Neural Correlates of Anticipation and Uncontrollability in Snake Phobia

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INTRODUCTION
Anticipation and uncontrollability have been implicated as major contributors to anxiety disorders in general (Barlow, 2002). Consistent with a large literature on brain responses to aversion, a recent study in our laboratory (Nitschke et al., 2006) implicated a number of brain regions in the anticipation of and response to aversive pictures, including the anterior cingulate cortex (ACC), insula, amygdala and orbital frontal cortex (OFC). The present event-related fMRI study enrolled volunteers both with and without specific phobia of snakes to identify the neural areas recruited in the anticipation of and response to videos of differing emotional content (snake, fish, disgust). Uncontrollability was manipulated by giving subjects control on half of the trials to avoid viewing the videos. Barlow’s theory of anxiety emphasizes uncontrollability as one of the most important generalized psychological influences on the development of specific phobia. Research on anxiety has investigated uncontrollability in general (Barlow, 2002). Consistent with a large literature on anxiety disorders in general (Barlow, 2002), our fMRI analysis procedures (artifact removal, head movement compensation and atlas based correction) were chosen to optimize data collection.

METHODS
Participants
Two groups of participants were studied. Snake phobics consisted of 12 participants (9 females, mean age 23, range 18-46) and Non-phobics consisted of 12 participants (4 females, mean age 23, range 19-30). Participants were right-handed and neurologically healthy. Non-phobics met criteria for DSM-IV (First et al. 1996). Snake phobics did not have a history of specific phobia of snakes and were not of other clinical disorders as assessed by the Structured Clinical Interview for the DSM-IV (SCID) (First et al. 2002). All clinical disorders including specific phobia of snakes were assessed by the SCID. Informed consent in accordance with rules set by the University of Wisconsin at Madison Human Subjects Committee was obtained from all participants prior to the experiment.

Stimuli
The stimuli consisted of 3 sets: snake, fish, and disgust videos (24 each). Each video was standardized for similar emotional content (e.g., arousal, valence, disgust, fear) during pilot rating sessions prior to the study. Physical attributes such as brightness, contrast, scene complexity and movement of the stimulus were also equalized. Videos were presented to participants in the scanner using Axscan graphics mounted on the head coil of a 3.0 Tesla GE NMR Scanner (TR=200 ms).

Procedure
Experimental Paradigm
Participants were administered several anxiety and phobia questionnaires, followed by a mock scanner session during which they practiced the experimental task. Each trial began with an anticipation period signaled by a cue. An S presented snake video, a F presented fish video, and a P presented disgust video. Subjects were instructed at the onset of the study that they would be receiving these videos. Uncontrollability was indicated by the color of the anticipation cue. A blue or yellow cue indicated a controllable trial, and the video that followed was controllable if subjects responded fast enough to avoid viewing the anticipated video. If a subject had an uncontrollable trial, they invariably received the video. When a subject had a controllable trial, if reaction time (RT) was fast enough to a red target square that followed the cue after a variable delay, they received a fixation cross rather than the anticipated video. Otherwise, they received the anticipated video. Of the 72 total video trials, half were rated as uncontrollable and the other half controllable. A success rate of approximately 50% was achieved with online monitoring of RT by DMX software. Each trial ended with one Likert online rating about the nature of the stimulus - valence, arousal, disgust, and fear - and counterbalanced across conditions.

HYPOTHESES
1. In phobics, anticipation of snake videos will activate regions identified in Nitschke et al. (2006), including the insula and amygdala.
2. Uncontrollability over video presentation will result in larger neural responses than when video presentation can be controlled.
3. Non-phobics are expected to show anticipation and uncontrollability effects for the disgust videos but not the snake videos.

RESULTS

Anticipation
In phobics, anticipation of snake videos activated ACC, bilateral insula and amygdala more than anticipation of fish and disgust videos (Figure 1, 2). In non-phobics, anticipation of disgust videos activated dorsal and perigenual ACC, bilateral insula and bilateral OFC more than anticipation of fish or snake videos. There was a significant difference between anticipation of fish and snake videos in non-phobics in that anticipation of snake videos activated the right insula. Activation effects were mirrored in the video response data (Figure 3).

Uncontrollability
The most salient stimulus for the phobic participant group showed accentuated activity in the insula and ACC when it was uncontrollable, versus controllable as a function of worry, as measured by the Penn State Worry Questionnaire (Figure 7) and, anxiety, as measured by the Hamilton Rating Scale for Anxiety (Figure 8).

CONCLUSIONS
1. As predicted, anticipation of aversive events led to greater activation in the ACC, bilateral insula, amygdala and OFC. For the phobics, this was especially the case for the anticipation of snake videos. The non-phobics predominantly showed anticipation effects for the disgust videos in comparison to the snake. Uncontrollability over video presentation resulted in larger neural responses than when video presentation could be controlled in phobics with elevated anxiety.

REFERENCES

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Data Analysis
Our fMRI analysis procedures (artifact removal, head movement compensation and atlas based correction) are detailed in previous publications (Mackiewicz et al., 2006) and are available as a protocol.

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