MRI-related anxiety levels change within and between repeated scanning sessions

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A B S T R A C T

Magnetic resonance imaging (MRI) scans frequently trigger state anxiety in individuals being scanned. It is not known, however, whether levels of MRI-related anxiety change over the course of a single scan or across repeated scanning experiences. Since changes in state anxiety are known to affect regional brain activity in healthy volunteers, systematic changes in levels of MRI-related anxiety could confound findings from neuroimaging studies. We assessed anxiety levels in eleven healthy male volunteers during a control period and during two MRI scanning sessions. Anxiety levels were highest during the first MRI scan, dropping to control levels or below by the second scan. In addition, anxiety fluctuated within scanning sessions, particularly during the first scan, with levels high at the beginning of the session, decreasing during mid-scan and then increasing again toward the end of the session. These results suggest that habituation in an MRI simulator before participating in a neuroimaging study could help to decrease fluctuations in MRI-related anxiety. Moreover, in studies that address several experimental questions within a single scanning session, experimental designs could be adapted to avoid potential confounds from within-scan variation in scanner-related anxiety.

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1. Introduction

Magnetic resonance imaging (MRI) is known as a physiologically non-invasive technique. Individuals being scanned, however, sometimes experience substantial anxiety as a result of the scanning procedures or environment. During clinical scans, 25–37% of patients experience anxiety of moderate intensity (Katz et al., 1994; MacIsaac et al., 1998), and intense, acute anxiety prevents completion of ~2% of scans (for review, see Dewey et al., 2007). The discrepancy between the number of people reporting anxiety and the number of prematurely terminated scans suggests that many “complete’s” still experience substantial anxiety. MRI-related anxiety is likely caused by the novelty of the experience, the confined and noisy space within the scanner, fear of suffocation or that the scanner will be harmful, and concern about anticipated findings (Katz et al., 1994; MacKenzie et al., 1995; McGlynn et al., 2007; Thorpe et al., 2008). This anxiety can occur in individuals who have no history of claustrophobia (Fishbain et al., 1988; Avrahami, 1990), and can be quite severe; i.e., comparable to anxiety levels experienced by individuals about to undergo elective abdominal surgery (Quirk et al., 1989).

Although MRI-related anxiety is common, little is known about how levels of state anxiety change within a single scanning session or over repeated scanning experiences. One study found both increases and decreases in reported anxiety levels from before to after a scan, depending on whether patients had a negative or positive/neutral experience of their scan (MacKenzie et al., 1995). In that study, however, anxiety levels were not monitored during the scanning procedures, so the time course of any changes during scanning is unknown. It is also not known how levels of state anxiety might change across repeated scans.

Our limited knowledge of scanner-related anxiety could be problematic for the interpretation of some functional neuroimaging studies, since changes in state anxiety have been found to affect regional brain activity (Damasio et al., 2000; Paquette et al., 2003; Bishop et al., 2004). For example, experimental induction of state anxiety is frequently linked to brain activation changes in regions including medial prefrontal cortex (Simpson et al., 2001), amygdala (Phan et al., 2002; Bishop et al., 2004) and orbitofrontal cortex (Damasio et al., 2000), among others. Differences in levels of combined state and trait anxiety have also been associated with variations in levels of neurochemicals in the orbitofrontal cortex, as measured using magnetic resonance spectroscopy in healthy volunteers (Grachev and Aplkarian, 2000). Furthermore, individual differences in levels of state anxiety can interact with task effects in healthy volunteers; for example, higher state anxiety was correlated with stronger insular responses to presentation of negative emotional material (Meriau et al., 2009).

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These findings suggest that changes in state anxiety related to MRI procedures could yield an effect of their own or else mask actual effects of manipulated variables. This is a particular concern for repeated–measures designs, which are commonly used to examine the neural correlates of psychiatric treatments. The brain regions affected by changes in state anxiety are similar to those implicated in mood disorders (e.g., Deckerbach et al., 2006; Konarski et al., 2007); thus, if levels of MRI-related anxiety were to change over repeated scans (e.g., because of habituation), any resulting differences in post-treatment regional brain activity could be mistakenly interpreted as treatment effects. Fluctuations in MRI-related anxiety could be a concern even for studies that involve only a single scan. Functional MRI (fMRI) studies often include several experiments within a single scanning session, usually in a fixed order. Systematic changes in levels of state anxiety during scanning sessions could lead to their own effect on regional brain activity and thus confound the interpretation of neuroimaging findings.

A final area for concern is the rapidly growing use of so-called ‘resting-state’ fMRI experiments. These studies examine the functional activation and connectivity of the human brain when participants are not instructed to engage in any particular task. A consistent network of regions is activated under such passive conditions, including medial prefrontal cortex, posterior cingulate, and medial temporal lobe structures, among others (Raichle et al., 2001; Raichle and Snyder, 2007). The function of this ‘default network’ is a topic of ongoing investigation, and changes in default network activation have been observed in various psychiatric conditions (Buckner et al., 2008; Broyd et al., 2009). Importantly, activation and connectivity within the default network appear to be susceptible to experimentally induced changes in participants’ emotional state during scanning (Harrison et al., 2008; Pitroda et al., 2008). Thus, variation in spontaneous anxiety due to MRI procedures could be an important confounding variable for resting-state fMRI studies.

In light of these considerations, this study was designed to systematically assess fluctuations in levels of state anxiety both within and between repeated scanning sessions. Time series of control measures of self-reported state anxiety and heart rate were first collected outside the scanner environment a week before the first MRI scan. Levels of state anxiety and heart rate were then monitored during two MRI scans conducted one week apart.

2. Methods

2.1. Participants

Twelve healthy, right-handed, MRI-naïve young men (mean age 22 years, range 20–25) participated in the experiment. Participants were recruited from a university student population through personal communication. Individuals were excluded from the study during initial screening if they reported any past or current neurological disease or psychiatric illness (assessed using the Mini International Neuropsychiatric Interview; Sheehan et al., 1998), regular cigarette smoking, use of illegal drugs, or alcohol misuse during the past year. All procedures were approved by the Research Ethics Board of the Capital District Health Authority (Nova Scotia), and participants gave informed consent prior to beginning the study. Participants completed all three phases of the study, except for one individual who did not complete the scans because of an acute anxiety attack (see below).

2.2. Measures

Self-reported anxiety was monitored using the nine-item Tension–Anxiety subscale of the Profile of Mood States (POMS; McNair et al., 1992). This subjective measure was selected because it is short enough to permit assessment of immediate anxiety levels repeatedly during the scans with only brief (30 s) interruptions to ongoing procedures. The POMS Tension–Anxiety subscale has excellent internal consistency (Kuder-Richardson coefficients ≥ 0.90) and is strongly correlated with other measures of anxiety (McNair et al., 1992). It has also been shown to effectively measure changes in mood associated with emotion-inducing conditions in healthy volunteers, such as anticipation of dental examinations (Pillard and Fisher, 1970) or viewing an anxiety-inducing autopsy film (Pillard et al., 1967).

As a physiological correlate of anxiety, we assessed heart rate in beats per minute (BPM). Changes in heart rate are known to be associated with regional differences in brain activation (Gianaros et al., 2004).

2.3. Control session

Procedures related to MRI scans have both relatively generic and unique features that could potentially be anxiety inducing. Generic features include the novelty of participating in a research study in an unfamiliar setting, physical isolation, and a lengthy period of relative immobility. Unique features are related to the scanner environment, including confinement in a narrow space and exposure to cycles of loud scanner noises. An initial control session was designed to mimic some of the generic features of MRI scan procedures, in order to permit assessment of anxiety-inducing effects that are related specifically to MRI scanning procedures. To accomplish this, participants were asked to lie quietly alone on a bed in a private bedroom for 60 min during a control session, conducted at the Chronobiology Laboratory at the QEII Health Sciences Centre. During the resting period, the POMS-TA was administered verbally by the experimenter five times via audio link, at intervals designed to mimic the timing of scheduled breaks in the planned MRI protocol (i.e., at 0, 8, 20, 35 and 50 min into the session). Heart rate was monitored with a finger pulse-oximeter and recorded every 30 s.

2.4. MRI sessions

All MRI scans were performed at the IWK Health Centre using a full-body 1.5 T GE Twinspeed scanner. The first MRI scan was conducted in the week following the control session, and the second scan one week later. To avoid possible time–of–day effects, the control session and the two scans took place at approximately the same time of day for each participant (15:00–18:00). Before beginning Scan 1, participants received a detailed verbal orientation to the scanning procedures, including information about the duration of the session. During the scans, participants were told how long each sequence would last, and they were informed when the end of the session was approaching. Participants were not given a task to perform during the scans but were asked to try to stay awake. The same MRI sequences were used during both Scan 1 and Scan 2 (see Table 1 for details). Total scan time was approximately 60 min.

The procedure for measuring anxiety levels during both scans was as follows: inside the MRI suite, immediately after the participant was positioned inside the scanner bore but before the scanning procedures started, the POMS-TA was administered verbally by an experimenter. During the scan, the POMS-TA was administered by audio link during short pauses between scanning runs (at ~8, 20, 35 and 50 min). Heart

<table>
<thead>
<tr>
<th>Scan type</th>
<th>Sequence</th>
<th>Duration (min:s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Localizer</td>
<td>FRFSE</td>
</tr>
<tr>
<td>2.</td>
<td>1H-MRS</td>
<td>PRESS</td>
</tr>
<tr>
<td>3.</td>
<td>1H-MRS</td>
<td>PRESS</td>
</tr>
<tr>
<td>4.</td>
<td>1H-MRS</td>
<td>PRESS</td>
</tr>
<tr>
<td>5.</td>
<td>T1 (anatomical)</td>
<td>SPGR</td>
</tr>
</tbody>
</table>

rate was monitored continuously during the scan with a finger pulse-oximeter and recorded at 30 s intervals.

2.5. Data analysis and statistics

Heart rate data were analyzed by first creating bins for each subject that corresponded to the time intervals between self-reports, then computing the mean heart rate for each time bin. Changes over time were analyzed using a repeated-measures ANOVA with factors of Session (Control Session, Scan 1, Scan 2) and Time Bin (0–8 min, 9–20 min, 21–35 min, 36–50 min, 51 min-session end). Changes in POMS-TA scores over time were analyzed using a repeated-measures ANOVA with factors of Session (Control Session, Scan 1, Scan 2) and Time (reports at 0, 8, 20, 35 and 50 min into the session). Significant main effects and interactions from each of the two ANOVAs were followed by simple-effects ANOVAs and trend analyses.

3. Results

3.1. Terminated scan

Out of the group of 12 healthy, young men, one participant experienced extreme anxiety upon being positioned within the MRI scanner, was unable to begin the scanning procedure and had to be excused from the study. He reported no prior history of claustrophobia or other anxiety disorders, and had not anticipated that the scan would cause him any discomfort, consistent with other reports of anxiety due to MR scanning (Fishbain et al., 1988; Avrahami, 1990). He was debriefed and offered follow-up psychological counseling.

3.2. Self-reports

For the remaining 11 participants, Fig. 1A shows that self-reported anxiety scores (as measured by the POMS-TA) varied significantly according to Session (F[2,20] = 18.8, P < 0.01) and Time (F[4,40] = 3.73, P < 0.05), with a significant interaction between Session and Time (F[8,80] = 2.02, P = 0.05). Anxiety was significantly higher overall during Scan 1 compared to Scan 2 (F[1,10] = 36.5, P < 0.001), while anxiety levels during Scan 2 did not differ significantly from those during the Control Session (F[1,10] = 2.45, P = 0.15). Anxiety levels were relatively constant during the Control session and during Scan 2 (Fig. 1A), but showed a pronounced quadratic trend during Scan 1: anxiety levels started high, decreased in mid-scan, and then increased again toward the end of Scan 1 (quadratic trend: F[1,10] = 9.74, P < 0.05).

3.3. Heart rate

There were significant effects of Session (F[2,20] = 3.71, P < 0.05) and Time Bin (F[4,40] = 7.57, P < 0.001) on heart rate, as well as a significant Session x Time Bin interaction (F[4,40] = 2.99, P < 0.001). Similar to the anxiety self-reports, heart rate was significantly higher during Scan 1 than Scan 2 (Fig. 1B; F[1,10] = 6.94, P < 0.05); however, heart rate during Scan 1 closely resembled that during the Control session (F < 1). Within sessions, significant quadratic trends were evident during both Scan 1 (F[1,10] = 13.3, P < 0.01) and Scan 2 (F[1,10] = 52.4, P < 0.001): heart rate was high at the beginning of both scans, decreased during the middle of the scan and increased again toward the end. This pattern was particularly pronounced during Scan 2 (Fig. 1B).

4. Discussion

This study assessed variation in MRI-related anxiety levels within and between repeated MRI scanning sessions. Our results indicate that anxiety levels in healthy young men fluctuate significantly over both these timescales. Self-reported anxiety and heart rate were both higher during the first scan compared to the second scan, probably reflecting initial anxiety about the scan procedures and environment, followed by habituation over sessions. During the second scan, self-reported anxiety returned to levels observed during the control session, while heart rate values decreased below those in the control session. The latter observation suggests that the novelty of the hospital environment and participation in a research study (even outside the scanner environment) may themselves have influenced physiological arousal. We observed significant habituation of both anxiety levels and heart rate with a delay of one week between scans; it remains to be determined whether these effects would be similar over longer delay intervals, such as might be used in psychiatric treatment studies.

We also observed changes in anxiety levels over the course of a single scanning session. During the first scan, self-reported anxiety and heart rate were both high at the beginning of the session and decreased in mid-scan, presumably reflecting within-session habituation to the scan procedures and environment. Both measures then increased somewhat toward the end of the session. Heart rate demonstrated

![Fig. 1. A. Mean self-reported anxiety, as measured by POMS-TA scores, across the three sessions. Higher POMS-TA scores indicate greater state anxiety. B. Mean heart rate across the three sessions (N = 11 for both A and B). Error bars show ±1 SEM.](image-url)
this quadratic trend clearly during both the first and second scans. The increases in anxiety level and heart rate toward the end of the scans could be related to anticipation of the session ending, since participants were informed when the end of the session was approaching. Alternatively, they could reflect restlessness and discomfort after an extended period of confinement and immobility. The latter interpretation suggests that future studies should assess the advisability of very long scanning sessions.

Because changes in anxiety levels are known to affect brain activation (Bishop et al., 2004), these data suggest that variation in MRI-related anxiety has the potential to influence neuroimaging results. For example, the heightened anxiety that was observed during the first scan could be associated with brain activation changes in anterior cingulate (Simpson et al., 2001), orbitofrontal cortex (Damasio et al., 2000) or amygdala (Phan et al., 2002), which are among the regions that have previously been shown to be influenced by state anxiety. Moreover, changes in cardiovascular variables, such as heart rate and sympathetic/parasympathetic tone, are also known to influence regional brain activity (Critchley et al., 2000; Critchley et al., 2003; Gnanaros et al., 2004). Habituation to the scanner, and the associated decrease in anxiety levels, would presumably reduce any such changes during a second scan. Habituation effects could also be expected over the course of a single scanning session, given that we found significant changes in MRI-related anxiety within each scan.

Our data were obtained from a group of healthy young men with no history of clinical anxiety, including the individual who was unable to participate because of acute anxiety. Given the homogeneity of our group, we do not know if these results are generalizable to other groups; however, one may speculate that the impact of MRI-related anxiety might be even more pronounced in other populations. For example, women are more likely than men to experience severe MRI-related anxiety, resulting in scan termination or necessitating sedation (Dewey et al., 2007). Other vulnerable populations may include patients with psychiatric illnesses and perhaps children or the elderly. Any effects assessed in these groups using a repeated-measures experimental design could therefore be more susceptible to being confounded with large changes in anxiety levels caused by a strong anxiety reaction to the first experience of scanning, followed by habituation. Alternatively, some groups could be prone to sensitization rather than habituation, if the initial experience of scanning were particularly aversive to them (MacKenzie et al., 1995). Further research is needed to examine levels of MRI-related anxiety in other populations, including women.

A second potential limit on the generalizability of our study stems from the absence of explicit task demands. In many fMRI studies, participants have a task to perform during the scans, while our participants simply rested quietly during each session. Since distraction typically reduces anxiety levels (e.g., Corah et al., 1979), it is possible that participants who have an engaging task to perform may show less variation in anxiety levels than our participants did. In many fMRI studies, however, the task consists of passively viewing stimuli, or is so easy or boring that participants are unlikely to be strongly engaged and distracted.

Moreover, other types of MRI studies do not include tasks. Magnetic resonance spectroscopy (MRS) studies, for example, typically do not include an explicit task, and resting-state fMRI studies are intended to investigate patterns of brain activity in the absence of explicit task demands (Raichle et al., 2001; Raichle and Snyder, 2007; Buckner et al., 2008). Thus, distraction resulting from task demands is unlikely to reduce the potential impact of changing arousal and anxiety levels across and within sessions for many types of MRI studies.

MRI-related anxiety may be reduced by giving participants detailed information about the scanning procedures before the experiment begins. A previous study reported that patients receiving a very comprehensive orientation procedure, which included an information booklet, exposure to recorded scanner noise, a tour of the control room, and strategies to reduce anxiety experienced less anxiety than controls given the usual basic instructions (Gray et al., 2000).

The practice of habituating participants in an MRI simulator before the actual scans may also be a valuable exercise. Previous research has demonstrated that even highly claustrophobic participants show steep decreases in anxiety upon repeated experience with an MRI simulator (Wood and McGlynn, 2000). Training in an MRI simulator could also reduce the number of prematurely terminated scans, which are costly and inconvenient to researchers, as well as stressful and disheartening for participants. If simulator training is not possible, an alternative approach would be to measure anxiety levels during scanning. These data could then be modeled as covariates in neuroimaging analyses, in an attempt to disentangle the influence of scan-related anxiety from experimental effects of interest. Both the anxiety self-reports and heart-rate measures we employed were easy to implement, and could be conducted with only minor interruptions to the scanning procedures.

Researchers may also wish to take within-scan changes in anxiety into account when planning a series of experiments to be performed within a single scanning session. In particular, we found that anxiety levels were highest at the beginning and end of each scan, and most stable in the middle of the session. Therefore it may be best to perform anatomical scans during the first and last 10 minutes of each scan, reserving the middle of the session for functional experiments.

In conclusion, we found changes in MRI-related anxiety levels in a group of healthy young men, both within and between MRI scanning sessions. These fluctuations, although highly reproducible, were relatively small, so it remains for future studies to determine whether changes of this magnitude can significantly affect neuroimaging results. If the results of such studies are positive, then researchers may be able to improve the sensitivity and validity of neuroimaging studies by taking MRI-related anxiety into account, allowing more reliable detection of subtle differences between controls and patients, or smaller within-subject changes over time.

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