



## Registered Reports

## Anticipatory stress associated with functional magnetic resonance imaging: Implications for psychosocial stress research



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## ABSTRACT

Stress tasks performed during functional magnetic resonance imaging (fMRI) elicit a relatively small cortisol response compared to stress tasks completed in a traditional behavioral laboratory, which may be due to apprehension of fMRI that elicits an anticipatory stress response. The present study investigated whether anticipatory stress is greater prior to research completed in an MRI environment than in a traditional behavioral laboratory. Anticipatory stress (indexed by cortisol) was greater prior to testing in the MRI environment than traditional behavioral laboratory. Furthermore, anticipation of fMRI elicited a cortisol response commensurate with the response to the stress task in the behavioral laboratory. However, in the MRI environment, post-stress cortisol was significantly lower than baseline cortisol. Taken together, these findings suggest the stress elicited by anticipation of fMRI may lead to acute elevations in cortisol prior to scanning, which may in turn disrupt the cortisol response to stress tasks performed during scanning.

## 1. Introduction

Excessive exposure to psychological stress disrupts emotion function and can lead to stress-related disorders (Chrousos and Gold, 1992). Thus, there is growing interest in neuroimaging techniques (e.g., functional magnetic resonance imaging; fMRI) to improve our understanding of the neural substrates of the psychosocial stress response (Allendorfer et al., 2014; Bali and Jaggi, 2015; Dedovic et al., 2009b; Pruessner et al., 2008). The most popular index of psychosocial stress in humans is the hormone cortisol, which is controlled by the hypothalamic-pituitary-adrenal (HPA) axis. Prior work has repeatedly demonstrated that psychosocial stress exposure in traditional behavioral laboratory settings elicits a significant cortisol response (Bali and Jaggi, 2015; Dickerson and Kemeny, 2004; Kirschbaum et al., 1993). However, similar effects have not always been demonstrated during fMRI (Allendorfer et al., 2014; Dedovic et al., 2009c; Pruessner et al., 2010). In fact, previous research has reported significantly greater cortisol levels before rather than after stress tasks completed during fMRI (Allendorfer et al., 2014; Chung et al., 2016; Hermans et al., 2011; Root

et al., 2009). Thus, anticipation of fMRI may elicit an anticipatory cortisol response before participants are exposed to the stress task itself. The observed decrease in cortisol following stress tasks completed in the MRI environment may result from an acute elevation in cortisol prior to scanning that is driven by anticipatory stress that is uniquely associated with fMRI methodology. However, no prior research has investigated anticipatory stress associated with fMRI by directly comparing cortisol levels prior to fMRI to levels measured prior to participating in a traditional behavioral study. Investigating the anticipatory distress associated with fMRI would help determine its impact on the results of experimental stress tasks performed in the MRI scanner.

Prior research suggests that many individuals experience stress during MRI scanning, especially those with no prior exposure to MRI (Tessner et al., 2006). However, preparing to safely and effectively participate in an fMRI study may also be distressing for many research participants. Volunteers for an fMRI study must complete a thorough safety screening and consent process prior to scanning due to the risk associated with the high magnetic fields used in fMRI research. The primary aim of safety screening is to ensure that participants have no

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ferromagnetic medical devices implanted inside their body or other safety issues that could cause harm when placed within a high magnetic field. Additional screening questions and safety concerns include, but are not limited to, tattoos containing metallic ink, pregnancy, claustrophobia, sensitivity to loud noises, and eye injuries involving metallic objects (e.g., metal slivers embedded in the eye). Additionally, participants must complete and sign a safety form to explicitly attest they have no conditions that would make undergoing MRI unsafe. Further, before entering the scanner room, participants are often inspected with a hand-held metal detector to ensure there is no metal on their body. They are also given instructions on certain safety-seeking behaviors to use during scanning (e.g., using a “squeeze ball” to set off an alarm and stop scanning), which may further increase anticipatory fear (Sloan and Telch, 2002).

While safety precautions are necessary to protect the well-being of participants, the novelty of the neuroimaging environment coupled with extensive safety precautions may direct participants' attention to the potential dangers of scanning, portraying fMRI as a threatening and potentially harmful procedure (Mason, 1968; Ursin and Eriksen, 2004). Additionally, participants are instructed before scanning to refrain from making even minor movements while in the scanner to prevent motion artifacts. The effort to remain still is compounded by the fact that participants are warned that they will be isolated and confined inside an uncomfortable machine that makes repetitive, loud, and startling noises (Burow et al., 2005; DeVries et al., 2003; Mason, 1968; Rudy et al., 1999). As a result, participants may anticipate and fear negative outcomes that could occur during scanning, such as physical harm, claustrophobia, or the inability to remain still (Brosschot et al., 2006; Mason, 1968; McGlynn et al., 2007). In fact, participants commonly report feelings of apprehension prior to scanning, such as fear of an unknown procedure, harm by the machine, suffocation, and restriction (McGlynn et al., 2007; Thorpe et al., 2008). In addition, the strict guidelines of MRI may lead participants to fear negative evaluation by the investigators (McGlynn et al., 2007). Further, the lack of control over the procedure and fear of social evaluation in the MRI environment may create an experience similar to an effective psychosocial stress task (Dickerson and Kemeny, 2004). Thus, simply being prepared to participate in an fMRI study may distress volunteers and elevate cortisol levels prior to scanning (Mason, 1968; McGlynn et al., 2007; Thorpe et al., 2008).

Many of the aforementioned feelings that participants experience prior to fMRI (e.g., uncontrollability, social evaluative threat, and fear of harm by the machine) are characteristic of physical and psychosocial threats. Previous research has demonstrated that exposure to physical or psychosocial threats activate the HPA axis, resulting in cortisol release (Chrousos and Gold, 1992; Dickerson and Kemeny, 2004; Gaab et al., 2005; Kirschbaum et al., 1993; Rohleder et al., 2007; Sapolsky et al., 2000). Furthermore, anticipation of physical or psychosocial threats can also elevate cortisol (Chrousos and Gold, 1992; Gaab et al., 2005; Mason, 1968; Turan, 2015). Subsequently, the acute increase in circulating cortisol levels, following a stressor, transiently inhibits HPA axis activation and suppresses further secretion of cortisol (Keller-Wood et al., 1983; Sapolsky et al., 1985; Sapolsky et al., 2000). Thus, if participants feel threatened by the preparation for an fMRI scan, the cortisol response to a subsequent stressor (e.g., a stress task) may be relatively weak, or even diminished, by cortisol's negative feedback loop.

The primary purpose of the present study was to determine whether anticipatory stress associated with MRI is greater than anticipatory stress in a traditional behavioral laboratory. Participants completed an experimental session in a traditional behavioral laboratory and in an MRI facility on two separate visits. Given the additional preparation, precautions, and environmental characteristics required for fMRI, we hypothesized that participants would experience greater anticipatory stress (indexed by cortisol) prior to testing in the fMRI environment than in a traditional behavioral laboratory.

## 2. Methods

### 2.1. Participants

Data from 57 right-handed volunteers (36 males, 21 females, mean age = 19.68, SEM = 0.15, age range = 17–22 years) recruited as part of a larger research project were included in this study. All 57 participants included in the analysis completed the project in the afternoon (traditional behavioral laboratory: 3:25 PM; SD =  $\pm$  69 min and MRI environment: 2:48 PM; SD =  $\pm$  55 min) to reduce the effects of diurnal rhythms on cortisol measurements. Participants provided written informed consent and all study procedures were approved by the University of Alabama at Birmingham Institutional Review Board.

### 2.2. Procedures

The study was completed on two non-sequential days. On the first day of testing, volunteers completed the Trier Social Stress Test (TSST) in a standard behavioral laboratory (TSST; Kirschbaum et al., 1993). The opportunity to volunteer for the subsequent MRI session that included the Montreal Imaging Stress Task (MIST) was not mentioned during recruitment or completion of the first assessment that included the TSST. Instead, volunteers were recruited independently for the MRI session, and returned at a later date to complete the MIST in an MRI setting (Dedovic et al., 2005). The average period of time between testing sessions was 6.4 months (i.e., mean = 190.89 days; SEM = 20.68 days; range = 25–937 days). The stress response was assessed by measuring cortisol and heart rate during both sessions. However, skin conductance response (SCR) was collected during the MIST only. SCR was collected during the MIST, in part, due to the nature of the larger neuroimaging project, which included another cognitive-emotional task that was completed after the MIST.

### 2.3. TSST

Upon arrival to the behavioral laboratory, participants were briefly introduced to the TSST during the informed consent process. Experimenters told participants they would complete a speech and math task which would be videotaped. In addition, experimenters explained heart rate and blood pressure would be measured during the task and multiple saliva samples would be collected to measure chemicals related to their body's reaction to stress. After acclimating to the lab environment and being interviewed for approximately 60 min, participants were asked to rest for 5 min (baseline) and then were introduced to the Trier Social Stress Test (Kirschbaum et al., 1993). The TSST consisted of a 5 min speech preparation period, a 5 min mock job interview, and a 5 min mental arithmetic task involving serial subtraction (Kirschbaum et al., 1993). During the mock job interview, participants were instructed to pretend that they were a job applicant delivering a speech in front of an evaluation panel in hopes of being hired. While giving the speech, participants sat approximately two meters away from a desk with two judges who wore white lab coats. The judges maintained neutral facial expressions and did not provide any positive verbal or nonverbal feedback. Participants were told the judges were trained to detect verbal and non-verbal stress signals and that their performance was also being video recorded. If participants ended their speech early, they were told to continue until the full 5 min had elapsed. Following the mock job interview, participants completed the arithmetic (i.e., serial subtraction) portion of the test. Participants were instructed to subtract backwards from 996 in increments of 13 as quickly and accurately as possible. After every mistake, one of the judges instructed participants to stop and start again at 996.

### 2.4. MIST

Participants returned on a second day to complete the MIST during

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