3 including resources (cost, space requirements), and accessibility (portability, commercial availability). Creators will need to ensure their chosen hardware is compatible with a software development platform or game engine (e.g. Unity3d™) to create VEs. These will determine immersion capabilities, options to integrate with other hardware and flexibility of user interactions.

3.2.2 ETVE Application

Exposure and Response Prevention (ERP), the most common OCD treatment (Abramowitz, 1996; Foa, 2010; Foa et al., 2005) can be limited by difficulty simulating intrusive thoughts (Lind et al., 2013). The ETVE project aimed to overcome this limitation by creating a flexible, customisable treatment tool using VR. Our initial VEs were specialised to the contamination subtype, that presents as excessive concerns regarding threat of illness and the sensation of being unclean (Radomsky & Rachman, 2004; Ruscio et al., 2010), and our hardware decision-making is summarised in Table 4.

Table 4

ETVE Equipment Decision Making

| Consideration | Decision-Making | Suitable | Unsuitable |
|---------------|--|--|--|
| Resources | Expanding to multiple settings, so somewhat portable preferred, with acceptable financial and resource costs – balance with commercial availability and reputation (for technical support and updates). Availability of clinical room space: limited in a hospital setting, so the option to assemble and disassemble easily in clinical rooms, and sufficient physical area to safely use the equipment and full virtual space, were important. | HMDs Portable/handheld | Projection displays |
| Immersion | High visual resolution for sufficient anxiety-provocation. Intuitive interactions. Contamination-based OCD means hand/body movements and minimising simulator sickness are important. | HMDs (movement tracked) Projection displays | Handheld devices Stationary HMD |
| Integration | Software open enough to be integrated with other technology for precise measurement. Control options from clinician-researcher interface. | HMDs (some) Projection displays | Handheld devices |
| Flexibility | Goal of ecologically valid treatment tool – need to be customisable user-by-user. Iterative design (modify VEs over time). | Systems with real-time manipulation software options | Handheld (difficult to customise during immersion) |

A HMD system with room-scale movement tracking that was sufficiently large to create a realistic sized kitchen and bathroom, and that was easily commercial available was deemed most suitable (see Table 4; Resources). The HTC™ Vive was selected, which utilises a HMD tracked within a defined space (up to 16 feet between base stations which detect movements), two wireless handheld controllers, and directional audio (over-ear headphones). Our system utilised an approximately 4 meter by 4 meter space, and we upgraded with a wireless adaptor commercially available for the HTC™ Vive to optimise free-movement and minimise risks (e.g. trip hazard of cable connecting to computer). The developer platform

utilised was Unity™, which was familiar for the Information Technology (IT) collaboration team, who were responsible for design modifications though not required for ongoing day-to-day system operations.

3.3 Design and Development

The VR software platform is utilised to create the VE content. In psychological contexts, VR systems may leverage or extend beyond standard gameplay applications, therefore requiring modification or the development of a new VE. In order to do so, clinical and research teams may obtain additional expertise, via external collaborations outside the team or internal up-skilling, such as employing team members with these skills to work onsite. VR system creators will frequently also benefit from interdisciplinary collaboration during the design phase, for example with end-users (e.g. clinicians, users) and stakeholders (e.g. hospital staff). This will ensure design features of VEs (e.g. virtual objects) are acceptable and appropriate (see Section 4 for additional discussion). Active consultation with end-users throughout the design process will enable creators to address perceived barriers, such as training needs (Liu et al., 2015; Ogourtsova et al., 2019). Sensory inputs can create virtual stimuli, that in turn are combined to create convincing virtual spaces (see Table 5). As an illustrative example, this could involve programming the familiar visual and audio features of a microwave, then adding an oven and refrigerator, to build a virtual kitchen environment.

Table 5

Sensory Input Considerations

| Input | Considerations |
|--------|---|
| Visual | Immersive systems reduce the amount of contradictory sensory input from the outside world (e.g. HMDs blocking out, projection displays overlaying real-world). Presence and realism will be enhanced by wider field of view, stereoscopy to create depth, andvection to induce cognitively perceived self-motion (Wiederhold & Bouchard, 2014). |

| | |
|----------------------------|---|
| Audio | Audio input increases realism and reduces interference noise from the external real-world. Spatialised audio, modified relative to head movements, is associated with higher presence than non-spatialised (Hendrix & Barfield, 1996). Dynamic auditory input may be paired to events or user input, while general background noises can also be programmed. |
| Tactile | Haptic feedback uses controller movements to mimic touch, via force and vibrations (Sallnäs et al., 2000). |
| Olfactory | Real-world smell cues that can be paired with virtual objects, and may thereby enhance the sense of presence (Hoffman et al., 1998). |
| Proprioception and walking | The systems involved in providing information about position, location, orientation, and movement of bodily parts will also impact user experience. Spatial presence requires tracking body movements and rapid virtual display updates. User movement may be achieved by a range of programming options, such as naturalistic walking, click-movement systems, treadmills, or walking in place. Walking enhances presence when participants associate themselves with the virtual body (Slater et al., 1995). Matching visual input to sensorimotor changes also reduces simulator sickness (Usoh et al., 1999), according to sensory conflict theory. |

Interfaces, that are the digital spaces where the user or clinician interacts with VR system, will also need to be developed. The clinician-researcher interface allows interaction with the computer running the VEs (see Figure 2). They may be responsible for real-time monitoring and modification of VEs, and controlling data collection with event-markers (notations in recordings of the precise time a particular occurrence commenced). Information collected should also permit post-VR review of experiences (e.g., event-markers identifying the time-window of a user's response). Stylistically, clinician-researcher interfaces should have automated processes, include a timeline of events, not permit accidental event triggering, and include predefined comment flags (Brinkman et al., 2010).

A user interface allows the user to interact with the VR system. VEs should feel 'real' for immersion and ecological validity. Active manipulation of environments, rather than passively reviewing pre-determined experiences, increases the sense of presence. For example,

walking around a landscape, rather than watching a movie of the landscape unfolding. It has been indicated that tracked-movement VR with greater visual fields of view and personalised features creates greater immersion than generalised stationary systems (Ling et al., 2014; Moreno & Mayer, 2004; Usoh et al., 1999). Challenges emerge balancing mimicking the objective real-world with extending upon reality to capitalise upon the opportunities of VR. To illustrate, a virtual room may be designed with familiar everyday features; however, once creators extend upon reality this can create a jarring reminder of the ‘un-real’ nature of the environment. Perhaps biofeedback statistics overlaying a realistic virtual room would increase the functionality but decrease user immersion and presence. The decision whether to include such features will be guided by the end goal of the VE, such as convincing immersion with high likelihood of learnings transferring back to the real-world, or creative virtual worlds that extend beyond the limitations of objective reality.

3.3.1 Recommendations

VE source. The VE may be built from scratch, or modified from existing systems. Given the relatively early phase of VR in psychology, developing from scratch is recommended, as yet there does not exist sufficient open-source software options to customise for most clinical populations. System creators should be aware that this will require considerable investment of time and cost, yet allows for a fully purpose-built system. Conversely, utilising existing programs has occurred in the field which speeds up the initial start time, though may create downstream challenges in customising to meet specific research or clinical purposes. Specifically, as the majority of available programs are built for gameplay applications, this may mean changing source code is problematic, hindering the flexibility of VEs and integration with other technologies. For example, a virtual car simulator may exist. However, without open access, changing features such as the amount of traffic would be extremely challenging. In order for VR to expand in the psychological space, systems will need

to be designed with adaptability at the forefront, given the perpetual evolution of technology (i.e. ‘future-proofed’, see Table 2 and Section 3.5), and where possible shared across research facilities to remove the need to start from scratch. Particular consideration must be directed towards opportunities of creating open-source systems. As this field progresses and more systems become available, the community of creators and software developers should consider knowledge dissemination (Graham et al., 2006) and open-source software sharing with other appropriately trained clinicians and researchers. This will address resource barriers (Ogourtsova et al., 2019) and permit diverse empirical evaluation of system reliability, validity, and usability, in keeping with open science principles of reproducibility and sustainability.

Collaborations. VR development requires interdisciplinary collaboration between creators, developers, end-users, and clinician-researchers throughout the decision-making processes (Glegg & Levac, 2015). The cost and accessibility of software developers may present an early barrier to development, so opportunities to share open-source software across sites will support expansion of VR into areas with lower accessibility. Given the variability within interdisciplinary teams, each person’s area of work will drive unique priorities, goals, and timelines within the project. Recommendations to mitigate this include collaboratively defining a ‘successful project’ early and agreeing on communication practices, such as preferred format and frequency. While the researcher may prioritise precise control over measurements, peer-reviewed papers and conference presentations, the software developer may preference applying the full extent of their knowledge to designing an aesthetically pleasing interface, ‘delivering’ the project and moving on. The extent and limits of each individual’s expertise should be discussed early, rather than assuming that a software developer will be proficient across all areas of IT. Maintaining a collaborative relationship with a software team over time is preferable, as an understanding of the system’s foundation will enable more efficient program modifications, remaining rapidly responsive to potential errors and changing

end-user needs. Ongoing collaboration may afford the researcher additional time to conduct comprehensive evaluation studies with technological support.

Sensory input. Generally, greater virtual mimicry of the real world, via naturalistic, detailed, dynamic interactions, creates heightened immersion (Bohil et al., 2011). VR systems that allow users to move freely by matching visual and sensorimotor inputs are therefore optimal. Advancements in screen resolutions heighten the convincingness of virtual objects. Challenges remain in constructing convincing virtual humans, particularly their appearance and the unpredictability of their behaviour. While pushing a glass of milk with defined force will cause it to spill, pushing a human could result in them crying, running away, or pushing back. Although promising options are emerging, programming two-way communication and movement interactions (e.g. crowds to move adaptively around the user) remain particularly challenging (Pelechano et al., 2008).

Audio should include general background noise (constant or programmed to loop on a timer) and dynamic sounds (commencing according to user actions). For example, a virtual shopping centre may have background music accompanied by cash register noises when a purchase is made. Although not truly able to touch virtual objects, creators should give consideration to how this sensation can be virtually achieved. The experience of weight when virtually moving an item can be achieved by consideration to object physics. Developers can program movement speeds to mimic a sense of resistance and weight. Additionally, the capabilities of handheld controllers can be creatively repurposed (e.g. holding virtual jelly, controllers vibrate).

Interfaces.

Clinician-researcher interface. Designs will need to consider both the appearance and capability of the interface. Interfaces that allow manipulation of the VE before and during user engagement will expand usability across population groups and for each individual. In social

phobia populations for example, system creators could program crowds into the VE before use, and include capability for the crowd to be manipulated in size and movements during use. Typically, VR systems are not designed to permit a non-user to manipulate the VE in real-time, so precise external control will require an interface that can rapidly modify the code in the VR platform.

Data collection and monitoring may be manual (button press, typing a note) or automated (synchronising an event-marker when specific actions occur in the VE). Automated processes are preferable, given reduced cognitive burden on the clinician-researcher (Brinkman et al., 2010), reducing the likelihood of errors and permitting greater opportunity to monitor and engage with users. For example, rather than a clinician-researcher operated button for every event, programming an event-marker for every handheld controller button press by the user. Creative solutions assist with the balance between pre-programming (automating processes) and flexibility (user-driven experience). For example, a sliding scale to increase the number of objects in an environment, rather than a button for every item.

User interface. To be perceived as realistic, the VE needs to mimic the real-world, responding dynamically to user input. For example, a steamy/dirty mirror may clear as a user wipes a cloth across it or food may burn if left in the oven too long. Additional opportunities exist in extending beyond reality. Multiple sources of information can be integrated into the user interface, such as providing biofeedback representations of real-time heart-rate within the VE.

3.3.2 ETVE Application

VE source. Custom VEs (see Table 6), coded using the Unity™ software platform, were built in collaboration between the research team and software developers. At the time of development, there were no suitable existing VEs which could be modified. The creators aimed to follow a full design process from conceptualisation to completion.

Collaborations. IT collaborations were initially external, then shifted towards a combination of external team members working on-site and upskilling internal team members. The latter became necessary for knowledge continuity, as IT teams worked on shorter timeframes than researchers and would depart to work on new projects. Communication at the project outset was via sporadic reciprocal site visits and email. This became insufficient, leading to unclear deadlines and goals. A VR facility was built at the research site, and an arrangement with external IT team members to work on-site created opportunity for weekly meetings and shifting to instant messaging systems. This was more effective as tasks were immediately and collaboratively prioritised, and supports the continuing establishment of an empirical evidence-base with software adaptations as technology evolves.

End-user collaborations were with OCD clinicians, hospital staff and people with lived experience, who were consulted to determine suitability of VE features (stimuli, exposure scenarios) as well as hardware acceptability. A VR system was set up at a hospital, which allowed researchers and OCD clinicians to test VE build iterations, and ensured the system continued to meet end-user needs.

Sensory input.

Table 6

Sensory Input Applications

| Input | ETVE Applications |
|--------|--|
| Visual | Three spaces were created; a kitchen, bathroom, and an elevator (practice area). To increase the sense of space, we included inaccessible but viewable areas around the defined movement space (e.g. room adjoining kitchen with frosted doors and windows to outdoors). Free exploration, rather than pre-determined, maximised realism. Given the end-users are people with OCD, we intended to create a VE with rooms that mimicked typical environments with familiar details (panel of buttons for elevator, refrigerator magnets). Stimuli specific to contamination-based OCD were layered in (e.g. unclean utensils). Additionally, wireless naturalistic walking technology meant the software developers designed the interactions with virtual objects to include appearances when observed from different angles, and to change with user-driven actions such as touching other items e.g. cloth |

| | |
|----------------------------|--|
| | touching a stain. To enable customisation for a range of user symptom severity, object appearance could be manipulated on a sliding scale of contamination (e.g. increasing stains). |
| Audio | General background noise (e.g. fluorescent light flickering), and dynamic object-specific sounds (e.g. hand-dryer) were compiled and programmed in unison with visual elements. |
| Tactile | Two handheld controllers enable manipulation of items in the virtual space. Haptic feedback allows mimicking of force/resistance. This was customised to features of the objects (e.g. milk bottle perceived to be heavier because it is slower to move with insufficient force). Additionally, we utilised the controller vibrations as a mobile phone notification, as an option for communicating exposure task instructions. |
| Olfaction | The requirement for additional researchers to manage olfactory cues in the real-world, combined with this being a relatively uncommon practice in the VR psychology field, determined that this feature would not be included in the initial ETVE environments. |
| Proprioception and walking | Rooms were perceived to be structured above one another, by making them accessible via an elevator, meaning the full movement area could be utilised for each room. The hardware selection enabled users to experience naturalistic walking, untethered to the computer due to the wireless adapter. |

Interfaces.

Clinician-researcher interface. Capabilities of the interface include pre-modification, such as the contamination sliding scale, and during-immersion customisation, via flexible order and timing of exposure events. The virtual session needed to match the traditional session structure of exposure-based therapy, allowing events to be arranged into a hierarchy on a client-by-client basis. Events commence when the clinician-researcher clicks a button, sending a message to a virtual mobile phone that provides task instructions to the user. This balanced flexibility with pre-programming of features, but required custom-built software to communicate with Unity™ and the physiology recording software (providing event-markers) simultaneously. Customisability of VEs was further achieved by a ‘drag-and-drop’ feature to add new stimuli.

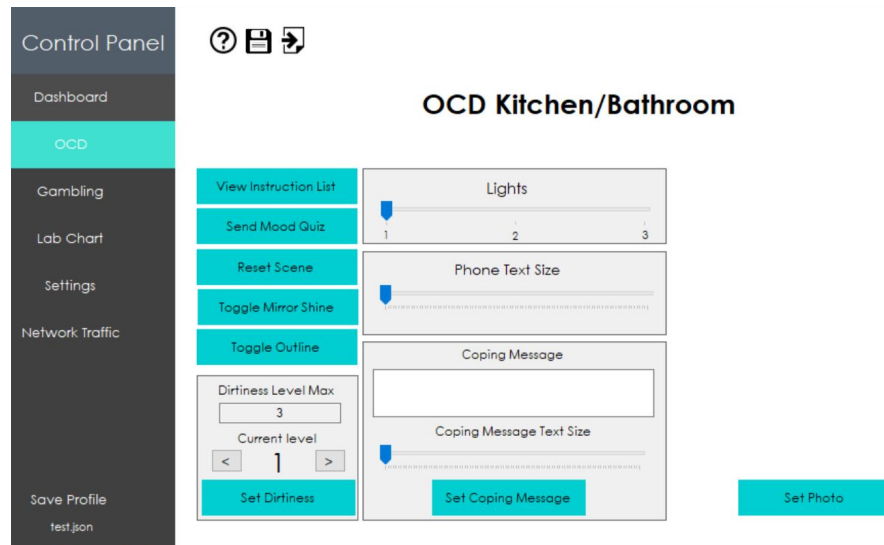


Figure 3. Clinician-Researcher Interface

User-interface. Users explore the VEs at their own will and pace, which meant objects were programmed to respond dynamically to user input, rather than on a fixed timeline (see Figures 3 and 4). Consequences of events varied depending on input, such as toilets flushing and making a noise when a button was pressed and stains on a bench spreading when food moves. Automation of event-marking was achieved from the user-end by programming a trigger when the handheld controller was clicked to be sent to the physiology software, representing contact with a virtual object.



Figure 4. User Interface: Kitchen VE with Phone Receiving Messages from Clinician-Researcher Interface

3.4 Technology Combinations

Research and clinical implementations each prioritise real-time monitoring and precise measurement to varying degrees. VR offers the ability to manipulate user experiences and precisely measure responses (e.g. psychophysiological, timing of affect changes) under controlled circumstances. Objective measures, such as physiology, could be provided as biofeedback in real-time (Repetto et al., 2009, 2013), or analysed post-VR as an indicator of emotional arousal (Wiederhold et al., 2002). Cognitive processes can also be investigated, for example indirectly via eye-tracking systems. Such data could index attentional bias (eye gaze focus), record signals such as pupil response, and reward/fear sensitivity. Preliminary studies have investigated the crossover of technologies (Bayliss & Ballard, 1998); however, integration with traditional neuroscience measures, such as EEG, remains limited.

3.4.1 Recommendations

Real-time monitoring. For the most part, VR systems and add-on technologies were not built to run collaboratively. Repurposing to meet specific needs will need to overcome challenges of closed Application Program Interfaces (APIs), hardware restrictions, and signal-noise interference. We recommend sourcing software experts to create workarounds and an interface to review data and VR experiences, and specialist technicians to manage hardware incompatibilities. Ideally, software visualisations will be integrated into a single clinician-researcher interface, rather than running multiple software programs synonymously (due to the associated lag-times, greater cognitive burden increasing errors).

Precise measurement. Traditional data collection methods, such as pen and paper questionnaires, would require breaks from immersion. They should be incorporated into VEs in a way that retains psychometric validity. Virtual versions of questionnaires could be designed, or if using a clinician avatar integrated into their communication. Subjective reporting measures could overlay the user interface, using handheld controller ‘point and click’

functionality to record responses. VR also offers opportunities to integrate cognitive and psychophysiological assessments that may otherwise be restricted to highly controlled laboratory environments, enabling the assessment of neuropsychological constructs in a portable, clinically-accessible manner (Foerster et al., 2016, 2019). In parallel, designers are working to create purpose-built VR and psychophysiology systems (e.g. HTC™ Vive Pro Eye), which are anticipated to advance and supersede the requirement to create workarounds. As technology advances, particularly with increased head and body movements, validation of acquired data quality is needed.

Monitoring and Recording. Balancing precise recording with user-driven, flexible interactions is challenging. Users' actions should directly generate event-marking of data where possible. This will require system creators to understand their system capabilities in depth. For example, programming digital messages from handheld controllers, so that when a button is pressed it will send a direct message to the data recording system.

3.4.2 ETVE Application

The ETVE system was designed for both clinical and research purposes. Therefore, technology combinations were required to collect research-grade data as well as provide real-time displays for user monitoring.

Psychophysiology recording was incorporated as an objective measure of affective arousal. Emotional states change rapidly in exposure therapy, requiring measures with relatively high frequency sampling rates (e.g. heart, respiration). Hardware specifications posed a challenge. The HMD was selected to be wireless, yet many research grade physiology systems are wired and tethered to a receiver. Software was also problematic to integrate in real-time, due to systems often having closed APIs.

We selected the AD Instruments Equivital LifeMonitor system (Hidalgo; Cambridge, U. K.); a research grade (Liu et al., 2013) physiology system that was designed for monitoring

under movement conditions (e.g. emergency services). The Equivital streams the acquired signals via Bluetooth to LabChart™ software which permits computer input as an event-marker. Our custom-built Control Panel synchronises a virtual task onset (message to Unity™) and automated event-marking (trigger to LabChart™). This feature was important, as other technology required manual button pressing, that would lead to lag-time and cognitive burden. Further considerations included direct streaming of physiology signals (not via amplifiers, avoiding lag-time which would invalidate data), and in real-time (not post-processed) to ensure precise synchronisation with virtual events.

3.5 Clinical Implementation

Translation of evidence-based tools into clinical practice is a well-documented challenge. Implementation research has highlighted the necessity to consider barriers, strategies, and evaluation of process outcomes to achieve the adoption of novel systems. Throughout design and development processes, collaborative engagement between stakeholders is important to ensure the identification and management of barriers, and to position the system as an acceptable, feasible, and appropriate tool (Proctor et al., 2009, 2011).

To date, the adoption of VR for psychological treatment has lagged behind the research (Glegg & Levac, 2015). Amongst mental health professionals favourable to VR, perceived usefulness of VR technology is the primary predictor of intention to use, rather than perceived cost or ease of use (Bertrand & Bouchard, 2008). Key identified barriers include feasibility factors (Proctor et al., 2011), such as clinicians' lack of knowledge and experience in the field (Glegg et al., 2013). Further research is required to explore the hurdles and facilitators for VR exposure-based therapy specifically, though broad predictions can be made from knowledge of other novel tools. For example, uptake being increased by an established evidence-base, broad acceptability, and high feasibility of implementation (e.g. sense of familiarity and

confidence, achievable financial and staffing resource investment, training opportunities) (Proctor et al., 2009, 2011).

As with any psychological tool, creators have a responsibility to consider the ethical consequences of implementation, including potential for misuse, consent procedures, and risks (Kellmeyer et al., 2019). Ethical consent procedures should be modified, requiring thorough understanding of possible VR specific risks, such as simulator sickness, disorientation, and dizziness. These will differ across populations, particularly those being treated for mental health conditions. Creators, researchers and clinicians will need to identify potential unique harms raised by the use of their virtual environments, beyond general risks such as simulator sickness, and propose management strategies specific to clinical populations (Rizzo et al., 2003). For example, unique vulnerabilities may exist for people with poor differentiation between reality and imagination, such as psychosis, though preliminary findings indicate engagement in co-design and safety in research settings (Botella et al., 2009; Foreman, 2010; Realpe et al., 2020), suggesting individuals should be screened on a patient-by-patient basis rather than excluded by diagnostic criteria alone. Virtual environments may also trigger traumatic memories, emotions or anxieties in vulnerable individuals. Developers will need to establish; would VR be safe to use in these individuals, how frequently and for how long can sessions be conducted, screening of vulnerable individuals, and what measures are in place to deal with adverse events if and when they occur.

The clinician-user relationship, and how this may be impacted by technology, should be considered by creators, particularly clinicians and researchers, in the design process. The physical presence of technologies in the therapeutic space could either be viewed as an opportunity, to enhance a sense of security and increase clients empowerment to express themselves (Riva, 2005), or as barrier impeding communication (e.g. eye contact). Given the impact of therapeutic alliance on client outcome (Martin et al., 2000) it is promising that

alliance appears comparable in some virtual and in-vivo studies (Anderson et al., 2013). In VR exposure-based therapy, clients' positive expectations enhance therapeutic gains (Price et al., 2008). Varied communication methods between user and clinician in VR require further research, with many studies either not reporting or not including this feature in their designs (Lindner et al., 2017; Repetto et al., 2013).

Creating an evidence base for VR applications includes establishing validation, equivalency with gold-standards, and efficacy, as well as evaluation of implementation strategy outcomes (Proctor et al., 2011). Should VR in psychology expand, future-proofing systems should be considered: incorporating end-user customisation that requires minimal computer programming skills (Persa et al., 2014), and open software where possible to enable upgrades that keep pace with technology improvements. This will allow rapid VE customisation, rather than returning to VE developers for every alteration, which would potentially create an insurmountable financial and time resource-demand for clinician-researchers. An illustrative sample of opportunities and challenges for clinical implementation within anxiety disorders is provided in Table 7.

Table 7

Examples of Opportunities, Challenges & Future Considerations for VR Exposure-Based Therapies

| Opportunity | Summary | Clinical Factors |
|---|--|--|
| Addressing and measuring each patient's unique symptoms | Carefully controlled stimuli onset timing and graded features, customised to each client's fear structure, improving treatment relevance. Immersive replication of anxiety-provoking scenarios in the clinician's office, including otherwise impractical stimuli. Precise response measurement. | Post-traumatic stress disorder exposure-based scenarios, such as warzones, that may be otherwise challenging to replicate, with user responses monitored in a synchronised manner to stimuli onsets. |
| Therapeutic engagement | Enhancing the relevance of exposure stimuli to each user could enhance trust in the therapeutic process | Treatment accessibility in remote locations, with typically fewer |

| | and alliance, important predictors of treatment outcome. Self-directed VR therapy programs to improve service accessibility. | psychological services, via self-directed or remote clinician supervision. |
|---------------------------------------|--|---|
| Challenge | Summary | Clinical Factors |
| Ethics and safety | Currently insufficient screening measures to assess suitability, consent protocols, and guidelines for specialists. Requires multi-disciplinary collaboration with ethicists, implementation researchers, people with lived experience etc. Provocation of ‘unwanted’ emotions is core to exposure-based treatment (Behr et al., 2005), so clinical risk management must be incorporated into software design. | Clinical formulation tools required to weigh prospective benefits of VR against risks, and compare these to existing best-practices. Training for clinicians to differentiate between anxiety symptoms and simulator sickness. |
| Symptom monitoring | Within-session communication capabilities to enable user and clinician-researcher to collaboratively modify or end session. Embed techniques to assess and monitor symptoms, including cognition that may undermine immersion e.g. rationalising, neutralising. | Necessity to circumvent hardware impeding communication, e.g. HMD obscuring non-verbal indicators of distress. Monitoring immersion breaking thoughts e.g. <i>‘It’s just a simulation and not real’</i> . |
| Future Consideration | Summary | Clinical Factors |
| Virtual humans | Future technology advancements will improve realism of virtual humans, including enhancing representations of the self. Opportunities for user and clinician to share the VE, enhancing responsiveness, engagement, immersion. Requires scientific evaluation to understand the sufficient level of detail to achieve cognitive acceptance and suspension of disbelief without costly superfluous programming. | Virtual bodies customised to match the user, e.g. body shape, could enhance transfer of therapeutic gains to the real-world. Interactions with realistic humans central to many psychological disorders e.g. public speaking anxiety. |
| Empirical evidence and implementation | Objective and subjective symptom provocation and clinical engagement evidence required, as well as replicated studies of validity, reliability and usability. Identification of predictors for favourable therapeutic outcome, session structuring protocols, and factors that enhance transfer gains to real-world. | Assessment and measurement of arousal and extinction processes. Treatment manuals including frequency and duration of sessions. Strategies to meet staff training and support needs, audit |

Knowledge dissemination. Implementation and success of implementation, evaluation. Review longer-term factors such as stakeholder feedback processes. feasibility, fidelity, responsiveness, sustainability (Proctor et al., 2009).

3.5.1 Recommendations

Acceptability, Appropriateness, Feasibility. Consultation is crucial at all stages of the project, and should be held with potential users, clinician-researchers, and stakeholders (e.g. hospital staff). Given the potential scepticism towards a novel tool, active involvement in the design process will increase likelihood of eventual adoption and reduce the frequency of adverse events. Early implementation oriented engagement should evaluate acceptability, appropriateness, and feasibility factors (Proctor et al., 2011). Specifically, stakeholders' perceptions of the system's palatability, relevance, and ability to be carried out in their setting. Furthermore, considerations may encompass self-identified needs and perceived benefits above existing treatments, concerns, and wishes of end-users. Clinically appealing systems will be feasible, including being cost-effective, portable to relocate within/between clinics, intuitive (i.e. high perceived confidence), and appealing to clients. Consideration of these factors will optimise interventions to be amenable to implementation, and in the longer-term should also deal with aspects of clinician-researcher training and support (Proctor et al., 2009). Collaboration should not cease once the system is finalised. Rather, designers should facilitate technology training, support implementation and VE revisions, and provide user manuals for set-up and troubleshooting, in deliberate, purposeful efforts to improve sustainable adoption.

Ethics. Access to the VR system, including VE software files, should be protected so it cannot be used by unqualified individuals unethically. Appropriately trained specialists should be responsible for overseeing the interdisciplinary design, use, and accessibility of systems. Without this guidance, software developers may not understand the unique vulnerability risks of VR, and potential trigger symptoms without a clinical purpose as a result

of poorly considered design features. Systems that establish an empirical evidence-base with clinician supervised immersion, should not then be freely available to the public for self-guided use, and creators must establish who is responsible for gatekeeping accessibility. At the user level, clinician-researchers will need to consider safety guidelines for their selected VR system, and incorporate these into risks advised during consent procedures, as well as a protocol for managing potential harm. The transfer and storage of clinical communications and identifiable information within VR systems, particularly in-home access, will need to ensure privacy and confidentiality (Yellowlees et al., 2012). Risks will uniquely present at the junction between hardware, software, and each user. Clinician-researchers should therefore develop and disseminate specialised assessment and consent protocols designed on the basis of findings that identify risks in specific populations.

Therapeutic alliance. The therapeutic alliance impacts research and clinical outcomes. An interesting challenge is balancing immersion (sense the VE is the only present experience), with a connection to an external person such as the clinician-researcher who is generally not within the VE. Incorporating this communication into the virtual space may be programmed, such as pre-recorded messages, or flexible, varying due to input from the clinician. The source and format also need to be determined, whether spoken (via microphone into headphones) or integrated into the VR system (avatar “speaks” to user, or written information appears). An iterative design process will ensure this trade-off meets user demands for each population group (Brinkman et al., 2010). Research validating VR systems in psychology should include measures of therapeutic alliance and session feedback, and findings compared across studies to evaluate suitability of VR in varied populations.

Evidence base and future proofing. A foundation of reliability, validity, and usability is built from replication across studies. Therefore, factors to enhance replication, such as easily sharing systems across sites, and applicability to broader population groups should be

incorporated. For VR to meet theorised opportunities, knowledge dissemination should encompass publishing detailed methodologies, design guidelines, and ethical considerations, tailored to best reach the intended end-user (Graham et al., 2006). In order to facilitate adoption, particular research attention must be directed towards evidence of the novel additional value of VR, to heighten perception of practical usefulness (Bertrand & Bouchard, 2008).

Future-proofed systems that incorporate simple customisation (e.g. adding new virtual objects) are more likely to be taken up by clinics. This modifiability allows clinicians to change the VE for each client's presentation without reliance on software developers. Thereby, the relevance for each user is improved beyond what they would typically experience in a clinician's office, such as a virtual airport rather than looking at pictures of an airport. In research, this permits the precise measurement of user responses under carefully controlled conditions with potentially greater ecological validity.

Beyond the individual system, open-source software will enable the breadth and depth of supporting literature to be expanded. Sharing software between clinical and research settings will diversify the sample generalisability and improve the evidence-base. These processes also encourage scientific rigour, as code will be reviewed by more researchers and developers. A sufficient empirical evidence-base will require careful balancing of timeframes, as technology may rapidly advance while clinical research depends upon the relatively slower cycle of research grants, empirical testing, and dissemination of findings.

3.5.2 ETVE Application

Acceptability, Appropriateness, Feasibility. Although not primarily an implementation study, a preliminary understanding of stakeholders perceptions of acceptability (agreeableness to the system), appropriateness (fit, relevance, compatibility), and feasibility (extent to which the system could be carried out within the setting) was garnered by incorporating clinicians and stakeholders throughout the design process in an active manner

(Proctor et al., 2009, 2011). To manage potential uptake barriers, we employed an iterative design process with user, clinician, and stakeholder feedback. From this process, virtual exposure tasks were modified, and system intuitiveness for the clinician-researcher and user were improved. Reservations regarding VR were discussed with both users and clinicians, such as whether hardware posed an issue given contamination concerns. Systems that allowed user-clinician interactions, had minimal resource demands, and the option to pack up equipment and use VR rooms for other purposes were considered beneficial. Commercially available systems were preferred, as they are designed to be user-friendly for a VR-naïve person and have lower monetary costs.

Ethics. Consent procedures included advising that there was some risk of mild nausea and physical discomfort (e.g. neck ache) while using the VR headset. Prior to facing aversive stimuli, users engaged with a neutral VE to familiarise themselves with the use of VR. This provided an opportunity for users who experienced any nausea from the technology to withdraw before cue exposure, though it should be noted that this places the onus upon the client to identify and report aversive symptoms which may be challenging in some circumstances (see Table 7; symptom monitoring). Researchers regularly asked users about their experiences during VR to ensure they were experiencing no or only acceptable nausea. These risks were further managed by each session lasting at maximum 30 minutes, in line with VR safety guidelines. Users could request a rest-break or withdraw at any time, which was an important consideration when designing communication capabilities during immersion. A provisional psychologist was present and a clinical psychologist was present/available at all sessions to deal with any adverse events triggered by the VR system.

Alliance. Real-time communication was important for symptom monitoring, therapeutic alliance, and feedback for research validation. Given the heterogeneity of presentations and cognitive processes in OCD, it was not possible to predict all possible client

responses. Immediate spoken communication was therefore crucial. Speaking via microphone to headphones did not add to the immersion, particularly without a virtual clinician. As such, a headset with one earphone removed permitted both VR audio input and communication. Once validated, future iterations may consider integrating communication into the VE to improve immersion.

A standardised measure of therapeutic alliance was administered following each exposure session. This data was collected to investigate the potential influence of VR on the therapeutic relationship, the findings of which will form part of our validation publication. In addition to psychometric information from a standardised tool, clinician-researchers also engaged in informal discussion with users about their experiences as part of the debrief process, to guide future modifications to the VR system.

Evidence-base and future proofing. Clinical implementation depends in part on a published evidence-base, which is underway with validation studies. Longer-term implementation will also require communication from researchers to clinicians about how to use the system and the benefits thereof, in an active dissemination strategy. At this initial stage, knowledge sharing was facilitated by an ETVE researcher at the clinic, demonstrating equipment, running VR sessions, and communicating instructional information. Future-proofing was also considered with designing customisability features (e.g. aforementioned ‘drag and drop’ functionality).

3.6 Future Directions

Currently, there are relatively few studies providing evidence of VR implementation in specific disorders (Opriş et al., 2012). Meta-analyses suggest VR exposure-based therapy treatment gains can transfer to real-world improvements in phobias and anxiety disorders (Morina et al., 2015; Opriş et al., 2012); however, comprehensive evidence of factors to maximise this remain to be seen.

3.6.1 Virtual Humans

Theoretically, VEs matching real-world experiences would associate with greater transfer of learning. Virtual humans would be anticipated to aid the therapeutic alliance, sense of presence, and ecological validity. Although improving, the realism of virtual humans remains limited, particularly in dynamic responses to unpredictable participant inputs (e.g. spontaneous conversation and behaviour). This extends to the participant seeing their own body in the virtual space. Technological advancements may permit customisable client bodies in the virtual space (e.g. skin tone, body shape). Research will need to compare participant responses to determine optimal solutions.

3.6.2 User Customisation

Ecological validity of VR exposure-based therapy will only be achieved when VEs can be modified to users unique presenting concerns, not just clinical groups generally. Given the practical constraints of therapy, the ability to bring the outside world into the clinician's office must be time efficient, clinician/user friendly, allow flexible modifications, and optimise the limitless possible stimuli. This may involve starting with a general library of open-source VEs, (rooms, outdoor areas) designed in collaboration with software teams, which can be customised by clinicians independently (e.g. adding specific stimuli). Without these capabilities, VEs may be more realistic than imaginal techniques, but they'll be less relevant, and therefore utility would arguably be limited given the higher investment.

3.6.3 Validity, Reliability, and Usability

The excitement surrounding VR's opportunities should not excuse this novel tool from scientific scrutiny. Replicated validity and reliability, and comparisons with current gold-standards, are necessary. Somewhat unique to VR exposure-based therapy is usability research, which looks at designing optimal interfaces, which can be time consuming and costly, in part due to the rapid changes in technology (Rizzo et al., 2004). Beyond such treatment efficacy

evidence, it is necessary to examine longer-term implementation factors such as sustainability over time (Proctor et al., 2009).

3.7 Conclusion

This article has presented considerations for creating VR systems in psychological research and practice, with the applied example of our novel OCD system. It is our intent that this will make VR design more approachable for clinician-researchers, as well as encourage the ongoing rigorous scientific examination of these systems. Scientific evidence for the use of VR will be possible by publishing methodologies for future researchers to improve upon, and ensuring tools are validated before being integrated into clinical practice. We anticipate that the future directions we have identified will allow this field to realise the opportunities promised in the literature.

CHAPTER FOUR: VALIDATION STUDY METHOD

Building upon the VR development process outlined in the preceding chapter, the methodological information for the validation study will now be provided. This aims to bridge the gap between conceptualisation and clinical testing.

4.1 Research Commencement: Collaborations and Development

In order to extend upon the development work outlined in Chapter Three, I then conducted a validation study, the results of which are explored in Chapter Five. There were overlapping procedures across these development and validation phases, including establishing and maintaining the partnership with The Melbourne Clinic which created a novel opportunity to specialise the system for clinical implementation.

The commencement phase of the overarching project involved team meetings with key stakeholders from both Monash and The Melbourne Clinic, including the research team, psychiatrists, and staff from the OCD program. Within these meetings the author provided the project rationale, proposed methodology, and introduced the chosen VR equipment. Feedback was obtained on these components. Subsequent modifications made to heighten clinical utility of virtual environments and system features included contamination variability, and flexibility in structuring and delivering of graded exposure hierarchies by providing a range of possible tasks.

Roundtable discussions also allowed for troubleshooting of anticipated barriers for implementation, including ensuring access to a location suitable for the VR system set-up, as well as virtual environment design, and broad recruitment policies. Potential hurdles to engaging the target population, clinicians, and more broadly the clinical setting, were also considered. At the patient focussed level, it was important to acknowledge the notable refusal rates for exposure sessions in contamination-based OCD patients. In light of these factors, the

perceived acceptability of the study design was regularly reviewed during the development phase of the project.

Taking a patient focussed perspective guided the equipment choices and design. Of particular concern was the selection of the psychophysiology system hardware, as sticky electrodes would potentially prove to be anxiety provoking. This one example is emblematic of the general approach taken: to not necessarily make VR fundamentally more approachable, rather to ensure the extra-ERP factors would not impede the ability for participants to uptake the core processes, being the exposure tasks. Discussions within the interdisciplinary team also covered the strategies for managing potential unwillingness of participants to make physical contact with the research equipment, as well as a strategy for facilitating their engagement in keeping with standard ERP processes, although it eventuated that participants did not raise such concerns, which will be elaborated upon later in this chapter.

Clinician perspectives were also actively incorporated in the design process, particularly regarding system features that they perceived to be most crucial to VR-based ERP acceptability. These included the capabilities to customise virtual environments on a patient-by-patient basis, which were considered to be a priority design feature, to enable modification of exposures for each patient's symptom profile. Additionally, clinicians reinforced the importance of environment design being based on common real-world places and items, rather than prioritising the stylistic appeal, in order to maximise ecological validity. As a result of these discussions, researchers were positioned to troubleshoot and overcome barriers to clinical uptake, incorporate end-user feedback into the development, and tailor features according to clinical acceptability. The team anticipated benefits of this design philosophy would include optimised levels of longer-term patient engagement with the system relative to standard approaches, given VR-based ERP would address their core symptoms in a useful and approachable manner.

To advance collaborations, I participated in several 3-week inpatient OCD programs with patient consent and the support of The Melbourne Clinic. Through this, a greater understanding of exposure procedures was gained which I could disseminate back to the software developers and research team to customise and adapt the system accordingly. Benefits from this engagement also included the establishment of trust between the author and both staff and patients. As many inpatients return for multiple stays, this involvement also garnered a positive ‘ripple effect’, thanks to informal communications amongst patients that supported recruitment, and expressed interest in both the study and VR for OCD generally.

This engagement with the inpatient program also facilitated one-on-one meetings with key program staff and patients to gain informal feedback on the proposed VR system and its content. Such an ‘end-user’ perspective was crucial to enable researchers to design VR-based ERP approaches tailored to patients' needs. In light of the valuable feedback from clinicians, patients, and other key stakeholders, the team expanded the number of available tasks and stimuli, as well as increased the opportunities for variability in contamination. Iterative design modifications maximised the likelihood of patient and clinician uptake, face validity, and appropriateness for the target population.

The experimental research sessions for the validation study were conducted at The Melbourne Clinic in a designated area of the hospital. It was anticipated that many of the participants would be affiliated with The Melbourne Clinic, and as such this location was chosen due to its convenience for participants, and for its general familiarity. As there is a relative scarcity of OCD inpatient programs in Australia, patients of The Melbourne Clinic OCD program include people from a diverse geographic region encompassing rural and urban environments. Flexible scheduling of research appointments, including times outside of business hours, enhanced the possibility of participant referrals, thereby furthering the diversity of the participant cohort. Therefore, basing the study on site near the inpatient area enhanced

the variability of the participant cohort by enabling patients to participate during their inpatient stay. Experiences garnered from this study highlight the benefits of locating VR-based ERP systems at existing clinical sites. Setting up in this manner provides opportunities to access large clinical cohorts, a dedicated physical space with clinical support, a sustained demand for services over time, and therefore improved access and equity of services.

During the recruitment phase, additional challenges inherent to the clinical population emerged, including general avoidance of ERP due to unfamiliarity, fear, and negative past experiences of psychological treatment. Often there was an extended period of time between patients expressing an interest in the study and following through with scheduling an appointment. This was described by patients as being due to an ‘internal battle’ between their strong motivating wishes of achieving wellness and contributing to research, versus their barriers of reluctance to engage in *in vivo* exposure. Despite these challenges, all participants who scheduled an appointment turned up for the study and engaged in exposure tasks, which bodes well for the future patient acceptability of VR-based ERP approaches in OCD.

4.2 Study Design

A repeated-measures study design was used with random allocation to a counterbalanced order. By having the same participants in both groups for comparison, this approach minimises the potential for inter-individual differences, such as medication, to confound the findings. In addition, participants engaged in both experimental conditions on the same day to minimise the possibility of confounding effects from concurrent psychological therapy between experimental sessions. This within-subjects design is best positioned to address the overarching research aims, namely investigating the comparability of OCD related experiences in VR to the existing benchmark of traditional, real-world ERP sessions. Should the virtual sessions be considered sufficiently similar to the real-world sessions, this would provide justification of validity. Future research would then be able to implement between-

subjects and longitudinal designs, to examine treatment efficacy. Building upon those evidentiary foundations, the effectiveness and suitability of VR for particular patients could be determined. Taken collectively, such a combination of future study designs would best inform the positioning of VR relative to existing treatment approaches, for example as an adjunct or alternative technique.

The two groups differed on the exposure method conditions, namely VR and *in vivo* ERP. Allocation was counterbalanced with half of the sample assigned to the VR condition followed by *in vivo*, and the other half vice versa. Counterbalancing in this manner ensured that the possibility of carryover effects from one session impacting another, such as practice or fatigue, were eliminated at a group comparison level. By randomly allocating participants to the comparison groups, the study design protects against any potential regression to the mean (Barnett et al., 2005). Clinician referral procedures commenced in January 2018, and active enrolment commenced in June 2018, with data collection occurring between July 2018 to June 2019.

4.3 Participants

Prior to commencing the experimental protocols, informed consent was obtained from each participant. The validation study sample comprised 22 participants aged 18 to 65 ($M = 32.91$, $SD = 9.84$), who were predominantly female (64%), unemployed (50%), living with family (64%), and single (50%), all of which are representative of typical OCD samples (Karno et al., 1988). Patients were mainly recruited through clinician referrals from inpatient and outpatient services, with advertising flyers placed in waiting areas. Protocols for clinician referral ensured patient confidentiality, by asking patients for consent prior to their contact details being shared with researchers. Patients approached in this manner were also given the option to contact researchers directly via details on the provided flyer. Clinicians emphasised that participation would have no impact on their treatment, and information acquired by The

Melbourne Clinic, such as medical history, would remain confidential. Clinicians were also not made aware of whether patients chose to participate or not.

Recruitment processes were also facilitated by referral from other research studies conducted at The Melbourne Clinic and Monash University. Any dual participation across studies did not overlap in psychotherapeutic processes nor timeline of participation. One such avenue of participant referral was established by embedding myself within the research offices of the hospital to conduct general research administrative activities. From this, I built working relationships with research staff which led to subsequent referral of participants across studies. In a similar manner, participants were also recruited from previous Monash University research studies. This led to a more demographically diverse sample, and more variability in symptom severity, given these participants were seeking outpatient community-based support rather than inpatient service engagement. In these circumstances, potential participants were contacted by researchers on the study that they originally participated in and provided with my contact details for the VR study.

Inclusion and exclusion criteria were determined prior to initiating the recruitment process, in keeping with standard research protocols. In this process, considerations were made to both the relative lack of safety guidelines for VR use in specific psychological conditions, and the expertise of the clinical setting, with the intent of mitigating potential risks. Participants were asked about co-morbid diagnoses that can include symptoms of conflating real and imagined experiences, such as schizophrenia. While VR is being investigated for use in conditions such as psychosis (Botella et al., 2009; Realpe et al., 2020), the experiences of such participants were deemed to be outside the area of expertise for management by the current team. Co-morbid diagnoses in these symptom categories were therefore considered exclusion criteria. Beyond these exclusions, participants were also required to meet inclusion criteria, that specified they must be:

1. Able to provide free and informed consent
2. Currently meeting diagnostic criteria for OCD with primary contamination concerns
3. Aged 18 years or older
4. Fluent in English
5. Able to engage with the outlined study protocol, including physical contact with psychophysiology and VR equipment. Notably, there were no instances of people declining to participate once they were informed of these requirements.

On the day of participation, clinical inclusion criteria were formally assessed in person using a clinical interview, the Mini International Neuropsychiatric Interview (MINI), the Yale Brown Obsessive Compulsive Scale (YBOCS-II), and self-reported diagnostic history. The facilitation of recruitment from clinician referral meant the majority of participants had a confirmed diagnosis of OCD, established by a psychiatrist and/or clinical psychologist. Regardless, the diagnosis was confirmed within the clinical interview on the day of participation, by administration of the MINI. The MINI is considered a validated, standardised approach to determining whether individuals meet DSM diagnostic criteria, including for OCD (Rapp et al., 2016; Sheehan et al., 1998). Additionally the YBOCS-II is considered the gold standard measure for OCD symptom severity with strong psychometric properties (Rapp et al., 2016). The content of the initial clinical interview is elaborated upon further in section 4.5.1 Clinical Interview. Within this interview, any people demonstrating an inability to comprehend study procedures and discuss the benefits and disadvantages of participation in an informed and balanced manner would be considered to be excluded from participating in the study. Participants were *not* excluded solely on the basis of other comorbid diagnoses such as Major Depressive Disorder, Anxiety, Eating Disorder, Personality Disorder, and/or ADHD. There are high rates of comorbidities with other mood disorders in OCD (American Psychiatric

Association, 2013a; Ruscio et al., 2010), and these conditions were not anticipated to interact detrimentally with the research protocol to create a safety risk.

Consideration to the ability of people to engage with the VR and psychophysiology equipment was considered of particular importance, due to the recruited sample having primary contamination concerns. Given this was the first study to use VR hardware requiring this amount of physical contact (i.e. the HMD and handheld controllers) in patients with these symptoms, it was unclear whether patients would find participation challenging due to contamination concerns. Therefore, during recruitment conversations each participant was asked about their prior experience with VR, as part of an explanation of the system, which included the extent of physical contact with the hardware. Discussing any questions or barriers to engagement at this stage ensured participants could make an informed choice. While there were initial hypothesised concerns within the clinical and research team about contact concerns being a barrier to enrolment, there were no instances of refusal at this screening stage, nor during any testing session. In actuality, informal feedback from potential participants indicated that they were excited and curious about the novel nature of the equipment, and keen to ‘try it out’ and contribute to a potential new treatment approach for OCD.

Ethics approval for this study was obtained from The Melbourne Clinic Human Research Ethics Committee (Professorial Unit; Healthscope) and this approval was secondarily registered with Monash University Human Research Ethics Committee.

4.4 Materials

The VR system has been described in Chapter Three, with additional information provided in this section for necessary context and links to the psychophysiology system. Other outcome measures utilised in the validation study are provided in Chapter Five, within the validation manuscript.

4.4.1 Virtual Reality System

All the VR sessions within this study utilised a HTC Vive system, which provided a HMD that is coupled with movement tracking base stations and hand controllers to enable interactivity. The base stations were attached to walls in diagonally opposed corners of the room to create a walkable space of approximately four metres by four metres, as per the manufacturer's specifications. HTC Vive's room scaling technology monitored the matching of the virtual space to the physical dimensions of the room by projecting a boundary grid in the participants view when they approached physical walls. Prior to entering the contamination focused environments, participants used a neutral virtual training space. This provided the opportunity to familiarise themselves with the hardware and software, prior to entering the symptom eliciting kitchen or bathroom environment.

4.4.2 Psychophysiology System

Emotional experiences of fear, anxiety and disgust may manifest in changes to heart and respiration rates (Kreibig, 2010), which provides an opportunity for objective measurement of these psychological states (Diemer et al., 2014; Freire et al., 2010; Meyerbröcker & Emmelkamp, 2010). Psychophysiological responsiveness is considered to be particularly marked for disgust experiences, as the direction of sympathetic-parasympathetic co-activation changes often relates to the specific nature of the feared stimuli. Disgust may manifest as decreased respiration when relating to vomiting, while faster inspiration and cardiac deactivation may relate to blood and injury (Kreibig, 2010).

While examinations of arousal and habituation processes in VR exposure-based therapy have been quantified using psychophysiological markers, a coherent pattern of response has not yet been established (Meyerbröcker & Emmelkamp, 2010). Heart rate changes during VR exposure-based therapy may be unclear as a consequence of the complexity of heart reactivity during fear, or from poorly-designed studies (Diemer et al., 2014). It is therefore important

immersive VR systems that aim to elicit emotional arousal consider more than one psychophysiological indicator and approach data acquisition in a theoretically driven way.

In order to measure these psychophysiological responses, both heart and respiration rates were recorded using a wireless monitoring system, in keeping with signals collected in previous literature (Laforest, Bouchard, Crétu, et al., 2016; Meyerbröker & Emmelkamp, 2010; Pallavicini et al., 2013). Prior studies have averaged recordings across relatively long durations, such as 20 minutes (Wiederhold et al., 2002). However, the inherently transient nature of these signals suggests that recordings should be partitioned into meaningful phases (referred to as epochs), such as anticipatory fear and contact-related disgust. As such, the acquired data was partitioned into *Instruction* and *Contact* phases. *Instruction* refers to when participants were informed of the exposure task to be faced, whereas *Contact* refers to when they made contact with the anxiety-provoking stimuli. Further details relating to these phases can be found in Chapter Five.

It must be noted that psychophysiological measurement in VR is particularly difficult from a logistical perspective, due to inherent challenges in integrating multiple hardware systems while still ensuring patient safety. Commercially available psychophysiology hardware is often tethered via cables to computers, which would cause an unacceptable trip hazard, especially as participants would not be able to see the cables due to the HMD. To enhance participant safety, mobility, and comfort, a wireless system was considered preferable, as it minimises the risk of physical interference between required equipment. An added advantage is that a wireless system would also decrease the complexity of manual set-up for the clinician or researcher guiding the VR sessions. On this basis, the selection of both the VR and psychophysiology equipment was guided towards wireless options that allowed users to move freely in a defined space. Beyond such hardware integration challenges, novel software

programs were also required. Future studies are also likely to find this a necessity, to develop programs that exist at the boundary between the two technologies and synchronise signals.

Based upon these criteria, an Equivital wireless monitoring system was selected. This system is a multi-parameter body-worn device permitting ambulatory monitoring of psychophysiological data in a valid, reliable, research grade manner (Y. Liu et al., 2013). Heart and respiration signals were acquired continuously (via the Sensor Electronics Module in the Equivital Sensor Belt) and real-time streamed via Bluetooth to the AD Instruments LabChart Pro analysis software v.8.1.6 for processing. Post-session, recordings were separated into VR and *in vivo* files. An additional benefit of this system was that participants could put on and take off the equipment relatively independently. This was important given it was anticipated some participants may face difficulty receiving assistance from the researcher in putting on equipment due to contamination concerns. As was the case with the VR hardware, there were no instances of refusal in our sample cohort in response to the psychophysiology equipment.

4.5 Procedure

4.5.1 Clinical Interview

Each experimental session commenced with a dedicated time period for rapport building between the participant and researcher. After this, time was allocated to establishing a sense of participant familiarity with the physical environment, as the testing room was separate from the main hospital. The explanatory statement was provided and discussed, and then signed informed consent paperwork completed. The majority of participants indicated the statement would elicit time consuming checking compulsions and therefore requested a collaborative approach with the researcher to go through these paperwork items with them. All participants were provided with explanations of the risks unique to VR and informed about what to expect from the immersion. They were provided the opportunity to discuss with researchers the manner in which the VR experience would differ from more conventional uses,

such as recreational gaming, in keeping with ethical guidelines for VR in psychological implementations (Behr et al., 2005; Yellowlees et al., 2012).

Following these procedures, a more detailed clinical interview was conducted to build an understanding of each participant's OCD symptoms and provide psychoeducation, with particular focus upon the principles of ERP and Subjective Unit of Distress (SUDs). SUDs are a self-report measure of client experience, commonly utilised in OCD settings to guide the development of exposure hierarchies and monitor treatment engagement and process (Wolpe, 1973). To ensure understanding and reliability in reporting, SUDs ratings were discussed in detail, for example regarding what '100 out of 100' represented. Information was gathered regarding feared stimuli, mental and behavioural compulsions, neutralising thoughts and avoidance behaviours to ensure a foundational level of researcher familiarity with each participant's key symptoms, as required to conduct an ERP session. A secondary benefit was building a sense of trust towards the researcher; ensuring each participant felt heard and their symptoms understood was an important foundation to establish, prior to working collaboratively through exposure sessions. The MINI and YBOCS-II were administered to record co-morbidities and OCD symptoms themes beyond contamination.

Tailored hierarchies were developed according to SUDs ratings, in keeping with standard ERP procedures (Abramowitz, 1996). Firstly, the researcher and participant collaboratively designed generic hierarchies for kitchen and bathroom settings guided by the collaborative formulation established in the interview. Secondly, the researcher independently designed a tailored, graded hierarchy for the kitchen and bathroom environments (i.e., without participant involvement). This two-step process was necessary so that the participant was not aware of the exact tasks prior to the exposure, so that data could be collected regarding the anticipatory fear onset within-session when the new task was provided. Going from generic to specific hierarchies was deemed necessary with dual considerations of research validity and

comparability (tasks needed to some degree be ‘available’ in the pre-programmed virtual environments) with the clinical need to address each participant’s unique symptoms. Participants were asked to select to use either a kitchen or bathroom environment on the basis of their unique symptom profile and contamination concerns. Collaborative discussion with the researcher supported this process, on the basis of the clinical formulation that was ascertained through the initial components of the clinical interview. Participants selected the environment they believed would be most relevant to their fear structure. Graded hierarchies were matched across the virtual and *in vivo* sessions.

4.5.2 Questionnaires

Questionnaire data was collected using the online survey platform, Qualtrics (Qualtrics, 2005). Demographic information collected included participants age, postcode, education, occupation, and number of people living in their home. Additionally, pre- and post- exposure questionnaires, including state anxiety and alliance measures, were completed using Qualtrics. Two participants were unable to complete the questionnaires independently due to OCD symptoms (re-reading and checking compulsions would reportedly generate a self-perceived unmanageable degree of uncertainty and discomfort). For these two participants, the researcher conducted a verbal interview using pen and paper. There were no refusals to use the computer for questionnaire purposes that were directly due to contamination concerns but planning for such an eventuality is important for an OCD VR-based ERP cohort.

4.5.3 Equipment Set-up

Following the initial questionnaires, each participant was shown the VR and psychophysiology equipment and provided with a rationale for its use (i.e. to understand people’s responses to exposures). The researcher also explained how VR works and what they would be able to experience during the virtual experience (i.e., walk around to explore the

areas, move and interact with objects in the environment, hear noises). These discussions broadly followed the following script:

“The environments are a kitchen and a bathroom. There are familiar objects in those rooms, for example a toaster in the kitchen. You have full control over which objects you want to touch, pick up, or use. We will agree on which tasks you feel prepared to try. In the VR, I will send reminders of those tasks to a virtual mobile phone. The controller will buzz when a text message comes to you. An example of an experience you could have in the VR environment is an instruction coming to the virtual mobile phone that reads "Touch the toaster with both hands". You would then walk over to the toaster and use the controllers to touch the toaster, perhaps press the buttons, with as much engagement as you feel capable to complete. Throughout the session you will be able to communicate verbally with the researcher. Just as with ERP sessions you may have done previously, you have control over when you do the tasks and how much you would like to do.”

The researcher then explained how to wear the VR and psychophysiology components, clarified any questions, and asked whether participants felt comfortable to use the equipment. There were no instances of reluctance nor refusals to continue participation following these introductions, rather participants indicated curiosity and motivation regarding a novel way of potentially conducting ERP. Many reported that they were especially eager to contribute to research because they wanted to see improvements in the manner that their symptoms could be managed in the future and the likelihood of greater treatment successes from more diversity in ERP options. Participants were able to put on the psychophysiology equipment independently

in a private room. The researcher reviewed data quality as it streamed to the software, and with participant consent confirmed adequate equipment fit if required or requested.

4.5.4 Exposure Sessions

As mentioned, participants were randomly allocated to equally sized groups to create counterbalancing, whereby each completed either VR or the *in vivo* session first, followed by a rest break and the other session. In the interest of clarity, the following discussion will be presented from the perspective of those who undertook the VR session first.

Participants were guided by the researcher to put on the VR equipment, and with participant consent the researcher adjusted the headset to ensure comfort. Immersion began with a virtual demonstration scene that allowed participants to become familiar with how to manoeuvre within the VR environment. This particular scene was located in an elevator, which was purposefully designed to not provoke any feelings of discomfort. The researcher prompted the participant to walk around in this demonstration area to become accustomed to the room size. Participants were asked to report when they saw the grid room boundary to ensure familiarity with this feature for safety purposes, which is projected by the VR system when users approach real-world physical walls. While in the demonstration scene, participants were asked if they experienced any nausea or physical discomfort as a result of the VR and reminded that they were free to take a break or cease participation at any point by notifying the researcher. By dedicating time for each person to trial the system prior to any therapeutic intervention, we aimed to identify and manage any risks arising from hardware and software (Behr et al., 2005). Throughout all VR sessions, there were no instances of participants experiencing physical discomfort nor requiring a break from immersion before sessions reached their natural conclusion. For the exposure component of the VR session, participants followed these steps:

1. Select either the kitchen or bathroom environment using the elevator selection panel.

The environment was chosen prior to immersion by the participant with clinician

support on the basis of which was most relevant to their obsessions and compulsions.

A range of contaminated objects which commonly elicit distress in people with contamination concerns would be visible in either environment.

2. Report SUDs upon entering their chosen room.
3. Walk around in the environment, immersing themselves.
4. Report readiness to engage in the first exposure task. The researcher then clicked a button on the Control Panel software, which sent a virtual text message to their virtual mobile phone (see Figure 5) and an event-marker to the physiology software.
5. Participants read the task instruction and reported their associated SUDs to the researcher (*Instruction* phase).
6. When ready, participants engaged with the first level of exposure (e.g. touch a light switch) involving some physical contact with an anxiety-eliciting item.
7. Report SUDs during each *Contact* commencement and at any time they wished to advise the researcher that their anxiety was changing. This additional reporting happened naturally as participants were typically familiar, or quickly became well-versed, with the process of SUDs in ERP sessions.
8. Engaged with the exposure task for as long as they felt was necessary and useful.
9. Either remain at the exposure level, or increase in the hierarchy if they reported they were willing and chose to do so, and their SUDs were at a clinically appropriate level (i.e. not at 100, SUDs had subsided to a degree that any increase was now within a clinically acceptable range relative to their previous task level of SUDs).
10. Repeat from step 4 at the next exposure task level up in the graded hierarchy.
11. Continue for the duration of the exposure session, to a maximum of 30 minutes, in keeping with technology health and safety guidelines. Participants ended the exposure session when they were no longer able to meet the conditions of step 9, due to their

SUDs increases making further progression through the hierarchy clinically inappropriate. At this point the participant returned to the neutral scene and removed themselves from the VR.

12. Complete psychological self-report questionnaires relating to therapeutic alliance, and state-based anxiety using the Qualtrics platform, and an engagement and adherence measure verbally with the researcher.

Messages on the screen of a virtual mobile phone were used to provide exposure task instructions (see Figure 5), which is a novel approach for providing the participant with information from the external environment while minimising the breaking of immersion. Analogous to the vibration of a mobile phone, this message prompt was tied to vibrating haptic feedback in the VR handheld controllers, which further enhanced immersion. This framework allowed the researcher to control the onset and content of the exposure instruction, in a manner that was responsive to participant needs.

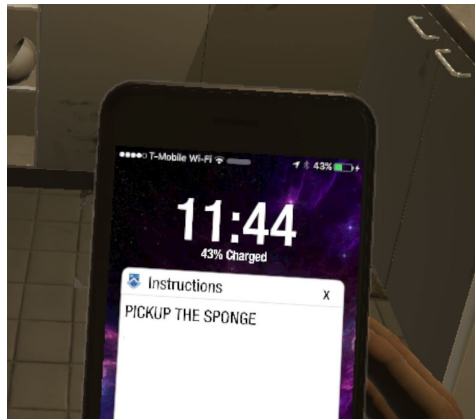


Figure 5. Virtual Mobile Phone Interface. The Controller Vibrates in the User’s Hand to Notify Them of an Exposure Task Instruction, Designed to Resemble a Real-World Mobile Phone Notification.

At the conclusion of the exposure session, the researcher and participant engaged in a short discussion regarding the VR experience. This typically involved participant feedback on what could be improved, relevance to their everyday experiences and whether they would

utilise VR-based ERP again. Participants were invited to remove the physiological measurement devices in private.

A rest break was provided between the two exposure sessions, of a duration that was guided by participant needs and symptom provocation levels, typically around 30 minutes. Upon return to the testing room following this break, rapport was re-established, and participants discussed their subjective anxiety. The second exposure session was only commenced when SUDs had returned to the pre-session baseline of the first exposure session.

The structure of the *in vivo* session followed the same procedure as the VR session, with matched hierarchies across sessions. Whichever environment was selected for the first session was used in the second, so both would be conducted again in the kitchen or bathroom, but not both. This was necessary for precise comparison of matched hierarchies. While some participants had engaged with previous research studies and clinical programs at The Melbourne Clinic, the *in vivo* environments were distinct from both the regions of the hospital these participants had been exposed to, and the broader clinical program spaces.

For the *in vivo* environments, it was deemed that a familiarisation environment was unnecessary, in contrast to the VR session as there was not the added element of technology acclimatisation required. However, to replicate the VR experience in a methodologically robust procedure, time was nonetheless allocated for participants to be present in a neutral space prior to exposure.

Event-marking in the psychophysiology software for the virtual and *in vivo* exposure *Instruction* phases was achieved via a button-press by the researcher. During the *Contact* phases event-markers were generated *in vivo* the researcher pressed a button, and in VR when the participant clicked the handheld controller button. Therefore, in the *Contact* phase a slight difference in onset may have occurred, though it is important to note any latency would be unlikely to miss a pronounced change as notably heart and respiration signals are relatively

lower in frequency compared to others, such as electroencephalography. The overall data quality was reinforced by recording the time of the event for manual cross-checking. This is discussed further in Chapter Six.

Once a participant completed both sessions, they were engaged in conversation about how they found the overall experience, comparisons between VR and *in vivo*, and whether they perceived a need for VR-based ERP in OCD. In recognition of their time, a 60 dollar retail gift-card was provided. Participants were reminded that in the event of any distress arising following participation, they should contact their treating medical specialist, and researchers confirmed there were no barriers to them receiving this support.

4.6 Data Analysis

The number of exposure levels completed from the hierarchy was participant driven—in keeping with standard ERP protocols—and as such the number of tasks completed varied across the sample. However, in order to have statistically robust, equal group sizes, the analysis required there to be a consistent number of levels to compare at a group level. At the conclusion of all data collection for the study, I assessed the number of levels completed by participants and only considered records from levels one through to six for the final analysis. This decision was made with consideration to minimising the amount of missing data, as it would have not been statistically sound to include twelve task levels when only a minority of participants completed more than six levels. Given the participant driven nature of task completion, there was a minority of participants who did not reach level six of the exposure hierarchy. This occurred when a participant's SUDs increased to a level deemed appropriate to end the ERP session. Specifically, cessation prior to level 6 happened during *in vivo* sessions for a total of 2 participants at *Instruction* and 4 at *Contact*, and during VR sessions for 1 participant at *Contact*. In these circumstances missing data was imputed using Expectation Maximisation (Tabachnick & Fidell, 2007). When compared to *in vivo*, all participants engaged with more,

or the same, amount of hierarchy levels in VR (i.e., no participants completed more tasks in Traditional than VR). Given the duration of each task completion was participant driven, the data was analysed at onset of *Instruction* and *Contact*, to account for any confound of dosage.

Psychophysiology data files were cleaned in LabChart software to remove additional or erroneous triggers, such as when participants pressed the handheld controller button multiple times for the same contact event, in which case the first trigger was selected and the markers immediately following removed in keeping with the manner of epoch definitions *in vivo*. Data cleaning was supported by manual cross-checking procedures, including recording the time and event-marker number for each exposure event to ensure the accuracy of final triggers.

4.6.1 Psychophysiology Acquisition and Data Extraction

As mentioned, psychophysiology data was collected for heart and respiration signals. In order to limit electrocardiogram (ECG) frequencies to a range between 1 and 30 Hz, the signal was filtered through a bandpass filter (Bailey et al., 1990). This process suppressed baseline wander stemming from periodic respiratory variation and muscle artefacts, which represent noise, while preserving the amplitude of the QRS and ST shape (Andreassi, 1995; Bailey et al., 1990; Buendía-Fuentes et al., 2012). On the low frequency side of the filter, it is known that no biological components or signals are authentically attributable to ECG below 0.67Hz, and 0.5Hz is known to distort T waves and ST segments. Additionally, low-pass filters above 40 Hz may modify the QRS amplitude (Buendía-Fuentes et al., 2012; Electrophysiology, 1996). Digital filters are considered appropriate methods to manage frequency cut-offs for signals stored in computer memory, without introducing phase-distortion (Buendía-Fuentes et al., 2012).

Heart beats were detected using standard human classifications, defining a typical QRS width as 80ms as to distinguish beats from other waves and noise. As the R wave components of the heartbeat should be at least 300ms apart in order to prevent erroneous classification of

T-waves/noises as QRS complexes, and to promote alignment at QRS maximum (as R is most easily identified). Averaging occurred across 4 beats to minimise noise and interference and provide a more accurate waveform. Beat markers and classification for inclusion were reviewed to ensure accurate detection of QRS complexes. ECG was converted to Heart Rate in beats per minute (HR/bpm) for analysis. These procedures have been similarly reported in previous VR exposure-based therapy research (Notzon et al., 2015).

Respiration signals were classified using LabChart human pre-sets, as a cyclic human signal of chest expansion that was acquired from the respiratory belt. This signal was converted into Respiration Rate in breaths per minute (RR/bpm) for analysis.

4.6.2 Psychophysiology Epoch Definitions

Session recordings were further divided into *Instruction* and *Contact* epochs, which were real-time event-marked in the psychophysiology file. Post-processing involved selecting and defining a consistent time window after each trigger onset. This consistency permitted comparability across participants and hierarchy levels, as epochs should be equivalent in duration for analysis (Shaffer & Ginsberg, 2017). Selected times were five and ten seconds for *Instruction* and *Contact* respectively. These epoch durations were determined as suitable on the basis of missing data considerations (events that had durations shorter than five or ten seconds) and consistent with theoretical explanations of the rapid anticipatory response associated with the task instruction, followed by a longer disgust reaction due to stimulus contact. Autonomic responses are most prominent immediately following initial exposure onset (De Vries-Bouw et al., 2011), which is what we aimed to capture. Therefore, epoch durations needed to be short enough to exclude longer habituation processes, as these are characterised by signals returning to baseline. If these extended time points were to be included, it would reduce the average value of the signal, and, perhaps minimise the potential for noticeable differences to be recorded between *in vivo* and VR sessions. This would be

misleading, suggesting that the autonomic arousal at anticipatory fear was lower. Therefore, it was important to select an epoch duration that included just the initial response, without averaging across a longer time period. LabChart was used to select and extract the epoch duration following each event-marker and transfer the calculated values to its inbuilt Data Pad functionality. From here, the values were transferred to SPSS for group level analysis (IBM, 2017).

Data accuracy was further supported by comparisons to published reports of psychophysiology in anxious populations. The mean and standard deviations of our signals were acceptably comparable (Dishman et al., 2000; Donahue et al., 2009; Freire et al., 2010; Harris et al., 2002; Jang et al., 2002; Laforest, Bouchard, Crétu, et al., 2016; Monk et al., 2001; Mühlberger et al., 2001; Notzon et al., 2015). Further details of the data analysis procedures can be found within Chapter Five, as part of the Validation manuscript.

4.7 Concluding Remarks

The outlined methodology was deployed to address the validation research aims for our novel VR-based ERP system. Specifically, the initial hypothesis that there would be no significant differences between the two exposure methods on subjective, objective, and therapeutic indicators obtained in this clinical sample. The empirical evidence to follow in Chapter Five outlines VR's comparability to the existing first-line approach to psychological treatment for OCD, being traditional ERP.

CHAPTER FIVE: VALIDATION MANUSCRIPT

After demonstrating the development and opportunities of this new novel VR-based ERP system for treating contamination-based OCD—as outlined in the first manuscript within Chapter Three—a validation study was required to support its efficacy. As traditional ERP is the current gold-standard in psychological treatment for this clinical population, the primary aim of this study was to compare patient responses in VR to traditional *in vivo* ERP. Equivalent findings across these two exposure methods, in conjunction with favourable participant engagement responses, would provide evidence for the validity of VR as a tool for use in ERP.

In order to compare virtual exposure to *in vivo*, the VR system was designed to include a range of flexible tasks that could be incorporated into graded hierarchies for participants. In light of the promises and pitfalls of VR exposure-based therapy identified in the earlier chapters of this thesis, we investigated a comprehensive array of responses to matched virtual and *in vivo* exposure experiences, including subjective psychological distress using the most common clinical index (SUDs), objective psychophysiological indicators of distress using both heart rate and respiration, and the key clinical factors of therapeutic alliance and exposure engagement.

This chapter presents the manuscript '*Exposure Therapy in a Virtual Environment: Validation in Obsessive Compulsive Disorder*' which is currently under review with a peer-reviewed journal. To my knowledge, this is the first comparative study between immersive VR and real-world *in vivo* ERP, for a clinical OCD sample, that considers a range of both symptom and clinical engagement measures. The evidence of therapeutic variables, such as alliance and engagement, presented herein are necessary to convincingly suggest that VR-based ERP can be translated into clinical practice. Additional notable contributions include precisely defined psychophysiological epochs and providing comparisons to the current gold-standard in psychological treatment with examination of statistical equivalence.

TITLE PAGE

**Exposure Therapy in a Virtual Environment:
Validation in Obsessive Compulsive Disorder**

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Abstract

Exposure and Response Prevention (ERP) is the current first-line psychological treatment for Obsessive-Compulsive Disorder (OCD). However, substantial inter-individual variability exists in treatment outcomes, including inadequate symptom improvements, and notable refusal and attrition rates. These are driven, in part, by impracticalities in simulating intrusive thoughts within clinical settings. Virtual Reality (VR) offers the potential of overcoming these limitations in a manner that allows for finely controlled anxiety-provoking scenarios to be created within supportive clinical settings. To validate the potential of VR for treating contamination-based OCD, 22 patients undertook a VR ERP session and a matched session of the current gold-standard of *in vivo* ERP. In VR, patients were immersed within a contamination environment that permitted flexible delivery of customisable, graded exposure tasks. The VR environment utilised HTC Vive hardware, to allow for patients to both interact with, and physically move through the environment. Subjective and objective measures of distress were recorded, including heart and respiration rates. These measures indicate virtual and *in vivo* ERP sessions provoke consistent anxiety profiles across an exposure hierarchy. Virtual exposure was advantageous for engagement and adherence to tasks, and the therapeutic alliance was upheld. VR is a promising mechanism for ERP in contamination OCD.

Keywords: Virtual Reality, Obsessive Compulsive Disorder, Exposure Therapy, Therapeutic Alliance, Anxiety, Psychophysiology

Abbreviations: Exposure and Response Prevention (ERP), Obsessive Compulsive Disorder (OCD), Subjective Units of Distress (SUDs), Virtual Reality (VR)

5.1 Introduction

Obsessive-compulsive disorder (OCD) is characterised by persistent intrusive and upsetting thoughts, images or urges (obsessions), and/or repetitive behaviours or mental acts (compulsions), that are performed to reduce discomfort (American Psychiatric Association, 2013a). Cognitive Behaviour Therapy including Exposure and Response Prevention (ERP) is the recommended first line non-pharmacological treatment for OCD (American Psychiatric Association, 2007, 2013b; National Institute for Health and Care Excellence, 2005; The Australian Psychological Society, 2018). Typically, ERP sessions utilise exposure hierarchies to assist clients to sequentially face anxiety provoking scenarios in a graded manner while simultaneously withholding compulsions to assist in learning new associations to feared stimuli (Abramowitz & Larsen, 2006; Powers et al., 2006). Despite a strong evidence-base, 15-25% of clients refuse ERP, a further 14-25% drop out prematurely (Abramowitz, 2006; Jenike, 2004; Ong et al., 2016; Öst et al., 2015; Schruers et al., 2005), and up to 41% of clients demonstrate inadequate treatment response (Simpson et al., 2006; Simpson, Foa, et al., 2008). These figures may partly stem from the impracticalities of simulating triggering situations and associated intrusive thoughts within clinical settings, which can feel removed from client's daily experiences, as well as low compliance with ERP between sessions (Lind et al., 2013). Given these substantial engagement and symptom-provocation shortfalls in standard ERP approaches, new avenues to provide evidence-based treatment are needed. Innovative technologies such as Virtual Reality (VR) offer a unique opportunity to create novel ERP tools that translate traditional strengths of ERP while addressing current limitations.

VR uses computer simulations to create immersive, carefully controlled three-dimensional environments. Audio-visual features mimic and extend reality, providing the opportunity of seemingly endless experiences that can be customised. Current technologies enable users to ambulate within virtual environments and choose their actions freely, which

heightens presence and distinguishes VR from more passive experiences like watching a movie. Virtual environments offer the opportunity to capture comprehensive, carefully controlled research data in these ecologically valid settings. These capabilities may also be leveraged to address barriers in traditional treatment delivery, potentially improving service uptake, targeted symptom provocation, and facilitating in-home therapeutic engagement. In doing so VR could overcome the challenge of replicating client's day-to-day experiences in a clinician's office. VR exposure sessions in post-traumatic stress disorder and specific phobias have been shown to significantly reduce disorder symptoms, and are not inferior to real-world *in vivo* exposure with respect to therapeutic outcomes (Gonçalves et al., 2012; Parsons & Rizzo, 2008; Rizzo et al., 2014). Given the similarities in underlying mechanisms of anxiety and stress disorders have led to commonalities in exposure-based treatment approaches, VR exposure-based therapy holds promise as a potential treatment tool for other similar disorders, such as OCD.

In ERP, the combination of both *in vivo* and imaginal exposures currently generate the greatest improvements in anxiety and OCD symptoms at post-treatment (Abramowitz, 1996; Gillihan et al., 2012). VR-based ERP for OCD could enhance upon these treatment modalities by simulating situations of the real-world in a more realistic manner. Additionally, exposures that may otherwise be perceived as dangerous or impractical *in vivo* could feel more 'safe' or feasible in VR. In order to validate virtual exposure tasks, it is crucial to demonstrate that provocation of disorder-specific emotions can occur in response to relevant virtual stimuli, to a comparable level to real-world exposure. Specific emotional experiences can be targeted in ERP depending on clients' symptom profiles. Fear and disgust dimensions are particularly relevant in several anxiety-related disorders, such as contamination-based OCD (Cisler et al., 2009). Evidence is building that subjective and objective measures of OCD-related anxiety can be heightened in VR, including the provocation of fear and disgust (Belloch et al., 2014; Inozu

et al., 2020; Kim et al., 2008, 2009; Laforest, Bouchard, Crétu, et al., 2016). VR-based ERP for OCD may also offer advantages beyond existing treatments, such as greater standardisation of exposures via precise control over graded tasks (Cloos, 2005).

Better designed studies are urgently needed in order to translate VR-based ERP into clinical practices. A systematic review concluded that there was an insufficient number of studies that compared VR to either *in vivo* or imaginal exposure (Diemer et al., 2014). This type of analysis remains vital to understanding the relative strengths and weaknesses of VR-based ERP as a treatment tool by using existing treatment modalities as a benchmark. Establishing this evidence will require studies to use clinical samples that meet diagnostic criteria and make comparisons to ‘treatment as usual’ groups. These are notable gaps in the literature to date, which in contamination-OCD has lacked control comparisons (Belloch et al., 2014) primarily focused upon sub-clinical samples (Inozu et al., 2020), non-immersive technology (Kim et al., 2008), and provided no comparison condition to existing best practices of *in vivo* treatment (Laforest et al., 2016).

Studies that concurrently measure clinically relevant objective and subjective responses to VR-based ERP and directly contrast with *in vivo* ERP are needed to ascertain the therapeutic utility of VR-based ERP. For instance, Subjective Units of Distress (SUDs), is the most commonly used self-report assessment of client experience. SUDs are used in developing treatment hierarchies and monitoring treatment engagement and process (Wolpe, 1973). In anxiety populations, including those who display contamination concerns, fear and disgust responses may also correspond with distinct heart and respiratory changes (Kreibig, 2010), providing an opportunity for parallel psychophysiological measurements to further quantify emotional experiences (Diemer et al., 2014; Freire et al., 2010; Meyerbröker & Emmelkamp, 2010). These advancements will provide important evidence for the utility of VR in eliciting relevant emotional engagement.

Beyond evidence of anxiety provocation, the clinical acceptability of new VR treatment tools must be addressed to facilitate translation into clinical practice. Clinicians' perception of 'usefulness' is a predictor of VR implementation (Bertrand & Bouchard, 2008) and limited understanding of benefits and insufficient training are reported as key barriers to VR uptake (Schwartzman et al., 2012). Research will need to measure and report clinical factors in order to improve clinicians' familiarity and likelihood of acceptance. In particular, any impact of VR on the therapeutic relationship and client engagement factors are important to ascertain as these are known predictors of treatment response (Abramowitz et al., 2002; Martin et al., 2000). It is also imperative that research examines the unique impact of technology on therapeutic alliance factors; either enhancing client's empowerment over their own treatment, or creating a barrier to communication (e.g. face-to-face engagement) (Meyerbröker & Emmelkamp, 2008; Riva, 2005).

In light of the above, this study aims to robustly validate a novel VR exposure system (development described elsewhere; Cullen et al., 2020). In a contamination-based OCD sample, we aimed to investigate the comparability of a session each of VR and Traditional *in vivo* ERP, across subjective and objective responses as measured by self-reported anxiety, therapeutic alliance and exposure engagement, and psychophysiological heart rate and respiration indicators of emotional response. These findings will help determine whether VR is a valid method for exposure therapy in OCD, using a clinically diagnosed sample to examine anxiety provocation and clinical indicators of engagement.

5.2 Method

5.2.1 Participants

Twenty-two consenting adult participants were recruited from OCD treatment clinics and the general public, via clinician referral, flyers (waiting rooms, support groups) and research databases. To be included in the study, participants needed to be 18 years and above,

meet primary diagnostic criteria for OCD according to the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (American Psychiatric Association, 2013a) using the Mini International Neuropsychiatric Inventory, endorse primary contamination concerns on the Yale-Brown Obsessive Compulsive Scale II (YBOCS-II; Goodman et al., 1989), and report stable psychoactive medication type and dosages in at least the prior three months, if prescribed. These criteria were assessed by a psychologist in a semi-structured clinical interview. Individuals were excluded for any co-morbid diagnostic history that may have posed a safety risk (given limited published safety protocols specialised for VR in psychological populations). Ethics approval was obtained from The Melbourne Clinic Research Ethics Committee and Monash University Human Research Ethics Committee. Additional methodological information is available elsewhere (Cullen, 2020; Cullen, Dowling, Segrave, Morrow, et al., n.d.).

5.2.2 Apparatus

VR Hardware and Software. A HTC Vive system with wireless adaptor for the head-mounted display was used, as this permits free movement within a defined walkable space. The visual display adapts according to participant actions, for example turning in a different direction and walking over to look at a new area in the environment. Two handheld wireless controllers enable the user to manipulate objects in the virtual environment. Custom virtual environments were built in Unity software (see Figure 6). Software design was collaborative and iterative, incorporating feedback from OCD patients and clinicians (detailed information; Cullen et al., 2020).

Psychophysiology hardware and signal acquisition. Physiological signals were acquired using the Equivital LifeMonitor wireless monitoring system (Y. Liu et al., 2013). Signals were live streamed via Bluetooth to the AD Instruments LabChart Pro analysis software v.8.1.6 and recorded. Custom built software integrated the physiology and VR

programs. This permitted real-time virtual environment modifications, such as making new stimuli available to commence an exposure task, with synchronised event-markers sent to the physiology software. Electrocardiogram (ECG) and respiration were measured via the Equivital Sensor Belt, which contains ECG electrodes and an expansion based respiratory belt transducer. Device sampling rates are predetermined at 256/s. A bandpass filter of 1 to 30 Hz was applied to the ECG signal (Andreassi, 1995; Bailey et al., 1990; Buendía-Fuentes et al., 2012).

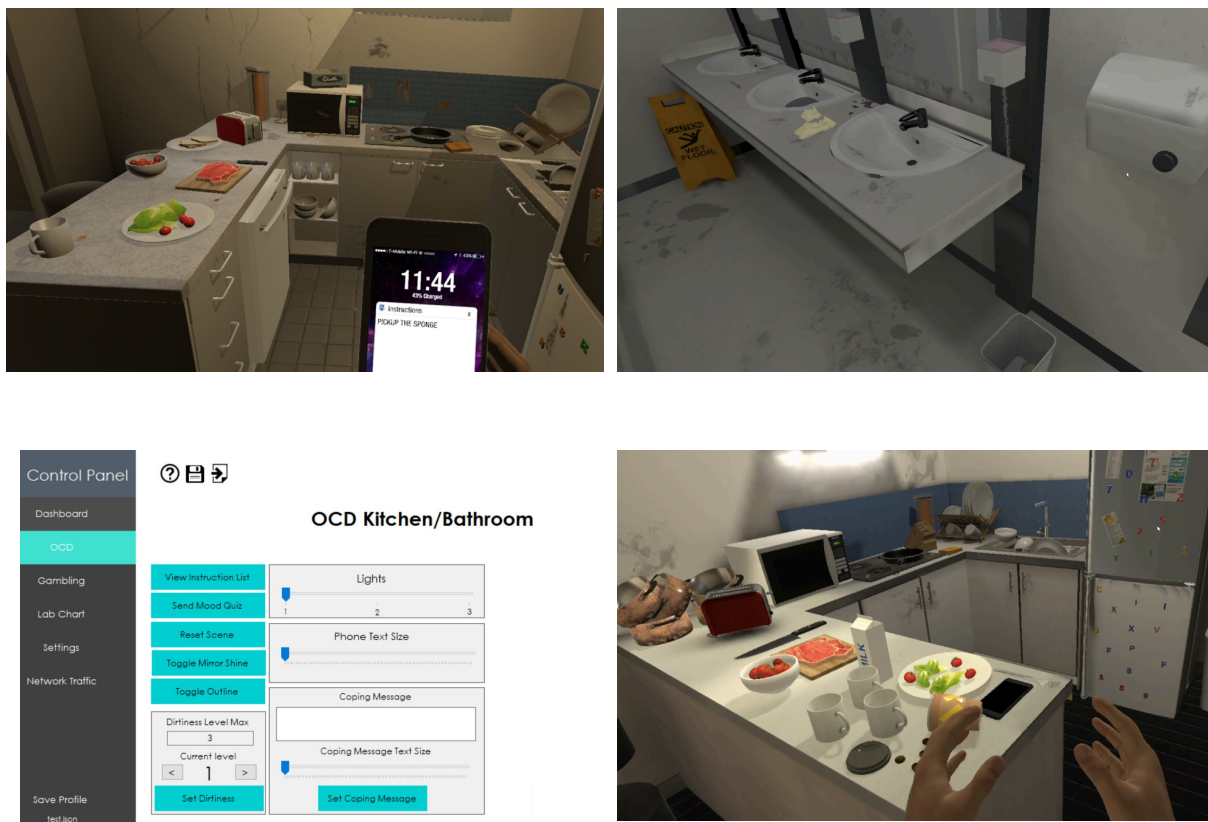


Figure 6. Sample of Virtual Environments and Control Panel Interface

5.2.3 Procedure

All recruited participants attended the sessions. This is notable given the typical rates of treatment refusal in OCD (Jenike, 2004; Öst et al., 2015; Schruers et al., 2005). The study design was repeated measures and counterbalanced with random allocation. For each participant, following informed consent, a clinical interview was conducted to characterise

OCD symptoms and provide psychoeducation to ensure familiarity with SUDs and ERP session structure. Participants and researchers developed exposure hierarchies according to SUDs ratings, in keeping with standard ERP procedures (Abramowitz, 1996). Generic hierarchies were collaboratively designed for kitchen and bathroom settings. Using this understanding of each participants symptoms, researchers translated this into a tailored hierarchy that would be expected to sequentially heighten anxiety for each participant. This was necessary to ensure that a distinct novel fear response could be exhibited when each task instruction was provided. This approach balanced research validity and comparability (pre-determined tasks able to be generated using the VR software) with the clinical need to address each participant's unique symptoms and elicit emotional responses. Participants selected to use either a kitchen or bathroom environment, and hierarchies were matched across virtual and traditional *in vivo*.

Pre-session measures were collected using an online questionnaire platform (Qualtrics, 2005), except for two participants who felt their OCD symptoms would impede completing a questionnaire, with data was collected via interview in these instances. Psychophysiology was recorded coincident with all VR and *in vivo* exposure activities. There were no refusals from participants due to the equipment (i.e., insurmountable fears of being contaminated), nor instances of simulator-sickness. Participants started either the virtual or *in vivo* session according to their randomised order. Within-session ERP data (SUDs, psychophysiology; see Materials within-session below) was recorded at two key points for each exposure task; *Instruction* and *Contact*. *Instruction* is when participants were informed of the task, whereas *Contact* refers to when they made contact with the anxiety-provoking stimuli. Consistent with standard therapy, session pace and the number of tasks were participant-driven, with support from the researchers (see Data Analysis for further exposure task level information). Communication between researcher and participant was possible throughout sessions to enable

engagement and ongoing monitoring. Post-exposure questionnaires were administered at the conclusion of each session.

A rest break between sessions was provided, of a duration that was guided by patient needs and symptom provocation levels, typically 20 to 30 minutes. The second exposure session followed the same procedure as above, on the same day. Participants were debriefed and provided a 60 dollar gift-card in appreciation of their time.

5.2.4 Materials

The State-Trait Anxiety Inventory (State subscale; STAI-S, Y-form) is a 20-item questionnaire that was used to measure current anxiety symptoms pre- and post-session. Higher summed Likert ratings represent greater severity. Psychometric properties indicate sound reliability and validity, with adequate discrimination between low and high stress situations (Barnes et al., 2002; Metzger, 1976; Spielberger et al., 1983).

The Session Rating Scale Version 3 (SRS), is considered a reliable, valid, and feasible tool to measure therapeutic alliance (Duncan et al., 2003), and is appropriate for session-by-session use. The Patient Adherence Scale for Exposure and Response Prevention Therapy (PEAS) was used to measure client engagement in exposure processes (quantity, quality, ritual prevention), as compliance is a known predictor of outcome (Abramowitz et al., 2002). The scale has excellent inter-rater reliability and good face and content validity (Maher et al., 2012; Simpson et al., 2010). The SRS and PEAS were administered at the conclusion of each exposure session.

Within-session. SUDs were measured on a 0 to 100 scale at defined points (including *Instruction* and *Contact* phases). Self-reported anxiety provocation is commonly operationalised using such fear ratings in clinical and research contexts (Carl et al., 2019; Meyerbröker & Emmelkamp, 2010; Morina et al., 2015).

ECG and respiration signals were acquired continuously with semi-automated real-time event marking of key times. For example, triggers were programmed to be sent to LabChart software automatically when participants pressed a button on the VR controller, indicating contact with objects. Recordings were post-processed using these markers into the *Instruction* and *Contact* windows, with the aim of examining fear and disgust responses respectively (Cisler et al., 2009; Diemer et al., 2014). By dividing these signals into meaningful epochs, we intended to capture detailed fluctuations in psychophysiological activity which relate to conceptually meaningful anxiety experiences.

5.2.5 Data Analysis

Psychophysiology data extraction. For heart rate, beats were classified according to standard human QRS classifications, averaged across 4 beats, and manually reviewed for detection accuracy. Respiration was classified using cyclic human chest expansion parameters (analysed as breaths per minute). Exposure hierarchy task levels 1 to 6 were extracted for analysis. Each task included *Instruction* and *Contact* event-markers. Post-processing defined consistent post-trigger epochs (5 and 10 seconds respectively) to allow inter-individual comparison. These time durations were driven by theoretical conceptualisations of rapid anticipatory fear and a relatively longer disgust reaction, and to exclude any longer habituation experience from being falsely calculated in the averaged value. Separating signals into these theoretically meaningful windows has a drawback of limiting identification of the acceleration and deceleration of signal responses between tasks, that have been theorised to be distinct for anxiety, fear, and disgust (Kreibig, 2010). Therefore, a secondary analysis was conducted that incorporated both *Instruction* and *Contact*, with the intent of capturing potential fluctuations in signals from one emotional state to the next.

Cleaning. Data for all measurements was transferred to SPSS Statistics v.25 software for analysis (IBM, 2017). One case was excluded from all within-session analyses due to

missing data for one ERP session (subsequent $n = 21$). Regarding specific signals, three cases were excluded from heart rate analyses due to anomalous signal features stemming from conflicting environmental signals and imperfect fitting of psychophysiology hardware belt to the participant (heart rate analysis $n = 18$). Where participants reached their upper threshold for subjective anxiety before hierarchy level six (*in vivo* sessions; 2 at *Instruction*, 4 at *Contact*, VR sessions; 1 at *Contact*), missing data was imputed using Expectation Maximisation (Tabachnick & Fidell, 2007). Out of range values and univariate outliers were winsorized. No multivariate outliers were identified. Normality was met, aside from a few instances whereby analysis proceeded due to more cases than dependent variables and equal group sizes. Assumptions were met for all analyses (Hills, 2011; Tabachnick & Fidell, 2007).

Statistical analysis and equivalence testing. Dependent t-tests were used to analyse pre- to post-session data and clinical factors. Within-session data was analysed using two-way Group x Level repeated-measures ANOVAs, with conservative Greenhouse-Geisser corrections under Sphericity violations (Tabachnick & Fidell, 2007). Groups were defined by method of exposure delivery: virtual or traditional (*in vivo*). The Level variable was the exposure hierarchy task levels from one to six. For each measured signal, ANOVAs were conducted on *Instruction* and *Contact* separately, as well as both phases incorporated into the same analysis (see Psychophysiology data extraction).

Heart rate and respiration analyses that identified no significant differences between groups were followed up with equivalence testing. These statistical tests were used to determine whether the non-significant differences in responses could be considered unimportant in scope, within the context of the research and signals (Mara & Cribbie, 2012). Two-one sided *t*-tests were used, in keeping with the paired nature of samples (Cribbie & Arpin-Cribbie, 2009). Traditional ERP is considered the current gold-standard, so equivalency tests examined whether VR was comparable to that benchmark. Critical mean differences were

the standard deviation of average *in vivo* heart and respiration rates. These measures were chosen given that the signals lend themselves to robust, objective levels of equivalence, unlike the subjective data, which meant ranges could be pre-defined according to Cribbie & Arpin-Cribbie (2009) recommendations of definitive, probable, or potential equivalence. From an initial alpha level of .05, a more stringent alpha was set at .01 for these tests, comparable to a Bonferroni adjusted value of approximately .008.

5.3 Results

The sample was aged 18 to 65 with $M(SD) = 32.91(9.84)$, predominantly female (64%), unemployed (50%), living with family (64%), and single (50%), which is representative of typical OCD samples (Karno et al., 1988). Highest education was Year 12 or bachelor's degree (32% of each). Total YBOCS-II score was $M(SD) = 29.41(6.51)$, ranging from 18 to 45. Psychiatric medication dosages were stable in the months preceding participation with 64% of the sample taking at least one psychoactive medication. Most common co-morbid diagnoses were depression and panic disorder (past and current). See Table 8 for further characterisation.

Table 8

OCD Symptom Severity, Psychoactive Medications, and Comorbidities for the Sample

| Demographic Information | Proportion of Sample |
|--|----------------------|
| YBOCS-II Total Score Categorisation | |
| Mild | 5% |
| Moderate | 45% |
| Severe | 45% |
| Very Severe | 5% |
| Psychoactive Medication Classes (current)* | |
| Selective Serotonin Reuptake Inhibitors | 41% |
| Tricyclic Antidepressants | 14% |
| Benzodiazepines | 10% |
| Atypical Antipsychotics | 5% |
| Anticonvulsants | 5% |

Co-morbid Psychiatric Diagnoses (past and current)

| | |
|--------------------------------|-----|
| Major Depressive Disorder | 64% |
| Panic Disorder | 23% |
| Generalised Anxiety Disorder | 18% |
| Post-Traumatic Stress Disorder | 5% |

*Note: Two participants were prescribed multiple psychoactive medications, as such the percentages in this table to do not sum to the above mention of 64% - as this referred to the proportion of the sample taking *some form* of psychoactive medication.

Within-Session SUDs. SUDs significantly increased across the hierarchy levels, with large effect sizes. There were no statistically significant differences attributable to group, nor interaction between group and level in determining SUDs, as shown in Figure 7 (*Instruction*: Group, $F(1, 40) = 1.38, p = .25$, Level, $F(3.51, 140.29) = 14.57, p < .001$, partial $\eta^2 = .27$, Group x Level, $F(3.51, 140.29) = 1.93, p = .12$. *Contact*: Group, $F(1,40) = 1.30, p = .26$, Level, $F(3.40, 136.06) = 17.87, p < .001$, partial $\eta^2 = .31$, Group x Level $F(3.40, 136.06) = .92, p = .44$).

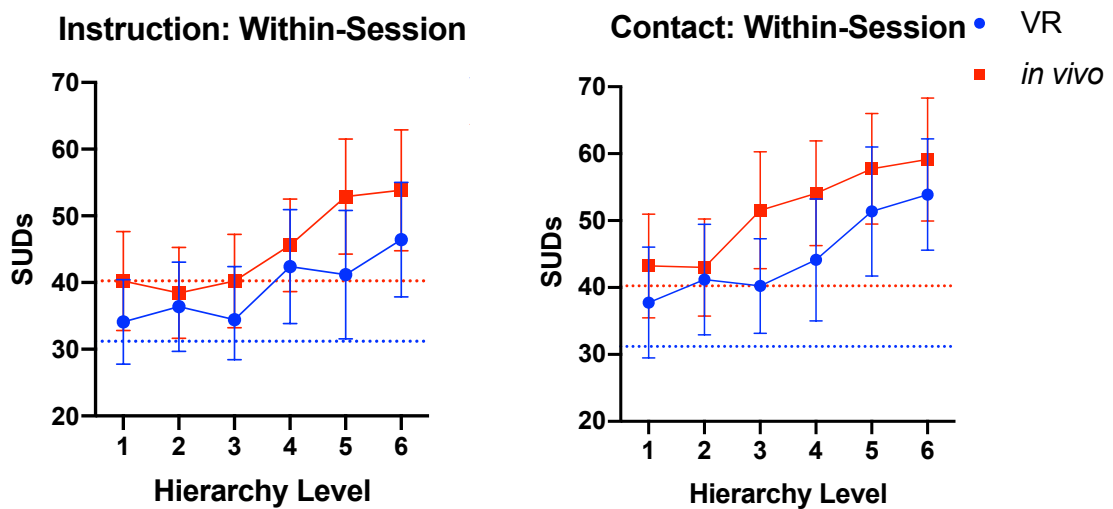


Figure 7. Profiles for SUDs at *Instruction* and *Contact* stages. Plot of Means with 95% Confidence Interval Bars. Trend Lines at Y-axis Represent Reported SUDs Once Within Environment, Before Task Onset.

Pre- and Post-Session Anxiety. Compared with the VR session, pre-session anxiety

was higher before *in vivo* exposure, $t(20) = 2.74, p = .013$, Cohen's $d = 0.45$ (medium), with a mean difference of 6.03, 95% CI [1.49, 10.98] (see Table 9). No significant differences in anxiety remained between the two exposure modalities after the sessions, $t(20) = 1.53, p = 0.14$.

Table 9

Mean Values for Clinical Variables of both Exposure Methods

| Measure | Virtual <i>M(SD)</i> | Traditional <i>in vivo</i> <i>M(SD)</i> |
|---------------------------------|-------------------------|--|
| Pre-Session Anxiety (STAI-S) | 42.29(13.47) | 48.52(12.82) |
| Post-Session Anxiety (STAI-S) | 43.19(13.15) | 47.71(14.36) |
| Therapeutic Alliance (SRS) | 38.05(2.72) | 36.86(2.99) |
| Engagement and Adherence (PEAS) | 16(2.61) | 14.86(2.94) |

Clinical factors. Engagement and adherence to exposure tasks in the Virtual session was higher, $t(20) = 2.17, p = .042$, Cohen's $d = 0.41$ (medium), with a mean difference of 1.14 between the two conditions, 95% CI of difference [0.04, 2.24]. Therapeutic alliance did not differ across exposure methods, $t(20) = 1.70, p = .11$. See Figure 8.

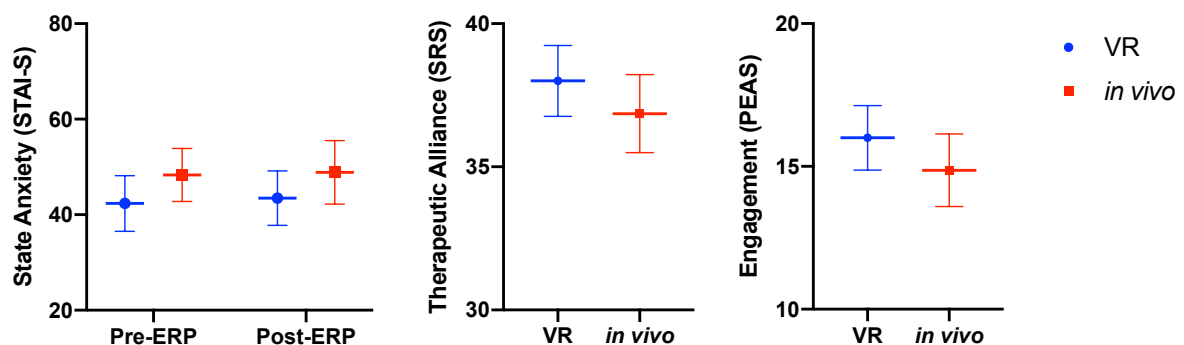


Figure 8. Comparisons of VR to *in vivo* Clinical Variables: Pre- and Post-ERP Anxiety Measured by STAI-S, Therapeutic Alliance Measured by SRS, and Exposure Engagement and

Adherence Measured by PEAS. Graphs Plot the Group Means with 95% Confidence Interval Error Bars.

Psychophysiological response. Across the exposure hierarchy levels, there were no significant increases in heart rate (*Instruction*: $F(2.98, 101.37) = 1.25, p = .30$, *Contact*: $F(2.96, 100.50) = .99, p = .40$) nor respiration rate (*Instruction*: $F(4.15, 165.95) = 2.22, p = .067$, *Contact*: $F(1, 40) = .10, p = .75$).

Heart rate at both phases, and respiration at *Contact*, also did not differ significantly between exposure methods, and no interaction effect was evident. Heart Rate *Instruction*: Group, $F(1, 34) = .54, p = .47$, Group x Level, $F(2.98, 101.37) = 1.04, p = .38$; *Contact*: Group, $F(1, 34) = .38, p = .54$, Group x Level, $F(2.96, 100.50) = .66, p = .58$. Respiration *Contact*: Group, $F(1, 40) = .10, p = .75$, Level, $F(4.37, 174.62) = 1.51, p = .19$, Group x Level, $F(4.37, 174.62) = .48, p = .77$. Equivalence testing for heart and respiration rate at each level met criteria for probable to definitive equivalence of the VR to *in vivo* standard.

A significant interaction effect and group differences were evident for respiration rate at the *Instruction* phases, *Instruction*: Group, $F(1, 40) = 6.01, p = .019$, partial $\eta^2 = .13$ (medium), Group x Level, $F(4.15, 165.95) = 2.64, p = .034$, partial $\eta^2 = .06$ (small to medium). Profiles displayed in Figure 9 exemplify the nature of this difference.

For each of the psychophysiological signals, a combined analysis of both *Instruction* and *Contact* was utilised to capture the change from one event to another. This was to explore potential accelerations and decelerations of signals across fear and disgust (for further information see earlier section: Statistical analysis and equivalence testing). For respiration, there was an interaction between group and level (Group, $F(1, 40) = 2.86, p = .099$, Level, $F(11, 40) = 1.71, p = .069$, Group x Level, $F(11, 40) = 2.00, p = .027$, partial $\eta^2 = .048$ (small to medium)) but this was not evident for heart rate (Group, $F(1, 34) = 0.47, p = .50$, Level, $F(5.48, 186.43) = 1.47, p = .20$, Group x Level, $F(5.48, 186.43) = 0.74, p = .61$), see Figure 9.

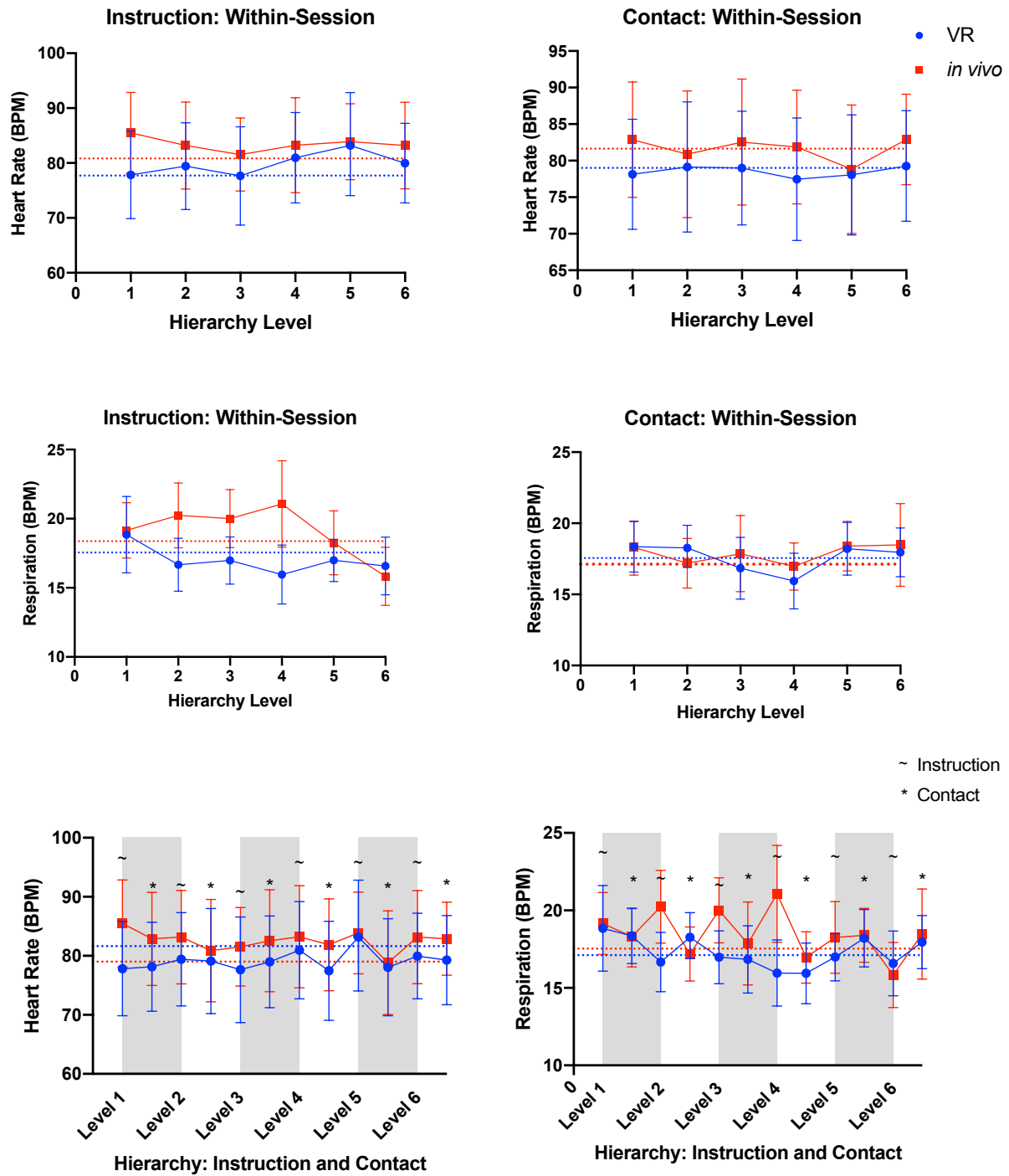


Figure 9. Heart (Beats Per Minute) and Respiration Rates (Breaths Per Minute) Responses During *Instruction* and *Contact* Phases across the Six Levels of the Hierarchy. 95% Confidence Intervals Presented as Bars. The Y-axis Dashed Plot Line Indicates the Average Baseline Level of Physiological Arousal that was Obtained when Participants First Entered the Environment Before ERP Commenced.

5.4 Discussion

For individuals with moderate-severe OCD, Virtual and Traditional *in vivo* exposure sessions resulted in comparable symptom provocation and clinical indicators. Self-reported anxiety increased across the exposure hierarchy for both exposure methods. Psychophysiological signals were also comparable; however, in neither method of exposure did they increase across levels. While pre-session anxiety was higher before *in vivo* ERP, this did not remain at post-session. Virtual exposure was advantageous for participant engagement and adherence to exposure tasks, and the therapeutic alliance was not adversely affected in VR. These findings provide evidence in support of VR as an exposure modality that can enhance participant engagement and elicit relevant anxiety symptoms while maintaining the therapeutic relationship.

For both exposure methods, the increase of SUDs across hierarchy levels indicates that the subjective experiences of distress from anxiety-related fear and disgust were comparable. The higher pre-session anxiety for Traditional suggests that participants may have expected *in vivo* to be more anxiety-provoking than virtual. On the basis of this finding, VR may offer a more acceptable ERP method for patients who would find *in vivo* unacceptably anxiety provoking pre-session, thereby overcoming traditional refusal and drop-out rates. Interestingly, this state anxiety disparity did not endure at post-session. Given that subjective distress heightened for both within-sessions, it may be that the subjective experiences of Virtual and *in vivo* were more alike than expected, explaining this absence of a difference at post-session. Taken together, our findings suggest that subjective distress can be heightened in VR exposure to a comparable degree to Traditional *in vivo*, consistent with the central tenets of ERP (Foa & Kozak, 1986). These results are consistent with previous findings that VR-based ERP can elicit relevant symptoms, suggesting utility for anxiety assessment and treatment purposes (Inozu et al., 2020; Kim et al., 2008; Kim et al., 2012; Laforest et al., 2016; Van Bennekom et al., 2017).

Contaminated VR environments have elicited anxiety, evidenced by measures such as increased STAI and heart rate, in people who have heightened fears of contamination but do not meet diagnostic criteria (Inozu et al., 2020) and people with OCD, to a greater degree than individuals without such concerns (Laforest, Bouchard, Crétu, et al., 2016). Our study shows not only that VR can elicit anxiety, but that the degree of anxiety elicited is consistent with the best-practice standard traditional therapy, providing considerable supportive evidence for VR implementation.

Therapeutic alliance showing no difference across groups is a clinically meaningful finding, consistent with previous speculation that VR technology could maintain rather than inhibit the therapeutic relationship by acting as a common ground between client and clinician (Coyle et al., 2007; Riva, 2005; Riva et al., 2002; Wrzesien et al., 2015). Although empirical studies that have compared VR exposure-based therapy to the traditional therapeutic alliance remain relatively limited, it appears there are no differences in contexts with and without technology for phobia treatment (Wrzesien et al., 2013) and that alliance can continue to be positively related to VR exposure-based therapy outcome in some disorders (Meyerbröcker & Emmelkamp, 2008).

Adherence and engagement in exposure tasks was higher in the virtual session than *in vivo*. This is particularly notable finding in OCD where there can be low levels of engagement and high no-show rates. The PEAS outcome measure represents the percentage of tasks attempted, the degree of engagement, and percentage of urges to ritualise successfully resisted. Additionally, when considering engagement from a technology design perspective, there were no instances of refusal due to the equipment (e.g., fear of contamination from VR handheld controllers). No simulator-sickness occurred, which may in part be accounted for by the ambulant technologies used that minimised the experience of sensorimotor discrepancy. Informal feedback from the participants in this study suggested that the novelty and nature (i.e.

safety) of VR heightened their likelihood of engagement in therapeutic processes. Further qualitative research may assist to explain these experiences and perspectives.

The psychophysiology data provides another valuable insight into participants experiences within sessions and are consistent with the self-report data showing an absence of significant differences between exposure methods. The only exception was a significant interaction (and group) effect at the fear-related stage of *Instruction* that emerged for respiration. This was reflected in the *Instruction* profile graph as higher breathing rate at the anticipation of the middle level exposure tasks for Traditional *in vivo* exposures, which was not evident in *Contact*. Aside from this, heart rate and respiration (*Contact* only) were comparable across groups. The absence of change in heart rate across an exposure hierarchy co-occurring with subjective anxiety and respiration changes is consistent with previous VR exposure-based therapy studies (Freire et al., 2010; Moore et al., 2002; Notzon et al., 2015; Wiederhold et al., 2002; Wilhelm et al., 2005). It is possible that heart rate differences may only emerge in the highest anxiety-provocation levels of virtual environments (Mühlberger et al., 2007). When considered more broadly, the increase in self-reported anxiety across a hierarchy without associated psychophysiology changes is an established clinical phenomenon, despite clients commonly reporting symptoms in physiological terms, such as racing heart or sweaty palms (Grossman et al., 2001; Mauss et al., 2005; Wilhelm et al., 2001). This incoherence has practical implications, such as casting doubt upon the ability of biofeedback systems to modify psychophysiological arousal in these patient groups (Henriques et al., 2011). For the purposes of our research questions, the key finding remains that the pattern of both the subjective and objective data obtained followed the same patterns in both VR and *in vivo* exposures.

5.4.1 Strengths, Limitations, and Future Directions

This is the first study to directly compare subjective, objective, and therapeutic responses to VR, in a sample of people diagnosed with OCD, to the existing benchmark of *in vivo* ERP.

These findings directly advance the existing literature by utilising a clinical sample, theoretically meaningful heart and respiration rate responses, measurement of clinical factors, and crucially by making comparisons to the current gold-standard in psychological treatment techniques. Acquiring high quality psychophysiology signals in a dynamic ambulatory environment is a considerable challenge. The current paradigm has successfully navigated this task, with mean heart rate and respiration data consistent with those previously reported in people with high anxiety (Dishman et al., 2000; Donahue et al., 2009; Freire et al., 2010; Laforest, Bouchard, Crétu, et al., 2016).

Future studies should investigate VR versus traditional ERP across multiple sessions to better understand longer-term client therapeutic outcomes and clinician perspectives. From a technology perspective, advances in VR will offer new opportunities to be tested, such as realistic virtual clinicians embedded in environments. Additionally, the breadth of empirical measurements should be expanded, including psychophysiology as objective evidence for anxiety arousal and extinction processes (Diemer et al., 2014), particularly as research-grade technologies become integrated with VR systems. Challenges for VR-based ERP in OCD will include managing cognitive and behavioural processes (e.g. neutralising, safety, “It’s just a game/simulation”) which may counteract presence and immersion.

5.5 Conclusion

By demonstrating responses that were consistent with the existing first line in therapeutic treatment for OCD, we provide validation evidence for this novel VR system. Traditional (*in vivo*) and virtual sessions elicited comparable increasing levels of anxiety across an exposure hierarchy, thereby meeting this core foundational requirement for ERP processes. Heightened patient engagement and lower pre-session anxiety support the notion that virtual exposures offer a more acceptable modality for ERP, potentially overcoming the current challenges of refusal rates in traditional therapy. Evidencing that the therapeutic alliance can be maintained

in VR is a unique and clinically meaningful contribution to the literature, suggesting technology may not pose a barrier when engagement is factored into design. Collectively, this multifaceted evidence highlights the exciting abilities for VR technology in OCD research and treatment applications, to advance the current best-practices in a novel and engaging manner.

CHAPTER SIX: DISCUSSION

To date, the realised promise of VR for psychology had not matched the hype, in part, due to a lack of methodological publications curtailing progress. The practical framework provided in Chapter Three fills this gap, providing detailed considerations and recommendations for clinicians and researchers to develop specialised VR-based ERP systems that improve upon existing treatment modalities. It is hoped that this will in turn increase the pace of scientific development relating to VR in psychology and highlight the importance of incorporating end-user engagement into clearly planned design procedures.

The development and validation process of this novel, immersive and customisable VR toolset, has demonstrated the importance of this work for the future treatment of OCD and related disorders. The VR-based ERP OCD field has been directly advanced by my work through the provision of multifaceted validity evidence when compared to the best-practice traditional psychotherapeutic benchmark. Findings presented in Chapter Five identified that VR exposures offer a clinically meaningful degree of equivalent emotional arousal and therapeutic alliance, with enhanced client engagement in exposure. This evidence of arousal and engagement positions VR-based ERP as a clinically acceptable tool to supplement ERP therapy for OCD.

My work has established the first immersive OCD VR-based ERP system that has been validated by comparing engagement and responses of a clinical sample to the gold-standard of *in vivo* ERP sessions. This is the first VR system to enable real-time customisable tasks and variable contamination to achieve processes consistent with standard ERP. Furthermore, this is also the first study to contrast psychophysiological responses in VR to those obtained *in vivo* with temporal and event-related specificity, as well as to provide evidence of comparable therapeutic alliance and greater exposure engagement in VR. Taken collectively, these findings provide robust, multifaceted evidence of the equivalence of VR-based ERP to the existing best-

practice of traditional exposure for OCD. Given ERP is the current first-line psychological treatment for OCD, the comparability of VR lends considerable credibility to its efficacy in this population. Not only can VR elicit disorder specific emotions; it can do so to an equivalent degree to existing best-practice.

The combination of customisable exposures, synchronised in real time through objective physiological data, and supported by quantified measures of therapeutic engagement, are novel in the provision of comprehensive theoretical and clinical evidence. These were yet to be addressed in VR exposure-based therapy, particularly the OCD literature. The validation results presented in Chapter Five both support and extend upon the growing area of literature that indicates VR exposure-based therapy is an effective technique for anxiety and stress disorders (Botella et al., 2007; Carl et al., 2019; Powers & Emmelkamp, 2008; Rizzo et al., 2014; Rothbaum et al., 2006; Wallach et al., 2009).

I will now position the central findings of my work into the context of the broader field of literature. In particular, I will discuss key learnings relating to VR hardware selection and software design, as well as research and clinical efficacy factors for VR-based ERP design purposes. I also examine the key limitations of the current work and explore recommendations for both future research, and ethical and clinical practice. I conclude this chapter by highlighting the exciting potentials for VR in psychological research and clinical implementation that have been uncovered during my research.

6.1 Key Findings and Implications

6.1.1 Advantages of Utilising Immersive VR Hardware

Traditional *in vivo* ERP modalities are either realistic but poorly controlled, such as visiting a public bathroom, or carefully graded but removed from everyday experiences, such as touching toilet paper in a clinician's office. Respectively, these limitations relate to patient reluctance to engage and insufficient symptom provocation. These are direct barriers to the

arousal and extinction processes that theoretically underpin effective ERP. In contrast, VR-based ERP offers the potential to exert fine control over the environment, and the degree of exposure, in a manner that can improve the relevancy of sessions and translate to patients' daily experiences. Careful control over exposures also permits precisely synchronised measurement of patient responses in both practical and research settings.

However, to this point the systems have not been in place to tailor VR experiences to fit a client's specific profile of symptoms, nor immersive enough for users to suspend their disbelief of the environment not being 'real'. This is not to say that these limitations were insurmountable, but rather due to the failure of the research community to match the pace of technological advancement and to capitalise upon opportunities for users to readily immerse themselves and experience convincing presence within the virtual environment.

Previous VR exposure-based therapy system designs in some cases restricted users to viewing a representation of themselves on a screen, similar to watching a movie (Matthews, Maunder, Scanlan, & Kirkby, 2017). The inability for users to experience a first-person perspective of themselves embedded in a virtual environment directly hindered presence. In contamination-based OCD this has been a significant limitation of VR systems, given that the sense of uncleanliness or proximity to contaminants is central to the symptom profile. Therefore, the first-person user perspective and naturalistic handheld controllers in our system appear to sustain the advantages of traditional ERP, allowing the feeling of contamination to be more realistically experienced by the user. It is important that novel approaches to OCD ERP build upon existing optimal treatment practices, rather than reinventing the wheel.

CAVE systems may offer higher visual specifications and immersion for OCD patients (Laforest, Bouchard, Crétu, et al., 2016), as compared to computer screen simulations. Yet projection-based displays are not easily transported for replication and implementation across research and clinical sites. Systems that cannot be used across multiple settings hold two

considerable drawbacks. Firstly, the burden is placed upon the patient to travel to the clinical setting, which reduces service accessibility, especially for people in rural or remote locations. Secondly, it causes challenges in creating a replicated evidence-base of systems across diverse populations. Although the software programs may be relatively easily shared across sites, the resource investment in setting up CAVE hardware across each service is unrealistic relative to the opportunities of portable HMD systems such as ours.

The HTC Vive, with its naturalistic handheld controllers, allowed our system to generate immersive virtual environments that can respond to user-driven manipulation. Furthermore, as the Vive was originally designed by manufacturers to be a consumer grade recreational gaming product, it is both widely available and relatively simple to set up, in a manner that makes it suitable for both professional and home environments. Consultations with the clinic identified that setting up this hardware on site was extremely feasible and acceptable in terms of resource investments. Thereby, selecting this system on the basis of these hardware features reinforces the truly translatable nature of this work, directly from the research laboratory into the clinic. As VR systems become increasingly commonplace, the developed system is also well positioned to be adapted into in-home, self-directed VR-based ERP tasks.

6.1.2 Software: Customisation, Ecological Validity and End-User Design

The development of specialised software is also an important consideration to achieve VR's promised opportunities. While previous systems were limited to a generic contamination environment with a few simple tasks (Belloch et al., 2014; Laforest, Bouchard, Crétu, et al., 2016), our system empowers patients and clinicians or researchers to exert choice and control over the VR-based ERP experience. Collaboratively, users and clinicians can flexibly determine when an exposure task commences and which anxiety-provoking items appear within the environment, as well as manipulate the overall degree of contamination. By tailoring the nature, onset, and duration of exposure tasks, the VR-based ERP experience can be

modified to address each individual's treatment needs in a way that is more relevant to daily experiences than imaginal approaches, thereby increasing both ecological and face validity.

Real-time customisation had not previously been explored, yet it is crucial to the application of clinical practice. Without such ability to enact flexible, dynamic modifications, it would be impossible to create a targeted treatment protocol for patients; consequently, many clinicians would not choose VR-based ERP over traditional approaches. My work evidences that currently available technology can facilitate these foundational ERP requirements. Without the capability to customise exposures for each patient, VR experiences would have limited practical functionality, and therefore perhaps no overall discernible benefit above imaginal ERP. Despite seeming more realistic, perhaps general VR-based ERP systems would only provoke general symptoms, not each patients' unique fear structure. As my research demonstrates, VR-based ERP systems can offer both heightened realism and customisation. From our findings, it is clear that VR can indeed be customised and tailored on an individual basis, and therefore offers a promising new mechanism for ERP.

End-user feedback from clinicians, patients, and key clinical stakeholders was an important component in establishing these software features. Collaborative involvement of clinicians and researchers at the clinic directly facilitated hardware selection, bidirectional knowledge transfer, and decision-making regarding the system's functions. Through early engagement with end-users, our software was specialised to meet a clear clinical need and to be usable from the perspective of implementing clinicians. Patients who were consulted reported high acceptability of the design and identified VR-based ERP would be a useful additional ERP modality, offering advantages beyond existing techniques, particularly for exposures where imaginal techniques would be insufficient to elicit anxiety and where *in vivo* was not practicable or possible. My work highlights the importance of gathering input from patients, clinical staff, and the implementing clinic management, in order to maximise the

likelihood of eventual uptake. An iterative, collaborative design process is most likely to overcome previously identified barriers to clinical uptake, such as clinicians' perceptions of VR system usefulness (Bertrand & Bouchard, 2008). Designing novel VR exposure-based therapy systems should always be guided by the requirements of clinical services to address a clear need, as without these involvements the end goal of clinical translation with sustained engagement would remain unachievable.

6.1.3 Therapeutic Alliance and Clinical Engagement

Clinical engagement indicators, particularly the therapeutic relationship, are important predictors of treatment outcome (Martin et al., 2000). These, however, have not been examined empirically in therapeutic VR use. The validation findings presented in Chapter Five show that the therapeutic alliance between clinician and patient can be preserved in the presence of VR. Previously, minimal reporting of the procedure for therapeutic communication and an absence of quantified measurement of the therapeutic alliance in studies limited the clinical applicability of VR exposure-based therapy findings (Lindner et al., 2017; Repetto et al., 2013). By enabling real-time, naturalistic communication between the participant and researcher in my study, the therapeutic relationship achieved the same quality in VR as *in vivo* sessions, as measured by the SRS. Contrary to concerns that VR may impede therapeutic communication (Rizzo et al., 2003), the present findings show that the alliance can be attained with VR hardware and software in the therapeutic space.

There has also been no prior empirical investigation of the engagement of patients using VR exposure-based therapies. The research evidence of effectiveness had not yet been matched by uptake and translation into clinical settings (Carl et al., 2019). My findings directly contribute to resolving this gap, providing evidence that patients using VR-based ERP may complete more exposure tasks, to an increased quality. Participant engagement and adherence to exposure tasks was significantly higher in the VR sessions, as compared to *in vivo* ERP. As

had been hypothesised (Riva, 2005), the higher scores on the PEAS measurement supports the idea that VR-based ERP enhances engagement. There were no instances of refusal from patients to participate due to hardware or software, reinforcing the acceptability of the VR-based ERP system to OCD patients and suggesting VR may make ERP more approachable for patients. Despite our initial concerns that our participants may have difficulty engaging with shared hardware, due to their primary contamination concerns, it bodes well for VR-based ERP implementation that this was not the case. These results further highlight the value of user engagement in the development of VR systems and that such processes should be a core part of future research into VR-based ERP to ensure its rapid clinical uptake.

The importance of clinical guidance and the therapeutic relationship in generating symptom improvements remain relevant in VR exposure-based therapy settings. As such, VR exposure-based therapy systems should not be treated as entirely stand-alone products, prescribed outside of a clinician-led treatment plan. VR competent clinicians will still be required. Based on my research, clinicians can be reassured that the therapeutic relationship can be maintained in VR-based ERP and that patients are likely to engage better than *in vivo*. These findings will therefore guide clinical decision-making regarding the implementation of VR exposure-based therapies. Future work should determine and report mechanisms that maximise rapport and clinical practices (Yellowlees et al., 2012).

6.1.4 Enhanced Treatment Opportunities for OCD

Elicitation of emotional arousal is a foundation of exposure therapy (Foa & Kozak, 1986), and necessary for clients to learn that anxiety is temporary and tolerable. In doing this, existing maladaptive fear structures can be replaced with new, adaptive, and competing learnings. Until now, it was previously unknown how OCD patient responses to VR-based ERP would correspond with *in vivo* sessions in this regard. As illustrated in Chapter Five, the two exposure methods can elicit comparable OCD related subjective distress to a clinically

meaningful degree. This finding is in keeping with results of VR exposure-based therapy in other psychological disorders (Carl et al., 2019), and preliminary feasibility work in OCD (Belloch et al., 2014; Laforest, Bouchard, Bossé, et al., 2016; Laforest, Bouchard, Crétu, et al., 2016).

Our study is one of very few in the OCD VR-based ERP field to sample from a clinically diagnosed population. Previously, the generalisability of findings was hampered by the reliance upon small (Laforest, Bouchard, Bossé, et al., 2016) and non-clinical samples, such as university students reporting dislike for contamination (Belloch et al., 2014; Inozu et al., 2020; Matthews et al., 2017; Van Bennekom et al., 2017). Our findings are therefore directly applicable to people with OCD, a critical step towards clinical implementation. Without studies such as ours, it would be impossible to suggest that VR-based ERP could be a therapeutic option. Future replication of our findings in a larger sample and in a range of clinical contexts is needed to strengthen the evidence-base for the use of VR-based ERP in OCD.

Direct involvement of patients in the system design was crucial to creating enhanced opportunities for OCD treatment. Improving patients' perception of treatment appropriateness and usefulness is important. Exposure sessions are inherently challenging as patients progressively confront significant fears. Our VR system has been designed to heighten the association between virtual exposures and the day-to-day experiences of patients through customisable, dynamic environments. By matching ERP experiences closely to real fear models, therapeutic gains are more likely to translate back into patients' everyday lives. Higher engagement in virtual exposures as compared to *in vivo*, as explored in the validation study, suggests VR-based ERP may offer a more approachable method of ERP for patients. By increasing patient acceptability of treatment options, current challenges of relatively high refusal and attrition may be addressed. These have clear flow on effects to the high burden of disease and morbidity reported in OCD (Ayuso-Mateos, 2006; Crino et al., 2005; James et al.,

2018; Murray et al., 2004; Ong et al., 2016; Öst et al., 2015; Slade et al., 2009). These findings suggest that VR-based ERP systems continue to offer a novel opportunity to heighten treatment acceptability while maintaining the ability to elicit symptoms.

6.1.5 Research Validation: Multifaceted Evidence of Arousal

In addition to the clinical contributions of my work, the quality and range of empirical evidence for VR exposure-based therapy has been directly improved, particularly due to the comparison to *in vivo* as the current gold standard. Comprehensive quantified assessment of participant emotional arousal in VR-based ERP has now been achieved through integration of subjective and objective measures. It was hypothesised that virtual and *in vivo* exposures would produce comparable participant responses. Analogous profiles were obtained across SUDs and heart rate and respiration measures for the two exposure methods. Thus, VR exposures appear to elicit comparable responses to the existing gold-standard benchmark. This is an important indicator in support of the effectiveness of VR-based ERP for OCD.

Logistical challenges of integrating VR hardware with external add-on research technologies were overcome, as evidenced by our functional implementation of wireless hardware and associated event triggering systems. The incorporation of psychophysiology acquisition capabilities substantially enhances the opportunities for research utilisation. The purpose-built Control Panel software was able to successfully address previous software challenges integrating VR and research systems for signal recording. Specifically, we overcame obstacles in the triggering of dynamic events in unpredictable environments, as well as analysing the non-standardised psychophysiological data generated by such an approach. This required considerable financial, time, and intellectual resource investments, substantially beyond the baseline investment in hardware to set-up a generic VR system.

Achieving this dynamic data in the present work is an advancement upon previous VR studies. Commonly, past work only analysed psychophysiology data by averaging across very

long epochs, such as greater than 20-minutes (Wiederhold et al., 2002), that would encompass a range of distinct emotions averaged into a relatively crude value that lacks temporal or event-related specificity. We developed a much more precise and theoretically relevant approach by carefully defining epochs related to emotional responses during exposures (being the *Instruction* anticipation and *Contact* disgust phases of 5 and 10 seconds respectively). However, there is still an open question regarding how to disentangle the meaning of changes in heart rate responsiveness within exposures, and how these correspond with specific emotional states. In light of our work, it would be recommended that future studies should continue to analyse psychophysiological data in such theoretically defined manners, to improve the ability to draw conclusions about the meaning ascribed to any signal variability.

Our validation findings, as presented in Chapter Five, displayed a trend of heart and respiration rates accelerating and decelerating that emerged between anticipation (*Instruction*) and fear (*Contact*) at higher exposure levels. This is in keeping with the notion that responsiveness in these signals can change relating to specific emotional experiences, such as disgust correlating with faster respiratory inspiration and cardiac deactivation to blood and injury stimuli (Kreibig, 2010). Taken collectively, this suggests improved insights regarding participants' physiological responses may be garnered by evaluating theoretically meaningful epochs in this way. This may be achieved in future work by exploring whether heart rate is consistently unchanged across hierarchies, as was predominantly evident in the present work, or whether signal increases only emerge at the highest levels of anxiety-provocation (Mühlberger et al., 2007).

Patients commonly report physiological changes such as racing heart or sweaty palms when anxious (Grossman et al., 2001; Mauss et al., 2005; Wilhelm et al., 2001). However, our results from the SUDs and psychophysiological measurements suggests that there may be a disconnect between subjective and objective responses across the exposure hierarchy.

Increasing self-reported anxiety in the absence of psychophysiological changes during emotional arousal is an established clinical phenomenon (Grossman et al., 2001; Mauss et al., 2005). This inconsistency has important practical implications, as it casts doubt upon the utility of efforts such as the modification of physiological arousal using biofeedback systems to provide symptom relief in psychological conditions (Henriques et al., 2011).

Conceptually, this discrepancy between subjective and objective measures indicates that there are higher-order unresolved issues regarding how different types of measurements are weighted and considered. In addition to the challenges of processing and interpreting such data which includes noise from measurement error, there is a lack of consensus in the relationship between signals and specific underlying emotions. Perhaps, there is not a direct, predictable relationship between measures like SUDs and heart rate. As such, although objective measurements are favoured by researchers, the connection back to clinical practice may be lost where subjective data is not also considered to be of high importance. If discrepancies exist between these two subjective and objective evidentiary sources, it remains to be seen which is the more robust, and under what circumstances a clinician would select to interpret one over the other. Certainly, the patients self-report of experiences will always be an important indicator to some degree. Until the nature of any direct relationship between psychophysiological signals and clinical symptoms are established, it remains best practice to continue gathering a range of measures to investigate user responses in virtual environments.

6.2 Limitations

While the evidence collected in the current work clearly establishes the benefits, particularly for symptom provocation and engagement, derived from the use of VR for an OCD cohort, there are a number of weaknesses in the study that need to be considered when implementing clinically. While the cohort was demographically consistent with typical OCD groups and considered a sufficiently powered and larger sample size than previous comparable

work (Laforest, Bouchard, Bossé, et al., 2016; Van Bennekom et al., 2017), further validation with increasingly larger sample sizes will be an important step in reinforcing these findings. In doing so, more socio-demographically diverse cohorts can be examined in a range of different clinical settings. This would ensure that the garnered results are truly representative and may be generalised to wider range of contexts. Future work should also develop and validate VR systems to address multiple OCD themes concurrently (e.g. checking, ordering), given the typically high co-occurrences within patients (Mataix-Cols et al., 2005; Ruscio et al., 2010). In doing so, a greater proportion of OCD patients would be included in the research, and longer-term be able to benefit therapeutically from any VR-based ERP systems. Additionally, further validation studies should investigate VR-based versus traditional ERP in between-subjects and longitudinal designs. The present work aimed to evidence the comparability of the two modalities, and given these findings, future work will now be positioned to examine longer-term client therapeutic outcomes and clinician perspectives, including changes in OCD symptoms across multiple sessions.

It is also important to note that the interpretation of psychophysiological data is often limited by measurement imprecision and challenges ascribing a specific emotional state to a precise signal change. For example, when the signal is acquired in ambulatory patients an unavoidably higher degree of noise will be present. Therefore, effective integration of psychophysiological measurement with VR will benefit from ongoing development and validation of robust data acquisition and analysis protocols. Physiological responses have been ascribed to both immersion and emotional arousal in the VR exposure-based therapy literature (Diemer et al., 2014), though as discussed earlier they may be inconsistent with self-reported anxiety (Grossman et al., 2001; Mauss et al., 2005; Wilhelm et al., 2001). Disentangling these relative contributions will require greater understanding of associated signal patterns. Despite these challenges in interpretation, the central research question for the validation study was

whether psychophysiological responses were consistent across the two exposure methods, and in this regard, findings confirmed our hypotheses that they were.

Across both the virtual and *in vivo* exposure sessions, event-marking in the psychophysiology recording for task instructions was achieved by researcher action. Specifically, a button-press that generated the virtual exposure *Instruction* onset also auto-generated an event-marker in the psychophysiology software. This process was consistent with the *in vivo* session, whereby a researcher initiated the button-press to mark the event onset. However, the two exposure paradigms differed in how event-markers were generated for the *Contact* phase; for the *in vivo* session the researcher controlled the event-marker onset with a button press when the participant began making contact with the feared stimuli, whereas for the VR session when the participant made contact by pressing their handheld controller this button press auto-generated the event-marker. These two approaches have implications for precision in the *Contact* phase and may have created an unavoidable difference in onset timing across modalities. However, heart and respiration rates are of a relatively lower frequency compared to other psychophysiology signals, such as electroencephalography (EEG). This means a small onset latency would be unlikely to miss a specific meaningful change, as would be the case in EEG recordings. Given this lower frequency, by defining epochs to be 5 to 10 seconds we aimed to collect a sufficient duration to gather meaningful data regarding signal changes. We further mitigated this potential limitation by conducting manual data cleaning procedures to review the epochs and ensure there were no circumstances of event-markers missing an acute acceleration or deceleration.

Designing hierarchies on the basis of SUDs is a standard process in ERP (Abramowitz, 1996). However, the potential for a mismatch between the patient's self-predicted and actual provoked anxiety in hierarchies is an unavoidable practical limitation. Patients may expect a task to elicit relatively low anxiety when designing a hierarchy but then may experience a much

greater increase in SUDs once in the session. This could exert undue influence on exposure method group averages for task levels. While unexpected variability of anxiety in a therapeutic setting can aid the transfer of treatment learnings back to an unpredictable real-world, in research settings this mismatch can complicate interpretation of the pattern of responses. The present study minimised this impact by utilising a repeated-measures design, matching the tasks and hierarchy across exposure methods, and focusing on the comparability of virtual to *in vivo* exposure.

Replicated research that uses the same VR exposure-based therapy systems across studies is limited, in both the present study and the broader literature. While the general evidentiary basis for VR exposure-based therapy has been growing, hardware and software approaches are fragmented. These issues are heightened by the rapidly evolving nature of the underlying technologies and differences in VR environments and protocols, which complicates the process of drawing comparisons and conclusions across studies. Given our work focused on the development and validation of a novel system, we are not positioned to rectify this broader challenge in the literature. Each VR exposure-based therapy system will require independent validation, then expanding efficacy evaluation across sites. In the present work, by developing a system that incorporated greater opportunities for standardisation and utility across settings, it is hoped that these protocols will be useful for future work. Individual VR exposure-based therapy systems will require replicated empirical testing and the generation of supporting information, such as normative data sets (Wiener et al., 2020). This further highlights the value of methodological publications, such as that presented within this thesis, as well as replicated empirical testing of systems across diverse locations and patient groups, as important areas for ongoing work.

6.3 Future Research Recommendations

6.3.1 Virtual Humans

Future improvements in the realism of virtual humans will create opportunities to design and measure user responses to virtual interactions. As VR advances, making this step will be of significant importance, given the centrality of human exchanges to many psychological disorders. If this is realised, there is the potential for a clinician and patient to realistically share the virtual environment, which could enhance the clinician's ability to responsively manage patient treatment and optimise the therapeutic relationship, or more simply to just increase immersion, and heighten ecological validity. However, any such applications must ensure that the representation of the clinician does not invoke a sensation of dissonance within the virtual environment that could cause immersion breaks. This would be particularly relevant when the clinician is known to the patient prior to the VR exposure-based therapy immersion.

Until shared VR sessions between clinician and patient are empirically evidenced to be efficacious and believable to the users, there is also scope for researching the optimal manner of external-to-internal communication. Optimising the therapeutic relationship may vary on a disorder-by-disorder or patient-by-patient basis. Best practices for managing the therapeutic relationship will require wide ranging comparisons, including but not limited to, technologies that can facilitate communication, such as microphone-to-headphone features, virtual clinicians, or a clinician avatar conveying messages from a real-world clinician. Of particular focus should be the ability to implement spontaneous and unpredictable human interactions, as doing so is important to truly achieving realistic immersion, and as such must be empirically tested.

Future research will also be able to capitalise upon improved virtual representations of the self, such as customised user bodies in the virtual space. The ability for users to see their

virtual selves in the environment may heighten presence. This may include looking down to their own virtual legs, seeing their hands move, and observing their reflected actions in mirrored surfaces. In relation to the present context of OCD, this should encompass the experience of contamination spreading onto the body, in a manner that would allow perceived transference back to the real-world. In order for users to cognitively accept such virtual representations of the self, VR exposure-based systems would need to include the ability to select features such as body shape, skin tone, and any distinguishing physical attributes. Inadequate matching may counterproductively generate rejection and detract from, rather than enhance, the sense of presence and the suspension of disbelief. Subsequent research will need to compare participant responses to these variable options for virtual humans in order to determine the optimal combinations of solutions.

6.3.2 Ecological Validity

Enhancing ecological validity will require the development of tools that enable even greater variability in the controlled modification of virtual environments than is currently available. The ability to customise virtual environments to disorder level symptoms and client needs in real time would be anticipated to improve immersion and clinical relevance. This may not require a completely custom-built environment for each patient, but rather the ability to embed features and markers in a non-specific environment that can heighten immersion and improve applicability for each person's treatment needs. Making such changes is important, as not all individual patients can have their symptoms provoked in a generic environment. All patients will require some degree of customisation to their symptom profile. As an example, a patient with OCD contamination concerns may have specific symptom drivers, requiring a bespoke solution with variability in the type of contaminant that provokes anxiety, such as HIV but not dirt and grime, and the potential to change environments and people in the VR-based ERP scenario, such as representations of some family members. Environmental modifications

and customisation were explored in Chapters Three and Four and should be expanded to be a standard feature of VR exposure-based therapy systems across other psychological disorders. It is important to note that although these features are crucial, they require considerable time and financial resource investments, which may make them out of reach for small clinics or independent researchers. As such, it is likely that larger institutions will be best positioned to develop and share systems.

The ability to replicate the outside world with these customisable VR features in a clinician's office must be time efficient within the confines of a psychological session; user friendly for clinicians and patients; and optimise the potentially limitless nature of virtual stimuli. It would be possible for a 'virtual library' of environments to be created that clinicians could independently adapt, without relying upon software developers. This could leverage existing frameworks, like the Unity Asset Store, which sells objects that can be embedded within virtual environments. In doing so, specific stimuli could be added to environments on a patient-by-patient basis. Augmenting the simulation with audio stimuli, in a similar fashion to spoken narratives used in imaginal exposure, would allow for an optimal combination of exposure opportunities, building upon the diversity offered by traditional approaches. For OCD populations, this could include spoken recordings from people familiar to the patient, or feared phrases and terms that would allow for carefully targeted cue exposures for a patient's symptoms profiles.

Of course, increasing the specificity of the virtual scenario will require additional resources, relative to a more generic approach. By probing the clinical value of environmental specificity, future studies can elucidate the worth of this increased realism for users, relative to imaginal techniques. Future work should continue to scientifically scrutinise advancements in VR capabilities to evidence validity, reliability, and usability of interfaces, while taking the required resources into account.

6.3.3 Improved Treatment Opportunities

While certain other disorders have shown that treatment gains across VR exposure-based therapy sessions are maintained when transferred back to the real-world (Morina et al., 2015; Oprea et al., 2012), further work is required to show if this too holds for patients with OCD, and for the VR-based ERP system developed in the current thesis. Future VR exposure-based therapy research treatment protocols should be designed to assess predictors of therapeutic response, and the frequency, duration, and number of sessions that will be required to generate clinically meaningful improvements. Establishing these VR exposure-based therapy protocols will also require robust tools to quantitatively measure immersion across various clinical populations. This will be necessary to determine and subsequently predict the time taken to reach a sufficient degree of immersion for treatment purposes. Responses to VR exposure-based therapy should be compared to existing best practices, and attention directed to whether VR exposure-based therapy offers any advantages regarding pace of symptom improvements, follow-up outcomes, or patient engagement. If human to human therapy is an option, VR proficient clinicians should still continue to weigh up the benefits for each client above existing best practices (Kellmeyer et al., 2019), and examine where VR is best placed in a stepped care approach.

Immersion breaking in VR exposure-based therapy occurs when the user's suspension of disbelief is lost. This can result from external factors, such as hearing a police siren in the real-world that provides a jolting reminder of the external world while within a virtual environment. Internal factors may also cause immersion breaks, and there may be unique characteristics of the OCD patient cohort that must be accounted for in light of this possibility. Cognitive rationalising through neutralising and other mental ritualising acts may be of particular concern, in which thoughts like *'It's just a simulation and not real'* may undermine the immersion, engagement, and the therapeutic processes. However, there is also the potential

that general cognitive and behavioural features of OCD could be targeted in parallel within the virtual environment, such as addressing intolerance of uncertainty and perfectionism, to add an increased layer of symptom provocation and treatment opportunities for appropriate patients.

Consideration must also be directed towards heightening the engagement of patients and clinicians with VR exposure-based therapy systems, and how protocols can be designed to advance this goal. Given participants displayed greater initial adherence and engagement in virtual exposures, as compared to the *in vivo* approach, VR-based ERP may provide an avenue for maximising ERP uptake. Our protocols included consultations with the OCD patients about what they perceived to be advantages and drawbacks of a VR-based ERP session, including serving as a ‘middle ground’ between imaginal and *in vivo* during the initial phase of ERP. Clinicians identified their uptake of systems would be maximised by systems that are cost-effective, able to be relocated within and across clinics, and straightforward in their design, providing capabilities that are familiar and intuitive. Gathering further patient-centred information about VR exposure-based therapy should be the focus of qualitative approaches in future research.

Further investigation is also required to understand VR-based ERP’s potential benefits for clients who would otherwise be ambivalent to ERP uptake. Our findings of higher engagement were bolstered by participants reporting that they saw VR holding utility as a ‘bridge’ into treatment uptake. Therefore, patients with severe symptoms or ERP reluctance that precludes initial engagement may find VR-based ERP more acceptable. Research will be required to understand which patients are most likely to respond, and measurement tools to predict the appropriateness of VR-based ERP for their treatment needs. More research will also be required to determine refusal and attrition rates from VR-based ERP in OCD relative to *in vivo*, given VR appears positioned to improve motivation to engage in treatment. Our study encountered no refusals: all scheduled participants attended their session and reported higher

exposure engagement scores in VR. However, our study design is not positioned to comment on the attrition rates and symptom improvements over a therapeutic course of VR-based ERP, which will require multiple ERP session research protocols.

6.4 Future Directions for Ethics and Clinical Practice of VR Exposure-Based Therapy

Potential safety risks exist for users with hardware, such as HMDs, and the virtual environments generated by software. Manufacturer health and safety protocols often outline general risks, such as simulator sickness and immersion after-effects; however, these must be customised to clinical populations (Rizzo et al., 2003). Furthermore, screening tools to identify unique risks for each individual user will be required before widespread VR exposure-based therapy implementation. These areas for future clinical and ethical investigation are explored further throughout the following sections.

6.4.1 Safety Considerations: Hardware and Software

Equipment risks can differ across users. For example, a CAVE system may present a low risk of physical harm for many people due to the projection-based visuals meaning that the user remains able to see their body and the real-world environment while immersed. However, HMDs that are tethered via cables to a computer could pose a falls risk, especially for users with poor gait or balance. Risks will uniquely present at the junction between hardware, software, and each user. In exposure therapy, management of software content risks presents a unique challenge because the provocation of unwanted emotions is a core component of treatment processes (Behr et al., 2005). Tailored assessment tools followed by consent procedures are therefore required to be developed.

Assessments to screen individuals before VR use should enable clinicians to identify symptoms that could impact safety and efficacy. Symptoms such as distorted reality and poor self-awareness may create unique vulnerabilities (Rizzo et al., 2003) that need to be considered to ensure that potential harms do not outweigh any prospective benefits of VR. The ethical use

of VR in a clinic requires evidence demonstrating that such novel approaches offer sufficient benefits above traditional human-to-human clinical practices (Kellmeyer et al., 2019). Determining suitability will involve predicting, assessing, and mitigating risks using reliable, valid tools and management procedures. This will be necessary on a patient-by-patient basis, on the foundations of systemic policies and procedures. Clinicians will also require guidelines to understand and weigh up the relative benefits of VR versus more traditional approaches, in light of the likely risks and benefits for each patient. Publication and dissemination of such guidelines will serve to advance the field with greater legitimacy.

6.4.2 Ethics Relating to Wellbeing, Communication, and Competency

Ethical considerations of patient, clinician, and societal well-being entail a number of professional responsibilities. Technology entering the therapeutic or research space will require new investigations to upholding these ethical standards. Clinician-user communication may be facilitated by the VR technology, including microphone-to-headphone features or clinician avatars that convey messages from an external real-world clinician into the virtual environment. Technology will change the manner that clinical communications and identifiable information are transferred and stored, and in light of this systems will need to be reviewed to ensure privacy and confidentiality (Yellowlees et al., 2012). Individuals are likely to continue to need some degree of human-to-human engagement and support. Professionals will, therefore, need to be upskilled in order to practice competently with appropriate expertise tailored to VR (Rizzo et al., 2003). In keeping with protocols for traditional psychological tools, the general accessibility of VR software will need to be protected to prevent unethical use, for example by people who are not qualified to complete assessments or deliver therapy. Legal and ethical codes of conduct for technology-based interventions should ideally be agile and responsive as hardware, software, and legislation evolve over time (Botella et al., 2009).

Communication between patient and clinician will need to not only be maintained within the exposure immersion, as described in my work, but extended outside strictly within-clinic VR experiences. This includes policies and procedures to support clients who undertake VR immersions external to the clinic. Patients self-directed uses of VR exposure-based therapy are likely to increase in prevalence as systems become more commercially available, affordable, and commonplace in people's homes. In-home use of VR presents unique opportunities, such as therapeutic homework tasks being set in VR, that would require their own evidence-base to be established prior to software dissemination to the public. 'Self-help' style VR therapy may improve engagement and accessibility for sub-clinical groups (Rizzo et al., 2003), as well as increase the frequency of completing therapeutic homework tasks; however, these users will still require support when unexpected challenges arise. In order to support such independent VR therapy, professional risk management procedures will need to be in place, including determining whether or not the clinician can provide real-time remote support while users engage in at-home VR exposure-based therapy. A clear definition of procedures and clinician availability would be vital, combined with realistic expectation management for patients regarding the nature of in-home support and any associated privacy concerns. These risks and support strategies must be incorporated into informed consent procedures at the outset of clinical engagements with VR exposure-based therapy systems.

Clinician's lack of confidence and understanding with VR (Bertrand & Bouchard, 2008) is but one example highlighting that substantial implementation research and action is required if VR is to enter common clinical practice. Examples that may pave the way for implementation include, increasing familiarity with VR through conference presentations and publications in scientific journals (Schwartzman et al., 2012), with particular focus upon development, validation and efficacy studies. Specialised professional development courses would logically follow as an opportunity to provide training to clinicians about VR

functionality and advantages. Furthermore, informal opportunities to translate research into clinical settings should be capitalised upon. This may include embedding researchers into clinics to conduct system set up, perform troubleshooting, and share written protocols. This would provide bidirectional benefits, in that the clinician grows to recognise the advantages of VR in practice, while the researcher may be able to collect important information from patients and clinicians about their experiences with the VR exposure-based therapy technology. Overall, these acceptability considerations highlight the importance of identifying barriers to implementation and building familiarity, to progress from promising research findings into clinical practice with clearly identifiable benefits.

6.5 Concluding Remarks

The expertise garnered from the design and creation of the customised system is now shared with the scientific community as practical considerations and recommendations presented in a development framework. Unlike many previous specialised VR systems, ours utilises truly immersive technology and provides the capability for virtual environments to be customised on a patient-by-patient basis, while synchronised research-grade psychophysiological data is automatically collected. By co-designing with clinicians and incorporating patient feedback in the design process, we have maximised the suitability of the system to address limitations of traditional ERP. Clinical and research settings will benefit from the ability to carefully control graded exposures that can be customised in an individual manner to account for heterogeneous symptom presentations. Looking to the future, such systems are positioned to provide treatments that enhance acceptability for clients and provide self-guided therapy in supplement to clinician-guided, thereby improving accessibility.

Robust validation evidence was provided through comparison to the gold-standard benchmark of *in vivo* exposure sessions, showing multifaceted comparability in subjective and objective measures of arousal across matched exposure hierarchies. Greater engagement and

adherence in VR relative to *in vivo* is an important finding that supports the notion VR offers a more acceptable treatment modality for patients. Outcomes were bolstered by establishing that the therapeutic alliance is maintained even with the presence of technology in the therapeutic space. By exploring the opportunities and challenges of implementing VR from a theoretical, practical, and applied perspective, my work provides evidence for the validity of VR-based ERP for patients with contamination-based OCD.

REFERENCES

- Abelson, J. L., Curtis, G. C., Sagher, O., Albucher, R. C., Harrigan, M., Taylor, S. F., Martis, B., & Giordani, B. (2005). Deep brain stimulation for refractory obsessive-compulsive disorder. *Biological Psychiatry*, 57(5), 510–516.
<https://doi.org/10.1016/j.biopsych.2004.11.042>
- Abramowitz, J. S. (1996). Variants of exposure and response prevention in the treatment of obsessive-compulsive disorder: A meta-analysis. *Behavior Therapy*, 27(4), 583–600.
[https://doi.org/10.1016/S0005-7894\(96\)80045-1](https://doi.org/10.1016/S0005-7894(96)80045-1)
- Abramowitz, J. S. (1997). Effectiveness of psychological and pharmacological treatments for obsessive-compulsive disorder: A quantitative review. *Journal of Consulting and Clinical Psychology*, 65(1), 44–52. <https://doi.org/10.1037/0022-006X.65.1.44>
- Abramowitz, J. S. (2006). The psychological treatment of obsessive-compulsive disorder. *Canadian Journal of Psychiatry*, 51(7), 407–416.
<https://doi.org/10.1383/psyt.3.6.68.38210>
- Abramowitz, J. S., Brigidi, B. D., & Roche, K. R. (2001). Cognitive-Behavioral Therapy for Obsessive-Compulsive Disorder: A Review of the Treatment Literature. *Research on Social Work Practice*, 11(3), 357–372. <https://doi.org/10.1177/104973150101100305>
- Abramowitz, J. S., Franklin, M. E., Zoellner, L. A., & Dibernardo, C. L. (2002). Treatment compliance and outcome in obsessive-compulsive disorder. *Behavior Modification*, 26(4), 447–463. <https://doi.org/10.1177/0145445502026004001>
- Abramowitz, J. S., & Larsen, K. E. (2006). Exposure Therapy for Obsessive-Compulsive Disorder. In D. C. S. Richard & D. Lauterbach (Eds.), *Handbook of Exposure Therapies* (pp. 185–208). Elsevier Science & Technology. <https://doi.org/10.1037/10673-010>
- Ackerman, D. L., & Greenland, S. (2002). Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder. *Journal of Clinical Psychopharmacology*,

- 22(3), 309–317. <https://doi.org/10.1097/00004714-200206000-00012>
- Adamovich, S. V., Fluet, G. G., Tunik, E., & Merians, A. S. (2009). Sensorimotor training in virtual reality: A review. *NeuroRehabilitation*, 25(1), 29–44. <https://doi.org/10.3233/NRE-2009-0497>
- Alonso, P., Pujol, J., Cardoner, N., Benlloch, L., Deus, J., Menchón, J. M., Capdevila, A., & Vallejo, J. (2001). Right prefrontal repetitive transcranial magnetic stimulation in obsessive-compulsive disorder: a double-blind, placebo-controlled study. *The American Journal of Psychiatry*, 158(7), 1143–1145. <https://doi.org/10.1176/appi.ajp.158.7.1143>
- American Psychiatric Association. (2007). Practice guideline for the treatment of patients with obsessive-compulsive disorder. *American Psychiatric Association*. http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm
- American Psychiatric Association. (2013a). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Author.
- American Psychiatric Association. (2013b). Guideline watch for the practice guideline for the treatment of patients with obsessive-compulsive disorder. *American Psychiatric Association*. <http://psychiatryonline.org/content.aspx?bookid=28§ionid=40634994>
- Amin, A. M., Tong, X., Gromala, D., & Shaw, C. D. (2017). Cardboard Mobile Virtual Reality as an Approach for Pain Distraction in Clinical Settings: Comparison, Exploration and Evaluation with Oculus Rift. *Proceedings of the 2017 CHI Conference Extended Abstracts on Human Factors in Computing Systems*, 2345–2351. <https://doi.org/10.1145/3027063.3053234>
- Anderson, P. L., Price, M., Edwards, S. M., Obasaju, M. A., Schmertz, S. K., Zimand, E., & Calamaras, M. R. (2013). Virtual reality exposure therapy for social anxiety disorder: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, 81(5), 751–760. <https://doi.org/10.1037/a0033559>

- Andreassi, J. (1995). *Psychophysiology: Human Behavior and Physiological Response* (3rd ed.). Lawrence Erlbaum Associates Publishers.
- Anholt, G. E., Aderka, I. M., Balkom, A. J. L. M. Van, Smit, J. H., & Schruers, K. (2014). Age of onset in obsessive-compulsive disorder: admixture analysis with a large sample. *Psychological Medicine*, 44(1), 185–194. <https://doi.org/10.1017/S0033291713000470>
- Ayuso-Mateos, J. L. (2006). Global burden of obsessive-compulsive disorder in the year 2000. *World Health Organisation*, 1–10. https://www.who.int/healthinfo/statistics/bod_obsessivecompulsive.pdf
- Bailey, J. J., Berson, A. S., Garson, A., Horan, L. G., Macfarlane, P. W., Mortara, D. W., & Zywiets, C. (1990). Recommendations for standardization and specifications in automated electrocardiography: Bandwidth and digital signal processing. *Circulation*, 81(2), 730–739. <https://doi.org/10.1161/01.CIR.81.2.730>
- Bandelow, B., Zohar, J., Hollander, E., Kasper, S., Möller, H. J., Allgulander, C., Ayuso-Gutierrez, J., Baldwin, D. S., Bunevicius, R., Cassano, G., Fineberg, N., Gabriels, L., Hindmarch, I., Kaiya, H., Klein, D. F., Lader, M., Lecrubier, Y., Lépine, J. P., Liebowitz, M. R., ... Vega, J. (2008). World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders - First revision. *World Journal of Biological Psychiatry*, 9(4), 248–312. <https://doi.org/10.1080/15622970802465807>
- Barnes, L. L. B., Harp, D., & Jung, W. S. (2002). Reliability generalization of scores on the Spielberger state-trait anxiety inventory. *Educational and Psychological Measurement*, 62(4), 603–618. <https://doi.org/10.1177/0013164402062004005>
- Barnett, A. G., van der Pols, J. C., & Dobson, A. J. (2005). Regression to the mean: What it is and how to deal with it. *International Journal of Epidemiology*, 34(1), 215–220. <https://doi.org/10.1093/ije/dyh299>

- Bayliss, J. D., & Ballard, D. H. (1998). *The Effects of Eye Tracking in a VR Helmet on EEG Recordings*. <http://hdl.handle.net/1802/409>
- Behr, K.-M., Nosper, A., Klimmt, C., & Hartmann, T. (2005). Some practical considerations of ethical issues in VR research. *Presence*, 14(6), 668–676. <https://doi.org/https://doi.org/10.1162/105474605775196535>
- Belloch, A., Cabedo, E., Carrió, C., Lozano-Quilis, J. A., Gil-Gómez, J. A., & Gil-Gómez, H. (2014). Virtual reality exposure for OCD: Is it feasible? *Revista de Psicopatología y Psicología Clínica*, 19(1), 37. <https://doi.org/10.5944/rppc.vol.19.num.1.2014.12981>
- Bertrand, M., & Bouchard, S. (2008). Applying the technology acceptance model to VR with people who are favorable to its use. *Journal of Cyber Therapy and Rehabilitation*, 1(2), 200–207. https://www.researchgate.net/publication/252084357_Applying_the_technology_acceptance_model_to_VR_with_people_who_are_favorable_to_its_use
- Bohil, C. J., Alicea, B., & Biocca, F. A. (2011). Virtual reality in neuroscience research and therapy. *Nature Reviews Neuroscience*, 12(12). <https://doi.org/10.1038/nrn3122>
- Botella, C., Garcia-Palacios, A., Baños, R. M., & Valencia, U. De. (2009). Cybertherapy: Advantages, Limitations, and Ethical Issues. *PsychNology Journal*, 7(1), 77–100. <http://repositori.uji.es/xmlui/handle/10234/97162>
- Botella, C., Gracia-Palacios, A., Villa, H., Baños, R. M., Quero, S., Alcañiz, M., & Riva, G. (2007). Virtual reality exposure in the treatment of panic disorder and agoraphobia: A controlled study. *Clinical Psychology and Psychotherapy*, 14(3), 164–175. <https://doi.org/10.1002/cpp.524>
- Bouchard, S., Dumoulin, S., Robillard, G., Guitard, T., Klinger, E., Forget, H., Loranger, C., & Roucaut, F. X. (2017). Virtual reality compared with in vivo exposure in the treatment of social anxiety disorder: A three-arm randomised controlled trial. *British Journal of*

- Psychiatry*, 210(4), 276–283. <https://doi.org/10.1192/bjp.bp.116.184234>
- Bradford, N. K., Caffery, L. J., & Smith, A. C. (2016). Telehealth services in rural and remote Australia: A systematic review of models of care and factors influencing success and sustainability. *Rural and Remote Health*, 16(4), 1–23.
- Brauer, L., Lewin, A., & Storch, E. (2011). A Review of Psychotherapy for Obsessive-Compulsive Disorder. *Mind & Brain*, 2(1), 38–44. <https://doi.org/10.1007/s11920-009-0043-8>
- Brinkman, W. P., Mast, C. Van Der, Sandino, G., Gunawan, L. T., & Emmelkamp, P. M. G. (2010). The therapist user interface of a virtual reality exposure therapy system in the treatment of fear of flying. *Interacting with Computers*, 22(4), 299–310. <https://doi.org/10.1016/j.intcom.2010.03.005>
- Buendía-Fuentes, F., Arnau-Vives, M. A., Arnau-Vives, A., Jiménez-Jiménez, Y., Rueda-Soriano, J., Zorio-Grima, E., Osa-Sáez, A., Martínez-Dolz, L. V., Almenar-Bonet, L., & Palencia-Pérez, M. A. (2012). High-Bandpass Filters in Electrocardiography: Source of Error in the Interpretation of the ST Segment. *ISRN Cardiology*, 2012, 1–10. <https://doi.org/10.5402/2012/706217>
- Calamari, J. E., Wiegartz, P. S., & Janeck, A. S. (1999). Obsessive-compulsive disorder subgroups: A symptom-based clustering approach. *Behaviour Research and Therapy*, 37(2), 113–125. [https://doi.org/10.1016/S0005-7967\(98\)00135-1](https://doi.org/10.1016/S0005-7967(98)00135-1)
- Carl, E., Stein, A. T., Levihn-Coon, A., Pogue, J. R., Rothbaum, B., Emmelkamp, P., Asmundson, G. J. G., Carlbring, P., & Powers, M. B. (2019). Virtual reality exposure therapy for anxiety and related disorders: A meta-analysis of randomized controlled trials. *Journal of Anxiety Disorders*, 61, 27–36. <https://doi.org/10.1016/j.janxdis.2018.08.003>
- Carmin, C., Wiegartz, P. S., & Wu, K. D. (2005). Self-directed Exposure in the Treatment of OCD. In J. S. Abramowitz & A. Houts (Eds.), *Concepts and controversies in obsessive-*

- compulsive disorder* (1st ed., pp. 333–358). Springer-Verlag New York.
<https://doi.org/10.1007/b101087>
- Carr, A. T. (1974). Compulsive Neurosis: A Review of the Literature. *Psychological Bulletin*, 81(5), 311–318. <https://doi.org/https://doi.org/10.1037/h0036473>
- Cherniack, E. P. (2011). Not just fun and games: applications of virtual reality in the identification and rehabilitation of cognitive disorders of the elderly. *Disability and Rehabilitation: Assistive Technology*, 6(4), 283–289.
<https://doi.org/10.3109/17483107.2010.542570>
- Chessa, M., Maiello, G., Borsari, A., & Bex, P. J. (2019). The Perceptual Quality of the Oculus Rift for Immersive Virtual Reality. *Human-Computer Interaction*, 34(1), 51–82.
<https://doi.org/10.1080/07370024.2016.1243478>
- Cisler, J. M., Olatunji, B. O., & Lohr, J. M. (2009). Digust, Fear, and the Anxiety Disorders: A Critical Review. *Clinical Psychology Review*, 29(1), 34–46.
<https://doi.org/10.1016/j.cpr.2008.09.007>
- Cloos, J.-M. (2005). The treatment of panic disorder. *Current Opinion in Psychiatry*, 18(1), 45–50.
https://journals.lww.com/co-psychiatry/Abstract/2005/01000/The_treatment_of_panic_disorder.9.aspx
- Coles, M. E., Heimberg, R. G., Frost, R. O., & Steketee, G. (2005). Not just right experiences and obsessive – compulsive features : Experimental and self-monitoring perspectives. *Behaviour Research and Therapy*, 43, 153–167.
<https://doi.org/10.1016/j.brat.2004.01.002>
- Constans, J. I., Foa, E. B., Franklin, M. E., & Mathews, A. (1995). Memory for actual and imagined events in OC checkers. *Behaviour Research and Therapy*, 33(6), 665–671.
[https://doi.org/https://doi.org/10.1016/0005-7967\(94\)00095-2](https://doi.org/https://doi.org/10.1016/0005-7967(94)00095-2)
- Cottraux, J., Note, I., Yao, S. N., Lafont, S., Note, B., Mollard, E., Bouvard, M., Sauteraud, A.,

- Bourgeois, M., & Dartigues, J.-F. (2001). A Randomized Controlled Trial of Cognitive Therapy versus Intensive Behavior Therapy in Obsessive Compulsive Disorder. *Psychotherapy and Psychosomatics*, 70, 288–297. <https://doi.org/https://doi.org/10.1159/000056269>
- Coyle, D., Doherty, G., Matthews, M., & Sharry, J. (2007). Computers in talk-based mental health interventions. *Interacting with Computers*, 19(4), 545–562. <https://doi.org/10.1016/j.intcom.2007.02.001>
- Craske, M. G., Kircanski, K., Zelikowsky, M., Mystkowski, J., Chowdhury, N., & Baker, A. (2008). Optimizing inhibitory learning during exposure therapy. *Behaviour Research and Therapy*, 46(1), 5–27. <https://doi.org/10.1016/j.brat.2007.10.003>
- Craske, M. G., Treanor, M., Conway, C. C., Zbozinek, T., & Vervliet, B. (2014). Maximizing exposure therapy: An inhibitory learning approach. *Behaviour Research and Therapy*, 58, 10–23. <https://doi.org/10.1016/j.brat.2014.04.006>
- Cribbie, R. A., & Arpin-Cribbie, C. A. (2009). Evaluating clinical significance through equivalence testing: Extending the normative comparisons approach. *Psychotherapy Research*, 19(6), 677–686. <https://doi.org/10.1080/10503300902926554>
- Crino, R., Slade, T., & Andrews, G. (2005). The Changing Prevalence and Severity of Obsessive- Compulsive Disorder Criteria From DSM-III to DSM-IV. *American Journal of Psychiatry*, 162(5), 876–882. <https://doi.org/https://doi.org/10.1176/appi.ajp.162.5.876>
- Cruz-Neira, C., Sandin, D. J., & DeFanti, T. A. (1993). Surround-screen projection-based virtual reality: the design and implementation of the CAVE. *Proceedings of the 20th Annual Conference on Computer Graphics and Interactive Techniques*, 135–142. <https://doi.org/https://doi.org/10.1145/166117.166134>
- Cullen, A. J. (2020). *Virtual Reality in Psychology: Development and Validation of an Exposure Therapy System*. Monash University, Australia.

- Cullen, A. J., Dowling, N. L., Segrave, R., Carter, A., & Yücel, M. (n.d.). *Exposure Therapy in a Virtual Environment: Validation in Obsessive Compulsive Disorder*.
- Cullen, A. J., Dowling, N. L., Segrave, R., Morrow, J., Carter, A., & Yücel, M. (n.d.). *Considerations and Practical Protocols for Using Virtual Reality in Psychological Research and Practice, as Evidenced Through Exposure-Based Therapy*.
- Cushman, F., & Morris, A. (2015). Habitual control of goal selection in humans. *Proceedings of the National Academy of Sciences*, 112(45). <https://doi.org/10.1073/pnas.1506367112>
- Cushman, L. A., Stein, K., & Duffy, C. J. (2008). Detecting navigational deficits in cognitive aging and Alzheimer disease using virtual reality. *Neurology*, 71(12), 888–895. <https://doi.org/10.1212/01.wnl.0000326262.67613.fe>
- Davis, S., Nesbitt, K., & Nalivaiko, E. (2015). Comparing the onset of cybersickness using the Oculus Rift and two virtual roller coasters. *Proceedings of the 11th Australasian Conference on Interactive Entertainment (IE 2015)*, 167, 3–14. <https://doi.org/10.17973/MMSJ.2015>
- De Vries-Bouw, M., Popma, A., Vermeiren, R., Doreleijers, T. A. H., Van De Ven, P. M., & Jansen, L. M. C. (2011). The predictive value of low heart rate and heart rate variability during stress for reoffending in delinquent male adolescents. *Psychophysiology*, 48(11), 1597–1604. <https://doi.org/10.1111/j.1469-8986.2011.01233.x>
- Denys, D., Mantione, M., Figee, M., Van Den Munckhof, P., Koerselman, F., Westenberg, H., Bosch, A., & Schuurman, R. (2010). Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. *Archives of General Psychiatry*, 67(10), 1061–1068. <https://doi.org/10.1001/archgenpsychiatry.2010.122>
- Dickinson, A. (1985). Actions and habits: the development of behavioural autonomy. *Philosophical Transactions of the Royal Society of London*, 308, 67–78. <https://doi.org/https://doi.org/10.1098/rstb.1985.0010>

- Diemer, J., Mühlberger, A., Pauli, P., Zwanzger, P., Diemer, J., Mühlberger, A., Pauli, P., Virtual, P. Z., Diemer, J., Hlberger, A. M. Ü., Pauli, P., & Zwanzger, P. (2014). Virtual reality exposure in anxiety disorders: Impact on psychophysiological reactivity. *The World Journal of Biological Psychiatry*, 15(6), 427–442. <https://doi.org/10.3109/15622975.2014.892632>
- Difede, J., Cukor, J., Patt, I., Giosan, C., & Hoffman, H. (2006). The application of virtual reality to the treatment of PTSD following the WTC attack. *Annals of the New York Academy of Sciences*, 1071(1), 500–501. <https://doi.org/10.1196/annals.1364.052>
- Dishman, R. K., Nakamura, Y., Garcia, M. E., Thompson, R. W., Dunn, A. L., & Blair, S. N. (2000). Heart rate variability, trait anxiety, and perceived stress among physically fit men and women. *International Journal of Psychophysiology*, 37(2), 121–133. [https://doi.org/10.1016/S0167-8760\(00\)00085-4](https://doi.org/10.1016/S0167-8760(00)00085-4)
- Dolan, R. J., & Dayan, P. (2013). Goals and Habits in the Brain. *Neuron Review*, 80(2), 312–325. <https://doi.org/10.1016/j.neuron.2013.09.007>
- Donahue, C. B., Kushner, M. G., Thuras, P. D., Murphy, T. G., Van Demark, J. B., & Adson, D. E. (2009). Effect of quetiapine vs. placebo on response to two virtual public speaking exposures in individuals with social phobia. *Journal of Anxiety Disorders*, 23(3), 362–368. <https://doi.org/10.1016/j.janxdis.2008.12.004>
- Dougherty, D. D., Baer, L., Cosgrove, G. R., Cassem, E. H., Price, B. H., Nierenberg, A. A., Jenike, M. A., & Rauch, S. L. (2002). Prospective long-term follow-up of 44 patients who received cingulotomy for treatment-refractory obsessive-compulsive disorder. *American Journal of Psychiatry*, 159(2), 269–275. <https://doi.org/10.1176/appi.ajp.159.2.269>
- Dougherty, D. D., Rauch, S. L., & Jenike, M. A. (2004). Pharmacotherapy for obsessive-compulsive disorder. *Journal of Clinical Psychology*, 60(11), 1195–1202. <https://doi.org/10.1002/jclp.20083>

- Dougherty, D. D., Rauch, S. L., & Jenike, M. A. (2015). Treatments for Obsessive-Compulsive Disorder. In P. E. Nathan & J. M. Gorman (Eds.), *A Guide to Treatments That Work* (4th ed., pp. 545–585). Oxford University Press.
<https://doi.org/10.1093/med:psych/9780199342211.003.0017>
- Duncan, B., Miller, S., Sparks, J., & Claud, D. (2003). The Session Rating Scale: Preliminary psychometric properties of a “working” alliance measure. *Journal of Brief Therapy*, 3(1), 3–12.
https://www.researchgate.net/profile/Barry_Duncan2/publication/280015889_The_Session_Rating_Scale_Preliminary_Psychometric_Properties_of_a_Working_Alliance_Measure/links/55b96a1a08aec0e5f43c33fa.pdf
- Ecker, W., & Gonner, S. (2008). Incompleteness and harm avoidance in OCD symptom dimensions. *Behaviour Research and Therapy*, 46, 895–904.
<https://doi.org/10.1016/j.brat.2008.04.002>
- Eddy, K. T., Dutra, L., Bradley, R., & Westen, D. (2004). A multidimensional meta-analysis of psychotherapy and pharmacotherapy for obsessive-compulsive disorder. *Clinical Psychology Review*, 24(8), 1011–1030. <https://doi.org/10.1016/j.cpr.2004.08.004>
- Egger, J., Gall, M., Wallner, J., Boechat, P., Hann, A., Li, X., Chen, X., & Schmalstieg, D. (2017). HTC Vive MeVisLab integration via OpenVR for medical applications. *PLoS ONE*, 12(3), 1–14. <https://doi.org/10.1371/journal.pone.0173972>
- Electrophysiology, T. force of the E. society of cardiology and the north A. society of pacing and. (1996). Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, 17, 354–381.
<https://doi.org/10.1161/01.CIR.93.5.1043>
- Emmelkamp, P. M. G. (2005). Technological innovations in clinical assessment and psychotherapy. *Psychotherapy and Psychosomatics*, 74(6), 336–343.

- <https://doi.org/10.1159/000087780>
- Farrand, S., Evans, A. H., Mangelsdorf, S., Loi, S. M., Mocellin, R., Borham, A., Bevilacqua, J. A., Blair-West, S., Walterfang, M. A., Bittar, R. G., & Velakoulis, D. (2018). Deep brain stimulation for severe treatment-resistant obsessive-compulsive disorder: An open-label case series. *Australian and New Zealand Journal of Psychiatry*, 52(7), 699–708. <https://doi.org/10.1177/0004867417731819>
- Farrell, M. J., Arnold, P., Pettifer, S., Adams, J., Graham, T., & MacManamon, M. (2003). Transfer of Route Learning from Virtual to Real Environments. *Journal of Experimental Psychology: Applied*, 9(4), 219–227. <https://doi.org/10.1037/1076-898X.9.4.219>
- Feinstein, S. B., Fallon, B. A., Petkova, E., & Liebowitz, M. R. (2003). Item-by-item factor analysis of the Yale-Brown Obsessive Compulsive Scale Symptom Checklist. *Journal of Neuropsychiatry and Clinical Neurosciences*, 15, 187–193. <https://doi.org/https://doi.org/10.1176/jnp.15.2.187>
- Fisher, P. L., & Wells, A. (2005). How effective are cognitive and behavioral treatments for obsessive-compulsive disorder? A clinical significance analysis. *Behaviour Research and Therapy*, 43(12), 1543–1558. <https://doi.org/10.1016/j.brat.2004.11.007>
- Foa, E. B. (2010). Cognitive behavioral therapy of obsessive-compulsive disorder. *Dialogues in Clinical Neuroscience*, 12(2), 199–207. <https://doi.org/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181959/>
- Foa, E. B., & Kozak, M. J. (1986). Emotional Processing of Fear: Exposure to Corrective Information. *Psychological Bulletin*, 99(1), 20–35. <https://doi.org/10.1037/0033-2909.99.1.20>
- Foa, E. B., & Kozak, M. J. (1995). DSM-IV field trial: obsessive-compulsive disorder. *The American Journal of Psychiatry*, 152(1), 90–96. <https://doi.org/10.1176/ajp.152.1.90>
- Foa, E. B., Liebowitz, M. R., Kozak, M. J., Davies, S., Campeas, R., Franklin, M. E., Huppert,

- J. D., Kjernisted, K., Rowan, V., Schmidt, A. B., Simpson, H. B., & Tu, X. (2005). Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. *American Journal of Psychiatry*, *162*(1), 151–161. <https://doi.org/10.1176/appi.ajp.162.1.151>
- Foa, E. B., Steketee, G., & Grayson, J. B. (1985). Imaginal and in vivo exposure: A comparison with obsessive-compulsive checkers. *Behavior Therapy*, *16*(3), 292–302. [https://doi.org/10.1016/S0005-7894\(85\)80017-4](https://doi.org/10.1016/S0005-7894(85)80017-4)
- Foa, E. B., Steketee, G., Grayson, J. B., Turner, R. M., & Latimer, P. R. (1984). Deliberate exposure and blocking of obsessive-compulsive rituals: Immediate and long-term effects. *Behavior Therapy*, *15*(5), 450–472. [https://doi.org/10.1016/S0005-7894\(84\)80049-0](https://doi.org/10.1016/S0005-7894(84)80049-0)
- Foa, E. B., Steketee, G., Turner, R. M., & Fischer, S. C. (1980). Effects of imaginal exposure to feared disasters in obsessive-compulsive checkers. *Behaviour Research and Therapy*, *18*(5), 449–455. [https://doi.org/10.1016/0005-7967\(80\)90010-8](https://doi.org/10.1016/0005-7967(80)90010-8)
- Foerster, R. M., Poth, C. H., Behler, C., Botsch, M., & Schneider, W. X. (2016). Using the virtual reality device Oculus Rift for neuropsychological assessment of visual processing capabilities. *Scientific Reports*, *6*(1), 1–10. <https://doi.org/10.1038/srep37016>
- Foerster, R. M., Poth, C. H., Behler, C., Botsch, M., & Schneider, W. X. (2019). Neuropsychological assessment of visual selective attention and processing capacity with head-mounted displays. *Neuropsychology*, *33*(3), 309–318. <https://doi.org/10.1037/neu0000517>
- Foreman, N. (2010). Virtual Reality in Psychology. *Themes in Science and Technology Education*, *2*(1–2), 225–252. <http://earthlab.uoi.gr/theste/index.php/theste/article/view/33>
- Foreman, N., Stanton-Fraser, D., Wilson, P. N., Duffy, H., & Parnell, R. (2005). Transfer of spatial knowledge to a two-level shopping mall in older people, following virtual exploration. *Environment and Behavior*, *37*(2), 275–292.

- <https://doi.org/10.1177/0013916504269649>
- Franklin, M. E., Abramowitz, J. S., Kozak, M. J., Levitt, J. T., & Foa, E. B. (2000). Effectiveness of exposure and ritual prevention for obsessive-compulsive disorder: randomized compared with nonrandomized samples. *Journal of Consulting and Clinical Psychology*, 68(4), 594–602. <https://doi.org/10.1037/0022-006X.68.4.594>
- Freeman, D. (2008). Studying and treating schizophrenia using virtual reality: A new paradigm. *Schizophrenia Bulletin*, 34(4), 605–610. <https://doi.org/10.1093/schbul/sbn020>
- Freeston, M. H., Ladouceur, R., Gagnon, F., Thibodeau, N., Rheume, J., Letarte, H., & Bujold, A. (1997). Cognitive-Behavioral Treatment of Obsessive Thoughts: A Controlled Study. *Journal of Consulting and Clinical Psychology*, 65(3), 405–413. <https://doi.org/10.1037/0022-006x.65.3.405>
- Freire, R. C., De Carvalho, M. R., Joffily, M., Zin, W. A., & Nardi, A. E. (2010). Anxiogenic properties of a computer simulation for panic disorder with agoraphobia. *Journal of Affective Disorders*, 125, 301–306. <https://doi.org/10.1016/j.jad.2009.12.031>
- Frost, R. O., & Steketee, G. (1997). Perfectionism in Obsessive-Compulsive Disorder Patients. *Behaviour Research and Therapy*, 35(4), 291–296. [https://doi.org/10.1016/S0005-7967\(96\)00108-8](https://doi.org/10.1016/S0005-7967(96)00108-8)
- Gabriëls, L., Cosyns, P., Nuttin, B., Demeulemeester, H., & Gybels, J. (2003). Deep brain stimulation for treatment-refractory obsessive-compulsive disorder: psychopathological and neuropsychological outcome in three cases. *Acta Psychiatrica Scandinavica*, 107(4), 275–282. <https://doi.org/10.1034/j.1600-0447.2003.00066.x>
- Garcia-Palacios, A., Botella, C., Hoffman, H., & Fabregat, S. (2007). Comparing acceptance and refusal rates of virtual reality exposure vs. in vivo exposure by patients with specific phobias. *Cyberpsychology and Behavior*, 10(5), 722–724. <https://doi.org/10.1089/cpb.2007.9962>

- Garcia-Palacios, A., Hoffman, H. G., See, S. K., Tsai, A., & Botella, C. (2001). Redefining therapeutic success with virtual reality exposure therapy. *Cyberpsychology and Behavior*, 4(3), 341–348. <https://doi.org/10.1089/109493101300210231>
- Gava, I., Barbui, C., Aguglia, E., Carlino, D., Churchill, R., De Vanna, M., & McGuire, H. F. (2007). Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD). *Cochrane Database of Systematic Reviews*, 2, 1–47. <https://doi.org/10.1002/14651858.CD005333.pub2>
- Gillan, C. M., Fineberg, N. A., & Robbins, T. W. (2017). A trans-diagnostic perspective on obsessive-compulsive disorder. *Psychological Medicine*, 47, 1528–1548. <https://doi.org/10.1017/S0033291716002786>
- Gillan, C. M., Morein-Zamir, S., Urcelay, G. P., Sule, A., Voon, V., Apergis-Schoute, A. M., Fineberg, N. A., Sahakian, B. J., & Robbins, T. W. (2014). Enhanced Avoidance Habits in Obsessive-Compulsive Disorder. *Biological Psychiatry*, 75(8), 631–638. <https://doi.org/10.1016/j.biopsych.2013.02.002>
- Gillan, C. M., Papmeyer, M., Morein-Zamir, S., Sahakian, B. J., Fineberg, N. A., Robbins, T. W., & de Wit, S. (2011). Disruption in the Balance Between Goal-Directed Behavior and Habit Learning in Obsessive-Compulsive Disorder. *American Journal of Psychiatry*, 168(7), 718–726. <https://doi.org/10.1176/appi.ajp.2011.10071062>
- Gillihan, S. J., Williams, M. T., Malcoun, E., Yadin, E., & Foa, E. B. (2012). Common pitfalls in exposure and response prevention (EX/RP) for OCD. *Journal of Obsessive-Compulsive and Related Disorders*, 1(4), 251–257. <https://doi.org/10.1016/j.jocrd.2012.05.002>
- Glegg, S. M. N., Holsti, L., Velikonja, D., Ansley, B., Brum, C., & Sartor, D. (2013). Factors influencing therapists' adoption of virtual reality for brain injury rehabilitation. *Cyberpsychology, Behavior, and Social Networking*, 16(5), 385–401. <https://doi.org/10.1089/cyber.2013.1506>

- Glegg, S. M. N., & Levac, D. E. (2015). Barriers, Facilitators and Interventions to Support Virtual Reality Implementation in Rehabilitation: A Scoping Review. *PM&R*, 10(11), 1237–1251. <https://doi.org/10.1016/j.pmrj.2018.07.004>
- Gonçalves, R., Pedrozo, A. L., Coutinho, E. S. F., Figueira, I., & Ventura, P. (2012). Efficacy of Virtual Reality Exposure Therapy in the Treatment of PTSD: A Systematic Review. *PLoS ONE*, 7(12), 1–8. <https://doi.org/10.1371/journal.pone.0048469>
- Goodman, W. K., Price, L. H., Rasmussen, S. A., Mazure, C., Delgado, P., Heninger, G. R., & Charney, D. S. (1989). The Yale–Brown Obsessive Compulsive Scale. *Archives of General Psychiatry*, 46(11), 1012–1016. <https://doi.org/10.1001/archpsyc.1989.01810110054008>
- Graham, I. D., Logan, J., Harrison, M. B., Straus, S. E., Tetroe, J., Caswell, W., & Robinson, N. (2006). Lost in knowledge translation: time for a map? *The Journal of Continuing Education in the Health Professions*, 26(1), 13–24. <https://doi.org/10.1002/chp.47>
- Gramann, K., Müller, H. J., Eick, E. M., & Schönebeck, B. (2005). Evidence of separable spatial representations in a virtual navigation task. *Journal of Experimental Psychology: Human Perception and Performance*, 31(6), 1199–1223. <https://doi.org/10.1037/0096-1523.31.6.1199>
- Graybiel, A. M., & Rauch, S. L. (2000). Toward a Neurobiology of Obsessive-Compulsive Disorder. *Neuron*, 28(4), 343–347. [https://doi.org/10.1016/S0896-6273\(00\)00113-6](https://doi.org/10.1016/S0896-6273(00)00113-6)
- Greenberg, B. D., Gabriels, L. A., Malone, D. A., Rezai, A. R., Friehs, G. M., Okun, M. S., Shapira, N. A., Foote, K. D., Cosyns, P. R., Kubu, C. S., Malloy, P. F., Salloway, S. P., Giftakis, J. E., Rise, M. T., MacHado, A. G., Baker, K. B., Stypulkowski, P. H., Goodman, W. K., Rasmussen, S. A., & Nuttin, B. J. (2010). Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive-compulsive disorder: Worldwide experience. *Molecular Psychiatry*, 15(1), 64–79. <https://doi.org/10.1038/mp.2008.55>

- Greist, J. H., Jefferson, J. W., Kobak, K. A., Katzelnick, D. J., & Serlin, R. C. (1995). Efficacy and tolerability of Serotonin transport inhibitors in Obsessive-Compulsive Disorder: A Meta-analysis. *Archives of General Psychiatry*, 52(1), 53–60. <https://doi.org/10.1001/archpsyc.1995.03950130053006>
- Grossman, P., Wilhelm, F. H., Kawachi, I., & Sparrow, D. (2001). Gender differences in psychophysiological responses to speech stress among older social phobics: Congruence and incongruence between self-evaluative and cardiovascular reactions. *Psychosomatic Medicine*, 63(5), 765–777. <https://doi.org/10.1097/00006842-200109000-00010>
- Grøtte, T., Solem, S., Vogel, P. A., Güzey, I. C., Hansen, B., & Myers, S. G. (2014). Metacognition, Responsibility, and Perfectionism in Obsessive-Compulsive Disorder. *Cognitive Therapy and Research*, 39, 41–50. <https://doi.org/10.1007/s10608-014-9635-7>
- Grunebaum, M. F., Ellis, S. P., Li, S., Oquendo, M. A., & Mann, J. J. (2004). Antidepressants and suicide risk in the United States, 1985-1999. *Journal of Clinical Psychiatry*, 65(11), 1456–1462. <https://doi.org/10.4088/JCP.v65n1103>
- Gujjar, K. R., van Wijk, A., Kumar, R., & de Jongh, A. (2019). Efficacy of virtual reality exposure therapy for the treatment of dental phobia in adults: A randomized controlled trial. *Journal of Anxiety Disorders*, 62, 100–108. <https://doi.org/10.1016/j.janxdis.2018.12.001>
- Harris, S. R., Kemmerling, R. L., & North, M. M. (2002). Brief virtual reality therapy for public speaking anxiety. *CyberPsychology & Behavior*, 5(6), 543–550. <https://doi.org/10.1089/109493102321018187>
- Hendrix, C., & Barfield, W. (1996). The sense of presence within auditory virtual environments. *Presence: Teleoperators & Virtual Environments*, 5(3), 290–301. <https://doi.org/10.1109/VRAIS.1995.512482>
- Henriques, G., Keffer, S., Abrahamson, C., & Horst, S. J. (2011). Exploring the Effectiveness

- of a Computer-Based Heart Rate Variability Biofeedback Program in Reducing Anxiety in College Students. *Applied Psychophysiology Biofeedback*, 36, 101–112. <https://doi.org/10.1007/s10484-011-9151-4>
- Heyman, I., Fombonne, E., Simmons, H., Ford, T., Meltzer, H., & Goodman, R. (2001). Prevalence of obsessive-compulsive disorder in the British nationwide survey of child mental health. *British Journal of Psychiatry*, 179, 324–329. <http://search.proquest.com/docview/57576532/>
- Hills, A. (2011). *Foolproof Guide to Statistics using IBM SPSS* (2nd ed.). Pearson Australia.
- Hodgson, R. J., & Rachman, S. (1972). The effects of contamination and washing in obsessional patients. *Behaviour Research and Therapy*, 10(2), 111–117. [https://doi.org/10.1016/S0005-7967\(72\)80003-2](https://doi.org/10.1016/S0005-7967(72)80003-2)
- Hoffman, H. G., Hollander, A., Schroder, K., Rousseau, S., & Furness, T. (1998). Physically touching and tasting virtual objects enhances the realism of virtual experiences. *Virtual Reality*, 3(4), 226–234. <https://doi.org/10.1007/bf01408703>
- Huppert, J. D., & Roth, D. A. (2003). Treating obsessive-compulsive disorder with exposure and response prevention. *The Behavior Analyst Today*, 4(1), 66–70. <https://doi.org/https://doi.org/10.1037/h0100012>
- IBM. (2017). *IBM SPSS Statistics for Macintosh* (No. 25). IBM Corp.
- Inozu, M., Celikcan, U., Akin, B., & Mustafaoğlu Cicek, N. (2020). The use of virtual reality (VR) exposure for reducing contamination fear and disgust: Can VR be an effective alternative exposure technique to in vivo? *Journal of Obsessive-Compulsive and Related Disorders*, 25. <https://doi.org/10.1016/j.jocrd.2020.100518>
- International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders. (2011). A conceptual framework for the revision of the ICD-10 classification of mental and behavioural disorders. *World Psychiatry*, 10(2), 86–92.

- <https://doi.org/https://doi.org/10.1002/j.2051-5545.2011.tb00022.x>
- James, S. L., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdollahpour, I., Abdulkader, R. S., Abebe, Z., Abera, S. F., Abil, O. Z., Abraha, H. N., Abu-Raddad, L. J., Abu-Rmeileh, N. M. E., Accrombessi, M. M. K., ... Murray, C. J. L. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 Diseases and Injuries for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, 392(10159), 1789–1858. [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7)
- Jang, D. P., Kim, I. Y., Nam, S. W., Wiederhold, B. K., Wiederhold, M. D., & Kim, S. I. (2002). Analysis of physiological response to two virtual environments: Driving and flying simulation. *Cyberpsychology and Behavior*, 5(1), 11–18. <https://doi.org/10.1089/109493102753685845>
- Jenike, M. A. (2004). Obsessive–Compulsive Disorder. *The New England Journal of Medicine*, 350(3), 256–263. <https://doi.org/10.1016/B978-0-12-385157-4.01073-3>
- Juan, M. C., Alcaniz, M., Monserrat, C., Botella, C., Bannos, R. M., & B, G. (2005). Using Augmented Reality to Treat Phobias. *IEEE Computer Graphics and Applications*, 25(6), 31–37. <https://doi.org/10.1109/MCG.2005.143>
- Kampmann, I. L., Emmelkamp, P. M. G., Hartanto, D., Brinkman, W. P., Zijlstra, B. J. H., & Morina, N. (2016). Exposure to virtual social interactions in the treatment of social anxiety disorder: A randomized controlled trial. *Behaviour Research and Therapy*, 77, 147–156. <https://doi.org/10.1016/j.brat.2015.12.016>
- Karno, M., Golding, J. M., Sorenson, S. B., & Burnam, M. A. (1988). The Epidemiology of Obsessive-Compulsive Disorder in Five US Communities. *Archives of General Psychiatry*, 45, 1094–1099. <https://doi.org/10.1001/archpsyc.1988.01800360042006>

- Kellmeyer, P. (2018). Neurophilosophical and Ethical Aspects of Virtual Reality Therapy in Neurology and Psychiatry. *Cambridge Quarterly of Healthcare Ethics*, 27(4), 610–627. <https://doi.org/10.1017/S0963180118000129>
- Kellmeyer, P., Biller-Andorno, N., & Meynen, G. (2019). Ethical tensions of virtual reality treatment in vulnerable patients. *Nature Medicine*, 25(8), 1185–1188. <https://doi.org/10.1038/s41591-019-0543-y>
- Kim, C. H., Cha, K. R., Kim, S. I., Kim, K. W., & Jon, D. I. (2008). Virtual reality assessment of checking symptoms in patients with obsessive compulsive disorder. *Journal of Affective Disorders*, 107, S121. <https://doi.org/10.1016/j.jad.2007.12.142>
- Kim, K., Kim, C.-H., Cha, K. R., Park, J., Han, K., Kim, Y. K., Kim, J.-J., Kim, I. Y., & Kim, S. I. (2008). Anxiety provocation and measurement using virtual reality in patients with obsessive-compulsive disorder. *CyberPsychology & Behavior*, 11(6), 637–641. <https://doi.org/10.1089/cpb.2008.0003>
- Kim, K., Kim, C. H., Kim, S. Y., Roh, D., & Kim, S. I. (2009). Virtual reality for obsessive-compulsive disorder: Past and the future. *Psychiatry Investigation*, 6(3), 115–121. <https://doi.org/10.4306/pi.2009.6.3.115>
- Kim, K., Roh, D., Kim, C. H., Cha, K. R., Rosenthal, M. Z., & Kim, S. I. (2012). Comparison of checking behavior in adults with or without checking symptom of obsessive-compulsive disorder using a novel computer-based measure. *Computer Methods and Programs in Biomedicine*, 108(1), 434–441. <https://doi.org/10.1016/j.cmpb.2012.03.014>
- Kircanski, K., & Peris, T. S. (2014). Exposure and Response Prevention Process Predicts Treatment Outcome in Youth with OCD. *Journal of Abnormal Child Psychology*, 543–552. <https://doi.org/10.1007/s10802-014-9917-2>
- Klinger, E., & Bouchard, S. (2005). Virtual Reality Therapy Versus Cognitive Behavior Therapy for Social Phobia: A Preliminary Controlled Study. *CyberPsychology &*

- Behavior & Behavior*, 8(1), 76–89. <https://doi.org/10.1089/cpb.2005.8.76>
- Kobak, K. A., Greist, J. H., Jefferson, J. W., Katzelnick, D. J., & Henk, H. J. (1998). Behavioral versus pharmacological treatments of obsessive compulsive disorder: a meta-analysis. *Psychopharmacology*, 136, 205–216. <http://dx.doi.org/10.1007/s002130050558>
- Kogan, C. S., Stein, D. J., Rebello, T. J., Keeley, J. W., Chan, K. J., Fineberg, N. A., Fontenelle, L. F., Grant, J. E., Matsunaga, H., Simpson, H. B., Thomsen, P. H., van den Heuvel, O. A., Veale, D., Grenier, J., Kulygina, M., Matsumoto, C., Domínguez-Martínez, T., Stona, A. C., Wang, Z., & Reed, G. M. (2020). Accuracy of diagnostic judgments using ICD-11 vs. ICD-10 diagnostic guidelines for obsessive-compulsive and related disorders. *Journal of Affective Disorders*, 273, 328–340. <https://doi.org/10.1016/j.jad.2020.03.103>
- Kozak, M. J., & Coles, M. E. (2005). Treatment for OCD: Unleashing the Power of Exposure. In J. S. Abramowitz & A. Houts (Eds.), *Concepts and controversies in obsessive-compulsive disorder* (1st ed., pp. 283–315). Springer-Verlag New York. https://doi.org/10.1007/0-387-23370-9_15
- Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology*, 84(3), 394–421. <https://doi.org/10.1016/j.biopsycho.2010.03.010>
- Krijn, M., Emmelkamp, P. M. G., Biemond, R., de Wilde de Ligny, C., Schuemie, M. J., & Van Der Mast, C. A. P. G. (2004). Treatment of acrophobia in virtual reality: The role of immersion and presence. *Behaviour Research and Therapy*, 42(2), 229–239. [https://doi.org/10.1016/S0005-7967\(03\)00139-6](https://doi.org/10.1016/S0005-7967(03)00139-6)
- Krijn, M., Emmelkamp, P. M. G., Olafsson, R. P., & Biemond, R. (2004). Virtual reality exposure therapy of anxiety disorders: A review. *Clinical Psychology Review*, 24(3), 259–281. <https://doi.org/10.1016/j.cpr.2004.04.001>
- Ladouceur, R., Gosselin, P., & Dugas, M. J. (2000). Experimental manipulation of intolerance of uncertainty : a study of a theoretical model of worry. *Behaviour Research and Therapy*,

- 38(9), 933--941. [https://doi.org/10.1016/S0005-7967\(99\)00133-3](https://doi.org/10.1016/S0005-7967(99)00133-3)
- Laforest, M., Bouchard, S., Bossé, J., & Mesly, O. (2016). 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. *Frontiers in Psychiatry*, 7, 1–13. <https://doi.org/10.3389/fpsy.2016.00099>
- Laforest, M., Bouchard, S., Crétu, A. M., & Mesly, O. (2016). Inducing an anxiety response using a contaminated virtual environment: Validation of a therapeutic tool for obsessive-compulsive disorder. *Frontiers in ICT*, 3, 1–11. <https://doi.org/10.3389/fict.2016.00018>
- Lam, J. N., & Steketee, G. (2008). Reducing Obsessions and Compulsions Through Behavior Therapy. *Psychoanalytic Inquiry*, 21(2), 157–182. <https://doi.org/10.1080/07351692109348930>
- Lang, P. J. (1977). Imagery in therapy: an information processing analysis of fear. *Behavior Therapy*, 8(5), 862–886. [https://doi.org/10.1016/S0005-7894\(77\)80157-3](https://doi.org/10.1016/S0005-7894(77)80157-3)
- Leckman, J. F., Denys, D., Simpson, H. B., Mataix-Cols, D., Hollander, E., Saxena, S., Miguel, E. C., Rauch, S. L., Goodman, W. K., Phillips, K. A., & Stein, D. J. (2010). Obsessive-compulsive disorder: A review of the diagnostic criteria and possible subtypes and dimensional specifiers for DSM-V. *Depression and Anxiety*, 27(6), 507–527. <https://doi.org/10.1002/da.20669>
- Lind, C., Boschen, M. J., & Morrissey, S. (2013). Technological advances in psychotherapy: Implications for the assessment and treatment of obsessive compulsive disorder. *Journal of Anxiety Disorders*, 27(1), 47–55. <https://doi.org/10.1016/j.janxdis.2012.09.004>
- Lindner, P., Miloff, A., Hamilton, W., Reuterskiöld, L., Andersson, G., Powers, M. B., & Carlbring, P. (2017). Creating state of the art, next-generation Virtual Reality exposure therapies for anxiety disorders using consumer hardware platforms: design considerations and future directions. *Cognitive Behaviour Therapy*, 46(5), 404–420.

- <https://doi.org/10.1080/16506073.2017.1280843>
- Ling, Y., Nefs, H. T., Morina, N., Heynderickx, I., & Brinkman, W. P. (2014). A meta-analysis on the relationship between self-reported presence and anxiety in virtual reality exposure therapy for anxiety disorders. *PLoS ONE*, 9(5), 1–12. <https://doi.org/10.1371/journal.pone.0096144>
- Lipsey, M. W., & Wilson, D. B. (1993). The Efficacy of Psychological, Educational, and Behavioral Treatment: Confirmation from meta-analysis. *American Psychologist*, 48(12), 1181–1209.
- Liu, L., Miguel Cruz, A., Rios Rincon, A., Buttar, V., Ranson, Q., & Goertzen, D. (2015). What factors determine therapists' acceptance of new technologies for rehabilitation-a study using the Unified Theory of Acceptance and Use of Technology (UTAUT). *Disability and Rehabilitation*, 37(5), 447–455. <https://doi.org/10.3109/09638288.2014.923529>
- Liu, Y., Zhu, S. H., Wang, G. H., Ye, F., & Li, P. Z. (2013). Validity and reliability of multiparameter physiological measurements recorded by the Equivital lifemonitor during activities of various intensities. *Journal of Occupational and Environmental Hygiene*, 10(2), 78–85. <https://doi.org/10.1080/15459624.2012.747404>
- Maher, M. J., Wang, Y., Zuckoff, A., Wall, M. M., Franklin, M., Foa, E. B., & Simpson, H. B. (2012). Predictors of patient adherence to cognitive-behavioral therapy for obsessive-compulsive disorder. *Psychotherapy and Psychosomatics*, 81(2), 124–126. <https://doi.org/10.1159/000330214>
- Mara, C. A., & Cribbie, R. A. (2012). Paired-samples tests of equivalence. *Communications in Statistics: Simulation and Computation*, 41(10), 1928–1943. <https://doi.org/10.1080/03610918.2011.626545>
- Martin, D. J., Garske, J. P., & Davis, M. K. (2000). Relation of the therapeutic alliance with

- outcome and other variables: A meta-analytic review. *Journal of Consulting and Clinical Psychology*, 68(3), 438–450. <https://doi.org/10.1037/0022-006X.68.3.438>
- Mataix-Cols, D., Rosario-Campos, M. C., & Leckman, J. F. (2005). A Multidimensional Model of Obsessive-Compulsive Disorder. *American Journal of Psychiatry*, 162(2), 228–238. <https://doi.org/10.1176/appi.ajp.162.2.228>
- Matthews, A. J., Maunder, R., Scanlan, J. D., & Kirkby, K. C. (2017). Online computer-aided vicarious exposure for OCD symptoms: A pilot study. *Journal of Behavior Therapy and Experimental Psychiatry*, 54, 25–34. <https://doi.org/10.1016/j.jbtep.2016.06.002>
- Mauss, I. B., McCarter, L., Levenson, R. W., Wilhelm, F. H., & Gross, J. J. (2005). The tie that binds? Coherence among emotion experience, behavior, and physiology. *Emotion*, 5(2), 175–190. <https://doi.org/10.1037/1528-3542.5.2.175>
- Mcevoy, P. M., & Mahoney, A. E. J. (2012). To Be Sure, To Be Sure: Intolerance of Uncertainty Mediates Symptoms of Various Anxiety Disorders and Depression. *Behavior Therapy*, 43(3), 533–545. <https://doi.org/10.1016/j.beth.2011.02.007>
- McLay, R. N., Ram, V., Murphy, J., Spira, J., Wood, D. P., Wiederhold, M. D., Wiederhold, B. K., Johnston, S., & Reeves, D. (2014). Effect of Virtual Reality PTSD Treatment on Mood and Neurocognitive Outcomes. *Cyberpsychology, Behavior, and Social Networking*, 17(7), 439–446. <https://doi.org/10.1089/cyber.2013.0383>
- McLay, R. N., Wood, D. P., Webb-Murphy, J. A., Spira, J. L., Wiederhold, M. D., Pyne, J. M., & Wiederhold, B. K. (2011). A randomized, controlled trial of virtual reality-graded exposure therapy for post-traumatic stress disorder in active duty service members with combat-related post-traumatic stress disorder. *Cyberpsychology, Behavior, and Social Networking*, 14(4), 223–229. <https://doi.org/10.1089/cyber.2011.0003>
- Merlo, L. J., Storch, E. A., Lehmkuhl, H. D., Jacob, M. L., Murphy, T. K., Goodman, W. K., & Geffken, G. R. (2010). Cognitive behavioral therapy plus motivational interviewing

- improves outcome for pediatric obsessive-compulsive disorder: A preliminary study. *Cognitive Behaviour Therapy*, 39(1), 24–27. <https://doi.org/10.1080/16506070902831773>
- Metzger, R. L. (1976). A reliability and validity study of the State-Trait Anxiety Inventory. *Journal of Clinical Psychology*, 0–2. [https://doi.org/10.1002/1097-4679\(197604\)32:2%3C276::AID-JCLP2270320215%3E3.0.CO;2-G](https://doi.org/10.1002/1097-4679(197604)32:2%3C276::AID-JCLP2270320215%3E3.0.CO;2-G)
- Meyerbroeker, K., Morina, N., Kerkhof, G. A., & Emmelkamp, P. M. G. (2013). Virtual reality exposure therapy does not provide any additional value in agoraphobic patients: A randomized controlled trial. *Psychotherapy and Psychosomatics*, 82(3), 170–176. <https://doi.org/10.1159/000342715>
- Meyerbröcker, K. (2014). Virtual Reality Exposure Therapy. In P. M. G. Emmelkamp & T. Ehring (Eds.), *The Wiley Handbook of Anxiety Disorders* (1st ed., pp. 1311–1324). John Wiley & Sons.
- Meyerbröcker, K., & Emmelkamp, P. M. G. (2008). Therapeutic processes in virtual reality exposure therapy: The role of cognitions and the therapeutic alliance. *Journal of CyberTherapy & Rehabilitation*, 1(3), 247–257. https://www.researchgate.net/publication/254918700_Therapeutic_processes_in_virtual_reality_exposure_therapy_The_role_of_cognitions_and_the_therapeutic_alliance
- Meyerbröcker, K., & Emmelkamp, P. M. G. (2010). Virtual reality exposure therapy in anxiety disorders: A systematic review of process-and-outcome studies. *Depression and Anxiety*, 27(10), 933–944. <https://doi.org/10.1002/da.20734>
- Minns, S., Levihn-Coon, A., Carl, E., Smits, J. A. J., Miller, W., Howard, D., Papini, S., Quiroz, S., Lee-Furman, E., Telch, M., Carlbring, P., Xanthopoulos, D., & Powers, M. B. (2018). Immersive 3D exposure-based treatment for spider fear: A randomized controlled trial. *Journal of Anxiety Disorders*, 58(May), 1–7.

- <https://doi.org/10.1016/j.janxdis.2018.05.006>
- Minns, S., Levihn-Coon, A., Carl, E., Smits, J. A. J., Miller, W., Howard, D., Papini, S., Quiroz, S., Lee-Furman, E., Telch, M., Carlbring, P., Xanthopoulos, D., & Powers, M. B. (2019). Immersive 3D exposure-based treatment for spider fear: A randomized controlled trial. *Journal of Anxiety Disorders*, 61, 37–44. <https://doi.org/10.1016/j.janxdis.2018.12.003>
- Monk, C., Kovenko, P., Ellman, L. M., Sloan, R. P., Bagiella, E., Gorman, J. M., & Pine, D. S. (2001). Enhanced stress reactivity in paediatric anxiety disorders: Implications for future cardiovascular health. *International Journal of Neuropsychopharmacology*, 4(2), 199–206. <https://doi.org/10.1017/S146114570100236X>
- Moore, K., Wiederhold, B. K., Wiederhold, M. D., & Riva, G. (2002). Panic and agoraphobia in a virtual world. *Cyberpsychology and Behavior*, 5(3), 197–202. <https://doi.org/10.1089/109493102760147178>
- Moreno, R., & Mayer, R. E. (2004). Personalized messages that promote science learning in virtual environments. *Journal of Educational Psychology*, 96(1), 165. <https://doi.org/10.1037/0022-0663.96.1.165>
- Morganti, F., Stefanini, S., & Riva, G. (2013). From allo- to egocentric spatial ability in early Alzheimer's disease: A study with virtual reality spatial tasks. *Cognitive Neuroscience*, 4(3–4), 171–180. <https://doi.org/10.1080/17588928.2013.854762>
- Morina, N., Ijntema, H., Meyerbröcker, K., & Emmelkamp, P. M. G. (2015). Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments. *Behaviour Research and Therapy*, 74, 18–24. <https://doi.org/10.1016/j.brat.2015.08.010>
- Mühlberger, A., Bülhoff, H. H., Wiedemann, G., & Pauli, P. (2007). Virtual Reality for the Psychophysiological Assessment of Phobic Fear: Responses During Virtual Tunnel Driving. *Psychological Assessment*, 19(3), 340–346. <https://doi.org/10.1037/1040->

3590.19.3.340

- Mühlberger, A., Herrmann, M. J., Wiedemann, G., Ellgring, H., & Pauli, P. (2001). Repeated exposure of flight phobics to flights in virtual reality. *Behaviour Research and Therapy*, 39(9), 1033–1050. [https://doi.org/10.1016/S0005-7967\(00\)00076-0](https://doi.org/10.1016/S0005-7967(00)00076-0)
- Munafò, M. R., Nosek, B. A., Bishop, D. V. M., Button, K. S., Chambers, C. D., Percie Du Sert, N., Simonsohn, U., Wagenmakers, E. J., Ware, J. J., & Ioannidis, J. P. A. (2017). A manifesto for reproducible science. *Nature Human Behaviour*, 1(1), 1–9. <https://doi.org/10.1038/s41562-016-0021>
- Murray, C. J. L., Lopez, A. D., & Wibulpolprasert, S. (2004). Monitoring global health: time for new solutions. *BMJ*, 329(7474), 1096–1100. <https://doi.org/10.1136/bmj.329.7474.1096>
- Myers, S. G., Fisher, P. L., & Wells, A. (2008). Belief domains of the Obsessive Beliefs Questionnaire-44 (OBQ-44) and their specific relationship with obsessive-compulsive symptoms. *Journal of Anxiety Disorders*, 22(3), 475–484. <https://doi.org/10.1016/j.janxdis.2007.03.012>
- Naesström, M., Blomstedt, P., & Bodlund, O. (2016). A systematic review of psychiatric indications for deep brain stimulation, with focus on major depressive and obsessive-compulsive disorder. *Nordic Journal of Psychiatry*, 70(7), 483–491. <https://doi.org/10.3109/08039488.2016.1162846>
- National Institute for Health and Care Excellence. (2005). Obsessive-compulsive disorder and body dysmorphic disorder: treatment. In *National Institute for Health and Care Excellence* (Issue November 2005, pp. 15–46). <https://www.nice.org.uk/guidance/cg31/resources/obsessivecompulsive-disorder-and-body-dysmorphic-disorder-treatment-975381519301>
- National Institute for Health and Care Excellence. (2018). Post-traumatic Stress Disorder. In

- National Institute for Health and Care Excellence*. www.nice.org.uk/guidance/ng116
- Niehorster, D. C., Li, L., & Lappe, M. (2017). The accuracy and precision of position and orientation tracking in the HTC vive virtual reality system for scientific research. *I-Perception*, 8(3), 1–23. <https://doi.org/10.1177/2041669517708205>
- Notzon, S., Deppermann, S., Fallgatter, A., Diemer, J., Kroczeck, A., Domschke, K., Zwanzger, P., & Ehrlis, A. C. (2015). Psychophysiological effects of an iTBS modulated virtual reality challenge including participants with spider phobia. *Biological Psychology*, 112, 66–76. <https://doi.org/10.1016/j.biopsycho.2015.10.003>
- Ogourtsova, T., Archambault, P. S., & Lamontagne, A. (2019). Exploring barriers and facilitators to the clinical use of virtual reality for post-stroke unilateral spatial neglect assessment. *Disability and Rehabilitation*, 41(3), 284–292. <https://doi.org/10.1080/09638288.2017.1387292>
- Olatunji, B. O., Davis, M. L., Powers, M. B., & Smits, J. A. J. (2013). Cognitive-behavioral therapy for obsessive-compulsive disorder: A meta-analysis of treatment outcome and moderators. *Journal of Psychiatric Research*, 47(1), 33–41. <https://doi.org/10.1016/j.jpsychires.2012.08.020>
- Ong, C. W., Clyde, J. W., Bluett, E. J., Levin, M. E., & Twohig, M. P. (2016). Dropout rates in exposure with response prevention for obsessive-compulsive disorder: What do the data really say? *Journal of Anxiety Disorders*, 40, 8–17. <https://doi.org/10.1016/j.janxdis.2016.03.006>
- Opriş, D., Pinteş, S., García-Palacios, A., Botella, C., Szamosközi, Ş., & David, D. (2012). Virtual reality exposure therapy in anxiety disorders: A quantitative meta-analysis. *Depression and Anxiety*, 29(2), 85–93. <https://doi.org/10.1002/da.20910>
- Optale, G., Urgesi, C., Busato, V., Marin, S., Piron, L., Priftis, K., Gamberini, L., Capodieci, S., & Bordin, A. (2010). Controlling memory impairment in elderly adults using virtual

- reality memory training: a randomized controlled pilot study. *Neurorehabilitation and Neural Repair*, 24(4), 348–357. <https://doi.org/10.1177/1545968309353328>
- Öst, L.-G., Havnen, A., Hansen, B., & Kvale, G. (2015). Cognitive behavioral treatments of obsessive–compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. *Clinical Psychology Review*, 40, 156–169. <https://doi.org/10.1016/j.cpr.2015.06.003>
- Pallavicini, F., Cipresso, P., Raspelli, S., Grassi, A., Serino, S., Vigna, C., Triberti, S., Villamira, M., Gaggioli, A., & Riva, G. (2013). Is virtual reality always an effective stressors for exposure treatments? Some insights from a controlled trial. *BMC Psychiatry*, 13(1), 52. <https://doi.org/10.1186/1471-244X-13-52>
- Pani, J. R., Chariker, J. H., Dawson, T. E., & Johnson, N. (2005). Acquiring new spatial intuitions: Learning to reason about rotations. *Cognitive Psychology*, 51(4), 285–333. <https://doi.org/10.1016/j.cogpsych.2005.06.002>
- Parsons, T. D., & McMahan, T. (2017). An initial validation of the Virtual Environment Grocery Store. *Journal of Neuroscience Methods*, 291, 13–19. <https://doi.org/10.1016/j.jneumeth.2017.07.027>
- Parsons, T. D., & Rizzo, A. A. (2008). Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, 39(3), 250–261. <https://doi.org/10.1016/j.jbtep.2007.07.007>
- Pearman, A. (2009). Predictors of subjective memory in young adults. *Journal of Adult Development*, 16(2), 101–107. <https://doi.org/10.1007/s10804-009-9063-1>
- Pelargos, P. E., Nagasawa, D. T., Lagman, C., Tenn, S., Demos, J. V., Lee, S. J., Bui, T. T., Barnette, N. E., Bhatt, N. S., Ung, N., Bari, A., Martin, N. A., & Yang, I. (2017). Utilizing virtual and augmented reality for educational and clinical enhancements in neurosurgery. *Journal of Clinical Neuroscience*, 35, 1–4. <https://doi.org/10.1016/j.jocn.2016.09.002>

- Pelechano, N., Stocker, C., Allbeck, J., & Badler, N. (2008). Being a part of the crowd: Towards validating VR crowds using presence. *Proceedings of the International Joint Conference on Autonomous Agents and Multiagent Systems, 1*, 136–142.
https://www.researchgate.net/publication/221455524_Being_a_Part_of_the_Crowd_Towards_Validating_VR_Crowds_Using_Presence
- Pelissolo, A., Zaoui, M., Aguayo, G., Yao, S. N., Roche, S., Ecochard, R., Gueyffier, F., Pull, C., Berthoz, A., & Jouvent, R. (2012). Virtual reality exposure therapy versus cognitive behavior therapy for panic disorder with agoraphobia: A randomized comparison study. *Journal of Cybertherapy Rehabilitation*, 5(1), 35–42.
<https://www.researchgate.net/publication/233997242>
- Pence, S. L., Ph, D., Sulkowski, M. L., Ed, M., Jordan, C., Ed, M., Storch, E. A., & Ph, D. (2010). When Exposures Go Wrong: Trouble- Shooting Guidelines for Managing Difficult Scenarios that Arise in Exposure-Based Treatment for Obsessive-Compulsive Disorder. *American Journal of Psychotherapy*, 64(1), 39–53.
<https://doi.org/10.1176/appi.psychotherapy.2010.64.1.39>
- Persa, G., Török, Á., Galambos, P., Sulykos, I., Kecskés-Kovács, K., Czigler, I., Honbolygó, F., Baranyi, P., & Csépe, V. (2014). Experimental framework for spatial cognition research in immersive virtual space. *2014 5th IEEE Conference on Cognitive Infocommunications (CogInfoCom)*, 587–593.
<https://doi.org/10.1109/CogInfoCom.2014.7020412>
- Powers, M. B., & Emmelkamp, P. M. G. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders*, 22(3), 561–569.
<https://doi.org/10.1016/j.janxdis.2007.04.006>
- Powers, M. B., Smits, J. A. J., Leyro, T. M., & Otto, M. W. (2006). Translational Research Perspectives on Maximizing the Effectiveness of Exposure Therapy. In D. S. C. Richard

- & D. L. Lauterbach (Eds.), *Handbook of Exposure Therapies* (pp. 109–126). Academic Press. <https://doi.org/10.1016/B978-012587421-2/50005-3>
- Pratt, D. R., Zyda, M., & Kelleher, K. (1995). Virtual reality: in the mind of the beholder. *Computer*, 28(7), 17–19.
- Price, M., Anderson, P., Henrich, C. C., & Rothbaum, B. O. (2008). Greater expectations: using hierarchical linear modeling to examine expectancy for treatment outcome as a predictor of treatment response. *Behavior Therapy*, 39(4), 398–405. <https://doi.org/10.1016/j.beth.2007.12.002>
- Proctor, E. K., Landsverk, J., Aarons, G., Chambers, D., Glisson, C., & Mittman, B. (2009). Implementation Research in Mental Health Services: an emerging science with conceptual, methodological, and training challenges. *Administration and Policy in Mental Health and Mental Health Services Research*, 36(1), 24–34. <https://doi.org/10.1007/s10488-008-0197-4>
- Proctor, E. K., Silmere, H., Raghavan, R., Hovmand, P., Aarons, G., Bunger, A., Griffey, R., & Hensley, M. (2011). Outcomes for implementation research: Conceptual distinctions, measurement challenges, and research agenda. *Administration and Policy in Mental Health and Mental Health Services Research*, 38(2), 65–76. <https://doi.org/10.1007/s10488-010-0319-7>
- Qualtrics. (2005). *Qualtrics* (June 2018). <https://www.qualtrics.com>
- Rachman, S. (1997). A cognitive theory of obsessions. *Behaviour Research and Therapy*, 35(9), 793–802. [https://doi.org/10.1016/S0005-7967\(97\)00040-5](https://doi.org/10.1016/S0005-7967(97)00040-5)
- Rachman, S. (1998). A cognitive theory of obsessions: elaborations. *Behaviour Research and Therapy*, 36, 385–401. [https://doi.org/10.1016/S0005-7967\(97\)10041-9](https://doi.org/10.1016/S0005-7967(97)10041-9)
- Rachman, S., De Silva, P., & Roper, G. (1976). The Spontaneous Decay of Compulsive Urges. *Behaviour Research and Therapy*, 14(6), 445–453. <https://doi.org/10.1016/0005->

7967(76)90091-7

- Rachman, S., Shafran, R., Radomsky, A. S., & Zysk, E. (2011). Reducing contamination by exposure plus safety behaviour. *Journal of Behavior Therapy and Experimental Psychiatry*, 42(3), 397–404. <https://doi.org/10.1016/j.jbtep.2011.02.010>
- Radomsky, A. S., & Rachman, S. (2004). Symmetry, ordering and arranging compulsive behaviour. *Behaviour Research and Therapy*, 42(8), 893–913. <https://doi.org/10.1016/j.brat.2003.07.001>
- Rapp, A. M., Bergman, R. L., Piacentini, J., & McGuire, J. F. (2016). Evidence-Based Assessment of Obsessive–Compulsive Disorder. *Journal of Central Nervous System Disease*, 8, JCNSD.S38359. <https://doi.org/10.4137/jcnsd.s38359>
- Realpe, A., Elahi, F., Bucci, S., Birchwood, M., Vlaev, I., Taylor, D., & Thompson, A. (2020). Co-designing a virtual world with young people to deliver social cognition therapy in early psychosis. *Early Intervention in Psychiatry*, 14(1), 37–43. <https://doi.org/10.1111/eip.12804>
- Reger, G. M., Holloway, K. M., Candy, C., Rothbaum, B. O., Difede, J., Rizzo, A. A., & Gahm, G. A. (2011). Effectiveness of virtual reality exposure therapy for active duty soldiers in a military mental health clinic. *Journal of Traumatic Stress*, 24(1), 93–96. <https://doi.org/10.1002/jts.20574>
- Reid, L. M., & MacLulich, A. M. J. (2006). Subjective memory complaints and cognitive impairment in older people. *Dementia and Geriatric Cognitive Disorders*, 22(5–6), 471–485. <https://doi.org/10.1159/000096295>
- Repetto, C., Gaggioli, A., Pallavicini, F., Cipresso, P., Raspelli, S., & Riva, G. (2013). Virtual reality and mobile phones in the treatment of generalized anxiety disorders: A phase-2 clinical trial. *Personal and Ubiquitous Computing*, 17(2), 253–260. <https://doi.org/10.1007/s00779-011-0467-0>

- Repetto, C., Gorini, A., Algeri, D., Vigna, C., Gaggioli, A., & Riva, G. (2009). The use of biofeedback in clinical virtual reality: The intrepid project. *Annual Review of CyberTherapy and Telemedicine*, 7(1), 128–132. <https://doi.org/10.3233/978-1-60750-017-9-128>
- Riva, G. (2005). Virtual Reality in Psychotherapy: Review. *CyberPsychology & Behavior*, 8(3), 220–230. <https://doi.org/10.1089/cpb.2005.8.220>
- Riva, G. (2009). Virtual reality: an experiential tool for clinical psychology. *British Journal of Guidance & Counselling*, 37(3), 337–345. <https://doi.org/10.1080/03069880902957056>
- Riva, G., Molinari, E., & Vincelli, F. (2002). Interaction and presence in the clinical relationship: Virtual reality (VR) as communicative medium between patient and therapist. *IEEE Transactions on Information Technology in Biomedicine*, 6(3), 198–205. <https://doi.org/10.1109/TITB.2002.802370>
- Rizzo, A. A., Difede, J., Rothbaum, B. O., Reger, G., Spitalnick, J., Cukor, J., & McLay, R. (2010). Development and early evaluation of the Virtual Iraq/Afghanistan exposure therapy system for combat-related PTSD. *Annals of the New York Academy of Sciences*, 1208(1), 114–125. <https://doi.org/10.1111/j.1749-6632.2010.05755.x>
- Rizzo, A. A., Hartholt, A., Grimani, M., Leeds, A., & Liewer, M. (2014). Virtual Reality Exposure Therapy for Combat-Related Posttraumatic Stress Disorder. *Computer*, 47(7), 31–37. <https://doi.org/10.1109/MC.2014.199>
- Rizzo, A. A., Schultheis, M., Kerns, K. A., Mateer, C., Rizzo, A. A., Schultheis, M., Kerns, K. A., & Mateer, C. (2004). Analysis of assets for virtual reality applications in neuropsychology. *Neuropsychological Rehabilitation*, 14(1–2), 207–239. <https://doi.org/10.1080/09602010343000183>
- Rizzo, A. A., Schultheis, M. T., & Rothbaum, B. O. (2003). Ethical Issues for the Use of Virtual Reality in the Psychological Sciences. In S. S. Bush & M. L. Drexler (Eds.), *Ethical Issues*

- in Clinical Neuropsychology* (pp. 243–280). Swets & Zeitlinger Publishers.
<http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.519.617&rep=rep1&type=pdf>
- Rolnick, A., & Lubow, R. E. (1991). Why is the driver rarely motion sick? The role of controllability in motion sickness. *Ergonomics*, 34(7), 867–879.
<https://doi.org/10.1080/00140139108964831>
- Roper, G., Rachman, S., & Hodgson, R. (1973). An experiment on obsessional checking. *Behaviour Research and Therapy*, 11(3), 271–277. [https://doi.org/10.1016/0005-7967\(73\)90003-X](https://doi.org/10.1016/0005-7967(73)90003-X)
- Rosa-Alcázar, A. I., Sánchez-Meca, J., Gómez-Conesa, A., & Marín-Martínez, F. (2008). Psychological treatment of obsessive-compulsive disorder: A meta-analysis. *Clinical Psychology Review*, 28(8), 1310–1325. <https://doi.org/10.1016/j.cpr.2008.07.001>
- Rose, F. D., Brooks, B. M., & Rizzo, A. A. (2005). Virtual reality in brain damage rehabilitation: review. *Cyberpsychology and Behavior*, 8(3), 241–271.
<https://doi.org/10.1089/cpb.2005.8.241>
- Rothbaum, B. O. (2005). Commentary on Riva, G. *CyberPsychology & Behavior*, 8(3), 239–240.
- Rothbaum, B. O., Anderson, P., Zimand, E., Hodges, L., Lang, D., & Wilson, J. (2006). Virtual reality exposure therapy and standard (in vivo) exposure therapy in the treatment of fear of flying. *Behavior Therapy*, 37, 80–90. <https://doi.org/10.1016/j.beth.2005.04.004>
- Ruscio, A. M., Stein, D. J., Chiu, W. T., & Kessler, R. C. (2010). The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. *Molecular Psychiatry*, 15, 53–63. <https://doi.org/10.1038/mp.2008.94>
- Saleh, C., & Fontaine, D. (2015). Deep Brain Stimulation for Psychiatric Diseases: What Are the Risks? *Current Psychiatry Reports*, 17(5). [https://doi.org/10.1007/s11920-015-0565-](https://doi.org/10.1007/s11920-015-0565-1)

- Salkovskis, P. M. (1985). Obsessional-Compulsive Problems: a Cognitive-Behavioural Analysis. *Behaviour Research and Therapy*, 23(5), 571–583. [https://doi.org/10.1016/0005-7967\(85\)90105-6](https://doi.org/10.1016/0005-7967(85)90105-6)
- Salkovskis, P. M. (1991). The Importance of Behaviour in the Maintenance of Anxiety and Panic: A Cognitive Account. *Behavioural Psychotherapy*, 19, 6–19. <https://doi.org/10.1017/S0141347300011472>
- Salkovskis, P. M., & Kirk, J. (1999). Obsessive-compulsive disorder. In D. M. Clark & C. G. Fairburn (Eds.), *Science and practice of cognitive behaviour therapy* (pp. 179–208). Oxford University Press. <https://doi.org/10.1093/med:psych/9780192627254.001.0001>
- Sallnäs, E.-L., Rasmussen-Gröhn, K., & Sjöström, C. (2000). Supporting Presence in Collaborative Environments by Haptic Force Feedback. *ACM Transactions on Computer-Human Interaction*, 7(4), 461–476. <https://doi.org/10.1145/365058.365086>
- Sanchez-Vives, M. V., & Slater, M. (2005). From presence to consciousness through virtual reality. *Nature Reviews Neuroscience*, 6(4), 332–339. <https://doi.org/10.1038/nrn1651>
- Schruers, K., Koning, K., Luermans, J., Haack, M. J., & Griez, E. (2005). Obsessive-compulsive disorder: A critical review of therapeutic perspectives. *Acta Psychiatrica Scandinavica*, 111(4), 261–271. <https://doi.org/10.1111/j.1600-0447.2004.00502.x>
- Schuemie, M. J. (2003). *Human-Computer Interaction and Presence in Virtual Reality Exposure Therapy*.
- Schwartzman, D., Segal, R., & Drapeau, M. (2012). Perceptions of virtual reality among therapists who do not apply this technology in clinical practice. *Psychological Services*, 9(3), 310–315. <https://doi.org/10.1037/a0026801>
- Shaffer, F., & Ginsberg, J. P. (2017). An Overview of Heart Rate Variability Metrics and Norms. *Frontiers in Public Health*, 5, 1–17. <https://doi.org/10.3389/fpubh.2017.00258>
- Shafran, R. (2005). Cognitive-behavioural models of OCD. In J. S. Abramowitz & A. C. Houts

- (Eds.), *Concepts and controversies in obsessive-compulsive disorder* (1st ed., pp. 229–260). Springer-Verlag New York. <https://doi.org/10.1007/b101087>
- Sharples, S., Cobb, S., Moody, A., & Wilson, J. R. (2008). Virtual reality induced symptoms and effects (VRISE): Comparison of head mounted display (HMD), desktop and projection display systems. *Displays*, 29(2), 58–69. <https://doi.org/10.1016/j.displa.2007.09.005>
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). 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. *Journal of Clinical Psychiatry*, 59(SUPPL. 20), 22–33.
- Simpson, H. B., Foa, E. B., Liebowitz, M. R., Ledley, D. R., Huppert, J. D., Cahill, S., Vermes, D., Schmidt, A. B., Hembree, E., Franklin, M., Campeas, R., Hahn, C.-G., & Petkova, E. (2008). A randomized, controlled trial of cognitive-behavioural therapy for augmenting pharmacotherapy in obsessive-compulsive disorder. *The American Journal of Psychiatry*, 165(5), 621–630. <https://doi.org/10.1176/appi.ajp.2007.07091440>
- Simpson, H. B., Huppert, J. D., Petkova, E., Foa, E. B., & Liebowitz, M. R. (2006). Response versus remission in obsessive-compulsive disorder. *Journal of Clinical Psychiatry*, 67(2), 269–276. <https://doi.org/10.4088/JCP.v67n0214>
- Simpson, H. B., Maher, M., Page, J. R., Gibbons, C. J., Franklin, M. E., & Foa, E. B. (2010). Development of a Patient Adherence Scale for Exposure and Response Prevention Therapy. *Behavior Therapy*, 41(1), 30–37. <https://doi.org/10.1016/j.beth.2008.12.002>
- Simpson, H. B., Zuckoff, A., Page, J. R., Franklin, M. E., & Foa, E. B. (2008). Adding motivational interviewing to exposure and ritual prevention for obsessive-compulsive disorder: An open pilot trial. *Cognitive Behaviour Therapy*, 37(1), 38–49.

- <https://doi.org/10.1080/16506070701743252>
- Slade, T., Johnston, A., Teesson, M., Whiteford, H., Burgess, P., Pirkis, J., & Saw, S. (2009). *The Mental Health of Australians 2. Report on the 2007 National Survey of Mental Health and Wellbeing* (pp. 23–28). [https://www.health.gov.au/internet/main/publishing.nsf/Content/A24556C814804A99CA257BF0001CAC45/\\$File/mha25.pdf](https://www.health.gov.au/internet/main/publishing.nsf/Content/A24556C814804A99CA257BF0001CAC45/$File/mha25.pdf)
- Slater, M., Usoh, M., & Steed, A. (1995). Taking steps: the influence of a walking technique on presence in virtual reality. *ACM Transactions on Computer-Human Interaction*, 2(3), 201–219. <https://doi.org/10.1145/210079.210084>
- Sookman, D., & Pinard, G. (2002). Overestimation of Threat and Intolerance of Uncertainty in Obsessive Compulsive Disorder. In R. O. Frost & G. Steketee (Eds.), *Cognitive approaches to obsessions and compulsions* (1st ed., pp. 63–89). Pergamon. <https://www.elsevier.com/books/cognitive-approaches-to-obsessions-and-compulsions/frost/978-0-08-043410-0>
- Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Consulting Psychologists Press.
- Stanley, M. A., & Turner, S. M. (1995). Current status of pharmacological and behavioral treatment of obsessive-compulsive disorder. *Behavior Therapy*, 26(1), 163–186. [https://doi.org/10.1016/S0005-7894\(05\)80089-9](https://doi.org/10.1016/S0005-7894(05)80089-9)
- Tabachnick, B. G., & Fidell, L. S. (2007). *Using Multivariate Statistics* (6th ed.). Pearson.
- Tarr, M. J., & Warren, W. H. (2002). Virtual reality in behavioral neuroscience and beyond. *Nature Neuroscience*, 5, 1089–1092. <https://doi.org/10.1038/nn948>
- Teo, W. P., Muthalib, M., Yamin, S., Hendy, A. M., Bramstedt, K., Kotsopoulos, E., Perrey, S., & Ayaz, H. (2016). Does a combination of virtual reality, neuromodulation and neuroimaging provide a comprehensive platform for neurorehabilitation? - A narrative

- review of the literature. *Frontiers in Human Neuroscience*, 10, 1–15.
<https://doi.org/10.3389/fnhum.2016.00284>
- The Australian Psychological Society. (2010). *Evidence-based Psychological Interventions in the Treatment of Mental Disorders: A Literature Review (Third Edition)*.
- The Australian Psychological Society. (2018). *Evidence-based psychological interventions in the treatment of mental disorders: A review of the literature (Fourth Edition)*.
- Thomson, C., Segrave, R., Gardner, J., & Carter, A. (2018). Patients' Weighing of the Long-Term Risks and Consequences Associated With Deep Brain Stimulation in Treatment-Resistant Depression. *AJOB Neuroscience*, 9(4), 243–245.
<https://doi.org/10.1080/21507740.2018.1561542>
- Tolin, D. F., Abramowitz, J. S., Brigidi, B. D., & Foa, E. B. (2003). Intolerance of uncertainty in obsessive-compulsive disorder. *Anxiety Disorders*, 17(2), 233–242.
[https://doi.org/10.1016/S0887-6185\(02\)00182-2](https://doi.org/10.1016/S0887-6185(02)00182-2)
- Usoh, M., Arthur, K., Whitton, M. C., Bastos, R., Steed, A., Slater, M., & Brooks, F. P. (1999). Walking > walking-in-place > flying, in virtual environments. *Proceedings of the 26th Annual Conference on Computer Graphics and Interactive Techniques*, 359–364.
<https://doi.org/10.1145/311535.311589>
- Valderhaug, R., Larsson, B., Götestam, K. G., & Piacentini, J. (2007). An open clinical trial of cognitive-behaviour therapy in children and adolescents with obsessive-compulsive disorder administered in regular outpatient clinics. *Behaviour Research and Therapy*, 45(3), 577–589. <https://doi.org/10.1016/j.brat.2006.04.011>
- Van Bennekom, M. J., Kasanmoentalib, M. S., De Koning, P. P., & Denys, D. (2017). A Virtual Reality Game to Assess Obsessive-Compulsive Disorder. *Cyberpsychology, Behavior, and Social Networking*, 20(11), 718–722. <https://doi.org/10.1089/cyber.2017.0107>
- van den Heuvel, O. A., Remijnse, P. L., Mataix-Cols, D., Vrenken, H., Groenewegen, H. J.,

- Uylings, H. B. M., Balkom, A. J. L. M. Van, & Veltman, D. J. (2009). The major symptom dimensions of obsessive-compulsive disorder are mediated by partially distinct neural systems. *Brain*, *132*, 853–868. <https://doi.org/10.1093/brain/awn267>
- Van Den Hout, M. A., Engelhard, I. M., Toffolo, M. B. J., & Van Uijen, S. L. (2011). Exposure plus response prevention versus exposure plus safety behaviours in reducing feelings of contamination, fear, danger and disgust. An extended replication of Rachman, Shafran, Radomsky & Zysk (2011). *Journal of Behavior Therapy and Experimental Psychiatry*, *42*(3), 364–370. <https://doi.org/10.1016/j.jbtep.2011.02.009>
- Vaswani, M., Linda, F. K., & Ramesh, S. (2003). Role of selective serotonin reuptake inhibitors in psychiatric disorders: A comprehensive review. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *27*(1), 85–102. [https://doi.org/10.1016/S0278-5846\(02\)00338-X](https://doi.org/10.1016/S0278-5846(02)00338-X)
- Veldhuis, J., Dieleman, J. P., Wohlfarth, T., Storosum, J. G., Brink, W. Van Den, Sturkenboom, M. C. J. M., Denys, D., Veldhuis, J., Dieleman, J. P., Wohlfarth, T., & Storosum, J. G. (2012). Incidence and prevalence of “ diagnosed OCD ” in a primary care, treatment seeking, population. *International Journal of Psychiatry in Clinical Practice*, *16*(2), 85–92. <https://doi.org/10.3109/13651501.2011.617454>
- Wallach, H. S., Safir, M. P., & Bar-Zvi, M. (2009). Virtual reality cognitive behavior therapy for public speaking anxiety: A randomized clinical trial. *Behavior Modification*, *33*(3), 314–338. <https://doi.org/10.1177/0145445509331926>
- Walshe, D. G., Lewis, E. J., Kim, S. I., O’Sullivan, K., & Wiederhold, B. K. (2003). Exploring the use of computer games and virtual reality in exposure therapy for fear of driving following a motor vehicle accident. *Cyberpsychology and Behavior*, *6*(3), 329–334. <https://doi.org/10.1089/109493103322011641>
- Weissman, M. M. (1998). Cross-National Epidemiology of Obsessive-Compulsive Disorder.

- CNS Spectrums*, 3(5), 6–9. <https://doi.org/10.1017/S1092852900007136>
- Wheaton, M. G., & Chen, S. R. (2020). Homework Completion in Treating Obsessive–Compulsive Disorder with Exposure and Ritual Prevention: A Review of the Empirical Literature. *Cognitive Therapy and Research*, 0123456789. <https://doi.org/10.1007/s10608-020-10125-0>
- Wiederhold, B. K., & Bouchard, S. (2014). Advances in virtual reality and anxiety disorders. In *Advances in virtual reality and anxiety disorders. Series in anxiety and related disorders*. [https://doi.org/10.1016/S1571-5078\(08\)00422-4](https://doi.org/10.1016/S1571-5078(08)00422-4)
- Wiederhold, B. K., Jang, D. P., Kim, S. I., & Wiederhold, M. D. (2002). Physiological monitoring as an objective tool in virtual reality therapy. *Cyberpsychology and Behavior*, 5(1), 77–82. <https://doi.org/10.1089/109493102753685908>
- Wiederhold, B. K., & Wiederhold, M. D. (2000). Lessons Learned From 600 Virtual Reality Sessions. *CyberPsychology & Behavior*, 3(3), 393–400. <https://doi.org/10.1089/10949310050078841>
- Wiener, J. M., Carroll, D., Moeller, S., Bibi, I., Ivanova, D., Allen, P., & Wolbers, T. (2020). A novel virtual-reality-based route-learning test suite: Assessing the effects of cognitive aging on navigation. *Behavior Research Methods*, 52(2), 630–640. <https://doi.org/10.3758/s13428-019-01264-8>
- Wilhelm, F. H., Kochar, A. S., Roth, W. T., & Gross, J. J. (2001). Social anxiety and response to touch: Incongruence between self-evaluative and physiological reactions. *Biological Psychology*, 58(3), 181–202. [https://doi.org/10.1016/S0301-0511\(01\)00113-2](https://doi.org/10.1016/S0301-0511(01)00113-2)
- Wilhelm, F. H., Pfaltz, M. C., Gross, J. J., Mauss, I. B., Kim, S. I., & Wiederhold, B. K. (2005). Mechanisms of virtual reality exposure therapy: The role of the behavioral activation and behavioral inhibition systems. *Applied Psychophysiology Biofeedback*, 30(3), 271–284. <https://doi.org/10.1007/s10484-005-6383-1>

- Williams, M. T., Mugno, B., Franklin, M., & Faber, S. (2013). Symptom dimensions in obsessive-compulsive disorder: Phenomenology and treatment outcomes with exposure and ritual prevention. *Psychopathology*, 46(6), 365–376.
<https://doi.org/10.1159/000348582>
- Wilson, C. J., Soranzo, A., & Sheffield, S. (2015). The Use of Virtual Reality in Psychology : A Case Study in Visual Perception. *Computational AndMathematicalMethods InMedicine*, 2015. <https://doi.org/10.1155/2015/151702>
- Wolpe, J. (1973). *The practice of behavior therapy*. Pergamon.
- Woody, S. R., & Teachman, B. A. (2000). Intersection of Disgust and Fear: Normative and Pathological Views. *Clinical Psychology: Science and Practice*, 7(3), 291–311.
<https://doi.org/10.1093/clipsy.7.3.291>
- World Health Organization. (2008). *Global Burden of Disease 2004 Update: Disability Weights for Diseases and Conditions*.
- World Health Organization. (2019). *The International Classification of Diseases* (11th ed.). World Health Organization.
- Wrzesien, M., Bretón-López, J., Botella, C., Burkhardt, J. M., Alcañiz, M., Pérez-Ara, M. Á., & Del Amo, A. R. (2013). How technology influences the therapeutic process: Evaluation of the patient-therapist relationship in augmented reality exposure therapy and in vivo exposure therapy. *Behavioural and Cognitive Psychotherapy*, 41(4), 505–509.
<https://doi.org/10.1017/S1352465813000088>
- Wrzesien, M., Burkhardt, J. M., Botella, C., & Alcañiz, M. (2015). Towards a Virtual Reality- and Augmented Reality-Mediated Therapeutic Process model: a theoretical revision of clinical issues and HCI issues. *Theoretical Issues in Ergonomics Science*, 16(2), 124–153.
<https://doi.org/10.1080/1463922X.2014.903307>
- Yamaguchi, T., Foloppe, D. A., Richard, P., Richard, E., & Allain, P. (2012). A dual-modal

- virtual reality kitchen for (re)learning of everyday cooking activities in Alzheimer's disease. *Presence: Teleoperators and Virtual Environments*, 21(1), 43–57.
https://doi.org/10.1162/PRES_a_00080
- Yellowlees, P. M., Holloway, K. M., & Parish, M. B. (2012). Therapy in virtual environments- clinical and ethical issues. *Telemedicine and E-Health*, 18(7), 558–564.
<https://doi.org/10.1089/tmj.2011.0195>
- Zhao, Y. C., Kennedy, G., Yukawa, K., Pyman, B., & Stephen O'Leary. (2011). Can virtual reality simulator be used as a training aid to improve cadaver temporal bone dissection? Results of a randomized blinded control trial. *The Laryngoscope*, 121(4), 831–837.
<https://doi.org/10.1002/lary.21287>