Approaches to Elicit and Attenuate Conditional Reinstatement of Fear for Specific Phobia

Kirra A. Krisch

BPsych (Hons)

School of Applied Psychology

Griffith Health

Griffith University, Gold Coast

Submitted in fulfilment of the requirements of the degree of Doctor of Philosophy in Clinical Psychology.

Submitted: December 2021

Principal Supervisor: Professor David Neumann

Associate Supervisor: Dr Mark Boschen

External Supervisor: Dr Siavash Bandarian-Balooch

Abstract

Exposure therapy is considered the most effective treatment for many of the anxiety disorders including specific phobia. Despite this, following successful exposure therapy many individuals experience return of fear symptoms. The return of fear following exposure therapy suggests that extinction does not result in a permanent unlearning of associations between a conditional stimuli (CS) and an unconditional stimuli (US). Reinstatement of fear is one proposed mechanism for return of fear. A standard reinstatement procedure involves a CS paired with an US during acquisition, the CS is presented alone during extinction, the US is presented without the CS in reinstatement, and then followed by test trials of the CS. Reinstatement of fear is observed in test. While there are extensive laboratory-based studies demonstrating reinstatement of fear, there is limited clinical research on the conditions that might elicit and attenuate the reinstatement effect. Re-exposure to aversive stimuli (e.g., pain) in a standard reinstatement procedure with fearful individuals could be considered an ethical problem due to the potential for causing harm and distress. It is common for individuals suffering from specific phobia to have multiple phobias, with approximately 75% of individuals fear more than one object or situation. There is limited research investigating individuals with multiple phobias. Furthermore, an unextinguished CS has elicited reinstatement of fear with rats termed conditional reinstatement, which potentially suggests that an untreated fear can elicit reinstatement of fear in clinical populations. Accordingly, the current thesis had three main aims. Firstly, to investigate whether an unextinguished CS will elicit reinstatement of fear. Secondly, whether exposure to an unextinguished CS can reduce reinstatement of fear. Thirdly, to extend the translational nature and

generalisability of the reinstatement research by conducting a laboratory-based experiment, a clinical-analogue experiment, and a case study intervention. In addressing these aims, the first experiment involved a laboratory-based learning task in virtual reality with 360 degree footage of a golden orb weaver (e.g., CS extinguished), a fancy rat (e.g., CS unextinguished) and a water python (e.g., CS -) with non-clinical participants ($N = 93$). The results showed reinstatement of fear can be triggered by an unextinguished CS and subsequent extinction of this unextinguished CS can attenuate reinstatement, as indicated by conditioned heart rate responses and shock expectancy ratings. Reinstatement of fear was not found for the control group. The findings of the first experiment provided the first evidence of how an unextinguished CS elicited and attenuated reinstatement in a non-clinical sample. In translating this finding to fearful individuals, a clinical-analogue experiment was implemented with 50 individuals who experience moderate to high fear towards rats and spiders. Extending the findings of the first study, exposure to an untreated fear reinstated fear to a treated fear and following virtual reality exposure therapy (VRET) attenuated this reinstatement, across subjective units of distress (SUDs), avoidance ratings and conditioned heart rate responses. The third study implemented a case study method with a participant who met criteria for specific phobia of rats and spiders. The purpose of the $N = 1$ design was to test an intervention based on the previous two studies. No reinstatement of fear was found from post-treatment to follow up, as indicated by SUDs ratings, avoidance ratings or conditioned heart rate responses. Overall, the results of the three translational studies demonstrated how exposure to different aversive events can trigger reinstatement and exposure with multifarious stimuli may enhance the long-term effectiveness of exposure

therapy for specific phobia. The clinical implications of the research program include the recommendation to conduct a comprehensive assessment of the number of feared objects and/or situations experienced by the client and to treat each individual fear through VRET or in vivo exposure therapy to reduce the occurrence of conditional reinstatement.

Statement of Originality

This work has not previously been submitted for a degree or diploma to any University. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

Kirra A. Krisch

Table of Contents

List of Tables

List of Figures

Figure 6.3.

Mean Heart Rate Change Scores for the CSext and CSunext across Phases for the MPS, Reinstatement and Control groups (error bars reflect the standard error of the mean)

Chapter 7

Figure 7.1.

SUDS of Maximum Fear Across Pre-treatment Assessments and Post-treatment Assessments and Minimum Fear During Steps of Each Hierarchy in Treatment

Acknowledgments

Firstly I wish to thank my supervisors, Professor David Neumann, Dr Siavash Bandarian and Dr Mark Boschen. Sia, I feel eternally grateful to you for being my mentor, a supervisor, teacher, now colleague and dear friend. Sia, thank you for accepting me unconditionally and your consistent support, no person has shaped my love for learning or journey to become a clinical psychologist more than you. I admire your enthusiasm and encouragement, connection to people, insight into the human psyche and persistence to continually learn and teach. David, thank you for your immense knowledge, guidance and patience, you have been the main contributor to my ability to conduct experimental research and inspire me to express myself with clarity as you always do. I am very appreciative of the dedication you have shown throughout my PhD. Mark, thank you for agreeing to come on board in the final stages of the my PhD, you alleviated my anxiety by knowing I had your encouragement and expertise. Thank you to the co-authors John Zhong and Dr Alex O'Donnell who contributed to some of the publications presented in this thesis. Thank you, John, for your outstanding problem solving abilities on the many technical issues we faced and the kindness you always show me. Alex, I appreciate all the hours we have spent sharing ideas.

I am so grateful to the support my family have provided, Mum, Dad, Kelly and George, thank you for all your care and love and thank you for fostering my love of learning. Thank you Te Rangimarie for all the sacrifices you have made to provide me more time to focus on my PhD, for bringing your whanau into my life and your unwavering love and support has made completing my thesis possible. I wish to acknowledge my fellow PhD friends and candidates for always being there to discuss

ideas and for their encouragement, especially Jared, Matt, Vinny, and Karlee. I am thankful for Lucy, Sarah, Kelly and Ebonie for not only the years you have supported me through my studies especially following the delay of the outbreak of COVID-19 but for the 16 years of friendship. I wish to acknowledge several of my close friends Karli, Tania, Sarah, Monique, Mana-Kura, Marcelo, Mika and Jess for their help with pilot testing, being a sounding board and emotional support.

Finally, I would like to extend my thanks and gratitude to all the participants who faced their fears with me.

Publications in Thesis

Included in this thesis are papers in *Chapters 3, 5, 6 and 7* which are co-authored with other researchers. My contribution to each co-authored paper is outlined at the front of the relevant chapter. The bibliographic details (if published or accepted)/status (if prepared or submitted for publication for these papers including all authors, are:

Chapter 3: Krisch K. A., Bandarian-Balooch S., O'Donnell A. W., & Neumann D. L. (published in 2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. In Z. Hill (Ed.), *Virtual reality: Advances in research and applications* (pp. 85–126). Nova Science.

Chapter 5: Krisch, K. A., Bandarian-Balooch, S., Neumann, D. L., & Zhong, J. (2020). Eliciting and attenuating reinstatement of fear: Effects of an unextinguished CS. *Learning and Motivation*, *71*. https://doi.org/10.1016/j.lmot.2020.101650.

Chapter 6: Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (submitted for publication in 2021). Reinstatement of fear: Immersive virtual reality exposure treatment to multifarious stimuli for individuals with multiple animal fears.

Chapter 7: Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (In preparation). Virtual reality exposure therapy for a case of multiple phobias: Reinstatement of fear.

Kirra A. Krisch

Supervisor: Professor David L. Neumann

Glossary of Terms and Acronyms

ABS	Australian Bureau of Statistics
ADIS-5	Anxiety Disorders Interview Schedule for DSM-5
APA	American Psychiatric Association
AR	Augmented Reality
BAT	Behavioural Avoidance Task
CAS	Clinical Anger Scale
CAVE	Computer Automatic Virtual Environment
CBT	Cognitive Behavioural Therapy
CR	Conditioned Response
CR Group	Conditioned Reinstatement Group
CSR	Clinical Severity Rating
CS	Conditioned Stimulus
CS+	Conditioned Stimulus plus
CS-	Conditioned Stimulus minus
CSext	Extinguished CS
CSunext	Unextinguished CS
DASS-21	Depression Anxiety and Stress Scale version 21
DSM-5	Diagnostic Statistical Manual of Mental Disorders version 5
EEG	Electroencephalogram
ECG	Electrocardiogram
FRQ	Fear of Rats Questionnaire
FSQ	Fear of Spiders Questionnaire

HMD	Head Mounted Display
HR	Heart Rate
MFS	Multiple Feared Stimuli Group
MPS	Multiple Phobic Stimuli Group
OCD	Obsessive-Compulsive Disorder
PTSD	Post-traumatic Stress Disorder
RJPQ	The Reality Judgement and Presence Questionnaire
ROF	Return of Fear
SCID-5	Structured Clinical Interview for DSM-5
SIAS	Social Interaction Anxiety Scale
SNAQ	Snake Anxiety Questionnaire
SPQ	Spider Phobia Questionnaire
SUDS	Subjective Units of Distress
UR Group	Unconditioned Reinstatement Group
US	Unconditioned Stimulus
VRET	Virtual Reality Exposure Therapy
VR	Virtual Reality

Chapter 1: Preamble

The present chapter provides an introduction and overview of the components of the thesis. The chapter introduces a brief background and theoretical underpinnings of the topic and the importance of examining return of fear and reinstatement of fear. An overview of how the aims are addressed across the components of the thesis is also given. The thesis consists of 8 chapters: a brief introduction and overview of the thesis (Chapter 1), a general introduction to anxiety disorders, treatment and reinstatement of fear (Chapter 2), as well as a published book chapter that reviews the literature of virtual reality exposure therapy (VRET) for specific phobia and return of fear (Chapter 3). The following chapter provides the aims of the research project more comprehensively (Chapter 4). The subsequent chapters include three studies. The first is a published journal article describing Experiment 1, which employed non-fearful participants (Chapter 5). The second is a manuscript describing Experiment 2 with moderate to high fearful participants which has been submitted for publication (Chapter 6). The third is a case study with an individual suffering from multiple animal type phobias (Chapter 7). The thesis concludes with the General discussion (Chapter 8).

Chapter 1: Introduction and Thesis Overview

Mental health disorders result in a significant burden at an economic, societal and individual level. The economic burden in the period of 2018-2019 was $10.6 billion in Australia (AIHW, 2021). Moreover, throughout the COVID-19 pandemic in 2020-2021 there has been a rise in both reported psychological distress and the use of mental health services (Aknin et al., 2021). One societal cost is reflected in how mental illness was the largest cause of disability burden in Australia in 2015, accounting for 24.3% of all disabilities (Ciobanu et al., 2018). Mental health disorders can be debilitating for individuals and can result in problems with self-esteem, relationships, employment, and reduced quality of life. Research investigating the long-term effectiveness of psychological treatments is important to reduce the burden associated with mental health disorders.

Globally and in Australia, the most common group of mental health disorders are the anxiety disorders (Australian Bureau of Statistics [ABS], 2019; Stein et al., 2017). Anxiety disorders are characterised by physiological arousal, worry and avoidance. The full range of anxiety disorders include social anxiety disorder, generalised anxiety disorder, health anxiety disorder, selective mutism, separation anxiety disorder, panic disorder, specific phobia, agoraphobia and substance/medication-induced anxiety disorder and anxiety disorder due to another medical condition (American Psychiatric Association [APA], 2013).

Specific phobia is the most prevalent anxiety disorder (Kessler & Wang, 2008; Van Houtem et al., 2013). Specific phobia is marked by persistent fear and avoidance of an object or situation that is out of proportion to the risk of harm the object or situation

poses and leads to impairment in functioning for the individual (APA, 2013). It has been found that 75% of individuals diagnosed with specific phobia meet criteria for more than one phobia (APA, 2013; Wittchen et al., 2002). However, studies typically employ samples of those with only one phobia. Furthermore, it has been found that those with multiple phobias are less likely to recover than those with pure specific phobia (Wittchen et al., 2002). For reasons such as these, research that considers the burden and treatment of individuals with multiple phobias is needed.

Several mechanisms have been proposed to be involved in the development of a specific phobia. Vicarious fear conditioning (Askew & Field, 2007; King et al., 1998; Marin et al., 2020; Rachman, 1977), modelling (Gerull & Rapee, 2002) and direct fear conditioning (Bouton & Bolles, 1979; Pavlov, 1927; Rachman, 1977; Wolpe, 1958) are implicated in the acquisition of fears. A study investigating the acquisition of specific animal phobias in adults demonstrated that 68% of the participants could not recall the acquisition of their phobia, 23% perceived their phobia resulted from an aversive encounter with the animal reflecting fear conditioning and 9% attributed their fears to vicarious and modelling experiences (Menzies & Clark, 1993a).

The acquisition of specific phobia has been explained within a Pavlovian conditioning framework (Pavlov, 1927). The explanation for direct conditioning results from the pairing of a neutral conditioned stimulus (CS; e.g., snake) and an aversive unconditioned stimulus (US; e.g., painful bite). Subsequent presentations of the CS evoke a conditioned fear response (CR; e.g., negative affect, increased heart rate). During this acquisition process, a CS-US association is learnt (Bouton, 2002; Bouton & Bolles, 1979). Extinction of the fear response can occur through repeated presentations of the CS

alone. The magnitude of the CR will diminish across the repeated presentations. Decades of research has supported the Pavlovian learning model of acquisition and extinction of conditioned fear responses (Bouton & Bolles, 1979; Bouton et al., 2006; Forcadell et al., 2017; Laborda et al., 2011; Leer & Engelhard, 2015; Neumann & Longbottom, 2008; Pavlov, 1927; Warren et al., 2014; Wolpe, 1958).

Fear conditioning procedures have been employed to test the process of both acquisition and extinction of fears. In a fear conditioning procedure, typically non-fearful participants are repeatedly presented with a CS+ (e.g., photographs or virtual geometric shapes, faces, spiders) paired with an aversive US (e.g., electric shocks, loud noises). In this acquisition phase, a CS- can be used as a control stimulus (e.g., other neutral stimuli) to assess learning. The CS- is not paired with the US. Participants have been found to demonstrate conditioned fear responses (e.g., CR) to the CS+ and not the CS- on a combination of different fear measures such as heart rate measures (e.g., Bandarian-Balooch et al., 2015; Culver et al., 2011; Matthews et al., 2015; Neumann & Waters, 2006) and self-reported US expectancy ratings (e.g., Bandarian-Balooch & Neumann, 2011; Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Warren et al., 2014).

Extinction involves presenting the feared stimulus (CS; e.g., spider) repeatedly across trials without the US (e.g., painful bite) and typically a reduction in the CR (e.g., fear) is observed. Earlier work suggested that the acquired fear (i.e., CS-US association) is erased during extinction (McClelland & Rumelhart, 1985; McCloskey & Cohen, 1989; Rescorla & Wagner, 1972). However, numerous studies have shown that the CR (e.g., fear) can return following extinction, which suggests that the CS-US association is not erased (Bouton, 2002; Bouton & Bolles, 1979; Bouton et al., 2021; Haesen & Vervliet,

2015; Leer & Engelhard, 2015; Thomas et al., 2009; Warren et al., 2014). The laboratory-based research on extinction provides evidence of the internal validity of the extinction process and mechanisms underlying return of fear, with the intent to inform clinical practice.

In extending the findings from the laboratory, the process of extinction has been translated to exposure therapy in clinical settings under a cognitive-behavioural therapy (CBT) model (Öst, 1989; Wolpe, 1958). Exposure therapy for specific phobia involves gradually presenting the feared object or situation until the fear reduces (Öst, 1989; Wolpe, 1958). The most well supported treatment for specific phobia is exposure therapy (Abramowitz et al., 2012; Craske, 1999; Craske, & Mystkowski, 2006) and this can be delivered in vivo (with real life stimuli), in virtual reality (with virtual stimuli), or imaginal (with imaginary stimuli).

Despite the efficacy of this treatment, many individuals with specific phobia have a relapse of symptoms. Rachman (1966) termed this return of fear. Rachman demonstrated that individuals with specific phobia of spiders who were treated with exposure therapy experienced a relapse of fear 24 hours following treatment. Following this seminal study, laboratory-based, clinical-analogue (e.g., a study conducted with moderately to high fearful samples) and clinical studies (e.g., a sample of those with a diagnosis of specific phobia) have investigated the four mechanisms of return of fear: renewal of fear, spontaneous recovery of fear, reinstatement of fear, re-acquisition of fear and more recently in the instrumental conditioning literature resurgence of fear (see Bouton, 2002; Bouton et al., 2021; and Chapter 2 of this thesis for more detail). Research

on the reinstatement of fear in humans is limited and the current thesis is focused on this mechanism.

Reinstatement of fear involves the demonstration that extinguished fear can be triggered after re-exposure to the original fear (e.g., US; painful spider bite; Pavlov, 1927; Rescorla & Heth, 1975b) or a different stimulus that becomes associated with the fear-eliciting US (Halladay et al., 2012; Rescorla & Heth, 1975b; Sokol & Lovibond, 2012). In a standard reinstatement procedure, a CS is paired with a US during acquisition, the CS is presented alone during extinction, the US is presented without the CS in a reinstatement phase, and finally there are test trials of the CS. Bouton's contextual memory model (Bouton, 1993, 2002, 2004) proposes that extinction does not destroy the CS-US association, but rather a CS-noUS association is learnt during extinction. Bouton proposed that reinstatement of fear occurs due to contextual conditioning involved in the presentation of the aversive stimulus in the reinstatement phase (Bouton, 2004) and the CS-noUS association is retrieved from memory if the reinstatement phase and test is conducted in the same context.

The majority of studies on the reinstatement effect have used laboratory protocols conducted with rats (Bouton & Bolles, 1979; Callen et al., 1984; Halladay et al., 2012; Hendry, 1982; Kim & Richardson, 2007; Rescorla & Heth, 1975b; Taslimi et al., 2018) and non-fearful human participants (Dirikx et al. 2007; Dunsmoor et al., 2014; Hermans et al., 2005; LaBar & Phelps, 2005; Sokol & Lovibond, 2012). The lack of reinstatement studies with clinical-analogue or clinical samples (Mystkowski et al., 2006; Rachman & Whittal, 1989; Shiban et al., 2015) limits the external validity of the reinstatement effect. Ethical and methodological considerations of conducting reinstatement research (e.g.,

presenting participants with a painful bite) have potentially prevented the reinstatement effect being tested with clinical samples (Boschen et al., 2009).

An innovative method by Halladay et al. (2012) demonstrated that presenting rats with an unextinguished CS (e.g., tone) reinstated fear responding to an extinguished CS (e.g., light). The unextinguished CS and extinguished CS were paired with the US in acquisition and the extinguished CS was presented alone in the extinction phase but the unextinguished CS was not presented in the extinction phase. A study that replicates Halladay et al.'s (2012) findings from rats to human participants could provide the opportunity to explore additional research directions and clinical implications. One clinical implication is that an unextinguished CS could translate to an untreated secondary feared object or situation and whether exposure to this secondary fear could reinstate fear to an extinguished primary feared object or situation. In the case that the findings of Halladay et al. (2012) extend to humans, there remains a risk that encountering an untreated fear may elicit reinstatement of fear following successful exposure therapy for a primary fear.

Consistent with this, previous research demonstrates that fear can be reinstated in rats with other aversive stimuli (Rescorla & Heth, 1975b; Sokol & Lovibond, 2012) and there is clinical evidence that following successful exposure therapy for anxiety that encountering aversive events can trigger reinstatement of fear (Jacobs & Nadel, 1985). As previously noted, 75% of individuals diagnosed with specific phobia meet criteria for more than one phobia (Wittchen et al., 2002). Given the importance of the generalisability of research, the current thesis aimed to extend the novel methodology from Halladay et al. (2012) to human participants with multiple fears. Moreover, this

approach will overcome the ethical problems of conducting reinstatement of fear with clinical-analogue and clinical samples. The present thesis further extended prior research by using virtual reality-based exposure to examine potential ways to reduce the reinstatement of fear in humans.

Rationale for Research Program

In summary, return of fear is common for the anxiety disorders including specific phobia. Compared to the other mechanisms of return of fear, reinstatement of fear has not been translated from the laboratory to clinical-analogue and clinical studies. As discussed, the small amount of empirical research with samples of individuals with multiple phobias is problematic. It is more common to be diagnosed with multiple phobias than a single phobia and for those with multiple phobias recovery is less likely (APA, 2013; Wittchen et al., 2002). Thus, understanding return of fear for those with multiple fears is valuable. The clinical implications of Halladay et al.'s (2012) findings of conditional reinstatement could be extended to humans. In extending the findings, an unextinguished CS could translate to an untreated fear triggering reinstatement to a fear successfully treated with exposure therapy (i.e., an extinguished CS). In this case, conditional reinstatement may increase the probability of the occurrence of return of fear. Importantly, no previous researchers have examined whether exposure to an unextinguished CS can elicit and reduce conditional reinstatement of fear. Overall, this leads to the research question of this thesis: *Can an untreated fear reinstate fear that has successfully been treated with exposure-based therapy in individuals with multiple phobias?*

Aims

To address the research question, the current thesis had three main aims. The first aim was to examine whether exposure to an unextinguished CS can elicit reinstatement of fear. The second aim was to determine whether exposure to an unextinguished CS can attenuate reinstatement of fear. The third aim was to extend reinstatement of fear research to human clinical-analogue and clinical samples. The aims of the thesis are addressed in Chapter 2 and Chapter 3 which together provide literature reviews on reinstatement research, a laboratory-based experiment with non-fearful participants (Chapter 4), a clinical-analogue study with those with a moderate to high fear of spiders and rats (Chapter 5), and an $N = 1$ case study with an individual suffering from multiple animal phobias (Chapter 6) and the general discussion which summarises the research project (Chapter 7). An overview for the components of the thesis and how the aims will be addressed is discussed next.

Overview of Chapter 2: Anxiety Disorders, Treatment and Return of Fear

Chapter 2 provides a literature review across the anxiety disorders, their treatment and the reinstatement of fear. The anxiety disorders, including specific phobia, are discussed in more depth than the current chapter and the number of different phobic objects and/or situations an individual fears is discussed as an important factor in research and treatment. The chapter highlights the mechanisms of acquisition, extinction and return of fear from a Pavlovian conditioning model (Pavlov, 1927) and Bouton's contextual memory model (Bouton, 1993, 2002, 2004). The laboratory-based reinstatement literature is reviewed and the lack of ecological validity is highlighted. Subsequently, the clinical-analogue and clinical reinstatement research is examined and the implications of the scarcity of this research are provided. It is noted that ethical

considerations could have hindered translating laboratory-based reinstatement findings to clinical research. Studies with more innovative approaches are discussed to overcome this problem including Halladay et al.'s (2012) finding of conditional reinstatement and how virtual reality technology could be a useful methodology to adopt in the present research. Specific theoretical and clinical implications for conditional reinstatement and the process of attenuation are reviewed.

Overview of Chapter 3: A Review of Virtual Reality Exposure Therapy for Specific Phobia and its Clinical Application to Reduce Return of Fear

Chapter 3 is a published book chapter which provides a literature review for VRET for treating specific phobia and attenuating return of fear. The theoretical background of exposure therapy, return of fear and challenges of traditional exposure-based treatments (i.e., in vivo and imaginal exposure) are discussed. The literature on VRET compared to traditional exposure-based treatments for return of fear is reviewed and the benefits of VRET for specific phobia include: it is seen as a more acceptable form of treatment to clients and it can be more feasible for difficult to obtain objects/situations and for multiple phobias. Presence, immersion and interactivity of virtual reality technology and the application of VRET to return of fear research is also considered.

A literature search for studies evaluating the effectiveness of VRET to reduce return of fear for specific phobia was conducted and 12 studies were used as the basis for the literature review. The review found that further research is needed to establish if VRET is equivalent to in vivo exposure in maintaining long-term treatment gains for specific phobia. In considering the use of VRET in clinical-analogue and clinical studies,

it also highlighted that spontaneous recovery and renewal of fear have received more attention than reinstatement and reacquisition of fear. Furthermore, the review indicated that VRET could be an effective methodology to overcome the ethical challenges associated with reinstatement of fear by providing an alternative modality to present reinstating stimuli. The book chapter explores the clinical implications for the use of VRET and provides future research directions for VRET in reducing return of fear for specific phobia.

Overview of Chapter 4: Overview of the Aims the Empirical Studies

Given that Chapters 5, 6 and 7 comprise the empirical work of the thesis and the preceding chapter provides a broader literature review of VRET for specific phobia to reduce the return of fear, the purpose of Chapter 4 is to provide a comprehensive explanation of the aims of the research project. Chapter 4 highlights the key findings from the literature review in Chapter 3 and provides a concise overview of the design, samples, measures and analyses of the three studies.

Overview of Chapter 5: Eliciting and attenuating reinstatement of fear: Effects of an unextinguished CS (Study 1).

The ethical considerations in conducting reinstatement of fear with clinical samples has hindered the translation of laboratory-based findings with rats to non-fearful human participants and to clinical research (Boschen et al., 2009). Understanding the key mechanisms underlying return of fear in experimentally controlled conditions with rats and non-fearful participants is the first step to be able to determine whether these methods can enhance the long-term effectiveness of exposure therapy (Bandarian-Balooch et al., 2013; Boschen et al., 2009). The finding that an unextinguished CS can

trigger reinstatement of fear with rats (Halladay et al., 2012) could be translated to how untreated fears could trigger reinstatement of fear with humans. Chapter 5 presents the first empirical study of the thesis. The first experiment addressed the first and second aims by examining whether an unextinguished CS can elicit reinstatement of fear to an extinguished CS and whether extinction to the unextinguished CS can attenuate reinstatement. Chapter 5 also addresses the third aim by extending findings from laboratory-based studies with rats (Halladay et al., 2012; Rescorla & Heth, 1975b) to human non-fearful participants.

A sample of 93 undergraduate psychology non-fearful participants were presented with 360 degree virtual reality footage of an extinguished CS (e.g., golden orb weaver) and an unextinguished CS (e.g., water python) both previously paired with a US (e.g., electro-tactile stimulus). In addition, a CS- (e.g., brown fancy rat) was presented alone. Shock expectancy ratings and conditioned heart rate responses were used as dependent measures. The findings from the study showed that reinstatement of fear can be elicited by an unextinguished CS. Moreover, the finding suggested that extinction to this unextinguished CS can reduce reinstatement in the sample of non-fearful human participants. The generalisability of this study to clinical settings is limited due to employing a non-fearful sample. To extend the translational nature of the project subsequent studies used more clinically relevant samples.

Overview of Chapter 6: Reinstatement of fear: Immersive virtual reality exposure treatment to multifarious stimuli for individuals with multiple animal fears (Study 2)

In comparison to the other mechanisms of return of fear, the focus on reinstatement research with clinical-analogue or clinical samples with specific phobia has been scarce (Mystkowski et al., 2006; Rachman & Whittal, 1989; Shiban et al., 2015). Translational reinstatement research from laboratory-based studies to clinical-analogue designs with relevant samples are integral to increase the generalisability and long-term effectiveness of exposure therapy for specific phobia. As previously discussed, those with specific phobia are known to meet criteria for multiple phobias of objects and/or situations but few studies employ samples of those with multiple fears.

Study 2 investigated the first aim of whether an unextinguished CS (e.g., fear of spiders) reinstated fear to a previously extinguished CS (e.g., fear of rats) and the second aim to assess whether exposure to the unextinguished CS can attenuate this conditional reinstatement. Study 2 also focused on addressing the third aim by extending previous laboratory-based research from Halladay et al. (2012), Rescorla and Heth (1975; Exp 2) and Study 1, to a clinical-analogue design. A sample of 50 participants with high fear levels of both spiders and rats was recruited. The study design used three groups, the reinstatement and multiple phobic stimuli group received exposure to the unextinguished CS and the control group did not. The multiple phobic stimuli group was the only group to receive a second VRET phase to determine whether exposure to the unextinguished CS can attenuate this conditional reinstatement.

As hypothesised, reinstatement of fear was found for the reinstatement and multiple phobic groups and not the control group as measured by avoidance ratings, subjective units of distress and heart rate change. Reinstatement of fear was attenuated for the multiple phobic stimuli group as evidenced by a significant decrease across all

measures. The clinical implications of the results for Study 2 suggest that clinicians should conduct a comprehensive assessment of fears and deliver exposure therapy for their client's multiple different fears to reduce the potential for conditional reinstatement of fear.

Overview of Chapter 7: Virtual Reality Exposure Therapy for a Case of Multiple Phobias: Examining Reinstatement of Fear (Study 3)

The present research culminates by generalising a novel intervention from laboratory-based research to a clinical-analogue study and to a case study with an individual suffering from two animal phobias (e.g., spiders and rats). In this way, the present thesis achieved the third aim. The third study implemented a case study method ($N = 1$) to test an intervention based on the previous two studies to examine whether conducting exposure to an unextinguished CS will reduce reinstatement with a participant who met criteria for specific phobia of two animal types (rats and spiders). An individualised VRET session was provided for the primary fear of rats. Following therapy, a reinstatement phase was delivered where the participant was exposed to their secondary fear of spiders. The participant then undertook an individualised exposure hierarchy in virtual reality for their fear of spiders and three follow-up sessions. Tau-U analyses of data trend and non-overlap for subjective units of distress, avoidance measured on a behavioural avoidance task (BAT) and heart rate change indicated that following successful VRET the primary fear of rats was reinstated by exposure to the untreated fear of spiders and VRET to the unextinguished CS attenuated reinstatement. The results provide further evidence of translating interventions from laboratory-based research to clinical-analogue to intervention-based research. Furthermore, the research

can be translated to clinical settings with planning for relapse prevention by incorporating exposure to other fears and phobias.

Overview of Chapter 8: General discussion

In the general discussion, the research project aims are reviewed. Specifically, the discussion focusses on how the findings across the studies extend previous research that an unextinguished CS can reinstate fear to an extinguished CS with humans (Halladay et al., 2012; Rescorla & Heth, 1975b) and provides an attenuation method for conditional reinstatement. The aim of the research project to overcome a gap in the translational nature of reinstatement research is addressed. The broader theoretical and clinical implications of the research project are discussed in depth. Key issues discussed include the wider applications for clinicians to assess for multiple fears and implement exposure to multifarious stimuli, other attenuation methods for conditional reinstatement of fear, and investigating whether conditional reinstatement could occur with other disorders. The strengths of the research project are highlighted. The limitations of the research project are provided including: the lack of interactivity in the virtual technology, not considering the role of disgust in two of three of the studies, the small clinical sample size and no longitudinal follow-ups. Future research directions across the research project are considered. Chapter 8 concludes by highlighting the importance of enhancing the long-term effectiveness of exposure-based treatments for individuals with multiple phobias and possible ways in which this can be achieved.

References

Abramowitz, J. S., Deacon, B. J., & Whiteside, S. P. (2012). *Exposure therapy for anxiety: Principles and practice*. Guilford Press.

Australian Bureau of Statistics (2019b). National Health Survey: first results, 2017-18. ABS cat. no. 4364.0.55.001. Canberra: ABS. https://www.abs.gov.au/statistics/health/health-conditions-and-risks/national-health-survey-first-results/latest-release

Australian Institute of Health and Welfare. (2021). *Mental health services in Australia.* Retrieved from https://www.aihw.gov.au/reports/mental-health-services/mental-health-services-in-australia

Aknin, L., De Neve, J. E., Dunn, E., Fancourt, D., Goldberg, E., Helliwell, J. F., ... & Ben Amor, Y. (2021; in press). Mental health during the first year of the COVID-19 pandemic: A review and recommendations for moving forward. *Perspectives on Psychological Science*.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

Askew, C., & Field, A. P. (2007). Vicarious learning and the development of fears in childhood. *Behaviour Research and Therapy*, *45*(11), 2616-2627. https://doi.org/10.1016/j.brat.2007.06.008

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2013). Renewal of fear: clinical-analogue findings. *In Psychology of fear: New developments* (pp. 1-27). Nova Science Publishers.

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 138-144. https://doi.org/10.1016/j.jbtep.2014.12.006

Boschen, M. J., Neumann, D. L., & Waters, A. M. (2009). Relapse of successfully treated anxiety and fear: Theoretical issues and recommendations for clinical practice. *Australian & New Zealand Journal of Psychiatry*, *43*(2), 89-100. https://doi.org/10.1080/00048670802607154

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*(1), 80. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology*, *19*(1S), 57. https://doi.org/10.1037/0278-6133.19.Suppl1.57

Bouton, M. E. (2002). Context, ambiguity, and unlearning: Sources of relapse after behavioral extinction. *Biological Psychiatry*, *52*(10), 976-986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning & Memory*, *11*(5), 485-494. http://www.learnmem.org/cgi/doi/10.1101/lm.78804.

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445-466. https://doi.org/10.1016/0023-9690(79)90057-2

Bouton, M. E., Maren, S., & McNally, G. P. (2021). Behavioral and neurobiological mechanisms of Pavlovian and instrumental extinction learning. *Physiological Reviews*, *101*(2), 611-681. https://doi.org/10.1152/physrev.00016.2020

Bouton, M. E., Westbrook, R. F., Corcoran, K. A., & Maren, S. (2006). Contextual and temporal modulation of extinction: behavioral and biological mechanisms. *Biological Psychiatry*, *60*(4), 352-360. https://doi.org/10.1016/j.biopsych.2005.12.015

Callen, E. J., McAllister, W. R., & McAllister, D. E. (1984). Investigations of the reinstatement of extinguished fear. *Learning and Motivation*, *15*(3), 302-320. https://doi.org/10.1016/0023-9690(84)90025-0

Ciobanu, L. G., Ferrari, A. J., Erskine, H. E., Santomauro, D. F., Charlson, F. J., Leung, J., ... & Baune, B. T. (2018). The prevalence and burden of mental and substance use disorders in Australia: Findings from the Global Burden of Disease Study 2015. *Australian & New Zealand Journal of Psychiatry*, *52*(5), 483-490. https://doi.org/10.1177/0004867417751641

Craske, M. G. (1999). *Anxiety disorders: psychological approaches to theory and treatment*. Westview Press. https://psycnet.apa.org/record/1998-06744-000

Craske, M .G., Hermans, D., & Vansteenwegen, D. (2006). *Fear and learning: Basic science to clinical application*, APA Books, Washington, DC.

Culver, N. C., Stoyanova, M., & Craske, M. G. (2011). Clinical relevance of retrieval cues for attenuating context renewal of fear. *Journal of Anxiety Disorders*, *25*(2), 284-292. https://doi.org/10.1016/j.janxdis.2010.10.002

Dirikx T., Hermans D., Vansteenwegen D., Baeyens, F., & Eelen P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, 38, 237-251. https://doi-org.10.1016/j.jbtep.2006.04.001

Dunsmoor, J. E., Ahs, F., Zielinski, D. J., & LaBar, K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, *113*, 157-164. https://doi-org.10.1016/j.nlm.2014.02.010

Forcadell, E., Torrents-Rodas, D., Vervliet, B., Leiva, D., Tortella-Feliu, M., & Fullana, M. A. (2017). Does fear extinction in the laboratory predict outcomes of exposure therapy? A treatment analog study. *International Journal of Psychophysiology*, *121*, 63-71. https://doi.org/10.1016/j.ijpsycho.2017.09.001

Gerull, F. C., & Rapee, R. M. (2002). Mother knows best: effects of maternal modelling on the acquisition of fear and avoidance behaviour in toddlers. *Behaviour Research and Therapy*, *40*(3), 279-287. https://doi.org/10.1016/S0005-7967(01)00013-4

Haesen, K., & Vervliet, B. (2015). Beyond extinction: Habituation eliminates conditioned skin conductance across contexts. *International Journal of Psychophysiology*, *98*(3), 529-534. https://doi.org/10.1016/j.ijpsycho.2014.11.010

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Hendry, J. S. (1982). Summation of undetected excitation following extinction of the CER. *Animal Learning & Behavior*, *10*(4), 476-482. https://doi.org/10.3758/BF03212287

Hermans, D., Dirikx, T., Vansteenwegenin, D., Baeyens, F., Van den Bergh, O., & Eelen, P. (2005). Reinstatement of fear responses in human aversive conditioning. *Behaviour Research and Therapy*, *43*(4), 533-551. https://doi.org/10.1016/j.brat.2004.03.013

Jacobs, W. J., & Nadel, L. (1985). Stress-induced recovery of fears and phobias. *Psychological Review*, *92*(4), 512. https://doi.org/10.1037/0033-295X.92.4.512

Kessler R. C., & Wang P .S. (2008). The Descriptive Epidemiology of Commonly Occurring Mental Disorders in the United States. *Annual Review Public Health*, *29*, 115-129. https://doi.org.10.1146/annurev.publhealth.29.020907.090847

King, N. J., Muris, P., & Ollendick, T. H. (2004). Specific phobia. In *Anxiety Disorders in Children and Adolescents* (pp. 263-279). Guilford Press. https://psycnet.apa.org/record/2004-16376-012

Kim, J. H., & Richardson, R. (2007). A developmental dissociation in reinstatement of an extinguished fear response in rats. *Neurobiology of Learning and Memory*, *88*(1), 48-57. https://doi.org/10.1016/j.nlm.2007.03.004

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2018). Effects of extended extinction and multiple extinction contexts on ABA renewal. *Learning and Motivation*, *63*, 1-10. https://doi.org/10.1016/j.lmot.2017.11.001

Krisch, K. A, Bandarian-Balooch, S., O'Donnell, A. W., & Neumann, D. L. (2016). *Virtual reality exposure therapy for specific phobia and its clinical application to*

reduce return of fear. Virtual reality: Advances in research and applications, Nova Science Publishers.

LaBar, K. S., & Phelps, E. A. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, *119*(3), 677. https://10.1037/0735-7044.119.3.677

Laborda, M. A., McConnell, B. L., & Miller, R. R. (2011). Behavioral techniques to reduce relapse after exposure therapy. *Associative learning and conditioning theory*, *1*, 79-104.

Leer, A., & Engelhard, I. M. (2015). Countering fear renewal: Changes in the UCS representation generalize across contexts. *Behavior Therapy*, *46*(2), 272-282. https://doi.org/10.1016/j.beth.2014.09.012

Marin, M. F., Bilodeau-Houle, A., Morand-Beaulieu, S., Brouillard, A., Herringa, R. J., & Milad, M. R. (2020). Vicarious conditioned fear acquisition and extinction in child–parent dyads. *Scientific Reports*, *10*(1), 1-10. https://doi.org/10.1038/s41598-020-74170-1

Matthews, A., Naran, N., & Kirkby, K. C. (2015). Symbolic online exposure for spider fear: habituation of fear, disgust and physiological arousal and predictors of symptom improvement. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 129-137. https://doi.org/10.1038/s41598-020-74170-1

McClelland, J. L., & Rumelhart, D. E. (1985). Distributed memory and the representation of general and specific information. *Journal of Experimental Psychology: General*, *114*(2), 159.

McCloskey, M., & Cohen, N. J. (1989). Catastrophic interference in connectionist networks: The sequential learning problem. In *Psychology of learning and motivation* (Vol. 24, pp. 109-165). Academic Press. https://doi.org/10.1016/S0079-7421(08)60536-8

Menzies, R. G., & Clark, J. C. (1993a). The etiology of childhood water phobia. Behaviour *Research and Therapy,* 31, 499–501. https://doi.org/10.1016/0005-7967(93)90131-D

Mystkowski, J. L., Craske, M. G., Echiverri, A. M., & Labus, J. S. (2006). Mental reinstatement of context and return of fear in spider-fearful participants. *Behavior Therapy*, *37*(1), 49-60. https://doi.org/10.1016/j.beth.2005.04.001

Neumann, D. L., & Longbottom, P. L. (2008). The renewal of extinguished conditioned fear with fear-relevant and fear-irrelevant stimuli by a context change after extinction. *Behaviour Research and Therapy*, *46*(2), 188-206. https://doi.org/10.1016/j.brat.2007.12.004

Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure. *Biological Psychology*, *73*(2), 175-185. https://doi.org/10.1016/j.biopsycho.2006.03.004

Öst, L. G. (1989). One-session treatment for specific phobias. *Behaviour Research and Therapy*, *27*(1), 1-7. https://doi.org/10.1016/0005-7967(89)90113-7

Pavlov IP. (1927). Conditioned reflexes. London: Oxford University Press.

Rachman, S. (1966). Studies in desensitization—II: Flooding. *Behaviour Research and Therapy*, *4*(1-2), 1-6. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman, S. (1977). The conditioning theory of fearacquisition: A critical examination. *Behaviour Research and Therapy*, *15*(5), 375-387. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman S., & Whittal M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, *27*, 513-520. https://doi.org/10.1016/0005-7967(89)90085-5

Rescorla, R. A., & Heth, C. D. (1975b). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*(1), 88. https://pubmed.ncbi.nlm.nih.gov/1151290/

Shiban Y., Schelhorn I., Pauli P., & Mühlberger A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, *71*, 45-53. https://doi.org/10.1016/j.brat.2015.05.014

Sokol, N., & Lovibond, P. F. (2012). Cross-US reinstatement of human conditioned fear: Return of old fears or emergence of new ones?. *Behaviour Research and Therapy*, *50*(5), 313-322. https://doi.org/10.1016/j.brat.2012.02.005

Stein, M. B., & Craske, M. G. (2017). Treating anxiety in 2017: Optimizing care to improve outcomes. *Jama*, *318*(3), 235-236. https://doi.org/10.1001/jama.2017.6996

Stinson, F. S., Dawson, D. A., Chou, S. P., Smith, S., Goldstein, R. B., Ruan, W. J., & Grant, B. F. (2007). The epidemiology of DSM-IV specific phobia in the USA: Results from the National Epidemiologic Survey on Alcohol and Related

Conditions. *Psychological Medicine*, *37*(7), 1047-1059. https://doi.org/10.1017/S0033291707000086

Taslimi, Z., Komaki, A., Haghparast, A., & Sarihi, A. (2018). Effects of acute and chronic restraint stress on reinstatement of extinguished methamphetamine-induced conditioned place preference in rats. *Basic and Clinical Neuroscience*, *9*(3), 157. https://doi.org.10.29252/nirp.bcn.9.3.157

Thomas, B. L., Vurbic, D., & Novak, C. (2009). Extensive extinction in multiple contexts eliminates the renewal of conditioned fear in rats. *Learning and Motivation*, *40*(2), 147-159. https://doi.org/10.1016/j.lmot.2008.10.002

Van Houtem C. M., Laine M. L., Boomsma D. I., Ligthart L., Van Wijk A. J., & De Jongh A. (2013). A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears. *Journal of Anxiety Disorders*, *27*, 379-388. https://doi.org/10.1016/j.janxdis.2013.04.007

Warren, V. T., Anderson, K. M., Kwon, C., Bosshardt, L., Jovanovic, T., Bradley, B., & Norrholm, S. D. (2014). Human fear extinction and return of fear using reconsolidation update mechanisms: The contribution of on-line expectancy ratings. *Neurobiology of Learning and Memory*, *113*, 165-173. https://doi.org/10.1016/j.nlm.2013.10.014

Wittchen, H. U., Lecrubier, Y., Beesdo, K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. *Anxiety Disorders*, 23-37. https://doi.org/10.1002/9780470986844.ch2

Wolpe, J. (1958). Psychotherapy by reciprocal inhibition. *Conditional reflex: a Pavlovian Journal of Research & Therapy*, *3*(4), 234-240. https://doi.org/10.1007/BF03000093

Chapter 2: Preamble

The proceeding chapter provided a brief background and rationale of the research project, presented the aims and an overview of the chapters of the thesis. Chapter 2 presents a more comprehensive review of anxiety disorders with a particular focus on specific phobia, exposure therapy, return of fear, the theoretical frameworks underlying exposure therapy and return of fear, and a literature review of reinstatement of fear and targeting multiple phobias. The summary section of Chapter 2 highlights the importance of translational reinstatement of fear research.

Chapter 2: Anxiety Disorders, Treatment and Return of Fear

The anxiety disorders are the most prevalent group of mental health disorders globally (Kessler et al., 2010; Stein et al., 2017), with higher comorbidity rates than for other mental health disorders (Toft et al., 2005). Consistent with this, in Australia, anxiety disorders are the most common mental health disorder, with 1 in 7 adults being diagnosed with an anxiety disorder (ABS, 2019). The common symptoms of anxiety across the disorder categories include muscle tension, rapid heart rate, dizziness, a dry throat, sweating, difficulty breathing, nausea and headaches. Excessive anxiety can disrupt our cognitive processes (Sapolsky et al., 1990) and short-term memory (Wehrenberg & Prinz, 2007). Anxiety disorders can impact relationships, employment and self-esteem (Wardenaar et al., 2017). The Diagnostic and Statistical Manual for Mental disorders fifth edition (DSM-5) includes an anxiety disorders category with the following specific disorders: generalized anxiety disorder, panic disorder, specific phobias, agoraphobia, social anxiety disorder and separation anxiety disorder (APA, 2013).

Specific phobia is the most prevalent anxiety disorder (Kessler & Wang, 2008; Van Houtem et al., 2013). Lifetime prevalence rates of specific phobia have been estimated to be between 10 to 12.5% (Kessler et al., 2008; LeBeau et al., 2010; Van Houtem et al., 2013). Specific phobia is characterised by persistent, distressing and impairing fear and avoidance of an object or situation that is out of proportion to the risk of harm the object or situation poses (APA, 2013). The DSM-5 categorises four subtypes of specific phobia: animal (e.g., snakes, spiders, rats, dogs), natural environment (e.g., heights, water, storms), situational (e.g., flying, enclosed spaces, driving) and blood-

injection injury (e.g., injections, blood tests). Animal phobia has the highest prevalence of the specific phobia subtypes (Curtis et al., 1998; Depla et al., 2008; LeBeau et al., 2010; Wardenaar et al., 2017).

Most individuals suffering from specific phobia fear on average three different phobic objects or situations (e.g., Curtis et al., 1998; LeBeau et al., 2010; Wittchen et al., 2002). Research examining the impairment specific phobias causes when a single object or situation is feared has shown that compared to other anxiety disorders, specific phobia causes less (Marks, 1987), similar (Becker et al., 2007; Depla et al. 2008; Stinson et al., 2007), or more severe impairment (Magee et al., 1996). However, a cross-national study by Wardenaar et al. (2017) including surveys from 22 countries demonstrated that when the number of phobic objects or situations increased, specific phobia led to higher impairment rates, greater comorbidity and reduced treatment-seeking, which is consistent with previous research (e.g., Burstein et al., 2012; Curtis et al., 1998; Stinson et al., 2007). The number of different phobic objects or situations an individual fears should thus be considered in research and treatment.

Regardless of the number of feared objects/situations, numerous individuals suffering from specific phobia do not seek treatment (Garcia-Palacios et al., 2001). However, for those individuals who receive treatment for specific phobia, exposure therapy is regarded as the gold standard for treatment (Abramowitz et al., 2012; Craske, 1999). Exposure therapy is an effective treatment involving gradually presenting the individual with the feared object or situation until the fear attenuates (Öst, 1989; Wolpe, 1958). The three main exposure-based approaches for specific phobia include in vivo

exposure (with real-life stimuli), VRET (with virtual stimuli) and imaginal exposure (with imagined stimuli; Bush, 2008).

The key mechanism underlying exposure therapy has been provided by the learning framework of Pavlovian conditioning (Pavlov, 1927). Extinction of conditioned fear involves repeated presentations of the feared stimulus without the aversive stimulus, resulting in a fear response no longer being observed. Extinction of a conditioned fear response corresponds to exposure therapy. After successful in vivo exposure treatment, approximately 35-50% of individuals experience a return of fear symptoms (Rachman, 1966; Rose & McGlynn, 1997; Vasey et al., 2012). For example, Rose and McGlynn (1997) conducted exposure therapy with 20 individuals suffering from snake phobia. At one-month post treatment, 25% of successfully treated individuals experienced a return of fear symptoms. The occurrence of fear symptoms following successful exposure is termed return of fear (ROF; Rachman, 1966, 1987).

Research has shown that Pavlovian conditioning can be applied to improve our understanding of the mechanisms that underlie ROF. Laboratory-based research with rats and humans has shown that the extinction process does not result in a destruction of the CS-US association learnt in acquisition (Bouton, 2002, 2004; Bouton & Bolles, 1979; Bouton et al., 2006; Effting & Kindt, 2007; Warren et al., 2014). This research has suggested that extinction results in new learning that the previously feared object need not be feared anymore (Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Lissek et al., 2008; Neumann, 2006; Vansteenwegen et al., 2007). Moreover, this research has shown that the extinction process can be modified to increase or reduce the likelihood of fear responses returning post extinction.

However, only a small proportion of laboratory-based return of fear findings have been reliably translated into clinical-analogue and clinical research (Bagley & Bandarian-Balooch, 2020; Bandarian-Balooch et al., 2013; Boschen et al., 2009; Jessup et al., 2020; Shiban et al., 2015; Vansteenwegen et al., 2007). Translating laboratory-based ROF findings to clinical research is important because it enhances the applicability of this research to clinical settings (Bandarian-Balooch et al., 2013; Boschen et al., 2009; Neumann & Longbottom, 2008), ultimately informing clinicians how the exposure therapy process can be modified to enhance long-term effectiveness. The translation of ROF research may occur through a progression from research on the extinction of fear responses in laboratory-based studies with rats and other non-human animals, to laboratory studies with non-phobic human individuals, to laboratory and field research to moderately fearful individuals, and finally to laboratory and clinical case studies and randomised controlled trial studies with phobic individuals.

The present chapter provides a review of the acquisition, extinction and return of fear with a particular emphasis on situations in which the individual fears multiple objects or situations. The chapter begins with discussing the acquisition, extinction and reinstatement of fear learning from the Pavlovian conditioning framework and Bouton's contextual memory model. Subsequently, the laboratory-based reinstatement literature and the ecological validity of these studies are reviewed. It is noted that the lack of clinical studies on reinstatement of fear is due to the inherent ethical challenges. A novel approach that was developed in a laboratory-based study with rats shows how an unextinguished CS can reinstate fear to an extinguished CS, termed conditional reinstatement. The implications of conditional reinstatement are explored such as how

the majority of those with specific phobia have multiple phobias and how untreated fears may remain a risk for reinstatement of fear to the primary fear. Theoretical models are applied to understand conditional reinstatement of fear and to provide suggestions of how it can be attenuated. Finally, the main points of this chapter are summarised.

The Acquisition, Extinction and Return of Fear

Pavlovian conditioning provides a learning model underpinning the acquisition and extinction of fear (Bouton & Bolles, 1979; Davey, 1992; Laborda et al., 2011; Neumann & Longbottom, 2008; Pavlov, 1927; Wolpe, 1958). The acquisition of specific phobia has been explained within a Pavlovian conditioning framework as resulting from the pairing of a neutral CS (e.g., snake) and an aversive US (e.g., pain). Subsequent presentations of the CS alone evokes a conditioned fear response (CR; e.g., fear). In laboratory-based studies, during the acquisition phase, a CS-US association is learnt and this learning is expressed as a CR. The magnitude of the CR thus gives an indication of the strength of the CS-US association.

In laboratory-based human studies, CRs are typically measured using a combination of physiological measures, such as heart rate, skin conductance, and startle eyeblinks (e.g., Matthews et al., 2015; Neumann & Waters, 2006; Neumann et al., 2008), self-reported US expectancy ratings or affective reactions (e.g., Bandarian-Balooch & Neumann, 2011; Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Neumann et al., 2008), and behavioural measures of affect (Pischek-Simpson et al., 2009). In clinical-analogue studies for specific phobia, CRs are typically measured using a combination of self-report subjective units of distress (SUDS), behavioural, and physiological measures (e.g., Bandarian-Balooch et al., 2015; Shiban et al., 2013).

Extinction of the conditioned fear response can be observed following acquisition. Procedurally, extinction requires repeated presentations of the feared stimulus without the aversive consequence (US). A progressive reduction in the magnitude of the CR is observed across the extinction trials. In clinical settings, the process of extinction is analogous to exposure therapy (Öst, 1989; Wolpe, 1958).

It has long been proposed that extinction results in the destruction of the CS-US association and thus removal of the original fear (McClelland & Rumelhart, 1985; Rescorla, 1972). More recent conditioning research using rats (e.g., Bouton, 2002, 2004; Bouton & Bolles, 1979; Laborda & Miller, 2013; Mozafari et al., 2020; Thomas et al., 2009) and human participants (e.g., Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Warren et al., 2014) has suggested that the return of the extinguished CR (e.g., fear) shows that the original CS-US association is not destroyed by the extinction process (see Bouton et al., 2021 for a review). Several authors note that extinction procedures may cause disruption of the CS-US association (Delamater & Westbrook, 2014; Rescorla, 2001).

Mechanisms of Return of Fear

Four mechanisms for the return of extinguished conditioned behaviour have been proposed: spontaneous recovery, reacquisition, renewal, and reinstatement within the Pavlovian conditioning literature and more recently the mechanism of resurgence has been examined within the instrumental conditioning literature (Boschen et al., 2009; Bouton, 2002; Bouton et al., 2021; Pavlov, 1927). In spontaneous recovery, extinguished fear can return when the extinguished CS is presented after a temporal context shift (Bouton, 2002, 2004; Pavlov, 1927). In reacquisition, extinguished fear can return after

another pairing of the CS and US and results in rapid formation of the CS-US association in similar conditions to those of acquisition, (Napier et al., 1992) or slow formation in similar conditions to extinction (Bouton, 1986). In renewal, there are typically three phases; acquisition, extinction, and test whereby extinguished fear can return when the physical context is changed after extinction (Bouton, 2002; Neumann, 2007; Neumann & Kitlertsirivatana, 2010). The renewal procedures re-eliciting fear differ by the context change after extinction, ABA renewal involves returning to the acquisition context following extinction and ABC or AAB renewal involves presenting the participant with a different context following extinction (Bouton, 2002). Reinstatement is the mechanism of particular interest to the proposed studies and involves presentations of the US following extinction, which can trigger the recovery of the extinguished response to the CS (Bouton, 1984; Bouton & Bolles, 1979; Pavlov, 1927; Rescorla & Heth, 1975b; Westbrook et al., 2002). Resurgence is a paradigm that has mainly been studied in instrumental learning and involves relapse to a behaviour that has previously been extinguished by presenting a secondary behaviour in extinction (Leitenberg et al., 1970; Nall & Shahan, 2020).

Recent neurobiology research examining the neural mechanisms of fear conditioning and extinction has provided further support for the existing theoretical accounts of extinction learning (Bouton et al., 2021). In fear acquisition it has been found that contextual information of the CS and US is processed in the hippocampus and medial prefrontal cortex and projected to the amygdala which triggers the conditioned response (see Bouton et al., 2021 for a review). The neural circuits proposed to be involved in the extinction process also include the amygdala, prefrontal cortex and

hippocampus (e.g., Farinelli et al., 2006; LeDoux, 2015). Extinction learning has been found to involve synaptic plasticity in the amygdala (e.g., Bocchio et al., 2017). Extinction has been found to occur as a result of infralimbic inhibition to the amygdala neurons and the infralimbic projections to the nucleus reuniens which may inhibit the recovery of contextual fear (e.g., Bocchio et al. 2017; Milad & Quirk; 2002). The behavioural and neurobiology literature not only provides insight into extinction learning but reflects how extinction does not result in the permanent unlearning of the CS-US association, by evidence of the recovery of conditioned responses (Bouton, 2002; Bouton et al., 2021).

Reinstatement of Extinguished Conditioned Responses

In reinstatement, extinguished fear can return after re-exposure to the US (Pavlov, 1927; Rescorla & Heth, 1975b) and typically occurs when this exposure is conducted in the extinction context (Bouton, 1984; Bouton & Bolles, 1979). A clinical example of reinstatement would involve a client who has overcome their fear of spiders by completing exposure therapy and subsequently experiences pain being bitten by a wasp, reinstating their initial fear. In a standard reinstatement procedure, a CS is paired with a US during acquisition, the CS is presented alone during extinction, and then the US is presented without the CS in a reinstatement phase and followed by test trials of the CS. For example, Hermans et al. (2005) were one of the first to investigate reinstatement with a non-fearful human sample and paired images of human faces (CS) with a shock (US). In the extinction phase each image was presented without the shock. Following this a reinstatement group was presented with four US presentations and a control group did not receive US presentations. Upon presentation of the CS again, a significant

reinstatement of US-expectancy ratings was observed in the reinstatement group and not in the control group.

Laboratory-based studies have produced reinstatement of extinguished conditioned responses on test trials with rats (Bouton & Bolles, 1979; Halladay et al, 2012; Kim & Richardson, 2007; Rescorla & Heth, 1975b; Taslimi et al., 2018) and human participants (Dirikx et al., 2007; Dunsmoor et al., 2014; Hermans et al., 2005; Neumann, 2008). Reinstatement of extinguished conditioned responses has been produced using a variety of different contexts, CSs, and USs (Best, 2014; Labar & Phelps, 2005; Shiban et al., 2015; Westbrook et al., 2002).

The reinstatement effect has been found when the CS is presented in test in the same context as where the US is presented following extinction (Bouton & Bolles, 1979; LaBar & Phelps, 2005). For example, LaBar and Phelps (2005) demonstrated the reinstatement effect in a differential conditioning paradigm by exposing human participants to four US presentations (i.e., loud noise) following extinction. In test, participants in the condition receiving the US presentations in the same context for all phases showed significantly higher skin conductance responses to the CS+ than participants who underwent the same procedure in a different context for the reinstatement phase. Reinstatement of extinguished conditioned responses has also been observed when the CS was presented in test in a different context to where the US was presented (Richardson et al., 1999; Westbrook et al., 2002). Taken together, these studies (Bouton, & Bolles, 1979; LaBar & Phelps, 2005; Richardson et al., 1999; Westbrook et al., 2002) demonstrate the importance of other cues, in this case contextual cues, in producing reinstatement of extinguished conditioned responses.

Various CSs, including geometric shapes (Gazendam & Kindt, 2012; Kattoor et al., 2013; LaBar & Phelps, 2005; Sevenster et al., 2012; Sokol & Lovibond, 2012), coloured lights (Milad, 2005; Norrholm et al., 2006) and neutral faces (Dirikx et al., 2004; Dirikx et al., 2007; Dirikx et al., 2009; Dunsmoor et al., 2014; Hermans et al., 2005; Kull et al., 2012), have been used in research on the reinstatement effect (Haaker et al., 2014). It has been argued that a limitation of this research is that the majority of stimuli (e.g., geometric shapes, coloured lights) used in previous studies lack ecological validity and thus are not generalisable to exposure therapy (Barry et al., 2014).

In addressing the criticism of poor ecological validity of CSs, Dunsmoor et al. (2014) used virtual reality human characters. One advantage of using virtual reality protocols to investigate ROF is that the conditions may more closely resemble real-life clinical situations (Dunsmoor et al., 2014; Krisch et al., 2016). However, the human faces used as CSs by Dunsmoor et al. (2014) were not fear-relevant and are potentially not generalisable to exposure therapy in clinical settings where exposure therapy is largely focused on treatment of fear relevant stimuli. Fear relevant stimuli are stimuli that have or are likely to cause harm to humans (Öhman & Mineka, 2001). Kindt and Soeter (2013) used fear-relevant CSs of photographs of spiders in their study. The authors propose that this methodology is more ecologically valid, given that anxiety disorders are more likely to be associated with fear-relevant stimuli that pose a survival threat, than with fear-irrelevant (e.g., geometric shapes; Kindt & Soeter, 2013; Öhman & Mineka, 2001). Therefore, currently there are few human reinstatement studies employing stimuli that closely resemble real-life objects (Kindt & Soeter, 2013) and situations (Dunsmoor et al., 2014).

In contrast to variations in the types of CSs used in reinstatement laboratory-based studies, the type of reinstating US has been more consistent. The most common US is an electrotactile stimulus (Dirikx et al., 2007; Haaker et al., 2014; Kull et al., 2012; Schiller et al, 2008). Other USs used in reinstatement research include an air blast to the throat (e.g., Norrholm et al., 2006), loud tones (e.g., LaBar & Phelps, 2005) and abdominal pain (e.g., Kattoor et al., 2012). Typically, the acquisition US is the same as the reinstatement US (Haaker et al., 2014). However, it has also been found that the reinstating stimulus can differ to the US employed in acquisition in both rats (e.g., Rescorla & Heth, 1975b) and humans (e.g., Sokol & Lovibond, 2012). The clinical implication of this potentially suggests diverse aversive experiences could reinstate return of fear. Despite the potential clinical implications of these studies, the reinstating stimuli have limited ecological validity and are not clinically relevant (e.g., an air blast or an electric shock does not correspond to the same sensation as being bitten by an animal). It has previously been proposed that in future studies it is necessary that ecologically valid reinstating stimuli be used with clinical samples (Haaker et al., 2014).

Several traditional learning models have been proposed to explain processes relevant in reinstatement, such as mediated conditioning (Westbrook et al., 2002) or the non-associative theory (Rescorla & Heth, 1975b). However, these models do not completely account for reinstatement of fear. Among the models that provide an explanation of reinstatement, Bouton's memory model of learning (1993), is the most widely recognised (e.g., Best, 2014; Hendry, 1982; Vervliet et al., 2013).

Bouton's Contextual Memory Model

Bouton's contextual memory model (Bouton, 1993, 2002, 2004) proposes that extinction does not reflect unlearning of the CS-US association, rather extinction reflects new learning that the CS is associated with the absence of the US. Through this process, a CS-noUS association is learnt during extinction. The two associations are stored in memory and the meaning of the association remains ambiguous (Bouton, 2002). According to this model, the context determines which association is retrieved and expressed in behaviour. The CS-noUS association is context specific and will not readily generalize between different contexts. Thus, the CS-noUS is only retrieved from memory in the extinction context. Conversely, the CS-US association is relatively context independent and will be retrieved from memory in all contexts, except for the extinction context (Bouton, 1993).

In the contextual memory model, it is suggested that reinstatement occurs due to the contextual conditioning involved in the presentation of the aversive stimulus in the reinstatement phase (Bouton, 2004). In a standard reinstatement phase the US is presented and associated with the background contextual cues. In the test phase, the contextual cues enhance the retrieval of the CS-US association formed in acquisition and thus fear is reinstated. Bouton (2002) proposed that contextual cues (e.g., lights, sounds, indoor and outdoor contexts) are the sum of features and thus are not inherently part of the US. The contextual memory model has been supported in neurobiology studies and supports how reinstatement may occur. In particular, in the test phase presenting the extinguished CS in a different context to where extinction occurred, the infralimbic neurons of the medial prefrontal cortex are inhibited (Laurent & Westbrook, 2009;

Marek et al., 2018; Milad & Quirk, 2002) and excitation in the hippocampus may mediate reinstatement, both allowing for the expression of the conditioned response.

The contextual memory model has highlighted the role of the sensory properties and contextual cues in triggering reinstatement. However, previous studies have highlighted that reinstatement may occur due to the sensory properties of the stimulus activating a representation of the affective properties of the US (Halladay et al., 2012; Kellett & Kokkinidis, 2004; Rescorla & Heth, 1975b). Stimulating the human amygdala has been found to evoke fear (Gloor, 1992) and consistent with this, Kellett and Kokkinidis (2004) found reinstatement of fear-potentiated startle was enhanced following electrical activation of the amygdala when presenting a stimulus in laboratory-rats but independently electrically stimulating the amygdala did not act as an US to trigger reinstatement.

In the contextual memory model, reinstatement is conceptualised as an inability to retrieve the CS-noUS association after re-exposure to the reinstating stimulus (Rescorla & Heth, 1975b) and typically occurs when this exposure is conducted in the extinction context (Bouton, 2002). Laboratory-based findings that examine reinstatement in different contexts and using various CSs, and USs may have important clinical implications for understanding the underlying mechanisms of relapse following exposure therapy. However, several challenges of investigating reinstatement of fear using a clinical sample have been identified in the literature (Boschen et al., 2009).

Challenges of Investigating Reinstatement of Fear in Clinical Research

Renewal of fear and spontaneous recovery of fear have been extensively translated from laboratory-based studies to clinical research (Bagley & Bandarian-

Balooch, 2020; Culver et al., 2011; Jessup et al., 2020; Vansteenwegen et al., 2007). However, due to ethical considerations there are a lack of studies investigating reinstatement of fear with a clinical sample (Boschen et al., 2009; Haaker et al., 2014; Hermans et al., 2005; Neumann, 2008). It has been considered unethical to have individuals undergo successful exposure therapy (e.g., for spider phobia) and subsequently expose them to a corresponding painful stimulus to reinstate fear (e.g., a US such as being bitten by a rat). Given the importance of preventing relapse in clinical phobic populations, further experimental studies and translations to clinical samples are needed to examine the reinstatement effect in more detail (Haaker et al., 2014).

Aiming to replicate reinstatement in a clinical-analogue study, Rachman and Whittal (1989) investigated reinstatement of fear using an electrotactile shock similar to that used in laboratory-based research. The researchers assigned 40 individuals highly fearful of spiders or snakes to a reinstatement or control group. The participants completed exposure treatment and two weeks later returned for the test session. The reinstatement group received an electric shock and the control group did not receive an electric shock. In contrast to laboratory-based research, there were no significant differences in heart rate or subjective fear between the two groups at test. The explanation for not finding a reinstatement effect was attributed to the electric shock not being sufficiently aversive to reinstate fear. In contrast, the use of an electric shock has been sufficiently aversive to elicit reinstatement of fear with non-fearful human participants (Dirikx et al., 2007; Haaker et al., 2013; Kull et al., 2012). An alternative explanation could be that presenting an electric shock to phobic participants is not as aversive as a presentation of the stimulus (e.g., spider or snake; Hermans et al., 2005).

The reinstating stimulus should be sufficiently aversive and clinically relevant and thus more generalizable to exposure therapy.

A Novel Approach to Investigating Reinstatement of Fear and Theoretical Explanations

Another method that holds promise for replicating reinstatement of fear in clinical-analogue research is using an unextinguished CS in the reinstatement phase. Halladay et al. (2012) examined if exposure to an unextinguished CS would reinstate conditional fear to an extinguished CS with groups of rats. The four groups differed according to the reinstatement phase. In acquisition, each group received presentations of the CSunextinguished (e.g., tone) and CSextinguished (e.g., light) paired with the US (e.g., footshock). In extinction, each group received presentations of the CSextinguished without the US. It was found that presenting rats with an unextinguished CS (e.g., tone) in the reinstatement phase reinstated initial fear in responding to an extinguished CS (e.g., light). Halladay et al. (2012) referred to the phenomenon of an unextinguished CS triggering reinstatement as conditional reinstatement. Additionally, Halladay et al. (2012) referred to standard reinstatement by an aversive US as unconditional reinstatement.

The results of Halladay et al. (2012) suggest that reinstatement of fear can be triggered by a broader variety of stimuli, including stimuli that may elicit fear due to a prior association with an aversive stimulus. Bouton's contextual memory model (1993, 2002, 2004) could potentially explain how conditional reinstatement occurs as a result of the contextual cues triggering an affective representation associated with the presentation of an unextinguished CS in the reinstatement phase. The proposed contextual cues outlined by Bouton and Swartzentruber (1991) included stimulus and background

features that can be encoded in learning and memory during acquisition. Incorporating this broader definition of context, the features of the stimulus could be considered contextual retrieval cues of the original fear learning. The unextinguished CS may reinstate the conditioned response of fear to the extinguished CS by the contextual cues (e.g., features of the background context and lights and tones are sensory changes to the environment) serving as a reminder of the acquisition context and eliciting the CS-US association in the test phase (Bouton, 1993, 1998; Brooks & Bouton, 1993).

In considering the theoretical implications of the findings reported by Halladay et al. (2012), it is possible that conditional reinstatement of fear occurred due to re-encountering the conditioned response of fear in the reinstatement phase. Halladay et al. (2012) specified that conditional reinstatement may have occurred due to the affective properties of the unextinguished CS rather than solely the sensory properties of the stimuli. Therefore, in Halladay et al. (2012) presenting the unextinguished CS (e.g., tone) to rats in the reinstatement phase potentially reinstated the conditioned response (e.g., fear) and retrieved the CS-US association to the extinguished CS (e.g., light). Furthermore, conditional reinstatement only occurred with an unextinguished CS and not a novel stimulus, indicating the importance of the emotional valence to recover conditional responding following extinction. The theoretical implications of Halladay et al. (2012) and Kellett and Kokkinidis (2004) highlight the importance of emotions in the understanding of fear conditioning. The clinical implications from Halladay et al. (2012) suggests that one fear can trigger other networks of fear in rats.

Translating the previous findings in rats (e.g., Halladay et al., 2012; Kellet & Kokkidinis, 2004; Rescorla & Heth, 1975b) to humans would have important clinical and

theoretical implications for fear conditioning, exposure therapy, and reinstatement of fear for anxiety disorders (i.e., specific phobia). In clinical settings it is known that individuals may have multiple feared objects or situations, even though they may present for treatment for their most problematic one. In such a situation, an unextinguished CS reinstating fear to an extinguished CS would translate to a secondary feared object or situation that does not undergo extinction. As a result, there remains the danger that reinstatement may be elicited to an extinguished primary feared object or situation.

If an unextinguished CS can reinstate fear to an extinguished CS in humans, this finding would support Foa and Kozak's (1986) emotional processing theory. Emotional processing theory proposes that fear activation occurs when an individual encounters stimuli that are represented in the fear network and are associated with the meaning of danger (Foa & Kozak, 1986). Emotional processing theory extended on Lang (1977) and proposes that the closer the match between the fear-evoking experience and the individuals fear structure, the greater degree of fear activation. Lang (1977) suggested that individuals with a specific phobia may have coherent fear structures that can be evoked with minimally matching information across stimuli and the fear structure can be easily activated due to misinterpreting the meaning of danger (e.g., a coiled garden hose may trigger fear in a snake phobic). The notion of diverse stimuli triggering reinstatement of fear by a different US (Rescorla & Heth, 1975b) and an unextinguished CS (Halladay et al., 2012) in not only rats but also humans, increases the likelihood of return of fear occurring in everyday life (Haaker et al., 2014).

Reinstatement research with humans has primarily focused on examining how fear acquisition and extinction processes can be modified to reliably produce

reinstatement of fear in laboratory-based studies. This research has enhanced our understanding of the mechanisms involved in the reinstatement effect. Until recently, there was no ethical methodology available that allowed translation of laboratory-based reinstatement research to clinical samples. The findings of Halladay et al. (2012), showing that reinstatement of fear can occur with an unextinguished CS in rats, suggests a method whereby reinstatement can be examined with parallel methodology with humans in laboratory-based and clinical-analogue settings. Furthermore, it is equally important to understand what learning or exposure processes can be modified to attenuate reinstatement of fear and ultimately enhance the long-term effectiveness of exposure therapy for specific phobia.

Attenuation of Reinstatement of Fear in Laboratory-based Studies

Research has identified multiple methods that can be used to attenuate reinstatement including gradual extinction with rats (Gershman et al., 2013), and humans (Shiban et al., 2015) and conducting extinction in multiple contexts (Dunsmoor et al., 2014). Gershman et al. (2013) examined whether gradual extinction would attenuate reinstatement of conditioned responses and spontaneous recovery with rats. A gradual extinction paradigm was employed with three groups of rats. The gradual extinction group was exposed to tones paired with a gradual decrease in the frequency of the shock. The standard group of rats were exposed to presentations of the tone without the US in the extinction phase. The gradual reverse group of rats was exposed to presentations of the tone paired with a gradual increase in the frequency of the shock. Gershman and colleagues (2013) found that gradually decreasing the shock during extinction significantly attenuated reinstatement of fear and spontaneous recovery of fear.

Furthermore, for the standard extinction and gradual reverse groups, attenuation of reinstatement of fear and spontaneous recovery of fear was not found.

Consistent with Gershman et al. (2013), gradual extinction has been found to be effective in attenuating reinstatement of fear with a human sample. In a laboratory-based experiment using virtual reality technology with human participants, Shiban et al. (2015) examined whether gradually reducing presentations of the US during extinction attenuated reinstatement of fear. The study suggested that virtual reality can be used to reliably reproduce and test methods to attenuate reinstatement of fear. The study employed a standard extinction group including a CS+ (e.g., spider) presented with an aversive air blast US and CS- (e.g., scorpion) presented without an aversive US. In the gradual extinction group, the CS+ was paired with gradually decreasing the intensity of the US (e.g., air blast 5 bar). In the reinstatement phase, the US was presented twice following by five test presentations of the CS+ and CS-. Reinstatement of fear was attenuated in the gradual extinction group. However, in the standard extinction group reinstatement was attenuated for the startle response but not for the skin conductance response or the expectancy ratings. The authors proposed that presenting the US in acquisition reactivates and destabilizes the state of the original fear memory, attenuating reinstatement of extinguished conditioned responses (Schiller et al., 2010). One reason for the non-significant findings for the skin conductance and expectancy ratings within the standard extinction group could be that the US (i.e., an air blast) was not sufficiently aversive to elicit a strong reinstatement effect. Thus, it is necessary for future research to consider the role of US aversiveness in triggering reinstatement of fear.

Other methods for attenuating reinstatement of fear have been explored with human participants. One method is conducting exposure in multiple contexts. Dunsmoor et al. (2014) examined whether extinction in multiple virtual contexts attenuated reinstatement, spontaneous recovery, and renewal of fear-potentiated startle. Participants were assigned to three groups: receiving extinction in multiple contexts, or a single novel context, or in the same context as acquisition. To examine spontaneous recovery of fear, all groups returned 24 hours later for test in the extinction context and in a novel context to examine renewal of fear. In this novel context three electric shocks were administered to examine reinstatement of fear. It was found that conducting extinction in multiple contexts attenuated reinstatement of fear but not spontaneous recovery and renewal of fear. A criticism of the methodology is that potential order effects may have contributed to the results, due to the researchers successively testing spontaneous recovery of fear, renewal of fear and reinstatement of fear and thus it may not represent a valid test of each return of fear mechanism. However, the study does provide empirical support for conducting extinction across various contexts as potentially attenuating reinstatement of fear.

Taken together, both studies (Dunsmoor et al., 2014; Shiban et al., 2015) employed methods that hold promise for attenuating reinstatement of fear. However, the reinstating methods have limited applicability to clinical settings. The reinstating stimulus in a real-life situation for an individual fearing spiders would be a spider bite and the use of an electric shock in the previous studies does not easily translate to clinical settings. It may be unethical to have a spider fearful individual bitten by another animal (e.g., wasp) and this accounts for why the previous studies employed an electric shock

and non-fearful samples. To determine if these methods attenuate reinstatement of fear following exposure therapy with high fearful or phobic individuals, it is necessary for future studies to employ a clinically relevant reinstating stimulus, which could be an unextinguished CS. A disadvantage of laboratory-based reinstatement research is that it remains uncertain about whether the mechanisms are directly applicable to clinical phenomenology, furthering the need for clinical-analogue experiments and clinical investigations (Vervliet et al., 2013). Ultimately, this suggests the importance of conducting clinical studies to increase the long-term effectiveness of exposure therapy. Thus, there is also a need for a novel approach to reduce reinstatement of fear using clinical samples.

Targeting Multiple Phobias and Attenuating Reinstatement of Fear

The finding that an unextinguished CS can trigger reinstatement (Halladay et al., 2012) to an extinguished CS is important, given that in clinical settings an unextinguished CS translates to a secondary feared object or situation. This conditional reinstatement is problematic, as it is common for individuals suffering from specific phobia to have multiple phobias; approximately 75% of individuals fear more than one object or situation (e.g., Curtis et al., 1998; LeBeau et al., 2010; Wittchen, et al., 2002). Furthermore, Wittchen et al. (2002) surveyed 3021 participants and found that over 50% of individuals suffering from specific phobia feared three or more different phobic objects or situations. Specifically, it was found that 26.4% of individuals feared two objects/situations, 23.5% individuals feared three objects/situations, 10.4% individuals feared four objects/situations and 17.3% feared more than four objects or situations (Wittchen et al., 2002). This comorbidity has been shown in the animal phobia subtype

(e.g., snakes and spiders; Ajdacic-Gross et al., 2016) and with various combinations of the subtypes (e.g., animal and environmental; animal and situational; Wittchen et al., 2002). The likelihood of recovering from specific phobia is inversely related to the number of fears, while 60% of individuals with pure specific phobia recover, only 30% of individuals with two to three multiple phobias recover (Wittchen et al., 2002).

The lower rates of recovery for those with multiple phobias demonstrates the importance of understanding whether exposure therapy for one fear generalises to other fears not targeted in treatment. While the research on multiple phobias is limited, a multiple baseline case study by Öst (1987) provides evidence that exposure therapy doesnot generalise across phobias. Öst (1987) provided exposure therapy to an adult woman diagnosed with specific phobias of rats, snakes, cats and worms using a one-session treatment. The results indicated clinically significant improvements for self-reported anxiety, behavioural avoidance and heart rate and blood pressure. Importantly, the fear, anxiety and avoidance of the specific animal phobia remained until it was targeted in treatment. A more recent multiple baseline study conducted by Farrell et al. (2020) with children diagnosed with specific phobia of dogs found that while exposure therapy significantly reduced their fear of dogs, there was no change in the other comorbid phobias (e.g., specific phobias of cats, blood injection, water, the dark, insects, toilets) from pre-treatment to 1-month follow-up. Thus, both studies (Farrell et al., 2020; Öst, 1987) demonstrate a lack of generalisability of exposure therapy across phobias not targeted in treatment. In contrast, Ollendick et al. (2010) and Ryan et al. (2017) demonstrated significant improvements up to 6 months post-treatment for non-treated phobias in children who participated for one session treatment for specific phobia. Due to the mixed findings further research focusing on whether exposure therapy for one fear generalises to other untreated fears is required.

The evidence of the high comorbidity of fears, the associated recovery rates for multiple phobias and the lack of generalisation across stimuli, suggests that a secondary phobia is a risk factor for conditional reinstatement of fear. Investigating conditional reinstatement of fear with human participants may increase the real-world applicability of reinstatement of fear. In a clinical example, an individual may undergo exposure therapy for a primary fear of spiders and have a secondary fear of snakes. Subsequent to successful exposure therapy for fear of spiders, the individual may encounter a snake andthis might trigger a reinstatement of the primary fear of spiders. This clinical example has more real-world applicability and may be more likely to occur than traditional reinstatement, such as an individual re-experiencing the US (e.g., a wasp bite), followingsuccessful exposure therapy. Therefore, this would suggest that an unextinguished CS, which could be translated to a clinical term of multifarious stimuli (e.g., multiple different stimuli such as: spider and snakes) may elicit reinstatement of fear. Throughoutthe thesis, when discussing laboratory findings the terms unextinguished CS and extinguished CS will be used and when discussing clinical relevant phenomena the termsmultifarious stimuli will be employed.

If the results from Halladay et al. (2012) extend to human participants, a simple encounter with another feared stimulus would significantly increase the likelihood of an individual experiencing reinstatement of fear. Bouton's contextual memory model (Bouton, 2002) could explain conditional reinstatement in humans by suggesting that encountering a secondary untreated fear and the associated contextual cues may enhance retrieval of the CS-US association which is relatively context-independent. Conditional reinstatement may be consistent with studies with rats that highlight the role of emotions in extinction and reinstatement and the important role of the contextual cues activating an

affective representation of the untreated fear (Halladay et al., 2012; Kellett & Kokkinidis, 2004; Rescorla and Heth, 1975b).

Based on the presumption that fear can be reinstated by a secondary fear with human participants, exposure to multifarious stimuli could be another method to reduce conditional reinstatement. Rowe and Craske (1998) and Shiban et al. (2015) have found that exposure to multiple similar stimuli (e.g., different types of spiders) reduced renewal of fear. Previous clinical-analogue studies have shown that exposure to multiple extinction contexts has been found to attenuate fear renewed by a context change (e.g., Bandarian-Balooch et al., 2015; Glautier et al., 2013; Shiban et al., 2015). Exposure to multiple extinction contexts has some similarity to exposure to multifarious stimuli in that it could increase the number of shared cues between extinction learning and subsequent exposure to the feared stimulus (Bouton, 2002). Thus, similar to renewal research on multiple extinction contexts and multiple similar stimuli, it is possible that exposure to multifarious stimuli can reliably reduce reinstatement of fear. This method has valuable clinical implications as it suggests clinicians should incorporate sessions with multifarious stimuli to prevent reinstatement of the primary fear due to an encounter of a secondary feared object. However, there is currently insufficient evidence to support this suggestion. There is little empirical research examining multiple phobias and no previous studies have examined whether exposure to multifarious stimuli can reduce conditional reinstatement of fear.

Summary and Conclusions

In summary, there is limited translational research investigating reinstatement of fear from laboratory studies to clinical studies particularly when compared to the other

mechanisms of return of fear. Challenges of investigating reinstatement of fear include ethical issues of the reinstating US and the lack of clinically relevant stimuli in previous research. Translational research from laboratory-based studies to clinical-analogue and clinical studies has important clinical implications for how to improve the long-term effectiveness of exposure therapy for the anxiety disorders including specific phobia. As noted, 75% of individuals experience multiple phobias and the likelihood of recovering from specific phobia is inversely associated with the number of fears (Wittchen et al., 2002). Novel approaches to investigating reinstatement of fear are needed to translate laboratory-based findings such as whether an unextinguished CS can elicit reinstatement of fear (Halladay et al., 2012) to clinical settings.

References

Abramowitz, J. S., Deacon, B. J., & Whiteside, S. P. (2012). *Exposure therapy for anxiety: Principles and practice*. Guilford Press.

Australian Bureau of Statistics (2019b). National Health Survey: first results, 2017-18. ABS cat. no. 4364.0.55.001. Canberra: ABS. https://www.abs.gov.au/statistics/health/health-conditions-and-risks/national-health-survey-first-results/latest-release

Australian Institute of Health and Welfare. (2021). *Mental health services in Australia.* Retrieved from https://www.aihw.gov.au/reports/mental-health-services/mental-health-services-in-australia

Aknin, L., De Neve, J. E., Dunn, E., Fancourt, D., Goldberg, E., Helliwell, J. F., ... & Ben Amor, Y. (2021). Mental health during the first year of the COVID-19 pandemic: A review and recommendations for moving forward. *Perspectives on Psychological Science*.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

Askew, C., & Field, A. P. (2007). Vicarious learning and the development of fears in childhood. *Behaviour Research and Therapy*, *45*(11), 2616-2627. https://doi.org/10.1016/j.brat.2007.06.008

Bagley, L. R., & Bandarian-Balooch, S. (2020). Attenuation of renewal of fear using context similarity with spider fearful individuals. *Learning and Motivation*, *70*, 101630. https://doi.org/10.1016/j.lmot.2020.101630

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2013). Renewal of fear: clinical-analogue findings. In *Psychology of fear: New developments* (pp. 1-27). Nova Science Publishers.

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 138-144. https://doi.org/10.1016/j.jbtep.2014.12.006

Barry, T. J., Griffith, J. W., De Rossi, S., & Hermans, D. (2014). Meet the Fribbles: Novel stimuli for use within behavioural research. *Frontiers in Psychology*, *5*, 103. https://doi.org/10.3389/fpsyg.2014.00103

Becker, E. S., Rinck, M., Türke, V., Kause, P., Goodwin, R., Neumer, S., & Margraf, J. (2007). Epidemiology of specific phobia subtypes: Findings from the Dresden Mental Health Study. *European Psychiatry*, *22*(2), 69-74. https://doi.org/10.1016/j.eurpsy.2006.09.006

Best, L. (2014). Generalization of Fear Effects in Reinstatement to a Discrete Stimulus. USC Aiken Psychology Theses. https://scholarcommons.sc.edu/aiken_psychology_theses/9

Bocchio, M., Nabavi, S., & Capogna, M. (2017). Synaptic plasticity, engrams, and network oscillations in amygdala circuits for storage and retrieval of emotional memories. *Neuron*, *94*(4), 731-743. https://doi.org/10.1016/j.neuron.2017.03.022

Boschen, M. J., Neumann, D. L., & Waters, A. M. (2009). Relapse of successfully treated anxiety and fear: Theoretical issues and recommendations for clinical practice. *Australian & New Zealand Journal of Psychiatry*, *43*(2), 89-100.

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*(1), 80. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology*, *19*(1S), 57. https://doi.org/10.1037/0278-6133.19.Suppl1.57

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological Psychiatry*, *52*(10), 976-986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning and Memory*, *11*(5), 485-494. http://www.learnmem.org/cgi/doi/10.1101/lm.78804.

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445-466. https://doi.org/10.1016/0023-9690(79)90057-2

Bouton, M. E., Maren, S., & McNally, G. P. (2021). Behavioral and neurobiological mechanisms of Pavlovian and instrumental extinction learning. *Physiological Reviews*, *101*(2), 611-681. https://doi.org/10.1152/physrev.00016.2020

Bouton, M. E., & Swartzentruber, D. (1991). Sources of relapse after extinction in Pavlovian and instrumental learning. *Clinical Psychology Review*, *11*(2), 123-140. https://doi.org/10.1016/0272-7358(91)90091-8

Bouton, M. E., Westbrook, R. F., Corcoran, K. A., & Maren, S. (2006). Contextual and temporal modulation of extinction: behavioral and biological mechanisms.

Biological Psychiatry, *60*(4), 352-360. https://doi.org/10.1016/j.biopsych.2005.12.015

Brooks, D. C., & Bouton, M. E. (1993). A retrieval cue for extinction attenuates spontaneous recovery. *Journal of Experimental Psychology: Animal Behavior Processes*, *19*(1), 77. https://doi.org/10.1037/0097-7403.19.1.77

Burstein, M., Georgiades, K., He, J. P., Schmitz, A., Feig, E., Khazanov, G. K., & Merikangas, K. (2012). Specific phobia among US adolescents: Phenomenology and typology. *Depression and Anxiety*, *29*(12), 1072-1082. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.22008

Bush, J. (2008). Viability of virtual reality exposure therapy as a treatment alternative. *Computers in Human Behavior*, *24*(3), 1032-1040. https://doi.org/10.1016/j.chb.2007.03.006

Callen, E. J., McAllister, W. R., & McAllister, D. E. (1984). Investigations of the reinstatement of extinguished fear. *Learning and Motivation*, *15*(3), 302-320. https://doi.org/10.1016/0023-9690(84)90025-0

Ciobanu, L. G., Ferrari, A. J., Erskine, H. E., Santomauro, D. F., Charlson, F. J., Leung, J., ... & Baune, B. T. (2018). The prevalence and burden of mental and substance use disorders in Australia: Findings from the Global Burden of Disease Study 2015. *Australian & New Zealand Journal of Psychiatry*, *52*(5), 483-490. https://doi.org/10.1177/0004867417751641

Craske, M. G. (1999). *Anxiety disorders: psychological approaches to theory and treatment*. Westview Press. https://psycnet.apa.org/record/1998-06744-000

Culver, N. C., Stoyanova, M., & Craske, M. G. (2011). Clinical relevance of retrieval cues for attenuating context renewal of fear. *Journal of Anxiety Disorders*, *25*(2), 284-292. https://doi.org/10.1016/j.janxdis.2010.10.002

Curtis, G., Magee, W. J., Eaton, W. W., Wittchen, H. U., & Kessler, R. C. (1998). Specific fears and phobias: Epidemiology and classification. *The British Journal of Psychiatry*, *173*(3), 212-217. https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/abs/specific-fears-and-phobias/E3E1FDE206DD1A47EFCCA2B41C5DA37C#metrics

Davey, G. C. (1992). Classical conditioning and the acquisition of human fears and phobias: A review and synthesis of the literature. *Advances in Behaviour Research and Therapy*, *14*(1), 29-66. https://doi.org/10.1016/0146-6402(92)90010-L

Delamater, A. R., & Westbrook, R. F. (2014). Psychological and neural mechanisms of experimental extinction: A selective review. *Neurobiology of Learning and Memory*, *108*, 38-51. https://doi.org/10.1016/j.nlm.2013.09.016

Depla, M. F., Margreet, L., van Balkom, A. J., & de Graaf, R. (2008). Specific fears and phobias in the general population: Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Social Psychiatry and Psychiatric Epidemiology*, *43*(3), 200-208. https://doi.org/10.1007/s00127-007-0291-z

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2004). Reinstatement of extinguished conditioned responses and negative stimulus valence as a pathway to return of fear in humans. *Learning & Memory*, *11*(5), 549-554. http://www.learnmem.org/cgi/doi/10.1101/lm.78004.

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, *38*(3), 237-251. https://doi.org/10.1016/j.jbtep.2006.04.001

Dirikx, T., Vansteenwegen, D., Eelen, P., & Hermans, D. (2009). Non-differential return of fear in humans after a reinstatement procedure. *Acta Psychologica*, *130*(3), 175-182. https://doi.org/10.1016/j.actpsy.2008.12.002

Dunsmoor, J. E., Ahs, F., Zielinski, D. J., & LaBar, K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, *113*, 157-164. https://doi-org.10.1016/j.nlm.2014.02.010

Effting, M., & Kindt, M. (2007). Contextual control of human fear associations in a renewal paradigm. *Behaviour Research and Therapy*, *45*(9), 2002-2018. https://doi.org/10.1016/j.brat.2007.02.011

Farinelli, M., Deschaux, O., Hugues, S., Thevenet, A., & Garcia, R. (2006). Hippocampal train stimulation modulates recallof fear extinction independently of prefrontalcortex synaptic plasticity and lesions. *Learning & Memory*, *13*(3), 329-334. http://www.learnmem.org/cgi/doi/10.1101/lm.204806

Farrell, L. J., Miyamoto, T., Donovan, C. L., Waters, A. M., Krisch, K. A., & Ollendick, T. H. (2021). Virtual reality one-Session treatment of child-specific phobia of dogs: A controlled, multiple baseline case aeries. *Behavior Therapy*, *52*(2), 478-491. https://www-clinicalkey-com-au.libraryproxy.griffith.edu.au/service/content/pdf/watermarked/1-s2.0-S0005789420300861.pdf?locale=en_AU&searchIndex=

Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: exposure to corrective information. *Psychological Bulletin*, *99*(1), 20. https://doi.org/10.1037/0033-2909.99.1.20

Forcadell, E., Torrents-Rodas, D., Vervliet, B., Leiva, D., Tortella-Feliu, M., & Fullana, M. A. (2017). Does fear extinction in the laboratory predict outcomes of exposure therapy? A treatment analog study. *International Journal of Psychophysiology*, *121*, 63-71. https://doi.org/10.1016/j.ijpsycho.2017.09.001

Garcia-Palacios, A., Hoffman, H. G., Kwong See, S., Tsai, A. M. Y., & Botella, C. (2001). Redefining therapeutic success with virtual reality exposure therapy. *CyberPsychology & Behavior*, *4*(3), 341-348. https://doi.org/10.1089/109493101300210231

Gazendam, F. J., & Kindt, M. (2012). Worrying affects associative fear learning: a startle fear conditioning study. *PLoS One*, *7*(4), e34882. https://doi.org/10.1371/journal.pone.0034882

Gershman, S. J., Jones, C. E., Norman, K. A., Monfils, M. H., & Niv, Y. (2013). Gradual extinction prevents the return of fear: Implications for the discovery of state. *Frontiers in Behavioral Neuroscience*, *7*, 164. https://doi.org/10.3389/fnbeh.2013.00164

Gerull, F. C., & Rapee, R. M. (2002). Mother knows best: Effects of maternal modelling on the acquisition of fear and avoidance behaviour in toddlers. *Behaviour Research and Therapy*, *40*(3), 279-287. https://doi.org/10.1016/S0005-7967(01)00013-4

Glautier, S., Elgueta, T., & Nelson, J. B. (2013). Extinction produces context inhibition and multiple-context extinction reduces response recovery in human predictive learning. *Learning & Behavior*, *41*(4), 341-352. https://doi.org/10.3758/s13420-013-0109-7

Gloor, P. (1992). Role of the amygdala in temporal lobe epilepsy. In J. P. Aggleton (Ed.), *The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction* (pp. 505–538). Wiley-Liss.

Haaker, J., Golkar, A., Hermans, D., & Lonsdorf, T. B. (2014). A review on human reinstatement studies: An overview and methodological challenges. *Learning & Memory*, *21*(9), 424-440. http://www.learnmem.org/cgi/doi/10.1101/lm.036053.114

Haesen, K., & Vervliet, B. (2015). Beyond extinction: Habituation eliminates conditioned skin conductance across contexts. *International Journal of Psychophysiology*, *98*(3), 529-534. https://doi.org/10.1016/j.ijpsycho.2014.11.010

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Hendry, J. S. (1982). Summation of undetected excitation following extinction of the CER. *Animal Learning & Behavior*, *10*(4), 476-482. https://doi.org/10.3758/BF03212287

Hermans, D., Dirikx, T., Vansteenwegenin, D., Baeyens, F., Van den Bergh, O., & Eelen, P. (2005). Reinstatement of fear responses in human aversive conditioning.

Behaviour Research and Therapy, *43*(4), 533-551. https://doi.org/10.1016/j.brat.2004.03.013

Jacobs, W. J., & Nadel, L. (1985). Stress-induced recovery of fears and phobias. *Psychological Review*, *92*(4), 512. https://doi.org/10.1037/0033-295X.92.4.512

Jessup, S. C., Tomarken, A., Viar-Paxton, M. A., & Olatunji, B. O. (2020). Effects of repeated exposure to fearful and disgusting stimuli on fear renewal in blood-injection-injury phobia. *Journal of Anxiety Disorders*, *74*, 102272. https://doi.org/10.1016/j.janxdis.2020.102272

Kattoor, J., Gizewski, E. R., Kotsis, V., Benson, S., Gramsch, C., Theysohn, N., ... & Elsenbruch, S. (2013). Fear conditioning in an abdominal pain model: Neural responses during associative learning and extinction in healthy subjects. *PloS one*, *8*(2), e51149. https://doi.org/10.1371/journal.pone.0051149

Kellett, J., & Kokkinidis, L. (2004). Extinction deficit and fear reinstatement after electrical stimulation of the amygdala: Implications for kindling-associated fear and anxiety. *Neuroscience*, *127*(2), 277-287. https://doi.org/10.1016/j.neuroscience.2004.05.011

Kessler R. C, & Wang P. S. (2008). The Descriptive Epidemiology of Commonly Occurring Mental Disorders in the United States. *Annual Review Public Health*, *29*, 115-129. https://doi.org.10.1146/annurev.publhealth.29.020907.090847

Kim, J. H., & Richardson, R. (2007). A developmental dissociation in reinstatement of an extinguished fear response in rats. *Neurobiology of Learning and Memory*, *88*(1), 48-57. https://doi.org/10.1016/j.nlm.2007.03.004

King, N. J., Muris, P., & Ollendick, T. H. (2004). Specific phobia. In *Anxiety Disorders in Children and Adolescents* (pp. 263-279). Guilford Press. https://psycnet.apa.org/record/2004-16376-012

Kindt, M., & Soeter, M. (2013). Reconsolidation in a human fear conditioning study: A test of extinction as updating mechanism. *Biological Psychology*, *92*(1), 43-50. https://doi.org/10.1016/j.biopsycho.2011.09.016

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2018). Effects of extended extinction and multiple extinction contexts on ABA renewal. *Learning and Motivation*, *63*, 1-10. https://doi.org/10.1016/j.lmot.2017.11.001

Krisch, K. A., Bandarian-Balooch, S., O'Donnell, A. W., & Neumann, D. L. (2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. *Virtual reality: Advances in research and applications*, 85-126.

Kull, S., Müller, B. H., Blechert, J., Wilhelm, F. H., & Michael, T. (2012). Reinstatement of fear in humans: autonomic and experiential responses in a differential conditioning paradigm. *Acta psychologica*, *140*(1), 43-49. https://doi.org/10.1016/j.actpsy.2012.02.007

LaBar, K. S., & Phelps, E. A. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, *119*(3), 677. https://10.1037/0735-7044.119.3.677

Laborda, M. A., McConnell, B. L., & Miller, R. R. (2011). Behavioral techniques to reduce relapse after exposure therapy. *Associative Learning and Conditioning Theory*, *1*, 79-104.

Laborda, M. A., & Miller, R. R. (2013). Preventing return of fear in an animal model of anxiety: Additive effects of massive extinction and extinction in multiple contexts. *Behavior Therapy*, *44*(2), 249-261. https://doi.org/10.1016/j.beth.2012.11.001

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

Laurent, V., & Westbrook, R. F. (2009). Inactivation of the infralimbic but not the prelimbic cortex impairs consolidation and retrieval of fear extinction. *Learning & Memory*, *16*(9), 520-529. http://www.learnmem.org/cgi/doi/10.1101/lm.1474609.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and Anxiety*, *27*(2), 148-167. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.20655

LeDoux, J. E. (2015). Feelings: What are they & how does the brain make them?. *Daedalus*, *144*(1), 96-111. https://doi.org/10.1162/DAED_a_00319

Leer, A., & Engelhard, I. M. (2015). Countering fear renewal: Changes in the UCS representation generalize across contexts. *Behavior Therapy*, *46*(2), 272-282. https://doi.org/10.1016/j.beth.2014.09.012

Leitenberg, H., Rawson, R. A., & Bath, K. (1970). Reinforcement of competing behavior during extinction. *Science*, *169*(3942), 301-303. https://doi.org/10.1126/science.169.3942.301

Lissek, S., Biggs, A. L., Rabin, S. J., Cornwell, B. R., Alvarez, R. P., Pine, D. S., & Grillon, C. (2008). Generalization of conditioned fear-potentiated startle in humans: experimental validation and clinical relevance. *Behaviour Research and Therapy*, *46*(5), 678-687. https://doi.org/10.1016/j.brat.2008.02.005

Magee, W. J., Eaton, W. W., Wittchen, H. U., McGonagle, K. A., & Kessler, R. C. (1996). Agoraphobia, simple phobia, and social phobia in the National Comorbidity Survey. *Archives of general psychiatry*, *53*(2), 159-168. https://doi.org.10.1001/archpsyc.1996.01830020077009

Marek, S., Siegel, J. S., Gordon, E. M., Raut, R. V., Gratton, C., Newbold, D. J., ... & Dosenbach, N. U. (2018). Spatial and temporal organization of the individual human cerebellum. *Neuron*, *100*(4), 977-993. https://doi.org/10.1016/j.neuron.2018.10.010

Marin, M. F., Bilodeau-Houle, A., Morand-Beaulieu, S., Brouillard, A., Herringa, R. J., & Milad, M. R. (2020). Vicarious conditioned fear acquisition and extinction in child–parent dyads. *Scientific Reports*, *10*(1), 1-10. https://doi.org/10.1038/s41598-020-74170-1

Marks, I. M. (1987). *Fears, phobias, and rituals: Panic, anxiety, and their disorders*. Oxford University Press on Demand.

Matthews, A., Naran, N., & Kirkby, K. C. (2015). Symbolic online exposure for spider fear: Habituation of fear, disgust and physiological arousal and predictors of symptom improvement. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 129-137. https://doi.org/10.1038/s41598-020-74170-1

McClelland, J. L., & Rumelhart, D. E. (1985). Distributed memory and the representation of general and specific information. *Journal of Experimental Psychology: General*, *114*(2), 159.

McCloskey, M., & Cohen, N. J. (1989). Catastrophic interference in connectionist networks: The sequential learning problem. In *Psychology of Learning and Motivation* (Vol. 24, pp. 109-165). Academic Press. https://doi.org/10.1016/S0079-7421(08)60536-8

Menzies, R. G., & Clark, J. C. (1993a). The etiology of childhood water phobia. Behaviour *Research and Therapy, 31*, 499–501. https://doi.org/10.1016/0005-7967(93)90131-D

Milad, M. R., Orr, S. P., Pitman, R. K., & Rauch, S. L. (2005). Context modulation of memory for fear extinction in humans. *Psychophysiology*, *42*(4), 456-464. https://doi.org/10.1111/j.1469-8986.2005.00302.x

Milad, M. R., & Quirk, G. J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, *420*(6911), 70-74. https://doi.org/10.1038/nature01138

Mozafari, R., Jamali, S., Pourhamzeh, M., Koruji, M., Ahadi, R., & Haghparast, A. (2020). The blockade of D1-and D2-like dopamine receptors within the dentate gyrus attenuates food deprivation stress-induced reinstatement of morphine-extinguished conditioned place preference in rats. *Pharmacology Biochemistry and Behavior*, *196*, 172967. https://doi.org/10.1016/j.pbb.2020.172967

Mystkowski, J. L., Craske, M. G., Echiverri, A. M., & Labus, J. S. (2006). Mental reinstatement of context and return of fear in spider-fearful participants. *Behavior Therapy*, *37*(1), 49-60. https://doi.org/10.1016/j.beth.2005.04.001

Nall, R. W., & Shahan, T. A. (2020). Resurgence of punishment-suppressed cocaine seeking in rats. *Experimental and Clinical Psychopharmacology*, *28*(3), 365. https://doi.org/10.1037/pha0000317

Napier, R. M., Macrae, M., & Kehoe, E. J. (1992). Rapid reacquisition in conditioning of the rabbit's nictitating membrane response. *Journal of Experimental Psychology: Animal Behavior Processes*, *18*(2), 182.

Neumann, D. L. (2007). The resistance of renewal to instructions that devalue the role of contextual cues in a conditioned suppression task with humans. *Learning and Motivation*, *38*(2), 105-127. https://doi.org/10.1016/j.lmot.2006.11.002

Neumann, D. L., & Longbottom, P. L. (2008). The renewal of extinguished conditioned fear with fear-relevant and fear-irrelevant stimuli by a context change after extinction. *Behaviour Research and Therapy*, *46*(2), 188-206. https://doi.org/10.1016/j.brat.2007.12.004

Neumann, D. L., & Kitlertsirivatana, E. (2010). Exposure to a novel context after extinction causes a renewal of extinguished conditioned responses: implications for the treatment of fear. *Behaviour Research and Therapy*, *48*(6), 565-570. https://doi.org/10.1016/j.brat.2010.03.002

Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure.

Biological Psychology, *73*(2), 175-185. https://doi.org/10.1016/j.biopsycho.2006.03.004

Neumann, D. L., Waters, A. M., & Westbury, H. R. (2008). The use of an unpleasant sound as the unconditional stimulus in aversive Pavlovian conditioning experiments that involve children and adolescent participants. *Behavior research methods*, *40*(2), 622-625. https://doi.org/10.3758/BRM.40.2.622

Norrholm, S. D., Jovanovic, T., Vervliet, B., Myers, K. M., Davis, M., Rothbaum, B. O., & Duncan, E. J. (2006). Conditioned fear extinction and reinstatement in a human fear-potentiated startle paradigm. *Learning & Memory*, *13*(6), 681-685. http://www.learnmem.org/cgi/doi/10.1101/lm.393906

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: toward an evolved module of fear and fear learning. *Psychological Review*, *108*(3), 483. https://doi.org/10.1037/0033-295X.108.3.483

Öst, L. G. (1987). Applied relaxation: description of a coping technique and review of controlled studies. *Behaviour Research and Therapy*, *25*(5), 397-409. https://doi.org/10.1016/0005-7967(87)90017-9

Öst, L. G. (1989). One-session treatment for specific phobias. *Behaviour Research and Therapy*, *27*(1), 1-7. https://doi.org/10.1016/0005-7967(89)90113-7

Pavlov IP. (1927). Conditioned reflexes. London: Oxford University Press.

Pischek-Simpson, L. K., Boschen, M. J., Neumann, D. L., & Waters, A. M. (2009). The development of an attentional bias for angry faces following Pavlovian fear conditioning. *Behaviour Research and Therapy*, *47*(4), 322-330. https://doi.org/10.1016/j.brat.2009.01.007

Rachman, S. (1966). Studies in desensitization—II: Flooding. *Behaviour Research and Therapy*, *4*(1-2), 1-6. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman, S. (1977). The conditioning theory of fear acquisition: A critical examination. *Behaviour Research and Therapy*, *15*(5), 375-387. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman, S., & Whittal, M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, 27, 513-520. https://doi.org/10.1016/0005-7967(89)90085-5

Rescorla, R. A. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement. *Current Research and Theory*, 64-99.

Rescorla, R. A. (2001). Retraining of extinguished Pavlovian stimuli. *Journal of Experimental Psychology: Animal Behavior Processes*, *27*(2), 115. https://doi.org/10.1037/0097-7403.27.2.115

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*(1), 88. https://pubmed.ncbi.nlm.nih.gov/1151290/

Richardson, R., Duffield, T. Q., Bailey, G. K., & Westbrook, R. F. (1999). Reinstatement of fear to an extinguished conditioned context. *Animal Learning & Behavior*, *27*(4), 399-415. https://doi.org/10.3758/BF03209977

Rose, M. P., & McGlynn, F. D. (1997). Toward a standard experiment for studying post-treatment return of fear. *Journal of Anxiety Disorders*, *11*(3), 263-277. https://doi.org/10.1016/S0887-6185(97)00010-8

Rowe, M. K., & Craske, M. G. (1998). Effects of varied-stimulus exposure training on fear reduction and return of fear. *Behaviour Research and Therapy*, *36*(7-8), 719-734. https://doi.org/10.1016/S0005-7967(97)10017-1

Ryan, S. M., Strege, M. V., Oar, E. L., & Ollendick, T. H. (2017). One session treatment for specific phobias in children: Comorbid anxiety disorders and treatment outcome. *Journal of Behavior Therapy and Experimental Psychiatry, 54,* 128-134.

Taslimi, Z., Komaki, A., Haghparast, A., & Sarihi, A. (2018). Effects of acute and chronic restraint stress on reinstatement of extinguished methamphetamine-induced conditioned place preference in rats. *Basic and Clinical Neuroscience*, *9*(3), 157. https://doi.org.10.29252/nirp.bcn.9.3.157

Thomas, B. L., Vurbic, D., & Novak, C. (2009). Extensive extinction in multiple contexts eliminates the renewal of conditioned fear in rats. *Learning and Motivation*, *40*(2), 147-159. https://doi.org/10.1016/j.lmot.2008.10.002

Sapolsky, R., Uno, H., Rebert, C., and Finch, C. (1990). Hippocampal damage with prolonged glucocorticoid exposure in primates. *Journal Neuroscience.* 10, 2897–2902. https://doi.org.10.1523/JNEUROSCI.10-09-02897.1990

Schiller, D., Cain, C. K., Curley, N. G., Schwartz, J. S., Stern, S. A., LeDoux, J. E., & Phelps, E. A. (2008). Evidence for recovery of fear following immediate extinction in rats and humans. *Learning & Memory*, *15*(6), 394-402. http://www.learnmem.org/cgi/doi/10.1101/lm.909208.

Sevenster, D., Beckers, T., & Kindt, M. (2012). Instructed extinction differentially affects the emotional and cognitive expression of associative fear memory. *Psychophysiology*, *49*(10), 1426-1435. https://doi.org/10.1111/j.1469-8986.2012.01450.x

Shiban, Y., Pauli, P., & Mühlberger, A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, *51*(2), 68-74. https://doi.org/10.1016/j.brat.2012.10.007

Shiban Y., Schelhorn I., Pauli P., & Mühlberger A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, 71, 45-53. https://doi.org/10.1016/j.brat.2015.05.014

Sokol, N., & Lovibond, P. F. (2012). Cross-US reinstatement of human conditioned fear: Return of old fears or emergence of new ones?. *Behaviour Research and Therapy*, *50*(5), 313-322. https://doi.org/10.1016/j.brat.2012.02.005

Stein, M. B., & Craske, M. G. (2017). Treating anxiety in 2017: Optimizing care to improve outcomes. *Jama*, *318*(3), 235-236. https://doi.org/10.1001/jama.2017.6996

Stinson, F. S., Dawson, D. A., Chou, S. P., Smith, S., Goldstein, R. B., Ruan, W. J., & Grant, B. F. (2007). The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine*, *37*(7), 1047-1059. https://doi.org/10.1017/S0033291707000086

Toft, T., Fink, P. E. R., Oernboel, E. V. A., Christensen, K. A. J., Frostholm, L., & Olesen, F. (2005). Mental disorders in primary care: Prevalence and co-morbidity among disorders. Results from the functional illness in primary care (FIP) study. *Psychological Medicine*, *35*(8), 1175-1184. https://doi.org.10.1017/S0033291705004459

Van Houtem C. M., Laine M. L., Boomsma D. I., Ligthart L., Van Wijk A. J., & De Jongh A. (2013). A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears. *Journal of Anxiety Disorders*, 27, 379-388. https://doi.org/10.1016/j.janxdis.2013.04.007

Vansteenwegen, D., Vervliet, B., Iberico, C., Baeyens, F., Van den Bergh, O., & Hermans, D. (2007). The repeated confrontation with videotapes of spiders in multiple contexts attenuates renewal of fear in spider-anxious students. *Behaviour Research and Therapy*, *45*(6), 1169-1179. https://doi.org/10.1016/j.brat.2006.08.023

Vervliet, B., Craske, M. G., & Hermans, D. (2013). Fear extinction and relapse: State of the art. *Annual Review of Clinical Psychology*, *9*, 215-248. https://doi.org/10.1146/annurev-clinpsy-050212-185542

Wardenaar, K. J., Lim, C. C., Al-Hamzawi, A. O., Alonso, J., Andrade, L. H., Benjet, C., ... & De Jonge, P. (2017). The cross-national epidemiology of specific phobia in the World Mental Health Surveys. *Psychological Medicine*, *47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Warren, V. T., Anderson, K. M., Kwon, C., Bosshardt, L., Jovanovic, T., Bradley, B., & Norrholm, S. D. (2014). Human fear extinction and return of fear using reconsolidation update mechanisms: The contribution of on-line expectancy ratings. *Neurobiology of Learning and Memory*, *113*, 165-173. https://doi.org/10.1016/j.nlm.2013.10.014

Wehrenberg, M., and Prinz, S. (2007). *The Anxious Brain: The Neurobiological Basis of Anxiety Disorders and how to Effectively Treat them.* New York, NY: W.W. Norton.

Westbrook, R. F., Iordanova, M., McNally, G., Richardson, R., & Harris, J. A. (2002). Reinstatement of fear to an extinguished conditioned stimulus: Two roles for context. *Journal of Experimental Psychology: Animal Behavior Processes*, *28*(1), 97. https://doi.org/10.1037/0097-7403.28.1.97

Wittchen, H. U., Lecrubier, Y., Beesdo, K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. *Anxiety Disorders*, 23-37. https://doi.org/10.1002/9780470986844.ch2

Wolpe, J. (1958). Psychotherapy by reciprocal inhibition. *Conditional reflex: a Pavlovian Journal of Research & Therapy*, *3*(4), 234-240. https://doi.org/10.1007/BF03000093

Chapter 3: Preamble

The previous chapters have highlighted the gap between the reinstatement effects produced in the laboratory and reinstatement of fear occurring in clinical-analogue and clinical samples. Chapters 1 and 2 reviewed the literature on the ethical constraints to conducting reinstatement of fear with clinical samples and drew attention to the lack of focus in research for those with multiple phobias. Chapter 3 is a published book chapter which aimed to review the use of virtual reality exposure therapy (VRET) in treating specific phobia with a particular focus on reducing return of fear. The theoretical frameworks underpinning exposure therapy and the mechanisms of return of fear are summarised. VRET is compared with traditional exposure-based treatments and factors impacting treatment choice are outlined. A key focus of this review is considering the generalisability of translating VRET research to clinical settings. The chapter provides suggestions for future research for VRET in reducing return of fear for specific phobia. Overall, and in the context of the thesis, Chapter 3 provides a methodology that may bridge the gap between reinstatement effects produced in the laboratory and reinstatement of fear in clinical settings.

STATEMENT OF CONTRIBUTION TO CO-AUTHORED PUBLISHED PAPER

This chapter includes a co-authored published book chapter. The bibliographic details of the published paper, including all authors are:

Krisch K. A,, Bandarian-Balooch S., O'Donnell A. W., & Neumann D. L. (2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. In Z. Hill (Ed.), *Virtual reality: Advances in research and applications* (pp. 85–126). Nova Science.

The candidate was responsible for manuscript preparation including: conducting the literature search and reviewing the literature, writing the substantial amount of the manuscript, submitting the manuscript and revising the manuscript in line with the reviewers edits under supervision. Dr Alexander O'Donnell wrote a section of the manuscript on virtual reality technology under supervision and Dr Siavash Bandarian wrote a section on summarizing the clinical applications of VRET in combination with in vivo exposure therapy. The formatting is consistent with the referencing style required at time of publication.

(Signed)_____(Date): 16/11/21
Kirra Krisch

(Countersigned)_____(Date): 16/11/21
Supervisor: Dr Siavash Bandarian

(Countersigned) _____ (Date): 30/11/21
Corresponding author: Dr Alexander O'Donnell

(Countersigned) _____ (Date): 16/11/21
Supervisor: Professor David Neumann

Chapter 3: A Review of Virtual Reality Exposure Therapy for Specific Phobia and its Clinical Application to Reduce Return of Fear

Kirra A. Krisch[1*], Siavash Bandarian-Balooch[1,2], Alexander W. O'Donnell[1], & David L. Neumann[1,2]

[1]School of Applied Psychology Griffith University, Australia

[2]Menzies Health Institute Queensland, Australia

Abstract

Virtual reality exposure treatment (VRET) is an emerging technique that overcomes many challenges of in vivo exposure-based treatments in clinical psychology. Research has examined VRET in treating a range of anxiety disorders, predominantly specific phobia. More recently, research has considered the effectiveness of VRET in reducing return of fear for specific phobia. Return of fear is a partial reappearance of anxiety symptoms following successful exposure treatment. There are four mechanisms underlying return of fear: renewal, spontaneous recovery, reacquisition, and reinstatement. This chapter reviews the use of VRET for specific phobia and the relative situations most applicable to VRET and traditional exposure-based treatments are outlined. Virtual reality technology and equipment for clinical settings are evaluated, with particular focus on emerging and accessible techniques that will facilitate further growth of VRET and allow for more individualised treatment plans. Recommendations for reducing return of fear using VRET for specific phobia are also made.

Keywords: Virtual reality; exposure therapy; specific phobia; return of fear

Introduction

Virtual reality technologies have been used as a supplement or as an alternative treatment to traditional exposure-based treatment for a range of anxiety disorders (Meyerbroker, & Emmelkamp, 2010; Opris et al., 2012). Traditional exposure-based treatments involve the individual imagining (i.e., imaginal exposure) or being repeatedly presented with the feared stimulus in person (i.e., in vivo) until the fear is reduced (Barlow, Craske, Cerny, & Klosko, 1989; Bush, 2008; Öst, 1989, Wolpe, 1958). In contrast, virtual reality exposure therapy (VRET) involves systematically exposing an individual to the feared object or situation within a virtual environment with the aim being to attenuate anxiety and fear (Pratt, Zyda, & Kelleher, 1995).

To deliver VRET, a clinician needs software to create a virtual environment and hardware to present the virtual environment to the client. Initial research and clinical applications of VRET were conducted exclusively with computer-generated graphics designed using the appropriate software (Rothbaum, Hodges, Watson, Kessler, & Opdyke, 1996). The hardware component of virtual reality consisted of two options: a Computer Automatic Virtual Environment (CAVE) or a Head Mounted Display (HMD). The CAVE system is a projection based virtual reality system involving a large cube composed of display screens that the user(s) will enter to immerse themselves in a virtual environment (Cruz-Neira, Sandin, & DeFanti, 1993; Heim, 1995). HMDs are wearable devices that remove vision of the outside world whilst providing immersive pictorial information from miniature visual displays and corresponding auditory information from speakers near the ears (Emmelkamp, 2005; Patterson, Winterbottom, & Pierce, 2006).

Previous VRET research has predominantly focused on the treatment of specific phobia (Emmelkamp, 2005; Emmelkamp, Bruynzeel, Drost, & Van Der Mast, 2001). Specific phobia is an anxiety disorder marked by excessive and persistent fear of an object or situation (APA, 2013). VRET for specific phobia involves presenting the individual with a virtual representation of the phobic stimulus or situation (Carlin, Hoffman, & Weghorst, 1997; Opris et al., 2012). VRET is particularly relevant for the treatment of several specific phobia types, including spider phobia (Garcia-Palacios, Hoffman, Carlin Furness, & Botella, 2002, Michaliszyn, Marchand, Bouchard, Martel, & Poirier-Bisson, 2010; Shiban, Schelhorn, Pauli, & Mühlberger, 2015), fear of flying (Krijn, et al., 2007; Maltby, Kirsch, Mayers, & Allen, 2002; Rothbaum et al., 2006), fear of heights (Emmelkamp et al., 2001; Rothbaum et al., 1995), and driving phobia (Wald & Taylor, 2000; 2003). This is because VRET can help minimise the challenges these phobia types have for in vivo treatment in terms of cost, health and safety, and feasibility (Bouchard, Cote, & Richard, 2007; Emmelkamp, 2005; Parsons, 2015).

In treating specific phobia, VRET can address many challenges of existing traditional exposure techniques (Bush, 2008; Parsons, 2015). Nevertheless, traditional exposure-based treatments remain as the treatment of choice for specific phobia (Abramowitz, Deacon, & Whiteside, 2012; Choy, Fyer, & Lipsitz, 2007; Emmelkamp, Bouman, & Scholing, 1992). However, subsequent to traditional exposure-based therapy up to 50% of individuals experience a reappearance of anxiety symptoms (Rachman, 1966; Rose & McGlynn, 1997; Vasey et al., 2012; Wolpe, 1958). This phenomenon is termed return of fear and is defined as the partial recurrence of anxiety symptoms post-successful exposure therapy (Rachman, 1966; Rachman, 1989). Four mechanisms

underlie return of fear: spontaneous recovery, renewal, reinstatement, and reacquisition (Rachman, 1966). It is important for clinicians to incorporate methods to reduce return of fear following therapy to ensure long-term treatment outcomes.

The current chapter will review studies on VRET for specific phobia with a focus on how VRET could be used to attenuate return of fear. The theoretical framework underpinning exposure-based therapies will be explained. Furthermore, the chapter will evaluate the use of VRET as an adjunct tool to in vivo exposure or as an alternative treatment for specific phobia. The effectiveness of VRET relative to in vivo treatment will be addressed in terms of specifically reducing return of fear. The research evidence for the generalisability of VRET will be evaluated. Virtual reality technology and equipment for clinical settings are also evaluated, with a particular focus on emerging and accessible techniques that will facilitate further growth of VRET and allow for more individualised treatment plans. Applications of VRET in clinical settings will be discussed and recommendations for clinicians will be provided.

Theoretical Framework of Exposure Therapy and Return of Fear

Pavlovian conditioning provides a learning model underpinning the acquisition and extinction of fear (Bouton & Bolles, 1979; Davey, 1992; Laborda, McConnell, & Miller, 2011; Neumann & Longbottom, 2008; Pavlov, 1927; Wolpe, 1958). The acquisition of specific phobia has been explained within a Pavlovian conditioning framework as resulting from the pairing of a neutral conditioned stimulus (CS; e.g. snake) and an aversive unconditioned stimulus (US; e.g. pain). Subsequent presentations of the CS alone evokes a conditioned fear response (CR; e.g. fear). In laboratory-based studies, CRs are typically measured using a combination of physiological measures, such

as heart rate, skin conductance, and startle eyeblinks (e.g. Matthews, Naran, & Kirkby, 2015; Neumann & Waters, 2006; Neumann, Waters, & Westbury, 2008), self-reported US expectancy ratings or affective reactions (e.g. Bandarian-Balooch & Neumann, 2011; Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Neumann, Waters, Westbury, & Henry, 2008), and behavioural measures of affect (Boschen, Parker, & Neumann, 2007; Pischek-Simpson, Boshen, Neumann, & Waters, 2009). In clinical-analogue studies for specific phobia, CRs are typically measured using a combination of self-report subjective units of distress, behavioural, and physiological measures (e.g. Bandarian-Balooch, Neumann, & Boschen, 2015; Shiban, Pauli, & Mühlberger, 2013). In laboratory based studies, during the acquisition phase, a CS-US association is learnt and this learning is expressed as a CR. The magnitude of the CR thus gives an indication of the strength of the CS-US association.

Extinction of the conditioned fear response can be observed following acquisition. Procedurally, extinction requires the repeated presentations of the feared stimulus without the aversive consequence (US). A progressive reduction in the magnitude of the CR is observed across the extinction trials. In clinical settings, the process of extinction is analogous to exposure therapy (Öst, 1989; Wolpe, 1958).

It was initially proposed that extinction results in the destruction of the CS-US association and thus removal of the original fear (McClelland & Rumelhart, 1985; Rescorla & Wagner 1972). More recent conditioning research using rats (e.g., Bouton, 2002, 2004; Bouton & Bolles, 1979; Thomas, Vubrik, & Novak, 2009; Laborda & Miller, 2013) and human participants (e.g., Bandarian-Balooch et al., 2015; Haesen & Vervliet, 2015; Leer & Engelhard, 2015; Neumann, Boschen & Waters, 2008; Warren et

al., 2014) has suggested that the return of the extinguished CR (e.g., fear) shows that the original CS-US association is not destroyed by the extinction process.

According to Bouton's contextual memory model (Bouton, 1993, 2002, 2004), extinction is a learning process wherein a new CS-noUS association is learnt and stored in memory along with the original CS-US association. Bouton (1993, 2002, 2004) proposed that upon presentation of the CS, it is the context which influences whether the CS-US association from acquisition or CS-noUS association from extinction is retrieved from memory and expressed in behaviour. The contextual memory model further states that the CS-US association will be retrieved in any context excluding the extinction context. In contrast, the CS-noUS association will be retrieved solely in the extinction context (Bouton, 1993, 2002, 2004).

The role of context in fear learning and extinction has been used to explain the four mechanisms of return of fear (Bouton, 2002, 2004; Bouton, Westbrook, Corcoran, & Maren, 2006). In spontaneous recovery, extinguished fear can return when the extinguished CS is presented after a temporal context shift (Bouton, 2002; 2004; Pavlov, 1927). In reinstatement, extinguished fear can return after re-exposure to the US (Rescorla & Heth, 1975b) and typically occurs when this exposure is conducted in the extinction context (Bouton, 2002). In reacquisition, extinguished fear can return after another pairing of the CS and US. The rate of reacquiring the fear is dependent on contextual cues (Bouton & Swartzentruber, 1991). In renewal, there are typically three phases; acquisition, extinction, and test whereby extinguished fear can return when the physical context is changed after extinction (Bouton, 2002; Neumann, 2007; Neumann & Kitlertsirivatana, 2010). These mechanisms highlight the role of contextual cues in

producing a return of fear. Equally important is research directed at methods to attenuate return of fear, ultimately contributing to improving exposure therapy approaches of specific phobia.

Numerous methods have been employed to attenuate renewal, spontaneous recovery, reinstatement, and reacquisition (see Boschen, Neumann, & Waters, 2009). One method that has been frequently studied is conducting extinction in multiple contexts. For instance, Dunsmoor, Ahs, Zielinski, and LaBar (2014) conducted extinction in multiple virtual contexts. In the acquisition phase, neutral CSs were used (e.g., virtual characters) with one CS paired with the US (e.g. electric shock) in context A (e.g. brick alleyway). In the extinction phase, the CSs were presented alone. One group received extinction in a single novel context B (e.g. blue wall alleyway), another group received extinction in multiple contexts (e.g. BCDA), and one group received extinction in the acquisition context (e.g. A). After 24 hours, participants returned for the test phase in the extinction context (spontaneous recovery) and a novel context (renewal and reinstatement test). Extinction in multiple contexts attenuated reinstatement of fear and renewal but did not attenuate spontaneous recovery. Bouton (1993; 2002; 2004) argued that conducting extinction in multiple contexts increases the number of shared cues between extinction and test contexts, thus attenuating return of fear. However, there are other explanations such as the theory of conditioned inhibition (Wagner & Rescorla, 1972) and generalisation decrement (Bouton, 2004; Capaldi & Lynch, 1967).

Researchers have explored contextual methods to attenuate return of fear using in vivo exposure, imaginal, and VRET. Return of fear researchers have manipulated a variety of physical contextual cues including lights, sounds, and indoor and outdoor

contexts (e.g., Milad et al., 2005; Neumann, 2006; Neumann, Lipp, & Cory). Sequentially more clinically relevant contextual cues have been manipulated in recent research with photographs (e.g., Neumann & Longbottom, 2008), videos (e.g., Vansteenwegen et al., 2007), and virtual reality (e.g., Alvarez, Johnson, & Grillon, 2007). The application of virtual reality may be particularly advantageous because it can provide a variety of visual and auditory contextual cues that could promote generalisation from the extinction context to the test context (Bandarian-Balooch, Neumann, & Boschen, 2012).

In sum, Pavlovian conditioning has provided a theoretical framework that underlies traditional exposure treatments. By extension, this framework can be applied to the use of VRET. Traditional exposure treatments and VRET can be differentiated according to the methods by which the researcher or clinician manipulates the contexts and stimuli. Moreover, there are distinct situations in which VRET, imaginal, and in vivo exposure may be preferred as a treatment option and applied in clinical settings.

Traditional Exposure-based Treatments For Specific Phobia and Associated Challenges

The two main traditional exposure-based treatments for specific phobia are in vivo exposure and imaginal exposure. Aside from considerations regarding their relative efficacy, there can be specific factors that influence whether one treatment approach is preferred over the other. These factors include the phobia type, therapist involvement, and client characteristics, and situational factors. Additional factors that may be relevant can include time demands, practicality, and cost.

Treatment Choice Dependent on Phobia Type

Several phobia types could be seen as more relevant for either imaginal or in vivo exposure. Imaginal exposure provides the client an opportunity to imagine specific situations or stimuli which would be difficult to confront in reality (Emmelkamp, 2005). For example, it is more feasible for a client suffering from a fear of floods to imagine this event rather than to delay exposure treatment until a flood occurs. Nevertheless, imaginal exposure could also be used in conjunction with in vivo exposure. For fear of spiders, for example, the therapist could conduct in vivo exposure sessions with the client continuing to do imaginal exposure in the absence of the therapist. Thus, it can be seen that some phobia types are more clinically relevant to be used with a specific treatment type. Accordingly, imaginal and in vivo exposure also differs with regard to therapist involvement. In delivering in vivo treatment, the therapist can model the exposure hierarchy steps to the client. For imaginal exposure, the therapist has limited control over the phobic-stimuli and situation compared to in vivo exposure (Bush, 2008).

Client Characteristics Impacting Treatment Choice

Similarly, client characteristics influence the choice of treatment type. Specifically, with in vivo exposure there is an increased likelihood of eliciting an anxious response from the client during therapy than there is with imaginal exposure (Bush, 2008; Krijn et al., 2004). It can be difficult for some clients to elicit an anxious response to an imagined stimulus and to visualise the specific situations or objects (Bush, 2008; Maltby et al., 2002). This indicates an advantage of in vivo exposure over that of imaginal exposure in that there is increased generalisability of extinction learning (Rothbaum et al., 2006). However, client's with more vivid imaginations may be able to imagine more exposure contexts and fear-relevant stimuli than is possible in reality.

Thus, the effectiveness of imaginal exposure is more dependent on client characteristics than in vivo exposure.

Situational Factors Impacting Treatment Choice

It is also necessary for clinicians to consider the relative cost considerations and client dropout rates of the imaginal and in vivo exposure. Imaginal exposure provides several benefits for the clinician and client such as fewer resources are required due to minimal or no set up costs (Bush, 2008). In vivo exposure, in contrast, can have high treatment costs (Kahan, Tanzer, Darvin, & Borer, 2000; Rothbaum, Hodges, Smith, Lee, & Smith, 2000). It is widely recognised in research on fear of flying that in vivo exposure therapy is not cost-effective (Kahan et al., 2000; Rothbaum et al., 1996; Rothbaum et al., 2000). This is due to the client typically having the responsibility to purchase the flights for themselves and the clinician (Botella, Osma, Garcia-Palacios, Quero, & Banos, 2004; Rothbaum et al., 1996; 2000). Mühlberger, Weik, Pauli, and Wiedemann (2006) has reported cost-considerations may limit the use of repeated exposure sessions for fear of flying which could ultimately help the client in reducing their fear.

Another disadvantage of in vivo exposure is client dropout. In vivo exposure can suffer from high attrition rates (Choy, Fyer, & Lipsitz, 2007; Garcia-Palacios et al., 2001). Choy, Fyer, and Lipsitz (2007) reviewed in vivo exposure studies for specific phobia and found participant dropout rates of up to 45%. Thus, this would limit the effectiveness of in vivo exposure.

Overall, it is important to recognise that there are important factors that influence clinical treatment decisions. Therefore, it is evident that phobia type, therapist involvement, client characteristics, and situational factors impact treatment choice.

However, the majority of the benefits and challenges reviewed here have not been the main focus of studies but are mostly derived from clinical observations. Therefore, the advantages and disadvantages of these treatments have not been systematically studied. Future research is needed to evaluate the clinical benefits and challenges of in vivo and imaginal exposure therapy. In addition to comparing these treatment approaches, there is also a need to compare them with more recent exposure treatments. VRET as an alternative therapy or used in conjunction with traditional exposure-based treatments may have the potential to overcome several of the challenges of in vivo and imaginal exposure.

VRET as a Method to Address Challenges with Traditional Treatments

An increasing number of researchers have emphasised how VRET can overcome challenges of in vivo exposure in clinical settings for a range of specific phobia types. The potential benefits of VRET include: feasibility, cost-effectiveness, high appeal to clients, treatment of multiple phobias, increased control, confidentiality, and safety. There is support for VRET as a more feasible treatment option than in vivo exposure therapy for specific phobia (Krijn et al., 2004; Opris et al., 2012). Emmelkamp et al. (2002) reported that a range of virtual exposure contexts and stimuli can conveniently be presented in the clinician's office. In their study, participants with acrophobia were exposed to spiders in multiple virtual contexts: a fire escape, a mall and a roof top patio at the top of a high rise in Amsterdam. This method has been found to increase the generalisability of extinction learning across contexts and consequently attenuate fear (Bandarian-Balooch, et al., 2011; Glautier, Elgueta, & Nelson, 2013; 2015; Shiban et al., 2013, 2015). Virtual reality exposure tasks can be more easily repeated as often as the

client requires (Rothbaum, Hodges, Anderson, Price, & Smith, 2002). Repeated exposure sessions in multiple virtual contexts is also considered more cost-effective.

It has been frequently reported that VRET is more cost-effective than in vivo exposure, predominately for fear of flying (Botella et al., 2004, Rothbaum et al., 1996; 2000; 2006). Mühlberger, Hermann, Wiedermann, Ellgring and Pauli (2001) used immersive VRET treatment sessions for fear of flying by including gradual steps of all aspects of flying with a commercial plane such as reaching take off position, take off, turbulence, descending, and landing. This VRET treatment plan would be more cost-effective if used for numerous clients than the cost of commercial aeroplane tickets for each individual. There are other phobia types where VRET could be feasible and cost-effective. For example, it would more affordable to present a virtual diving context than to do in vivo exposure in a shark diving cage for a client with a fear of sharks. Previously a criticism of VRET costs was the affordability of the virtual reality equipment (Maltby et al., 2002). However, recently virtual reality equipment has become more widely available and affordable (Rothbaum et al., 2002).

As previously mentioned, in vivo exposure for specific phobia has been linked to low rates of seeking treatment. VRET as an alternative treatment has been found to have higher treatment appeal and could contribute to overcoming the issue of low treatment participation rates. Garcia-Palacios et al. (2001) surveyed 777 individuals with high spider fear who had not received treatment regarding their preferences for VRET or in vivo exposure treatment. It was found that 81-89% of participants significantly preferred VRET over in vivo. This treatment preference has also been found with a clinical sample. Rothbaum et al. (2000) provided wait-list participants with a choice prior to treatment to

receive VRET or in vivo treatment for fear of flying. In this clinical trial, 14 of 15 participants preferred VRET over in vivo. An explanation for these findings is that specific phobia sufferers may find VRET an attractive alternative to in vivo due to the less threatening nature of virtual representations of the feared object or situation (Garcia-Palacios et al., 2001; Opris et al., 2012). The greater treatment acceptance for VRET suggests that this technique could address the low treatment rates of in vivo exposure by encouraging clients to seek treatment.

Another potential benefit of VRET is that it can be applied easily in clinical settings to treat the high prevalence of comorbid fears in specific phobia (e.g., fear of both snakes and spiders). This has important clinical implications as it has been found that 75% of sufferers of specific phobia fear more than one phobic object or situation (APA, 2013). In implementing virtual reality technologies in therapy a range of fear-relevant stimuli can easily be presented to the client (Krijn et al., 2007). However, there are no studies examining the effects of VRET for the treatment of comorbid fears. Future research could address this gap by identifying comorbid phobia types and employ VRET to enhance accessibility to a broad range of stimuli in clinical settings.

In clinical settings, VRET offers increased confidentiality, safety and control. In vivo exposure presents an increased risk to client confidentiality, as the exposure tasks are typically conducted in a public place, such as a hotel elevator or airport. The therapist's office can be used to facilitate VRET in a confidential and safe environment (Botella et al., 2004; Rothbaum et al., 2000). Similarly, VRET allows for greater safety and control when providing treatment, due to the minimisation of unexpected situations (e.g. an elevator breaking down). Clinical-analogue studies have employed virtual

representations of phobic stimuli; this results in increased experimental control (Michaliszyn et al., 2010; Rothbaum et al., 2002). An example of this can be found in studies of fear of flying, where weather conditions can be manipulated or stimuli can be varied (e.g. different sized aircraft) to provide multiple extinction contexts. Therefore, in specific situations (e.g., fear of flying or agoraphobia) VRET may be the preferred treatment.

The benefits of VRET have been demonstrated but pragmatic concerns over price, accessibility, and the required skills of the clinician have impeded the widespread transition of the research into clinical practice. The cost of VR equipment and the associated cost and time to develop virtual worlds to be used in treatment can be prohibitive to some clinicians. In addition, technical expertise is required to set up and operate the VR equipment. VRET is highly technology dependent and this may require additional training for therapists. However, recent advances in technologies have begun to address many of the concerns regarding VRET and thus making is a more viable treatment option for clinicians.

Emerging Virtual Reality Technologies: Considerations from a VRET Perspective

Recent advancements in technological capabilities have produced changes in the resources available to conduct VRET. Camera technology allowing the live-action filming of immersive videos with 360º of viewing is an important new development in virtual reality (Metz, 2015). When viewed through a HMD, the image and sounds from the immersive video presented will track the movement of the viewer's head. This process provides the viewer with an immersive experience designed to be perceived as more realistic than a standard 180º video.

The combination of HMD systems and immersive 360º video has the potential to improve VRET in two key ways. Firstly, the new technology may enhance the subjective feeling of being in the virtual environment. This subjective feeling is known as presence. Secondly, it can address a range of limitations of virtual reality in clinical settings. These limitations include accessibility, levels of immersion and presence, individualising virtual environments for clients, and motion sickness. Despite potentially improving the use of virtual reality in psychological contexts, the use of video also has its own limitations that need to be addressed. Specifically, immersive videos offer minimal interactivity which was a central feature of the traditional computer generated virtual environments and a key component of some definitions of virtual reality.

Presence in Virtual Reality

Similar to traditional exposure therapy methods, the effectiveness of VRET is dependent on an ability to evoke a fear response in the client when confronted with a fearful stimulus until the fear response is no longer observed (Richard, Lauterbach, & Gloster, 2007). The ability to evoke a realistic response from a virtual environment is dependent on the user having the subjective feeling of presence (Diemer, Alpers, Peperkom, Shiban, & Mühlberger, 2015; Price & Anderson, 2007). Presence is defined as a subjective sense of being in a virtual environment even when physically situated in another (Witmer & Singer, 1998). Related to presence is immersion. Immersion can have physical and mental elements wherein it is dependent upon the technical capabilities of the system to create a realistic virtual environment (Slater & Wilbur, 1997). Despite being distinguished by objective (technological capabilities) and subjective (consciousness) factors (Slater & Wilbur, 1997), the two concepts of immersion and

presence are often used interchangeably adding to confusion in the literature (McMahan, 2003). Considering the two factors independently is important because a realistic and immersive virtual environment is a determinant of a subjective state of presence in the environment (Lombard & Ditton, 1997). Therefore, factors that contribute to enhancing the immersive nature of a virtual environment is also likely to increase a sense of presence.

Presence is affected by a range of factors related to immersion. A sense of presence is aided when the proprioceptive information provided in the virtual environment mirrors that of the real world (Sanchez-Vives & Slater, 2005; Slater, Usoh, & Steed, 1995). The proprioceptive system automatically provides information about the movement and location of the body in relation to the environment (Park, Toole, & Lee, 1999). Therefore, factors that can assist the realistic processing of proprioceptive information will enhance presence. Factors known to facilitate proprioceptive information include a wide field of view, the activation of multiple sensory systems, the realism of the displayed environment, and a realistic latency period between input to the environment and a response. Importantly, these factors are also components of an immersive virtual environment (Sanchez-Vives & Slater, 2005) and are therefore dependent on technological capabilities.

Based upon the relationship between immersion and presence, clinicians could use modern technologies to enhance the perception of presence during VRET. HMDs need a wide field of view for the user to process realistic simulation (Anderson, 1996). Modern HMDs are now being produced with a field of view as wide as the human eye's peripheral vision to produce realistic perceptions of depth and increased presence

(Oscillada, 2015). Modern HMDs have custom graphics processors capable of displaying stereoscopic images (Winchester, 2016). Problems associated with latency between input and the response are also being addressed, with modern HMDs being manufactured with tailored hardware to cope with low latency performance (Raaen & Kjellmo, 2015). A yet to be tested proposition is that immersive videos can improve presence due to the realistic nature of the stimuli presented. Live-action filmed material is more realistic and has higher levels of ecological validity than computer generated graphics. One of the benefits of realistic virtual environments is higher levels of presence (Coelho, Tichon, Hine, Wallis, & Riva, 2006).

Advantages of Modern HMDs and Immersive Videos

The ability to administer VRET is dependent upon having the resources to acquire a HMD and produce a virtual environment. Recently, more powerful computers, more user-friendly hardware, and the removal of wires from the hardware systems have allowed virtual reality technologies to be mass-produced and available to a recreational consumer population (He, 2016). The implication of this rise in popularity is that virtual reality can be a tool psychologists can utilise to allow widespread, affordable, and immediately accessible solutions for problems psychologists routinely deal with. In addition, 360º video cameras are more affordable and available (Goldman, 2016). In comparison to the traditional method of computer generated graphics and animations, a device capable of filming a virtual environment is more accessible to consumers without an in-depth knowledge of graphic design software and computer coding. Clinicians are better able to film a scene and convert the footage to an immersive video than to create a computer-generated virtual world.

A review of decades of research has revealed that clients require individualised treatments in psychological interventions (Norcross & Wampold, 2011). Effective treatment plans actively engage patients with the treatment process, allow readjustments based on session-to-session assessment of progress, identify client specific cognitions, emotions, beliefs, and behaviours, use multiple techniques, and address potential comorbid disorders (Wilson, 2007). More specifically to VRET, individually tailored treatment involves exposure to increasingly fear provoking stimuli and environments that act as triggers of fear. Immersive videos provide a flexible system that can easily facilitate individualised treatments. Different stimuli and contexts relevant to the treatment for individual clients can be filmed and presented on a HMD with relative ease in most cases, in comparison to a computer generated animation. For example, if a client presents with a fear of dogs, the ability to incorporate an immersive video of a dog that is similar to a dog the client is likely to encounter post-treatment (e.g. a next door neighbour's dog) can enhance the long-term effectiveness of treatment due to reducing the potential for relapse (Bandarian-Balooch et al., 2011).

A considerable obstacle that needs to be overcome in the administration of VRET is the motion sickness that typically accompanies the use of HMDs. Viewing a virtual environment that incorporates motion or movement can induce nausea, vomiting, cold sweating, increased salivation, drowsiness, and pain in some people (Durlach & Mavor, 1995). Two things known to increase the likelihood of experiencing virtual reality induced motion sickness is poor image update times and extended periods of time immersed in the virtual environment (Bush, 2008).

The issue of motion sickness can have serious implications during treatment if the client associates the nauseated feelings with the feared object. For example, if a client presents with a fear of snakes, the client could be presented with a naturalistic immersive video with a snake covered in some shrubbery. If the snake were to start moving out of the shrubbery it would most likely attract the attention of the client who would quickly turn their head and attention to orientate at the source of movement. If the immersive video were to lag and not provide a realistic image, motion sickness could be experienced by the client. These physiological symptoms could become associated with the snake and in doing so strengthen the aversive response to snakes. For this reason, it is recommended that clinicians use HMDs that track the user's head orientation and position to give precise timing for individual frames (Smith, 2015). These technological developments essentially allow the technology to present the virtual environment in a realistic manner and improve treatment.

The Issue of Interactivity in Immersive Videos

Despite the flexibility offered by immersive videos, a potential disadvantage is a lack of interactivity. Traditional definitions of virtual reality emphasise the interaction between the user and system (Wiederhold & Wiederhold, 2005) and immersive videos do not offer considerable levels of interaction beyond basic head movements to focus attention on specific areas of the virtual environment. The debate surrounding the validity of labelling immersive videos as virtual reality is occurring in technological circles (Smith, 2015) and amongst clinical psychologists (Bouchard, et al., 2007). Nevertheless, the discussion regarding the correct terminology for immersive videos is distinct from the discussion regarding the utility and efficacy of using immersive videos

in psychological treatments. In research exploring the role of virtual reality in treating anxiety disorders, it is not uncommon to remove control over the interactivity from the participant as to ensure that they are exposed to a specific manipulation or procedure (Troger, Ewald, Glotzbach, Pauli, & Mühlberger, 2012). However, there are differences between the procedures needed to research VRET and the clinical applications of VRET.

The limited interaction of immersive videos can be problematic in clinical settings for two reasons. Firstly, for treatment effects to generalize to real-life situations, it is important for the client to approach the feared stimulus under their own volition. This requirement is based on the assumption that the client will overcome their fear by voluntarily being exposed to stimuli that cause strong fear responses for protracted periods of time (Rachman, 2004). An immersive video could remove that voluntary approach as the client has no control over the exposure process (e.g., proximal distance to the fearful stimuli) once the film commences. Secondly, the lack of client control once the immersive video begins is an ethical concern. Exposing a fearful client to anxiety provoking situations that are difficult to retreat from can cause the client undue distress.

The two problems posed by immersive video may be possible to overcome. In VRET, issues associated with voluntary approach and increased distress can be addressed by using different immersive videos rather than a continuous video. If a continuous exposure video is used, the only method of controlling the pace of exposure would be for the therapist and client to negotiate planned avoidance strategies or distractions such as the client closing their eyes, removing the HMD, or focusing on other salient stimuli in the virtual environment. However, employing planned avoidance and distractor strategies during the exposure process has been found to result in less fear reduction than sustained

attention to the fearful stimuli (Kamphuis & Telch, 2000). Thus, a more preferable method of promoting voluntary client approach during the exposure process is to use a different video clip for each step of the exposure hierarchy and allowing the client to decide when they are ready to proceed to the next step of exposure. This process during treatment sessions gives the client control over their volitional approach of the feared stimulus by allowing them to approach the immersive videos voluntarily. An alternative approach would be to allow the client to dictate the speed at which the immersive video is played, allowing them to voluntarily approach the feared object at a faster or slower pace. These methods also overcome the ethical problem of causing the client undue distress and gives the client the same control as for in vivo based exposure therapy.

The preceding discussion of user friendly HMDs and immersive video cameras has highlighted the easiest way to implement VRET in psychology clinics. Nevertheless, it is possible for clinicians to create and use animated virtual environments using computer software. Freely available software can be downloaded online to create a virtual environment without the clinician having to purchase a 360º camera system or locate the filmed stimuli. The previously noted drawback to this technique is the need to develop skills in computer graphics and coding languages in addition to investing time into the creation process. However, it is important to note that the recent development of immersive video technologies has meant that research on VRET has almost exclusively used the older, less user friendly, computer-generated animations.

Review of VRET and Return of Fear for Specific Phobia

A literature search for studies evaluating the effectiveness of VRET to reduce return of fear for specific phobia was conducted. Search terms involved a combination of

the following key terms: “virtual reality” AND “exposure therapy” AND “specific phobia” OR “anxiety disorders” OR “return of fear” OR “in vivo” and OR “treatment outcome”. Science Direct and Clinical Key were searched and this resulted in 64 articles. Following this, Google Scholar was searched and this resulted in 1,710 hits. The resulting articles were screened for relevance at the title and abstract level and subsequently at the article level. Articles were screened to exclude review articles, articles not including virtual reality, and non-psychology related articles. In total, 12 studies that focused on VRET and return of fear for specific phobia were used as the basis for the literature review. A summary of the findings from primarily clinical-analogue studies examining the effectiveness of VRET and methods attenuating return of fear are presented in Table 3.1. The studies included in the review all employed HMDs as opposed to CAVE systems, as modern HMDs are small, inexpensive, portable, user-friendly, and equally effective (Bush, 2008; Krijn et al., 2004). The review determined that VRET and associated methods can be considered effective in attenuating return of fear for specific phobia.

Return of fear has been an enduring issue for in vivo exposure therapy and has been extensively studied for specific phobia (e.g. Rachman, 1966; 1987; Boschen et al., 2009). In contrast, VRET is a relatively new treatment and there is limited literature investigating the occurrence of return of fear for this treatment. Previous reviews have found VRET and in vivo exposure therapy to be equally effective in the short-term for a range of specific phobia types (see Bush, 2008; Opris et al., 2012; Powers & Emmelkamp, 2008). Nonetheless, due to the clinical implications it is important to

establish the equivalence of VRET to in vivo exposure in terms of reducing fear in the long term, particularly in regards to return of fear.

Currently, return of fear VRET research has only explored fear of flying (Botella et al., 2004; Kahan et al., 2000; Matbly et al., 2002, Mühlberger et al., 2001, Rothbaum et al., 2002; Wiederhold & Wiederhold, 2003) acrophobia (Emmelkamp et al., 2002; Krijn et al., 2004), and spider phobia (Michalizyn et al., 2010; Shiban et al., 2015). These studies have explored methods that are applicable to VRET to attenuate spontaneous recovery, reinstatement, and renewal of fear.

Table 3.1

A Summary of VRET Studies on Specific Phobia with Various Follow up Tests and Procedures

Authors	Phobia type	*N*	Procedure	Test in reality	Follow up	Return of fear mechanism
Botella et al. (2004)	Fear of flying	9	Clinical-analogue	Yes	12 months	Spontaneous recovery of fear
Emmelkamp (2002)	Acrophobia	33	Clinical-analogue	Yes	6 months	Spontaneous recovery of fear
Kahan et al. (2000)	Fear of flying	31	Clinical-analogue	Yes	Average of 8 months	Spontaneous recovery of fear
Maltby et al. (2002)	Fear of flying	45	Clinical-analogue	Yes	6 months	Spontaneous recovery of fear
Michaliszyn et al. (2010)	Spider phobia	41	Clinical-analogue	No	3 months	Spontaneous recovery of fear
Mühlberger et al. (2001)	Fear of flying	30	Clinical-analogue	No	3 months	Spontaneous recovery of fear
Mühlberger et al. (2003)	Fear of flying	45	Clinical-analogue	Yes	6 months	Spontaneous recovery of fear
Rothbaum et al. (2002)	Fear of flying	24	Clinical-analogue	Yes	12 months	Spontaneous recovery of fear
Shiban et al. (2013)	Spider phobia	40	Clinical-analogue	Yes	-	Renewal of fear
Shiban, et al. (2015)	Spider phobia	30	Clinical-analogue	Yes	3 weeks	Renewal of fear
Shiban et al. (2015)	Non fearful	31	Fear-conditioning	No	24 hours	Reinstatement of fear
Wiederhold and Wiederhold, (2003)	Fear of flying	30	Clinical-analogue	Yes	3 years	Spontaneous recovery of fear

Spontaneous Recovery of Fear

Spontaneous recovery of fear has been explored in the majority of studies, although it has not always been the focus of the research or explicitly reported. As highlighted in Table 3.1, researchers have used a variety of follow-up time periods, procedures, and specific phobia types. Prior studies aiming to reduce spontaneous recovery using VRET have primarily explored fear of flying. As noted previously, this could be due to VRET representing a cost-effective and feasible treatment option for fear of flying when compared to other phobia types.

Several treatments have been used in conjunction with and compared with VRET to prevent spontaneous recovery of fear of flying. Kahan et al. (2000) explored the effects of a combination of VRET, relaxation, and cognitive strategies on reducing fear of flying. At an average of 8 months following treatment, 68% of participants reported they had taken an aeroplane flight. The authors reported some participants' experienced spontaneous recovery of fear as indicated by increased subjective units of distress from post-treatment to follow up. This study did not include a treatment comparison group or a control group. Therefore, it remains unclear whether the cognitive, behavioural, or virtual reality exposure components independently or in combination contributed to the treatment outcomes.

Rothbaum et al. (2002) compared a VRET group, an in vivo exposure group and a wait-list control group to treat fear of flying. At post-treatment, the VRET and in vivo group were equally as effective as demonstrated by the reduction of fear on self-report measures. During the 12 month follow-up, 92% of participants in the VRET group and 91% of participants in the in vivo group had undertaken a flight on a commercial airline. However, at follow up 17% of individuals experienced spontaneous recovery of fear as indicated by avoidance of flying. The authors reported no significant differences in avoidance of flying

between VRET and in vivo and concluded the treatments are equally effective in maintaining treatment gains.

Similar to the research on fear of flying, Michaliszyn et al. (2010) evaluated VRET and in vivo exposure on reducing spontaneous recovery for fear of spiders. In this clinical-analogue study, spider phobic participants were randomly assigned to a VRET group, in vivo group, or wait-list control. No significant differences were observed between VRET and in vivo immediately post-treatment. At the 3 month follow-up there was a slight advantage for in vivo exposure, with greater improvement on one self-report measure compared to VRET. In contrast, Emmelkamp et al. (2002) found in vivo exposure and VRET to be equally effective post-treatment and at follow up for acrophobia. Follow-up testing was conducted using self-report measures and a behavioural avoidance task and there were no significant differences on these measures between the post-treatment test and the six month follow up. Thus, treatment gains were maintained and a spontaneous recovery effect was not observed for VRET or in vivo exposure therapy.

Despite the fact that VRET is considered an effective long-term treatment, the studies reviewed so far have not isolated the specific components of VRET that might contribute to treatment efficacy (e.g. Kahan et al., 2000). Mühlberger, Wiedemann and Pauli (2003) aimed to examine the effective VRET components to reduce fear of flying and spontaneous recovery of fear. Three experimental groups were employed: cognitive treatment with VR exposure and motion simulation, cognitive treatment in conjunction with VR exposure without motion simulation, and cognitive treatment alone. Fear of flying was significantly reduced in the VRET groups when compared to the cognitive treatment group immediately post-treatment and after 6 months. In the cognitive treatment group, there was significant spontaneous recovery of self-reported fear when compared to the VRET groups. The visual and acoustic stimuli were found to be the most important components in reducing fear of

flying. However, there were no differences between VRET used in conjunction with motion simulation or not. These findings have important clinical implications, suggesting that it is not necessary to apply motion simulation in VRET. This may overcome the cost and technical challenges associated with the use of virtual reality in clinical settings. Thus, this could contribute to the widespread use of virtual reality and ease of clinical application of VRET.

Another treatment component of VRET that may be a method to reduce spontaneous recovery of fear is physiological and visual feedback. Wiederhold and Wiederhold (2003) randomly assigned participants to either virtual reality with physiological and visual feedback (VRETpm), virtual reality with physiological feedback (VRETno), or imaginal exposure therapy (IET) for fear of flying. Several physiological measures were employed as feedback including electroencephalogram (EEG), respiration rate, skin resistance, heart rate, and peripheral skin temperature. Following treatment, a 3 year follow-up was conducted. Similar to Botella et al. (2004), 100% of the participants in the VRETpm group had flown on a plane during the follow-up. Furthermore, 80% of participants in the VRETno group and 10% of participants in the IET group had flown on a plane without medication to control their anxiety. However, spontaneous recovery of anxiety symptoms occurred for some participants. These findings indicate that virtual reality with physiological monitoring and feedback is a more effective method to reduce spontaneous recovery of fear of flying than imaginal exposure or VRET with physiological feedback only. The specific components of VRET that make it effective in the long-term shown in this research using the technology (Mühlberger et al., 2003; Wiederhold & Wiederhold, 2003) are valuable to clinicians. However, previous research has explored numerous methods to reliably attenuate return of fear for in vivo exposure (for a review, see Bandarian-Balooch, Neumann, & Boschen, 2012; Boschen et al., 2009) and these may be applicable to VRET as well.

One method to attenuate return of fear that has been extensively studied with in vivo exposure therapy is conducting extinction in multiple contexts. It is important for studies to establish if this method can be generalised and applied in virtual reality to attenuate spontaneous recovery of fear. Presenting exposure in multiple contexts in VRET potentially enables the clinician to conveniently provide a range of situations not otherwise available in in vivo exposure therapy. Botella et al. (2004) used a multiple baseline design to examine if fear of flying participants would experience a return of fear in a 12 month period. The treatment involved numerous virtual contexts from pre-flight (e.g. packing, listening to air traffic news), arriving at the airport (e.g. hear and see planes taking off), and the flight (e.g. captain reporting details about weather, taking off, different weather and landing). At the 12 month follow-up, 100% of the participants had undertaken a flight and improvement on all anxiety measures except one was maintained from post-test to follow-up. The effectiveness of this treatment in reducing spontaneous recovery of fear could be due to conducting exposure in multiple contexts and realistic nature of these virtual contexts. However, as there is no control or other treatment comparison group, conclusions cannot be drawn from this study.

Similarly, Maltby et al. (2002) conducted exposure in multiple contexts (i.e. smooth, turbulent and stormy weather conditions) to treat fear of flying with two experimental groups: an attention-placebo group and a VRET group. The results showed that both groups had similar rates of flying during in vivo test flights. However, the VRET group had significantly reduced self-reported anxiety during test when compared to the attention-placebo group. A 6 month follow-up was conducted and a significant spontaneous recovery effect was observed on four of the five self-report post-assessment measures. The VRET group outperformed the attention-placebo group on one flight anxiety measure. Thus, VRET could be to some extent more effective in the long-term. A limitation of this study is that the follow-up did not

include a test flight but was assessed by retrospective subjective units of distress during flights undertaken in the last 6 months. Taken together, these studies (Botella et al., 2004; Maltby et al., 2002) potentially suggest that the method of using multiple extinction contexts generalises to VRET and it may be more feasible for clinicians to implement this technique in therapy.

According to Brooks and Bouton, (1993), the method of using multiple extinction contexts to reduce spontaneous is due to the use of extinction cues (i.e., contextual stimuli encoded with the extinction memory) presented immediately prior to the spontaneous recovery test. In Botella et al. (2004) and Maltby et al. (2002) there were potentially many extinction cues (e.g. planes taking off) present immediately prior to the spontaneous recovery test (e.g. undertaking flight). This may have activated the CS-noUS association and subsequently attenuated spontaneous recovery of fear. Therefore, the use of multiple temporal and physical contexts may increase the retrieval of the extinction memory in the long-term (Bouton, 2004; Brooks & Bouton, 1993; 1994) and reduce the potential for return of fear.

Another method of attenuating return of fear that has been found to be effective in laboratory-based studies with animals (Laborda & Miller, 2013; Thomas, et al., 2009) and humans (Krisch, Bandarian-Balooch, & Neumann, 2016) is conducting extended exposure sessions. Mühlberger et al. (2001) found that a single session involving repeated exposure (i.e. six exposure sessions) in virtual reality for fear of flying was more effective in reducing spontaneous recovery than a single session of relaxation training. Follow-up testing was conducted three months after treatment by exposing participants to another virtual flight. Both groups had reduced their fear responses when compared to pre-test as indicated by self-report and psychophysiological measures (i.e. heart rate and skin conductance level). VRET was more effective in reducing fear responses than relaxation training. It could be suggested

that extended exposure would attenuate spontaneous recovery due to strengthening the CS-noUS association through extended exposure to contextual stimuli (Denniston, Chang, & Miller, 2003). Thus, enhancing the generalisation of the CS-noUS association learnt in extinction to the follow-up test. However, further laboratory-based research with human participants is needed to determine if extended exposure is an effective method to reduce spontaneous recovery and the other mechanisms of return of fear.

Renewal of Fear

In the human return of fear literature, renewal is the most frequently studied mechanism (e.g., Bandarian-Balooch, Neumann, & Boschen, 2013; Neumann & Waters, 2006; Warren et al., 2014) and the primary method of attenuation explored in previous studies is conducting extinction in multiple contexts.

Two studies have examined the use of virtual reality to investigate the effects of multiple extinction contexts on renewal of fear of spiders (Shiban et al., 2013; Shiban et al., 2015). Shiban et al. (2013) exposed a spider-phobic sample to a virtual spider in either one virtual context or multiple virtual contexts. The authors manipulated the contexts by adjusting the colour of the illumination of the virtual room. The results showed that conducting exposure in multiple virtual contexts reduced self-reported fear, skin conductance responses, and behavioural measures of fear during a renewal test. Therefore, exposure in multiple virtual contexts may have enhanced the retrieval of the CS-noUS association in test.

Another clinical-analogue study by Shiban et al. (2015) examined whether multiple virtual stimuli and multiple virtual extinction contexts could independently and in combination reduce renewal of fear of spiders. In the renewal test it was found that both methods independently attenuated renewal and combining multiple stimuli and contexts did not result in a further attenuation of renewal. The findings suggest that VRET can be feasibly

conducted in a variety of contexts and with different types of feared stimuli from within the therapist's office to improve the long-term effects of treatment.

Reinstatement of Fear

Another mechanism of return of fear that requires further investigation in the context of VRET is reinstatement. Unfortunately, reinstatement has received less focus in clinical research due to ethical considerations with human participants. VRET could be considered an efficient technique to overcome the challenges involved in examining reinstatement of fear in clinical settings. However, there has been extensive laboratory-based research on reinstatement with animals (e.g. Bouton & King, 1983; Rescorla & Heth, 1975b) and humans (Neumann, 2008; Neumann, Lipp, & McHugh, 2014).

Of particular relevance for VRET is the laboratory-based study reported by Shiban, Wittmann, Weißinger, and Mühlberger (2015), because virtual reality technology was used to investigate attenuation of reinstatement of fear responses in humans. Shiban et al. (2015) aimed to examine the effects of gradual extinction on reinstatement of fear. The study employed a standard extinction group including a CS+ (e.g. spider) and CS- (e.g. scorpion) presented without an aversive US. In the gradual extinction group, the CS+ was paired with gradually decreasing the intensity of the US (e.g. air puff). In the reinstatement phase, the US was presented twice following by five presentations of the CS+ and CS-. In the test phase, it was found that gradual extinction reduced reinstatement in fear potentiated startle responses. The authors proposed that presenting the US in acquisition reactivates and destabilizes the state of the original fear memory, attenuating reinstatement extinguished conditioned responses (Schiller et al., 2010). Overall, this study suggested that virtual reality technology can be used to reliably reproduce and attenuate reinstatement of fear.

Conclusions of research on VRET and return of fear

In general, the review suggests that further research is needed to establish if VRET is equivalent to in vivo exposure in maintaining long-term treatment gains and thus reducing return of fear of flying, heights, and spiders. Future research could examine whether VRET is a useful treatment for other phobia types such as fear of sharks or vomiting. The review has also highlighted the limited number of clinical-analogue studies investigating the methods to attenuate reinstatement and reacquisition which could be due to ethical considerations (Boschen, Neumann, & Waters, 2008; Neumann, 2008; Hermans, Craske, Mineka, & Lovibond, 2006). Re-exposing fearful individuals to aversive stimuli (e.g. pain or the original feared object) could be considered an ethical dilemma due to the potential for causing unnecessary harm and distress. VRET could be an efficient methodology to address these ethical challenges if it could provide an alternative modality to present reinstating stimuli following virtual exposure. Overall, past studies indicate that there may be several methods to use VRET to reduce the likelihood of relapse in clinical settings.

The Generalisability of Virtual Reality Exposure Therapy Research to Clinical Settings

In clinical settings and VRET research it is important to ensure that treatment effects generalise from virtual reality environments to real stimuli and contexts. As noted previously, VRET presents an opportunity to examine a diverse range of stimuli and contexts that may not be possible to target with in vivo studies. As outlined in the previous section of this chapter, the manipulation of contextual changes in virtual reality has been found to generalise to real contexts and real phobic stimuli (Alvarez et al., 2007; Dunsmoor et al., 2014; Emmelkamp et al., 2002; Shiban et al., 2013; Shiban et al., 2015).

In reviewing previous studies using virtual contexts and stimuli, there have been inconsistencies in the methods used to measure treatment outcomes. It has been proposed that measuring successful treatment outcomes with VRET is a methodological problem of this area of research (Kahan et al., 2000). In particular, it has been argued that to determine

whether VRET attenuates fear responses the test phase must be conducted with a real stimulus in a real-life context. As noted previously, Michaliszyn et al. (2010) compared VRET, in vivo, and wait-list control conditions for treating fear of spiders. In the test phase the VRET group was presented with a virtual black widow spider in a virtual context. In contrast, the in vivo group was presented with two live spiders in a real context. Thus, the treatments cannot validly be compared due to methodological differences during the test phase. Similarly, Mühlberger et al. (2001) exposed participants to virtual reality test flights rather than conducting an in vivo flight during test. Conversely, Kahan et al. (2000), Maltby et al. (2002), Rothbaum et al. (2002) conducted VRET with participants fearful of flying and measured treatment outcome by whether or not participants undertook an actual flight. Clients completing exposure therapy will encounter real world stimuli and contexts, and thus a valid measure of treatment success in VRET is whether treatment gains are generalisable to real stimuli and contexts. Future studies should conduct a pre-test and a post-test in both virtual reality and in real-life contexts.

The ecological validity of VRET has also been examined in research by conducting behavioural measures of fear in real-life contexts. It is important that the behavioural avoidance tasks represent a valid test of fear and thus the final task needs to be designed to be sufficiently anxiety-provoking for the client. Shiban et al. (2013) had participants complete a post-test behavioural avoidance task involving participants pulling on a crank that made a plastic box containing a spider move towards them. This task would not be sufficiently difficult for a client to overcome following successful exposure therapy. To increase the difficulty in a following study, Shiban and colleagues (2015) requested participants to touch the box, open the box, and touch the spider with a pencil. The criteria for treatment completion should be confronting and handling the actual feared-stimulus. In another clinical-analogue study Emmelkamp et al. (2002) compared in vivo exposure and VRET with

the behavioural task involving all participants climbing stairs at 38 m high. This final behavioural avoidance task is a reliable measure of whether VRET can be generalised to a real phobic-stimulus. Therefore, future research should include a pre-test and a post-test behavioural avoidance task involving handling the feared stimulus.

In clinical-analogue research, it is essential for participants to be screened to ensure they meet criteria for moderate to high fear of a specific object or situation. Öst, Brandberg, and Alm (1997) criticised fear of flying studies for not including pre-treatment test flights. In response to this criticism, previous studies have excluded participants based on their completion of the final step of a pre-test behavioural avoidance task with fear of heights (e.g. Emmelkamp et al., 2002; Krijn et al., 2004) and spiders (Michaliszyn et al., 2010). In contrast, Mühlberger et al. (2001) and Wiederhold and Widerhold (2003) did not conduct a pre-test behavioural avoidance task but used self-report questionnaires. Pre-treatment and post-treatment behavioural measures could be considered as a methodological control to ensure real differences exist between the comparison treatments (Maltby et al., 2002).

Previous studies have reported inconsistent findings of whether VRET elicits the same level of anxiety as in vivo exposure (Michaliszyn et al., 2010) or not (Emmelkamp et al., 2002; Krijn et al., 2004). This discrepancy may raise concerns of the ecological validity of VRET in clinical settings. Rothbaum et al. (2002) found that 73% of participants in the VRET group used drugs and alcohol to cope with flights compared to 30% for in vivo exposure group. It could be suggested that in this study following VRET participants were more anxious in undertaking flights compared to those completing in vivo exposure and may use coping strategies to control this anxiety. Similarly, Krijn et al. (2004) reported that 5 out of 10 participants dropped out in the VRET condition due to the inability of VRET to elicit anxiety. However, these studies also found that VRET is as equally effective in the long-term as in vivo exposure therapy (Emmelkamp et al., 2002; Rothbaum et al., 2002), indicating

VRET generalises to real stimuli and contexts. The studies suggesting VRET may not evoke anxiety equivalent to in vivo exposure may have used virtual reality technologies and environments that may not elicit a sufficient level of presence (Bush, 2008; Krijn et al., 2004). Furthermore, a recent study confirmed an anxiety-provoking context in virtual reality triggers hippocampus activity the same as real-life anxiety-provoking contexts (Andreatta et al., 2015). The conclusions of research on VRET and return of fear suggest limitations and strengths of the generalisability of VRET research to clinical settings.

Summary of Clinical Applications of VRET in Combination with In Vivo Exposure Therapy

There are multiple limitations that present challenges to effective exposure therapy for the specific phobias in clinical settings. These include limited client financial resources, limited physical access to real-life fear evoking stimuli, and limited client treatment motivation. Primarily due to these limitations, just over two decades of research has been exploring VRET as an alternative to in vivo and imaginal exposure therapy. However, the current review identified that there is not enough evidence to suggest that VRET can be used as a long-term effective treatment alternative to in vivo exposure therapy. Instead, the current review suggests that VRET and in vivo exposure therapy could be combined to overcome the challenges posed by the limitations clinicians frequently encounter when providing exposure therapy. Moreover, whenever possible, methods to attenuate return of fear should be applied in the exposure process to enhance the long-term effectiveness of treatment. This section summarizes how VRET can be used in combination with in vivo exposure therapy and methods of attenuating return of fear to provide long-term effective specific phobia treatment in clinical settings. Clinical practice examples are provided.

VRET in Combination with In Vivo Exposure Therapy when Client Financial Resources are Limited

There are multiple specific phobias where in vivo exposure will require the therapist and client to travel to the feared stimulus, demanding additional therapist time and increasing the financial cost of therapy for the client. Effective in vivo exposure therapy for these specific phobias becomes challenging in clinical situations where client resources are limited. Some examples of specific phobias requiring resources and time for access include fear of sharks (animal subtype specific phobia), fear of heights (natural environment subtype specific phobia), fear of medical procedures (blood-injection-injury type subtype specific phobia), and fear of flying (situation subtype specific phobia). The current review showed that the type of specific phobia most commonly associated with high in vivo exposure therapy financial costs is fear of flying in commercial aeroplanes as it involves travel and commercial flight ticket expenses (Botella, Rothbaum et al., 1996; 2000; 2006; Mühlberger et al., 2001).

It has long been suggested that when in vivo exposure therapy for fear of flying in aeroplanes is not financially affordable, VRET can be used to supplement in vivo exposure therapy (Botella, Rothbaum et al., 1996; 2000; 2006; Mühlberger et al., 2001). In clinical practice, for example, in vivo exposure can be used for feared stimuli and situations that are commonly associated with fear of flying in aeroplanes, such as packing a suitcase, traveling to the airport, waiting in the baggage check-in line, and having a coffee at the airport while waiting for their flight. Subsequently, for exposure to the aeroplane flight itself, VRET can be used in the therapist's office or at the airport, until the client reports being prepared to take a commercial flight without the presence of the therapist. Subsequently to taking a commercial flight, the client can receive extended VRET to further enhance the long-term effectiveness of treatment (Denniston et al., 2003; Laborda & Miller, 2013; Mühlberger et al., 2001; Thomas, et al., 2009). This clinical example shows that combining VRET and in vivo exposure

therapy allows the client to receive long-term effective exposure therapy to the complete process of taking a commercial aeroplane flight without the added financial cost of having a therapist accompany them on the flight.

VRET in Combination with In Vivo Exposure Therapy when there is Limited Physical Access to Real-life Feared Stimuli

The efficacy of exposure therapy may, at least in part, lie in its utilization of real-life feared stimuli and situations. Thus, limited physical access to real-life feared stimuli poses two challenges to providing effective in vivo exposure therapy in clinical settings, both of which can potentially be overcome by combining VRET with in vivo exposure therapy. The first challenge it poses in clinical settings is that in situations where the feared stimulus is not readily available or at all accessible, relying on vivo exposure therapy alone may not be possible. The current review has suggested that in those situations, VRET in combination with in vivo exposure may be a long-term effective alternative.

In a clinical example, consider a client who resides in Sweden and is avoiding travel to Australia due to fearing an encounter with crocodiles. The client can receive treatment in Sweden using VRET until they report no longer experiencing debilitating fear of crocodiles. Upon arriving in Australia, the client could undergo in vivo exposure therapy to crocodiles until they report no longer being worried about future encounters with a crocodile in safe environments. VRET and in vivo exposure can be conducted in contexts where the feared stimulus is likely to be encountered post fear habituation to promote the long-term effectiveness of treatment (Bandarian-Balooch & Neumann, 2011). This clinical example shows that VRET can be used in combination with in vivo exposure to overcome a common challenge of in vivo exposure therapy without compromising long-term treatment effectiveness.

The second challenge that limited physical access to feared stimuli poses in clinical settings is that the specific phobias frequently involve feared stimuli that cannot be readily stored in clinics (e.g., living animals). In vivo exposure therapy for these phobias may require clinicians to repeatedly allocate time and resources to gain access to the same or similar feared stimuli over time. This challenge is particularly problematic in community clinics where clinician time and resources are typically restricted and multiple clients with one or more specific phobias may present for treatment within a short time span. VRET can overcome this challenge because it allows live action filming, digital storage (Metz, 2015), and clinician sharing of a multitude of feared stimuli. This promotes rapid long-term access to a broad set of feared stimuli. A benefit of this rapid long-term access is that clinicians can provide effective exposure therapy to multiple clients with different phobias or one client with multiple phobias with little time and resources expended in preparing access to the feared stimuli between clients. Again, a combination of VRET and in vivo exposure therapy is suggested whenever possible.

In clinical practice, for example, a client presenting with fear of needles and fear of thunder could receive in vivo exposure therapy for their fear of needles followed by VRET for their fear of thunder without the clinician needing to allocate significant resources and time to physically access these feared stimuli between sessions. To promote the long-term effectiveness of treatment, the VRET can be used to present the multiple combinations of the feared stimuli in multiple contexts (Shiban et al., 2013, 2015). This clinical example shows that VRET can be combined with in vivo exposure therapy in clinical settings to promote flexible and effective clinical treatment for specific phobias.

VRET in Combination with In Vivo Exposure Therapy when there is Limited Client Motivation

Limited client motivation poses a great challenge to effective treatment of specific phobia because it is likely to result in client refusal to seek (Garcia-Palacios et al., 2001; Opris et al., 2012) or to complete exposure therapy. The current review showed that individuals who are unlikely to agree to in vivo exposure therapy may instead agree to VRET, providing clinicians with a method to overcome the challenge posed to in vivo exposure therapy when client motivation is limited. In these situations, for long-term effective and generalizable treatment that is appealing to individuals with specific phobia, it is suggested that VRET be conducted prior to rather than instead of in vivo exposure therapy. Initial successful completion of VRET ideally results in an increased sense of mastery and self-efficacy (Bandura, 1977), which potentially translates into increased motivation to engage in in vivo exposure therapy.

In a clinical example, a client presenting to treatment for a phobia of heights while simultaneously reporting limited motivation to engage in in vivo exposure therapy may be encouraged to initially undergo VRET. Upon successful completion of VRET, the client can be encouraged to undergo in vivo exposure therapy. To promote the long-term effectiveness of treatment, both VRET and in vivo exposure therapy could be conducted in multiple contexts (Bandarian-Balooch & Neumann, 2011, Bandarian-Balooch, 2012, 2015; Shiban et al., 2013; 2015). This clinical example highlights that a combination of VRET and in vivo exposure therapy is required to deliver appealing and long-term effective treatment for specific phobia.

Conclusion

The current chapter reviewed the clinical applications of VRET for treating specific phobia. The acquisition of specific phobia and extinction of fear has been explained within a Pavlovian conditioning framework (Bouton, 1993; Pavlov, 1927). Recent conditioning models indicate that the original fear memory is not removed by exposure therapy. This is

evident in return of fear research and highlights the importance of examining spontaneous recovery, renewal, reinstatement and reacquisition of fear to enhance long-term treatment outcomes. The mechanisms of return of fear represent a challenge for the clinician to ensure long-term treatment success. The conclusions from research using VRET provide specific methods that can be applied to enhance treatment outcomes and suggest the value of ensuring treatment gains are generalisable to real stimuli and contexts.

The current chapter outlined specific situations in which either imaginal, in vivo exposure or VRET would be the preferred treatment option. Currently, virtual reality technology is more affordable and accessible than ever before and this could contribute to an increase of clinicians implementing VRET to treat specific phobia. VRET can be seen to overcome challenges associated with vivo exposure-based treatments for specific phobia. Specifically, it can be used to provide a range of fear-relevant stimuli and contexts. Emerging virtual reality technologies can assist in presenting methods found to attenuate return of fear.

VRET and in vivo are considered to be equally effective in the short-term (Powers & Emmelkamp, 2008). The current chapter reviewed the long-term effectiveness of these treatments to reduce return of fear and indicated that further evidence is needed to establish equivalency between the treatments. Overall, the review identified that VRET could be used in conjunction with in vivo exposure therapy to address limited client financial resources, limited physical access to real-life fear evoking stimuli, and limited client treatment motivation. Therefore, the current chapter provided support for the clinical application of VRET as a supplementary tool to attenuate return of fear for specific phobia.

References

Abramowitz, J. S., Deacon, B. J., & Whiteside, S. P. (2012). *Exposure therapy for anxiety: Principles and practice*. Guilford Press.

Alvarez, R. P., Johnson, L., & Grillon, C. (2007). Contextual-specificity of short-delay extinction in humans: renewal of fear-potentiated startle in a virtual environment. *Learning & Memory*, *14*, 247-253. doi: 10.1101/lm.493707

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

Anderson, D. (1996). *U.S. Patent No. 5,483,307*. Washington, DC: U.S. Patent and Trademark Office.

Andreatta, M., Glotzbach-Schoon, E., Mühlberger, A., Schulz, S. M., Wiemer, J., & Pauli, P. (2015). Initial and sustained brain responses to contextual conditioned anxiety in humans. *Cortex*, *63*, 352-363. doi: 10.1016/j.cortex.2014.09.014

Bandarian-Balooch, S., & Neumann, D. (2011). Effects of multiple contexts and context similarity on the renewal of extinguished conditioned behaviour in an ABA design with humans. *Learning and Motivation*, *42*, 53-63. doi: 10.1016/j.lmot.2010.08.008

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2012). Extinction treatment in multiple contexts attenuates ABC renewal in humans. *Behaviour Research and Therapy*, *50*, 604-609. doi: 10.1016/j.brat.2012.06.003

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2013). Renewal of fear: Clinical-analogue findings. In M. N. Pucella (Ed.), *Psychology of fear: Ne*w developments. Nova Science Publishers.

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful

individuals. *Journal of Behavior Therapy and Experimental Psychiatry, 47*, 138-144. doi: 10.1016/j.jbtep.2014.12.006.

Bandura, A. (1977). Self-efficacy: Toward a unifying theory of behavioral change. *Psychological Review*, *84*, 191-2015. doi: 10.1037/0033-295X.84.2.191

Barlow, D. H., Craske, M. G., Cerny, J. A., & Klosko, J. S. (1989). Behavioral treatment of panic disorder. *Behavior Therapy*, *20*, 261-282. doi: 10.1016/S0005-7967(97)10006-7

Botella, C., Osma, J., García-Palacios, A., Quero, S., & Baños, R. M. (2004). Treatment of flying phobia using virtual reality: Data from a 1-year follow-up using a multiple baseline design. *Clinical Psychology & Psychotherapy*, *11*, 311-323. doi: 10.1002/cpp.404

Bouchard, S., Cote, S., & Richard, D. (2007). Virtual reality applications for exposure. In D. Richard & D. Lauterbach (Eds.), *Handbook of Exposure Therapy* (pp. 347-388). California, USA: Elsevier Inc.

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*, 80-9. doi: 10.1037//0033-2909.114.1.80

Bouton, M. E. (2002). Context, ambiguity, and unlearning: Sources of relapse after behavioral extinction. *Biological Psychiatry, 52*, 976-986. doi: 10.1016/S0006-3223(02)01546-9

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning & Memory*, *11*, 485-494. doi: 10.1101/lm.78804

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation, 10*, 445-466. doi: 10.1016/0023-9690(79)90057-2

Bouton, M. E., & King, D. A. (1983). Contextual control of the extinction of conditioned fear: Tests for the associative value of the context. *Journal of Experimental Psychology: Animal Behavior Processes*, *9*, 248-265. doi: 10.1037/0097-7403.9.3.248

Bouton, M. E., & Swartzentruber, D. (1989). Slow reacquisition following extinction: Context, encoding, and retrieval mechanisms. *Journal of Experimental Psychology: Animal Behavior Processes*, *15*, 43-53. doi: 10.1037/0097-7403.15.1.43

Bouton, M. E., Westbrook, R. F., Corcoran, K. A., & Maren, S. (2006). Contextual and temporal modulation of extinction: behavioral and biological mechanisms. *Biological Psychiatry*, *60*, 352-360. doi: 10.1016/j.biopsych.2005.12.015

Boschen, M. J., Parker, I., & Neumann, D. L. (2007). Changes in implicit associations do not occur simultaneously to Pavlovian conditioning of physiological anxiety responses. *Journal of Anxiety Disorders, 21,* 788-803. doi: 10.1016/j.janxdis.2006.11.007

Brooks, D. C., & Bouton, M. E. (1993). A retrieval cue for extinction attenuates spontaneous recovery. *Journal of Experimental Psychology: Animal Behavior Processes*, *19*, 77-89. 10.1037/0097-7403.19.1.77

Bush, J. (2008). Viability of virtual reality exposure therapy as a treatment alternative. *Computers in Human Behavior*, *24*, 1032-1040. doi: 10.1016/j.chb.2007.03.006

Capaldi, E. J., & Lynch, D. (1967). Repeated shifts in reward magnitude: Evidence in favor of an associational and absolute (noncontextual) interpretation. *Journal of Experimental Psychology*, *75*, 226-235. doi: 10.1037/h0043125

Carlin, A. S., Hoffman, H. G., & Weghorst, S. (1997). Virtual reality and tactile augmentation in the treatment of spider phobia: a case report.*Behaviour research and therapy*, *35*, 153-158. doi: 10.1016/S0005-7967(96)00085-X

Choy, Y., Fyer, A. J., & Lipsitz, J. D. (2007). Treatment of specific phobia in adults. *Clinical Psychology Review*, *27*, 266-286. doi: 10.1016/j.cpr.2006.10.002

Coelho, C., Tichon, J., Hine, T., Wallis, G., & Riva, G. (2006). Media presence and inner presence: The sense of presence in virtual reality technologies. In G. Riva, M. T. Anguera, B. K. Wiederhold, & F. Mantovani, *From Communication to Presence: Cognition, Emotions and Culture Towards the Ultimate Communicative Experience* (pp. 25-45). Netherlands: IOS Press.

Cruz-Neira, C., Sandin, D., & DeFanti, T. (1993). Surround-screen projection-based virtual reality: The design and implementation of the CAVE. In M. Whitton, *Proceedings of the 20th Annual Conference on Computer Graphics and Interactive Techniques* (pp. 135-142). doi: 10.1145/166117.166134

Davey, G. C. (1992). Classical conditioning and the acquisition of human fears and phobias: A review and synthesis of the literature. *Advances in Behaviour Research and Therapy*, *14*, 29-66. doi: 10.1016/0146-6402(92)90010-L

Denniston, J. C., Chang, R. C., & Miller, R. R. (2003). Massive extinction treatment attenuates the renewal effect. *Learning and Motivation*, *34*, 68-86. doi: 10.1016/S0023-9690(02)00508-8

Diemer, J., Alpers, G., Peperkorn, H., Shiban, Y., & Mühlberger, A. (2015). The impact of perception and presence on emotional reactions: A review of research in virtual reality. *Frontiers in Psychology, 6*, 1-9. doi: 10.3389/fpsyg.2015.00026

Dunsmoor, J. E., Ahs, F., Zielinski, D. J., & LaBar, K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, *113*, 157-164. doi: 10.1016/j.nlm.2014.02.010

Durlach, N. & Mavor, A. (1995). *Virtual Reality: Scientific and Technological Challenges*. Washington DC: National Academy Press.

Emmelkamp P. M. (1982) *Phobic and obsessive–compulsive disorders: Theory, research, and practice.* New York: Plenum Press.

Emmelkamp, P. M. (2005). Technological innovations in clinical assessment and psychotherapy. *Psychotherapy and Psychosomatics*, *74*, 336-343. doi: 10.1159/000087780

Emmelkamp, P. M., Bouman, T. K., & Scholing, A. (1992). *Anxiety disorders: A practitioner's guide*. Wiley.

Emmelkamp, P. M. G., Krijn, M., Hulsbosch, A. M., De Vries, S., Schuemie, M. J., & Van der Mast, C. A. P. G. (2002). Virtual reality treatment versus exposure in vivo: a comparative evaluation in acrophobia. *Behaviour Research and Therapy*, *40*, 509-516.

Emmelkamp, P. M., Bruynzeel, M., Drost, L., & van der Mast, C. A. G. (2001). Virtual reality treatment in acrophobia: a comparison with exposure in vivo. *CyberPsychology & Behavior*, *4*, 335-339. doi: 10.1089/109493101300210222

Garcia-Palacios, A., Hoffman, H., Carlin, A., Furness, T. U., & Botella, C. (2002). Virtual reality in the treatment of spider phobia: a controlled study. *Behaviour Research and Therapy*, *40*, 983-993.

Glautier, S., Elgueta, T., & Nelson, J. B. (2013). Extinction produces context inhibition and multiple-context extinction reduces response recovery in human predictive learning. *Learning & Behavior*, *41*, 341-352. doi: 10.3758/s13420-013-0109-7

Goldman, J. (2016, February). Street view your life: These are the 360-degree cameras coming for 2016. *CNET Mobile World Congress*. Retrieved from: http://www.cnet.com/au/news/360-degree-cameras-2016/

Haesen, K., & Vervliet, B. (2015). Beyond extinction: Habituation eliminates conditioned skin conductance across contexts. *International Journal of Psychophysiology*, *98*(3), 529-534. doi: 10.1016/j.ijpsycho.2014.11.010

He, P. (2016). Virtual reality for budget smartphones. *Young Scientists Journal*, *18*, 50-57.

Heim, M. (1995). The design of virtual reality. In M. Featherstone & R. Burrows (Eds.), *Cyberspace Cyberbodies Cyberpunk: Cultures of Technological Embodiment* (pp. 65–78). London: Sage Publications.

Hermans, D., Craske, M. G., Mineka, S., & Lovibond, P. F. (2006). Extinction in human fear conditioning. *Biological psychiatry*, *60*, 361-368. doi: 10.1016/j.biopsych.2005.10.006

Kahan, M., Tanzer, J., Darvin, D., & Borer, F. (2000). Virtual reality-assisted cognitive-behavioral treatment for fear of flying: Acute treatment and follow-up. *CyberPsychology & Behavior*, *3*, 387-392. doi: 10.1089/10949310050078832.

Kamphuis, H. J., & Telch, J. M. (2000). Effects of distraction and guided threat appraisal on fear reduction during exposure-based treatments for specific fears. *Behaviour Research and Therapy*, *38*, 1163-1181. doi: 10.1016/S0005-7967(99)00147-3

Krijn, M., Emmelkamp, P., Biemond, R., de Wilde de Ligny, C., Schuemie, M., & van der Mast, C. (2004). Treatment of acrophobia in virtual reality: The role of immersion and presence. *Behaviour Research and Therapy*, *42*, 229-239. doi: 10.1016/S0005-7967(03)00139-6

Krijn, M., Emmelkamp, P. M., Ólafsson, R. P., Bouwman, M., Van Gerwen, L. J., Spinhoven, P.,... & Van der Mast, C. A. (2007). Fear of flying treatment methods: virtual reality exposure vs. cognitive behavioral therapy. *Aviation, Space, and Environmental Medicine*, *78*, 121-128. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/17310883

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2016). *Effects of extended extinction and multiple extinction contexts on ABA renewal.* Manuscript in preparation, School of Applied Psychology, Griffith University, Gold Coast, Australia.

Laborda, M. A., McConnell, B. L., & Miller, R. R. (2011). Behavioral techniques to reduce relapse after exposure therapy. In T. R. Schactman & S. Reilly (Eds.), *Associative*

learning and conditioning theory: Human and non-human applications (pp. 79-104). New York: Oxford University Press.

Laborda, M. A., & Miller, R. R. (2013). Preventing return of fear in an animal model of anxiety: Additive effects of massive extinction and extinction in multiple contexts. *Behavior Therapy*, *44*, 249-261. doi: 10.1016/j.beth.2012.11.001

Leer, A., & Engelhard, I. M. (2015). Countering Fear Renewal: Changes in the UCS Representation Generalize Across Contexts. *Behavior Therapy*, *46*, 272-282. doi: 10.1016/j.beth.2014.09.012

Lombard, M., & Ditton, T. (1997). At the heart of it all: The concept of presence. *Journal of Computer-Mediated Communication*, *3*. doi: 10.1111/j.1083-6101.1997.tb00072.x

Maltby, N., Kirsch, I., Mayers, M., & Allen, G. J. (2002). Virtual reality exposure therapy for the treatment of fear of flying: A controlled investigation. *Journal of Consulting and Clinical Psychology*, *70*, 1112-1118. doi: 10.1037/0022-006X.70.5.1112

McMahan, A. (2003). Immersion, engagement and presence. In M. Wolf & B. Perrson (Eds.), *The Video Game Theory Reader* (pp. 67-86). New York: Routledge.

Matthews, A., Naran, N., & Kirkby, K. C. (2015). Symbolic online exposure for spider fear: Habituation of fear, disgust and physiological arousal and predictors of symptom improvement. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 129-137. doi: 10.1016/j.jbtep.2014.12.003

Metz, R. (2015, December). Four important things to expect in virtual reality in 2016. *MIT Technology Review*, Retrieved from: https://www.technologyreview.com/s/545011/four-important-things-to-expect-in-virtual-reality-in-2016/

Meyerbröker, K., & Emmelkamp, P. M. (2010). Virtual reality exposure therapy in anxiety disorders: a systematic review of process-and-outcome studies. *Depression and Anxiety*, *27*, 933-944. doi: 10.1002/da.20734

Michaliszyn, D., Marchand, A., Bouchard, S., Martel, M. O., & Poirier-Bisson, J. (2010). A randomized, controlled clinical trial of in virtuo and in vivo exposure for spider phobia. *Cyberpsychology, Behavior, and Social Networking*, *13*, 689-695. doi: 10.1089/cyber.2009.0277

Milad, M. R., Quinn, B. T., Pitman, R. K., Orr, S. P., Fischl, B., & Rauch, S. L. (2005). Thickness of ventromedial prefrontal cortex in humans is correlated with extinction memory. *Proceedings of the National Academy of Sciences of the United States of America*, *102*, 10706-10711. doi: 10.1073/pnas.0502441102

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*, 1033-1050. doi: 10.1016/S0005-7967(00)00076-0

Mühlberger, A., Weik, A., Pauli, P., & Wiedemann, G. (2006). One-session virtual reality exposure treatment for fear of flying: 1-year follow-up and graduation flight accompaniment effects. *Psychotherapy Research*, *16*, 26-40. doi: 10.1080/10503300500090944

Mühlberger, A.,Wiedemann, G., & Pauli, P. (2003). Efficacy of a one session virtual reality exposure treatment for fear of flying. *Psychotherapy Research*, *13*, 323–336. doi: 10.1093/ptr/kpg030

Neumann, D.L. (2006).The effects of physical context changes and multiple extinction contexts on two forms of renewal in a conditioned suppression task with humans. *Learning and Motivation, 37,* 149-175. doi: 10.1016/j.lmot.2005.06.004

Neumann, D. L. (2007). The resistance of renewal to instructions that devalue the role of contextual cues in a conditioned suppression task with humans. *Learning and Motivation, 38,* 105-127. doi: 10.1016/j.lmot.2006.11.002

Neumann, D. L. (2008). The effects of context changes on the reinstatement of extinguished conditioned behavior in a conditioned suppression task with humans. *Learning and Motivation, 39,* 114-135.

Neumann, D. L., Boschen, M. J., & Waters, A. M. (2008). The Return of Extinguished Conditioned Behaviour in Humans: Research findings and Clinical Implications. In L.N. Piccard (Ed.), *Biological psychology*: *New research* (pp, 1-42). Nova Science Publishers.

Neumann, D. L., & Kitlertsirivatana, E. (2010). Exposure to a novel context after extinction causes a renewal of extinguished conditioned responses: implications for the treatment of fear. *Behaviour Research and Therapy*, *48*(6), 565-570. doi: 10.1016/j.brat.2010.03.002

Neumann, D. L., Lipp, O. V., & McHugh, M. J. (2012). The relationship between different measures of fear learning following tests for reinstatement and spontaneous recovery of extinguished conditioned fear. *Beyond the Lab: Applications of Cognitive Research in Memory and Learning* (pp. 83-108). Hauppauge NY: Nova Science Publishers Inc

Neumann, D. L., & Longbottom, P. L. (2008). The renewal of extinguished conditioned fear with fear-relevant and fear-irrelevant stimuli by a context change after extinction. *Behaviour Research and Therapy*, *46*, 188-206. doi:10.1016/j.brat.2007.12.004

Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure. *Biological Psychology*, *73*, 175-185. doi: 10.1016/j.biopsycho.2006.03.004

Neumann, D. L., Waters, A. M., & Westbury, H. R. (2008). The use of an unpleasant sound as the unconditional stimulus in aversive Pavlovian conditioning experiments that involve children and adolescent participants. *Behavior Research Methods, 40,* 622-625. doi: 10.3758/BRM.40.2.622

Norcross, J., & Wampold, B. (2011). What works for whom: Tailoring psychotherapy to the person. *Journal of clinical Psychology: In Session, 67*, 127-132. doi: 10.1002/jclp.20764

Opris, D., Pintea, S., García-Palacios, A., Botella, C., Szamosközi, S., & David, D. (2012). Virtual reality exposure therapy in anxiety disorders: a quantitative meta-analysis. *Depression and Anxiety*, *29*, 85-93. doi: 10.1002/da.20910

Oscillada, J. M. (2015, May). Comparison chart of FOV (field of view) of VR headsets. *VR Times*. Retrieved from http://www.virtualrealitytimes.com/2015/05/24/chart-fov-field-of-view-vr-headsets/

Öst, L. G. (1989). One-session treatment for specific phobias. *Behaviour Research and Therapy*, *27*, 1-7. doi: 10.1016/005-7967(89)90113-7

Öst, L. G., Brandberg, M., & Alm, T. (1997). One versus five sessions of exposure in the treatment of flying phobia. *Behaviour Research and Therapy*, *35*, 987-996. doi: 10.1016/S0005-7967(97)00077-6

Park, S., Toole, T., & Lee, S. (1999). Functional roles of the proprioceptive system in the control of goal-directed movement. *Perceptual and Motor Skill, 88*, 631-647. doi: 10.2466/PMS.88.2.631-647

Parsons, T. D. (2015). Virtual Reality Exposure Therapy for Anxiety and Specific Phobias. In M. Khosrow-Pour (Ed.), *Encyclopedia of Information Science and Technology, Third Edition* (pp. 6475-6483). Hershey, PA: Information Science Reference.

Patteron, R., Winterbottom, M., & Pierce, B. (2006). Perceptual issues in the use of head-mounted visual displays. *Human Factors*, *48*, 555-573. doi: 10.1518/001872006778606877

Pavlov, I. P. (1927). Conditioned reflexes. London: Oxford University Press.

Pischek-Simpson, L. K., Boschen, M. J., Neumann, D. L., & Waters, A. M. (2009). The development of an attentional bias for angry faces following Pavlovian fear conditioning. *Behaviour Research and Therapy, 47,* 322-330. doi: 10.1016/j.brat.2009.01.007

Powers, M. B., & Emmelkamp, P. M. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders*, *22*, 561-569. doi: 10.1016/j.janxdis.2007.04.006

Pratt, D. R., Zyda, M., & Kelleher, K. (1995). Virtual reality: in the mind of the beholder. *Computer*, *28*, 17-19. doi: 10.1109/2.386986

Price, M., & Anderson, P. (2007). The role of presence in virtual reality exposure therapy. *Journal of Anxiety Disorders*, *21*, 742-751. doi: 10.1016/j.janxdis.2006.11.002

Raaen, K. & Kjellmo, I. (2015). Measuring latency in virtual reality systems. In. K. Chorianopoulos, M. Divitini, J. B. Haugem L. Jaccheri, & R. Malaka (Eds.), *Entertainment Computing – ICEC 2015* (pp. 457-462). doi: 10.1007/978-3-319-24589-8_40

Rachman, S. (1966). Studies in desensitization—III: Speed of generalization. *Behaviour Research and Therapy*, *4*, 7-15. doi: 10.1016/0005-7967(66)90038-6

Rachman, S. (1989). The return of fear: Review and prospect. *Clinical Psychology Review*, *9*, 147-168. doi: 10.1016/0272-7358(89)90025-1

Rachman, S. (2004). Fear and courage: A psychological perspective. *Social Research, 71*, 149-176. Retrieved from: http://www.jstor.org/40971664

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*, 88-96. doi: 10.1037/0097-7403.1.1.88

Rescorla, R. A., & Wagner, A. R. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement. *Classical conditioning II: Current research and theory*, *2*, 64-99. Retrieved from: https://sites.ualberta.ca/~egray/teaching

Richard, C., Lauterbach, D., & Gloster, A. (2007). Description, mechanisms of action, and assessment. In D. Richard & D. Lauterbach (Eds.), *Handbook of Exposure Therapy* (pp. 1-28). California, USA: Elsevier Inc.

Rose, M. P., & McGlynn, F. D. (1997). Toward a standard experiment for studying post-treatment return of fear. *Journal of Anxiety Disorders*, *11*, 263-277. doi: 10.1016/S0887-6185(97)00010-8

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. doi: 10.1016/j.beth.2005.04.004

Rothbaum, B. O., Hodges, L., Anderson, P. L., Price, L., & Smith, S. (2002). Twelve-month follow-up of virtual reality and standard exposure therapies for the fear of flying. *Journal of Consulting and Clinical Psychology*, *70*, 428-432. 10.1037//0022-006X.70.2.428

Rothbaum, B. O., Hodges, L. F., Kooper, R., Opdyke, D., Williford, J. S., & North, M. (1995). Virtual reality graded exposure in the treatment of acrophobia: A case report. *Behavior Therapy*, *26*, 547-554. doi: 10.1016/S0005-7894(05)80100-5

Rothbaum, B., Hodges, L., Watson, B., Kessler, G., & Opdyke, D. (1996). Virtual reality exposure therapy in the treatment of fear of flying: A case report. *Behaviour Research and Therapy, 34*, 477-481. doi: 10.1016/0005-7967(96)00007-1

Rothbaum, B. O., Hodges, L., Smith, S., Lee, J. H., & Price, L. (2000). A controlled study of virtual reality exposure therapy for the fear of flying. *Journal of consulting and Clinical Psychology*, *68*, 1020. doi: 0.1037//0022-006X.68.6.1020

Sanchez-Vives, M., & Slater, M. (2005). From presence to consciousness through virtual reality. *Nature Reviews Neuroscience*, *6*, 332-339. doi: 10.1038/nrn1651

Shiban, Y., Pauli, P., & Mühlberger, A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, *51*, 68-74. doi: 10.1016/j.brat.2012.10.007

Shiban, Y., Schelhorn, I., Pauli, P., & Mühlberger, A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, *71*, 45-53. doi: 10.1016/j.brat.2015.05.014

Shiban, Y., Wittmann, J., Weißinger, M., & Mühlberger, A. (2015). Gradual extinction reduces reinstatement. *Frontiers in Behavioral Neuroscience*, *9*. doi: 10.3389/fnbeh.2015.00254

Slater, M., & Wilbur, S. (1997). A framework for immersive virtual environments (FIVE): Speculations on the role of presence in virtual environments. *Presence: Teleoperators and virtual environments, 6*, 603-616. doi: 10.1162/pres.1997.6.6.603

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*, 201-219. doi: 10.1145/210079.210084

Smith, W. (2015, November). Stop calling google cardboard's 360 degree videos 'VR.' *Wired*. Retrieved from http://www.wired.com/2015/11/360-video-isnt-virtual-reality/

Thomas, B. L., Vurbic, D., & Novak, C. (2009). Extensive extinction in multiple contexts eliminates renewal of conditioned fear in rats. *Learning and Motivation, 40,* 147-159. doi: 10.1016/j.lmot.2008.10.002

Troger, C., Ewald, H., Glotzbach, E., Pauli, P., & Muhlberger, A. (2012). Does pre-exposure inhibit fear context conditioning? A virtual reality study. *Journal of Neural Transmission, 119*, 709-719. doi: 10.1007/s00702-011-0757-8

Vansteenwegen, D., Vervliet, B., Iberico, C., Baeyens, F., Van den Bergh, O., & Hermans, D. (2007). The repeated confrontation with videotapes of spiders in multiple contexts attenuates renewal of fear in spider-anxious students. *Behaviour Research and Therapy*, *45*, 1169-1179. doi: 10.1016/j.brat.2006.08.023

Vasey, M. W., Harbaugh, C. N., Buffington, A. G., Jones, C. R., & Fazio, R. H. (2012). Predicting return of fear following exposure therapy with an implicit measure of attitudes. *Behaviour Research and Therapy*, *50*, 767-774. doi: 10.1016/j.brat.2012.08.007

Wagner, A. R., & Rescorla, R. A. (1972). Inhibition in Pavlovian conditioning: Applications of a theory. In R. A. Boakes & M. S. Haliday (Eds.), *Inhibition and learning* (pp. 301-336). New York: Academic Press.

Wald, J., & Taylor, S. (2000). Efficacy of virtual reality exposure therapy to treat driving phobia: a case report. *Journal of Behavior Therapy and Experimental Psychiatry*, *31*, 249-257. doi: 10.1016/S0005-7916(01)00009-X

Wald, J., & Taylor, S. (2003). Preliminary research on the efficacy of virtual reality exposure therapy to treat driving phobia. *CyberPsychology & Behavior*, *6*, 459-465. doi: 10.1089/109493103769710488

Warren, V. T., Anderson, K. M., Kwon, C., Bosshardt, L., Jovanovic, T., Bradley, B., & Norrholm, S. D. (2014). Human fear extinction and return of fear using reconsolidation update mechanisms: The contribution of on-line expectancy ratings. *Neurobiology of Learning and Memory*, *113*, 165-173. doi: 10.1016/j.nlm.2013.10.014

Wiederhold, B., & Wiederhold, M. (2005). *Virtual Reality Therapy for Anxiety Disorders: Advances in Evaluation and Treatment*. Washington DC: American Psychological Association.

Wilson, G. T. (2007). Manual-based treatment: Evolution and evaluation. In T. Treat, R. Bootzin, & T. Baker (Eds.), *Psychological Clinical Science*. New York: Taylor & Francis Group.

Winchester, H. (2016, July). Occulus rift v playstation VR: What is the best gaming VR headset? *Wearable*. Retrieved from http://www.wareable.com/project-morpheus/oculus-rift-versus-project-morpheus

Witmer, B., & Singer, M. (1998). Measuring presence in virtual environments: A perspective questionnaire. *Presence: Teleoperators and Virtual Environments, 7*, 225-240. doi: 10.1162/105474698565686

Wolpe, J. (1958). *Psychotherapy by reciprocal inhibition*. Stanford, CA: Stanford University Press.

Chapter 4: Preamble

The findings from the preceding book chapter influenced the decision to use VRET as a methodology in the research project to overcome the limitations of previous reinstatement research. The current chapter presents an overview of the aims of the research project and summarises the methodology in the two experiments and one case study. As briefly discussed in Chapter 1, the three aims of the research project will be further explored in Chapter 4.

Chapter 4: Overview of the Aims of the Empirical Studies

As outlined in the previous chapter, VRET could be implemented to present multiple feared stimuli and help overcome the ethical issues associated with conducting reinstatement of fear with fearful individuals. This is aligned with the gaps in the literature discussed in Chapters 1 and 2, namely that the research into reinstatement of fear in general and with clinical samples in particular is lacking (Rachman & Whittal, 1989; Shiban et al., 2013; 2015). The impact that reinstatement of fear may have for relapse following treatment for specific phobia is unknown and this prevents modifications to exposure therapy to increase efficacy and long-term effectiveness. Furthermore, despite the prevalence of multiple phobias in the population (APA, 2013; Burstein et al., 2012; Wardenaar et al., 2017; Wittchen et al., 2002), participants with multiple phobias are not typically included in empirical investigations. Previous research has found a lack of extinction generalisation across feared animal type stimuli (Farrell et al., 2020; Öst, 1987) and there are no previous studies on reinstatement of fear for those with multiple phobias.

Laboratory-based research with rats has demonstrated that aversive stimuli other than the US can trigger reinstatement (Halladay et al., 2012; Rescorla & Heth, 1975). In generalising the findings to a human clinical sample, it remains to be determined if untreated fears could evoke reinstatement of fear and if exposure therapy to the untreated fear could attenuate this fear reinstatement. The clinical implications involve how a secondary fear may be a risk factor for return of fear via conditional reinstatement of fear. It is unknown whether exposure to an unextinguished CS can elicit and reduce conditional reinstatement of fear in humans or in a clinical sample. The current research project aims are:

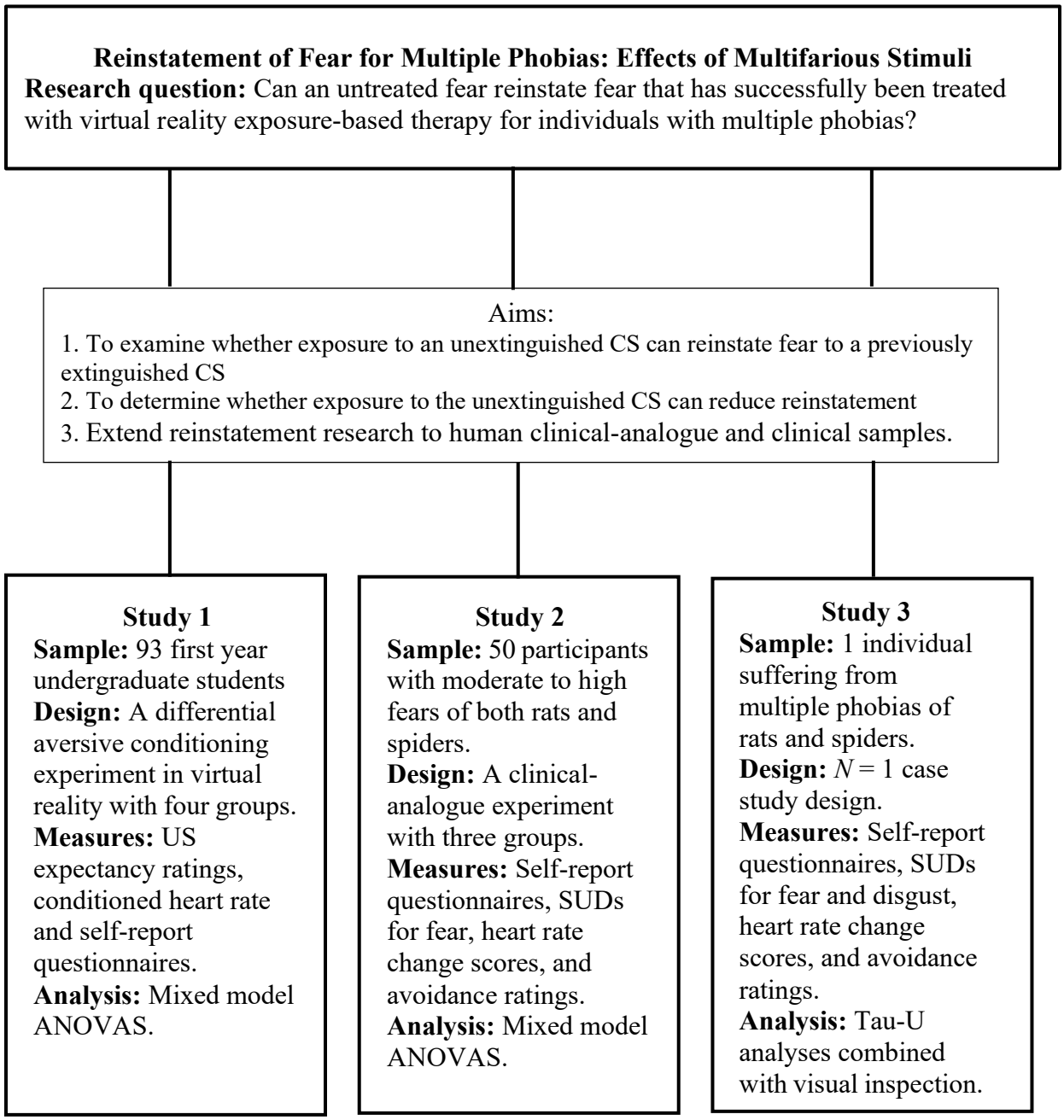
1. To examine whether exposure to an unextinguished CS can elicit reinstatement of fear in a non-fearful sample, moderate to high fearful sample, and a clinical case with an individual suffering from multiple phobias.

2. To determine whether exposure to an unextinguished CS can attenuate reinstatement of fear across a non-fearful sample, moderate to high fearful sample, and a clinical case with an individual suffering from multiple phobias.
3. To extend reinstatement of fear research from laboratory-based research with rats to human clinical-analogue and clinical samples.

The aims of the thesis were addressed across two experiments and a clinical case study. Following on from the comprehensive overview of the studies presented in Chapter 1, the following Figure 4.1 provides a concise overview of the design, samples, measures and analyses of the three studies.

Figure 4.1.

An Overview of the Three Studies and the Sample, Design, Measures and Analyses



References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

Burstein, M., Georgiades, K., He, J. P., Schmitz, A., Feig, E., Khazanov, G. K., & Merikangas, K. (2012). Specific phobia among US adolescents: phenomenology and typology. *Depression and Anxiety*, *29*(12), 1072-1082. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.22008

Farrell, L. J., Miyamoto, T., Donovan, C. L., Waters, A. M., Krisch, K. A., & Ollendick, T. H. (2021). Virtual reality one-Session treatment of child-specific phobia of dogs: A controlled, multiple baseline case aeries. *Behavior Therapy*, *52*(2), 478-491. https://www-clinicalkey-com-au.libraryproxy.griffith.edu.au/service/content/pdf/watermarked/1-s2.0-S0005789420300861.pdf?locale=en_AU&searchIndex=

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Öst, L. G. (1987). Applied relaxation: description of a coping technique and review of controlled studies. *Behaviour Research and Therapy*, *25*(5), 397-409. https://doi.org/10.1016/0005-7967(87)90017-9

Rachman S, Whittal M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, 27, 513-520. https://doi.org/10.1016/0005-7967(89)90085-5

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*(1), 88. https://pubmed.ncbi.nlm.nih.gov/1151290/

Shiban, Y., Pauli, P., & Mühlberger, A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, *51*(2), 68-74. https://doi.org/10.1016/j.brat.2012.10.007

Shiban Y., Schelhorn I., Pauli P., & Mühlberger A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, 71, 45-53. https://doi.org/10.1016/j.brat.2015.05.014

Wardenaar, K. J., Lim, C. C., Al-Hamzawi, A. O., Alonso, J., Andrade, L. H., Benjet, C., ... & De Jonge, P. (2017). The cross-national epidemiology of specific phobia in the World Mental Health Surveys. *Psychological Medicine*, *47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Wittchen, H. U., Lecrubier, Y., Beesdo, K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. *Anxiety Disorders*, 23-37. https://doi.org/10.1002/9780470986844.ch2

Chapter 5: Preamble

As highlighted in Chapter 4, the experiment presented in Chapter 5 aims to examine whether reinstatement of fear can be triggered by an excitatory CS that did not undergo extinction treatment and whether extinction to the excitatory CS can reduce reinstatement of fear. More broadly, Chapter 5 aims to bridge the gap between animal and clinical research. Chapter 5 includes a human non-fearful sample of 93 undergraduate psychology students who participated in a differential aversive conditioning procedure within a virtual reality environment.

STATEMENT OF CONTRIBUTION TO CO-AUTHORED PUBLISHED PAPER

This chapter includes a co-authored published journal article. The bibliographic details of the published paper, including all authors are:

Krisch, K. A., Bandarian-Balooch, S., Neumann, D. L., & Zhong, J. (2020). Eliciting and attenuating reinstatement of fear: Effects of an unextinguished CS. *Learning and Motivation*, *71*, 101650. https://doi.org/10.1016/j.lmot.2020.101650.

The candidate was responsible for manuscript preparation including a review of the literature, design and development of the experiment protocol, data collection, analysis and writing the manuscript. The supervisors provided advice and reviewed drafts. John Zhong provided programming support that assisted with the design of the experiment and drafting of the manuscripts technical sections. The *Learning and Motivation* journal permits the inclusion of a published manuscript for scholarly purposes in a thesis or dissertation (with full acknowledgement of the original article). The formatting is consistent with the journal requirements.

(Signed) _____(Date): 16/11/21
Kirra Krisch

(Countersigned) _____ (Date): 16/11/21
Corresponding author of paper: Dr Siavash Bandarian

(Countersigned)_____(Date): 16/11/21
Supervisor: Professor David Neumann

(Countersigned)_____(Date): 18/11/21
Supervisor: John Zhong

Chapter 5: Eliciting and Attenuating Reinstatement of Fear: Effects of an Unextinguished CS

School of Applied Psychology, Griffith University

Kirra A. Krisch[1], Siavash Bandarian-Balooch[1,2], David L. Neumann[1] & John Zhong[1]

[1]School of Applied Psychology Griffith University, Australia

[2]Menzies Health Institute Queensland, Australia

Abstract

Reinstatement of fear is a proposed mechanism for return of fear following exposure therapy. A standard reinstatement procedure in the laboratory involves a conditional stimulus (CS) paired with an unconditional stimulus (US) during acquisition (i.e., CS+), and a CS paired without an US (CS-) during acquisition. In extinction the CS+ and CS- are presented alone, then the US is presented without the CS in reinstatement, and followed by test trials of the CS. The current study examined whether reinstatement of fear can be triggered by a CS that was previously paired with the US (i.e., unextinguished CS) and reduced by extinction to the CSextinguished and CSunextinguished but not the CS- in a sample of first year psychology students (expectancy data $N = 93$; heart rate data $N = 73$). A differential aversive conditioning procedure presented within a virtual reality environment was used to examine reinstatement of the US expectancy and conditioned heart rate responses. As predicted, presentation of an unextinguished CS reinstated fear of a second previously extinguished CS. Moreover, conducting extinction with multiple stimuli attenuated this reinstatement of fear as indexed by self-report and heart rate measures. The present results suggest that therapy should include exposure to multiple stimuli to reduce the likelihood of reinstatement of fear.

Keywords: Reinstatement of fear; extinction of fear; virtual reality exposure therapy; anxiety

1. Introduction

Specific phobia is the most prevalent anxiety disorder (Kessler and Wang, 2008; Van Houtem et al., 2013) with lifetime prevalence rates estimated between 10% and 12.5% (Kessler et al., 2005; Van Houtem et al., 2013). It is common for individuals suffering from specific phobia to have multiple phobias, approximately 75% of individuals fear more than one object or situation (e.g., Curtis et al., 1998; LeBeau et al., 2010; Wittchen et al., 2003). Furthermore, Wittchen et al. (2003) surveyed 3021 participants and found over 50% of individuals suffering from specific phobia feared three or more different phobic objects or situations. The likelihood of recovering from specific phobia is inversely related to the number of fears, while 60% of individuals with pure specific phobia recover, only 30% of individuals with two to three multiple phobias recover (Wittchen et al., 2003).

Exposure therapy has been found to be the gold standard treatment for specific phobia (Abramowitz et al., 2012; Craske, 1999). In vivo exposure (with real-life stimuli) and virtual reality exposure therapy (VRET; with virtual stimuli) are two exposure-based approaches that have shown to be comparably effective in treating specific phobia (Bush, 2008). Subsequent to successful in vivo exposure treatment, approximately 35-50% of individuals experience a return of fear (ROF; Rachman, 1966, 1987; Rose and McGlynn, 1997; Vasey et al., 2012).

Exposure therapy has been explained within the learning framework provided by Pavlovian conditioning. Extinction of conditioned fear involves repeated presentations of the feared stimulus without the aversive stimulus, resulting in a fear response no longer being observed (Pavlov, 1927). Thus, the process of extinction is analogous to exposure therapy.

Pavlovian conditioning can also be applied help understand the mechanisms that underlie return of fear, such as reinstatement, renewal, spontaneous recovery and reacquisition. Reinstatement of fear is the process of how extinguished fear can return after re-exposure to the US (Rescorla and Heth, 1975). Reinstatement of extinguished conditioned

responses in laboratory-based studies has been observed on test trials with animals (Bouton and Bolles, 1979; Halladay et al., 2012; Kim and Richardson, 2007; Rescorla and Heth, 1975; Vurbic and Bouton, 2011) and human participants (Culver et al., 2015; Dirikx et al., 2007; Dunsmoor et al., 2014; Mertens et al., 2019). In a standard reinstatement procedure, a CS is paired with a US during acquisition, the CS is presented alone during extinction, and then the US is presented without the CS in a reinstatement phase, and followed by test trials of the CS.

Reinstatement of extinguished conditioned responses have been produced by a variety of USs such as: an electrotactile stimulus (Dirikx et al., 2007; Glotzbach-Schoon et al., 2015; Haaker et al., 2014; Kull et al., 2012; Neumann et al., 2012; Schiller et al., 2008), an air blast to the throat (e.g., Norrholm et al., 2006), loud tones (e.g., LaBar and Phelps, 2005), and abdominal pain (e.g., Kattoor et al., 2012). The number of US presentations in the reinstatement phase has vastly differed between studies with several studies using: 2 US presentations (Dirikz et al., 2004; Dirikx, 2009; Milad et al., 2005), 3 US presentations (Golkar et al., 2013; Golkar & Ohman, 2012; Haaker et al., 2013; Kindt and Soeter, 2013; Kull et al., 2012; Lonsdorf et al., 2004; Norrholm et al., 2006; Sevenster et al., 2012; Sokol & Lovibond, 2012), 4 US presentations (Herman et al., 2005; LaBar and Phelps 2005; Schiller et al., 2008) and up to 6 presentations (Neumann, 2008). While the reinstatement effect has been produced in diverse laboratory-based studies, attempts to reproduce these results in studies focused on individuals diagnosed with specific phobia following exposure therapy, have been largely unsuccessful (Rachman and Whittal, 1989; Shiban et al., 2015). Previous research employing one presentation of a US such as an air blast and electrotactile stimulus have found these USs were not sufficiently aversive to elicit reinstatement of fear with clinical-analogue and clinical samples (Rachman and Whittal, 1989; Shiban et al., 2015). The lack of success in producing reinstatement effects which generalise from the laboratory to

clinical-analogues and clinical samples has impeded our understanding of reinstatement of fear in phobic populations.

However, Halladay et al. (2012) developed a novel method to reinstate fear in rats in a laboratory-based procedure that holds particular promise for reinstatement studies with humans. Halladay et al. (2012) examined if exposure to an unextinguished CS would reinstate fear to an extinguished CS with groups of rats. The four groups differed according to the reinstatement phase. In acquisition, each group received presentations of the CSunextinguished (e.g., tone) and CSextinguished (e.g., light) paired with the US (e.g., footshock). In extinction, each group received presentations of the CSextinguished (i.e., light) without the US. It was found that presenting rats with an unextinguished CS (i.e., tone) in the reinstatement phase reinstated initial fear in responding to the extinguished CS (i.e., light). Halladay et al. (2012) referred to this phenomenon as conditional reinstatement. The results of Halladay et al. (2012) suggest that reinstatement of fear can be triggered by a broader variety of stimuli, including stimuli that may elicit fear due to a prior association with an aversive stimulus.

The finding that an excitatory CS can result in reinstatement (Halladay et al., 2012) is important, given that, in clinical settings an excitatory CS translates to a secondary feared object or situation. As noted, on average individuals with specific phobia will fear three different phobic objects or situations (e.g., Curtis et al., 1998; LeBeau et al., 2010; Wittchen et al., 2002) and importantly the likelihood of relapse is higher for those that have multiple phobias than for those that suffer from one phobia. Thus, the potential that exposure to a feared stimulus that was not part of treatment may increase the likelihood of reinstatement to the treated fear. Investigating conditional reinstatement of fear with human participants may thus increase the real-world applicability of reinstatement of fear. In a clinical example an individual may undergo exposure therapy for a primary fear of spiders and have a secondary

fear of snakes. Following successful exposure therapy for fear of spiders the individual may encounter a snake and this might trigger a reinstatement of the primary fear of spiders. Importantly, this example may be more likely to occur than standard unconditional reinstatement, such as an individual re-experiencing the US (e.g., a spider bite).

Bouton's contextual memory model (1998, 2002, 2004) can potentially explain how conditional reinstatement occurs. In the reinstatement phase, contextual cues will become associated with the presentation of an unextinguished CS. Subsequently, in the test phase, the contextual cues enhance the retrieval of the CS-US association during the presentation of the extinguished CS to produce conditional reinstatement of fear. While it is important to understand the theoretical underpinnings of conditional reinstatement, it is also valuable to understand how the exposure process can be modified to attenuate reinstatement of fear and ultimately enhance the long-term effectiveness of exposure therapy for specific phobia.

Research has identified several methods that can attenuate reinstatement such as: gradual extinction with rats (Gershman et al., 2013), and non-fearful humans (Shiban et al., 2015), secondary extinction with rats (Vurbic and Bouton, 2011) and with non-fearful human samples (Mertens et al., 2019). Conducting extinction in multiple contexts (Dunsmoor et al., 2014) has also been found to attenuate reinstatement of fear in humans. Based on the presumption that fear can be reinstated by a secondary fear with human participants, exposure to multiple feared stimuli could be a method to reduce conditional reinstatement. Previous clinical-analogue studies have found that exposure to multiple similar stimuli (e.g., different types of spiders) reduced renewal of fear (Rowe and Craske, 1998; Shiban et al., 2015). Exposure to multiple similar stimuli has been proposed to increase the number of shared cues between extinction learning and subsequent exposure to the stimulus (Bouton, 1993, 2002, 2004). Similar to renewal research on multiple similar stimuli, it is possible that different feared stimuli could increase shared cues between the extinction context and subsequent

exposure of the extinguished CS. Thus, exposure to different feared stimuli (e.g., snakes and spiders) could reliably reduce reinstatement of fear.

The current study investigated whether an ecological valid unextinguished CS will reinstate fear and whether exposure to this unextinguished CS can reduce reinstatement of fear in a human non-clinical sample. A differential aversive conditioning procedure with virtual reality was used to examine reinstatement of the expectancy of the US (e.g. an electric shock) and conditioned heart rate responses, by presenting the CSextinguished (e.g., virtual representation of a spider) and CSunextinguished (e.g., virtual representation of a snake) paired with the US. The CS- (e.g., virtual representation of a rat) was presented alone. One advantage of using virtual reality protocols to investigate ROF is that the conditions may more closely resemble real-life clinical situations (Dunsmoor et al., 2014; Krisch et al., 2016). The experiment consisted of six phases: acquisition, first extinction, reinstatement, first test, second extinction, and second test phase.

The experiment employed four groups: an Unconditional Reinstatement (UR) group, a Conditional Reinstatement (CR) group, a Multiple Feared Stimuli (MFS) group, and a Control group. In previous studies reinstatement typically occurs after 2-4 US presentations and the most common is 3 US presentations (Golkar et al., 2013; Golkar and Ohman, 2012; Haaker et al., 2013; Kindt and Soeter, 2013; Kull et al., 2012; Lonsdorf et al., 2004; Norrholm et al., 2006; Sevenster et al., 2012; Sokol & Lovibond, 2012). In several previous studies using feared stimuli (e.g., spiders and snakes) 1 US presentation of an electroctactile stimulus or air blast has not been sufficiently aversive to produce reinstatement of fear (Rachman and Whittal, 1989; Shiban et al., 2015). Thus, the UR group received 3 presentations of the US in the reinstatement phase. The UR group did not undergo a second extinction phase. In the reinstatement phase presenting the CSunextinguished more than once may result in extinction. The CR group received one presentation of the CSunextinguised in

the reinstatement phase without a second extinction phase. The MFS group received one presentation of the CSunextinguised in the reinstatement phase and a second extinction to the CSunextinguished. The control group was not presented with a reinstatement phase and did not receive a second extinction phase. It was hypothesised that shock expectancy and conditioned heart rate responses would be larger in the CR and UR groups than in Control group during the first test phase. No differences are expected between the CR group and UR group. These results would thus demonstrate the reinstatement effect when an unextinguished CS is used. It was also hypothesised that the reinstatement effect would be smaller for the MFS group than for the CR group during the second test phase. This finding would thus demonstrate the effects of extinction to an unextinguished CS results in attenuation of the reinstatement effect.

2. Materials and Method

2.1 Participants

The sample included one hundred and one first year students enrolled in psychology courses from Griffith University (77 females and 35 males) with mean age of 22.04 years (*SD* = 6.56, age range = 17- 49). Participants provided informed written consent and received course credit for participating. Three participants were excluded for not responding to 70% of the trials and five participants were excluded for failing to learn the contingencies in acquisition. The final sample for the expectancy data included 93 participants who were randomly assigned to one of four experimental groups; Unconditional Reinstatement (UR; *n* = 23), Conditional Reinstatement (CR; *n* = 21), Multiple Feared Stimuli (MFS; *n* = 26), or the Control group (*n* = 23). The groups were labelled according to the reinstatement phase (see Table 5.1). Shiban et al. (2015) revealed a partial-eta squared effect size of $\eta_p^2 = 0.32$, for the increase in CS+ expectancy ratings compared to the CS- at test. In the current study, to achieve a power of .90 with a α two-tailed = .05, 18 participants per group was required. The

heart rate data for 20 participants could not be analysed due to software error, resulting in a final total sample size of 73 for heart rate analyses. The final sample sizes in each group for conditioned heart rate analyses were UR n = 18, CR; n = 19, MFS n = 17, and the Control group n = 19. Ethical approval was granted by the Griffith University Human Research committee.

Table 5.1.

Conditional Stimuli and Number of Trials across Phases for Each Group

Groups	Phases					
	Acquisition	Extinction	Reinstatement	Test 1	Extinction 2	Test 2
UR	10 CS_{ext} US	12 CS_{ext}	3 US	1 CS_{ext}	-	1 CS_{ext}
	10 CS_{unext} US	12 CS-		1 CS_{unext}		1 CS_{unext}
	10 CS-			1 CS-		1 CS-
CR	10 CS_{ext} US	12 CS_{ext}	1 CS_{unext}	1 CS_{ext}	-	1 CS_{ext}
	10 CS_{unext} US	12 CS-		1 CS_{unext}		1 CS_{unext}
	10 CS-			1 CS-		1 CS-
MFS	10 CS_{ext} US	12 CS_{ext}	1 CS_{unext}	1 CS_{ext}	12 CS_{unext}	1 CS_{ext}
	10 CS_{unext} US	12 CS-		1 CS_{unext}		1 CS_{unext}
	10 CS-			1 CS-		1 CS-
Control	10 CS_{ext} US	12 CS_{ext}	-	1 CS_{ext}	-	1 CS_{ext}
	10 CS_{unext} US	12 CS-		1 CS_{unext}		1 CS_{unext}
	10 CS-			1 CS-		1 CS-

Note. UR = Unconditioned Reinstatement group; CR = Conditioned Reinstatement group; MFS = Multiple Feared Stimuli group; CSext = Conditional stimulus extinguished; CS_{unext} = Conditional stimulus unextinguished; US = Unconditional Stimulus; CS - = Conditional Stimulus without an aversive US; 10, 12, 3 and 1 refer to the number of trials.

2.2 Apparatus

Participants completed the task in a 2.2 x 3 m square room. The virtual CSs (CS extinguished and CS unextinguished) were presented through an Oculus Rift Virtual Reality headset. The Samsung Gear 360º video camera was used to record the video footage to be

presented in the experiment. A golden orb weaver (*Nephila edulis*), a water python (*Liasis mackloti*), and a brown rat (*Rattus norvegicus*) were filmed as the CSext, the CSunext, and CS-.The virtual reality environment featured the spider, snake, and rat in an office context and participants viewed this environment from a first person perspective. Additional 360^{o} video footage from this context without featuring the spider, snake, and rat was also recorded. The US was a 200 ms electrotactile stimulus produced by an IWORX S1100 stimulus isolator and presented through two ADInstruments MLA1010B Ag/AgCl electrodes that were attached to the participant's non-dominant arm. Custom written software was created to set the timing and sequence of the CS and US presentations. Heart rate (HR) was recorded by electrocardiography (ECG) signals in conjunction with an ADInstruments Model ML11GSR Bio amp. Three ADInstruments MLA1010B Ag/AgCl electrodes were used. The signal was bandpass filtered using cut-offs of 0.3 Hz to 300 Hz and acquired using a sampling rate of 1000 Hz.

Questionnaires were used to examine equivalency between the groups in fear of the animals used as CSs. For fear of snakes, the Snake Anxiety Questionnaire (SNAQ; Klorman et al., 1974) was administered. The SNAQ consists of 30 true of false items and was found to have high internal consistency in the current study (Cronbach's $\alpha = .89$), similar to previous research ($\alpha = .73$ - .89; Klorman et al., 1974). The Spider Phobia Questionnaire (SPQ; Klorman et al., 1974) was administered to examine fear of spiders and consists of 31 true or false items. In the present study, the SPQ showed high internal consistency (Cronbach's $\alpha = .89$), consistent with previous research ($\alpha = .83$ - .90; Klorman et al. 1974). A fear of rats questionnaire was adapted from the Fear of Spiders Questionnaire (FSQ) using established methodology (Botella et al. 2010) where the term spider is supplanted with the term rat. In the present study, the FSQ demonstrated high internal consistency (Cronbach's $\alpha = .90$), consistent with previous research ($\alpha = .92$; Szymanski and O'Donohue, 1995).

To measure the participants' presence, reality judgement and immersion in the virtual reality context, the Reality Judgement and Presence Questionnaire (Baños et al., 2000) was administered. The Reality Judgement and Presence Questionnaire (RJPQ; Baños et al., 2000) is measured on a 10-point likert scale format, ranging from 0 = *Not at all* to 10 = *Absolutely*. The Reality Judgement and Presence Questionnaire demonstrated high internal consistency for the total scale (Cronbach's α = .91), similar to previous research (Cronbach's α = .82; Baños et al., 2000). Additionally, The Depression Anxiety Stress Scales 21-item version (DASS-21; Lovibond and Lovibond, 1995) was administered to examine equivalency of depression, stress, and anxiety between the groups. The DASS-21 is measured on a 4-point severity scale, ranging from 0 = *Did not apply to me at all* to 3 = *Applied to me very much, or most of the time*. The DASS-21 showed high internal consistency (Cronbach's α = .91) in the present study, consistent with previous research (α = .84 - .91; Lovibond and Lovibond, 1995).

2.3 Procedure

Each participant completed the experiment individually and the duration of the experiment was approximately 50 minutes. Participants provided written consent to participate and the procedure of the experiment proper was explained to the participants using standardised instructions. The participants completed an online survey including demographic questions and the SPQ, the SNAQ, and the DASS-21. The ECG electrodes were placed on the participant's chest, specifically below the right clavicle, below the left clavicle and on the lower chest left of the umbilicus. The electrotactile stimulus electrodes were attached to the participant's dominant forearm. The US was set at an intensity the participant reported as "unpleasant, but not painful" and held at this set current throughout the experiment (Bandarian-Balooch et al., 2011; Krisch, Bandarian-Balooch and Neumann, 2018; Neumann and Kitlertsirivatana, 2010; Pischek-Simpson et al., 2009). Participants were

informed that they would be presented with virtual reality 360 degree footage of a rat, spider and snake in an office context.

A summary of the experimental phases and trial types for all groups can be seen in Table 5.1. The initial CS presented in each phase was counterbalanced across participants and the order of presentation of the CSs throughout the remaining trials was randomized, but the same CS was never presented more than two times in a row. The CSext and CSunext were accompanied with an electrotactile stimulus (US) in acquisition. The CS- was not accompanied by the US. In acquisition all participants were prompted to provide expectancy ratings on acquisition during Trials 1, 4, 7, and 10 for the CSext, the CSunext, and the CS-. The US was presented to all groups in acquisition for the CSext and CSunext and not for the CS-. In the reinstatement phase the UR group received three presentations of the US and the CR and MFS groups received one presentation of the CSunext. During the first extinction phase participants in all groups provided expectancy ratings during trials 1, 4, 5, 8, 9, and 12. All groups responded once to each of the three CSs during the test phases. The MFS group provided expectancy ratings during the second extinction phase during trials 1, 4, 5, 8, 9, and 12 (see Table 5.1). The Control group had a time gap equivalent to the duration of the Reinstatement phase in the MFS and UR groups before the first test and this involved viewing footage from the office context without featuring the spider, snake, or rat. The UR, CR, and Control groups had a time gap equivalent to the Extinction phase in the MFS group before the second test. The inter-trial intervals were randomised between 7.5 s, 10 s, and 12.5 s. At the end of the experiment proper the electrodes were removed and participants were requested to complete the RJPQ.

2.4 Design

The dependent variables were shock expectancy ratings and heart rate. The between-subjects independent variables for the initial phases of the experiment (Acquisition, first

extinction and first test) was Design with three levels (UR, CR, Control). The CR and MFS groups received the same acquisition, first extinction, and first test. Thus, the CR+MFS group in this set of analyses represents the combination of the two groups. For the second test phase, the between-subjects independent variable was Design with three levels (CR, MFS, Control). For all analyses the within subjects independent variables were CS with three levels (CSext, CSunext, CS-) and Trial with four levels (acquisition) or four to six levels (first and second extinction).

3. Results

3.1 Scoring and Statistical Analyses

Heart rate responses were scored from the time between successive R-peaks of the ECG using a threshold peak detector and examined for artefacts using a custom written program developed in Labview. Heart rates were calculated in successive 500 ms epochs prior to and during each CS presentation. The epochs contained in the 3 s immediately prior to the CS onset were used as the baseline from which the heart rates in the epochs 3 s following the CS were expressed as a change. The primary measure of conditioned heart rate responses was the peak heart rate acceleration during the 3 s following the CS presentation (Öhman, 1982).

One-way ANOVAs were conducted to check for differences between the groups for scores on the DASS-21 (M = 13.67, SD = 10.30), SPQ (M = 11.09, SD = 6.20), FSQ (M = 5.5, SD = 4.66), SNAQ (M = 9.68, SD = 6.45), RJPQ (M = 103.05, SD = 32.38), shock level (M = 8.00 SD = 1.54), age (M = 22.22, SD = 6.36). No significant differences between the groups were found for any measure, all $Fs < .010$, $p > .05$. A chi square analysis confirmed that gender distribution did not differ across the groups for either the expectancy data, χ^2 (3) = 2.16, p = .54 or heart rate data, χ^2 (3) = 0.82, p = .85.

Mixed factorial ANOVAs were conducted for the expectancy ratings and heart-rate change responses. The between-subjects independent variable for the initial set of analyses (acquisition, first extinction and first test) was Design with three levels (UR, CR, Control). The CR and MFS groups received the same acquisition, first extinction, and first test phase. Thus, the CR group in this set of analyses represented the combination of the two groups. For the second test, the between-subjects independent variable was Design with two levels (CR, MFS). For all analyses, the within-subjects independent variables were CS with three levels (CS_{ext}, $CS_{unext,}$ CS-). In addition, a second within-subjects independent variable of Trial with four levels (acquisition) or six levels (first extinction and second extinction) was used. Trial was not a factor for the test phase because there was only one trial in this phase.

The assumption of homogeneity of variance across groups was met. The assumptions of homogeneity of covariances, variables normally distributed and sphericity were violated for the expectancy ratings. A square root transformation was applied to the conditioned heart rate responses to normalise the distributions. Huynh-Feldt corrections were applied to adjust the degrees of freedom for the violation of sphericity.

3.2 Expectancy of Shock

Figure 5.1 shows the participants' expectancy ratings for all experimental phases in the UR, CR, MFS, and Control groups. In acquisition, participants learned differential shock expectancy. During the first extinction phase, expectancy of shock for the CSextinguished was extinguished. Reinstatement of shock expectancy was found for the CSextinguished and the CSunextinguished in the CR and UR groups and not in the Control group at the first test. Reinstatement was attenuated through extinction to the CSunextinguished for the MFS group at the second test.

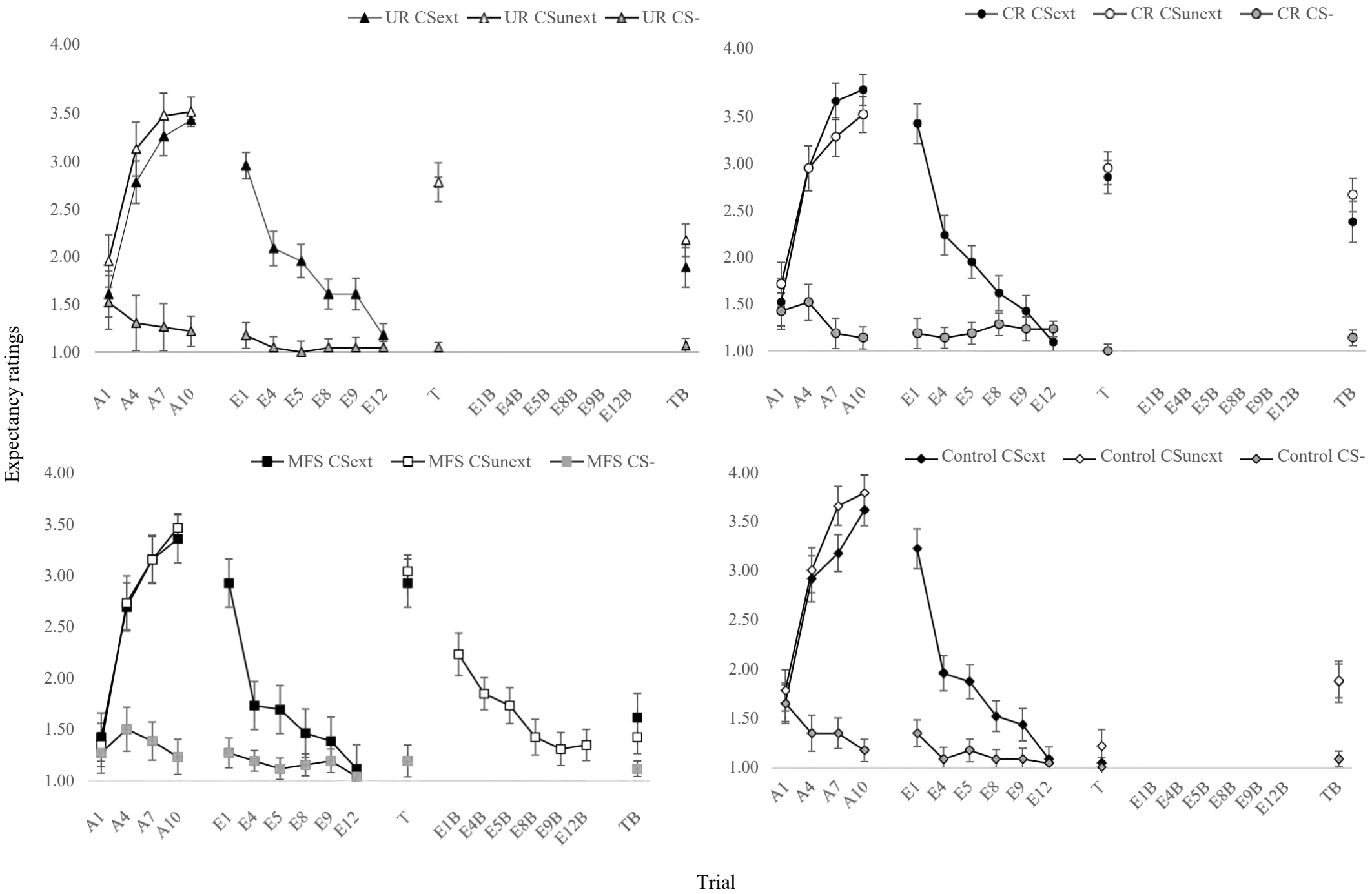


Figure 5.1. Mean shock expectancy ratings across acquisition, first extinction, first test, second extinction, and second test phases for the UR (n = 23; Male = 5;

Female = 18), CR (*n* = 21; Male = 7; Female = 14), MFS (*n* = 26; Male = 9; Female = 17), and Control (*n* = 23; Male = 8; Female = 15). Error bars represent the standard error of the mean**.**

3.2.1 Acquisition phase.

To investigate whether participants learned to expect the shock following the CSext and CSunext but not following the CS-, a 4 × 3 × 4 (Design × CS × Trial) mixed factorial ANOVA was conducted. The analyses revealed a significant CS × Trial interaction, $F(5.30, 471.81) = 64.81$, $p < .001$, $\eta_p^2 = .42$, a significant main effect of CS, $F(1.68, 149.48) = 221.43$, $p < .001$, $\eta_p^2 = .71$, and a significant main effect of Trial, $F(2.57, 229.03) = 118.31$, $p < .001$, $\eta_p^2 = .57$. Planned comparisons were employed by conducting multiple *t*-tests to investigate the significant two-way interaction by comparing the CSext, CSunext and CS- separately at each level of Trial. Shock expectancy ratings were significantly higher for the CSext and CSunext than the CS- towards the end of the acquisition phase on trials, 4, 7 and 10, all *t*s > 8.8, *p*s < .001, *d*s > 1.74. Thus, participants successfully learned to expect the shock following the CSext and CSunext but not after the CS- by trial 4 of acquisition.

3.2.2 Extinction phase.

To investigate differential expectancy of the CSs during extinction**,** a 4 × 2 × 6 (Design × CS × Trial) mixed factorial ANOVA was conducted, with the CS factor composed of the CSext and CS-. A significant CS × Trial interaction was revealed, $F(3.33, 296.17) = 83.15$, $p < .001$, $\eta_p^2 = .48$, as well as a significant main effect of CS, $F(1, 89) = 136.84$, $p < .001$, $\eta_p^2 = .61$, and a significant main effect of Trial, $F(3.19, 283.61) = 8.44$, $p < .001$, $\eta_p^2 = .50$. Multiple planned *t*-tests were conducted to compare the first extinction trial and final extinction trials for the CSext, demonstrating a significant decline of expectancy of shock ratings for the CSext towards the end of extinction phase trials , 5, 8, 9, 12, all *t*s > 4.62, $p < .001$, $d > 0.91$. In comparing the CSext and CS- there were no significant differences on the last extinction trials, all *t*s < 0.62, *p*s > .05, showing successful extinction of the conditioned responses.

3.2.3 Last extinction trial to first test phase.

The first test of reinstatement compared the last extinction trial to the test trial by a 4 × 2 × 2 (Design × CS × Trial) mixed factorial ANOVA. The analyses revealed all significant main effects and interactions were subsumed under a significant Design × CS × Trial interaction, $F(3, 89) = 21.07$, $p < .001$, $\eta_p^2 = .42$, a significant CS × Trial interaction, $F(3, 89) = 176.81$, $p < .001$, $\eta_p^2 = .67$, a significant CS × Design interaction, $F(3, 89) = 20.44$, $p < .001$, $\eta_p^2 = .41$, a significant Design × Trial interaction, $F(3, 89) = 24.27$, $p < .001$, $\eta_p^2 = .45$, and significant main effect of CS, $F(1, 89) = 223.59$, $p < .001$, $\eta_p^2 = .72$, Design, $F(3, 89) = 23.67$, $p < .001$, $\eta_p^2 = .44$, and Trial, $F(1, 89) = 197.10$, $p < .001$, $\eta_p^2 = .69$. Multiple planned *t*-tests were conducted to further examine the significant three-way interaction by comparing the last extinction trial and test trial separately for the CSext and CS- for each group. There was a significant increase in expectancy ratings for the CSext from the last extinction trial to the test trial for the CR group, $t(102) = 8.94$, $p < .001$, $d = 1.77$, and UR group, $t(102) = 9.37$, $p < .001$, $d = 1.85$. For the Control group there were no significant differences for the CSext, from the last extinction trial to the test trial. Thus, the results demonstrated that reinstatement of shock expectancy occurred for the CR and UR groups and not for the control group. No significant differences were found for the CS- from the last extinction trial to the first test trial for the CR, UR, and Control groups, all ts < 0.12, ps > .05.

3.2.4 Test phase one.

To further test for reinstatement, a 3 × 3 (Design × CS) mixed factorial ANOVA was conducted and a Design × CS interaction was revealed, $F(1.44, 128.24) = 20.62$, $p < .001$, $\eta_p^2 = .41$. A significant main effect of CS was also found, $F(4.32, 128.24) = 222.57$, $p < .001$, $\eta_p^2 = .71$. Planned comparisons were used to address the hypotheses and the significant interaction was examined using *t* tests comparing the CSext, CSunext, and CS- separately for each group. For the UR group, significantly higher expectancy ratings were found for the CSext than for CS-, $t(102) = 9.77$, $p < .001$, $d = 1.97$, and for the CSunext

compared to the CS-, $t(102) = 9.94$, $p < .001$, $d = 1.97$. For the CR group significantly higher expectancy ratings were found for the CSext than for CS-, $t(102) = 9.93$, $p < .001$, $d = 1.97$, and for the CSunext compared to the CS-, $t(102) = 10.67$, $p < .001$, $d = 2.11$. Expectancy ratings did not significantly differ between the CSext and CSunext for the CR or UR groups. Thus, confirming that unconditional and conditional reinstatement occurred for the experimental groups. For the Control group, the CSext, CSunext and the CS- did not significantly differ on the test trial, all ts < 0.24, ps > .05, confirming that reinstatement did not occur for the control group.

3.2.5 Extinction phase two.

A repeated measures ANOVA was conducted to examine if extinction of the CSunext occurred in extinction phase two for the MFS group. Expectancy ratings to the CSunext stimulus across the six extinction trials was used in this analysis. A significant effect was found, $F(1.00, 25.00) = 28.33$, $p < .001$, $\eta_p^2 = .53$. Further analyses confirmed a significant decline of expectancy of shock ratings was found for the CSunext towards the end of extinction trials 8, 9, 12, all ts > 4.21, ps < .001, ds > 1.70. Thus, showing successful extinction of the conditioned response.

3.2.6 Test phase two.

To examine if reinstatement was attenuated in the MFS group compared to the CR group a 2 × 3 (Design × CS) mixed factorial ANOVA was conducted. A significant Design × CS interaction, $F(5.73, 169.83) = 3.85$, $p = 0.002$, ηp2 = .12, and significant main effects of CS, $F(1.91, 169.83) = 53.54$, $p < .001$, $\eta p^2 = .38$, and Design, $F(3, 89) = 5.98$, $p < .001$, $\eta p^2 = .17$, were found. Planned

comparisons were used to address the hypotheses and the predicted interaction was examined using t-tests comparing the CSext, CSunext, and CS- separately for each group. The MFS group had no significant differences for the CSext, CSunext and CS-, all ts < 1.44, all ps >

.05, and confirmed the hypothesis that reinstatement was attenuated through extinction to the CSunextinguished. The CR group the CSext and CSunext than for the CS-, *t*s > 3.18, all *p*s < .05, all *d*s > 1.27, indicating attenuation of reinstatement of fear did not occur in the CR group.

3.3 Heart Rate Change

The participants' conditioned heart rate responses for all experimental phases in the UR, CR, MFS and Control groups in shown in Figure 5.2. Consistent with the shock expectancy results, acquisition of conditioned heart rate responses occurred. In the first extinction phase, conditioned heart rate responses for the CSextinguished were extinguished. In the first test phase, reinstatement of conditioned heart rate responses occurred for the CSextinguished and the CSunextinguished in the CR and UR groups and not in the Control group. Reinstatement of fear was attenuated through extinction to the CSunextinguished at the second test.

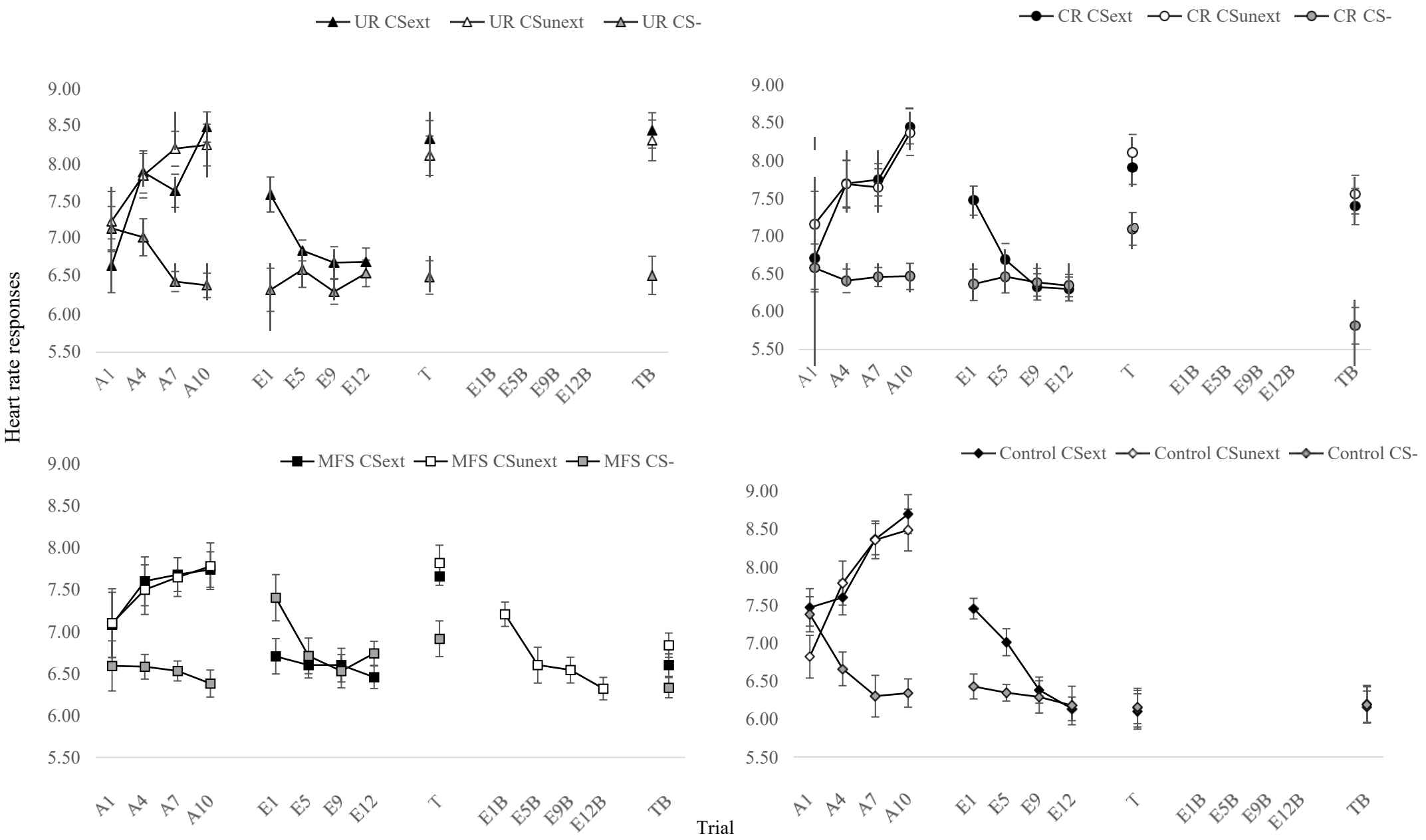


Figure 5.2. Heart rate responses across acquisition, first extinction, first test, second extinction and second test phases for the UR (n = 18; Male = 5; Female = 13), CR (n = 19; Male = 6; Female = 14), MFS (n = 17; Male = 7; Female = 10) and Control (n = 19; Male = 7; Female = 12) groups.Error bars represent the standard error of the mean.

3.3.1 Acquisition phase.

A 4 × 3 × 4 (Design × CS × Trial) mixed factorial ANOVA for heart rate change revealed a significant CS × Trial interaction, $F(6, 336) = 9.10$, $p < .001$, $\eta_p^2 = .14$, a significant main effect of CS, $F(2, 112) = 44.37$, $p < .001$, $\eta_p^2 = .44$, and a significant main effect of Trial, $F(3, 168) = 9.29$, $p < .001$, $\eta_p^2 = .14$. Planned comparisons compared the CSext, CSunext, and CS- separately at each level of Trial. Heart rate change was significantly more positive for the CSext and CSunext than the CS- towards the end of the acquisition phase trials, 4, 7 and 10, all *t*s > 5.92, *p*s < .001, *d*s > 6.83, thus confirming acquisition of conditioned heart rate responses.

3.3.2 Extinction phase.

A 4 × 2 × 4 (Design × CS × Trial) mixed factorial ANOVA showed a significant CS × Trial interaction, $F(3.00, 177) = 8.88$, $p < .001$, $\eta_p^2 = .13$, a significant main effect of CS, $F(1.00,59.00) = 17.52$, $p < .001$, $\eta_p^2 = .23$, and a significant main effect of Trial, $F(3.00, 177) = 9.82$, $p < .001$, $\eta_p^2 = .14$. Planned comparisons showed a significant decrease of heart rate change scores for the CSext across the extinction trials 1, 5, 9, 12, all *t*s > 4.73, $p < .001$, $d > 5.47$. No significant differences in heart rate change were found for the CS- across the extinction trials, *t*s < .05, *p*s > .05, or between the CSext and CS- on the last extinction trials 9 and 12, all *t*s < .08, *p*s > .05.

3.3.3 Last extinction trial to first test phase.

A 3 × 2 × 2 (Design × CS × Trial) mixed factorial ANOVA was conducted as the first test of reinstatement. Significant main effects and interactions were subsumed under a significant Design × CS × Trial interaction, $F(3.00, 65.00) = 3.85$, $p < .01$, $\eta_p^2 = .15$. Specifically, a significant CS × Trial interaction, $F(3.00, 65.00) = 23.13$, $p < .001$, $\eta_p^2 = .26$, a significant Design × Trial interaction, $F(3.00, 65.00) = = 7.03$, $p < .001$, $\eta_p^2 = .25$, and significant main effects of CS, $F(1.00, 65.00) = 33.84$, $p < .001$, $\eta_p^2 = .34$, Design, $F(1.00,$

65.00) = 10.53, $p < .001$, $\eta_p^2 = .34$, and Trial, $F(1.00, 65.00) = 43.37$, $p < .001$, $\eta_p^2 = .40$. Planned t-tests compared the last extinction trial and test trial separately for the CSext and CS- for each group. There was a significant increase for the heart rate change responses for the CSext from the last extinction trial to the test trial for the CR group, $t(65) = 4.26$, $p < .001$, $d = 1.06$, and UR group, $t(65) = 3.37$, $p < .001$, $d = .84$. For the Control group there were no significant differences for the CSext, from the last extinction trial to the test trial. No significant differences were found for the CS- from the last extinction trial to the first test trial for the CR, UR, and Control groups, all ts < 0.91, ps > .05. Overall the results confirmed reinstatement for the experimental groups and not the Control group.

3.3.4 Test phase one.

To further test reinstatement, a 3 × 2 (Design × CS) mixed factorial ANOVA was conducted. A Design × CS interaction, $F(4.00, 96.00) = 2.63$, $p < .05$, $\eta_p^2 = .10$, and a significant main effect of CS, $F(2.00, 96.00) = 9\ .11$, $p < .001$, $\eta_p^2 = .16$, was found. Planned comparisons showed that in the UR group, heart rate was higher for the CSext than for the CS-, $t(68) = 3.31$, $p = .002$, $d = 0.80$, and higher for the CSunext than for the CS-, $t(68) = 2.94$, $p = .005$, $d = 0.71$. For the CR group, HR change was more positive for the CSext than for the CS-, $t(68) = 2.71$, $p < .001$, $d = .65$, and for the CSunext than for the CS-, $t(68) = 3.72$, $p < .001$, $d = .90$. Mean heart rate change did not significantly differ between the CSext and CSunext for the CR or UR groups. The findings for heart rate change confirmed that unconditional and conditional reinstatement occurred for the experimental groups. For the Control group, the CSext, CSunext and the CS- heart rate change did not significantly differ on the test trial, all ts < 0.07, ps > .05, demonstrating that reinstatement did not occur in the control group.

3.3.5 Extinction phase two.

To examine whether extinction of the CSunext occurred for the MFS group, a repeated measures ANOVA. A significant effect of Trial was found, $F(2.11, 48.00) = 5.99$, $p < .001$, $\eta_p^2 = .27$, and multiple planned comparisons were conducted to compare the first extinction trial and final extinction trials for the CSunext. A significant decrease of mean heart rate change was found for the CSunext towards the end of extinction trials 5, 9, 12, all ts > 3.98, ps < .001, ds > 0.97.

3.3.6 Test phase two.

To determine whether reinstatement was attenuated in the MFS group compared to the CR group a 2 × 3 (Design × CS) mixed factorial ANOVA was conducted. A significant Design × CS interaction, $F(1.67, 53.33) = 7.78$, $p = .002$, $\eta_p^2 = .20$, and a significant main effect of CS, $F(1.67, 53.33) = 20.78$, $p < .001$, $\eta_p^2 = .39$, were revealed. For the MFS group, there were no significant differences in the heart rate change scores for the CSunext, CSext, and CS-, all ts < 1.64, all ps > .05, all ds < .45, demonstrating attenuation of the reinstatement of fear responses. For the CR group there were significantly higher heart rate change scores for the CSunext and the CSext than for the CS-, all ts > 5.70, all ps < .05, all ds > 1.57, indicating that attenuation of reinstatement of fear did not occur.

4. Discussion

The current study examined whether reinstatement of fear can be triggered by an excitatory CS that did not undergo extinction treatment and whether this reinstatement would be reduced by extinction to the excitatory CS, in a human non-clinical sample. Taken together, the shock expectancy ratings and conditioned heart rate responses indicate that reinstatement of fear can be triggered by an unextinguished CS and subsequent extinction of this unextinguished CS can attenuate reinstatement. The hypothesis that shock expectancy and conditioned heart rate responses would be larger in the reinstatement groups (UR, CR, MFS) than in the Control group in the first test phase was confirmed. As predicted, no

significant differences in the magnitude of the reinstatement effect were found between the CR and UR groups in the first test phase, indicating the equivalence of conditional reinstatement to traditional unconditional reinstatement. Taken together, the results showed that conditioned fear can be reinstated by an excitatory CS (i.e., the unextinguished CS) in a non-clinical human sample.

The results are consistent with previous findings by Halladay et al. (2012) that an unextinguished CS can trigger reinstatement to an extinguished CS in rats. The current findings are similar to previous studies demonstrating reinstatement by presenting the same aversive US in the acquisition and reinstatement phases (Culver et al., 2015; Dirikx et al., 2007; Dunsmoor et al., 2014; Glotzbach-Schoon et al., 2015; Haaker et al., 2014; Kattoor et al., 2012; Kull et al., 2012; LaBar and Phelps, 2005; Mertens et al., 2019; Neumann et al., 2012; Norrholm et al., 2006; Schiller et al., 2008), or after presentation of a different US in the reinstatement phase (Rescorla and Heth, 1975). Halladay et al. (2012) proposed several models that can explain conditional reinstatement. One particular model suggests that in extinction the CS presentations without the US may contribute to this context becoming a "negative occasion setter" that modifies the ability of the CS to predict the US (Bouton, 1993; Brooks and Bouton, 1993; Halladay et al., 2012; Holland and Lamare, 1984; Holland, 1989; Schmajuk and Holland, 1998). In accounting for conditional reinstatement, it has been suggested that encountering the CSunext in the reinstatement phase prevents the CSunext from continuing to be a negative occasion setter for the extinguished CS (Bouton and Swartzentruber, 1986; Halladay et al. 2012). Bouton (1993, 2002, 2004) proposed that reinstatement occurs due to re-exposure to the US promoting retrieval of the CS-US association. Halladay et al. (2012) applied Bouton's contextual memory model (Bouton, 1993) to account for conditional reinstatement by suggesting the CSunext reinstated responding to the CSextinguished by promoting the retrieval of the CS-US association in the

reinstatement phase. Taken together, the current finding and previous research (Halladay et al., 2012) suggests it may be exposure to the conditioned response that results in reinstatement. In interpreting this finding, it appears rats and humans retrieve associations not only by the re-experience of pain but also the re-experience of fear itself. Thus, if an individual encounters another fear such as fear of snakes this may serve to remind them of their initial fear of spiders and this initial fear may be reinstated.

The current finding that later experiences of fear can reinstate earlier fears has important theoretical, research and clinical practice implications. The current experiment has implications for laboratory research as it provides methodology that may increase the success of producing reinstatement effects. In utilising virtual reality, the current study was able to employ more ecologically valid feared stimuli through the use of 360 degree footage and this could be applied in future laboratory, clinical-analogue research and in clinical practice. Theoretically, the present findings implicate the importance of emotions in our understanding of fear conditioning, specifically how one fear can trigger other networks of fear, as opposed to reinstatement occurring due to the sensory properties of feared stimuli (Halladay et al., 2012; Rescorla and Heth, 1975). Furthermore, the present findings provide a more ethical and clinically relevant experimental paradigm that may be translated from laboratory research to clinical-analogue research. For example: instead of providing electric shocks or loud noises as aversive USs in the reinstatement phase, future research could employ feared stimuli as the CSext and CSunext. Future research could aim to investigate whether conditional reinstatement occurs due to the re-experience of the US or re-experience the conditioned response (fear) or a combination of both. To the authors knowledge the current study is the first to demonstrate the effects of conditional reinstatement in a human sample.

The hypothesis of whether reinstatement would be smaller for the MFS group compared to the CR group during the second test phase was also supported. This indicates

extinction to an unextinguished CS results in attenuation of conditional reinstatement. The present finding that extinction to different feared stimuli attenuated reinstatement is consistent with studies demonstrating multiple similar stimuli (i.e., different types of spiders; Rowe and Craske, 1998; Shiban et al., 2015) and multiple contexts (Bandarian-Balooch et al., 2015; Dunsmoor et al., 2014; Glautier et al., 2013; Shiban et al., 2013) attenuated renewal of fear. Similar theoretical frameworks have been used to explain the mechanisms and attenuation methods of renewal and reinstatement of fear (Bouton, 1993; Bouton and Bolles, 1979). Bouton's contextual memory model has also been used to explain attenuation of renewal by conducting extinction to multiple similar stimuli (e.g., Rowe and Craske, 2000) and multiple contexts (e.g., Bandarian-Balooch et al., 2015; Glautier et al., 2013). Specifically, by the overlap of contextual cues from the extinction context facilitating retrieval CS-noUS association and thus attenuating renewal of fear. In the current study extinction to the previously unextinguished CS in the MFS group may have increased the number of shared contextual cues from the second extinction phase and resulted in enhancing the CS-noUS association. Thus, the CS-noUS association would be more likely to be retrieved in the second test phase and can explain the attenuation of reinstatement.

Given that 75% of individuals with specific phobia have multiple fears (American Psychiatric Association, 2013; Curtis et al., 1998; LeBeau et al., 2010) and the likelihood of recovering from specific phobia is inversely related to the number of fears (Wittchen et al., 2003), the current findings could be valuable for clinicians using exposure to treat specific phobias. In translating the findings to clinical practice it suggests the importance of considering how a client's fear may be reinstated following successful exposure therapy and how exposure to their other fears may reduce the likelihood of reinstatement or relapse. Specifically, clinicians could conduct a comprehensive assessment of their clients' specific fears of objects or situations, even if the client only reports a primary fear. Clinicians could

also incorporate exposure to different feared stimuli to reduce reinstatement of fear. Clinical-analogue research designs can be utilized to test the effects of whether a secondary phobia (e.g., fear of spiders) can reinstate a primary or earlier developed phobia (e.g., fear of snakes) and whether conducting exposure treatment to the secondary phobia will attenuate the conditional reinstatement effect.

A limitation of the current study is the use of a non-clinical sample which limits the real-world generalisability of the current findings. This limitation was addressed partly by using CSs that are commonly the source of phobias in the population and by using an immersive VR environment. Future research should aim to extend the current research by examining conditional reinstatement and methods to attenuate conditional reinstatement using a clinical-analogue sample. While gender did not differ significantly across the groups in the current study, future research could investigate sex differences for reinstatement of fear. Specifically, in considering the evidence that women have a higher occurrence of animal phobias than men (Altemus et al., 2016; Donner and Lowry, 2013).

Overall, the current results provide the first evidence that an unextinguished CS can reinstate fear in a human sample and extends the evidence for the methodology of conditional reinstatement proposed by Halladay et al. (2012). Furthermore, the current findings highlight the importance of how secondary fears may elicit reinstatement of fear to previously extinguished fears and future research is required to examine whether this occurs in a clinical-analogue or clinical-analogue sample. Another important finding is that conducting extinction with different feared stimuli attenuated this reinstatement of fear as indexed by self-report, and physiological measures. Clinicians working with individuals with multiple fears or phobias could conduct exposure therapy with multiple different feared stimuli to reduce the likelihood of reinstatement of fear.

References

Abramowitz JS, Deacon BJ, Whiteside SP. (2012). *Exposure therapy for anxiety: Principles and practice*. Guilford Press.

Altemus et al. (2016). Sex differences in anxiety and depression clinical perspectives. *Frontiers in Neuroendocrinology*, *35*, 320-330. doi:10.1016/j.yfrne.2014.05.004

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.

Bandarian-Balooch S, & Neumann DL. (2011). Effects of multiple contexts and context similarity on the renewal of extinguished conditioned behaviour in an ABA design with humans. *Learning and Motivation*, **42**: 53-63. doi: 10.1016/j.lmot.2010.08.008

Bandarian-Balooch S, Neumann, DL, Boschen MJ. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry,* **47**: 138-144. doi: 10.1016/j.jbtep.2014.12.006.

Baños RM, Botella C, Garcia-Palacios A, Villa H, Perpiñá C, Alcaniz M. (2000). Presence and reality judgment in virtual environments: A unitary construct?. *CyberPsychology & Behavior*, **3,** 327-335.

Borstein PH, Knapp M. (1981). Self-control desensitization with a multi-phobic boy: A multiple baseline design. *Journal of Behavior Therapy and Experimental Psychiatry*, **12**: 281-285. doi: 10.1016/0005-7916(81)90059-8

Botella C, Bretón-López J, Quero S, Baños R, García-Palacios A. (2010). Treating cockroach phobia with augmented reality. *Behaviour Therapy*, **41**: 401-413. doi:10.1016/j.beth.2009.07.002

Bouton M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, **114**: 80-90. doi: 10.1037//0033-2909.114.1.80

Bouton ME. (2002). Context, ambiguity, and unlearning: Sources of relapse after behavioral extinction. *Biological Psychiatry,* **52**: 976-986. doi: 10.1016/S0006-3223(02)01546-9

Bouton ME. (2004). Context and behavioral processes in extinction. *Learning & Memory*, **11**: 485-494. doi: 10.1101/lm.78804

Bouton ME, Bolles RC. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, **10**: 445-466. doi: 10.1016/0023-9690(79)90057-2

Bouton ME and Swartzentruber D. (1986). Analysis of the associative and occasion-setting properties of contexts participating in a Pavlovian discrimination. *Journal Experimental. Psychology: Animal Behaviour Processes.* **12**: 333–350. Retrieved from: https://psycnet.apa.org/doiLanding?doi=10.1037%2F0097-7403.12.4.333

Brooks DC, Bouton ME. (1993). A retrieval cue for extinction attenuates spontaneous recovery. *Journal of Experimental Psychology: Animal Behavior Processes*, **19**(1): 77. Retrieved from: https://oce-ovid-com.libraryproxy.griffith.edu.au/article/00004783-199301000-00009/HTML

Bush J. (2008). Viability of virtual reality exposure therapy as a treatment alternative. *Computers in Human Behavior*, **24:** 1032-1040. doi: 10.1016/j.chb.2007.03.006

Culver NC, Vervliet B, Craske MG. (2015). Compound extinction: using the Rescorla–Wagner model to maximize exposure therapy effects for anxiety disorders. *Clinical Psychological Science*, **3**: 335-348. doi: 10.1177/2167702614542103

Dirikx T, Hermans D, Vansteenwegen D, Baeyens, F, Eelen P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, **38**: 237-251. doi: 10.1016/j.jbtep.2006.04.001

Donner & Lowry (2013). Sex differences in anxiety and emotional behavior. *Pflugers Arch*, *465*, 601–626. doi: 10.1007/s00424-013-1271-7

Dunsmoor JE, Ahs F, Zielinski DJ, LaBar KS. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, **113**: 157-164. doi: 10.1016/j.nlm.2014.02.010

Glotzbach-Schoon E, Andreatta M, Mühlberger A, Pauli P. (2015). Reinstatement of contextual anxiety in humans: Effects of state anxiety. *International Journal of Psychophysiology*, *98*, 557-566. doi: 10.1016/j.ijpsycho.2015.07.013

Haaker J, Golkar A, Hermans D. Lonsdorf TB. (2014). A review on human reinstatement studies: an overview and methodological challenges. *Learning & Memory*, **21**: 424-440. doi: 10.1101/lm.036053.114

Halladay LR, Zelikowsky M, Blair HT, Fanselow MS. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, **6**: 1-7. doi: 10.3389/fnbeh.2012.00018

Holland PC. (1989). Transfer of negative occasion setting and conditioned inhibition across conditioned and unconditioned stimuli. *J. Exp. Psychol. Anim. Behav. Process.,* **15**: 311–328. doi: 10.1037/0097-7403.15.4.311

Holland PC, Lamare J. (1984). Transfer of inhibition after serial and simultaneous feature negative discrimination training. *Learning and Motivation,* **15**: 219–243. doi: 10.1016/0023-9690(84)90020-1

Kattoor J, Gizewski ER, Kotsis V, Benson S, Gramsch C, Theysohn N, Maderwald S, Forsting M, Schedlowski M & Elsenbruch S. (2013). Fear conditioning in an abdominal pain model: neural responses during associative learning and extinction in healthy subjects. *PloS one*, **8**. doi: 10.1371/journal.pone.0051149

Kessler RC, Wang PS. (2008). The Descriptive Epidemiology of Commonly Occurring Mental Disorders in the United States. *Annual Review Public Health*, **29**: 115-129. doi: 10.1146/annurev.publhealth.29.020907.090847

Kim JH, Richardson R. (2007). A developmental dissociation in reinstatement of an extinguished fear response in rats. *Neurobiology of learning and memory*, **88**: 48-57. doi: 10.1016/j.nlm.2007.03.004

Klorman R, Weerts TC, Hastings JE, Melamed BG, Lang PJ. (1974). Psychometric description of some specific-fear questionnaires. *Behavior Therapy*, **5**: 401-409. doi:10.1016/S0005-7894(74)80008-0

Krisch KA, Bandarian-Balooch S, O'Donnell AW, Neumann DL. (2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. In Z. Hill (Ed.), *Virtual reality: Advances in research and applications* (pp. 85–126). Nova Science.

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2018). Effects of extended extinction and multiple extinction contexts on ABA renewal. *Learning and Motivation*, ***63***, 1-10. doi: 10.1016/j.lmot.2017.11.001

Kull S,Müller BH, Blechert J, Wilhelm FH, Michael T. (2012). Reinstatement of fear in humans: autonomic and experiential responses in a differential conditioning paradigm. *Acta Psychologica*, **140:** 43-49. doi: 10.1016/j.actpsy.2012.02.007

LaBar KS, Phelps EA. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, **119**: 677-686. doi: 10.1037/0735-7044.119.3.677.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and Anxiety*, **27**, 148-167.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and Anxiety*, *27*(2), 148-167. doi: 10.1002/da.20655

Liberman RP, Smith V. (1972). A multiple baseline study of systematic desensitization in a patient with multiple phobias. *Behavior Therapy*, **3**: 597-603. doi: 10.1016/S0005-7894(72)80009-1

Lonsdorf, E. V., Eberly, L. E., & Pusey, A. E. (2004). Sex differences in learning in chimpanzees. *Nature*, **428**, 715-716. doi: 10.1038/428715a

Lovibond PF, Lovibond SH. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*, **33**: 335-343. doi: 10.1016/0005-7967(94)00075-U

Mertens G, Leer A, van Dis EAM, Vermeer L, Steenhuizen A, van der Veen L, Engelhard IM. (2019). Secondary extinction reduces reinstatement of threat expectancy and conditioned skin conductance responses in human fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, **62**:103-111. doi: 10.1016/j.jbtep.2018.09.007

Neumann DL. (2007). The resistance of renewal to instructions that devalue the role of contextual cues in a conditioned suppression task with humans. *Learning and Motivation*, **38**, 105-127. doi: 10.1016/j.lmot.2006.11.002

Neumann DL, Kitlertsirivatana E. (2010). Exposure to a novel context after extinction causes a renewal of extinguished conditioned responses: Implications for the treatment of fear. *Behaviour Research and Therapy,* **48**: 565-570. doi:10.1016/j.brat.2010.03.002

Neumann D, Lipp O, McHugh M. (2012). The relationship between different measures of fear learning following tests for reinstatement and spontaneous recovery of extinguished conditioned fear. In G. Andrews and D.L. Neumann (Eds.), *Beyond the Lab: Applications of Cognitive Research in Memory and Learning,* (pp. 83-108). New York, U.S.A: Nova Science.

Neumann DL, Longbottom PL. (2008). The renewal of extinguished conditioned fear with fear-relevant and fear-irrelevant stimuli by a context change after extinction. *Behaviour Research and Therapy*, **46**: 188-206. doi:10.1016/j.brat.2007.12.004

Norrholm SD, Jovanovic T, Vervliet B, Myers KM, Davis M, Rothbaum BO, Duncan EJ. (2006). Conditioned fear extinction and reinstatement in a human fear-potentiated startle paradigm. *Learning & Memory*, **13**: 681-685. doi: 10.1101/lm.393906

Öhman A. (1982). *The orienting response during Pavlovian conditioning*. Department of Psychology, University of Uppsala.

Pavlov IP. (1927). Conditioned reflexes. London: Oxford University Press.

Pischek-Simpson, LK, Boschen, MJ, Neumann, DL, & Waters, AM. (2009). The development of an attentional bias for angry faces following Pavlovian fear conditioning. *Behaviour Research and Therapy, 47,* 322-330. doi:10.1016/j.brat.2009.01.007

Rachman, S. (1966). Studies in desensitization—III: Speed of generalization. *Behaviour Research and Therapy*, **4**: 7-15. Retrieved from: http://www.sciencedirect.com/science/article/pii/0005796766900386

Rachman S, Robinson S, Lopatka C. (1987). Is incomplete fear-reduction followed by a return of fear? *Behaviour Research and Therapy*, **25**: 67-69. doi:10.1016/0005-7967(87)90116-1

Rachman S, Whittal M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, **27**: 513-520. doi: 10.1016/0005-7967(89)90085-5

Rescorla RA, Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, **1**: 88. doi: 10.1037/0097-7403.1.1.88

Rose MP, McGlynn FD. (1997). Toward a standard experiment for studying post-treatment return of fear. *Journal of Anxiety Disorders*, **11**: 263-277.

Rowe MK, Craske MG. (1998). Effects of varied-stimulus exposure training on fear reduction and return of fear. *Behaviour Research and Therapy*, **36**: 719-734. doi: 10.1016/S0005-7967(97)10017-1

Schiller D, Cain CK, Curley NG, Schwartz, JS Stern SA, LeDoux JE, Phelps EA. (2008). Evidence for recovery of fear following immediate extinction in rats and humans. *Learning & Memory*, **15**: 394-402. doi: 10.1101/lm.909208

Sevenster, D., Beckers, T., & Kindt, M. (2012). Instructed extinction differentially affects the emotional and cognitive expression of associative fear memory. *Psychophysiology*, **49**, 1426-1435.

Shiban Y, Pauli P, Mühlberger A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, **51**: 68-74. doi: 10.1016/j.brat.2012.10.007

Shiban Y, Schelhorn I, Pauli P, Mühlberger A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, **71**: 45-53. doi: 10.1016/j.brat.2015.05.014

Schmajuk NA, Holland PC. (1998). *Occasion Setting: Associative Learning and Cognition in Animals.* Washington, DC: American Psychological Association.

Szymanski J, O'Donohue W. (1995). Fear of spiders' questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry*, **26**: 31-34. doi:10.1016/0005-7916(94)00072-T

Van Houtem CM, Laine ML, Boomsma DI, Ligthart L, Van Wijk AJ, De Jongh A. (2013). A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears. *Journal of Anxiety Disorders*, **27**: 379-388. doi:10.1016/j.janxdis.2013.04.007

Vasey MW, Harbaugh CN, Buffington AG, Jones CR, Fazio RH. (2012). Predicting return of fear following exposure therapy with an implicit measure of attitudes. *Behaviour Research and Therapy*, **50**: 767-774. doi: 10.1016/j.brat.2012.08.007

Vurbic D, Bouton ME. (2011). Secondary extinction in Pavlovian fear conditioning. *Learning & Behavior*, **39**: 202-211. doi: 10.3758/s13420-011-0017-7

Wittchen H.U., Lecrubier Y., Beesdo K., Nocon A. (2002) Relationships Among Anxiety Disorders: Patterns and Implications. In D. Nutt & J. Ballenger (Ed.), *Anxiety disorders,* (pp. 23-37). Oxford, UK: Blackwell Science Ltd.

Chapter 6: Preamble

In aiming to extend the previous findings in Chapter 5 to a fearful human sample, Chapter 6 presents a clinical-analogue experiment involving 50 participants with moderate to high fear of both spiders and rats. Chapter 6 examined whether exposure to a CS that has not undergone exposure-based treatment (i.e., an unextinguished CS; spider) can elicit and attenuate reinstatement of fear to another feared stimulus (i.e., an extinguished CS; rat).

STATEMENT OF CONTRIBUTION TO CO-AUTHORED PUBLISHED PAPER

This chapter includes a co-authored peer reviewed journal article that has been submitted for publication. The bibliographic details of the paper, including all authors are: Krisch K.A., Bandarian, S., & Neumann, D.L. (submitted). Reinstatement of fear: exposure treatment to multifarious stimuli for individuals with multiple animal fears.

The candidate was responsible for manuscript preparation including a review of the literature, design and development of the experiment protocol, data collection, analysis, writing the manuscript under supervision, and submitting the manuscript.

(Signed)_____(Date): 16/11/2021
Kirra Krisch

(Countersigned)_____(Date): 16/11/2021
Supervisor: Dr Siavash Bandarian

(Countersigned)_____(Date): 16/11/2021
Supervisor: Professor David Neumann

Chapter 6: Reinstatement of Fear: Exposure Treatment to Multifarious Stimuli for Individuals with Multiple Animal Fears

School of Applied Psychology, Griffith University

Kirra A. Krisch[1], Siavash Bandarian[1], & David L. Neumann[1]

[1]School of Applied Psychology Griffith University, Australia

Please direct correspondence to: Kirra Krisch, School of Applied Psychology, Griffith University (Gold Coast Campus), Mail: GRIFFITH UNIVERSITY QLD, Queensland, 4222, Australia, Kirra.Krisch@gmail.com, Telephone +61(0)7 567 880128.

Abstract

Background and Objectives

Reinstatement is a mechanism for the return of fear following exposure therapy for specific phobia and other anxiety disorders. Reinstatement in the context of multiple feared stimuli is poorly understood despite most individuals fearing more than one object/situation. The current study investigated whether exposure to a conditional stimulus (CS) that has not undergone extinction (i.e., an unextinguished CS; spider) can elicit and attenuate reinstatement of fear to another feared stimulus (i.e., an extinguished CS; rat).

Methods

Fifty individuals with moderate to high fear of both spiders and rats underwent virtual reality exposure treatment (VRET). The reinstatement and multiple phobic stimuli (MPS) groups received the unextinguished CS in the reinstatement phase and the control group did not. Furthermore, the MPS group received VRET for the unextinguished CS.

Results

Presentation of the unextinguished CS reinstated fear of a previously extinguished CS and VRET to the second feared CS attenuated this reinstatement of fear as measured by avoidance ratings, subjective units of distress, and heart rate change.

Limitations

The experimenter was not blind to the conditions and the same experimenter was used throughout all phases of the study.

Conclusions Clinicians should conduct a comprehensive assessment of feared objects/situations and provide exposure treatment for multiple different fears to reduce the likelihood of reinstatement in their clients.

Key words: Reinstatement of fear; specific phobias; multiple phobias; return of fear; exposure therapy; virtual reality exposure therapy

Introduction

Exposure therapy is an evidence-based treatment that involves gradually presenting the individual with the feared stimuli until the fear reduces to non-clinical levels. Exposure therapy can be conducted in vivo (i.e., with real life stimuli), virtual (i.e., with virtual reality simulated stimuli), and imaginal (i.e., with mental imagery). In vivo exposure therapy has been found to be the most effective treatment for specific phobia (Öst, 1989; Wolpe, 1968). Nonetheless, in vivo exposure therapy has been found to be one of the least implemented interventions in clinical settings (see Pittig et al., 2019). VRET is more acceptable to those with specific phobia than in vivo (Garcia-Palacios et al., 2001), more feasible (Krijn et al., 2004; Opris et al., 2012), and has been used to conduct extinction for multiple fears (Krisch et al., 2020). A problem with all forms of exposure therapy is that many individuals experience a return of fear following successful treatment (Abramowitz et al., 2012; Craske, 1999; Rachman, 1966, 1987; Rose & McGlynn, 1997; Vasey et al., 2012).

Classical conditioning research has demonstrated that reinstatement can be an underlying mechanism of return of fear (e.g., Bouton & Bolles, 1979; Dunsmoor et al., 2014; Mertens et al., 2019; Rescorla & Heth, 1975). Standard reinstatement of fear occurs when extinguished fear returns following re-exposure to the unconditional stimulus (US; Rescorla & Heth, 1975). Reinstatement of fear findings have been translated from animal (Bouton & Bolles, 1979; Gershman et al., 2013; Halladay et al., 2012; Kim & Richardson, 2007; Rescorla & Heth, 1975; Vurbic & Bouton, 2011), to non-phobic human participants (Dirikx et al. 2007; Dunsmoor et al., 2014; Hermans et al., 2005; LaBar & Phelps, 2005; Mertens et al., 2019; Zbozinek et al., 2015), and to limited clinical-analogue samples (Rachman & Whittal, 1989; Shiban et al., 2015). Ethical considerations may have interfered with the process of generalising laboratory-based findings to clinical studies, including the challenges of exposing an individual to an ecologically valid aversive US (e.g., exposing participants to the

pain of a bite to reinstate their fear of spiders). The lack of clinical-analogue and clinical studies investigating the reinstatement effect is problematic because it limits our understanding of how the reinstatement effect is elicited and attenuated in people who suffer from phobias.

A further limit to the clinical understanding of reinstatement is that few studies have considered individuals with multiple fears. The majority of individuals who have a specific phobia will have multiple fears of objects and/or situations (Burstein et al., 2003; Curtis et al., 1998; LeBeau et al., 2010; Wittchen et al., 2003). Multiple phobias have been linked to higher rates of severity, impairment, and comorbidity with other anxiety disorders compared to single phobias (Burstein et al., 2012; Wardenar et al., 2017). A small number of clinical-analogue and clinical studies with humans have shown that exposure treatment to one fear does not generalise to other untreated fears (Burstein et al., 2003; Farrell et al., 2020; Liberman & Smith, 1972; Öst, 1989).

Rachman and Whittal (1989) investigated reinstatement of fear with a sample of spider and snake phobics using an electrotactile shock similar to that used in laboratory-based research and a reinstatement effect was not found. The authors proposed that the null effect was due to the US not being sufficiently aversive to reinstate fear with a clinical sample. The ethical issues of eliciting reinstatement and the aversiveness and ecological validity of the US may explain the lack of reinstatement research with clinical-analogue samples. Further research is necessary to enhance the real world generalisability of the findings and to develop novel interventions for clinical settings.

Previous research by Halladay et al. (2012) and Rescorla and Heth (1975; Exp 2) with rats indicated that an unextinguished CS can reinstate the conditioned response to an extinguished CS. The approach could be translated to human clinical-analogue and clinical samples. Standard reinstatement has been found to occur even when the reinstating stimulus

differs from the US employed in acquisition in both rats (e.g., Rescorla & Heth, 1975) and humans (e.g., Sokol & Lovibond, 2012). Halladay et al.'s (2012) findings demonstrated that conditional reinstatement (i.e., exposing rats to an unextinguished CS tone) reinstated their initial fear to the extinguished CS (i.e., light). In translating these findings with rats to non-phobic human samples, Krisch et al. (2020) found that reinstatement can be triggered by a second fear-eliciting CS that has not undergone extinction (i.e., unextinguished CS) and subsequent extinction of this second fear can attenuate this conditional reinstatement.

These studies demonstrate that exposure to the conditioned response of fear alone, even in the absence of re-experiencing the US, results in reinstatement for rats and non-fearful human participants. The clinical implications are important because they suggest that reinstatement of fear could occur due to fear provoking events. For example, an individual who has overcome their fear of rats and then subsequently experiences a strong fear reaction to spiders may have their fear of rats reinstated. Furthermore, the previous findings indicate that untreated fears may be a risk factor for reinstatement of fear (Halladay et al., 2012; Krisch et al., 2020; Rescorla & Heth, 1975). However, further studies using clinical-analogue and clinical samples are necessary to provide evidence for whether conditional reinstatement occurs in these populations and how it can be attenuated.

While there are limited studies investigating conditional reinstatement of fear and how to attenuate this type of reinstatement (Krisch et al., 2020), parallels could be drawn between attenuating standard reinstatement of fear and conditional reinstatement of fear. Gradual extinction, involving progressively decreasing the intensity of the US (Shiban et al., 2015) and conducting exposure in multiple contexts (Dunsmoor et al., 2014) have been found to attenuate reinstatement of fear. However, the reinstating stimulus was an electric shock in these studies and such an approach is not as ecologically valid for individuals fearing spiders. Using an alternative approach, Krisch et al. (2020) found that conducting extinction with

multifarious stimuli (i.e., multiple different stimuli) attenuated conditional reinstatement of fear as measured by self-report and heart rate.

Several theoretical models could account for the process of eliciting and attenuating conditional reinstatement. Bouton and colleagues (Bouton, 1984; Bouton & Bolles, 1979; Bouton et al., 2021) proposed that in a standard reinstatement procedure, the CS-US association is triggered in fear acquisition and is not unlearned in extinction. Instead, a CS-noUS association is activated during extinction. Reinstatement is conceptualised in this model as being caused by contextual cues in the background triggering the CS-US association during US re-exposure. Previous findings of conditional reinstatement (e.g., Halladay et al., 2012; Krisch et al., 2020) could also be attributed to the contextual cues of presenting the unextinguished CS eliciting the CS-US association by acting as a reminder to the acquisition context. Despite this interpretation, the context alone has been not been found to elicit reinstatement of fear (Halladay et al., 2012; Krisch et al., 2020) and stimulating the amygdala in rats while presenting a novel stimuli has enhanced reinstatement of fear (Kellett & Kokkinidis, 2004).

An alternative explanation has suggested that the affective properties and stimulus valence of the reinstating stimulus functions to reinstate fear in humans (Zbozinek et al., 2015). The valence-reinstatement theory (Dirikx, et al., 2004; Dirikx, et al., 2007; Hermans, et al., 2005) may account for conditional reinstatement due to the unextinguished CS having negative valence and the physiological arousal level in reinstatement serving as a reminder of the valence from the acquisition context and in turn activating the CS-US association. There are several theoretical accounts emphasising the context and affective properties of the stimuli that provide insight into conditional reinstatement.

The current study aimed to extend previous research (Halladay et al., 2012; Krisch et al., 2020) to examine whether an unextinguished CS will reinstate fear and whether exposure

to this unextinguished CS can reduce reinstatement to the primary fear. The sample consisted of individuals with moderate to high fear of both a spider and rat. The participants were randomly assigned to either a Multiple phobic stimuli (MPS) group, Reinstatement group, or Control group. The MPS and Reinstatement groups underwent a conditional reinstatement procedure and the control group did not. The MPS group received VRET to both the CSextinguished and CSunextinguished while the other groups only received VRET to the CSextinguished. All participants provided avoidance ratings, subjective units of distress, and measures of heart rate to measure fear (e.g., Bandarian-Balooch et al., 2015; Mühlberger et al., 2001). It was hypothesised that reinstatement of fear would be found for the Reinstatement group but not in the Control group. It was also predicted that reinstatement of fear will be attenuated for the MPS group compared to the Reinstatement group.

1. Materials and Methods

1.1 Participants.

The total sample was 84 individuals. However, 33 participants had to be excluded from the study due to not being able to participate in either of the follow up sessions due to restrictions following the outbreak of COVID-19. One participant was excluded at the screening stage due to not meeting criteria for moderate to high fear of spiders. The final sample included 50 individuals (27 females and 23 males; age: M = 23.06 years; SD = 7.01) with a moderate to high fear of both spiders and rats as indicated by scores on the Fear of Spiders Questionnaire (FSQ; M = 81.94; SD = 22.24) and Fear of Rats Questionnaire (the FSQ supplanted with the term rat; FRQ; M = 77.37; SD = 19.82) being in the moderate to high range (Lindner et al., 2020; Szymanski & O'Donohue, 1995).

Recruitment involved locally posted advertisements and a website where undergraduate psychology students could elect to sign up. Participants signed up due to receiving treatment benefits and/or in exchange for partial course credit. Participants were

randomly assigned to either a Reinstatement group (n = 18), a MPS group (n = 17), or a Control group (n = 15; see Table 6.1). Shiban et al. (2015) revealed a partial-eta squared effect size of $\eta_p^2 = 0.52$, for the startle response at the reinstatement test, using 15 participants per group. In the current study, to achieve a power of .90 with a α two-tailed = .05, a minimum of 15 participants per group was required.

1.2 Therapist

The experimenter and therapist was the principal author and is a registered psychologist with several years of experience using exposure therapy to treat a range of anxiety disorders. The principal author conducted this experiment as part of the research component of her clinical psychology PhD. The second author whom is a clinical psychologist with extensive experience with exposure therapy also provided supervision to the experimenter. A standardized treatment manual was developed and adhered to for all participants.

Table 6.1.

The Conditional Stimuli and Number of Sessions across the Reinstatement, Multiple Phobic Stimulus (MPS) and Control Groups

Group	Sessions						
	Day 1			Day 14			
	Pre-test	Exposure 1	Post-test 1	Reinstatement	Follow-up 1	Exposure 2 Post-test 2	Follow-up 2
Reinstatement							
n = 9	CSext (spider)	CSext (spider)	CSext (spider)	CSunext (rat)	CSext (spider)	-	CSext (spider) CSunext (rat)
n = 9	CSext (rat)	CSext (rat)	CSext (rat)	CSunext (spider)	CSext (rat)	-	CSext (rat) CSunext(spider)
MPS							
n = 8	CSext (spider)	CSext (spider)	CSext (spider)	CSunext (rat)	CSext (spider)	CSunext (rat)	CSext (spider) CSunext (rat)
n = 9	CSext (rat)	CSext (rat)	CSext (rat)	CSunext (spider)	CSext (rat)	CSunext (spider)	CSext (rat) CSunext(spider)
Control							
n = 8	CSext (spider)	CSext (spider)	CSext (spider)	-	CSext (spider)	-	CSext (spider) CSunext (rat)
n = 7	CSext (rat)	CSext (rat)	CSext (rat)	-	CSext (rat)	-	CSext (rat) CSunext(spider)

Note. CSext reflects the extinguished CS, and CSunext reflects the unextinguished CS.

1.3 Apparatus.

The CS_{ext} and CS_{unext} were a golden orb weaver (*Nephila edulis*) and a fancy rat (*Rattus norvegicus domestica*). The order and nature of the stimuli were counterbalanced. For the first exposure session in each group, half the participants were exposed to the rat and half the participants were exposed to the spider (see Table 6.1). An Oculus Virtual reality headset and Skybox software were used to present the 360-degree virtual reality footage of the spider and rat in an office context. The Behavioural Avoidance Task (BAT) was used to measure the participant's avoidance of the spider and rat (see Table 6.2). Pilot testing was conducted to determine the specific steps for the BAT. A corresponding virtual reality 8-step hierarchy was recorded using the Samsung Gear 360º video camera from a first person perspective and separate videos represented each step. The BAT was scored in accordance with previous research (Bandarian-Balooch et al., 2015), specifically each step the participant completed resulted in subtracting an avoidance point. A higher score on the BAT reflects greater avoidance. During the BAT, subjective units of distress (SUDS) ratings (i.e., 0-100 scale) were recorded to measure self-reported fear and higher SUDS ratings indicated higher fear of the spider or rat, consistent with previous research (e.g., Krijn et al., 2004; Michaliszyn et al., 2010). A Polar V800 Watch was used to measure heart rate change. Previous research provides evidence for its validity as a research tool and the heart rate change parameters have been found to be consistent with ECG recordings (Giles et al., 2016).

Table 6.2.

The 8-step Exposure Hierarchy and Corresponding Virtual Reality and In Vivo BAT

BAT Scores	Step	Action Required at Each Step
8	1	Stand 2 metres away from the spider/rat in a closed container.
7	2	Stand 1 metre away from the spider/rat in a closed container.
6	3	Focus on the spider/rat from 50cm away in a closed container.
5	4	Place your gloved hands on the glass of the closed container.
4	5	Place your gloved hands inside the top of the open container.
3	6	Place your gloved hands inside the container 10cm away from the spider/rat.
2	7	Place a short stick next to a spider/rat inside the container.
1	8	Touch/interact with a spider/rat with a short stick inside the container.

Note. BAT = Behavioural Avoidance Task., higher scores indicate higher avoidance of the spider/rat.

1.4. Description measures.

The FSQ and FRQ (FSQ supplanted with the term rat) were administered to assess for fears of spiders and rats (Szymanski & O'Donohue, 1995). The FSQ and FRQ includes 18 items, with a Likert response format score 1 = *Not at all* to 7 = *very much*, with the total score range of 18–126. The FSQ and FRQ demonstrated high internal consistency respectively (Cronbach's α = .89 and Cronbach's α = .90), consistent with previous research (α = .92; Szymanski & O'Donohue, 1995). The Depression Anxiety Stress Scales 21-item version (DASS-21; Lovibond & Lovibond, 1995) was administered to examine equivalency of depression, stress, and anxiety between the groups. The DASS-21 is measured on a 4-point severity scale, ranging from 0 = *Did not apply to me at all* to 3 = *Applied to me very much, or most of the time*. The DASS-21 showed high internal consistency (Cronbach's α = .92) in the present study and this is consistent with Lovibond & Lovibond (1995; α = .84 - .91).

To determine the participants' presence and immersion in the virtual reality context, the Reality Judgement and Presence Questionnaire (RJPQ; Baños et al., 2000) was used. The RJPQ (Baños et al., 2000) is measured on a 10-point Likert scale format,

ranging from 0 = *Not at all* to 10 = *Absolutely*. In accordance with previous research the overall RJPQ has good internal consistency (Cronbach's α = .82; Baños et al., 2000) but internal consistency has not been reported for the subscales. In the present study, for the Reality judgement scale Cronbach's α = .88, for Internal/External correspondence subscale Cronbach's α = .85, and for the Attention/Absorption subscale Cronbach's α = .82.

1.4 Procedure.

The experimental procedure consisted of three sessions for all groups and a different number of phases for each group (refer to Table 6.1). All participants provided informed consent prior to participation. The participants were instructed to attach the Polar heart rate sensor across their sternum. During the pre-treatment assessment, an online survey was administered which included demographic questions, the FSQ, the FRQ (Szymanski & O'Donohue, 1995), the DASS-21 (Lovibond & Lovibond, 1995), and the RJPQ (Baños et al., 2000). During the survey, a 5-minute acclimatisation and 5-minute HR baseline were recorded. Subsequently, the SUDS scale was explained to the participants. Participants were informed that during the sessions they would be asked "How fearful are you now?" and participants were instructed to respond with numbers indicated their level of fear by verbally responding with any number from 0 – 100. To further screen participants for a moderate to high level fear of spiders and rats, participants completed an in vivo BAT involving selecting which step on the hierarchy they would be willing to complete. Participants were requested to provide predicted SUDS ratings if they completed step 8 of the BAT with both animals. The VRET session was completed once the final step of the VRET exposure hierarchies was concluded.

VRET has been conducted in previous return of fear studies for specific phobia (e.g., Botella et al., 2010; Emmelkamp et al., 2002; Shiban et al., 2013; Shiban et al., 2015), but the present protocol involved more ecologically valid stimuli by the use of 360 degree footage of real life stimuli. Psychoeducation on exposure therapy and VRET

was provided to each participant. Participants were informed they would see 360 degree footage of the same spider and/or rat and room as the in vivo BAT and they can interact with the virtual environment as it responds to their head movements. Participants were requested to provide predicted SUDs ratings prior to each step of the hierarchy and SUDs ratings during each step. In the initial session all groups completed VRET for the extinguished CS, which was either the rat or the spider dependent on counterbalancing. The Oculus rift headset was positioned, and the exposure session began with the first step of the hierarchy. Heart rate was measured at specific intervals throughout the VRET and BATs. The participant was encouraged to progress through the steps at their own pace. The steps were able to be repeated until the participant reported their fear below 15 on the SUDs scale and suggested they were willing to go to the next step. Each participant was able to successfully complete treatment as demonstrated by completing all the steps of the hierarchy. Debriefing was initiated with the participant post-treatment.

Post VRET, all participants completed an in vivo BAT to determine if any changes post-treatment generalised to real life stimuli. In the reinstatement phase, participants in the Reinstatement and MPS groups were instructed to select a step of the hierarchy to complete with the unextinguished CS. The control group did not complete a reinstatement phase.

The second session involved recording a 5-minute HR acclimatisation and 5-minute HR baseline and all groups completed an in vivo BAT for the extinguished CS. The MPS group received another VRET session for the unextinguished CS and the other groups did not. The third session involved re-administering the survey conducted at pre-assessment whilst HR acclimatisation and baseline periods were recorded. At this third session, all groups completed an in vivo BAT for the spider and rat.

2. Results

2.1 General Analyses

The dependent variables were heart rate change, avoidance ratings and SUDS ratings. Heart rate change scores were calculated by subtracting the maximum heart rate in each phase from the maximum heart rate observed during the baseline phase. The between-subjects independent variables for the analyses were Design with 3 levels (Reinstatement, MPS, and Control). The within-subjects independent variable for the initial analyses (pre-test to post-test 1, post-test 1 to follow-up 1) was Time with 2 levels and for follow-up 2 the within-subjects independent variable was CS with 2 levels (CSext and CSunext). The groups did not differ significantly across scores for the FSQ, FRQ, DASS-21, and RJPQ subscales, or age, or for arousal evoked by the two CSs (compared HR acclimatization and HR baseline data), all $Fs < 1.5$, $p > .05$. A chi square analysis confirmed that gender distribution did not differ across the groups, χ^2 (2) = 2.16, $p = .32$. Following VRET, 14% of the participants did not complete the final step of the in vivo BAT. Post-hoc analyses used *t*-tests adjusted for Type I error with a Bonferroni correction. The statistical significance was set at an α-level of .05. The treatment results will be presented across phases for the SUDS, avoidance and HR change data (see Figure 6.1, 6.2 and 6.3).

Figure 6.1.

Mean Subjective Units of Distress (SUDS) Ratings for the CSext and CSunext Across Phases for the MPS, Reinstatement and Control groups (error bars reflect the standard error of the mean)

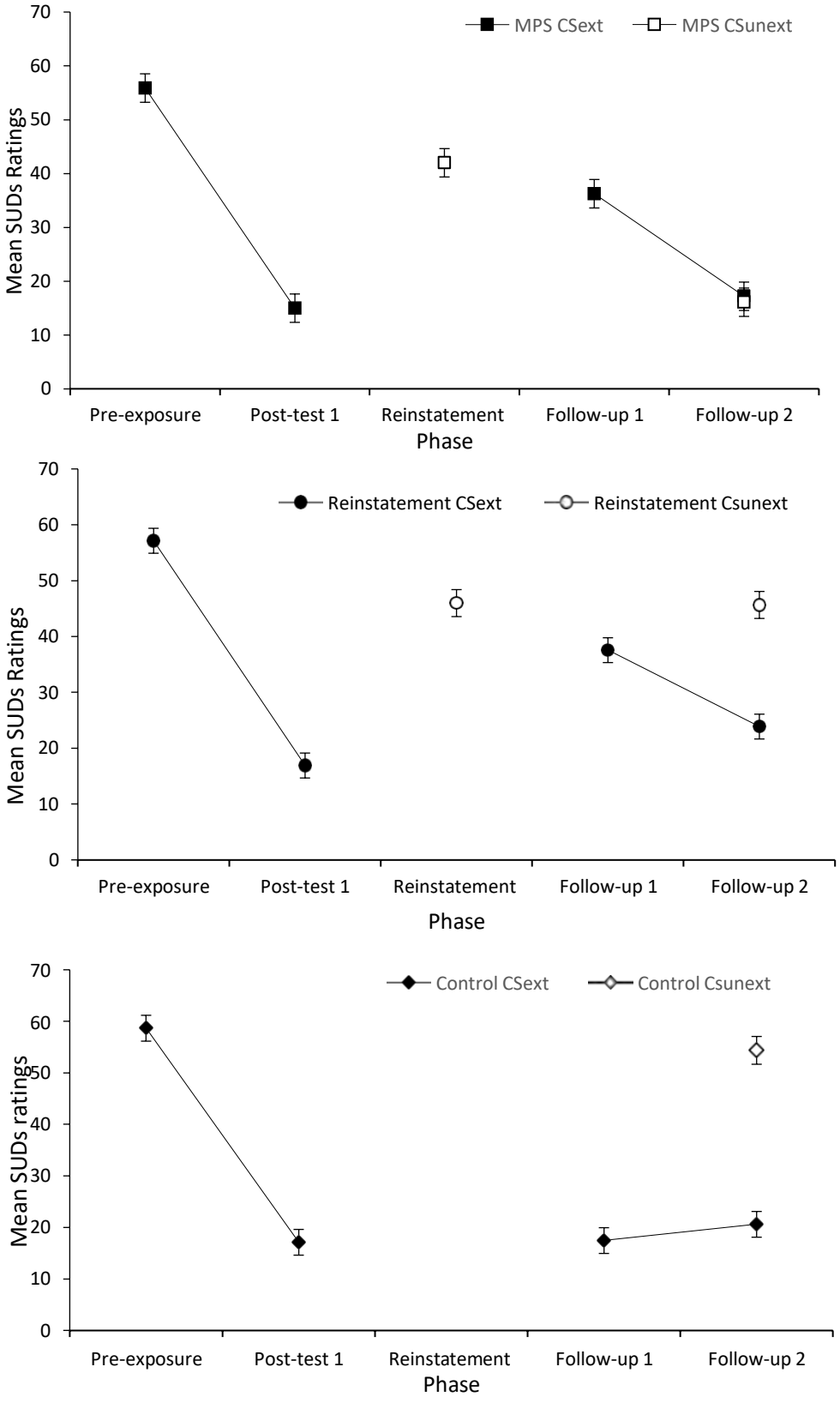


Figure 6.2.

Mean Avoidance Ratings Scores for the CSext and CSunext Across Phases for the MPS, Reinstatement and Control groups (error bars reflect the standard error of the mean)

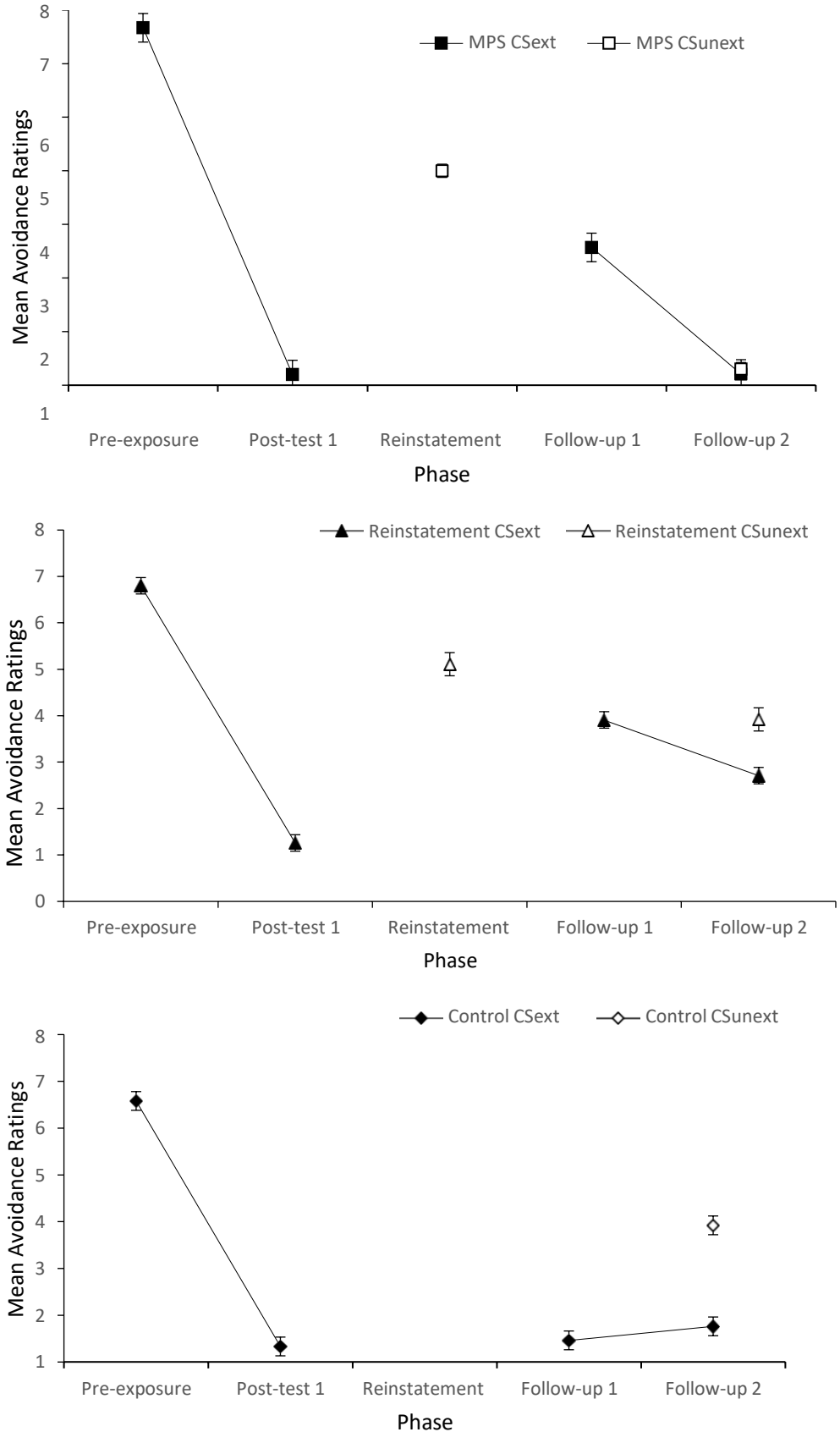
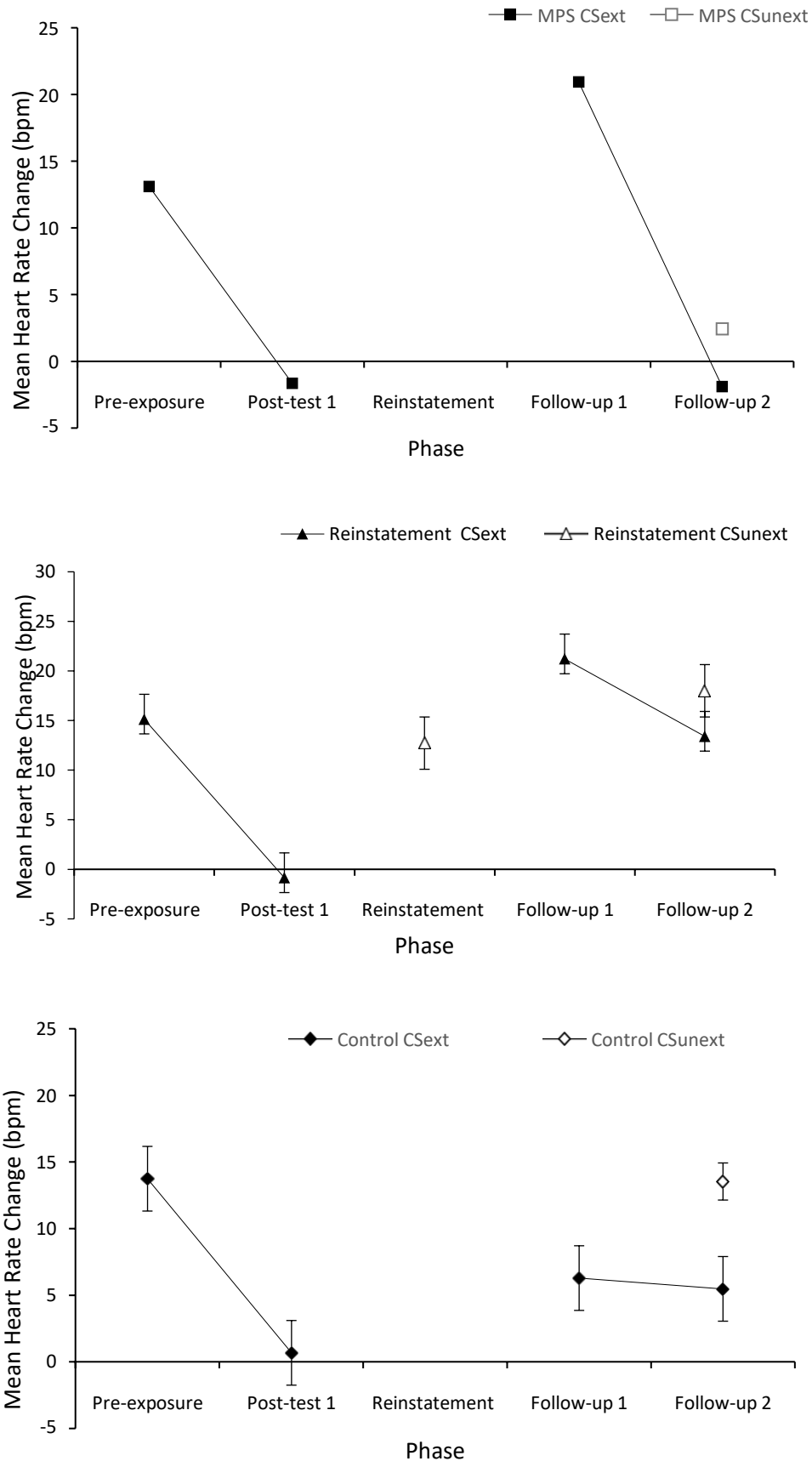


Figure 6.3.

Mean Heart Rate Change Scores for the CSext and CSunext Across Phases for the MPS, Reinstatement and Control groups (error bars reflect the standard error of the mean)



Reinstatement

Post-test 1 to follow-up 1

A series of 3 × 2 (Design × Time) mixed factorial ANOVAs were conducted to determine whether a reinstatement effect occurred for the Reinstatement Group relative to the Control group in avoidance ratings, SUDs ratings and HR change. As shown in Figures 1 to 3, the three groups did not significantly differ at post-test 1 indicating the exposure treatment was equivalent. However, there was a significant increase between post-test 1 and follow-up 1 in measures of fear observed across SUDs, avoidance and HR change for the MPS and Reinstatement groups but not the Control group.

SUDs Ratings. A significant Design × Time interaction, $F(1, 47) = 6.95$, $p = < .01$, $\eta_p^2 = .23$, and a significant main effect of Time, $F(1, 47) = 24.87$, $p = < .001$, $\eta_p^2 = .35$, and Design, $F(1, 47) = 6.24$, $p = < .05$, $\eta_p^2 = .21$, was observed for SUDs ratings. Within-group post-hoc analyses showed the MPS group and Reinstatement group reported significantly higher levels of fear at follow-up 1 compared to post-test 1, thus demonstrating the reinstatement effect following exposure to the CSunext, all ts > 3.19, ps < .01, ds > .90. For the Control group there were no significant differences in SUDs ratings between post-test 1 and follow-up 1, $t(47) = 1.34$, $p > .05$, thus demonstrating the reinstatement effect did not occur in this group. Between-groups post-hoc analyses at post-test 1 showed no significant differences for the SUDs ratings between the three groups, all ts < 1.75, ps > .05. At follow-up 1, the MPS and the Reinstatement group reported significantly higher levels of fear than the Control group, all ts > 2.75, ps < .05, ds > .80 and no significant differences were found between the MPS and Reinstatement group, $t(47) = 1.05$, $p > .05$.

Avoidance Ratings. Post-test 1 to follow-up 1 analyses showed a significant Design × Time interaction, $F(1, 48) = 12.46$, $p = < .001$, $\eta_p^2 = .34$, a significant main effect of Time, $F(1, 48) = 65.37$, $p = < .001$, $\eta_p^2 = .58$, and a main effect of Design, $F(1,$

48) = 5.75, p = .001, η_p^2 = .25. Within-group post-hoc analyses depicted a significant increase in avoidance for the Reinstatement and MPS groups between post-test 1 and follow-up 1, all ts > 3.72, ps < .01, ds > .95. No significant differences across phases were found for Control group, $t(47) = 0.51$, $p > .05$. Post-hoc analyses conducted between-groups revealed at follow-up 1 the Reinstatement and MPS groups had significantly higher avoidance ratings compared to the Control group, all ts > 2.83, ps < .05, ds > .83. At post-test 1, no significant differences for the SUDs ratings were found between the groups, all ts < 0.47, ps > .05.

Heart Rate Change. The results for heart rate change showed a significant Design × Time interaction, $F(1, 45) = 7.89$, p = .001, η_p^2 = .26, and subsumed under the interaction, a significant main effect of Time, $F(1, 45) = 83.89$, p = < .001, η_p^2 = .65, and Design, $F(1, 45) = 5.27$, p = < .05, η_p^2 = .19. Within-group post-hoc analyses demonstrated heart rate change scores increased for all the groups from post-test 1 to follow-up 1, all ts > 2.18, ps < .05, ds > .62. Between-group post-hoc analyses showed heart rate change scores were higher for the Reinstatement and MPS groups compared to the Control group at follow up 1, all ts > 2.39, ps < .05 , ds > .70. At post-test 1 there were no significant differences for heart rate change across the groups, all ts < .14, ps > .05.

Follow-up 2

A series of 3 × 2 (Design × CS) mixed factorial ANOVAs were conducted for the dependent variables to determine whether exposure to the CSunext in the MPS group resulted in significantly lower levels of fear for the CSunext and CSext compared to the Reinstatement and Control groups. Planned comparisons using t-tests were used to address the hypotheses and the predicted interaction was examined by comparing the CSext, and CSunext, separately for each group.

SUDs ratings. The results for the follow-up 2 analyses for SUDs ratings revealed a significant Design × CS interaction, $F(1, 42) = 11.23$, $p = <.001$, $\eta_p^2 = .35$. A significant main effects for CS, $F(1, 42) = 45.69$, $p < .001$, $\eta_p^2 = .53$, and Design, $F(1, 42) = 16.45$, $p = .001$, $\eta_p^2 = .44$, were found. Between-group post-hoc comparisons showed that the Reinstatement and Control groups reported significantly higher levels of fear for the CSunext compared to the CSext, all ts > 4.33, ps < .001, ds > 1.21. For the MPS group no significant differences between the CSext and CSunext were found at follow-up 2, $t(42) = 0.20$, $p > .05$.Within-group post-hoc analyses revealed that there were no significant differences between the three groups for the CSext at follow-up 2, all ts > .56, ps > .05, ds = .17. For the CSunext, the MPS group had significantly lower fear ratings than the Reinstatement and Control groups, all ts > 5.96, ps < .001, ds > 1.83. No significant differences were found between the Reinstatement and Control groups for the CSunext, $t(42) = 1.72$, $p > .05$, $d = .53$.

Avoidance ratings. Follow-up 2 analyses for avoidance showed a significant Design × CS interaction, $F(1, 42) = 9.45$, $p = <.001$, $\eta_p^2 = .30$, main effect of CS, $F(1, 42) = 31.83$, $p < .001$, $\eta_p^2 = .43$, and main effect of Design, $F(1, 42) = 23.86$, $p = .001$, $\eta_p^2 = .92$. Post-hoc analyses within-groups indicated that avoidance ratings for the MPS group did not significantly differ between the CSext and CSunext, $t(42) = 5.07$, $p > .05$, $d = 1.49$. In comparing the CSunext and CSext, the Reinstatement and Control groups had significantly higher avoidance for the CSunext, all ts > 5.87, ps < .001, ds > 1.81. The between-group analyses showed that for the CSext there were no significant differences between the three groups, all ts < 1.96, ps > .05. Further, for the CSunext the MPS group demonstrated higher avoidance than the Reinstatement and Control groups, all ts > 2.15, ps < .001, ds > 0.96.

HR change. A significant Design × CS interaction was revealed, $F(1, 46) = 5.21$, $p = <.01$, $\eta_p^2 = .19$, in addition to a significant main effect of CS, $F(1, 46) = 58.77$,

$p < .001$, $\eta_p^2 = .56$, and Design, $F(1, 46) = 11.95$, $p = .001$, $\eta_p^2 = .34$. For the within-group analyses, heart rate change scores for the CSext and CSunext did not significantly differ in the MPS group, $t(42) = 1.78$, $p > .05$, and the heart rate change scores were significantly higher for the CSunext compared to the CSext for both the Reinstatement and control group, all ts > 5.68, ps < .001, ds > 1.67. Between-group analyses suggested significantly lower heart rate change scores for the CSext in the MPS group than the Reinstatement and Control groups, all ts > 4.37, ps < .001, ds > 1.95. The heart rate change scores for the CSext were not significantly different between the Reinstatement and control groups, $t(42) = 0.89$, $p > .05$. In regards to the CSunext, the MPS group had significantly lower heart rate change scores compared to the Reinstatement and Control groups, all ts > 0.54, ps < .05, ds > 0.24. Again, no significant differences were found for the CSunext for the Reinstatement and Control groups, $t(42) = 0.82$, $p > .05$.

Discussion

Consistent with the hypotheses, the findings revealed that reinstatement of fear can be elicited following exposure to a second untreated feared stimulus in a moderate to high fearful sample, but that this reinstatement can be attenuated by conducting exposure to the second feared stimulus. Across the subjective ratings, avoidance ratings and heart rate change measures, the reinstatement group demonstrated higher levels of reinstatement of fear compared to the control group, thus supporting the first hypothesis. The finding that exposure to multifarious stimuli attenuated reinstatement of fear was demonstrated at follow-up 2 with the MPS group having significantly lower levels of fear than the Reinstatement and Control groups across all measures for the extinguished CS and unextinguished CS.

The current findings extend previous work by Halladay et al. (2012), Krisch et al. (2020) and Rescorla and Heth (1975) by demonstrating that an unextinguished CS can trigger reinstatement of fear in not only rats and a non-clinical sample, but also

individuals with multiple moderate to high animal fears. In the present study, extinguished fear returned following exposure to the unextinguished CS conducted in the extinction context. Theoretically, the current findings of eliciting conditional reinstatement can be partially explained by Bouton's contextual memory model (Bouton, 1993, 2000). The contextual features of the unextinguished CS may have retrieved the CS-US association by acting as a reminder of the acquisition context (Bouton, 1993), as the unextinguished CS had not been presented previously in the current study.

Neurobiological research may provide further insight into why reinstatement of fear may occur in preparations such as that used in the present study. In the acquisition of the fear, contextual information of the CS is processed in the hippocampus and medial prefrontal cortex which activates the amygdala and triggers the conditioned response (e.g., fear) and forms the CS-US association (Bouton et al., 2021). The role of synaptic plasticity in the amygdala is crucial for extinction learning and thus the CS-noUS association to be learnt (e.g., Bocchio et al., 2017). The contextual cues of the unextinguished CS in the reinstatement phase may activate the infralimbic neurons to the amygdala (Laurent & Westbrook, 2009; Marek et al., 2018; Milad & Quirk, 2002) and this experience of fear may trigger the fear to be reinstated for the extinguished CS, similar to how stimulating the amygdala has enhanced reinstatement of fear in rats (Kellett & Kokkidinis, 2004).

In accordance with Krisch et al. (2020), the current finding that exposure to multifarious stimuli attenuates reinstatement of fear extends the applicability of reinstatement to individuals with multiple moderate to high animal fears. Reinstatement of fear was higher in the group that did not undergo exposure treatment to their second fear and this suggests the importance of conducting exposure to multiple fears. The conditioned response of fear may be elicited by the unextinguished CS (e.g., the rat may

bite me) and activate fear in the amygdala and reinstate fear to the primary fear through activating a similar conditioned response (e.g., the spider may bite me). Further, exposure to the unextinguished CS may aid the synaptic plasticity of the amygdala and the learning of the CS-noUS association (i.e., the rat does not bite me). Thus, other models are relevant to interpret the current findings. The valence-reinstatement theory (Dirikx, et al., 2004; Dirikx, et al., 2007; Hermans, et al., 2005) may explain conditional reinstatement as the second untreated fear may be perceived with negative valence and elicit arousal that triggers the CS-US association. Further research is necessary to understand the theoretical underpinnings of conditional reinstatement of fear and the importance of contextual features and affective properties.

The current study contributes to the scarce reinstatement of fear research with clinical-analogue samples and exposure to multiple fears, supporting the suggestion that exposure treatment to one fear does not necessarily generalise to other untreated fears (Burstein et al., 2003; Farrell et al., 2020; Liberman & Smith, 1972; Öst, 1989). The clinical implications of the present findings are valuable in indicating that untreated fears and potentially aversive events may be a risk factor for reinstatement of fear occurring for individuals with multiple fears. The current study adds to previous research which has highlighted how not only phobia subtype but the number of fears (Burstein et al., 2012; Curtis et al., 1998; Kendler et al., 1992), may be clinically meaningful to categorise specific phobia in diagnostic nomenclature such as the DSM editions (American Psychological Society, 2013).

The current findings suggest clinicians should conduct a comprehensive assessment if an individual meets criteria for specific phobia and rank order the severity of the number of fears. Clinicians could administer the Anxiety Disorders Interview Schedule for DSM-5 (Brown & Barlow, 2014) which is a clinical semi-structured interview enabling severity ratings of each fear and explores comorbid conditions. To

maximise the effectiveness of exposure therapy for those experiencing multiple phobias, different exposure hierarchies could be developed for each fear and if time and access to stimuli is limited, VRET could be used as homework. The current results highlight the importance of relapse prevention planning and clinicians should aim to inform clients of the risk of being triggered by their other fears and be encouraged to continue exposure therapy for their untreated fears.

A strength of the current study was increasing the ecological validity compared to previous reinstatement studies by using 360 degree footage of the same spider and rat used in the VRET and in vivo BAT. However, the generalisability of the study could be improved by employing a clinical sample of individuals diagnosed with specific phobia rather than individuals with moderate to high fear. The finding that 14% of the participants did not successfully complete the final step of the in vivo BAT (instead completing the second last step) is consistent with previous VRET studies with an in vivo BAT (Farrell et al., 2020). In interpreting this finding, it could support prior research that VRET is not as effective in the long term or in eliciting an anxiety response as in vivo exposure therapy (see Krisch et al., 2018 for a review; Michaliszyn et al., 2010). Another limitation is that the experimenter was not blind to the conditions and the same experimenter was used throughout all phases of the study. Future research should use different experimenters who are blind to the conditions and who treat a clinical sample of those with multiple specific phobias by conducting exposure in vivo. Such an approach would enable further investigation of the effectiveness of in vivo exposure compared to VRET and to increase the generalisability of the findings to clinical settings. Finally, the present findings are limited to adult participants and further work is required to examine the generality to younger age groups given the observed developmental differences in reinstatement (Waters et al., 2017).

In summary, multiple phobias are more common than single phobias and have a higher risk of return of fear and have been largely dismissed in the literature. The present study extended previous research on conditional reinstatement of fear (Halladay et al., 2012; Krisch et al., 2020; Rescorla & Heth, 1975). Individuals with multiple moderate to high fears are at risk that an untreated fear will increase the likelihood of reinstatement. Clinicians are recommended to target other fears during treatment to reduce the risk of their client experiencing relapse in the future. To enhance the long term effectiveness of exposure therapy for specific phobia, VRET may also be used as homework if time and access is limited.

Acknowledgments

The authors would like to acknowledge John Zhong for his help with setting up the virtual reality technology.

Declarations of interest

There are no competing interests to declare.

Role of Funding Organisations

The research was funded by the principal author's PhD funds and Griffith University.

References

Abramowitz JS, Deacon BJ, Whiteside SP. (2012). *Exposure therapy for anxiety: Principles and practice*. Guilford Press.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 138-144. https://doi.org/10.1016/j.jbtep.2014.12.006

Baños R. M., Botella C., Garcia-Palacios A., Villa H., Perpiñá C., & Alcaniz M. (2000). Presence and reality judgment in virtual environments: A unitary construct?. *CyberPsychology & Behavior*, 3, 327-335. https://doi.org/10.1089/10949310050078760

Bocchio, M., Nabavi, S., & Capogna, M. (2017). Synaptic plasticity, engrams, and network oscillations in amygdala circuits for storage and retrieval of emotional memories. *Neuron*, *94*(4), 731-743. https://doi.org/10.1016/j.neuron.2017.03.022

Borstein P.H., Knapp M. (1981). Self-control desensitization with a multi-phobic boy: A multiple baseline design. *Journal of Behavior Therapy and Experimental Psychiatry*, 12, 281-285. https://doi.org/10.1016/0005-7916(81)90059-8

Botella C., Bretón-López J., Quero S., Baños R., García-Palacios A. (2010). Treating cockroach phobia with augmented reality. *Behaviour Therapy*, 41, 401-413. https://doi.org.10.1016/j.beth.2009.07.002

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*(1), 80. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology*, *19*(1S), 57. https://doi.org/10.1037/0278-6133.19.Suppl1.57

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological Psychiatry*, *52*(10), 976-986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning & Memory*, *11*(5), 485-494. http://www.learnmem.org/cgi/doi/10.1101/lm.78804.

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445-466. https://doi.org/10.1016/0023-9690(79)90057-2

Bouton, M. E., Maren, S., & McNally, G. P. (2021). Behavioral and neurobiological mechanisms of Pavlovian and instrumental extinction learning. *Physiological Reviews*, *101*(2), 611-681. https://doi.org/10.1152/physrev.00016.2020

Brown, T. A., & Barlow, D. H. (2014). *Anxiety and related disorders interview schedule for DSM-5 (ADIS-5L): Lifetime version. Client interview schedule*. Oxford University Press.

Burstein, M., Georgiades, K., He, J. P., Schmitz, A., Feig, E., Khazanov, G. K., & Merikangas, K. (2012). Specific phobia among US adolescents: Phenomenology and typology. *Depression and Anxiety*, *29*(12), 1072-1082. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.22008

Craske, M. G. (1999). *Anxiety disorders: psychological approaches to theory and treatment*. Westview Press. https://psycnet.apa.org/record/1998-06744-000

Curtis, G., Magee, W. J., Eaton, W. W., Wittchen, H. U., & Kessler, R. C. (1998). Specific fears and phobias: Epidemiology and classification. *The British Journal of Psychiatry*, *173*(3), 212-217. https://www.cambridge.org/core/journals/the-

british-journal-of-psychiatry/article/abs/specific-fears-and-phobias/E3E1FDE206DD1A47EFCCA2B41C5DA37C#metrics

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2004). Reinstatement of extinguished conditioned responses and negative stimulus valence as a pathway to return of fear in humans. *Learning & Memory*, *11*(5), 549-554. http://www.learnmem.org/cgi/doi/10.1101/lm.78004

Dirikx T., Hermans D., Vansteenwegen D., Baeyens, F., & Eelen P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, 38, 237-251. https://doi-org.10.1016/j.jbtep.2006.04.001

Dunsmoor, J. E., Ahs F., Zielinski D. J., LaBar K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, 113, 157-164. https://doi.org.10.1016/j.nlm.2014.02.010

Emmelkamp, P. M., Krijn, M., Hulsbosch, A. M., De Vries, S., Schuemie, M. J., & van der Mast, C. A. (2002). Virtual reality treatment versus exposure in vivo: a comparative evaluation in acrophobia. *Behaviour Research and Therapy*, *40*(5), 509-516. https://doi.org.10.1016/S0005-7967(01)00023-7

Farrell, L. J., Miyamoto, T., Donovan, C. L., Waters, A. M., Krisch, K. A., & Ollendick, T. H. (2021). Virtual reality one-Session treatment of child-specific phobia of dogs: A controlled, multiple baseline case aeries. *Behavior Therapy*, *52*(2), 478-491. https://www-clinicalkey-com-au.libraryproxy.griffith.edu.au/service/content/pdf/watermarked/1-s2.0-S0005789420300861.pdf?locale=en_AU&searchIndex=

Garcia-Palacios, A., Hoffman, H. G., Kwong See, S., Tsai, A. M. Y., & Botella, C. (2001). Redefining therapeutic success with virtual reality exposure therapy.

CyberPsychology & Behavior, *4*(3), 341-348. https://doi.org/10.1089/109493101300210231

Gershman, S. J., Jones, C. E., Norman, K. A., Monfils, M. H., & Niv, Y. (2013). Gradual extinction prevents the return of fear: Implications for the discovery of state. *Frontiers in Behavioral Neuroscience*, *7*, 164. https://doi.org/10.3389/fnbeh.2013.00164

Giles, D., Draper, N., & Neil, W (2016). Validity of the Polar V800 heart rate monitor to measure RR intervals at rest. *European Journal Applied Physiology,* 116**,** 563–571. https://doi.org/10.1007/s00421-015-3303-9

Hermans, D., Dirikx, T., Vansteenwegenin, D., Baeyens, F., Van den Bergh, O., & Eelen, P. (2005). Reinstatement of fear responses in human aversive conditioning. *Behaviour Research and Therapy*, *43*(4), 533-551. https://doi.org/10.1016/j.brat.2004.03.013

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Kellett, J., & Kokkinidis, L. (2004). Extinction deficit and fear reinstatement after electrical stimulation of the amygdala: Implications for kindling-associated fear and anxiety. *Neuroscience*, *127*(2), 277-287. https://doi.org/10.1016/j.neuroscience.2004.05.011

Kendler, K.S., Neale, M.C., Kessler, R.C., Heath, A.C., & Eaves, L.J. (1992). The genetic epidemiology of phobias in women: The interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. *Arch Gen Psychiatry, 49*, 273-281. http://doi.org.10.1001/archpsyc.1992.01820040025003

Kim, J. H., & Richardson, R. (2007). A developmental dissociation in reinstatement of an extinguished fear response in rats. *Neurobiology of Learning and Memory*, *88*(1), 48-57. https://doi.org/10.1016/j.nlm.2007.03.004

Krijn, M., Emmelkamp, P. M., 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

Krisch K. A., Bandarian-Balooch S., O'Donnell A. W., Neumann D. L. (2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. In Z. Hill (Ed.), *Virtual reality: Advances in research and applications* (pp. 85–126). Nova Science.

Krisch, K. A., Bandarian-Balooch, S., Neumann, D. L., & Zhong, J. (2020). Eliciting and attenuating reinstatement of fear: Effects of an unextinguished CS. *Learning and Motivation*, *71*, 101650.

LaBar, K. S., & Phelps, E. A. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, *119*(3), 677. https://10.1037/0735-7044.119.3.677

Laurent, V., & Westbrook, R. F. (2009). Inactivation of the infralimbic but not the prelimbic cortex impairs consolidation and retrieval of fear extinction. *Learning & Memory*, *16*(9), 520-529. http://www.learnmem.org/cgi/doi/10.1101/lm.1474609.

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and Anxiety*, *27*(2), 148-167. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.20655

Liberman R. P, & Smith V. (1972). A multiple baseline study of systematic desensitization in a patient with multiple phobias. *Behavior Therapy, 3*, 597-603. https://doi.org.10.1016/S0005-7894(72)80009-1

Lindner, P., Miloff, A., Bergman, C., Andersson, G., Hamilton, W., & Carlbring, P. (2020). Gamified, automated virtual reality exposure therapy for fear of spiders: A single-subject trial under simulated real-world conditions. *Frontiers in Psychiatry*, *11*, 116. https://doi.org/10.3389/fpsyt.2020.00116

Lovibond P. F, & Lovibond S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*, 33, 335-343 https://doi.org/10.1016/0005-7967(94)00075-U

Marek, R., Xu, L., Sullivan, R. K., & Sah, P. (2018). Excitatory connections between the prelimbic and infralimbic medial prefrontal cortex show a role for the prelimbic cortex in fear extinction. *Nature Neuroscience*, *21*(5), 654-658. https://doi.org/10.1038/s41593-018-0137-x

Mertens, G., Leer, A., van Dis, E. A. M., Vermeer, L., Steenhuizen, A., van der Veen, L., & Engelhard, I. M. (2019). Secondary extinction reduces reinstatement of threat expectancy and conditioned skin conductance responses in human fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, *62*, 103-111. https://doi.org/10.1016/j.jbtep.2018.09.007

Michaliszyn, D., Marchand, A., Bouchard, S., Martel, M. O., & Poirier-Bisson, J. (2010). A randomized, controlled clinical trial of in virtuo and in vivo exposure for spider phobia. *Cyberpsychology, Behavior, and Social Networking*, *13*(6), 689-695. https://doi-org.libraryproxy.griffith.edu.au/10.1089/cyber.2009.0277

Milad, M. R., & Quirk, G. J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, *420*(6911), 70-74. https://doi-org.libraryproxy.griffith.edu.au/10.1038/nature01138

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

Ollendick, T. H., Öst, L. G., Reuterskiöld, L., & Costa, N. (2010). Comorbidity in youth with specific phobias: Impact of comorbidity on treatment outcome and the impact of treatment on comorbid disorders. *Behaviour Research and Therapy*, *48*(9), 827-831. https://doi.org/10.1016/j.brat.2010.05.024

Opriş, D., Pintea, 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.libraryproxy.griffith.edu.au/10.1002/da.20910

Öst, L. G. (1989). One-session treatment for specific phobias. *Behaviour Research and Therapy*, *27*(1), 1-7. https://doi-org.10.1016/0005-7967(89)90113-7

Pavlov I. P. (1927). Conditioned reflexes. London: Oxford University Press.

Pittig, A., Kotter, R., & Hoyer, J. (2019). The struggle of behavioral therapists with exposure: self-reported practicability, negative beliefs, and therapist distress about exposure-based interventions. *Behavior Therapy*, *50*(2), 353-366. https://doi.org/10.1016/j.beth.2018.07.003

Rachman, S. (1966). Studies in desensitization—III: Speed of generalization. *Behaviour Research and Therapy*, *4*, 7-15. Retrieved from: http://www.sciencedirect.com/science/article/pii/0005796766900386

Rachman, S., Robinson S., & Lopatka C. (1987). Is incomplete fear-reduction followed by a return of fear? *Behaviour Research and Therapy*, *25*, 67-69.

https://doi.org.10.1016/0005-7967(87)90116-1

Rachman, S., & Whittal M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, *27*, 513-520. https://doi.org.10.1016/0005-7967(89)90085-5

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*, 88. https://doi.org.10.1037/0097-7403.1.1.88

Rose, M. P., & McGlynn, F.D. (1997). Toward a standard experiment for studying post-treatment return of fear. *Journal of Anxiety Disorders*, *11*, 263-277. https://doi.org/10.1016/S0887-6185(97)00010-8

Shiban, Y., Pauli P., & Mühlberger, A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, *51*, 68-74. https://doi.org.10.1016/j.brat.2012.10.007

Shiban, Y., Schelhorn I., Pauli P., & Mühlberger, A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, *71*, 45-53. https://doi.org.10.1016/j.brat.2015.05.014

Sokol, N., & Lovibond, P. F. (2012). Cross-US reinstatement of human conditioned fear: return of old fears or emergence of new ones?. *Behaviour research and therapy*, *50*(5), 313-322. https://doi.org/10.1016/j.brat.2012.02.005

Szymanski, J., & O'Donohue, W. (1995). Fear of spiders' questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry*, *26*, 31-34. https://doi.org.10.1016/0005-7916(94)00072-T

Vasey, M. W., Harbaugh C. N., Buffington A. G., Jones C. R., Fazio R. H. (2012). Predicting return of fear following exposure therapy with an implicit measure of attitudes. *Behaviour Research and Therapy*, *50*, 767-774. https://doi.org.10.1016/j.brat.2012.08.007

Vurbic, D., & Bouton M. E. (2011). Secondary extinction in Pavlovian fear conditioning. *Learning & Behavior*, 39, 202-211. https://doi.org.10.3758/s13420-011-0017-7

Waters, A. M., Theresiana, C., Neumann, D. L., & Craske, M. G. (2017). Developmental differences in aversive conditioning, extinction, and reinstatement: A study with children, adolescents, and adults. *Journal of Experimental Child Psychology 159,* 263-278. https://doi.org/10.1016/j.jecp.2017.02.012

Wardenaar, K. J., Lim, C. C., Al-Hamzawi, A. O., Alonso, J., Andrade, L. H., Benjet, C., ... & De Jonge, P. (2017). The cross-national epidemiology of specific phobia in the World Mental Health Surveys. *Psychological Medicine*, *47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Wittchen, H. U, Lecrubier Y., Beesdo K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. In D. Nutt & J. Ballenger (Ed.), *Anxiety disorders,* (pp. 23-37). Oxford, UK: Blackwell Science Ltd.

Wolpe, J. (1968). Psychotherapy by reciprocal inhibition. *Conditional reflex: a Pavlovian Journal of Research & Therapy*, *3*(4), 234-240.

Zbozinek, T. D., Holmes, E. A., & Craske, M. G. (2015). The effect of positive mood induction on reducing reinstatement fear: Relevance for long term outcomes of exposure therapy. *Behaviour Research and Therapy*, *71*, 65-75. https://doi.org/10.1016/j.brat.2015.05.016

Chapter 7: Preamble

As highlighted in the previous chapters, an important aim of the current research project was to extend the reinstatement of fear literature to clinical samples. In addressing this aim, an $N = 1$ case study was used. The study involved providing VRET to an individual with multiple animal type phobias (i.e., phobias to rats and spiders) and it aimed to improve the generalisability of the research and provide evidence for an intervention that may aid the long-term effectiveness of exposure therapy for specific phobia. The study is presented in manuscript format although at the time of this PhD thesis submission it has not been submitted for publication to a peer reviewed journal.

Chapter 7: Virtual Reality Exposure Therapy for a Case of Multiple Phobias: Examining Reinstatement of Fear

School of Applied Psychology, Griffith University

Kirra A. Krisch[1], Siavash Bandarian & David L. Neumann

[1]School of Applied Psychology Griffith University, Australia

[2]Menzies Health Institute Queensland, Australia

Please direct correspondence to: Kirra Krisch, School of Applied Psychology, Griffith University (Gold Coast Campus), Mail: GRIFFITH UNIVERSITY QLD, Queensland, 4222, Australia, Kirra.Krisch@griffithuni.edu.au, Telephone +61(0)7 567 880128.

Abstract

Individuals with specific phobia fear on average 3 different objects or situations. Despite this, laboratory-based and clinical-analogue research with specific phobia samples have focused on single fears. Following successful exposure therapy, many individuals experience a reinstatement of fear following a fear-provoking encounter. The current case study aimed to determine whether an untreated fear (i.e., an unextinguished CS) can elicit reinstatement to an extinguished fear (termed conditional reinstatement) and whether exposure to this untreated fear can attenuate conditional reinstatement of fear in an individual with multiple animal type phobias. Diagnostic severity and status was measured with the Structured Clinical Interview for the DSM-5 (SCID-5, First et al., 2015). Subjective units of distress (SUDs), avoidance during a behavioural avoidance task (BAT) and heart rate was measured throughout the sessions. Tau-U analyses of data trend and non-overlap indicated that exposure to a spider (e.g., an unextinguished CS) attenuated conditional reinstatement of rats and spiders across all measures. To reduce reinstatement of fear following successful exposure therapy, clinicians could comprehensively assess and treat multiple fears using virtual reality exposure therapy.

Keywords: exposure therapy; reinstatement of fear; case study; multiple phobias; return of fear; specific phobia

Introduction

It is estimated that more than 40% of the general population fear one or more object or situation at some point during their lifetime (Curtis, 1998; Depla et al., 2008; Oosterink et al., 2009). In the case that this fear becomes persistent, and the fear is excessive to the threat posed, it is considered a specific phobia (American Psychiatric Association, 2013). Specific phobias are the most prevalent group of mental health disorders (Kessler & Wang, 2008; LeBeau et al., 2010; Van Houtem et al., 2013). The Diagnostic and Statistical Manual for Mental disorders (fifth edition; DSM-5) identifies five main subtypes of specific phobia: animal-type, natural environment type, situational type, blood-injury type, and other (American Psychiatric Association [APA], 2013).

The DSM-5 emphasises that most people with specific phobia fear more than one object or situation (APA, 2013). Wittchen et al. (2003) surveyed 3021 participants and found that 75% of individuals suffering from specific phobia feared more than one object or situation and over 50% of feared three or more different phobic objects or situations. It has been found that those suffering from multiple phobias exhibit elevated severity and impairment, higher comorbidity with other disorders, reduced treatment-seeking and lower likelihood of recovery (Burstein et al., 2012; Stinson et al., 2007; Wardenaar et al., 2017). Despite this evidence, the assessment and treatment of multiple phobias has received little attention in the literature.

Specific phobias have been found to have a multifaceted etiology (King et al., 2004; Ollendick & Muris, 2015). Genetic vulnerability, neurobiology, parenting practices, temperament, direct and indirect conditioning, have all been implicated in phobia acquisition (see Ollendick & Muris, 2015 for a review). Rachman (1977, 1991) proposed a model involving three pathways of fear acquisition. Specifically, the classical conditioning pathway (Pavlov, 1927; Wolpe, 1958) whereby an individual

encounters a CS paired with an aversive US and results in a conditioned fear response (e.g., an individual is bitten by a spider). Indirect pathways include how fears and phobias can be learnt by observing other people's responses to an object or situation (e.g., a child modelling their parents fear and avoidance of rats) or by vicarious fear learning involving viewing information that an object or situation is threatening (e.g., watching a television show where a snake bites someone).

Irrespective of how a phobia is acquired, exposure therapy is the most effective treatment (Craske, 1999; Olatunji et al., 2010; Öst, 1989; Wolpe, 1968). Subsequent to effective exposure therapy treatment, 35-50% of individuals report a return of anxiety symptoms which Rachman (1966, 1977) termed return of fear. Reinstatement of fear is one of the least studied mechanisms of return of fear. Reinstatement of fear can occur after re-exposure to the unconditional stimulus (US) following successful exposure therapy (Mertens et al., 2019; Rachman & Whittal, 1989; Rescorla & Heth, 1975; Shiban et al., 2015; Zbozinek et al., 2015). A clinical example of reinstatement would be an individual who has overcome their phobia of spiders through exposure therapy and then has their fear of spiders reinstated after being bitten by a scorpion. Translating this clinical example to explore the underlying mechanisms of reinstatement in research has been difficult. It would violate ethics in human research to subject participants to painful bites and it would be challenging to replicate this phenomenon.

Due to the ethical and practical limitations, reinstatement of fear studies have been predominately conducted using laboratory-based experiments with animals and non-fearful human participants (Bouton & Bolles, 1979; Dirikx et al. 2007; Dunsmoor et al., 2014; Gershman et al., 2013; Halladay et al., 2012; Hermans et al., 2005; Kim & Richardson, 2007; LaBar & Phelps, 2005; Mertens et al., 2019; Rescorla & Heth, 1975; Vurbic & Bouton, 2011; Zbozinek et al., 2015). Reinstatement of fear research has not typically employed clinical samples (Boschen et al., 2009; Haaker et al., 2014; Hermans

et al., 2005; Neumann, 2008). Halladay et al.'s (2012) and Rescorla and Heth's (1975; Exp 2) findings that an unextinguished CS can reinstate the conditioned response to an extinguished CS in rats demonstrated that other aversive encounters could trigger reinstatement. Halladay et al. (2012) termed this conditional reinstatement. Extending these findings could potentially bridge the gap in research between animal and non-fearful samples to clinical-analogue and clinical samples. A clinical example of conditional reinstatement is a client who has multiple animal type phobias who has overcome their fear of spiders by completing exposure therapy and subsequently experiences an aversive encounter with a secondary untreated fear of rats, reinstating their initial fear. Therefore, the clinical implications of Halladay et al. (2012) and Rescorla and Heth (1975) are valuable in suggesting that exposure therapy to the conditioned response may reinstate fear without necessarily re-experiencing the US and this increases the likelihood of reinstatement of fear occurring.

To date, research that has specifically treated multiple phobias or included multiple phobias in the sample has focused primarily on paediatric samples. In studies involving paediatric samples with comorbid specific phobias (Borstein & Knapp; 1981; Farrell et al., 2020) and an adult case study of one session treatment for individual multiple animal type phobias (Öst, 1987), it has been found that treatment effects did not generalise across the non-treated fears. In Ollendick et al. (2010) and Ryan et al. (2017) exposure to the primary anxiety disorder did result in a significant reduction to comorbid phobias up to 6 months post-treatment but participants still remained fearful. Thus, there is conflicting evidence that successful exposure to a primary fear generalises to untreated fears for individuals with comorbid phobias during treatment.

While the presence of comorbid phobias has been found to reduce the likelihood of seeking treatment and the effectiveness of treatment (Burstein et al., 2012; Stinson et

al., 2007; Wardenaar et al., 2017), there are no studies to date that have explored if reinstatement of fear occurs for those with multiple phobias. In clinical settings, treatment for specific phobia tends to focus on treatment for a single phobia due to limited access to multiple feared stimuli and a lack of affordable long-term treatments. Given the high rates of those with comorbid phobias, high probability of return of fear occurring and the importance of continuing to enhance the long-term effectiveness of exposure therapy, further research is needed to understand whether untreated fears can reinstate fear to a treated fear.

In addressing this gap in the literature, Krisch et al. (2020) and Krisch et al. (2021) extended previous laboratory-based research with animals (Halladay et al., 2012; Rescorla & Heth, 1975; Sokol & Lovibond, 2012). The authors found that an untreated fear (i.e., unextinguished CS; spider) triggered reinstatement to a successfully treated fear (i.e., extinguished CS; snake) in non-fearful participants (Krisch et al., 2020) and moderately to high fearful participants (Krisch et al., 2021). Moreover, Krisch et al. (2020) and Krisch et al. (2021) demonstrated that reinstatement was attenuated by conducting exposure to the extinguished CS (termed multifarious stimuli) and highlighted the use of VRET as a methodology to present multiple fears. However, this research has limited external validity due to not examining conditional reinstatement with a clinical sample.

Due to individuals with specific phobia having a preference for VRET compared to in vivo and the additional control of stimuli provided with virtual reality technology (Garcia-Palacios et al., 2001; Rothbaum et al., 2000), VRET may be an effective method to address multiple phobias and reinstatement of fear that may be triggered by untreated fears (Krisch et al., 2016). Previous studies using VRET and in vivo treatment for specific phobia have also been predominately limited to single phobias (i.e., Garcia et al., 2001; Michaliszyn et al., 2010; Minns et al., 2018). For example: Malbos et al.

(2020) utilised a *N* = 1 design to examine the effectiveness of treatment for specific phobia of sharks. The case study demonstrates how clinicians can utilise virtual reality technology for stimuli which are difficult and expensive to access in vivo. However, the study was also limited by relying solely on self-report measures. Krisch et al. (2020) and Krisch et al. (2021) employed VRET and used self-report, physiological and behavioural measures of fear. However, the studies by Krisch et al. (2020; 2021) were limited by not using a clinical sample of individuals suffering from phobia.

The generalisability of prior research has been restricted by not employing a clinical sample of those with multiple phobias. To the authors' knowledge there are no current studies investigating whether conditional reinstatement occurs with those meeting criteria for multiple phobias. Furthermore, conducting VRET with multifarious stimuli to reduce conditional reinstatement of fear in a clinical sample is yet to be investigated. Therefore, the present study aims to examine whether individualised VRET treatment can reduce conditional reinstatement of fear. The current study examined whether a modified version of OST VRET treatment can be effective in the treatment of an individual with comorbid animal-type phobias. In achieving this aim, a case study method with an individual experiencing multiple phobias was utilised. The method also allowed for recommendations regarding the long-term effectiveness of treatment for individuals suffering from multiple phobias to be developed.

Case summary

Eva is a 25 year old female who self-referred for treatment due to experiencing persistent anxiety and avoidance of rats and spiders. A comprehensive assessment was conducted including a structured clinical interview, behavioural approach task and self-report measures of her fears of rats and spiders. Based on this assessment, she was diagnosed with Specific Phobia of two animal types (rats and spiders) and social anxiety disorder.

Presenting problems and history

Eva described a persistent and intense fear when encountering rats (domesticated or undomesticated) and spiders. The fears of rats and spiders led to significant avoidance and impacted her employment and her leisure time. Eva's employment is in community settings where she conducts home visits. During these situations she described herself as being hypervigilant and avoidant of rats and spiders. Eva described avoiding places where she had previously seen rats and spiders including her garage and particular outdoor spaces such as parks. For example, if Eva was to see a spider in one room of the house she would need someone to remove it or kill it and even then she would avoid that room for several days.

Assessment and descriptive measures

Apparatus

The phobic stimuli employed were a fancy rat (*Rattus norvegicus domestica*) with black and white colouring and measuring 21.86 cm in length and a golden orb weaver (*Nephila edulis*) with the length of the body approximately 3 cm and legs spanning 9 cm. A 13-step graded exposure hierarchy was developed collaboratively with the client for both the rat and spider. The exposure hierarchy steps were recorded with a Samsung Gear 360º video camera from a first-person perspective. During the filming the person wore a laboratory coat, blue pants and blue shoe covers. In order to increase immersion in the virtual reality context, Eva was requested to wear the same attire. Eva was presented with the rat and spider for the in vivo behavioural avoidance tasks (BATs) and in virtual reality through Skybox software and an Oculus rift headset (see Table 7.1). A box was designed for the study to present the phobic stimuli. It had a glass viewing screen so Eva could view the animals and it had cardboard sides to prevent the animals escaping. In addition, sleeves were fixed to the sides of the box for Eva to place her hands inside. Eva's heart rate was recorded throughout assessment,

treatment, and follow-up with a Polar V800 watch. Heart rate change scores were calculated by subtracting the heart rate during the BATs from baseline at each VRET session, with positive changes scores indicating higher heart rate during the BATs. Prior studies have demonstrated the validity of the Polar V800 watch in measuring fear with the heart rate change parameters (Bandarian-Balooch et al., 2015; Carpenter et al., 2021; Preusser et al., 2017) and it has been found that heart rate measurements taken with wearable watches correspond to electrocardiography (ECG) recordings (Giles et al., 2016).

Table 7.1.

The Steps for the Virtual Reality Exposure Hierarchy and Corresponding In Vivo Behavioural Avoidance Task for Rats and Spiders

1	Stand 2 metres away while viewing animal in a closed container.
2	Stand 1 metre away while viewing animal in a closed container.
3	Stand 50 cm away while viewing animal in a closed container.
4	Place hands on top of open container while viewing animal.
5	Hands inside sleeves at top of open container.
6	Hold the stick next to animal inside container.
7	Touch the animal with the stick in the open container.
8	Touch animal with gloved hands inside the open container.
9	Hands on table with animal not contained without touching animal.
10	Touch animal on table with gloved hands.
11	Place animal on gloved hands.
12	Place animal on arms.
13	Hold animal on hands close to face.

Structured Clinical Interview for Disorders in the DSM-5 research version

In assessing whether Eva met criteria for specific phobia and other comorbid diagnoses, the Structured Clinical Interview for Disorders in the DSM-5 research version was administered (SCID-5-RV; First et al., 2015). Diagnoses assigned a Clinical Severity Rating (CSR) of four or above, on a 0 (*not present*) to 8 (*very severe*) scale, are considered clinically significant and 4 and below are considered subclinical features of the disorder. Eva was rated a CSR score of 7 for her phobia of rats, a CSR score of 6 for her phobia of spiders and a CSR score of 4 for her social anxiety. As part of the SCID-5 administration Eva was asked what would be the most difficult in facing the feared stimuli. Eva indicated her strongest phobic belief was the same for both the rat and spider. Eva endorsed her fear was that both animals would bite her face and cause pain. In discussing her fears, Eva outlined how rats and spiders elicited both a fear and disgust response.

Fear of Spiders Questionnaire and Fear of Rats Questionnaire

The Fear of Spiders Questionnaire (FSQ) and FRQ (FSQ supplanted with the term rat) were administered to assess Eva's fears of spiders and rats (Szymanski & O'Donohue, 1995). The FSQ and FRQ contain 18 items and the total score range of 18 to 126, with the higher the score indicating more fear and avoidance. In previous studies the cut-off score for a phobia has been a score of 97 on the FSQ representing two standard deviations above the mean (Garcia et al., 2001) and a score below 65 has been found to represent meaningful clinical change following treatment (Michaliszyn et al., 2010).

Avoidance Ratings

The BATs were used to measure Eva's avoidance of the rat and spider. The distances in the BAT corresponded to the 13-step gradual exposure hierarchy collaboratively developed with the client (see Table 7.1) but the BAT was conducted in vivo. During each BAT, Eva was requested to complete the highest step she was willing

to and the therapist remained in another room but in Eva's sight. The scoring of the BAT was consistent with previous research (Bandarian-Balooch et al., 2015; Michaliszyn et al., 2010), with each step the client completed resulting in subtracting an avoidance point such that a higher score on the BAT indicates greater avoidance.

Subjects Units of Distress

During the BATs and exposure treatment, subjective units of distress (SUDS; Wolpe, 1973) ratings (i.e., 0-100 scale) were recorded to measure self-reported fear and disgust individually. Higher SUDS ratings reflected more fear and disgust of the spider or rat. The SUDS ratings were measured on a 100 point scale (0 = *no fear/disgust*, 25 = *mild fear or disgust*, 50 = *moderate fear or disgust*, 75 = *severe fear or disgust,* and 100 = *very severe fear or disgust*). Eva was requested to verbally report both her fear and disgust before and during each BAT and step of the exposure hierarchies.

The Social Interaction Anxiety Scale

The Social Interaction Anxiety Scale (SIAS) is a 20 item self-report scale developed to measure social interaction anxiety and has been used to monitor social anxiety symptoms. Higher scores indicate more issues with social interaction anxiety and the cut off score has been reported as 36 for detecting the likelihood of social anxiety disorder (Peters, 2000). There is evidence of clinician-rated severity and the SIAS being moderately correlated (Brown, et al., 1997). Due to Eva endorsing many items for social anxiety on the SCID-5 the SIAS was included as a control measure.

The Clinical Anger Scale

The Clinical Anger Scale (CAS) is a valid self-report measure assessing the psychological symptoms presumed to have relevance in the understanding and treatment of clinical anger. The CAS was administered in the study as a control measure across the phases.

Formulation

Eva reported that her mother modelled fear, anxiety, and avoidance of rats and spiders to keep Eva safe and to reduce her mother's own distress during fear provoking encounters. The avoidance of rats and spiders and subsequent immediate short-term reduction in fear may have been negatively reinforcing her avoidance behaviours. Eva's persistent avoidance could also have maintained a long-term pattern of avoidant responding that was exacerbated and maintained through lack of opportunities to learn that her fears are irrational and that she could cope with her fear of rats and spiders. Eva shared a salient episodic memory that may have contributed to her conditioned fear of rats through vicarious learning (Rachman, 1977) reporting that around the age of five years she felt terrified and disgusted seeing a movie scene where a rat chewed through human flesh.

Eva demonstrated insight into her phobias and was highly motivated to engage in VRET treatment and not willing to try in vivo exposure. Eva was highly educated, enjoyed her work, and did not wish for her phobias to continue to impact her life.

Assessment process

Across the study, Eva completed four pre-treatment assessments, treatment sessions, and four follow-up assessments (see Table 7.2 for how the assessments were spaced). The study protocol received ethical approval from Griffith University's ethics review committee. At the initial pre-treatment assessment, Eva provided her verbal and written consent to participate in the study and confidentiality was discussed. Subsequently, the SCID-5 and the self-report questionnaires (e.g., the FSQ, FRQ, SIAS, CAS) were administered and the SUDS ratings were explained. During the initial assessment, Eva also completed the step of the in vivo BAT she was willing with both a spider and rat and her heart rate was recorded. For the following pre-assessment sessions, Eva completed the self-report questionnaires and the BATs. A treatment

rationale for exposure therapy and VRET was provided and the exposure hierarchies were collaboratively developed with Eva.

Treatment, Reinstatement phase and Follow-up

The initial treatment session involved discussing the treatment procedure, and self-report questionnaires while recording a baseline measure of her heart rate. Attire including blue gloves, a laboratory coat, pants and shoe covers were provided to Eva to assist with immersion in the virtual context. The Oculus rift headset was positioned by the client. Following this Eva completed the VRET with the rat as this was Eva's primary phobia and Eva was asked to verbally provide her SUDs ratings for fear and disgust prior and during each step of the hierarchy. A step was considered completed once Eva reported a fear level of 20 or lower and Eva indicated she was ready to begin the next step. The VRET treatment sessions were completed once Eva reached the final step of the individualised VRET hierarchy for both the spider and rat. Eva's heart rate was measured throughout the first and second treatment sessions. A post-test in vivo BAT with the rat was conducted following VRET for the rat. A reinstatement phase involved the therapist requesting Eva to select the highest step on the hierarchy she was willing to complete with the spider in vivo exposure (i.e.,unextinguished CS). Debriefing on the process of exposure therapy and Eva's experiences was conducted. The second treatment session followed the same procedurewith the spider and without the reinstatement phase and concluded with a BAT for boththe rat and spider. Debriefing also occurred at the conclusion of the VRET.

The follow-up assessments were conducted at one hour, one week, one month and two months post the second treatment session. The SCID-5 was administered at the first post-treatment session. At each follow-up session the self-report questionnaires (e.g., the FSQ, FRQ, SIAS, CAS) and BATs were conducted with the SUDs ratings and heart rate recorded.

Results

The results were analysed with Tau-U calculations. Tau-U is an index used for analyses in single-case data combining nonoverlap between phases with intervention phase trend (Parker & Hagan-Burke, 2007; Parker et al., 2011). The current study used Tau-U analyses across an AB design and visual inspection is used as it is considered an important factor in single-case data (Brossart et al., 2014; Shadish et al., 2015). Phase A consisted of 4 data points at pre-treatment and phase B consisted of 4 data points at follow-up across the heart rate change, CAS, SIAS FSQ, FRQ, SUDS ratings and avoidance ratings in the BATs. The SCID-5 (First et al., 2015) was re-administered at the first follow-up to assess if Eva met criteria for specific phobia of rats and spider and for social anxiety disorder. The CAS and SIAS scores were analysed with Tau-U and there was no difference between pre-assessment and post-treatment (see Table 7.2), Tau-Us < - 0.17, *ps* > .17.

SCID-5 follow-up

The SCID-5-RV was conducted at follow-up and the results indicated that following VRET Eva no longer met criteria for specific phobia (rat CSR = 3; spider CRS = 3). As expected, her social anxiety disorder (CSR = 6) remained unchanged indicating the treatment did not generalise for comorbid anxiety disorders that were not targeted in treatment.

Pre-treatment results

The pre-treatment heart rate change scores, FRQ, FSQ, avoidance ratings and SUDs ratings for the CSext and CSunext were analysed using Tau-U and did not indicate a significant trend at Phase A, all Tau-Us < -1.13, *ps* > .05. The pre-treatment scores were significantly high for both the FRQ and FSQ and met the clinical cut off scores being above 97 (see Table 7.1). Across the pre-treatment assessments Eva selected to stand 1 metre from the CS extinguished (i.e., rat) in a closed container (i.e., avoidance rating of 12, see Table 7.2). For the CS unextinguished (i.e., spider) at pre-

treatment Eva was able to stand 1 metre to 50 cm away from the spider in a closed container (i.e., avoidance ratings of 12-11). In completing the BATs at pre-treatment Eva reported her SUDS ratings for fear and disgust within the moderate to severe range for both the rat and spider (see Figure 7.1). Thus, Eva's pre-treatment results did not significantly change at baseline across all measures.

Table 7.2.

Eva's Avoidance ratings (0-10), HR Change Scores, FRQ and FSQ scores, CAS and SIAS Scores between Initial Assessment and the Final Follow-up Test

	Avoidance ratings		HR change		FRQ	FSQ	CAS	SIAS
	Rat (CSext)	Spider (CSunext)	Rat (CSext)	Spider (CSunext)				
1 month pre-treatment	12	11	27	24	105	99	3	36
3 weeks pre-treatment	12	10	30	23	115	97	3	37
2 weeks pre-treatment	12	12	26	20	111	98	4	36
1 hour pre-treatment	12	11	31	25	117	98	4	36
Post-treatment CSext	2	-	10	-	-	-	-	-
Reinstatement	-	7	-	22	-	-	-	-
Post-reinstatement	5	-	20	-	-	-	-	-
Post-treatment CSunext (1 hour post)	2	2	17	8	49	64	4	37
Follow-up 1 (1 week post)	2	2	11	10	51	65	3	35
Follow-up 2 (1 month post)	2	2	15	13	52	66	4	36
Follow-up 3 (2 months post)	2	2	15	14	52	66	3	36

Note. HR represents heart rate, FRQ = Fear of rats questionnaire; FSQ = Fear of spiders questionnaire, CAS = Clinical anger scale, SIAS = social interaction anxiety scale, CSext = extinguished CS, CSunext = unextinguished CS and dashes represents not assessed.

Follow-up results

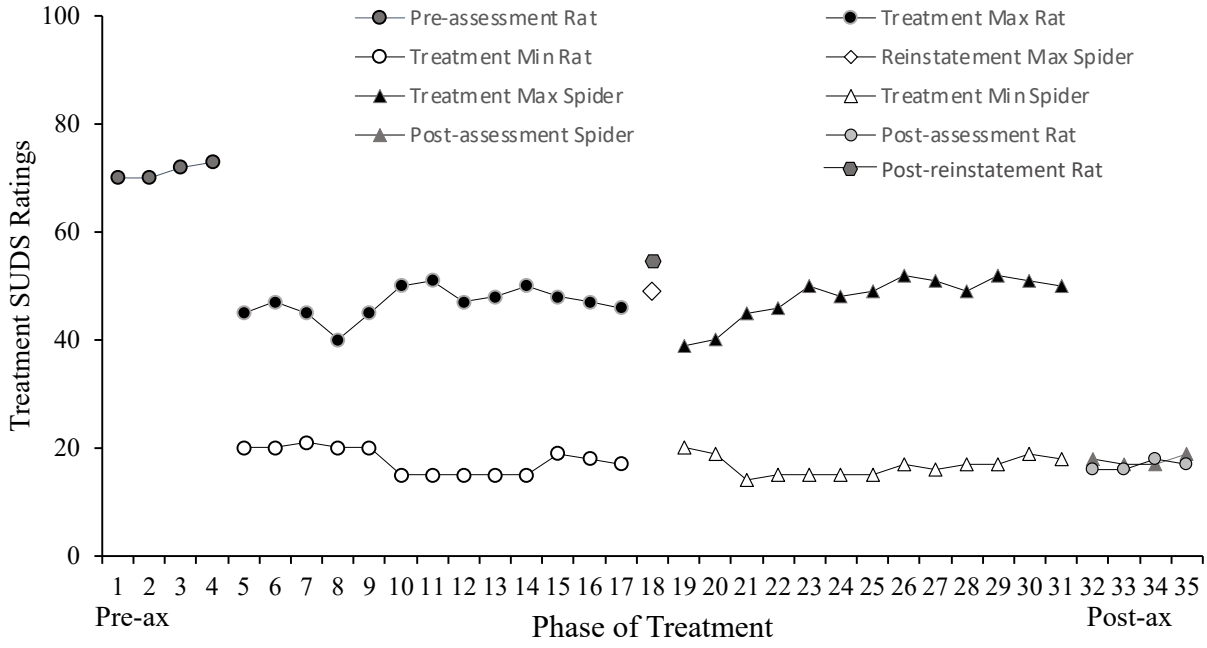
Across the follow-up assessments Eva's heart rate changes scores for the CSext and CSunext significantly decreased as indicated by a significant non-overlap between pre-treatment and post-treatment scores at Phase B, both Tau-U's = -1.00, *ps* = .02. In contrasting phase A and phase B scores with trend analyses all heart rate change scores were significant, both Tau-U's < -1.00, *p*'s = .001, suggesting heart rate change scores had significantly attenuated from pre-treatment to follow-up. The follow-up scores on the FRQ and FSQ had significantly decreased as indicated by a significant non-overlap between pre-treatment and post-treatment scores at Phase B, both Tau-U's = -1.00, *ps* = .02. Further, in contrasting phase A and phase B scores with trend analyses the FRQ and FSQ scores were significant, both Tau-U's < -1.00, *p*'s = .001, indicating the scores had significantly reduced from pre-treatment to follow-up. Eva's scores at post-treatment and follow-up were below the clinical cut-off for a phobia on the FSQ and FRQ (Michaliszyn et al., 2010; see Table 7.2 for scores). For the avoidance ratings the Tau-U analyses did not indicate a significant trend for phase B for the rat or the spider, Tau-Us = -1.00, *ps* = .02, suggesting Eva's avoidance ratings did not change due to time. Eva's avoidance of rats and spiders did not return to pre-treatment levels as indicated by contrasting phase A and phase B and the significant 100% fear reduction trends, Tau-Us = -1.00, *ps* = .001.

The SUDs ratings are presented in more detail than the other measures (see Figure 7.1). During the reinstatement phase, Eva's SUDs ratings of fear and disgust towards the spider (i.e., unextinguished CS) were within the moderate to severe range. Following the reinstatement phase involving in vivo exposure to the spider Eva reported an increase in fear and disgust ratings towards the rat (i.e., extinguished CS; see Figure 7.1). The Tau-U analyses could not be used to examine the reinstatement phase. At follow-up, the Tau-U analyses did not indicate a significant trend for phase B scores for

the rat or spider, Tau-U's = -1.00, *ps* = .02. Specifically, Eva's self-reported fear levels did not change due to spontaneous recovery effects. Tau-U analyses contrasting phase A and phase B scores revealed a significant 100% trend of attenuation for her fear and disgust of rats and spiders, Tau-U's = -1.00, $p < .001$. Thus, Eva's scores on the measures administered follow-up indicate reinstatement of fear did not occur.

Figure 7.1.

SUDS of Maximum Fear Across Pre-treatment assessments and Post-treatment Assessments and Minimum Fear During Steps of Each Hierarchy in Treatment



Discussion

The current study provides the first reported evidence that an untreated fear may reinstate fear for a treated fear in an individual who suffers from multiple phobias. Furthermore, it has shown that VRET can be used to present multifarious stimuli and attenuate this conditional reinstatement of fear for this population. Across measures of self-reported fear and disgust, avoidance, clinical interviews, and heart rate change there was a reliable reduction following the completion of individual VRET hierarchies with a rat and a spider. Importantly, reinstatement of fear assessed by these measures did not

occur at the 2 month follow-up. As expected, the findings across the control measures (e.g., SIAS, CAS) suggested that Eva's social anxiety and clinical anger symptoms did not significantly change from baseline to post-treatment. In extending Halladay et al. (2012), Krisch et al. (2020) and Krisch et al. (2021) and Rescorla and Heth (1975), the current study highlights that conditional reinstatement of fear occurs and that exposure to multifarious stimuli can reduce conditional reinstatement of fear in an individual with multiple animal type phobias. Moreover, the current study has further supported the use of VRET for addressing the ethical constraints of conditional reinstatement of fear with a clinical sample.

Consistent with prior research, the present results indicate VRET is an effective methodology for reducing specific fears (Malbos et al., 2020; Michaliszyn et al., 2010; Minns et al., 2018) and that exposure treatment to one fear did not generalise to the other untargeted fear (Borstein & Knapp, 1981; Farrell et al., 2020; Öst, 1987). It is noted that Eva completed both hierarchies in VRET and progressed to the second last step of the in vivo BAT rather than to completion. Similarly, participants in previous VRET studies also did not complete the final step of the in vivo BAT (Farrell et al., 2020; Krisch et al., 2021), even when the final step involved considerably less interaction with the animal (e.g., touching inside the cage near a spider in Michaliszyn et al., 2010). The current findings could reflect that Eva needed further VRET sessions to completely attenuate her fear and disgust. The case study findings provided further support for the notion that individuals with specific phobia prefer VRET over in vivo treatment (Garcia-Palacios et al., 2001; Opris et al., 2012; Rothbaum et al., 2000). At the beginning of the study, Eva reported she would not wish to undertake in vivo exposure as she perceived it as more anxiety provoking than VRET. However, at the end of the study Eva reported feeling more confident to undertake in vivo exposure in the future. An interpretation of the findings indicate VRET could be used to treat

secondary fears or be combined with in vivo exposure therapy as an initial step in the treatment program (Krisch et al., 2016).

Several models could be used to interpret conditional reinstatement. Bouton's contextual memory model (Bouton, 1993, 2000, 2002) suggests that exposure does not destroy the CS-US association from acquisition. Instead during exposure, the CS-noUS association is learnt and the context determines which is recalled. The present findings for conditional reinstatement could be explained by how the contextual cues of the unextinguished CS may have retrieved the CS-US association by serving as a reminder of the acquisition context (Bouton, 1993). In the test phase these cues enhanced the CS-US association formed in acquisition to be recalled and thus fear is reinstated. One issue with this interpretation is that in the case study Eva reported different experiences for how she acquired her phobias and it is possible that she does not accurately recall the acquisition contexts. The context for reinstatement and the BAT did share similarities but did differ by being conducted in VRET and in vivo, respectively. In the SCID-5 Eva endorsed a similar phobic belief across both spiders and rats which was that both animals would cause a painful bite to her face. Such beliefs may represent the conditioned response. Conditional reinstatement may have occurred due to the contextual cues of the unextinguished CS (i.e., spider) which may have activated the equivalent conditioned response (i.e., fear from being bitten) and reinstatement of fear may have occurred to the extinguished CS (i.e., rat).

Further evidence suggesting that the context triggers an affective response that then leads to reinstatement of fear comes from laboratory research conducted with animals. Kellett and Kokkidinis (2004) presented a stimulus and stimulated the amygdala in rats and this resulted in reinstatement of previously extinguished fear. Neurobiology studies demonstrate the importance of synaptic plasticity in the amygdala in exposure therapy for the CS-noUS association to be formed (Bocchio et al., 2017)

and the contextual cues of the unextinguished CS in the reinstatement phase may lead to amygdala activation and the conditioned response being triggered (Laurent & Westbrook, 2009; Marek et al., 2018; Milad & Quirk, 2002). Future research is necessary to understand the theoretical framework for conditional reinstatement of fear.

Clinical applications of the present results could aid in the assessment and treatment of specific phobias in the context of high rates for comorbid phobias. In terms of assessing for specific phobia, structured clinical interviews provide a comprehensive protocol and may increase the likelihood of identifying comorbid specific phobia which may be overlooked in the diagnostic process. The ADIS-5 and SCID-5 include several animal type categories (i.e., spiders, snakes, dogs, insects/bees and other (First et al., 2015; Szymanski & O'Donohue, 1995). However, given that other animal type fears are common (Van Houtem et al., 2013), in conducting an ADIS-5/SCID-5 the clinician should aim to list several other fear types to the client (e.g., rats and birds).

For over 50 years there has been extensive evidence that exposure therapy is the most effective treatment for the anxiety disorders and specific phobia but many clinicians do not conduct this treatment (Deacon et al., 2013; Pittig et al., 2019). Psychotherapists have suggested that practicality, negative beliefs, and therapist distress are barriers which interfere with their willingness to conduct exposure therapy (Deacon et al., 2013; Pittig et al., 2019). Conducting in vivo exposure therapy has not been associated with greater harm occurring to the client (see Olatunji et al., 2009), however VRET is a valuable treatment as psychotherapsists and individuals with anxiety disorders may be more likely to implement and access this treatment modality. The present case study provides guidelines on the application of VRET in clinical settings and due to the affordability of virtual reality technology, psychology private practices and community settings could provide VRET and provide VRET homework and consider it in relapse prevention planning.

A combination of measures of fear including physiological, self-report, and behavioural were included in the case study contributing to the validity to the findings (Haaker et al., 2014). The assessments and treatment were delivered by the same therapist which may have biased the results. A more valid and reliable approach would be to have independent assessors and therapists blind to the assessment and treatment timepoints and to include further assessment and post-treatment data points. The follow-up was completed across a 2 month timeframe and future research should aim to conduct follow-ups over a longer period. While control measures were included in the *N* =1 design, in future, a manipulation for conditional reinstatement could be included in a larger clinical sample of those with multiple phobias. The research questions could be investigated in a multiple baseline design or a clinical trial. More broadly, future research could determine whether return of fear is more common for those with multiple phobias than a single phobia.

In conclusion, the *N* = 1 study reported here has provided evidence that conditional reinstatement as measured by self-report, behavioural and physiological measures of fear occurs for those with multiple phobias and that it can be reduced by multifarious stimuli being presented in VRET. The current study continued the translational nature of return of fear research by bridging the gap between laboratory-based studies of conditional reinstatement with animals and non-fearful humans (Halladay et al., 2012; Rescorla & Heth, 1975; Sokol & Lovibond, 2012; Krisch et al., 2020; Krisch et al., 2021) to a clinical sample of those with comorbid phobias. While having some limitations relative to in vivo exposure, VRET is a valid approach for addressing the previous ethical issues of conducting reinstatement research with humans (Boschen et al., 2009; Haaker et al., 2014; Hermans et al., 2005; Neumann, 2008). Moreover, VRET may increase the chances of psychotherapists administering this evidence-based intervention and individuals with specific phobia with historically low treatment

seeking may be more likely to access VRET. It is recommended that clinicians provide a comprehensive assessment of the number of phobias through a structured clinical interview and understand the phobic beliefs. If time and access is inadequate, clinicians should consider providing VRET for secondary phobias and consider the effects of conditional reinstatement in relapse prevention planning.

References

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 138-144. https://doi.org/10.1016/j.jbtep.2014.12.006

Bocchio, M., Nabavi, S., & Capogna, M. (2017). Synaptic plasticity, engrams, and network oscillations in amygdala circuits for storage and retrieval of emotional memories. *Neuron*, *94*(4), 731-743. https://doi.org/10.1016/j.neuron.2017.03.022

Borstein, P. H., & Knapp M. (1981). Self-control desensitization with a multi-phobic boy: A multiple baseline design. *Journal of Behavior Therapy and Experimental Psychiatry*, 12, 281-285. https://doi.org/10.1016/0005-7916(81)90059-8

Boschen, M. J., Neumann, D. L., & Waters, A. M. (2009). Relapse of successfully treated anxiety and fear: theoretical issues and recommendations for clinical practice. *Australian & New Zealand Journal of Psychiatry*, *43*(2), 89-100. https://doi.org/10.1080/00048670802607154

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*(1), 80. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology*, *19*(1S), 57. https://doi.org/10.1037/0278-6133.19.Suppl1.57

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological Psychiatry*, *52*(10), 976-986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445-466. https://doi.org/10.1016/0023-9690(79)90057-2

Burstein, M., Georgiades, K., He, J. P., Schmitz, A., Feig, E., Khazanov, G. K., & Merikangas, K. (2012). Specific phobia among US adolescents: phenomenology and typology. *Depression and Anxiety*, *29*(12), 1072-1082. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.22008

Brossart, D. F., Vannest, K. J., Davis, J. L., & Patience, M. A. (2014). Incorporating nonoverlap indices with visual analysis for quantifying intervention effectiveness in single-case experimental designs. *Neuropsychological Rehabilitation*, 24, 464–491. https://doi.org.10.1080/09602011.2013.868361

Brown, T. A., & Barlow, D. H. (2014). *Anxiety and related disorders interview schedule for DSM-5 (ADIS-5L).: Lifetime version. Client interview schedule*. Oxford University Press.

Brown, E. J., Turovsky, J., Heimberg, R. G., Juster, H. R., Brown, T. A., & Barlow, D. H. (1997). Validation of the social interaction anxiety scale and the social phobia scale across the anxiety disorders. *Psychological Assessment*, 1, 21-27.

Carpenter, J. K., Moskow, D. M., & Hofmann, S. G. (2021). *Enhanced mental reinstatement of exposure to improve extinction generalization: A study on claustrophobia and MRI fear* [unpublished manuscript]. Department of Psychological and Brain Sciences, Boston University. https://doi.org/10.31234/osf.io/yrj3m

Craske, M. G. (1999). *Anxiety disorders: psychological approaches to theory and treatment*. Westview Press. https://psycnet.apa.org/record/1998-06744-000

Curtis, G., Magee, W. J., Eaton, W. W., Wittchen, H. U., & Kessler, R. C. (1998). Specific fears and phobias: Epidemiology and classification. *The British Journal of Psychiatry*, *173*(3), 212-217. https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/abs/specific-fears-and-phobias/E3E1FDE206DD1A47EFCCA2B41C5DA37C#metrics

Depla, M. F., Margreet, L., van Balkom, A. J., & de Graaf, R. (2008). Specific fears and phobias in the general population: results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Social Psychiatry and Psychiatric Epidemiology*, *43*(3), 200-208. https://doi.org/10.1007/s00127-007-0291-z

Deacon, B. J., Farrell N. R. (2013). Therapist Barriers to the Dissemination of Exposure Therapy. In: Deacon BJ, editor. *Handbook of Treating Variants and Complications in Anxiety Disorders*. https://doi-org.10.1007/978-1-4614-6458-7_23

Dirikx, T, Hermans D, Vansteenwegen, D, Baeyens, F, Eelen P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, 38, 237-251. https://doi-org.10.1016/j.jbtep.2006.04.001

Dunsmoor, J. E., Ahs, F., Zielinski, D. J., & LaBar, K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, *113*, 157-164. https://doi-org.10.1016/j.nlm.2014.02.010

Farrell, L. J., Miyamoto, T., Donovan, C. L., Waters, A. M., Krisch, K. A., & Ollendick, T. H. (2021). Virtual Reality One-Session Treatment of Child-Specific Phobia of Dogs: A Controlled, Multiple Baseline Case Series. *Behavior Therapy*, *52*(2),

478-491. https://www-clinicalkey-com-au.libraryproxy.griffith.edu.au/service/content/pdf/watermarked/1-s2.0-S0005789420300861.pdf?locale=en_AU&searchIndex=

First, M. B., Williams J. B .W., Karg R. S., & Spitzer R. L. (2015). Structured Clinical Interview for DSM-5—Research Version (SCID-5 for DSM-5, Research Version; SCID-5-RV). Arlington, VA, American Psychiatric Association.

Garcia-Palacios, A., Hoffman, H., Carlin, A., Furness III, T. A., & Botella, C. (2002). Virtual reality in the treatment of spider phobia: a controlled study. *Behaviour Research and Therapy*, *40*(9), 983-993.4 https://doi.org/10.1016/S0005-7967(01)00068-7

Gershman, S. J., Jones, C. E., Norman, K. A., Monfils, M. H., & Niv, Y. (2013). Gradual extinction prevents the return of fear: implications for the discovery of state. *Frontiers in Behavioral Neuroscience*, *7*, 164. https://doi.org/10.3389/fnbeh.2013.00164

Giles, D., Draper, N., & Neil, W (2016). Validity of the Polar V800 heart rate monitor to measure RR intervals at rest. *European Journal Applied Physiology,* 116**,** 563–571. https://doi.org/10.1007/s00421-015-3303-9

Haaker, J., Golkar, A., Hermans, D., & Lonsdorf, T. B. (2014). A review on human reinstatement studies: an overview and methodological challenges. *Learning & Memory*, *21*(9), 424-440. http://www.learnmem.org/cgi/doi/10.1101/lm.036053.114

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Hermans, D., Dirikx, T., Vansteenwegenin, D., Baeyens, F., Van den Bergh, O., & Eelen, P. (2005). Reinstatement of fear responses in human aversive

conditioning. *Behaviour Research and Therapy*, *43*(4), 533-551. https://doi.org/10.1016/j.brat.2004.03.013

Kessler, R.C., & Wang P.S. (2008). The Descriptive Epidemiology of Commonly Occurring Mental Disorders in the United States. *Annual Review Public Health*, 29, 115-129. https://doi.org/10.1146/annurev.publhealth.29.020907.090847

Kim, J. H., & Richardson, R. (2007). A developmental dissociation in reinstatement of an extinguished fear response in rats. *Neurobiology of Learning and Memory*, *88*(1), 48-57. https://doi.org/10.1016/j.nlm.2007.03.004

King, N. J., Muris, P., & Ollendick, T. H. (2004). Specific phobia. In *Anxiety Disorders in Children and Adolescents* (pp. 263-279). Guilford Press. https://psycnet.apa.org/record/2004-16376-012

Klorman, R., Weerts, T. C., Hastings, J. E., Melamed, B. G., & Lang, P. J. (1974). Psychometric description of some specific-fear questionnaires. *Behavior therapy*, *5*(3), 401-409. https://doi.org/10.1016/S0005-7894(74)80008-0

Krisch, K. A., Bandarian-Balooch, S., Neumann, D. L., & Zhong, J. (2020). Eliciting and attenuating reinstatement of fear: Effects of an unextinguished CS. *Learning and Motivation*, *71*, 101650. https://doi.org/10.1016/j.lmot.2020.101650

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2021). *Reinstatement of Fear: Exposure Treatment to Multifarious Stimuli for Individuals with Multiple Animal Fears* [Unpublished manuscript]. School of Applied Psychology, Griffith University.

Krisch, K., Bandarian-Balooch, S., O'Donnell, A. & Neumann, D. L. (2016). Virtual reality exposure therapy for specific phobia and its clinical application to reduce return of fear. *In: Hill, Z. (Ed.), Virtual Reality: Advances in Research and Applications.* Nova Publishers.

LaBar, K. S., & Phelps, E. A. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, *119*(3), 677. https://10.1037/0735-7044.119.3.677

LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and Anxiety*, *27*(2), 148-167. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.20655

Lipsitz, J. D., Fyer, A. J., Paterniti, A., & Klein, D. F. (2001). Emetophobia: Preliminary results of an Internet survey. *Depression and Anxiety*, *14*(2), 149-152. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.1058

Malbos, E., Burgess, G. H., & Lançon, C. (2020). Virtual reality and fear of shark attack: a case study for the treatment of squalophobia. *Clinical Case Studies*, *19*(5), 339-354. https://doi-org.10.1177/1534650120940014⟩

Mattick, R. P., & Clarke, J. C. (1998). Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. *Behaviour Research and Therapy*, 36(4), 455-470. https://doi.org/10.1016/S0005-7967(97)10031-6

Mertens, G., Leer, A., van Dis, E. A. M., Vermeer, L., Steenhuizen, A., van der Veen, L., & Engelhard, I. M. (2019). Secondary extinction reduces reinstatement of threat expectancy and conditioned skin conductance responses in human fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, *62*, 103-111. https://doi.org/10.1016/j.jbtep.2018.09.007

Michaliszyn, D., Marchand, A., Bouchard, S., Martel, M. O., & Poirier-Bisson, J. (2010). A randomized, controlled clinical trial of in virtuo and in vivo exposure for spider phobia. *Cyberpsychology, Behavior, and Social Networking*, *13*(6), 689-695. https://doi-org.libraryproxy.griffith.edu.au/10.1089/cyber.2009.0277

Minns, S., Levihn-Coon, A., Carl, E., Smits, J. A., Miller, W., Howard, D., ... & Powers, M. B. (2018). Immersive 3D exposure-based treatment for spider fear: A randomized controlled trial. *Journal of Anxiety Disorders*, *58*, 1-7. https://doi.org/10.1016/j.janxdis.2018.12.003

Neumann, D. L. (2008). The effects of context changes on the reinstatement of extinguished conditioned behavior in a conditioned suppression task with humans. *Learning and Motivation*, *39*(2), 114-135. https://doi.org/10.1016/j.lmot.2007.09.003

Olatunji, B. O., Cisler, J. M., & Deacon, B. J. (2010). Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. *Psychiatric Clinics*, *33*(3), 557-577. https://doi.org/10.1016/j.psc.2010.04.002

Olatunji, B. O., Deacon, B. J., & Abramowitz, J. S. (2009). The cruelest cure? Ethical issues in the implementation of exposure-based treatments. *Cognitive and Behavioral Practice*, *16*(2), 172-180. https://doi.org/10.1016/j.cbpra.2008.07.003

Ollendick, T. H., & Muris, P. (2015). The scientific legacy of Little Hans and Little Albert: Future directions for research on specific phobias in youth. *Journal of Clinical Child & Adolescent Psychology*, *44*(4), 689-706. https://doi-org.libraryproxy.griffith.edu.au/10.1080/15374416.2015.1020543

Ollendick, T. H., Öst, L. G., Reuterskiöld, L., & Costa, N. (2010). Comorbidity in youth with specific phobias: Impact of comorbidity on treatment outcome and the impact of treatment on comorbid disorders. *Behaviour Research and Therapy*, *48*(9), 827-831. https://doi.org/10.1016/j.brat.2010.05.024

Oosterink, F. M., De Jongh, A., & Hoogstraten, J. (2009b). Prevalence of dental fear and phobia relative to other fear and phobia subtypes. *European journal of oral*

sciences, *117*(2), 135-143. https://doi-org.libraryproxy.griffith.edu.au/10.1111/j.1600-0722.2008.00602.x

Opriş, D., Pintea, 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

Öst, L. G. (1987). Applied relaxation: description of a coping technique and review of controlled studies. *Behaviour Research and Therapy*, *25*(5), 397-409. https://doi.org/10.1016/0005-7967(87)90017-9

Öst, L. G. (1989). One-session treatment for specific phobias. *Behaviour Research and Therapy*, *27*(1), 1-7. https://doi.org/10.1016/0005-7967(89)90113-7

Parker, R. I., & Hagan-Burke, S. (2007). Useful effect size interpretations for single case research. *Behavior Therapy*, *38*(1), 95-105. https://doi.org/10.1016/j.beth.2006.05.002

Parker, R. I., Vannest, K. J., Davis, J. L., & Sauber, S. B. (2011). Combining nonoverlap and trend for single-case research: Tau-U. *Behavior Therapy*, *42*(2), 284-299. https://doi.org/10.1016/j.beth.2010.08.006

Pavlov, I. P. (1927). Conditioned reflexes. London: Oxford University Press.

Peters, L. (2000). Discriminant validity of the Social Phobia and Anxiety Inventory (SPAI), the Social Phobia Scale (SPS) and the Social Interaction Anxiety Scale (SIAS). *Behaviour Research and Therapy*, 38, 943-950. https://doi.org/10.1016/S0005-7967(99)00131-X

Pittig, A., Kotter, R., & Hoyer, J. (2019). The struggle of behavioral therapists with exposure: self-reported practicability, negative beliefs, and therapist distress about exposure-based interventions. *Behavior Therapy*, *50*(2), 353-366. https://doi.org/10.1016/j.beth.2018.07.003

Preusser, F., Margraf, J., & Zlomuzica, A. (2017). Generalization of extinguished fear to untreated fear stimuli after exposure. *Neuropsychopharmacology*, *42*(13), 2545-2552. https://doi.org/10.1038/npp.2017.119

Rachman, S. (1966). Studies in desensitization—II: Flooding. *Behaviour Research and Therapy*, *4*(1-2), 1-6. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman, S. (1977). The conditioning theory of fearacquisition: A critical examination. *Behaviour Research and Therapy*, *15*(5), 375-387. https://doi.org/10.1016/0005-7967(66)90037-4

Rachman, S. (1991). Neo-conditioning and the classical theory of fear acquisition. *Clinical Psychology Review*, *11*(2), 155-173. https://doi.org/10.1016/0272-7358(91)90093-A

Rachman S, Whittal M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, 27, 513-520. https://doi.org/10.1016/0005-7967(89)90085-5

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*(1), 88. https://pubmed.ncbi.nlm.nih.gov/1151290/

Rothbaum, B. O., Hodges, L., Smith, S., Lee, J. H., & Price, L. (2000). A controlled study of virtual reality exposure therapy for the fear of flying. *Journal of Consulting and Clinical Psychology*, *68*(6), 1020. https://doi.org/10.1037//0022-006X.68.6.1020

Ryan, S. M., Strege, M. V., Oar, E. L., & Ollendick, T. H. (2017). One session treatment for specific phobias in children: Comorbid anxiety disorders and treatment outcome. *Journal of Behavior Therapy and Experimental Psychiatry, 54,* 128-134.

Shadish, W. R., Hedges, L. V., Horner, R. H., & Odom, S. L. (2015). The Role of Between-Case Effect Size in Conducting, Interpreting, and Summarizing Single-

Case Research. NCER 2015-002. *National Center for Education Research*. https://eric.ed.gov/?id=ED562991

Shiban Y., Schelhorn I., Pauli, P., & Mühlberger, A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, 71, 45-53. https://doi.org/10.1016/j.brat.2015.05.014

Snell, W. E., Jr., Gum, S., Shuck, R. L., Mosley, J. A., & Hite, T. L.. (1995). The Clinical Anger Scale: Preliminary reliability and validity. *Journal of Clinical Psychology*, 51, 215-226. https://doi-org.libraryproxy.griffith.edu.au/10.1002/1097-4679(199503)51:2<215::AID-JCLP2270510211>3.0.CO;2-Z

Sokol, N., & Lovibond, P. F. (2012). Cross-US reinstatement of human conditioned fear: return of old fears or emergence of new ones?. *Behaviour Research and Therapy*, *50*(5), 313-322. https://doi.org/10.1016/j.brat.2012.02.005

Stinson, F. S., Dawson, D. A., Chou, S. P., Smith, S., Goldstein, R. B., Ruan, W. J., & Grant, B. F. (2007). The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine*, *37*(7), 1047-1059. https://doi.org/10.1017/S0033291707000086

Van Houtem, C.M., Laine M.L., Boomsma D.I., Ligthart L., Van Wijk A.J., De Jongh A. (2013). A review and meta-analysis of the heritability of specific phobia subtypes and corresponding fears. *Journal of Anxiety Disorders*, 27, 379-388. https://doi.org/10.1016/j.janxdis.2013.04.007

Vurbic, D., & Bouton, M. E. (2011). Secondary extinction in Pavlovian fear conditioning. *Learning & Behavior*, *39*(3), 202-211. https://doi.org/10.3758/s13420-011-0017-7

Wardenaar, K. J., Lim, C. C., Al-Hamzawi, A. O., Alonso, J., Andrade, L. H., Benjet, C., ... & De Jonge, P. (2017). The cross-national epidemiology of specific

phobia in the World Mental Health Surveys. *Psychological Medicine*, *47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Wittchen, H. U., Lecrubier, Y., Beesdo, K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. *Anxiety Disorders*, 23-37. https://doi-org.libraryproxy.griffith.edu.au/10.1002/9780470986844.ch2

Wolpe, J. (1958). Psychotherapy by reciprocal inhibition. *Conditional reflex: a Pavlovian Journal of Research & Therapy*, *3*(4), 234-240. https://doi.org/10.1007/BF03000093

Zbozinek, T. D., Holmes, E. A., & Craske, M. G. (2015). The effect of positive mood induction on reducing reinstatement fear: Relevance for long term outcomes of exposure therapy. *Behaviour Research and Therapy*, *71*, 65-75. https://doi.org/10.1016/j.brat.2015.05.016

Chapter 8: Preamble

The general discussion summarises the broader theoretical and clinical implications and contributions of the research project. The aims of the thesis are reiterated in accordance with how these were addressed across the research project. A summary of the integrated findings across the research project are provided and the theoretical frameworks used to explain the findings are evaluated. The assessment and treatment of multiple phobias, alternate methods to attenuate reinstatement of fear and the applicability of the findings to other mental health disorders are outlined as contributions to the field and future research directions. Strengths, limitations and specific recommendations for overcoming these limitations are specified. The thesis concludes with emphasising the clinical relevance of the research program.

Chapter 8: General Discussion

Overview of Rationale and Aims

Multiple phobias are associated with lower treatment-seeking and recovery rates compared for sufferers when compared to single phobias (Burstein et al., 2012; Curtis et al., 1998; Stinson et al., 2007; Wardenaar et al., 2017). While it is more common to meet criteria for multiple phobias (APA, 2013; Wittchen et al., 2003), there is limited research into understanding return of fear for those with multiple phobias. Prior to the current research project being conducted there was little translational research investigating reinstatement of fear from laboratory studies to clinical studies. Translational research has significant theoretical and clinical implications for how to enhance the long-term effectiveness of exposure therapy for specific phobia. In extending previous work (e.g., Halladay et al., 2012; Rescorla & Heth, 1975; Sokol & Lovibond, 2012), the present project aimed to answer the research question, can an untreated fear reinstate fear that has successfully been treated with virtual exposure-based therapy for individuals with multiple phobias? More specifically, the current research program aimed to:

1) Examine whether exposure to an unextinguished CS can elicit reinstatement of fear
2) Determine the extent to which exposure to an unextinguished CS can attenuate reinstatement of fear
3) Extend reinstatement of fear research to human clinical-analogue and clinical samples

The thesis introduced the topic and rationale for the research project (Chapter 1 and 2) and provided a literature review of VRET research focused on specific phobia and return of fear (Chapter 3). The methodology from Chapter 3 was then highlighted in Chapter 4 in which the aims of the research project were described. Subsequently, the research project addressed the aims in two experimental studies (Chapter 5 and 6) and

then extended those findings to a case study with an individual suffering from multiple phobias (Chapter 7). This final chapter synthesises the findings across the research project and provides the broader theoretical and clinical implications including: the assessment and treatment of multiple phobias, alternate methods to attenuate reinstatement of fear and the applicability of the findings to other mental health disorders. Subsequently, the strengths, the limitations and future research directions across the research project are discussed and the main points of the thesis are summarised.

Summary of Findings of Eliciting and Attenuating Conditional Reinstatement

The results across the three studies provided evidence for an unextinguished CS triggering reinstatement of fear to a previously extinguished CS. The experiment presented in Chapter 5 found that an excitatory CS which was not presented in the extinction phase could elicit reinstatement of conditioned heart rate responses and US expectancy to an extinguished CS in a human non-clinical sample ($N = 93$). Furthermore, extinction to the excitatory CS attenuated reinstatement in this study. The differential aversive conditioning experiment achieved the first and second aims of the thesis and represented the first step in addressing the third aim by extending previous laboratory-based findings in the animal literature (e.g., Halladay et al., 2012; Rescorla & Heth, 1975) to a human non-clinical sample. In aiming to contribute to the limited clinical-analogue reinstatement research (Rachman & Whittal, 1989; Shiban et al., 2015), a clinical-analogue experiment using a sample of 50 individuals with moderate to high fear levels of both spiders and rats was reported in Chapter 6. The clinical-analogue experiment showed that reinstatement of conditioned heart rate responses, avoidance ratings, and self-reported fear was triggered to a treated fear (e.g., extinguished CS) by exposure to an untreated fear (e.g., extinguished CS). Subsequently, reinstatement was reduced by VRET to the untreated fear. While the

clinical-analogue experiment contributed to the translational nature of previous research, the generalisability was limited by not employing a clinical sample with a diagnosis of phobia.

The research project concluded with a clinical case study of an individual experiencing multiple animal type phobias. The individual received individualised VRET to the primary phobia (e.g., fears of rats), received in vivo exposure to an untreated fear (e.g., fear of spiders) and subsequently received individualised VRET to the untreated fear. Visual inspection of the data did demonstrate a reinstatement of SUDs, heart rate change, and avoidance ratings following exposure to the untreated fear. However, due to the $N = 1$ design it was difficult to analyse a manipulation of conditional reinstatement. As expected, the Tau-U analyses revealed that the individual's level of fear were not reinstated across the follow-ups.

Taking the three studies together, the conditional reinstatement effect was produced in a controlled laboratory setting, to a clinical-analogue design with moderate to high fearful participants, and a case study using an individualised one session VRET for each animal type phobia. Overall, the three studies offer a further theoretical understanding of how other aversive events can trigger reinstatement (Halladay et al., 2012; Rescorla & Heth, 1975; Sokol & Lovibond, 2012) and offers an approach to reduce the risk of this form of reinstatement.

Theoretical Applications of the Integrated Findings

Several theoretical models have been applied to explain the findings across the research project. Bouton's contextual memory model (Bouton, 1993, 2002, 2004; Bouton & Bolles, 1979) has been utilised to, at least partially, explain the findings of conditional reinstatement across the research program. The CS-noUS has been proposed to only be retrieved from memory in the extinction context (Bouton, 1993) and the CS-US association is relatively context independent and will be retrieved from memory in

all contexts, except for the extinction context (Bouton, 1993). The findings of conditional reinstatement could reflect that the CS-US association was retrieved by similar contextual cues of the unextinguished CS and extinguished CS (e.g., unpredictable movements and the participant perceiving they have no control over the animal). In applying this model, it would be expected to that the attenuation of the primary fear or extinguished CS (e.g., rat) would generalise to the unextinguished CS (spider) due to retrieving similar contextual cues and thus the CS-noUS association. However, this did not occur across the three studies of the research project.

The findings from the current study are also inconsistent with previous generalisation of extinction findings for how exposure to treated stimuli (i.e., spiders) partially reduced fear to a conceptually and perceptually related untreated stimuli (i.e., cockroaches; Preusser et al., 2017). The similarity between the treated stimuli and untreated stimuli may explain the differences between the results (Dunsmoor & Murphy, 2015; Dunsmoor & Paz, 2015), as spiders and cockroaches have been proposed to be more conceptually and perceptually related than spiders, rats and snakes. Furthermore, spiders and rats also have distinctions such as animal class (e.g., arachnid compared to a mammal), and different features (e.g., spiders have an exoskeleton, no tail and 8 legs compared to rats which have an endoskeleton, a tail, and 4 legs). The findings presented in Chapter 5 and 6 indicated that the context alone did not elicit reinstatement, consistent with Halladay et al. (2012). While the role of context has been useful to explain renewal of fear (Bouton, 1993, 2002) and reinstatement of fear, other theoretical frameworks may also account for the finding of conditional reinstatement.

In highlighting the affective properties of the stimulus, the valence-reinstatement theory (Dirikx, et al., 2004; Dirikx, et al., 2007; Hermans, et al., 2005; Zbozinek et al., 2015) may account for conditional reinstatement. According to this theory, the negative valence and the physiological arousal level of presenting the unextinguished CS in the

reinstatement phase may have acted as a reminder of the valence from acquisition and subsequently retrieved the CS-US association. Valence ratings were not recorded for any CSs across the studies in this thesis. Accordingly, future research investigating conditional reinstatement of fear measuring negative valence is required to determine the theoretical underpinnings. Further support for the affective properties is found in the neurobiology literature, Kellett and Kokkinidis (2004) demonstrated that stimulating the amygdala without a stimulus did not trigger reinstatement in rats but presenting rats with a novel stimulus while stimulating the amygdala resulted in reinstatement of fear. It may be that both contextual cues and affective properties are necessary to trigger reinstatement of fear and this appears to be supported in the neurobiology research.

The role of fear and other emotions included in Bouton's contextual memory model (Bouton, 1993, 2000, 2004) and within a CBT framework, has been lacking to some extent. In the case study presented in Chapter 7, the participant's underlying phobic beliefs (e.g., animal will cause fear and pain by biting me) were equivalent across her phobia of rats and spiders. The experience of fear may not only be considered as an outcome of the conditioned response but integral in triggering reinstatement in humans. Similar to the phobic belief reported in Study 3, the participants in Hemyari et al.'s (2020) and Hisa's (2003) studies stated that the primary fear was due to perceiving the rats may bite them. In the current study exposure to the secondary fear or unextinguished CS could have evoked a previous experience of fear and this may be sufficient to retrieve the CS-US association. Further neurobiology research is integral in continuing to understand the underlying neural circuitry depending on the context and affective properties of the stimulus in the reinstatement of fear phenomenon. Therapeutic approaches that base the techniques on evidence from neurobiology and consider the role of emotions such as memory reconsolidation or intensive short-term dynamic psychotherapy may be helpful to understand reinstatement of fear more

broadly. Taken together, the theoretical frameworks for reinstatement may not be mutually exclusive (Haaker et al., 2014), and several models may explain the findings of the current research program (Vervliet et al., 2013).

The Assessment and Treatment of Multiple Phobias and Reducing Reinstatement

The clinical applications of the findings involve conducting a comprehensive assessment of the number of phobic stimuli and modifying existing treatment approaches to reduce the likelihood of conditional reinstatement occurring. Given the importance of assessing for the number of fears (APA, 2013; Wittchen et al., 2002) to reduce the likelihood of conditional reinstatement, the SCID-5 with CSR ratings and specific fear questionnaires (e.g., FRQ and FSQ) were administered in the case study as part of a comprehensive assessment for specific phobia and differential diagnosis. In previous research, the ADIS-5 and Fear Survey Schedule for Children which measures children's fear towards 80 different objects and situations (FSSC; Ollendick, 1983) are typically administered in paediatric samples with anxiety disorders including specific phobia (Farrell et al., 2020; Oar et al., 2015; Ollendick et al., 2010).

However, in clinical-analogue studies with adult specific phobia samples, it appears more common to conduct self-report questionnaires for particular phobias rather than structured clinical interviews. This may result in a higher probability of inclusion of comorbid specific phobias and other disorders in adult samples. As previously mentioned, as the number of phobias increase, specific phobia resulted in reduced treatment seeking and recovery rates (Burstein et al., 2012; Curtis et al., 1998; Stinson et al., 2007; Wardenaar et al., 2017). Future studies could consider assessing the number of fears each participant endorses and measuring any differences in treatment outcomes or return of fear rates between those with single phobias or comorbid phobias. A thorough assessment of the number of fears across paediatric and adult samples

would further our understanding of the efficacy of treatments for those with comorbid phobias.

Virtual reality has recently been used in treatment in clinical settings, however virtual reality could be beneficial in the assessment of comorbid phobias and, in turn, guide treatment planning. For example, clinicians could conduct virtual BATs for an individual with numerous self-reported fears to establish a behavioural measure to assist with determining the severity and impairment for each fear. This may assist clinicians to determine treatment planning for each phobia and provide evidence for prioritising the primary phobia and subsequently using in vivo or VRET to reduce the secondary fear. As previously discussed in Chapter 3, if time, cost and/or accessibility to the stimuli is an issue in treatment, VRET could be used to conduct exposure for the different fears (e.g., fear of sharks and a blood-injection phobia). Furthermore, due to client preference for VRET (Garcia-Palacios et al., 2001) compared to in vivo exposure therapy, VRET may represent a step in the exposure hierarchy planning for multiple phobias.

The findings of the current research project suggest that the treatment of multiple phobias is important to reduce the chances of reinstatement of fear. In treating comorbid phobias it is recommended for clinicians to conduct exposure therapy in vivo for each individual feared object and/or situation. For example, an individual may meet criteria for a specific phobia for spiders and heights and if feasible the clinician could develop and conduct separate exposure hierarchies for each fear. In accordance with the present findings the primary fear should be prioritised in treatment until successful extinction of the fear has occurred and then the secondary fear should be treated.

The research project suggests that following successful exposure therapy for specific phobia that the clinician should aim to have relapse prevention planning sessions. The sessions should incorporate psychoeducation of how encountering other aversive events or untreated fears could trigger a reinstatement of their original fears.

Furthermore, suggestions for clients for how to complete exposure in vivo or in virtual reality at home could be included in the relapse prevention planning. The clinician may need to conduct booster sessions with multifarious stimuli following treatment if return of fear occurs. In considering that return of fear and relapse may not be completely eliminated, treatment programs could emphasise the importance of continuing to find opportunities to practice exposure therapy and generalise extinction learning. Modifications to exposure therapy and relapse prevention planning could increase long-term effectiveness of this treatment.

A Research Paradigm to Test Other Methods of Attenuation

The research paradigm presented in the three studies, which involved presenting VRET for an unextinguished CS, could be extended to test whether other methods can reduce standard and conditional reinstatement of fear. In particular, the experimental paradigm employed across the present studies is more clinically relevant and ethical than previous approaches (e.g., LaBar & Phelps, 2005; Norrholm et al., 2006; Kattoor et al., 2012) and could be applied in future research. Alternate methods for reducing conditional reinstatement were beyond the scope of the thesis. Conducting extinction gradually (Shiban et al., 2015), and in multiple contexts (Dunsmoor et al., 2014) in virtual reality has been found to attenuate standard reinstatement of fear and future research could investigate the possibility that these methods to reduce conditional reinstatement of fear.

Researchers have investigated more methods to reduce renewal of fear compared to the other mechanism of return of fear (Bagley & Bandarian-Balooch, 2020; Culver et al., 2011; Jessup et al., 2020; Olatunji et al., 2017; Schlund et al., 2020; Vansteenwegen et al., 2007). The methods implemented to attenuate renewal of fear could be applied to reinstatement of fear. Given that multifarious stimuli can reduce conditional reinstatement of fear and multiple similar stimuli attenuated renewal of fear (Rowe &

Craske, 1998; Shiban et al., 2015), it is possible multiple similar stimuli could attenuate reinstatement. For instance: Shiban et al. (2015) examined the effects of VRET in multiple contexts and multiple similar stimuli on eliciting renewal of fear and found that virtual multiple similar stimuli reduced renewal of fear, while virtual multiple contexts did not. Thus, applying the current research paradigm and investigating the effects of multiple similar stimuli on reinstatement of fear may be worthwhile. Furthermore, the combination of methods did not demonstrate a summation effect (Shiban et al., 2015). In contrast, a combination of methods has been found to be effective in attenuating renewal of fear including: multiple extinction contexts and context similarity in humans (Bandarian-Balooch & Neumann, 2011) and extended extinction and multiple extinction contexts in rats (Thomas et al., 2009) and in humans (Krisch et al., 2018). Given that the reinstatement research with fearful and phobic samples has not sufficiently progressed since Rachman and Whittal (1989), alternative methods of attenuation may be helpful to reduce the likelihood of standard and conditional reinstatement occurring for those with specific phobia.

Broader Application of Aversive Events Triggering Reinstatement

The implications of the research project in conjunction with previous studies (Halladay et al., 2012; Rescorla & Heth, 1975; Sokol & Lovibond, 2012) indicate the importance of other aversive experiences in triggering reinstatement. Clinical examples of reinstatement being triggered due to traumatic events have been noted in the literature. Jacobs and Nadel (1985) described a client who had successfully overcome his phobia of heights and subsequently experienced a traumatic car accident involving losing his wife and son. Following this experience of fear his height phobia and several related fears reappeared. Consistent with the current research project the client in the above example implies that encountering an untreated fear can reinstate a previously extinguished fear. An interpretation of this clinical example extends beyond the current

findings by suggesting an experience of fear during a traumatic event or novel experience of fear can return an individual's previous anxiety disorder. The current findings may suggest that following traumatic experiences phobias could be reassessed and in the case that fear has returned, a booster session for that fear should be conducted, as well as addressing any dysfunction associated with the traumatic event. This client example from the literature implicates the role of fear and how aversive events can trigger conditional reinstatement of fear in non-phobia disorders.

Relapse is common following successful exposure therapy for numerous disorders. Return of fear and the Pavlovian conditioning model have been implicated in social anxiety (Plotkin, 2001; Yeung et al., 2021), panic disorder (Arch & Craske, 2011), obsessive-compulsive disorder (OCD; Abramowitz, & Arch, 2014), PTSD (Wicking et al., 2016), and substance use disorder (Lay & Khoo, 2021). Taking into account the high comorbidity rates in mental health disorders (Roca et al., 2009; Wardenaar et al., 2017), further empirical investigations could extend the current findings by examining whether conditional reinstatement will occur in other disorders. It remains to be determined in empirically based studies whether exposure to an untreated fear can reinstate conditioned responding to a clinical problem associated with anxiety or fear but is not a phobia. For example: a client who received successful exposure and response prevention for contamination-related OCD and subsequently encountered a cockroach (for which they had an underlying phobia for) and the client then reported an increase in anxiety, obsessions and compulsions. Thus, a broader research question yet to be answered is if conditional reinstatement can be evoked by experiences of anxiety and fear in non-phobia disorders.

Strengths

Several strengths of the research project are noted, including the use of clinically relevant stimuli, control groups and multiple measures of fear. The research project

employed clinically relevant reinstating stimuli (e.g., immersive real 360 degree footage of specific animals and in vivo presentations of the animals) as opposed to the majority of previous reinstatement research which used photographs or videos of neutral faces or geometric shapes (Dirikx et al., 2004; Dirikx et al., 2007; Dirikx et al., 2009; Dunsmoor et al., 2014; Hermans et al., 2005; Gazendam & Kindt, 2012; Katoor et al., 2013; Kull et al., 2012; LaBar & Phelps, 2005, Milad et al., 2005; Norrholm et al., 2006; Sokol & Lovibond, 2012). Thus, the methodology used in the present study increased the generalisability to clinical settings (Dunsmoor & Murphy, 2014). The inclusion of control groups in reinstatement studies with human participants is not common (see Haaker et al., 2014 for a review). Control groups were implemented in the first experiment and second clinical-analogue study, therefore increasing the internal validity of the conclusions. The case study did not include a control participant in the design. However, control measures were found to have not changed as a function of the intervention.

Several studies have assessed return of fear solely through self-report measures (Dirikx et al., 2004; Hermans et al., 2005; Kindt & Soeter, 2013; Kull et al., 2012), which limits the validity of the findings (Haaker et al., 2014). The use of multiple fear indices is evidence-based due to the increase of information from various sources (Lonsdorf et al., 2017) and reflects the conceptualisation of fear as defined by three response systems (e.g., overt behaviour, verbal-cognitive, and physiological; Lang, 1968). In the present research program, fear was assessed through physiological, and self-report measures across all 3 studies and 2 out of 3 studies included physiological, self-report and behavioural measures of fear, which is consistent with some previous return of fear research (Bandarian-Balooch et al., 2015; Haaker et al., 2013b; Kindt & Soeter, 2013; Sokol & Lovibond, 2012; Shiban, et al., 2013; 2015).

Limitations and Future Research Directions

Measures of Fear

Despite the multiple psychophysiological measures of fear employed in the present research project, this may not be consistent with the specific indices used in previous research. In particular, the physiological measures differ widely in return of fear research and may result in difficulties replicating and comparing findings (Lonsdorf et al., 2017). Heart change scores were used in all three studies as the physiological measure of fear in line with some prior conditioning studies (Bandarian-Balooch et al., 2015; Culver et al., 2011; Matthews et al., 2015; Neumann & Waters, 2006). Although skin conductance is the most widely evidenced physiological index, and is found to assess associative learning and corresponds with other indices of fear learning (Constantinou et al., 2021; Lonsdorf et al., 2017). It may have been more useful and consistent with prior research to use skin conductance than heart rate as a physiological measure of fear.

As discussed previously, neurobiology research has continued to advance our understanding of reinstatement of fear. Theoretical models can be explicitly tested using the following neuroimaging techniques: electroencephalography (EEG), functional magnetic resonance imaging and functional near-infrared spectroscopy. Bouton's contextual memory model (Bouton, 1993, 2002, 2004) highlighted how extinction does not destroy the original fear learning but reflects new learning, and this has been supported in neurobiology research (Bouton et al., 2021; Myers & Davis, 2002; Quirk & Mueller, 2008). The neural processes underlying extinction in Pavlovian conditioning have been found to involve a three-part neural circuit inclusive of the amygdala, hippocampus and pre-frontal cortex (Bouton et al., 2021). Thus, there are many parallels between the behavioural and neurobiology research of extinction and theoretical models can be tested in both types of research. In continuing this research a biobehavioural model of extinction and return of fear may emerge (Bouton et al., 2021). Portable

electroencephalogram (EEG) measures could be implemented (which are now more accessible) to further understand the neural processes underlying extinction and return of fear (Xu & Zhong, 2018). To compare findings across conditioning studies, researchers could aim for methodological coherence by implementing consistent measures of fear, as highlighted in Lonsdorf et al. (2015) and portable measures of EEG could be used for clinical studies.

Clinical Sample Sizes

The research program employed a moderate sample size in the clinical-analogue study in Chapter 6 and a $N = 1$ design with an individual with multiple phobias in Chapter 7. The findings provide some evidence of eliciting and attenuating conditional reinstatement in clinical samples. In comparison, testing the hypotheses from the research project in a larger clinical sample would allow for more accurate and representative results and would further support the translation of the findings and implications to clinical settings. The high occurrence of comorbid phobias in the population (APA, 2013) may aid recruitment of a large clinical sample. Nevertheless, it has been found that individuals with comorbid phobias are less likely to seek treatment (Burstein et al., 2012; Curtis et al., 1998; Stinson et al., 2007; Wardenaar et al., 2017) and this may represent a challenge in recruiting a larger clinical sample size.

Multiple baseline designs may represent the next step in continuing the translational nature of the current research. Multiple baseline designs conducted concurrently or non-concurrently provide an ethical alternative to reversal designs and flexibility and control for novel clinical research to be conducted (Jarrett & Ollendick, 2012; Kazdin, 1980; Watson & Workman, 1981). Given that examining the current topic involves a specialised population of those with comorbid phobias a multiple baseline design may be more feasible than a randomised control trial (RCT). Similar to previous studies investigating treatment of specific phobia using multiple baseline

designs (Botella et al., 2004; Farrell et al., 2020; Oar et al., 2015; Wald, 2004), examining whether an untreated fear can trigger reinstatement to a treated fear could be examined with a larger sample of those with multiple phobias in a multiple baseline design.

The Lengths of Follow-up

The methodology of return of fear research varies (Lonsdorf et al., 2017) and so does the length of follow-up tests. In measuring return of fear, longer follow-up tests would be more representative of long-term treatment effectiveness. Across the research projects, the time period for the follow-up tests significantly varied. In Study 1 (Chapter 5) conditional reinstatement was examined with non-fearful participants with no follow-up testing which is consistent with similar research conducted on the same day (Vansteenwegen et al., 2007) or 24 hours later (Dunsmoor et al., 2014; Shiban et al., 2015). In the clinical-analogue study presented in Chapter 6, the follow-up was conducted 2 weeks post-treatment and in the case study in Chapter 7 several follow-up tests were conducted with a maximum length of three months post-treatment. The present research project had shorter follow-up periods compared to return of fear research, ranging across 24 hours (Shiban et al., 2015), 3 weeks (Rowe & Craske, 1998; Shiban et al., 2013), 3 months (Michaliszyn et al. 2010), 6 months (Botella et al., 2016; Emmelkamp, 2002; Hemyari et al., 2020; Maltby et al., 2002), 12 months (Botella et al., 2004; Rothbaum et al., 2002) and 3 years (Wiederhold & Wiederhold, 2003). In understanding the research topic the length of follow-up tests are integral to determine whether reinstatement of fear occurs and longitudinal assessments would be a valuable future research direction.

The Role of Disgust

The present research project examined reinstatement of fear for multiple animal type phobias. However, disgust is an emotion that has been implicated in the animal

subtype of specific phobia (Olatunji & Deacon, 2008; Thorpe & Salkovskis, 1998; Tolin et al., 1997). Disgust is an emotion involving revulsion towards contamination (Olatunji et al., 2010) and a mechanism of disease avoidance (Oaten et al., 2009). In comparing non-fearful participants, spider-fearful participants demonstrated significantly increased fear and disgust responding to spiders (Olatunji & Deacon, 2008; Thorpe & Salkovskis, 1998; Tolin et al., 1997). Important to the current research project, Edwards and Salkovskis (2006) found exposure to a spider led to a return of self-reported fear and disgust ratings but exposure to a disgust-eliciting stimulus resulted in higher disgust ratings but not fear ratings. Disgust sensitivity has been found to be higher for those with spider fears (Armfield & Mattiske, 1996; De Jong & Merckelbach, 1998; Sawchuk et al., 2000; Thorpe & Salkovskis, 1998; Tolin et al., 1977). The majority of research on disgust and anxiety disorders is focused on spider phobia and blood-injection phobia.

While rats have been associated with a cross-cultural disgust response due to disease avoidance (Davey et al., 1998), rats have not received much attention in the literature. The handling of rats is necessary in many educational programs and research careers especially in medicine and thus further research could examine this type of phobia (Hemyari et al., 2020). Despite the growing evidence of the role of disgust in spider, rat and snake fears it was not considered in Study 1 (Chapter 5) or Study 2 (Chapter 6). However, in the final study (Chapter 7) SUDS ratings were recorded for fear and disgust across the VRET hierarchies. While the role of disgust was beyond the scope of the thesis, it could be argued that disgust had an influence on the reinstatement effects in Study 1 and Study 2. In future reinstatement of fear research with multiple animal type phobias, disgust could be measured during the BATs as seen in Chapter 7, pilot testing could be conducted to determine if one animal is more disgust-eliciting than others, and global disgust sensitivity could also be measured.

The Use of VRET Compared to In Vivo Exposure Therapy

The VRET methodology in the research project was necessary to overcome the ethical challenges inherent in conducting reinstatement of fear research in clinical samples. Nonetheless, as highlighted in Chapter 3, the findings of the literature review demonstrate that further research may be needed to elucidate if VRET is equivalent in effectiveness to in vivo exposure therapy in the long-term. The completion rates of in vivo BATs following in vivo exposure therapy (Bandarian-Balooch et al., 2015; Oar et al., 2015; Öst, 1987) appear to be higher than the completion rates of in vivo BATs following VRET in Study 2 and 3 and previous studies (Farrell et al., 2020). While acknowledging this may reflect a superiority for in vivo exposure, a meta-analysis has found that in vivo exposure therapy, VRET, and augmented reality exposure therapy were similarly efficacious in treating small animal phobias (Suso-Ribera et al., 2019). In vivo exposure was more effective compared to VRET and augmented reality exposure therapy in distance covered in the BATs in participants who had higher avoidance ratings in the pre-treatment BATs (Suso-Ribera et al., 2019), potentially indicating that those with higher levels of fear may respond to in vivo exposure to overcome avoidance compared to the other treatment modalities.

As outlined in Chapter 3, HMDs and immersive video footage increase the ecological validity of the stimuli and thus it was chosen for the research project (Metz, 2015). However, the minimal interactivity with the stimuli has been discussed as a limitation in Chapter 3, thereby potentially limiting the sense of immersion in the virtual environment. In improving the immersion of the three studies, hand controls could have been employed, in turn greater perceived interaction with the stimuli may have led to increased self-efficacy and coping.

Augmented reality (AR) which combines VR with experiences in vivo allows for increased immersion for participants. Botella et al. (2016) conducted a RCT which

examined the efficacy between exposure therapy conducted in AR or in vivo for spider and cockroach phobia. At post-treatment in vivo exposure led to greater reductions than AR but there were no differences at follow-up between the treatments (Botella et al., 2016). The technology used in this study involved 3D virtual spiders and cockroaches transposed into real time. Augmented reality of anxiety-provoking stimuli could be implemented for multiple phobias, other anxiety disorders and other mental health disorders such as OCD and PTSD. As the VR and AR technology continues to progress, the feasibility and effectiveness of treatments will too.

Conclusion

In overcoming the ethical challenges of eliciting reinstatement of fear in human participants, the research project narrowed the gap between laboratory-based research and clinical research. The empirical studies presented in this thesis included a combination of more controlled laboratory-based research and clinical research which is integral to improve our understanding of comorbid phobias, reinstatement of fear and improve existing exposure-based treatments. The literature review and results across the experiment with non-fearful participants, the clinical-analogue study with moderate to high fearful participants, and the case study indicate the importance of addressing comorbid phobias and conducting exposure with multifarious stimuli. Importantly, the consistency of the novel findings across the laboratory-based and clinical studies is an approach reflective of the combination of scientific and clinical progress in the wider research field. Clinicians should conduct a comprehensive assessment of the number of feared objects and/or situations and treat each individual fear through VRET or in vivo exposure therapy to reduce the occurrence of conditional reinstatement. Return of fear is a precursor for relapse and the occurrence of reinstatement of fear following aversive events could be conceptualised as an opportunity to build resilience and continue to practice generalising exposure techniques to previously extinguished or new fears.

There remains great potential to extend the research area by examining conditional reinstatement and multifarious stimuli in other mental health disorders and alternate methods to attenuate reinstatement of fear, could optimise the long-term effectiveness of exposure therapy.

Disclosure Statement

The author declares there are no conflicts of interest.

Informed Consent

All participants across the studies provided informed consent verbally and by completing consent forms.

Ethical Approval

Ethical approval was granted for each study by the Griffith University Human Research Ethics Committee.

References

Abramowitz, J. S., & Arch, J. J. (2014). Strategies for improving long-term outcomes in cognitive behavioral therapy for obsessive-compulsive disorder: Insights from learning theory. *Cognitive and Behavioral Practice*, *21*(1), 20-31. https://doi.org/10.1016/j.cbpra.2013.06.004

Antony M. M., Brown T. A., & Barlow D. H (1997). Heterogeneity among specific phobia types in DSM-IV. *Behaviour Research and Therapy, 35*(12), 1089-1100. https://doi.org/10.1016/S0005-7967(97)80003-4

Arch, J. J., & Craske, M. G. (2011). Addressing relapse in cognitive behavioral therapy for panic disorder: Methods for optimizing long-term treatment outcomes. *Cognitive and Behavioral Practice*, *18*(3), 306-315. https://doi.org/10.1016/j.cbpra.2010.05.006

Armfield, J. M., & Mattiske, J. K. (1996). Vulnerability representation: the role of perceived dangerousness, uncontrollability, unpredictability and disgustingness in spider fear. *Behaviour Research and Therapy*, *34*(11-12), 899-909. https://doi.org/10.1016/S0005-7967(96)00045-9

Bandarian-Balooch, S. B., & Neumann, D. L. (2011). Effects of multiple contexts and context similarity on the renewal of extinguished conditioned behaviour in an ABA design with humans. *Learning and Motivation*, *42*(1), 53-63. https://doi.org/10.1016/j.lmot.2010.08.008

Bandarian-Balooch, S., Neumann, D. L., & Boschen, M. J. (2015). Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 138-144. https://doi.org/10.1016/j.jbtep.2014.12.006

Botella, C. M., Juan, M. C., Baños, R. M., Alcañiz, M., Guillén, V., & Rey, B. (2005). Mixing realities? An application of augmented reality for the treatment of

cockroach phobia. *Cyberpsychology & Behavior*, *8*(2), 162-171. https://doi-org.libraryproxy.griffith.edu.au/10.1089/cpb.2005.8.162

Botella, C., Pérez-Ara, M. Á., Bretón-López, J., Quero, S., García-Palacios, A., & Baños, R. M. (2016). In vivo versus augmented reality exposure in the treatment of small animal phobia: a randomized controlled trial. *PloS one*, *11*(2), e0148237. https://doi.org/10.1371/journal.pone.0148237

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *114*(1), 80. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology*, *19*(1S), 57. https://doi.org/10.1037/0278-6133.19.Suppl1.57

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological Psychiatry*, *52*(10), 976-986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445-466. https://doi.org/10.1016/0023-9690(79)90057-2

Bouton, M. E., Maren, S., & McNally, G. P. (2021). Behavioral and neurobiological mechanisms of Pavlovian and instrumental extinction learning. *Physiological Reviews*, *101*(2), 611-681. https://doi.org/10.1152/physrev.00016.2020

Burstein, M., Georgiades, K., He, J. P., Schmitz, A., Feig, E., Khazanov, G. K., & Merikangas, K. (2012). Specific phobia among US adolescents: phenomenology and typology. *Depression and Anxiety*, *29*(12), 1072-1082. https://doi-org.libraryproxy.griffith.edu.au/10.1002/da.22008

Constantinou, E., Purves, K. L., McGregor, T., Lester, K. J., Barry, T. J., Treanor, M., ... & Eley, T. C. (2021). Measuring fear: Association among different measures of fear learning. *Journal of Behavior Therapy and Experimental Psychiatry*, *70*, 101618. https://doi.org/10.1016/j.jbtep.2020.101618

Culver, N. C., Stoyanova, M., & Craske, M. G. (2011). Clinical relevance of retrieval cues for attenuating context renewal of fear. *Journal of Anxiety Disorders*, *25*(2), 284-292. https://doi.org/10.1016/j.janxdis.2010.10.002

Curtis, G., Magee, W. J., Eaton, W. W., Wittchen, H. U., & Kessler, R. C. (1998). Specific fears and phobias: Epidemiology and classification. *The British Journal of Psychiatry*, *173*(3), 212-217. https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/abs/specific-fears-and-phobias/E3E1FDE206DD1A47EFCCA2B41C5DA37C#metrics

Davey, G. C., Buckland, G., Tantow, B., & Dallos, R. (1998). Disgust and eating disorders. *European Eating Disorders Review: The Professional Journal of the Eating Disorders Association*, *6*(3), 201-211. https://doi.org/10.1016/0146-6402(92)90010-L

Depla, M. F., Margreet, L., van Balkom, A. J., & de Graaf, R. (2008). Specific fears and phobias in the general population: results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Social Psychiatry and Psychiatric Epidemiology*, *43*(3), 200-208. https://doi.org/10.1007/s00127-007-0291-z

de Jong, P. J., & Merckelbach, H. (1998). Blood-injection-injury phobia and fear of spiders: Domain specific individual differences in disgust sensitivity. *Personality and Individual Differences*, *24*(2), 153-158. https://doi.org/10.1016/S0191-8869(97)00178-5

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2004). Reinstatement of extinguished conditioned responses and negative stimulus

valence as a pathway to return of fear in humans. *Learning & Memory*, *11*(5), 549-554. http://www.learnmem.org/cgi/doi/10.1101/lm.78004

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2007). Reinstatement of conditioned responses in human differential fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, *38*(3), 237-251. https://doi.org/10.1016/j.jbtep.2006.04.001

Dirikx, T., Vansteenwegen, D., Eelen, P., & Hermans, D. (2009). Non-differential return of fear in humans after a reinstatement procedure. *Acta Psychologica*, *130*(3), 175-182. https://doi.org/10.1016/j.actpsy.2008.12.002

Dunsmoor, J. E., Ahs, F., Zielinski, D. J., & LaBar, K. S. (2014). Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiology of Learning and Memory*, *113*, 157-164. https://doi-org.10.1016/j.nlm.2014.02.010

Dunsmoor, J. E., & Murphy, G. L. (2015). Categories, concepts, and conditioning: how humans generalize fear. *Trends in cognitive sciences*, *19*(2), 73-77. https://doi.org/10.1016/j.tics.2014.12.003

Dunsmoor, J. E., & Paz, R. (2015). Fear generalization and anxiety: behavioral and neural mechanisms. *Biological psychiatry*, *78*(5), 336-343. https://doi.org/10.1016/j.biopsych.2015.04.010

Edwards, S., & Salkovskis, P. M. (2006). An experimental demonstration that fear, but not disgust, is associated with return of fear in phobias. *Journal of Anxiety Disorders*, *20*(1), 58-71. https://doi.org/10.1016/j.janxdis.2004.11.007

Emmelkamp, P. M., Krijn, M., Hulsbosch, A. M., De Vries, S., Schuemie, M. J., & van der Mast, C. A. (2002). Virtual reality treatment versus exposure in vivo: a comparative evaluation in acrophobia. *Behaviour research and therapy*, *40*(5), 509-516. https://doi.org/10.1016/S0005-7967(01)00023-7

Farrell, L. J., Miyamoto, T., Donovan, C. L., Waters, A. M., Krisch, K. A., & Ollendick, T. H. (2021). Virtual reality one-Session treatment of child-specific phobia of dogs: A controlled, multiple baseline case aeries. *Behavior Therapy*, *52*(2), 478-491. https://www-clinicalkey-com-au.libraryproxy.griffith.edu.au/service/content/pdf/watermarked/1-s2.0-S0005789420300861.pdf?locale=en_AU&searchIndex=

Garcia-Palacios, A., Hoffman, H. G., Kwong See, S., Tsai, A. M. Y., & Botella, C. (2001). Redefining therapeutic success with virtual reality exposure therapy. *CyberPsychology & Behavior*, *4*(3), 341-348. https://doi.org/10.1089/109493101300210231

Gazendam, F. J., & Kindt, M. (2012). Worrying affects associative fear learning: a startle fear conditioning study. *PLoS One*, *7*(4), e34882. https://doi.org/10.1371/journal.pone.0034882

Haaker J, Golkar A, Hermans D. Lonsdorf TB. (2014). A review on human reinstatement studies: an overview and methodological challenges. *Learning & Memory*, 21, 424-440. http://www.learnmem.org/cgi/doi/10.1101/lm.036053.114.

Halladay, L. R., Zelikowsky, M., Blair, H. T., & Fanselow, M. S. (2012). Reinstatement of extinguished fear by an unextinguished conditional stimulus. *Frontiers in Behavioral Neuroscience*, *6*, 18. https://doi.org/10.3389/fnbeh.2012.00018

Hemyari, C., Dolatshahi, B., Sahraian, A., Koohi-Hosseinabadi, O., & Zomorodian, K. (2020). Evaluation of the Effectiveness of One-and Multi-Session Exposure-Based Treatments in Reducing Biological and Psychological Responses to Rat Phobia Among Students. *Psychology Research and Behavior Management*, *13*, 665. https://doi.org.10.2147/PRBM.S256781

Hermans, D., Dirikx, T., Vansteenwegenin, D., Baeyens, F., Van den Bergh, O., & Eelen, P. (2005). Reinstatement of fear responses in human aversive conditioning. *Behaviour Research and Therapy*, *43*(4), 533-551. https://doi.org/10.1016/j.brat.2004.03.013

Hisa, C. C. (2003). Four day cognitive behavioral treatment of a rat phobic. *Cuad Hispanoam Psicol*, *3*(1), 17-22.

Hofmann, S. G., Lehman, C. L., & Barlow, D. H. (1997). How specific are specific phobias?. *Journal of Behavior Therapy and Experimental Psychiatry*, *28*(3), 233-240. https://doi.org/10.1016/S0005-7916(97)00012-8

Jacobs, W. J., & Nadel, L. (1985). Stress-induced recovery of fears and phobias. *Psychological Review*, *92*(4), 512. https://doi.org/10.1037/0033-295X.92.4.512

Jarrett, M. A., & Ollendick, T. H. (2012). Treatment of comorbid attention-deficit/hyperactivity disorder and anxiety in children: A multiple baseline design analysis. *Journal of Consulting and Clinical Psychology*, *80*(2), 239.

Jessup, S. C., Tomarken, A., Viar-Paxton, M. A., & Olatunji, B. O. (2020). Effects of repeated exposure to fearful and disgusting stimuli on fear renewal in blood-injection-injury phobia. *Journal of Anxiety Disorders*, *74*, 102272. https://doi.org/10.1016/j.janxdis.2020.102272

Kattoor, J., Gizewski, E. R., Kotsis, V., Benson, S., Gramsch, C., Theysohn, N., ... & Elsenbruch, S. (2013). Fear conditioning in an abdominal pain model: neural responses during associative learning and extinction in healthy subjects. *PloS one*, *8*(2), e51149. https://doi.org/10.1371/journal.pone.0051149

Kazdin, A. E. (1980). Obstacles in using randomization tests in single-case experimentation. *Journal of Educational Statistics*, *5*(3), 253-260. https://doi.org/10.3102/10769986005003253

Kellett, J., & Kokkinidis, L. (2004). Extinction deficit and fear reinstatement after electrical stimulation of the amygdala: Implications for kindling-associated fear and anxiety. *Neuroscience*, *127*(2), 277-287. https://doi.org/10.1016/j.neuroscience.2004.05.011

Kindt, M., & Soeter, M. (2013). Reconsolidation in a human fear conditioning study: a test of extinction as updating mechanism. *Biological Psychology*, *92*(1), 43-50. https://doi.org/10.1016/j.biopsycho.2011.09.016

Krisch, K. A., Bandarian-Balooch, S., & Neumann, D. L. (2018). Effects of extended extinction and multiple extinction contexts on ABA renewal. *Learning and Motivation*, *63*, 1-10. https://doi.org/10.1016/j.lmot.2017.11.001

Kull, S., Müller, B. H., Blechert, J., Wilhelm, F. H., & Michael, T. (2012). Reinstatement of fear in humans: autonomic and experiential responses in a differential conditioning paradigm. *Acta psychologica*, *140*(1), 43-49. https://doi.org/10.1016/j.actpsy.2012.02.007

LaBar, K. S., & Phelps, E. A. (2005). Reinstatement of conditioned fear in humans is context dependent and impaired in amnesia. *Behavioral Neuroscience*, *119*(3), 677. https://10.1037/0735-7044.119.3.677

Lang, P. J. (1968). Fear reduction and fear behavior: Problems in treating a construct. In *Research in psychotherapy conference, 3rd, May-Jun, 1966, Chicago, IL, US*. American Psychological Association. https://doi.org/10.1037/10546-004

Lay, B. P. P., & Khoo, S. Y. S. (2021). Associative processes in addiction relapse models: A review of their Pavlovian and instrumental mechanisms, history, and terminology. *Neuroanatomy and Behaviour*, *3*, e18-e18. http://dx.doi.org/10.23668/psycharchives.4900

Lipsitz, J. D., Barlow, D. H., Mannuzza, S., Hofmann, S. G., & Fyer, A. J. (2002). Clinical features of four DSM-IV–Specific Phobia subtypes. *The Journal of Nervous and Mental Disease*, *190*(7), 471-478.

Lonsdorf T. B., Haaker J., & Kalisch R. (2014b). Long-term expression of human contextual fear and extinction memories involves amygdala, hippocampus and ventromedial prefrontal cortex: A reinstatement study in two independent samples. *Social Cognition Affect Neuroscience,* https://doi.org.10.1093/scan/nsu018

Lonsdorf, T. B., Menz, M. M., Andreatta, M., Fullana, M. A., Golkar, A., Haaker, J., ... & Merz, C. J. (2017). Don't fear 'fear conditioning': Methodological considerations for the design and analysis of studies on human fear acquisition, extinction, and return of fear. *Neuroscience & Biobehavioral Reviews*, *77*, 247-285. https://doi.org/10.1016/j.neubiorev.2017.02.026

Maltby, N., Kirsch, I., Mayers, M., & Allen, G. J. (2002). Virtual reality exposure therapy for the treatment of fear of flying: A controlled investigation. *Journal of Consulting and Clinical Psychology*, *70*(5), 1112. https://doi.org.10.1037//0022-006X.70.5.1112

Marks, I. M. (1987). *Fears, phobias, and rituals: Panic, anxiety, and their disorders*. Oxford University Press on Demand.

Matthews, A., Naran, N., & Kirkby, K. C. (2015). Symbolic online exposure for spider fear: habituation of fear, disgust and physiological arousal and predictors of symptom improvement. *Journal of Behavior Therapy and Experimental Psychiatry*, *47*, 129-137. https://doi.org/10.1038/s41598-020-74170-1

Metz, R. (2015, December). Four important things to expect in virtual reality in 2016. *MIT Technology Review*. https://www.technologyreview.com/s/545011/four-important-things-to-expect-in-virtual-reality-in-2016/

Michaliszyn, D., Marchand, A., Bouchard, S., Martel, M. O., & Poirier-Bisson, J. (2010). A randomized, controlled clinical trial of in virtuo and in vivo exposure for spider phobia. *Cyberpsychology, Behavior, and Social Networking*, *13*(6), 689-695. https://doi-org.libraryproxy.griffith.edu.au/10.1089/cyber.2009.0277

Milad, M. R., Orr, S. P., Pitman, R. K., & Rauch, S. L. (2005). Context modulation of memory for fear extinction in humans. *Psychophysiology*, *42*(4), 456-464. https://doi.org/10.1111/j.1469-8986.2005.00302.x

Myers, K. M., & Davis, M. (2002). Behavioral and neural analysis of extinction. *Neuron*, *36*(4), 567-584. https://doi.org/10.1016/S0896-6273(02)01064-4

Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure. *Biological Psychology*, *73*(2), 175-185. https://doi.org/10.1016/j.biopsycho.2006.03.004

Norrholm, S. D., Jovanovic, T., Vervliet, B., Myers, K. M., Davis, M., Rothbaum, B. O., & Duncan, E. J. (2006). Conditioned fear extinction and reinstatement in a human fear-potentiated startle paradigm. *Learning & Memory*, *13*(6), 681-685. http://www.learnmem.org/cgi/doi/10.1101/lm.393906

Oar, E. L., Farrell, L. J., & Ollendick, T. H. (2015). One session treatment for specific phobias: An adaptation for paediatric blood–injection–injury phobia in youth. *Clinical Child and Family Psychology Review*, *18*(4), 370-394. https://doi.org/10.1007/s10567-015-0189-3

Oaten, M., Stevenson, R. J., & Case, T. I. (2009). Disgust as a disease-avoidance mechanism. *Psychological Bulletin*, *135*(2), 303. https://doi.org/10.1037/a0014823

Olatunji, B. O., Cisler, J., McKay, D., & Phillips, M. L. (2010). Is disgust associated with psychopathology? Emerging research in the anxiety disorders. *Psychiatry Research*, *175*(1-2), 1-10. https://doi.org/10.1016/j.psychres.2009.04.007

Olatunji, B. O., & Deacon, B. (2008). Specificity of disgust sensitivity in the prediction of fear and disgust responding to a brief spider exposure. *Journal of Anxiety Disorders*, *22*(2), 328-336. https://doi.org/10.1016/j.janxdis.2007.03.007

Olatunji, B. O., Tomarken, A., Wentworth, B., & Fritzsche, L. (2017). Effects of exposure in single and multiple contexts on fear renewal: The moderating role of threat-specific and nonspecific emotionality. *Journal of Behavior Therapy and Experimental Psychiatry*, *54*, 270-277. https://doi.org/10.1016/j.jbtep.2016.09.004

Ollendick, T. H. (1983). Reliability and validity of the revised fear survey schedule for children (FSSC-R). *Behaviour Research and Therapy*, *21*(6), 685-692. https://doi.org/10.1016/0005-7967(83)90087-6

Ollendick, T. H., Öst, L. G., Reuterskiöld, L., & Costa, N. (2010). Comorbidity in youth with specific phobias: Impact of comorbidity on treatment outcome and the impact of treatment on comorbid disorders. *Behaviour Research and Therapy*, *48*(9), 827-831 https://doi.org/10.1016/j.brat.2010.05.024

Öst, L. G. (1987). Applied relaxation: description of a coping technique and review of controlled studies. *Behaviour Research and Therapy*, *25*(5), 397-409. https://doi.org/10.1016/0005-7967(87)90017-9

Plotkin, D. P. (2001). *The effects of interoceptive exposure on fear reduction and return of fear in individuals with public speaking anxiety*. University of California, Los Angeles.

Preusser, F., Margraf, J., & Zlomuzica, A. (2017). Generalization of extinguished fear to untreated fear stimuli after exposure. *Neuropsychopharmacology*, *42*(13), 2545-2552. https://doi.org/10.1038/npp.2017.119

Quirk, G. J., & Mueller, D. (2008). Neural mechanisms of extinction learning and retrieval. *Neuropsychopharmacology*, *33*(1), 56-72. https://doi.org/10.1038/sj.npp.1301555

Rachman S, & Whittal, M. (1989). The effect of an aversive event on the return of fear. *Behaviour Research and Therapy*, 27, 513-520. https://doi.org/10.1016/0005-7967(89)90085-5

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*(1), 88. https://pubmed.ncbi.nlm.nih.gov/1151290/

Roca, M., Gili, M., Garcia-Garcia, M., Salva, J., Vives, M., Campayo, J. G., & Comas, A. (2009). Prevalence and comorbidity of common mental disorders in primary care. *Journal of Affective Disorders*, *119*(1-3), 52-58. https://doi.org/10.1016/j.jad.2009.03.014

Rothbaum, B. O., Hodges, L., Anderson, P. L., Price, L., & Smith, S. (2002). Twelve-month follow-up of virtual reality and standard exposure therapies for the fear of flying. *Journal of Consulting and Clinical Psychology*, *70*, 428-432. 10.1037//0022-006X.70.2.428

Rowe, M. K., & Craske, M. G. (1998). Effects of varied-stimulus exposure training on fear reduction and return of fear. *Behaviour Research and Therapy*, *36*(7-8), 719-734. https://doi.org/10.1016/S0005-7967(97)10017-1

Sawchuk, C. N., Lohr, J. M., Tolin, D. F., Lee, T. C., & Kleinknecht, R. A. (2000). Disgust sensitivity and contamination fears in spider and blood–injection–injury

phobias. *Behaviour Research and Therapy*, *38*(8), 753-762. https://doi.org/10.1016/S0005-7967(99)00093-5

Schlund, M. W., Ludlum, M., Magee, S. K., Tone, E. B., Brewer, A., Richman, D. M., & Dymond, S. (2020). Renewal of fear and avoidance in humans to escalating threat: Implications for translational research on anxiety disorders. *Journal of the Experimental Analysis of Behavior*, *113*(1), 153-171. https://doi.org/10.1002/jeab.565

Shiban, Y., Pauli, P., & Mühlberger, A. (2013). Effect of multiple context exposure on renewal in spider phobia. *Behaviour Research and Therapy*, *51*(2), 68-74. https://doi.org/10.1016/j.brat.2012.10.007

Shiban, Y., Schelhorn I., Pauli P., & Mühlberger A. (2015). Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: A randomized clinical trial in virtual reality. *Behaviour Research and Therapy*, 71, 45-53. https://doi.org/10.1016/j.brat.2015.05.014

Sokol, N., & Lovibond, P. F. (2012). Cross-US reinstatement of human conditioned fear: return of old fears or emergence of new ones?. *Behaviour Research and Therapy*, *50*(5), 313-322. https://doi.org/10.1016/j.brat.2012.02.005

Stinson, F. S., Dawson, D. A., Chou, S. P., Smith, S., Goldstein, R. B., Ruan, W. J., & Grant, B. F. (2007). The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine*, *37*(7), 1047-1059. https://doi.org/10.1017/S0033291707000086

Suso-Ribera, C., Fernández-Álvarez, J., García-Palacios, A., Hoffman, H. G., Bretón-López, J., Baños, R. M., ... & Botella, C. (2019). Virtual reality, augmented reality, and in vivo exposure therapy: a preliminary comparison of treatment

efficacy in small animal phobia. *Cyberpsychology, Behavior, and Social Networking*, *22*(1), 31-38. https://doi.org/10.1089/cyber.2017.0672

Thomas, B. L., Vurbic, D., & Novak, C. (2009). Extensive extinction in multiple contexts eliminates the renewal of conditioned fear in rats. *Learning and Motivation*, *40*(2), 147-159. https://doi.org/10.1016/j.lmot.2008.10.002

Thorpe, S. J., & Salkovskis, P. M. (1998). Studies on the role of disgust in the acquisition and maintenance of specific phobias. *Behaviour research and therapy*, *36*(9), 877-893. https://doi.org/10.1016/S0005-7967(98)00066-7

Tolin, D. F., Lohr, J. M., Sawchuk, C. N., & Lee, T. C. (1997). Disgust and disgust sensitivity in blood-injection-injury and spider phobia. *Behaviour Research and Therapy*, *35*(10), 949-953. https://doi.org/10.1016/S0005-7967(97)00048-X

Vansteenwegen, D., Vervliet, B., Iberico, C., Baeyens, F., Van den Bergh, O., & Hermans, D. (2007). The repeated confrontation with videotapes of spiders in multiple contexts attenuates renewal of fear in spider-anxious students. *Behaviour Research and Therapy*, *45*(6), 1169-1179. https://doi.org/10.1016/j.brat.2006.08.023

Vervliet, B., Craske, M. G., & Hermans, D. (2013). Fear extinction and relapse: state of the art. *Annual Review of Clinical Psychology*, *9*, 215-248. https://doi.org/10.1146/annurev-clinpsy-050212-185542

Wald, J. (2004). Efficacy of virtual reality exposure therapy for driving phobia: A multiple baseline across-subjects design. *Behavior Therapy*, *35*(3), 621-635. https://doi.org/10.1016/S0005-7894(04)80035-2

Wardenaar, K. J., Lim, C. C., Al-Hamzawi, A. O., Alonso, J., Andrade, L. H., Benjet, C., ... & De Jonge, P. (2017). The cross-national epidemiology of specific phobia in the World Mental Health Surveys. *Psychological Medicine*, *47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Watson, P. J., & Workman, E. A. (1981). The non-concurrent multiple baseline across-individuals design: An extension of the traditional multiple baseline design. *Journal of Behavior Therapy and Experimental Psychiatry*, *12*(3), 257-259. https://doi.org/10.1016/0005-7916(81)90055-0

Wicking, M., Steiger, F., Nees, F., Diener, S. J., Grimm, O., Ruttorf, M., ... & Flor, H. (2016). Deficient fear extinction memory in posttraumatic stress disorder. *Neurobiology of Learning and Memory*, *136*, 116-126. https://doi.org/10.1016/j.nlm.2016.09.016

Wiederhold, B. K., & Wiederhold, M. D. (2003). Three-year follow-up for virtual reality exposure for fear of flying. *CyberPsychology & Behavior*, *6*(4), 441-445. https://doi.org/10.1089/109493103322278844

Wittchen, H. U., Lecrubier, Y., Beesdo, K., & Nocon, A. (2002). Relationships Among Anxiety Disorders: Patterns and Implications. *Anxiety Disorders*, 23-37. https://doi.org/10.1002/9780470986844.ch2

Xu, J., & Zhong, B. (2018). Review on portable EEG technology in educational research. *Computers in Human Behavior*, *81*, 340-349. https://doi.org/10.1016/j.chb.2017.12.037

Yeung, R. C., Lee, C. M., & Fernandes, M. A. (2021). The influence of social anxiety-provoking contexts on context reinstatement effects. *Quarterly Journal of Experimental Psychology*, 1747021821998489. https://doi.org/10.1177/1747021821998489

Zbozinek, T. D., Holmes, E. A., & Craske, M. G. (2015). The effect of positive mood induction on reducing reinstatement fear: Relevance for long term outcomes of exposure therapy. *Behaviour Research and Therapy*, *71*, 65-75. https://doi.org/10.1016/j.brat.2015.05.016