

# Neural Basis of Virtual Exposure Treatment

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**Abstract.** Virtual reality exposure therapy (VRET) is an increasingly common treatment for a range of anxiety disorder, specific phobias, PTSD and addictions, however neural mechanisms supporting VRET are yet to be understood. This review summarises existing studies which investigated the neural basis of VRET. Searches of electronic databases were performed using keywords related to VRET, mental disorders and neuroimaging. The search yielded 32 studies, and of these, 5 studies met inclusion criteria. Results indicated the role of prefrontal cortex in VRET, although more research is needed.

**Keywords.** VRET, neuroimaging, review, prefrontal cortex, anxiety disorders

## 1. Introduction

Virtual Reality Exposure Therapy (VRET) has shown promise in the treatment of a range of anxiety disorders [1], however, neural mechanisms underlying its efficacy are still not well understood [2]. Combining VRET with neuroimaging would help to understand its neural mechanisms, aid tailoring of more efficient VRET interventions, evaluate treatment effects and directions in research and clinical application.

A meta-analysis assessing neuroimaging studies of anxiety, phobia, PTSD and emotional processing, identified a “fear network” consisting of the prefrontal cortex (PFC) and amygdala. Healthy controls showed greater activity in the medial prefrontal cortex (MPFC) and dorsolateral prefrontal cortex (DLPFC) when exposed to aversive stimuli. Activity in these areas has an inverse relationship with the activity in the amygdala. Conversely, patients with anxiety showed decreased activity in DLPFC and MPFC inversely correlated with activity in the amygdala when exposed to anxiogenic stimuli [3]. Previous studies demonstrated that exposure therapy (EP) restores a balance within a fear circuit [4]. Although neural mechanisms underlying traditional (EP) are well documented, the neural basis of VRET and its effect on brain activity are still poorly understood [2]. The aim of this paper is to review and summarise an existing literature on the neural basis of VRET.

## 2. Methods

The aim of this review was to investigate what existing literature tells us of the impact of virtual exposure treatment on brain function. The objective was to identify brain areas and patterns of neural activity triggered by VRET.

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### *2.1. Search and analysis strategy*

We performed a systematic online database search on PubMed, MEDLINE, ISI Web of Science, and Google Scholar by entering various combinations of search items: VRET, virtual reality exposure, fMRI, PET, EEG, neuroimaging. Studies were included if they used (1) any combination of VRET and neuroimaging, (2) were performed on either healthy or patients with anxiety, phobia, PTSD or addiction, (3) activity in the neural fear circuit was reported. All studies that met inclusion criteria were critically reviewed in terms of study aims and objectives, methodology, population, sample size and technology.

### *2.2. Results*

The search yielded thirty - two studies, and of these, five studies met inclusion criteria. We identified four studies employing fMRI and one using EEG. In each of those studies, VRET was delivered through HMD. All five studies are summarised below.

### *2.3. Studies*

Three studies investigated neuronal mechanisms of VRET for addiction treatment. Lee et al. used fMRI to compare the efficacy of using 2D images and 3D VR as a tool for delivering VRET for smoking cessation. Participants in the 2D condition showed increased brain activity when viewing smoking-related cues in the right superior frontal gyrus, right middle frontal gyrus, and left orbital gyrus, left anterior cingulate gyrus, left supplementary motor area, right inferior temporal gyrus, right lingual gyrus, and right precuneus. Participants in VR exposed to smoking-related cues in VR, additionally showed increased activity in the left superior temporal gyrus, right superior frontal gyrus, and left inferior occipital gyrus, indicating more attention, visual balance and spatial orientation. The findings indicated that 3D VR may be superior to 2D images regarding ecological validity [5]. Another fMRI study conducted by Moon et al. studied eight participants on a six session VRET smoking cessation program, during which they were exposed to cues in the virtual bar which could trigger cigarette cravings. The fMRI scan was performed before and after the treatment. The results revealed increased activity in the left inferior frontal gyrus and left superior frontal gyrus in response to smoking-related cues [6]. Lee et al. compared the effect of ten sessions of VRET for alcohol dependence (ADP) patients with healthy controls using EEG. The results revealed increased alpha waves in PFC after treatment in ADP patients [7].

Only two studies investigated the neural basis of VRET for anxiety disorders. Clemente et al used fMRI to assess brain activity during VRET for assessment of specific phobia. Eleven participants with a mild phobia of small animals were exposed to simulations of these animals in VR. Results revealed increased activity in the right DLPFC (superior frontal gyrus). Activity was also found in the occipital lobe related to increased visual attention. Although authors concluded that activity in PFC is related to the self-awareness, they suggested it could be related to suppression of fear when exposed to the threatening stimuli [8]. Roy et al. was the only randomized controlled trial (RTC) employing brain imaging techniques to investigate

VRET for PTSD. Functional Magnetic Resonance (fMRI) was used before and after the treatment to assess improvement in brain function after VRET and found decreased activity in the amygdala, anterior cingulate cortex and increased activity in lateral prefrontal cortex [2].

### 3. Discussion

This review evaluated existing studies investigating neural mechanisms underlying VRET. In line with previous neuroimaging studies, this review indicated an essential role of PFC in VRET, in particular DLPFC and MPFC. The role is that of regulation of emotion and fear inhibition to reduce fear responses. In turn this reduces of anxiety, phobias and PTSD symptoms, as well as craving in addictions through inhibitory function. Successful VRET treatment should restore balance within the prefrontal - amygdalar fear circuit. Unfortunately, due to the small number of studies, there is limited evidence of how VRET affects brain function. Moreover, all existing studies evaluated the effect of VRET delivered through HMD.

There is a need for better designed randomized controlled trials, with larger samples, employing different VR systems, to verify the efficacy of VRET and its impact on brain function. So far there are no studies the effect of VRET in CAVE-like VR on brain activity.

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