



## Brain, body, and cognition: Neural, physiological and self-report correlates of phobic and normative fear



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### ABSTRACT

The phobic fear response appears to resemble an intense form of normal threat responding that can be induced in a nonthreatening situation. However, normative and phobic fear are rarely contrasted directly, thus the degree to which these two types of fear elicit similar neural and bodily responses is not well understood. To examine biological correlates of normal and phobic fear, 21 snake phobic and 21 nonphobic controls saw videos of slithering snakes, attacking snakes and fish in an event-related fMRI design. Simultaneous electrodermal, pupillary, and self-reported affective responses were collected. Nonphobic fear activated a network of threat-responsive brain regions and involved pupillary dilation, electrodermal response and self-reported affect selective to the attacking snakes. Phobic fear recruited a large array of brain regions including those active in normal fear plus additional structures and also engendered increased pupil dilation, electrodermal and self-reported responses that were greater to any snake versus fish. Importantly, phobics showed greater between- and within-subject concordance among neural, electrodermal, pupillary, and subjective report measures. These results suggest phobic responses recruit overlapping but more strongly activated and more extensive networks of brain activity as compared to normative fear, and are characterized by greater concordance among neural activation, peripheral physiology and self-report. It is yet unclear whether concordance is unique to psychopathology, or rather simply an indicator of the intense fear seen in the phobic response, but these results underscore the importance of synchrony between brain, body, and cognition during the phobic reaction.

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### 1. Introduction

The expression of fear is associated with an adaptive set of behaviors and central and autonomic nervous system responses that serve to protect the organism in the face of danger (Ohman & Mineka, 2001). When presented with a threat, physiological changes including increased heart rate (Moratti & Keil, 2005; Sartory, Rachman, & Grey, 1977) and dilated pupils (Reinhard, Lachnit, & König, 2006) ready the body to fight or flee. This evolutionarily adaptive response becomes maladaptive in simple phobic fear, in which an intense fear response can be provoked by a stimulus not immediately threatening to the body, such as a photograph of a snake. Autonomic reactions to phobic provocation mimic those in normative fear responding (Davidson, Marshall, Tomarken,

& Henriques, 2000; Sarlo, Palomba, Angrilli, & Stegagno, 2002), and neuroimaging studies of phobic fear demonstrate activation in visual, motor, affective, and sensory brain networks (Schienle, Schaefer, Hermann, Rohrmann, & Vaitl, 2007; Straube, Mentzel, & Miltner, 2006). These networks overlap with regions implicated in fear conditioning (Knight, Cheng, Smith, Stein, & Helmstetter, 2004; Phelps, Delgado, Nearing, & LeDoux, 2004), and presentation of fearful images (Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; Sabatinelli, Bradley, Fitzsimmons, & Lang, 2005), which find activation patterns involving similar regions such as the supplementary motor area and amygdala.

Despite similarities in autonomic responding and overlapping brain networks, some sequelae may be unique to phobic fear. Behavioral avoidance (Hamm, Cuthbert, Globisch, & Vaitl, 1997) and increased environmental vigilance (Kindt & Brosschot, 1997; Koch, O'Neill, Sawchuk, & Connolly, 2002) have been strongly associated with phobic fear. In addition, although phobics often overestimate the inherent danger of their feared stimuli (e.g. Arntz, Lavy, Van den Berg, & Van Rijsoort, 1993; Mizes, Landolf-Fritsche,

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& Grossman-McKee, 1987), many phobics also recognize that their fear is irrational and are quite embarrassed by it (Davidson, 2005; Mayer, Merckelbach & Muris, 2000). This apparent conflict between explicit cognition and emotional reaction may be explained by the uncontrollable, automatic nature of the phobic reaction and its involvement of many brain and bodily systems (Ohman & Mineka, 2001). This conflict may also lead to increased attempt at emotion regulation during fear provocation in phobic individuals, in an effort to dampen or control the reaction, although they are ultimately unable to do so (Hermann et al., 2009).

This uncontrollable and automatic sensation across multiple body systems is suggestive of the theory of concordance, the notion that indices of emotion should correlate, or cohere. However, empirical support for this theory has been mixed (Fernández-Dols, Sánchez, Carrera, & Ruiz-Belda, 1997; Matsumoto, Nezlek, & Koopmann, 2007; Rosenberg & Ekman, 1994), even in the study of specific phobia (Duinen, Schruers, & Griez, 2010). Particularly important are negative findings for correlation between subjective self-report and physiology (e.g. Gross & Levenson, 1993), which call into question the reliability of self-reported experiences of emotion. However, the concordance of systems associated with emotion has been observed to vary as a function of perceived intensity, with higher intensity responding linked to greater systemic concordance (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005; Rosenberg & Ekman, 1997). Intense phobic responses have likewise shown concordance between self-reported fear and physiological response (Sartory et al., 1977), and this concordance may be important to intense experiences that feel subjectively automatic or overwhelming.

The current study sought to contrast normative and phobic fear to discern similarities and distinctions in their neural and physiological correlates. To this end, phobic and nonphobic participants were presented with videos of snakes, both threatening clips of snakes striking in the direction of the viewer, and nonthreatening snakes slithering along the ground. In this way, the normative reaction of a nonphobic person to an attacking fearful snake stimulus can be compared to the phobic response to a less obviously threatening snake and a more complete picture of fear can be obtained. We hypothesized that normative fear would recruit regions frequently associated with threat and fear such as the amygdala, thalamus and insula (Hariri et al., 2003; Williams et al., 2005). In contrast, we hypothesized the neural correlates of phobic fear would involve an overlapping, but much more extensive set of brain regions. Unlike normative threat responding, phobic fear is often associated with feelings of disgust (de Jong, Peters, & Vanderhallen, 2002), and greater environmental awareness (Öhman, Flykt, & Esteves, 2001). Therefore, we hypothesized that phobia-specific activation in the insula (Wicker, Keyeere, Plially, Gallese, & Rizzolatti, 2003) and visual processing regions in temporal and parietal cortices (Lloyd, Morrison, & Roberts, 2006) would be observed. Further, as phobics report embarrassment and self-consciousness during fear responses (Davidson, 2005), we expected prefrontal activation unique to phobic fear in regions associated with emotion regulation (Goldin, McRae, Ramel, & Gross, 2008).

We were also specifically interested in whether responses would correlate across the multiple systems being measured, and whether this occurred in both phobic and normative fear. To test for concordance during phobic fear provocation across multiple systems, we collected self-reported affect, functional brain data and several measures of peripheral physiology. Given the intensity of phobic symptom provocation, we hypothesized that phobic fear would be associated with greater and more consistent relationships among indices.

## 2. Methods

### 2.1. Participants

A total of 24 snake phobic and 25 nonphobic control female subjects were enrolled in the study. Potential participants were recruited through an Introductory Psychology class and flyers displayed throughout the community requesting participants for a study of snake phobia. Exclusion criteria for all subjects included MRI contraindication (e.g. pacemaker), claustrophobia, left-handedness, and history of head trauma. Enrollment was limited to females due to the higher incidence of snake phobia in women as compared to men; creating a sample that was balanced across gender in the snake-phobic group may have proven difficult. Eligible phobic participants scored greater than 18 on the Snake Questionnaire (SNAQ; Klieger, 1987); control participants scored 3 or less. Diagnostic interviews were not conducted to evaluate phobics for clinically relevant simple phobia because it was felt that the rarity of snakes in Wisconsin limited the daily impact of the fear; restricting the sample to clinical significance was unnecessarily strict. Three phobic subjects completed the simulation session but were not scanned: two subjects discontinued their enrollment due to fear of the stimuli and one subject could not be comfortably positioned in the MRI simulation mock scanner used to prepare participants for the scanning environment. Technical difficulties caused data from four control subjects to be unusable, due to spatial warping of the functional data and/or problems with acquisition of functional data. The final sample size was 42, 21 of each phobic and control participants. The average age of phobic participants was 19.6 years; control subjects were on average 20.4 years old.

### 2.2. Procedure

Enrolled participants first completed a simulation session in a mock MRI scanner to familiarize them with the scanning environment and ensure tolerability of the fearful stimuli. Subjects were placed in the mock MRI scanner and shown stimuli similar but not identical to those used in the experimental trials. The real MRI scanning session occurred a few days to at most two weeks later, during which video clips were presented as MR images, pupillary response, and electrodermal activity data were collected. After MR scanning, subjects rated half of the video clips (randomly presented, half counterbalanced) presented on a computer outside the scanner. Valence and arousal ratings were collected for each video clip on a 1–7 Likert scale. Written informed consent was given in accordance with the Human Subjects Committee of the University of Wisconsin and subjects were paid eighty dollars for participation.

### 2.3. Design and materials

Subjects were presented with 48 video clips approximately 2 s in duration, 16 exemplars each of 3 types of videos. Video clip types included: snakes threatening in the direction of the camera, snakes slithering across the ground, and fish. Clips were selected from a variety of nature programs. Slithering snakes and fish were equated for direction of movement, i.e. toward versus away from the camera. Clips were presented in random order in an event-related design with an average of 8 s of black screen between clips (average ITI = 10 s, range 8–12 s).

#### 2.3.1. Pupillary, electrodermal and self-report data collection and analysis

An iView × system (v. 1.3.31) with eyetracking capabilities was integrated with the fiber optic goggles used to present the video stimuli. Horizontal pupil diameter was acquired during fMRI scanning at a sampling rate of 60 Hz, and data were processed using algorithms developed by Siegle, Steinhauer, and Thase (2004) using Matlab software (MathWorks, Natick, MA). Blinks were identified and removed using amplitude thresholds and remaining data were Z-scored within each participant. Pupillary data were lost from 2 phobic subjects for which heavy eye makeup caused difficulties in the software identifying the pupil. In remaining subjects, for each video the average pupillary diameter was calculated for an 8-s window from video onset, and the average response across all video presentations of each type threatening snake, slithering snake and fish were entered into a Video Type × Group ANOVA. Estimated pupil response for individual videos were used for the concordance analyses described below.

Electrodermal response (EDA) was also collected simultaneous to fMRI trials, using 8 mm Ag–Ag/Cl electrodes placed on the distal phalanges of the index and middle fingers of the left hand. EDA signal was processed with a Matlab routine developed in-house which low-pass filtered the data (0.7 Hz cutoff), and identified peaks exceeding 0.05  $\mu$ S in height. Due to the cold temperature in the scan room and high-frequency noise interference from the MR signal, only 13 subjects from each group showed a reliable EDA response, which was defined as having at least 2 identified peaks exceeding the 0.05  $\mu$ S cutoff from each of the 3 video conditions. For these subjects, amplitude and frequency of response was calculated across each video type, and these values were entered into separate Video Type × Group ANOVAs. Generally, participants excluded from EDA analyses did not show suprathreshold responses to the fish videos, and to the slithering snakes for control participants. Had all data been included, the resultant ANOVAs would have been highly imbalanced.

Self-reported valence and arousal ratings were collected after completion of MR data acquisition on a computer outside the scanning room. To constrain the length of

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