Psychiatry Research: Neuroimaging 214 (2013) 444–451

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Neural correlation of successful cognitive behaviour therapy for spider phobia: A magnetoencephalography study

Barry Wright [a,*], Ben Alderson-Day [a], Garreth Prendergast [b], Juliette Kennedy [a], Sophie Bennett [a], Mary Docherty [a], Clare Whitton [a], Laura Manea [a], Andre Gouws [b], Heather Tomlinson [a], Gary Green [b]

[a] Lime Trees Child, Family & Adolescent Unit, North Yorkshire and York Primary Care Trust, York, United Kingdom
[b] York Neuroimaging Centre, University of York, York, United Kingdom

ARTICLE INFO

Article history:
Received 23 August 2012
Received in revised form
4 July 2013
Accepted 13 September 2013

Keywords:
Simple phobia
Magnetoencephalography
Neuroimaging
Psychological therapy
Brain activation
Fear

ABSTRACT

Cognitive behavioural therapy (CBT) can be an effective treatment for spider phobia, but the underlying neural correlates of therapeutic change are yet to be specified. The present study used magnetoencephalography (MEG) to study responses within the first half second, to phobogenic stimuli in a group of individuals with spider phobia prior to treatment ($n=12$) and then in nine of them following successful CBT (where they could touch and manage live large common house spiders) at least 9 months later. We also compared responses to a group of age-matched healthy control participants ($n=11$). Participants viewed static photographs of real spiders, other fear-inducing images (e.g. snakes, sharks) and neutral stimuli (e.g. kittens). Beamforming methods were used to localise sources of significant power changes in response to stimuli. Prior to treatment, participants with spider phobia showed a significant maximum response in the right frontal pole when viewing images of real spiders specifically. No significant frontal response was observed for either control participants or participants with spider phobia post-treatment. In addition, participants' subjective ratings of spider stimuli significantly predicted peak responses in right frontal regions. The implications for understanding brain-based effects of cognitive therapies are discussed.

1. Introduction

Lifetime prevalence estimates for specific phobia range from 10% to 18% of the general population (Bijl et al., 1998; Kessler et al., 2005; Moffitt et al., 2010). One of the most common specific phobias is fear of spiders, which is reported to affect up to 1.2% of men and 5.6% of women (Fredrikson et al., 1996).

Treatment methods for specific phobias vary in their effectiveness (Choy et al., 2007). For spider phobia, successful treatment has involved aspects of exposure therapy and techniques from cognitive behavioural therapy (CBT) (Öst, 1996; Öst et al.,1991). Such methods can lead to significant reductions in patient-reported phobia and achievement of key functional goals, such as being able to remove a spider from the room (Wright et al., in preparation).

The success of talking therapy methods has led to efforts to identify the underlying neural correlates of spider phobia and how they change with therapy (Johanson et al., 1998, 2006; Paquette et al., 2003; Straube et al., 2006). In a study of 16 women with severe phobia using positron emission tomography (PET), Johanson et al. (1998) reported changes in regional cerebral blood flow (rCBF) in right frontal regions in response to videos of spiders (compared to rest and neutral images). However, specific changes were moderated by how participants managed their anxiety when viewing phobogenic stimuli: those that reported intense panic showed decreases in right frontal rCBF (in relation to rest), whereas those who reported being able to control their anxiety displayed increases in the same areas (Johanson et al., 1998). In a follow-up study that compared rCBF responses before and after a course of cognitive therapy (Johanson et al., 2006), participants who initially reported an anxiety response showed increases in right prefrontal cortex following successful treatment.

The importance of right prefrontal cortical regions in particular was supported in studies by Schienle et al. (2005) and Paquette et al. (2003). Using the greater spatial resolution of functional magnetic resonance imaging (fMRI), Schienle's group (2005) reported increased activation of the right dorsolateral prefrontal cortex (DLPFC), amygdala and right hippocampus in response to static images of spiders. Paquette et al. (2003) observed activation in right DLPFC prior to a course of CBT in participants with spider

* Correspondence to: Lime Trees Child, Family & Adolescent Unit, CAMHS, 31 Shipton Road, York, YO30 5RE, UK. Tel.: +44 1904726610; fax: +44 1904 632893.
E-mail address: barry.wright1@nhs.net (B. Wright).

0925-4927/$ - see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.pscychresns.2013.09.011

phobia, but no such response following treatment. Changes following similar therapeutic interventions have also been observed in the anterior cingulate cortex and insula (Straube et al., 2006) and amygdala, fusiform gyrus and medial orbitofrontal cortex (OFC) (Schienle et al., 2007). In the longer term, reductions in phobia following treatment have been associated with increases in medial OFC, which have been interpreted as reflecting improvement in emotional self-regulation (Schienle et al., 2009).

While the above MRI studies have identified the main brain areas associated with improvements following treatment, they lack the temporal resolution required to examine the time course of the phobic response. This is significant, as responses to phobogenic stimuli can be rapid (Globisch et al., 1999; Carlsson et al., 2004). Increased potentiation of the startle reflex has been reported to occur as early as 300 ms post-stimulus in participants viewing phobia-specific images (Globisch et al., 1999), an effect that can be induced with presentation times as short as 150 ms. Using a masking paradigm, Carlsson et al. (2004) reported phobia-specific PET responses in the amygdala and surrounding areas even when phobogenic target stimuli were only presented for 14 ms. Phobic participants are faster than controls in identifying spiders and show increased P300 and P400 responses to spider stimuli (Kolassa et al., 2005), with P300 increases also seen in spider phobia EEG studies (Leutgeb et al., 2009; Scharmüller et al., 2011). In addition, the onset of the BOLD response in the amygdala to spider images has also been reported to be earlier in phobic participants (Larson et al., 2006).

Because of this, it is important to complement existing findings on therapeutic change in the phobic response with data using electrophysiological methods, which have high temporal resolution. Electroencephalography (EEG) and magnetoencephalography (MEG), in contrast to MRI, allow for examination of the early (i.e. under one second) phobic response. Commonly this greater temporal resolution is associated with a loss of spatial resolution: most electroencephalographic methods of analysis are constrained to reporting changes in sensor-space. However, when combined with spatial filtering techniques such as Beamforming, MEG in particular allows for the reconstruction of multiple sources of activity inside the skull, at a greater spatial resolution than standard electrophysiological methods of analysis. This makes it an ideal tool for examining changes in the phobic responses with therapy.

The present study is the first (to our knowledge) to use MEG to examine changes to the early phobic response to spider stimuli. This was done first by comparing MEG responses in a group of participants with spider phobia and a group of age-matched, healthy controls, viewing images of spiders, other fear-inducing but non-phobogenic stimuli (e.g. snakes, sharks) and neutral stimuli. To then examine therapy-related changes, spider phobic participants completed a 6-month course of CBT, and were scanned in a second session. Following previous findings, we hypothesised that changes to the phobic responses would be observable in the right prefrontal cortex in particular.

2. Method

2.1. Participants

Twelve young people and adults (2M/10F; Age mean [S.D.]=27.84 [9.71], range=16–44) were recruited from the local area (York and North Yorkshire) via referral from their GP to mental health services for spider phobia treatment. Following referral all participants were assessed by an experienced clinician. They were only included if they were between 16 and 45 and met all the ICD-10 Research Diagnostic Criteria for phobic disorder involving spiders (World Health Organisation, 1993). We used a clinical interview with an experienced consultant psychiatrist and semi-structured questionnaire to achieve this. Exclusion criteria included any serious mental illness that required acute treatment that would preclude CBT as a practical method of treatment. In the event none of the participants had any mental health or neurological co-morbidities, with the exception of one participant with a history of depression, but who was healthy at the time of study. No-one was taking any psychotropic medication. There were no ethnic or language based exclusions. Eleven controls, group-matched for age and gender, were recruited via posters in community settings (2M/9F; Age mean [S.D.]=29.21 [10.30], range=18–45; t (21)= −0.33, P=0.746, n.s., unpaired t-test used). All participants were right handed with the exception of one participant in the phobic group and two participants in the control group.

The study received ethical approval and all participants gave fully informed consent after receiving information about the study.

2.2. Design

A mixed design was deployed across two stages: first, between-groups analysis comparing pre-treatment phobic participants (SP) and controls (Ctrl). Second, within-groups analysis compared phobic participants pre- (SP1) and post-treatment (SP2), for those participants who completed the course of therapy.

2.3. Treatment

Phobic participants received cognitive behaviour therapy described in detail elsewhere (Wright et al., in preparation) and was intended to be as comprehensive as possible based on the evidence base (without cost effectiveness restrictions). It comprised a mixture of desensitisation, habituation, in vivo exposure and a range of cognitive techniques and homework. Participants underwent a mean of 14 sessions. They were scanned before treatment and also after successful completion of treatment. The average length of time between each scan was 14.11 months. Success was defined as being able to cope with touching live spiders, capturing a large common spider in a jar and successfully releasing it outside, and a subjective feeling of being able to cope with spiders. All bar one participant were able to let large common English spiders walk repeatedly on their hands by the end of treatment. Outcomes of treatment were also assessed quantitatively using three questionnaires: the Fear of Spiders questionnaire (Szymanski and O'Donohue, 1995), the Fear Survey Schedule (Wolpe and Lang, 1964) and the Beck Anxiety Inventory (Beck et al., 1988). Scores on each questionnaire were compared pre- and post-treatment.

2.4. Procedure

All participants completed the MEG and MRI scanning protocols in a single session. (Structural MRI scans were required for localisation of MEG data). MEG was completed pre- and post-treatment in phobic subjects and once in controls. Phobic participants on their second visit were not required to complete a second MRI scan: their original structural data were used for co-registration.

The MEG session was divided into three scanning runs (blocks): cartoons, plastic objects, and real images (i.e. photos), with the first two runs designated as practice conditions, and the latter as a test condition. Each of these runs included three types of images. These were neutral images, fear inducing images (non-spider), and spider images chosen after pilot testing for fear ratings. Within each of these there were three images (e.g. in the non-spider fear real photo run there was (i) an aggressive dog, (ii) a shark and (iii) a snake). These were presented in a random order within each run, with each image appearing 33 times to allow brain scan capture. Before each run, participants were shown the images for that run while sat in the scanner with the door open. They were asked to rate them on level of fear from 1 to 9 (9 being most scary) to verify fearfulness. Finally, participants were asked if they were happy to view the images during the scan. On confirmed consent the participant the door was then closed and the scan begun.

Images were projected onto a white screen with a visual angle of $16^\circ \times 21^\circ$ (h × w). All images were presented for 500 ms (defined as the "active" period henceforth), followed by a fixation cross for 600 ms (the "passive" period). A total of 297 images were presented, taking just under 6 min. During scanning, participants were asked to keep still at all times and maintain their attention on the image or the fixation cross. Image presentation was conducted in E-Prime (Schneider et al., 2002).

Data were collected at the York NeuroImaging Centre using a 4D NeuroImaging MAGNES 3600 (a magnetometer based 248 channel whole-head MEG system), at a sample rate of 678.17 Hz with a bandwidth of 200 Hz. The MAGNES 3600 uses the magnetic fields measured by a reference array to perform online noise reduction. The noise reduction is performed using a weighted sum of the reference channels based upon site-specific noise calibrations.

Each participant completed a structural MRI scan after completing the MEG session. A GE 3.0 T Signa Excite HDx MRI scanner was used to acquire T1 structural images for each participant using a 3D FSPGR (Sagittal Isotropic 3D Fast Spoiled Gradient Recall Echo – structural T1 weighted scan). Acquisition parameters were as follows: Matrix size: 256 × 256 × 176, FOV: 290 × 290 × 176 mm^3, Slice thickness: 1.13 × 1.13 × 1.0 mm^3, TR 8.03 ms, TE 3.07 ms, Flip angle 20", PSD: efgre3d.