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(Don't) panic in the scanner! How panic patients with agoraphobia experience a functional magnetic resonance imaging session

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Abstract

Although functional magnetic resonance imaging (fMRI) has gained increasing importance in investigating neural substrates of anxiety disorders, less is known about the stress eliciting properties of the scanner environment itself. The aim of the study was to investigate feasibility, self-reported distress and anxiety management strategies during an fMRI experiment in a comprehensive sample of patients with panic disorder and agoraphobia (PD/AG). Within the national research network PANIC-NET, n=89 patients and n=90 controls participated in a multicenter fMRI study. Subjects completed a retrospective questionnaire on self-reported distress, including a habituation profile and exploratory questions about helpful strategies. Drop-out rates

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and fMRI quality parameters were employed as markers of study feasibility. Different anxiety measures were used to identify patients particularly vulnerable to increased scanner anxiety and impaired data quality. Three (3.5%) patients terminated the session prematurely. While drop-out rates were comparable for patients and controls, data quality was moderately impaired in patients. Distress was significantly elevated in patients compared to controls; claustrophobic anxiety was furthermore associated with pronounced distress and lower fMRI data quality in patients. Patients reported helpful strategies, including motivational factors and cognitive coping strategies. The feasibility of large-scale fMRI studies on PD/AG patients could be proved. Study designs should nevertheless acknowledge that the MRI setting may enhance stress reactions. Future studies are needed to investigate the relationship between self-reported distress and fMRI data in patient groups that are subject to neuroimaging research.
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1. Introduction

Although functional magnetic resonance imaging (fMRI) has gained increasing importance in investigating neural substrates of anxiety disorders (Paulus, 2008), less is known about the stress eliciting properties of the scanner environment itself. Reports about routine care patients indicate that an MRI examination can produce subjective distress (Dantendorfer et al., 1997; Flaherty and Hoskinson, 1989; Kilborn and Labbe, 1990; Mackenzie et al., 1995; McIsaac et al., 1998) or trigger long-term claustrophobia (Fishbain et al., 1988; Kilborn and Labbe, 1990) and panic attacks (Spiegelhalder et al., 2009) in subjects with no previous psychiatric history. Pre-existing claustrophobia may moreover predict distress and panic symptoms in the scanner (McIsaac et al., 1998). Adverse reactions not only constitute a significant problem for patients: they can affect the performance of (f)MRI studies by increasing the number of declined appointments, premature terminations of scans, or impair data quality (Dantendorfer et al., 1997).

Scanner distress ranges from moderate apprehension (approx. 30%), to severe panic and claustrophobia experienced by 5–10% of routine care patients (Melendez and McCrank, 1993). Among anxiety patients, those suffering from panic disorder and agoraphobia (PD/AG) are particularly vulnerable to the stress eliciting properties of the MRI, which is a highly agoraphobic/claustrophobic stimulus. Comprehensive assessments of scanner distress in PD are still lacking, but Bystritsky et al. (2001) found elevated panic symptoms in patients compared to controls. Maddock et al. (2003) stated that four out of six patients reported feeling anxious throughout the scan. Pillay et al. (2006) observed that although all eight patients were able to complete the scan, they showed initial signs of hesitation. Interpretation of these observations is however limited by the small number of patients and lack of quantitative assessment tools.

The aim of the present study was to investigate scanner-related effects on self-reported distress and data quality in a multicenter fMRI study on n = 89 PD/AG patients, addressing the following research questions:

1) Are large-scale fMRI studies in PD/AG patients (dropout-rates, data quality) feasible?
2) Do patients and controls differ in their amount of distress before, during and after the session?
3) Can we identify vulnerable patients using different measures of anxiety?
4) Management strategies: what can we do to make patients feel more comfortable?

2. Experimental procedures

2.1. Multicenter study PANIC NET

The fMRI study was embedded within a national research network (PANIC-NET; Arolt et al., 2009; Gloster et al., 2009) that is characterized by a multilevel and multicenter research structure, encompassing a randomized controlled clinical trial on cognitive behavioural therapy (CBT) and experimental add-on studies on fear circuit mechanisms in PD/AG. Eight centers participated in the clinical trial (Aachen, Berlin-Adlershof, Berlin-Charité, Bremen, Dresden, Greifswald, Münster, and Würzburg) treating n = 369 patients who met DSM-IV criteria for PD/AG. Four centers (Aachen, Berlin-Charité, Dresden, and Münster) also participated in the fMRI study which had been approved by all responsible ethics committees of the participating centers (research cluster P7: "Neuronal plasticity following cognitive-behavioral therapy in patients with panic disorder: a multicenter 3-Tesla study using fMRI").

2.2. Subjects

Eighty-nine PD/AG patients and 90 healthy controls participated in the fMRI study; n = 87 patients also participated in the clinical trial. Patient inclusion criteria encompassed a primary diagnosis of PD/AG according to the criteria of DSM-IVTR as assessed by the Composite International Diagnostic Interview (CAPI-WHO-CIDI; DIAX-CIDI version; Wittchen and Pfister, 1997), a score ≥18 at the Hamilton-Anxiety-Scale (SIGH-A; Shear et al., 2001), a score ≥4 at the Clinical Global Impressions Scale (CGI; Guy, 1976), age between 18 and 60 years. Exclusion criteria encompassed psychotic or bipolar I disorders, current threshold alcohol or substance dependence, current suicidal tendency, borderline personality disorder, organic mental disorders, concurrent psychotherapeutic/psychopharmacological treatments, severe cardiovascular, renal, and neurological diseases, colour blindness and any MRI-related exclusion criteria. Exclusion criteria were either assessed by entry into the clinical trial or prior to participation in the fMRI study. The control group was matched for gender, education, age, and handedness. Subjects were excluded in case of any current or lifetime diagnosis of any mental disorder (except misuse of alcohol and nicotine dependence), neurological disorders, central-nervous medication within the last four weeks, colour blindness, and MRI-related contraindications.

2.3. Procedure

Following inclusion into the clinical trial, patients were asked for participation in the fMRI study. Controls were recruited via advertisements and flyers. Subjects were scheduled an

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