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Neurophysiological correlates of habituation during exposure in spider phobia

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Abstract

Imaging studies using symptom-provocation paradigms in specific phobia have yielded contradictory results, possibly reflecting a failure to account for habituation processes. Given that a single session of exposure in vivo can result in significant improvement in specific phobia, we used prolonged exposure to phobic stimuli to identify CNS regions showing habituation. Eighteen subjects (12 with spider phobia, 6 healthy controls) underwent $H_2^{15}O$-positron emission tomography while being continuously presented with pictures of spiders or butterflies. Results showed main effects (spiders>butterflies) in the phobia group in the left fusiform gyrus (FG) and the right parahippocampal gyrus (PHG), with bilateral perirhinal cortex and right limbic areas approaching significance. Group×condition effects were found in the right amygdala and PHG. During spider scans, large habituation effects were observed in the anterior medial temporal lobe (MTL) bilaterally. Regression analyses demonstrated that state anxiety was correlated with activity in left amygdala, bilateral perirhinal cortex, right FG, and periaquaductal grey; by contrast, phobic fear was only associated with right-sided hippocampal activity. We conclude that prolonged exposure to phobic stimuli is associated with a significant decrease in bilateral anterior MTL regional cerebral blood flow. Right anterior MTL, identified when comparing phobic vs. neutral stimuli and habituation to phobic vs. neutral stimuli in the phobia group, implicates this region in phobic fear. Analyses of covariance suggest a further functional segregation with state anxiety being linked to enhanced activity in amygdala,

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perirhinal cortex, and tegmentum, and phobic fear with enhanced right hippocampal activity, suggesting a neuroanatomical differentiation between emotional-vegetative and cognitive aspects of (phobic) fear.

Keywords: Spider phobia; Positron emission tomography; Exposure; Habituation

1. Introduction

Specific phobia is a psychiatric disorder characterized by marked and persistent fear of circumscribed objects or situations, such as snakes, spiders, and being in a tunnel or elevator (American Psychiatric Association, 1994). Subjects with a specific phobia readily concede that their fears are exaggerated, but they nevertheless go to great lengths to avoid phobic stimuli. The etiology of specific phobias is unknown, although both constitutional and environmental factors may contribute to their pathogenesis (Fyer, 1998). Subtypes of specific phobias (animal, blood/injury, and situational phobias) tend to cluster in families (Skre et al., 2000; Kendler et al., 2002). In addition, previous traumatic experiences and/or vicarious learning may predispose to their onset (Lichtenstein and Annas, 2000). Exposure therapy, involving exposing patients to feared situations, is the gold standard for treatment of specific phobia. This treatment is based on the idea that anxiety subsides through a process of habituation. Habituation refers to a decline in fear responses, particularly physiological responses, with repeated exposures to fear-provoking stimuli. Several studies provide supportive evidence for the role of habituation in exposure therapy, with self-reported fear and physiological arousal showing a decline across exposure sessions, consistent with habituation (Emmelkamp, 2004).

Over the past decade, brain-imaging techniques, such as positron emission tomography (PET) and single photon emission computed tomography (SPECT), have been used to investigate the neuroanatomical substrate of specific phobias, particularly animal phobias. These studies typically involve exposing subjects to phobic objects such as snakes or spiders, either pictures or live animals, during scanning. To date, these studies have yielded conflicting results. Whereas Mountz et al. (1989) in an early PET study reported negative results, subsequent studies such as those of Wik et al. (1993) found increased regional cerebral blood flow (rCBF) in secondary visual cortex but decreased rCBF in hippocampus and orbitofrontal, prefrontal, temporopolar, and posterior cingulate cortex with exposure to phobic stimuli. In a follow-up study (Fredrikson et al., 1995), intravenous diazepam did not effect rCBF changes or influence subjective/physiological fear indices. Johanson et al. (1998), using ^{133}Xe-SPECT, reported decreased right lateral prefrontal flow during presentation of a spider video compared with a neutral video, particularly in near-panicking subjects. In contrast, Rauch et al. (1995), in their subjects with small animal phobia, found increased rCBF in left posterior orbitofrontal, left insular, and left somatosensory cortex, as well as in right anterior temporal and anterior cingulate cortex, but not in the amygdala complex during presentation of phobic objects compared with baseline. Similar findings were reported by Reiman (1997).

Inconsistencies in previous findings may reflect methodological differences such as imaging modality, stimulus paradigms (eyes open or closed, visual stimuli vs. touch), and data-analytic techniques (region of interest vs. voxel by voxel methods). In addition, few studies have controlled for decrements in subjects' responses in time, due to habituation after repeated exposure to phobic stimuli. Reiman (1997) attempted to reduce habituation effects by placing the snake closer to the subject with successive scans. To our knowledge, only a preliminary report by Drevets et al. (1995) addressed the effects of repeated stimulation (using 'live' animals) on patterns of CNS activation in subjects with small animal phobia, where increased activity during habituation in left posterior orbitofrontal cortex alone was found. In normal volunteers, several studies have shown that responses to fearful stimuli, particularly in anterior medial temporal cortex, may decrease rapidly over time (Breiter et al., 1996; Buchel et al., 1999; Thomas