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Doctoral Dissertation

Safety prediction driven by action mediates fear responses to height

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Abstract

Previous studies on fear extinction have primarily focused on repeated exposure to fear-inducing context without negative consequences. However, it is also possible that an individual can reduce fear responses by predicting that they can transition to a safe environment through their own actions, even if a fear-inducing context appears. Here, by conducting two virtual reality (VR) experiments (Exp 1 and Exp 2) involving height and flight scenarios, I examined whether participants' fear responses to height decrease after actively experiencing low-altitude VR flight, which allowed them to predict that they would be in a safe state by flying even if they fell from a height. Specifically, participants in the flight group actively flew over the city in VR for more than 7 minutes (active flight task). By contrast, participants in the control group passively watched the VR flight video (passive viewing task), which differed from the flight group only in that they could not control the course of the flight. Before and after the active flight or passive viewing task, both groups walked on a plank while having their skin conductance response (SCR) and subjective fear score (SFS) measured. In both Exp 1 and Exp 2, the active flight group exhibited a greater reduction in both SCR and SFS compared to the control group. Furthermore, a multivariate regression analysis of SCR using the questionnaires from Exp 2 revealed that the safety prediction driven by action has a positive contribution to the SCR reduction in the flight group. These results clarified that the ability to transition to safe states by self-actions can reduce physiological and subjective fear responses.

Chapter 1. General Introduction

1.1 Fear extinction learning

Fear extinction refers to the decrement in conditioned fear responses that occurs with repeated presentation of a conditioned fear stimulus that is unreinforced (Milad MR & Quirk GJ 2002). This process has been researched in neurobehavioral and psychological science for several decades, driving a recent surge in cellular, molecular, and computational studies due to its significant clinical relevance for treating psychiatric disorders (Phelps EA et al. 2004; Myers KM & Davis M 2007).

Through fear conditioning, an organism can associate neutral cues (conditioned stimulus, e.g., a visual stimulus such as a shape) with aversive outcomes (unconditioned stimulus, e.g., shock, loud tone). After several acquisition trials, the subject learns that the conditioned stimulus predicts the unconditioned stimulus, and subsequent presentation of the conditioned stimulus elicits fear responses, including freezing in the rodent and skin conductance responses in the human. This learned association can also be extinguished by repeatedly presenting the learned threat cue without the aversive outcome, a process known as fear extinction (LaBar KS et al. 1998; Milad MR et al. 2002; Phelps EA et al. 2004).

Threat responses acquired during Pavlovian threat conditioning often return after extinction learning, thereby patients with anxiety disorders often experience a relapse in symptoms after exposure therapy. Accordingly, there is a need for alternative methods to reduce threat response persistently. Recent

studies suggest a promising approach: safety learning incorporating "proactive coping," where individuals exert control to change an aversive situation, could provide a more robust alternative to standard extinction learning (Boeke EA et al. 2017).

Understanding the mechanisms of fear extinction is crucial for developing novel exposure-based therapies to treat phobias. Given the common theoretical premise that exposure therapy relies on mechanisms shared with fear extinction learning, research has sought to explore efficient ways to augment exposure-based therapies.

1.1.1 Biological mechanism of fear extinction

Research in rodents utilizing lesions, pharmacological manipulations, and electrophysiology has provided an increasingly detailed model of the neural circuitry of fear extinction. This extensive work suggests that the acquisition, storage, retrieval, and contextual modulation of fear extinction are supported by complex interactions among the amygdala, the ventral medial prefrontal cortex (vmPFC), and the hippocampus (Milad and Quirk, 2012). Specifically, the amygdala is understood to facilitate the initial acquisition and consolidation of the new extinction learning (Herry C et al. 2006; Sotres-Bayon F et al. 2007) while simultaneously preserving the original fear memory (Repa et al., 2001; Hartley and Phelps, 2010). The vmPFC, particularly its infralimbic (IL) region, is crucial for consolidating and retrieving the extinction memory, likely by inhibiting fear expression via

reciprocal connections with the amygdala (Quirk GJ et al. 2000; Milad MR and Quirk GJ, 2002). Furthermore, the hippocampus mediates the context-specific retrieval of the extinction memory, controlling whether the original fear response returns, via projections to both the vmPFC and the amygdala (Bouton ME, 2004; Maren S et al. 2013).

Human functional neuroimaging findings align closely with animal research, demonstrating that fear extinction depends on the integrated functioning of a conserved neural network involving the amygdala, ventromedial prefrontal cortex (vmPFC), and hippocampus (Milad MR & Quirk GJ, 2012). This cross-species consistency underscores that the neural substrates of fear extinction represent a phylogenetically fundamental mechanism, highly preserved from rodents to humans.

Mechanistically, it is proposed that when an extinguished cue is presented within the extinction training context, the hippocampus activates the vmPFC. This, in turn, stimulates inhibitory interneurons in the basolateral amygdala (BLA), which suppress output neurons in the central amygdala (CeA), thereby preventing conditioned fear responses (Herry C et al., 2010).

Functional MRI (fMRI) studies in humans have provided empirical support for this circuitry. For instance, amygdala activity significantly increases in response to the conditioned stimulus during the initial phases of extinction learning (Phelps EA et al., 2004). Subsequently, the success of extinction has been consistently associated with increased activity in the vmPFC (Kalisch R et al., 2006; Milad MR et al., 2007; Phelps EA et al., 2004). Taken together,

these findings indicate that a distinct and evolutionary conserved interaction among the amygdala, vmPFC, and hippocampus underlies the mammalian capacity for fear extinction.

1.1.2 Active avoidance

Hartley et al. demonstrated that instrumental control over receipt of shock reduced subsequent expression of a conditioned fear of shock. They showed the effects of stressor controllability, with escapable stress (ES) diminishing conditioned fear expression one week later (Hartley CA et al. 2014). Whereas ES participants exhibited successful extinction and an absence of fear recovery, fear expression in Inescapable participants was not significantly reduced through extinction learning and remained elevated the following day.

Previous studies using fMRI have suggested that active avoidance learning is based on different neural mechanisms than extinction learning. Boeke et al. showed that the experience of active control over shock reduced the conditioned fear response (Boeke EA et al. 2017). Subjects who learned to prevent a shock through an action (Master subjects) maintained low threat responses after safety learning and showed attenuated threat conditioning with novel stimuli, in contrast to those who underwent yoked extinction (Yoke subjects). In the avoidance and extinction phase, Master subjects showed an increase of striatal BOLD responses to shock omission compared with Yoke subjects. These findings suggest a differential role for the striatum in human active avoidance versus extinction learning and indicate that active avoidance

may be more effective than extinction in persistently diminishing threat responses.

The fear conditioning and extinction model has been used widely to examine the neural substrates underlying fear processes in animals and humans. While insights derived from fear conditioning are valuable for understanding fear, it is important that this model does not necessarily capture the etiology of specific phobias. This is primarily because the core symptoms of many specific phobias are often considered innate or evolutionarily prepared, rather than solely arising from associative learning or experience.

Consequently, research investigating fear extinction in phobic patients must extend beyond the confines of laboratory-based conditioned fear paradigms to include assessments conducted in ecologically relevant environments. This necessity explains the recent shift towards utilizing Virtual Reality (VR) technology in phobia research (Freitas JRS et al 2021).

1.2 Fear of heights

Acrophobia (fear of heights) is classified as a specific phobia according to major diagnostic systems, including the DSM-5 and ICD-10. It is characterized by the fear of real or simulated heights (standing on a balcony, climbing stairs, looking down from a height, etc.) It provokes severe anxiety, distress, and other debilitating symptoms like dizziness (Brandt T & Huppert D 2014; Francová A et al. 2025).

Acrophobia is recognized as one of the most prevalent anxiety disorders among specific phobias, with lifetime prevalence rates reported to range from 3.1% to 6.4% (Depla MF et al. 2008; LeBeau RT et al. 2010; Kapfhammer HP et al. 2015). As a chronic disorder, it can significantly impair an individual's life, inhibiting their ability to perform routine daily tasks (Arroll B et al. 2017).

These defensive fear reactions involve subjective fear, avoidance, and escape behaviors, accompanied by an increase in sympathetic nervous system activity as a defense mechanism against the feared state. Consequently, the measurement of the Skin Conductance Response (SCR), which captures sympathetic activation via electrodermal activity (sweating), is commonly employed as the standard physiological method for quantifying fear in acrophobia research (Diemer J et al. 2016; Bzdúšková D et al. 2022).

1.2.1 Neural basis of fear of heights

As a fundamental survival mechanism, fear of heights triggers a suite of physiological and behavioral responses in mammals, most notably increased heart rate, freezing, and avoidance. Such defensive reactions to height-related threats are well-documented as being evolutionarily conserved across various species, ranging from rodents to primates (Walk RD & Gibson EJ 1961). On the other hand, irrational or excessive fear of heights can lead to acrophobia, which interferes with normal daily activity (Depla MF et al. 2008; Arroll B et al. 2017). Although the fear of heights is an evolutionarily conserved

mechanism essential for survival, the specific neural circuits involved in processing height-related threats have long been poorly understood. However, recent advances in molecular biology in mouse models, as well as human epigenetic and fMRI studies, are progressively elucidating the complex neurobiological foundations of acrophobia.

Liu J et al. (2021) investigated the neural basis of height fear in freely behaving mice, specifically focusing on the basolateral amygdala (BLA). They identified a discrete set of BLA neurons that exhibited robust increases in firing rate, alongside elevated heart rate and freezing, selectively when the mouse was exposed to a high place. Crucially, these neurons were only activated by height threats, but not by other typical fear stimuli such as looming, acoustic startle, predatory odor, or general anxiety-inducing conditions. Furthermore, these BLA neurons were shown to process contextual threats; after fear conditioning, they developed conditioned responses to the context, but not the cue, suggesting a convergence in the processing of dangerous contextual information. The authors concluded that this unique BLA subpopulation likely integrates strong visual–vestibular inputs with plastic spatial/contextual information received from hippocampal inputs, allowing for the flexible encoding of high-place and contextual fear.

Shang Wet al. (2024) showed advanced mouse models to unravel the specific brain circuitry governing the physiological response to height threats. They discovered that the fear response is driven primarily by visual input, not vestibular input, yet is independent of the primary visual cortex (V1) and the superior colliculus (SC). This finding strongly suggests a subconscious, non-

image-forming visual pathway mediates the rapid, pre-attentive defensive response to height exposure. Crucially, the investigation identified a novel pathway connecting the ventral lateral geniculate nucleus (vLGN) to the lateral/ventrolateral periaqueductal gray (l/vlPAG) that mediates the enhancement of this fear response. The vLGN, a key component of the caudal prethalamus, acts as an integrative hub, and its inhibition significantly diminishes defensive behaviors. Furthermore, they demonstrated two distinct pathways with opposing functional roles in the height threat response: the vLGN to l/vlPAG pathway, which enhances the expression of fear of heights, and the SC to LPMR pathway, which attenuates it.

Hang Y et al (2022) identified that acrophobia is characterized by abnormal spontaneous neural activity in brain regions responsible for emotional regulation and visual processing, specifically showing lower activity in the prefrontal and orbitofrontal cortices alongside higher activity in the fusiform gyrus. The study further revealed weakened functional connectivity between these frontal regions and visual areas, with these deficits correlating directly with increased behavioral avoidance and anxiety symptoms. These results suggest that acrophobia may stem from a neurobiological impairment in the ability to appropriately inhibit threat responses and regulate fear-related behavior through cognitive and visual integration.

1.2.2 Treatment for fear of heights

In a systematic assess the efficacy of the treatments for acrophobia (Aroll B et al. 2017), treatments were categorized into several methods. Desensitization, where clients are gradually exposed to image or imagined fearful situations while employing relaxation techniques (Baker BL et al. 1973; Ressler KJ et al. 2004); In Vivo Exposure, which involves direct, real-world confrontation with height scenarios (Emmelkamp PM et al. 2002); and Virtual Reality Exposure (VRE), which utilizes computer-generated environments(Emmelkamp PM et al. 2002).

The first systematic review to compare all documented therapies for acrophobia (Aroll B et al. 2017) concluded that Desensitisation, In Vivo Exposure, and Virtual Reality Exposure (VRE) are probably effective treatments in the short term. However, this review highlighted several limitations regarding long-term efficacy: In Vivo Exposure was not found to be effective in the long term, and long-term follow-up data for Desensitisation were unavailable. Furthermore, the efficacy of VRE therapy varied depending on the measurement tool used, showing positive results on the Acrophobia Thematic Questionnaire (ATHQ) but not the Acrophobia Questionnaire (AQ).This review revealed that while some therapies are effective in the short term, their long-term efficacy remains questionable. The authors also noted that the observed equivalence between different therapies may be due to a Type II statistical error rather than true parity in effectiveness.

1.3 Exposure therapy

In the meta-analysis of exposure therapy in patients with different anxiety disorders (panic disorder, generalized anxiety disorder and social phobia), Bandelowet B al. (2015) found considerable pre-post effect sizes of d = 1.3. The underlying mechanisms of ET are not yet well understood and are subject of discussion (e.g. Craske MG et al., 2014; Rupp C et al., 2017). A systematic review (Böhnlein J et al. 2020) that investigated the factors influencing the success of exposure therapy concluded that two emotional factors significantly predicted treatment outcome: low trait anxiety and high motivation prior to the exposure therapy.

1.3.1 Virtual reality exposure therapy (VRET)

Currently, VR is considered one of the most effective tools for the treatment of phobias. Its immense potential stems from two key advantages: the precise control it affords in a laboratory setting and its great experimental flexibility. VR offers capabilities that can even surpass the constraints of reality, making it invaluable for phobia research. Numerous clinical trials and meta-analytic reviews have provided robust evidence supporting the utility of VR in treating phobias (Freitas JRS et al. 2021).

Specific phobias are among the most prevalent psychiatric disorders, causing chronic and adverse effects on everyday life (Kessler RC et al. 2012). These disorders exhibit a high rate of comorbidity, particularly with other anxiety

disorders, depression, and somatoform disorders (Trumpf et al. 2010). Consequently, international guidelines recommend exposure therapy as the standard treatment (Natl. Inst. Health Clin. Excell. 2011).

Exposure therapy is a form of cognitive behavioral therapy that aims to gradually reduce anxiety toward a feared situation by repeatedly experiencing the feared stimulus. However, the use of actual fear stimuli in in vivo exposure raises ethical concerns. Furthermore, the traditional requirement for prolonged, regular hospital visits contributes to both the psychological and economic burden on the patient .

Against this background, Virtual Reality Exposure Therapy (VRET) has become commonly utilized over the last two decades (Emmelkamp PMG. 2021). VRET offers distinct advantages, particularly in the ease with which a therapist can control the intensity, duration, and frequency of the fear stimulus. Additionally, VRET is considered more accessible than conventional in vivo exposure due to its lack of location constraint. Because VRET avoids the use of actual fear stimuli, it is also associated with reduced psychological distress for the patient (Boeldt D et al. 2019).

VRET is considered a modern variant of exposure therapy, wherein patients are exposed to their specific fear stimuli within a controlled VR environment and learn that their most feared scenario does not occur (Emmelkamp PMG et al. 2021). VRET enables individualized, gradual, controlled, immersive exposure that is easy for therapists to implement and often more acceptable to patients than in vivo or imaginal exposure (Boeldt D et al. 2019).

VRET has demonstrated its efficacy across multiple meta-analytic studies, showing therapeutic outcomes comparable to those achieved through in vivo exposure therapy ((Powers MB & Emmelkamp PMG 2008 ; Parsons TD & Rizzo AA 2008; Opriş D et al 2012; Morina N et al 2015). A systematic review of VRET efficacy for phobias reveals that VR is an effective treatment for phobias and is useful for studying specific issues, such as behavioral manipulations, that can enhance treatment outcomes (Botella C et al. 2017). The review identified eleven studies that fulfilled the selection criteria and contained pertinent information regarding the efficacy of VRET for the treatment of phobias. Consistent with previous meta-analyses (Parsons TD & Rizzo AA 2008; Powers MB & Emmelkamp PMG 2008; Botella C et al. 2017) further confirmed VRET's potential in treating phobias.

Few systematic reviews have specifically investigated deterioration rates following Virtual Reality (VR) therapy for anxiety disorders. Nevertheless, a recent study by (Fernandez-Alvarez et al. 2019) examined deterioration rates of VR therapy across 15 Randomized Controlled Trials (RCTs) for anxiety disorders. Deterioration was established using the Reliable Change Index (RCI) (Jacobson NS et al. 1984). The overall findings indicated that VR therapy deterioration rates were comparable to those observed in other active therapeutic approaches and were significantly lower than rates for patients in waiting-list control groups. Despite these encouraging results, further research is required to fully investigate the potential for long-term deterioration specifically in phobia treatment.

1.3.2 VRET for fear of heights

Some randomized controlled trials (RCTs) have demonstrated the efficacy of VRET in treating phobias. For instance, an initial Randomized Controlled Trial (RCT) demonstrated that VRET was as effective as in vivo exposure for patients with acrophobia, with the effects sustained at the 6-month follow-up (Emmelkamp PMG et al. 2002). More recently, research has focused on the feasibility of self-guided applications; an RCT using a smartphone-based VR cognitive behavioral therapy (VR CBT) for acrophobia revealed a significant reduction of symptoms post-treatment and at follow-up, concluding that VRET could be used as a stand-alone treatment without the guidance of a therapist (Donker T et al. 2019). Furthermore, a large RCT confirmed that an automated psychological intervention delivered by immersive VR is highly effective for the reduction of fear of heights, with treatment effects being at least equivalent to, and most likely superior to, the best face-to-face psychological intervention (Freeman D et al. 2018).

Bentz et al. (2021) demonstrated that repeated use of their stand-alone, smartphone-based Virtual Reality Exposure app significantly reduced avoidance behavior, as measured by the Behavioral Avoidance Test (BAT) in a real-life height situation, with an effect size comparable to in vivo treatments.

1.4 Aim of the study

The ability to flexibly readjust fear behavior when circumstances change is crucial for adaptive behavior. Specifically, when an individual transitions from a dangerous to a safe environment, it is essential to adjust the fear response and update safety predictions accordingly. However, the mechanism underlying the influence of state transition learning on fear mitigation remains largely unexplored.

Previous studies suggest that learning based on prediction and action, rather than solely on repeated experience, may also be effective for fear extinction. Instructed extinction, where fear is reduced by explicit teaching that the environment is safe ("no more danger"), suggests a reduction of fear mediated by explicit safety learning. Furthermore, active avoidance, where fear responses diminish after learning an action to prevent an aversive outcome (e.g., electric shock), has also been demonstrated as an effective strategy. These fear reduction, mediated by instruction and active avoidance behavior, may represent a distinct, novel mechanism of fear extinction driven by learning state transitions through self-initiated action. However, the detailed mechanism remains unclear. It is hypothesized that if action facilitates the learning of novel, safe environmental state transitions, this prediction-based fear extinction may also be effective for specific phobias like fear of heights.

This dissertation aims to elucidate the mechanisms of prediction-based fear extinction through VR experiments. Specifically, it investigates whether a

single experience of transitioning to an active safe state can induce fear extinction and subsequently reduce fear responses to heights.

To test this, participants with a fear of heights were randomly assigned to either a flight group or a control group. Participants in the flight group engaged in a "Flight task," flying over a virtual city for more than seven minutes. Those in the control group performed a "Passive viewing task," in which they watched a recording of the flight; this condition differed from the flight group only in the absence of volitional control over the flight path. Both before and after these tasks, all participants performed a plank task, during which their skin conductance responses (SCR) and subjective fear scores (SFS) were recorded. Additionally, a multivariate regression of SCR using the questionnaires collected after VR experiment revealed that the flight-dependent safety prediction has a positive contribution to the SCR reduction in the flight group. These results clarified that the ability to transition to safe states by self-actions can reduce physiological and subjective fear responses.

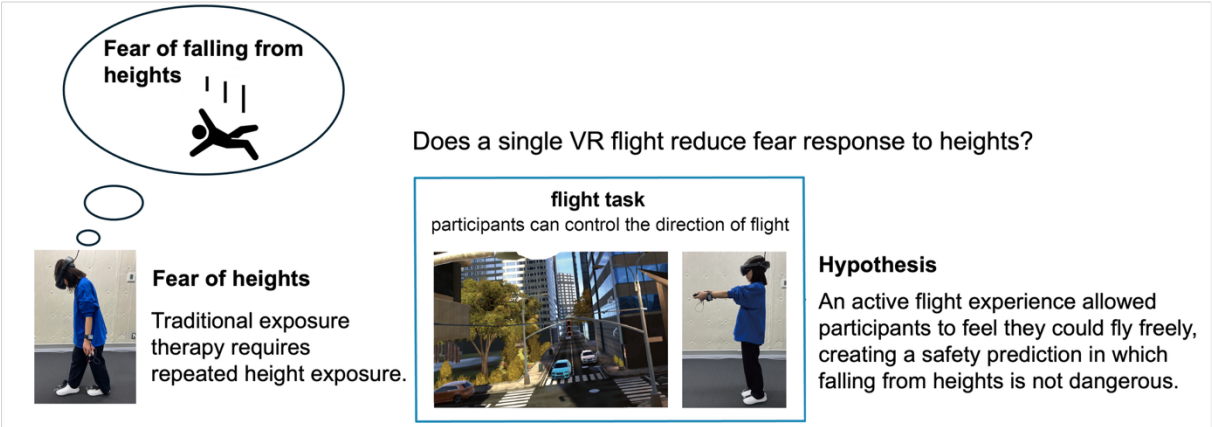


Fig. 1. Overview of the study. The aim of this study was to examine whether a single VR experience can reduce fear responses in individuals with a tendency toward acrophobia. I hypothesized that giving participants the ability to fly, enabling a transition to a safe state, would reduce fear responses to heights.

Chapter 2. Transition ability to safe states reduces fear responses to height[1]

2.1 Introduction

Discriminating between safe and dangerous environments is a crucial ability for animal survival. To implement this function, fear extinction plays an

[1] Portions of this chapter have been previously published in Proceedings of the National Academy of Sciences (Fujino M & Haruno M., 2025; https://www.pnas.org/doi/abs/10.1073/pnas.2416920122).
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essential role, where an individual learns to reduce or eliminate a conditioned fear response. Fear extinction has been mainly constructed and examined using repeated exposures to an already-learned threat cue without any aversive outcome (LaBar KS et al. 1998; Milad MR & Quirk GJ 2002; Phelps EA et al. 2004), which allows an agent to learn the new knowledge that the given context is safe.

However, it is also possible that an individual can reduce fear responses by predicting that they can transition to a safe environment even if a fear-inducing context appears. Previous studies reported that explicit instructions about safety facilitate the extinction of fear responses (Mertens G et al. 2018). Instructed extinction is a paradigm where participants are verbally informed after fear acquisition that the unconditioned stimulus will no longer be presented (Pittig A & Wong AH 2021; Luck CC & Lipp OV 2016). Although devices for delivering the unconditioned stimulus (such as shock electrodes or headphones) are often removed in studies of instructed extinction, I focus here on studies that did not remove such devices, since the removal completely changes the context. These previous studies demonstrated not only that instructions promote fear extinction (Cook SA & Harris RE 1937; Lipp OV & Edwards MS 2002), but also that they do not reduce the fear response immediately after the instruction (Wickens DD et al. 1963; Sevenster D et al. 2012; Luck CC & Lipp OV 2015; Bridger WH & Mandel IJ 1965; Mandel IJ & Bridger WH 1967) (e.g., Wickens DD et al 1963, Fig. 2 & 3). More recent studies showed that the skin conductance response (SCR) of the instructed groups decreases only after the second trial (Sevenster D, 2012, Fig. 4).

Although one study reported that the SCR of the instructed groups decreased in the first block of extinction, the precise effect of the instruction was not identified since the SCR of the two trials were averaged to compute the mean value within a block (Luck CC & Lipp OV 2015, Fig. 1). Altogether, these previous studies suggest that verbally instructed extinction mainly accelerates outcome-based extinction processes but does not represent purely prediction-based extinction.

In recent studies of fear extinction, an 'action' plays a more important role in enhancing fear extinction than previously believed (Collins KA et al. 2014; Morriss J et al. 2018; Bouton ME et al. 2021; Alemany-González M et al. 2024). Collins KA (2014) developed a virtual active avoidance task during fMRI scanning, where participants learned through trial and error to move a marker to prevent electric shocks. The study demonstrated that successful adaptive coping is modulated by a neural network involving the amygdala, striarum and mPFC, specifically revealing that the degree of connectivity between these regions predicts an individual's adaptive coping performance (Collins KA et al. 2014). Morriss J et al. (2018) investigated how the opportunity to perform an avoidance behavior modulates physiological fear by measuring skin conductance responses during a conditioning task that included both avoidable and unavoidable threats. Their results revealed that when participants were given the option to avoid a threat, their physiological arousal, measured as the difference in SCR between threat and safety cues, was significantly reduced. In other words, the conditioned response is effectively attenuated whenever an avoidance is available.

In the active avoidance paradigm, an agent learns that a behavioral response or action in the presence of a fear-inducing stimulus can avoid the negative outcome (LeDoux JE et al. 2017). A study comparing subjects with active avoidance training and classical extinction training reported that active avoidance improved fear extinction and prevented the spontaneous recovery of fear (Hartley A et al. 2014). A human functional MRI study of active avoidance showed that experiences of active control over threat engage the striatum during avoidance learning and reduce threat responses (Boeke EA et al. 2017).

Although these results clarified that an ‘action’ enhances fear extinction, they did not dissociate two possibilities: the action contributes to the reduction of association (i.e., fear memory) between the context and outcome in the repeated exposure, or the action-dependent prediction alone reduces fear responses. This inability was because active avoidance itself can be realized by either mechanism. In other words, since previous experiments of active avoidance were conducted using repeated exposures, determining whether predicting the transition to safe states contributes to the reduction of fear responses is not straightforward. To address this gap, it is necessary to introduce a new safe state during the experiment.

In addition, although previous extinction studies often rely on the association between an abstract cue and aversive stimulus, it was demonstrated that biologically fear-relevant stimuli, such as pictures of spiders and snakes, show greater resistance to extinction when used as conditioned stimulus compared to fear-irrelevant stimuli like pictures of butterflies or flowers (Hugdahl K

1978; Hugdahl K & Öhman A 1977; Ohman A et al. 1975; Soares JJF & Öhman A 1993). According to Seligman's preparedness theory (Seligman MEP 1971), humans are predisposed to quickly develop and maintain fears of certain stimuli that historically pose survival threats. It is therefore important to study the fear extinction mechanisms for innate and phylogenetic fear-relevant stimuli that also concern phobias (e.g., acrophobia). The important property of these stimuli is that people cannot erase or reduce fear responses easily even if they are cognitively aware that the stimuli are safe.

Virtual reality (VR) is a powerful tool to provide effective and well-designed behavioral contexts for experiments. Because of the advantage that participants do not need to expose themselves to the fear stimuli, several recent studies on acrophobia have utilized VR-simulated height environments (Bentz D et al. 2021). Based on the established observations that a 3D display of height in VR reliably induces strong and consistent fear responses (Yilmaz Balban M et al. 2021), our experiments (Exp 1 and Exp 2, Figure 2) used VR to examine whether the transition ability to safe states alone can reduce fear responses. Specifically, this study tested whether participants' physiological and subjective fear responses to height decrease after active low-altitude flight in VR. Importantly, participants could infer that they are in a safe state even if they fell from the height. In other words, the participants can simulate state transitions from falling (dangerous state) to a safe state by flying.

More specifically, I first conducted Exp 1 to examine the effect of active flight experience on fear responses. Ninety participants with moderate or higher levels of acrophobia were randomly assigned to the flight group and the

control group (Figure 2B). After they walked on a plank in VR (1st plank task), the flight group flew over the city (< 5 m) in VR for 7 minutes (Figure 2C). By contrast, the control group watched a video of a flight group participant's flight experience (passive viewing task). Therefore, only the flight group could control the course of the flight. Participants in both groups were asked to walk on the plank again (2nd plank task). SCR was measured as a physiological index of the fear response (Figure 2A). In addition to physiological data, a 7-item questionnaire and the subjective fear score (SFS), representing the self-reported level of fear during the two plank tasks, were collected. In Experiment 2 (74 participants), the same paradigm was used with several modifications to further explore the factors contributing to the reduction of fear responses in the flight group by incorporating new items into the original virtual reality questionnaire administered after the task.

2.2 Materials and Methods

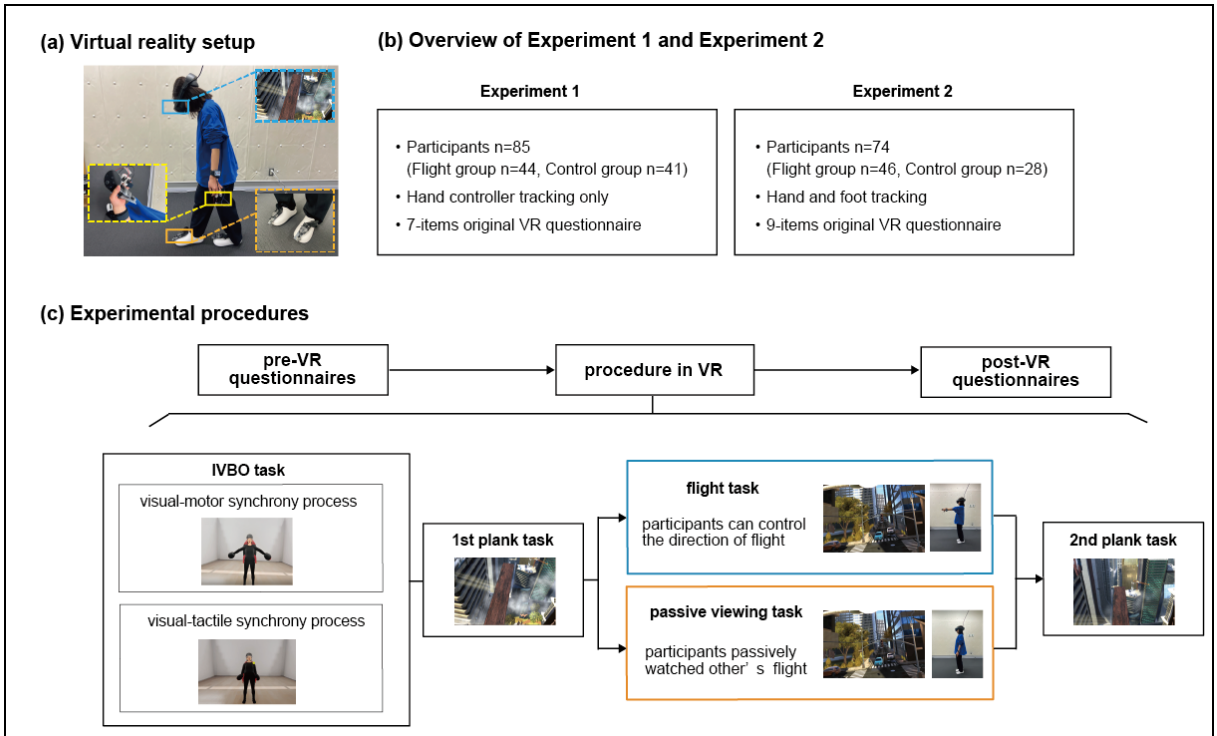


Fig. 2. (A) VR setup. The SCR was measured during the VR tasks. (B) Overview of Experiment 1 (Exp 1) and Experiment 2 (Exp 2). Exp 1 and Exp 2 differed only in the number of participants, VR foot tracking, and questionnaire items. (C) Experimental procedures. All participants completed pre- and post-VR questionnaires. After putting on the VR headset, they were involved in the illusion of a virtual body ownership (IVBO) task, which consisted of visual-motor synchrony and visual-tactile synchrony processes. In the visual-motor synchrony process, participants moved their arms and saw their avatar's arm move in the same way. In the visual-tactile synchrony process, participants watched a ball roll over their avatar's arm while simultaneously feeling a ball roll over their own arm. They also walked on a

plank at a high altitude (first plank task). Participants in the flight group flew over the city in VR for 7 min (<5 m high, active flight task), while participants in the control group watched a video of a flight group participant's flight (passive viewing task). All participants then experienced the second plank task.

2.2.1 Participants

The experimental protocol was approved by the ethics committee of the National Institute of Information and Communications Technology (B210142205) and carried out with approval and in accordance with all guidelines. Participants gave written informed consent.

In Exp 1, since reported effect sizes for VR-assisted therapy for anxiety disorders are moderate (Cohen's d=1.1) [46], I used G-power with an effect size of 0.5 (medium) and 80% power at a significance level of 0.05 and obtained the target sample size of 102. Therefore, I aimed at collecting 100 participants, finally recruiting 99 (31 females, mean ± s.d. age 22.3 ± 2.5 years) who had a fear of heights. All participants in Exp 1 met the criteria of having a pre HIQ score of moderate or above (≥ 30) and a positive pre-SCR value. The participants were randomly assigned to the flight (n = 49) and control (n = 50) groups. 8 participants were excluded for VR sickness during the VR tasks, and 1 was excluded due to an incomplete task

performance (i.e., falling from a plank). Therefore, I analyzed 44 participants in the flight group and 41 participants in the control group.

In Exp 2, 89 participants (34 females, mean ± SD age = 22.5 ± 2.6 years) were recruited. Due to technical problems, 7 participants did not complete the experiment. Additionally, 5, 2 and 1 participants were excluded due to VR sickness, low pre-experiment HIQ scores, and a negative pre-SCR value, respectively. Therefore, the final dataset for analysis included 74 participants (n = 46 in the flight group, n = 28 in the control group). To better understand the factors underlying the reduction of fear responses in the flight group, a larger number of participants was recruited for this group in Experiment 2.

The participants in Exp 1 and Exp 2 were independent, and no participants took part in both experiments. Participants received a total compensation of 4,000 yen for their participation.

2.2.2 VR setup

The main equipment was the Meta Quest Pro (Figure 2A) made by Meta that displays a 3D scene in stereo with a field of view of 106 degrees (horizontal). The device uses two screens, one per eye, each having a display resolution of 1800×1920. Its weight was 722 g. Participants could see virtual representations of their body by looking down towards their body and by looking at their virtual body on a virtual mirror. The task program was executed on a desktop computer with an Intel Core i7-12700 CPU, with 64GB

of RAM and an Nvidia GeForce RTX 3080, running on Windows 10. The task program was developed using Unreal Engine 5.0.

In Exp 2, foot tracking was added during the plank task (Figure 2A). This allowed participants to observe their virtual feet moving in synchrony with their real foot movements when they looked down.

2.2.3 Experimental procedures

The VR experiment consisted of 4 tasks: the virtual body ownership task, the 1st plank task, the active flight task or passive viewing task, and the 2nd plank task (Figure 2C). Participants experienced the tasks from the first-person perspective and used an avatar of the same gender as themselves. SCR was recorded during all tasks except for the virtual body ownership task (Figure 2A). Questionnaires were also completed by participants both before and after the experiment. Participants wore a virtual reality headset and underwent the experimental session for a duration of approximately 30 minutes.

Illusion of virtual body ownership (IVBO) task

It is established that the use of virtual avatars with synchronous multisensory experiences induces the sense of embodying a virtual body (Bohil CJ et al. 2011). Also, virtual avatars and synchronous multisensory correlations in VR enhance its effectiveness in clinical settings by inducing a sense of embodying

a virtual body (Blanke O 2012). Therefore, I conducted the illusion of a virtual body ownership (IVBO) task (Lugrin JL et al. 2015), which consisted of visual-motor synchrony (Gonzalez-Franco M et al. 2010) and visual-tactile synchrony (Blanke O 2012) processes, both essential for inducing IVBO (Kokkinara E & Slater M 2014).

In the visual-motor synchrony process, participants moved their head and arm for three minutes and observed their avatars' movements. In the visual-tactile synchrony process, the participants watched a ball roll over their avatar's arm while simultaneously feeling a ball roll over their arm (controlled by an experimenter). The motion of the ball in VR was synchronized with the motion of the ball on the real arm.

1st and 2nd Plank tasks

A commercial virtual reality game, “Richie's Plank Experience” by Toast VR, was utilized to induce fear responses to heights. Participants performed the plank task (i.e., walking on a plank at high altitude) before and after the active flight or passive viewing task.

The avatars controlled by the participants stood in front of an elevator and, after watching a car or bus pass in front of them, the participants rode the elevator to the 80th floor of the building, a height of about 300 meters, and were asked to walk on the plank. If the participants stepped off the plank, they would fall to the ground. After the plank task, they were also asked to report their SFS on a Likert scale of 0 to 10. Participants were instructed to walk to the end of the platform and return (with a time limit of 70 seconds in Exp 2). Before the second plank task, the flight group participants were instructed that they would be able to fly by the same procedure as the flight task.

Previous studies have consistently demonstrated that VR tasks involving walking on a narrow platform or plank at elevated heights induce significant subjective and objective fear (Basbasse YE et al. 2023; Maymon CN et al. 2024).

Active flight and passive viewing tasks

After the first plank task, participants in the flight group were engaged in the low-altitude virtual city flight, which lasted for 7 minutes. The rationale for establishing this specific time frame was twofold. First, preliminary pilot experiments indicated that approximately 5 to 7 minutes was the time required for nearly all participants to successfully acquire the necessary ability for self-directed flight within the virtual environment. Second, the duration of both the flight and the passive viewing task was conservatively limited to seven minutes, as exposure exceeding ten minutes was anticipated to increase the potential risk of VR sickness.

They were to fly lower than 5 meters to minimize the habituation to height. They could freely choose flight directions. By contrast, the control group participants passively watched a video of a VR flight experienced by a flight-group participant. I adopted the low-altitude flight to minimize the possibility that habituation to height contributes to the reduction of fear responses.

2.2.4 Skin conductance response (SCR) measurement

Each participant's SCR was analyzed using a peak-to-base measurement. This specific methodology was selected because the experimental design of the plank tasks deviated from the canonical fear conditioning paradigm in several key aspects.

First, while standard fear conditioning typically utilizes a brief unconditioned stimulus (US), such as an electric shock lasting less than few seconds, the current experiment involved a prolonged high-altitude exposure in virtual reality (VR) ranging from 30 to 60 seconds. Second, unlike traditional paradigms that require dozens of repetitive trials, the plank tasks in this study were administered only twice: once before and once after the intervention.

Given these temporal and structural differences, the peak-to-base calculation was deemed the most appropriate method for quantifying the fear index, following established procedures in neuroscientific literature (Milad MR et al. 2007; Indovina I et al. 2011; Gerlicher AM et al. 2018; Cortese A et al. 2024).

The baseline SCR was defined as the average of 60 seconds before starting the plank task. The SCR fear index was calculated by subtracting the baseline SCR from the maximum SCR during the plank task for the first and second plank tasks (pre-SCR fear and post-SCR fear indices, respectively). I defined the delta SCR fear index as the post-SCR fear index subtracted from the pre-SCR fear index.

2.2.5 Questionnaires

The following questionnaires were administered before, during, and after the virtual reality tasks (Figure 2C).

Attitude Toward Heights Questionnaire (ATHQ)

Before the VR tasks, all participants completed the Attitude Toward Heights Questionnaire (Abelson JL & Curtis GC 1989), a 6 item self-report acrophobia questionnaire. Participants were required to rate their attitude toward heights, including perceptions such as safe versus dangerous or threatening versus unthreatening, on a Likert scale ranging from 0 to 10. Consequently, the total score ranged from 0 to 60, where higher scores indicated a more significant fear of heights.

Heights Interpretation Questionnaire (HIQ)

Before the VR active flight or passive viewing task, all participants filled the Heights Interpretation Questionnaire (HIQ) (Steinman SA & Teachman BA 2011), which provides the self-reported acrophobia level. Participants were asked to rate anxious fears (e.g., whether they would have a panic attack at high altitudes) when imagining two different height situations (e.g., being on a ladder against a two-story house and on 15th-floor balcony). This score ranged from 16 to 80, with again higher scores indicating a greater fear of heights.

Inclusion criteria were that a participant had to be older than 18 years and have a fear of heights corresponding to a Heights Interpretation Questionnaire (HIQ) (Steinman SA & Teachman BA 2011) score of 30 or higher. I used the same cutoff as in a previous treatment trial (Freeman D et al. 2018) to decide at least a moderate fear of heights.

Original VR Questionnaire

An original questionnaire was developed by referring to the Standardized Embodiment Questionnaire (Tabel 1) proposed in a previous study (Gonzalez-Franco M & Peck TC 2018). After the VR tasks, all participants completed this questionnaire, which has 7 (Exp 1) or 9 (Exp 2) self-report questions about their feelings during the active flight or passive viewing task. This questionnaire commonly quantifies the illusion of virtual body ownership, identification with the avatar, presence, fear of falling, controllability (of the virtual self-body during active flight or during passive viewing), and VR sickness. In Exp 2, I additionally included safety prediction and enjoyment. Each score ranged from 1 (totally disagree) to 5 (totally agree). VR sickness score was used only to exclude participants who exhibited symptoms of VR sickness.

	Original VR Questionnaire (Exp 1 & Exp2)	
	Variable	Question
Q1	Body ownership lookdown	I felt that the avatar I saw when I looked down was my body.
Q2	Body ownership mirror	I felt as if the avatar I saw when looking in the mirror was my own body.
Q3	Identity	I felt identification with the avatar.

Q4	Presence	I had the sensation of being in the environment (5 is the sensation I would normally have in a place).
Q5	Fear of falling	I feared falling during the active task/passive viewing task.
Q6	Controllability	It felt like I could control the movement of my virtual body during the active flight/passive viewing task.
Q7	VR sickness	I felt VR sickness (e.g., sick, headache, dizziness).
	Original VR Questionnaire (Only Exp 2)	
Q8	Safety prediction	During the active flight task/passive viewing task, I felt falling off the plank was not dangerous because I could fly.
Q9	Enjoyment	I enjoyed the active flight task/passive viewing task.

Table 1. Original VR Questionnaire score Participants filled in the questionnaire immediately after the VR tasks. In Exp 2, two additional items, safety prediction and enjoyment, were included. Each item was scored on a 1 to 5 scale, which indicates minimum and maximum agreement, respectively.

2.5.4 Subjective Fear Score (SFS)

After each of the two plank tasks, all participants reported their fear levels on a Likert scale ranging from 0 to 10, with a higher score indicating a greater

fear of heights. The SFS for the first and second plank tasks defined the pre- and post-SFS fear indices, and the delta SFS fear index was calculated by subtracting the latter from the former.

2.2.6 Statistical analysis

A statistical analysis of SCR was performed in two steps. First, a paired t-test was conducted on the SCR fear index between the flight and control conditions. Second, group-level significance was assessed by Welch's t-test on the delta SCR fear index. All t-tests were one-sided unless otherwise indicated. A comparison of SFS between the two conditions and between groups was done using paired t-tests and the Mann–Whitney U test, respectively. I used the statsmodels 0.11.1 package in Python to assess the statistical significance of differences and set the significance level at $p < 0.05$. I also used the Mann-Whitney U test to compare the original VR questionnaire scores between the two groups.

2.2.7 Multivariate regression analysis

I employed a multivariate linear regression to identify the factors that contributed to the delta SCR. I adopted the ordinary least squares (OLS) method using the OLS function from the statsmodels.regression.linear_model module in Python.

2.3 Results

2.3.1 Questionnaire Outcomes

I first describe results for the questionnaires (ATHQ, HIQ and the original VR questionnaire) and the SFS in the two tasks and then move on to the results of the SCR data analysis.

I confirmed the baseline balance of fear of heights between the flight and control groups by using the pre-ATHQ and pre-HIQ scores. The two groups were not different in the level of fear of heights according to Welch's t-test (Exp1, ATHQ: $t(74)=-1.9$, $p=0.062$; HIQ: $t(82)=-1.8$, $p=0.080$; Exp 2, ATHQ: $t(56)=-1.52$, $p=0.13$; HIQ: $t(52)=-1.84$, $p=0.071$; two-tailed test). There was no significant difference in the initial fear levels between the two groups, though the control group showed a nominally higher mean. Consequently, the significant reduction of fear responses in the flight group cannot be attributed to a higher initial level of fear of heights.

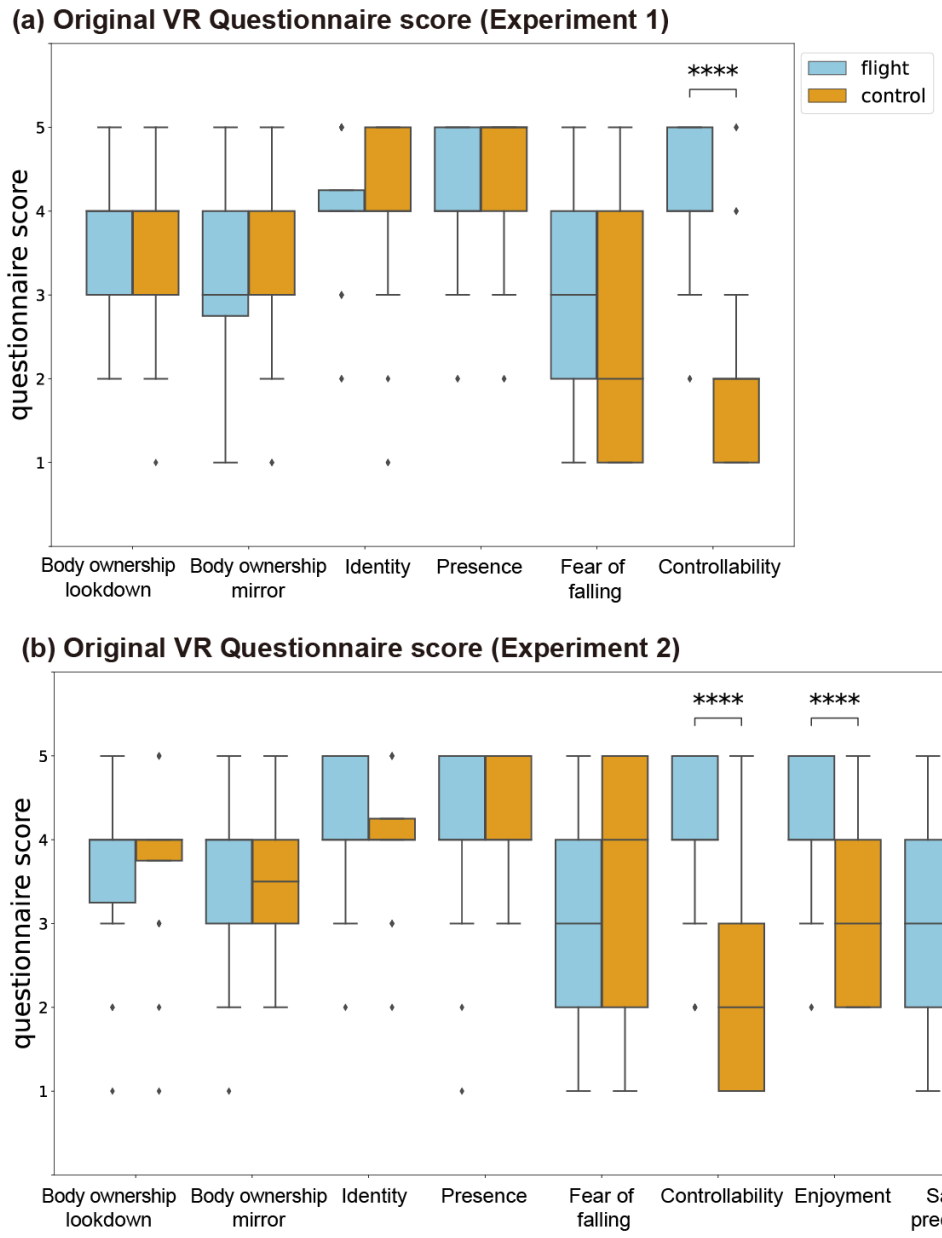


Fig. 3. (A) Scores from the original VR questionnaire in Exp 1. The Mann–Whitney U test revealed that only the controllability score was significantly

different between the flight and control groups (U = 1784.0, ****P = 9.0 × 10 −11). (B) Scores from the original VR questionnaire in Exp 2, which included additional items for enjoyment and safety prediction compared to the questionnaire used in Exp 1. The flight group showed significantly higher scores in controllability and enjoyment in comparison with the control group (Controllability: U = 1092.0, ****P = 1.1 × 10−6; Enjoyment: U = 1008.0, ****P = 9.0 × 10−5). The central line in the boxplot indicates the median and the box limits indicate the first and third quartile. The whiskers denote the interval within 1.5 times the interquartile range of the median. Data points outside this range are shown individually. ****P < 0.0001.

Figure 3A and 3B shows the results from the original VR questionnaire (Table 1) for the flight and control groups in Exp 1 (Figure 3A) and Exp 2 (Figure 3B). In both experiments, the average scores for body ownership lookdown, body ownership mirror, identity, and presence exceeded 3.2, suggesting that participants in both groups were similarly and reasonably immersed in the VR setup and their virtual body. No significant differences were found between the groups for these scores. The controllability score was different between the two groups: the flight group showed a higher controllability score (Exp 1: U= 1784.0, ****p=9.0×10^{-11}; Exp 2: U= 1092.0, ****p=1.1×10^{-6}), showing that active flight experience produced a strong sense of control of the virtual body movement during flight.

In Exp 2, I included two additional factors, enjoyment and safety prediction, as potential predictors of the reduction of fear responses (Figure 3B). The enjoyment score was significantly higher in the flight group compared to the control group (U= 1008.0, ****p=9.0×10^{-5}).

2.3.2 Subjective Fear Score

I first performed a within-group analysis of the pre- and post- SFS indices. The SFS score was significantly decreased in both groups (Exp 1, flight group: $t(43) = 10.2$, $p = 2.1 \times 10^{-13}$, control group: $t(40) = 8.43$, $p = 1.1 \times 10^{-10}$; Exp 2, flight group: $t(45) = 10.0$, $p = 2.6 \times 10^{-13}$, control group: $t(27) = 7.30$, $p = 3.6 \times 10^{-8}$; paired t-test). I next conducted a between-group comparison for the delta SFS index, which describes the difference between the pre- and post-SFS indices. As shown in Figure 4A and 4B, the flight group showed a significantly higher delta SFS index than the control group (Exp 1: U = 1088.5, *p = 0.047; Exp 2: U = 851.5, **p = 0.0079; Mann-Whitney U test), indicating that active flight experience reduces subjective fear responses.

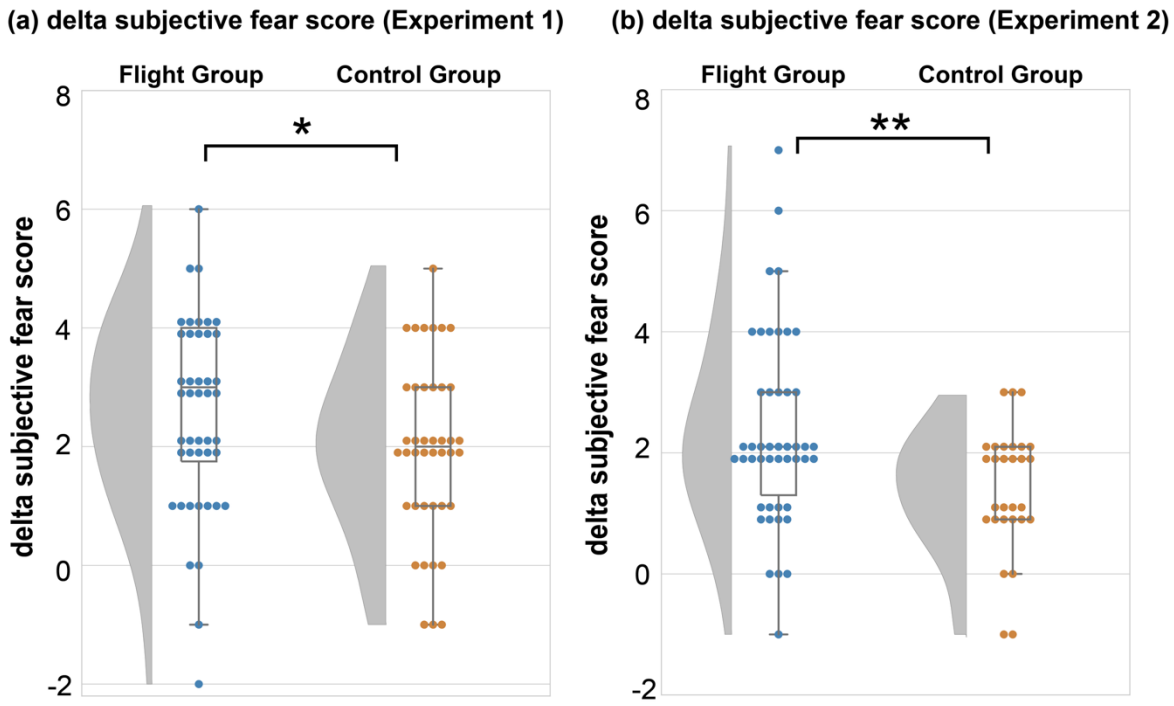


Fig. 4. (A) Group comparison of the delta SFS index in Exp 1. Each data point represents a participant's score. Blue, flight group; orange, control group. There was a significant difference between the flight and control groups (U = 1088.5, *P = 0.047, Mann–Whitney U test). (B) Group comparison of the delta SFS index in Exp 2. There was a significant difference between the flight and control groups (U = 851.5, **P = 0.0079, Mann–Whitney U test). *P < 0.05, **P < 0.01.

2.3.3 Skin Conductance Responses

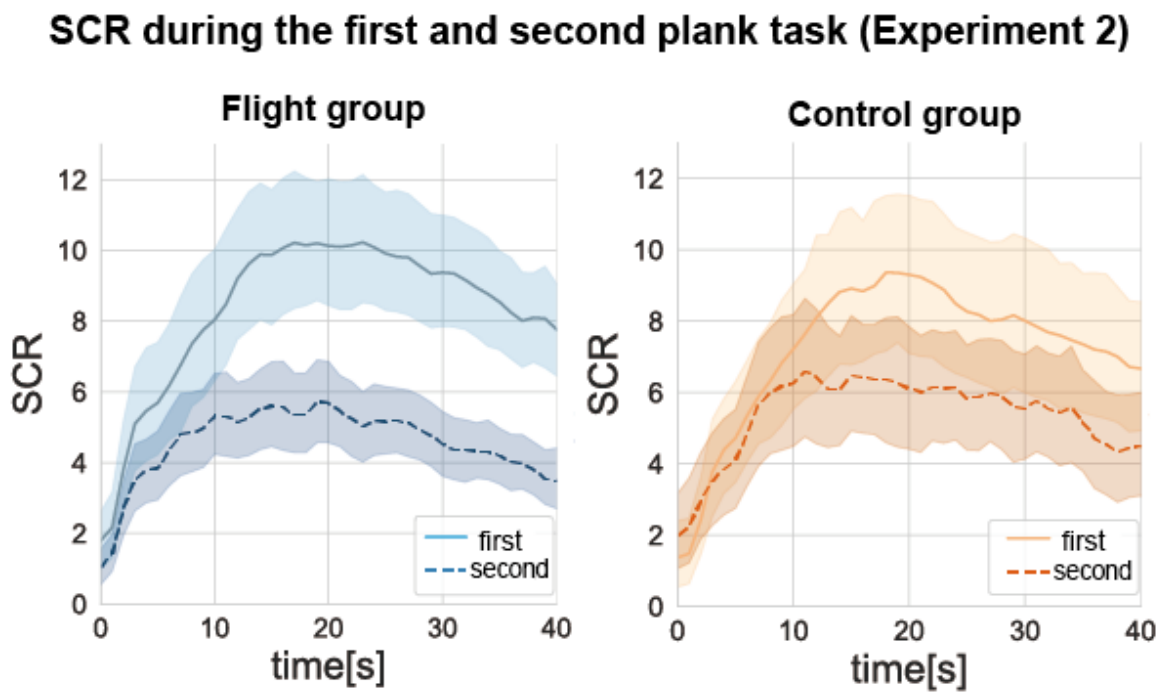


Fig. 5. (A) The time course of SCR during the plank task for participants in the flight group (Left) and control group (Right) in Exp 2. The x-axis value of 0 represents the time point at which the plank task began. In Experiment 2, a fixed time limit was implemented to facilitate a direct comparison of SCR between groups at consistent time points. The SCR values were determined by calculating the average response for each second of the task and subsequently subtracting the baseline, which was defined as the mean SCR recorded during the 60 seconds before the start of the plank task. The solid line represents the first plank task, while the dashed line represents the second plank task. Each line shows the mean SCR of all participants within the respective group, and the shaded area around the line indicates the 95% CI.

Figure 5 displays the time series of the SCR during the first and second plank tasks for flight and control participants in Exp 2, where I calculated the average of the SCR raw data per second and subtracted the baseline SCR. This analysis was possible in Exp 2 because I set a time limit of 70 seconds in the plank task for all participants. The SCR signals increased rapidly after the start of the plank task in both groups (x = 0 represents the start of the plank task). A remarkable observation is that the pre- and post-SCR showed visible differences in the flight group but not in the control group. More specifically, the flight group showed a higher pre-SCR than post-SCR, while the two SCR values were comparable in the control group.

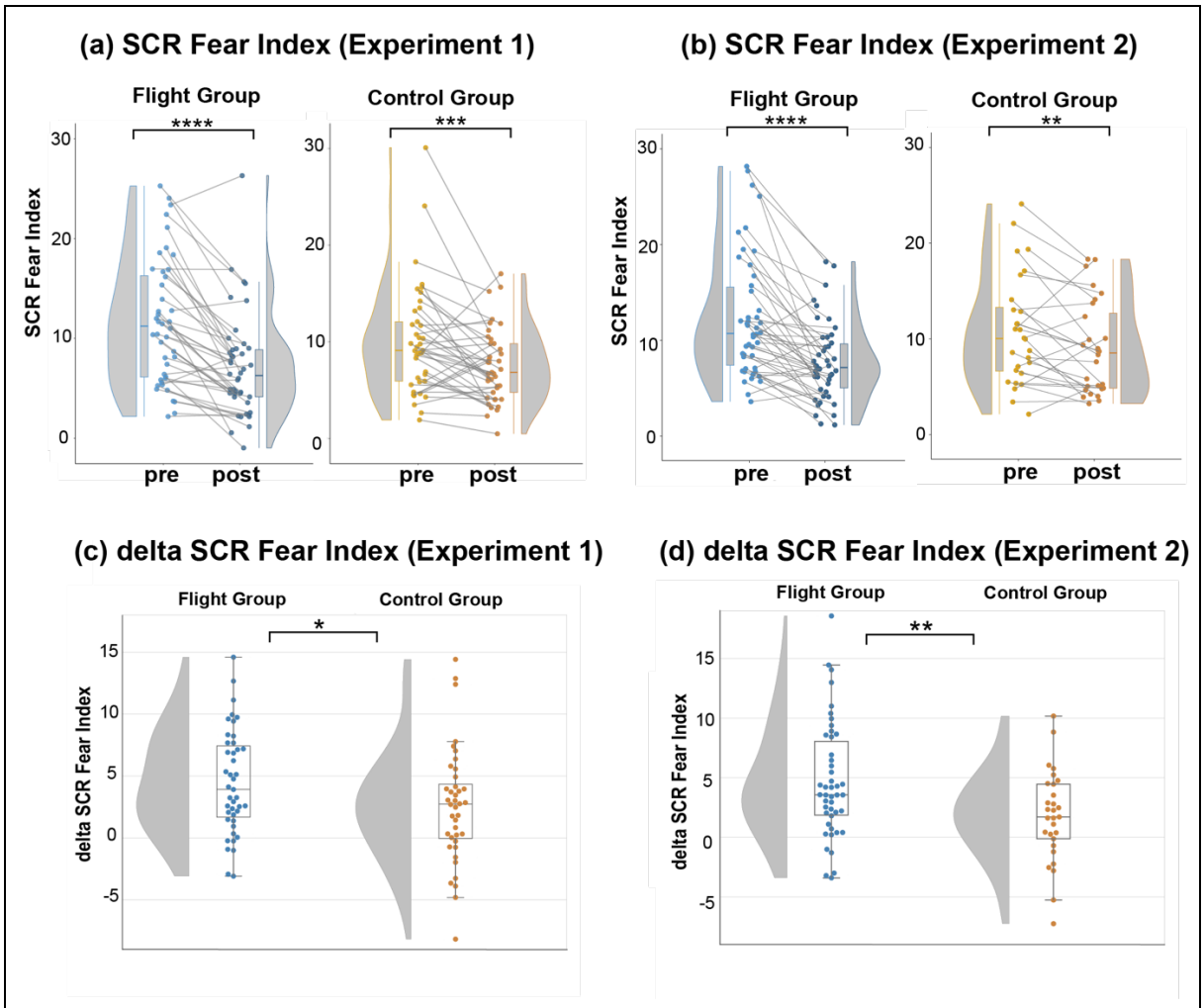


Fig. 6. (A and B) Analysis of SCR. SCR fear index of each participant during the first and second plank tasks in Exp 1 (A) and Exp 2 (B). SCR fear indices showed a significant decrease in both the flight and control groups (Exp 1, flight group: t(43) = 7.3, ****P = 2.2 × 10−9, control group: t(40) = 3.5, ***P = 5.7 × 10−4; Exp 2, flight group: t(45) = 6.5, ****P = 2.5 × 10−8, control group: t(27) = 2.6, **P = 0.0080; paired t test). (c and d) Delta SCR fear indices of each participant. The flight group showed a higher delta SCR fear

index than the control group (Exp 1: t(80) = 2.2, *P = 0.017; Exp 2: t(67) = 2.7, **P = 0.0039; Welch's t test).

To quantify the intuitive observations described above, I conducted a statistical analysis of the SCR data for all participants. Figure 6A and Figure 6B display the pre- and post-SCR fear indices for the flight and control groups in Exp 1 and Exp 2. I first conducted the Kolmogorov–Smirnov test to examine whether pre-SCRs (distributions) are different between the flight and control groups but there is no significant difference (Exp 1: D= 0.20, p=0.31; Exp 2: D= 0.19, p=0.50; two-tailed test). A significant decrease in the post-SCR fear index was observed in both groups during Exp 1 (flight group: t(43) = 7.3, $p = 2.2 \times 10^{-9}$; control group: t(40) = 3.5, $p = 5.7 \times 10^{-4}$; paired t-test, Fig. 6A). This decrease was validated in Exp 2 (flight group: t(43) = 7.3, $p = 2.2 \times 10^{-9}$; control group: t(40) = 3.5, $p = 5.7 \times 10^{-4}$; paired t-test; Figure 6B).

I conducted a between-group comparison for the delta SCR fear index, which is defined as the difference between the pre- and post- SCR fear indices. Figure 6C and Figure 6D illustrate that the flight group showed a larger delta SCR fear index than the control group in both experiments (Exp 1: t(86) = 2.2, *p = 0.017; Exp 2: t(67) = 2.7; **p = 0.0039, Welch's t-test). Additionally, I conducted the same analysis by excluding participants who exhibited a pre-SCR larger than 20 to remove the effect of high pre-SCR. The analysis confirmed that the group difference in the delta SCR fear index remained statistically significant across both experiments (Exp 1: t(76)= 2.6, **p=

0.0058; Exp 2: t(52)= 1.9; *p= 0.029, Welch's t-test; see also Fig. S1). These results altogether demonstrate that the active flight experience reduces physiological fear responses.

Previous sections have demonstrated that the active flight experience, as observed in the flight group, reduces both subjective fear scores and physiological fear responses. To further identify the specific factors contributing to the significantly larger delta SCR fear index in the flight group, a multivariate linear regression analysis was conducted. This analysis used 8 items (excluding VR sickness) of the original VR questionnaire and the ATHQ score collected in Exp 2. For the items with significant group differences (controllability) and the additional items in Exp 2 (i.e., enjoyment and safety prediction), I also incorporated interaction terms with the group. Thus, there are 13 regressors in total (Table 2).

Variables	**coefficient**	**P > |t|**
Body ownership lookdown	0.6188	0.455
Body ownership mirror	0.1262	0.865
Identity	-1.3185	0.157
Presence	0.3176	0.687
Fear of falling	0.0904	0.823
Controllability * Flight	-0.3460	0.585
Controllability * Control	0.6821	0.288
Enjoyment * Flight	-0.0257	0.970
Enjoyment * Control	-0.6740	0.444
Safety prediction * Flight	1.2552	**0.034**
Safety prediction * Control	0.0173	0.982
Pre-ATHQ	-0.3103	**0.003**
Post-ATHQ	0.1275	0.075

Table 2. Multivariate regression analysis of the delta SCR fear index. This table shows the results of the multivariate regression analysis regarding the

delta SCR fear index. The standardized β coefficients are displayed based on the questionnaire scores obtained in Experiment 2. The analysis revealed significant effects for safety prediction * Flight and pre-ATHQ.

I found a significant effect of safety prediction * Flight ($\beta_{standardized}$ = 1.26, $t(60) = 2.17$, *$p = 0.034$, two-tailed), revealing that higher safety prediction scores in the flight group are associated with lower SCR levels during the second plank task in comparison with the first plank task. I also found the effect of pre-ATHQ ($\beta_{standardized}$ = -0.32, $t(60) = -3.078$, **$p = 0.003$, two-tailed), confirming that participants with high pre-ATHQ tend to maintain high levels of fear responses during the second plank task.

In addition, an OLS regression analysis was conducted using the same questionnaire items as predictors and delta SFS as the dependent variable. This analysis revealed a significant effect of the Safety Prediction * Flight item ($\beta_{standardized} = 0.639$, $t(60) = 4.16$, $p < 0.001$, two-tailed). Specifically, participants who reported stronger predictions or confidence that the situation was safe during VR flight exhibited larger reductions in subjective fear (delta SFS). This finding further supports the involvement of safety prediction in fear reduction during the VR flight experience.

To examine whether changes in questionnaire-based acrophobia measures captured short-term fluctuations in subjective fear, a multivariate regression analysis was conducted. Changes in ATHQ scores (delta ATHQ) were entered as the independent variable, and changes in subjective fear ratings (delta SFS)

were used as the dependent variable. An ordinary least squares (OLS) regression model was fitted to the data.

In Exp 1, the regression analysis revealed no significant association between changes in ATHQ scores and reductions in subjective fear. The model explained virtually none of the variance in delta SFS ($R^2 = 0.000$, adjusted $R^2 = -0.012$), and the overall model was not significant ($F(1,83) = 0.005$, $p = 0.946$). The regression coefficient for delta ATHQ was close to zero ($\beta = -0.001$, $SE = 0.017$), indicating that changes in ATHQ scores did not predict short-term changes in subjective fear during the experimental session.

In contrast, when foot tracking was added during height walking in Exp 2, a different pattern emerged. Under this enhanced sensorimotor condition, changes in ATHQ scores showed a significant association with reductions in subjective fear ($R^2 = 0.148$, adjusted $R^2 = 0.136$; $F(1,72) = 12.52$, $p = 0.0007$). Participants who exhibited larger decreases in ATHQ scores also demonstrated greater reductions in delta SFS during the exp 2 ($\beta = 0.071$, $SE = 0.020$, $t = 3.54$, $p = 0.001$).

Thus, while Exp 1 showed a dissociation between questionnaire-based acrophobia measures and short-term subjective fear modulation, Exp 2 revealed a significant correspondence between these measures when immersive bodily interaction was increased through foot tracking.

To assess the relationship between objective fear responses and subjective fear ratings, correlation analyses were conducted separately for Experiment 1 and Experiment 2.

In Experiment 1, the correlation between objective fear responses and subjective fear scores was close to zero when all participants were considered ($r = -0.05$). Similarly weak associations were observed within each group, with a correlation of $r = -0.15$ in the flight group and $r = -0.04$ in the control group. These results indicate little to no correspondence between objective and subjective indices of fear during the single-session VR exposure in Experiment 1.

In Experiment 2, modest correlations were observed. Across all participants, the correlation between objective fear responses and subjective fear scores was $r = 0.17$. When examined by group, the flight group showed a near-zero correlation ($r = 0.04$), whereas the control group exhibited a somewhat larger, though still weak, positive correlation ($r = 0.26$).

2.4 Discussion

In this study, I conducted two VR experiments of heights and reported that the transition ability to safe states by self-actions can reduce physiological and subjective fear responses. More specifically, I tested whether participants' fear responses to heights decrease after active and low-altitude flight experiences: participants in the flight group flew over the city in VR, while participants in

the control group passively watched the flight video. Before and after the active flight or passive viewing task, both groups walked on a plank while their SCR was measured. I found that the flight group showed a larger reduction in both subjective and physiological fear responses than the control group. The multivariate linear regression of SCR data using questionnaire scores as regressors also revealed that the safety prediction based on the flight experience contributes to the SCR reduction (delta SCR fear index) in the flight group, suggesting that the active flight experience allowed participants to feel that they could fly freely, creating a new state in which falling from heights is not dangerous.

One may think that the differential physiological and subjective fear responses in the flight and control groups arose from the different immersion levels produced by active flight and passive viewing, respectively. However, I found not only that questionnaire scores of identity and presence were not different in the two groups (Fig. 3A and B) but also that these indices did not explain the delta SCR fear index in the flight group (Table 2), revealing that the level of immersion is not the cause of the differential fear responses. Instead, this study showed that the safety prediction based on the flight experience explains the delta SCR fear index in the flight group (Table 2). In addition, several participants commented in the post experiment interview that after the active flight task, they predicted not falling to the ground because of their flying ability such that the second plank task elicited less fear than the first. These results support our view that predicting the transition to safe states by self-actions can reduce physiological and subjective fear responses.

These findings are consistent with a previous study which reported that the sense of control by actions contributes to reduced fear responses (Hofmann SG & Hay AC 2018). In comparison, the present study revealed that the transition ability to safe states by self-actions alone can decrease physiological fear responses. In other words, the prediction of action-based state transitions can directly reduce fear responses rather than accelerate context–outcome association learning based on repeated exposures of the context–outcome pairs.

A previous study reported that active avoidance produced longer-lasting reductions in fear responses than Pavlovian avoidance (Hartley A et al. 2014; Boeke EA et al. 2017). Although these results clarified that an action enhances fear extinction, they did not identify the underlying mechanisms. The fear reduction by action-based prediction of state transitions we report in this study may account for this extra efficiency of fear extinction achieved by self-actions.

These findings may also be relevant to the distinction between model-free and model-based reinforcement learning (Daw ND et al. 2005; Gläscher J et al. 2010; Daw ND et al. 2011). The traditional approach for fear extinction with repeated exposure can be regarded as a form of model-free reinforcement learning that constructs associations among the cue (context) and outcomes, and potentially actions (O'Doherty et al., 2017). These associations are used to predict future outcomes and select behavior. In the case of fear extinction, an agent constructs a new association between context and nonaversive outcomes based on exposures (Dunsmoor JE et al. 2015). By contrast, model-based reinforcement learning predicts future outcomes by explicitly considering

context (or state) transitions by actions (Daw ND et al. 2011). It uses state transition probabilities associated with actions to calculate the expected outcome for each action. The model-based approach may well suggest a different mechanism for fear extinction based on state transitions, where the acquisition of the transition ability to safe states by an action reduces fear responses. The present results demonstrate that the prediction of action-based state transitions directly reduces fear responses, a finding consistent with the model-based learning view. Nevertheless, additional research is necessary to confirm this hypothesis. Whereas previous research on acrophobia VR exposure mainly measured the subjective state (Donker T et al. 2019; Freeman D et al. 2018; Arroll B et al. 2017; Rimer E et al. 2021), the present study showed significant reductions in both subjective and physiological fear responses. Overall, the observed correlations between objective and subjective fear measures were small in both experiments, suggesting that these indices capture partially dissociable aspects of fear. The consistently weak associations in the flight group, particularly in Experiment 2, may reflect the engagement of higher-level cognitive or predictive processes that modulate subjective fear independently of physiological fear responses. In contrast, the slightly stronger association observed in the control group in Experiment 2 suggests that, in the absence of active control or agency, subjective fear may more closely track objective fear responses. Together, these findings highlight a dissociation between subjective and objective fear measures and underscore the importance of assessing both dimensions when characterizing fear modulation in immersive VR environments. It is notable that SCR and SFS did not fully correlate with each other, consistent with previous studies

(Taschereau-Dumouchel V et al. 2022; Hollenstein T & Lanteigne D 2014). Several studies suggested that physiological measurements, such as skin conductance response, represent automatic, defensive responses that are not necessarily conscious responses (LeDoux JE & Brown R 2017; LeDoux JE & Pine DS 2016; LeDoux JE 2017). Other studies reported that brain regions decoding subjective fear ratings and SCR are different (Taschereau-Dumouchel V et al. 2020). Identification of the neural substrates underlying our subjective fear ratings and SCR observations is an important future research topic.

There are several limitations in the present study. Since this study was entirely conducted in VR, it is unclear whether the effects transfer to the real world. However, previous studies have shown that a single VR experience can change interpersonal attitudes (Peck TC et al. 2013) and cognitive task performance (Banakou D et al. 2018) in the real world, suggesting that VR flight experiences may also reduce the fear of heights in real-world high altitudes. In addition, because fear responses were measured only once after the active flight task, long-term effects remain unexplored. Therefore, it is important to test whether the VR flight experiences of people with acrophobia can reduce their fear responses to real-world high places, such as rooftops, and to examine the long-term effects of the reduction. Such studies may show the clinical usefulness of the prediction-based extinction mechanism in developing more effective treatment methodologies for phobias than traditional exposure therapy.

Despite these limitations, this study demonstrated that active, low-altitude VR flights can reduce physiological and subjective fear of heights by triggering

the prediction of transitioning to safe states by self-action even after falling, providing evidence of the fear extinction mechanism using the action-based prediction of safety.

2.5 Appendix

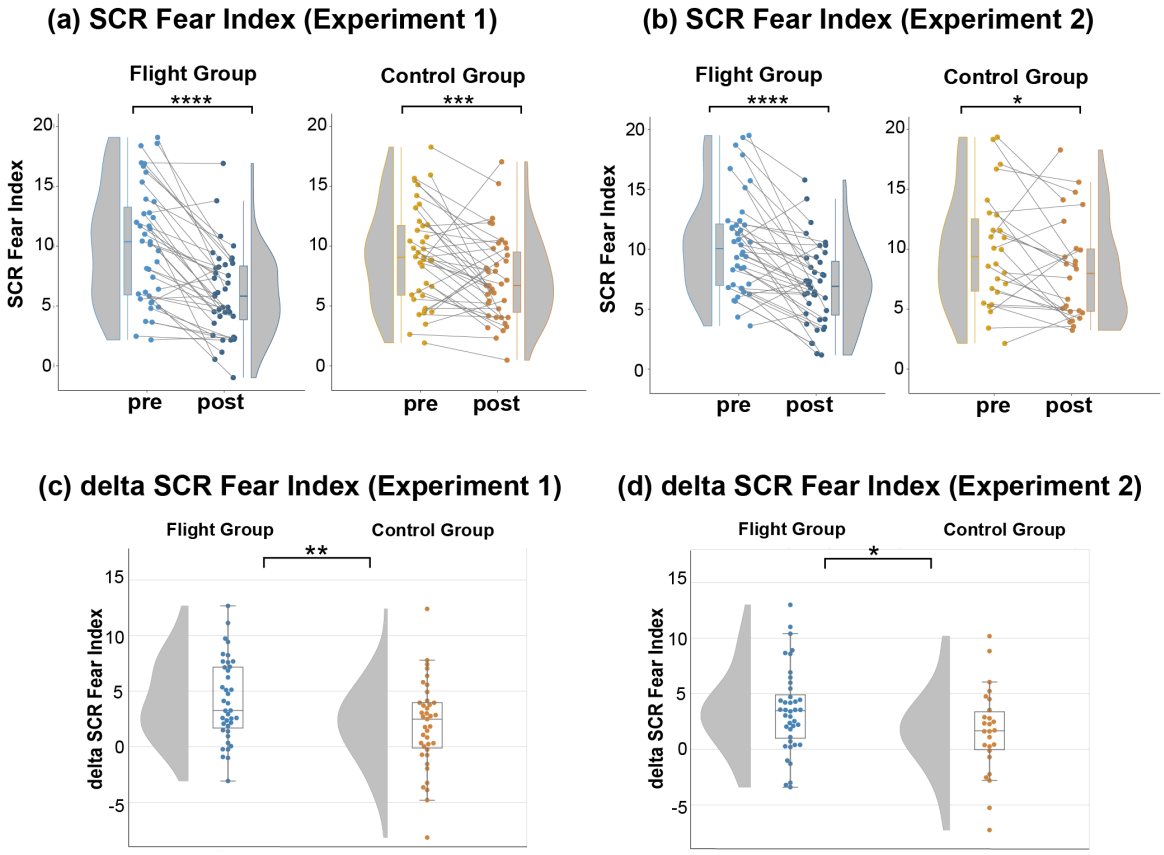


Fig. S1. To rule out the possibility that differences in pre-SCR fear index contribute to the significant difference in delta SCR fear index, participants with pre-SCR fear index above 20 were excluded. In Exp 1, 5 participants from the flight group and 2 from the control group, and in Exp 2, 6 from the flight group and 2 from the control group were excluded. Re-analysis with the same methods as in the original analysis showed that post-SCR fear index significantly decreased compared to pre-SCR fear index in both groups (Exp

1: flight group: t(38)= 7.1, ****p=9.2*10-9 ; control group: t(38)= 3.1, **p=0.0018, Exp 2: flight group: t(39)= 5.8, ****p=4.3*10-7; control group: t(25)= 2.1, *p= 0.021, paired t test, Fig. S1A and B). Moreover, the significant difference in delta SCR fear index between the two groups also remained (Exp 1: t(76)= 2.6, **p= 0.0058, Exp 2: t(52)= 1.9, *p= 0.029, Welch's t-test, Fig. S1C and D). These results suggest that the significant difference in delta SCR fear index between the two groups is not attributable to the difference in pre-SCR fear index.

Chapter 3. General Discussion and Conclusion

The present study offers novel insights into the behavioral mechanisms underlying fear extinction in acrophobia, specifically within the context of innate, evolutionarily preserved fear. I demonstrated that a single, active VR flight experience successfully established the prediction, "this environment is safe," resulting in a significant reduction in the fear response to heights. While previous research has highlighted that active avoidance and instructed extinction can enhance fear extinction, it has remained unclear whether this efficacy stems from a fundamentally new mechanism, which is learning state transitions through action, or merely the acceleration of conventional extinction based on repeated experience. The key finding is that the acquisition of novel flying ability facilitated the rapid updating of safety predictions, allowing for substantial extinction learning to occur after just a single active trial.

The novelty of this research lies in two primary areas. First, by comparing the fear reduction between the group actively undergoing the VR flight experience and the group passively viewing the same movie, I provided behavioral evidence for a novel prediction-based fear extinction. This extinction is unique in that the safety prediction is generated not purely by repetition, but by the subject's newly acquired ability to control state transitions. Such a complex, ability-dependent safety prediction has not been previously reported and may represent a distinctly human cognitive mechanism for fear processing.

Second, prediction-based fear extinction demonstrated effectiveness against prepared fear, which is innate fear rather than purely acquired through conditioned fear. Acrophobia is rooted in a conserved defensive response across species, and related phobias (such as fear of heights or snakes) are notoriously resistant to extinction compared to conditioned fears induced by stimuli like electric shocks. These results suggest a therapeutic approach for patients suffering from phobias that have historically shown lower treatment efficacy.

Furthermore, this study addresses some challenges common in conventional exposure therapy. Traditional exposure therapy often requires a minimum of three sessions spanning several weeks, demand constant guidance from a clinician, impose significant financial and psychological burdens on patients, and consequently suffer from high dropout rates. By using commercially available VR game for exposure, our approach paves the way for a more accessible, cost-effective, and less psychologically demanding (lower dropout rate) treatment. This low-threshold intervention holds immense promise for bridging the gap between available and utilized treatments for acrophobia.

Several limitations should be considered when interpreting the findings of this study. As follow-up assessments were not implemented in the current study, the long-term duration of this extinction is currently undetermined. Previous VRET interventions for acrophobia, such as those utilizing an avatar therapist (Freeman D et al., 2018) or multi-session standardized exposure (Francová et al., 2025), showed that therapeutic benefits were maintained for up to two months. However, there is no follow-up data in this study, a direct comparison

of the sustained impact of our novel mechanism is impossible. Follow-up assessments are necessary to establish how long the effect is sustained.

Second, the generalizability of our findings is limited by the participant pool. Most participants had only mild-to-moderate score of fear of heights. The regression analysis showed that participants with high pre-ATHQ scores remained highly SCR even after the intervention. This suggests that the single-session VR flight may be insufficient for individuals with severe acrophobia that significantly impairs daily functioning, potentially necessitating a longer duration or repeated use of the exposure intervention for this population.

Finally, this study only compared fear responses within the VR environment. The extent to which this demonstrated fear reduction translates to a decrease in real-world fear of heights remains an open question. Future research must address this critical translational aspect by utilizing a Behavioral Avoidance Test (BAT) in a real-life height situation to fully validate the clinical utility of this prediction-based extinction mechanism.

A crucial area for future research lies in assessing the neural mechanism underlying the prediction-based extinction demonstrated in this study. Specifically, a key question remains: does the human brain activity observed during the active VR flight experience involve circuits distinct from the regions and functions previously identified in studies of active avoidance or instructed extinction? Based on prior research in both humans and rodents, the fear reduction achieved through active avoidance training is mediated by a neural circuit involving the ventromedial prefrontal cortex (vmPFC) and the

striatum, which are critically engaged by behavioral control over aversive stimuli and prevent fear recovery (Moscarello and LeDoux, 2013; Ramirez F et al., 2015; Hartley A et al., 2014; Boeke EA et al., 2017). Furthermore, recent models suggest a functional segregation within the vmPFC, positing that the anterior vmPFC is the key hub for safety computation and integration of coping predictions, while the posterior vmPFC processes threat (Tashjian SM et al. 2021). Based on their theory, engaging in the VR flight experience may increase the neural activity of the anterior vmPFC, which is involved in safety computation.

While traditional fMRI studies on human fear extinction have predominantly relied on static images, electric shocks, and button presses in environments that differ significantly from the real world, the emerging field of immersive neuroscience is rapidly advancing the use of wide-field immersive virtual reality within fMRI scanners (Lenormand D& Piolino P, 2022; Park J et al., 2024). By integrating brain imaging techniques with virtual reality to authentically replicate threatening environments, the underlying neural mechanisms of prediction-based extinction will likely be further elucidated.

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Chapter 6. Publications and Presentations

Peer-review journal articles

1. Fujino, M., & Haruno, M. (2025). Transition ability to safe states reduces fear responses to height. *Proceedings of the National Academy of Sciences,* 122(20), e2416920122.

International conferences

Poster presentation

1. "VR-fMRI reveals greater amygdala activity and fear responses with 3D compared to 2D presentation of fearful movies," Cognitive Neuroscience Society (CNS) 2025, Boston MA, March 2025.

2. "Model-based extinction of the fear of heights by active flight experience in VR," Neuroscience 2023, Washington D.C., November 2023.

Domestic conferences

Poster presentation

1. Fujino M, Ando H, Haruno M, "Virtual Reality experience of active flight reduces the fear response to heights", Workshop of the Mechanism on Brain and Mind, January 2023.

2. Fujino M, Haruno M, "Virtual Reality experience of active flight reduces the fear response to heights", The 46th Annual Meeting of the Japan Neuroscience Society August 2023.

3. Fujino M, Haruno M, “Virtual reality experience of active flight reduces the fear response to heights”,「行動変容生物学」第 4 回領域会議、December 2024.

4. Fujino M, Wada A, Haruno M, “VR-fMRI reveals greater amygdala activity and fear responses with 3D compared to 2D presentation of fearful movies”, Workshop of the Mechanism on Brain and Mind, March 2025.

5. Fujino M, Wada A, Haruno M, “VR-fMRI reveals greater amygdala activity and fear responses with 3D compared to 2D presentation of fearful movies”,「行動変容生物学」第 5 回領域会議, June 2025.

6. Fujino M, Wada A, Haruno M, “VR-fMRI reveals greater amygdala activity and fear responses with 3D compared to 2D presentation of fearful movies”, The 48th Annual Meeting of the Japan Neuroscience Society July 2025.

Awards

1. Excellent Poster Award, Workshop of the Mechanism on Brain and Mind, January 2023.

2. Excellent Poster Award, Workshop of the Mechanism on Brain and Mind, March 2025.