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The temporal unfolding of face processing in social anxiety disorder — a MEG study

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ABSTRACT

The current study is the first to use magnetoencephalography (MEG) to examine how individuals with social anxiety disorder (SAD) process emotional facial expressions (EFEs). We expected that, compared to healthy controls (HCs), participants with SAD will show an early (<200 ms post-stimulus) over-activation in the insula and the fusiform gyrus (FG, associated with the N170/M170 component), and later (>200 ms post-stimulus) over-activation in the dorsolateral prefrontal cortex (DLPFC). Individuals with SAD (n = 12) and healthy controls (HCs, n = 12) were presented with photographs of facial displays during MEG recording. As compared to the HC group, the SAD group showed a reduced M170 (right FG under-activation around 130–200 ms); early reduced activation in the right insula, and lower insular sensitivity to the type of EFE displayed. In addition, the SAD group showed a late over-activation in the right DLPFC. This unique EFE processing pattern in SAD suggests an early under-activation of cortical areas, possibly related to reduced emphasis on high spatial frequency information and greater early emphasis on low spatial frequency information. The late DLPFC over-activation in the SAD group may correlate to failures of cognitive control in this disorder. The importance of a temporal perspective for the understanding of facial processing in psychopathology is underlined.

1. Introduction

Social anxiety disorder (SAD) is the most common anxiety disorder in the community, with an estimated life-time prevalence rate as high as 13% (Furmark, 2002). Individuals with social anxiety (SA) are agonized by the potential risk of performing inadequately in social situations or showing overt signs of nervousness with resultant embarrassment or humiliation (American-Psychiatric-Association, 1994). The processing of emotional facial expressions (EFEs) is an important aspect in social functioning, as they enable people to quickly infer other persons' thoughts, feelings, intentions and motivations (e.g., Said et al., 2011). Such nonverbal aspects of human interaction are especially relevant for individuals suffering from SA, for whom social evaluation is a primary concern.

Over the years, neuroimaging paradigms have been recruited to the study of EFE processing in SAD. Face processing entails several neural systems (Vuilleumier and Pourtois, 2007). First, the limbic system, including the amygdala and insula regions, processes coarse, low spatial frequency (LSF) information from the face (Vuilleumier et al., 2003). LSF information is important mainly for decoding emotional expressions (Langner et al., 2009). The amygdala and insula are involved in the detection of emotional, social or threatening stimuli (Anderson et al., 2003; Calder et al., 2001; Schienle et al., 2002), and their activity is modulated by the type of facial expression (Adolphs, 2002). MEG studies have shown that the activity of both areas is observed during the early stages of emotional face processing: the amygdala around 40 milliseconds (ms) (Garvert et al., 2014) and the insula around 150 ms post-stimulus onset (Bayle and Taylor, 2010; Chen et al., 2009). Moreover, Luo et al. (2007) found early event related synchronizations (ERS) in response to fearful faces in the amygdala at around 30 ms, and for angry expressions at around 150 ms.

This quick limbic processing pathway may be partly independent of a second, slower system involving the extrastriate visual cortex, including the fusiform gyrus (FG) (Vuilleumier et al., 2002; Vuilleumier et al., 2003; Williams et al., 2004). The "fusiform face area" (Kanwisher et al., 1997) in the FG has a key role in face perception, and is a part of a specialized neural system for face processing (Kanwisher and Yovel, 2006). This second stage of processing extracts finer and more elaborate high spatial frequency (HSF) features (Vuilleumier et al., 2003), important

Abbreviations: AFNI, analysis of functional neuroimages; BDI, Beck Depression Inventory; DLPFC, dorsolateral prefrontal cortex; EEG, electroencephalography; EFE, emotional facial expressions; FG, fusiform gyrus; FMRI, functional magnetic resonance imaging; FNE, fear of negative evaluation; HC, healthy control; HSF, high spatial frequency; LSAS, Liebowitz Social Anxiety Scale; LSF, low spatial frequency; MEG, magnetoencephalography; SA, social anxiety; SAD, social anxiety disorder; SAM, synthetic aperture modeling; TMS, transcranial magnetic stimulation.

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for precise recognition of identity and more detailed analysis of facial traits, such as age (Alorda et al., 2007; Winston et al., 2003). This slower processing of faces in the FG is usually associated with the N170 electroencephalography (EEG) component, or M170 in magnetoencephalography (MEG) (Taylor et al., 2011). The N170/M170 face-selective component (Bentin et al., 1996) indexes the late stages of structural encoding of faces which include a configurational analysis of whole faces. As such, the N170 is maximal to face stimuli that are optimal for face recognition and identification (Eimer, 2000); and is correlated with successful face categorization and identification (Liu et al., 2002).

In addition to the abovementioned systems, the processing of EFEs also requires top-down mechanisms, aimed at inhibiting emotional reactions to threatening stimuli and associated with prefrontal activation (Davidson, 2002; Ochsner and Gross, 2005). The dorsolateral prefrontal cortex (DLPFC) is important in this aspect as it initiates emotion regulation by inhibiting the amygdala (Siegle et al., 2007). The importance of the DLPFC region in the ability to disengage attention from faces was illustrated when transcranial magnetic stimulation (TMS) of the right prefrontal cortex resulted in impaired disengagement from angry faces, associated with decreased activation within the right DLPFC (De Raedt et al., 2010). In addition, a recent study showed that participants with high rumination scores (brooders) display higher DLPFC activity when attempting to disengage attention from negative EFEs (Vanderhasselt et al., 2011), suggesting that brooders need to recruit more attentional control (manifest as the DLPFC activity) in order to successfully disengage from negative information. MEG studies suggest that the frontal involvement in EFE processing arrives rather late in the processing stream: at around 250 ms post-stimulus (in Taylor et al., 2011); or around 160–210 ms (in Luo et al., 2007).

Haxby et al. (2000, 2002) described the EFE processing system as comprised of a core system which includes face-specific areas (including the FG and superior temporal sulcus, STS) which perform the visual analysis of faces; and an extended neural system, aimed at extracting important social information from faces, such as temporary mood states and intentions, as well as more stable personality characteristics. This extended system is comprised of brain structures which are involved in other functions, such as directing attention (e.g., frontal areas) or emotional processing (such as the amygdala and insula) (Haxby et al., 2002).

Due to the importance of facial expressions in social interaction and in SA, various studies explored the neural correlates of EFE processing in SAD, using both fMRI and EEG. Findings from fMRI studies have consistently shown that SADs present enhanced activation in limbic areas (such as the amygdala and insula) when viewing threatening faces (Evans et al., 2008; Gentili et al., 2008; Stein et al., 2002; Straube et al., 2005), as well as neutral ones (Birbaumer et al., 1998; Cooney et al., 2006). In contrast, the findings regarding the role of FG in face processing yielded a conflicting pattern of results using both fMRI and EEG methodologies. First, using fMRI, Straube et al. (2004) found that participants with SAD exhibited stronger FG activation compared to healthy controls (HCs), during categorization of face pictures as schematic or photographic, and also during free viewing of angry, happy and neutral faces (Straube et al., 2005). On the other hand, Gentili et al. (2008) found *weaker* activation in the left FG in SADs (compared to HCs), when performing a one-back repetition detection task based on face identity. Similarly, Beaton et al. showed in two studies that shy participants present *weaker* right FG activation to faces (compared to non-shy controls), when judging the faces' familiarity (Beaton et al., 2009) or gender (Beaton et al., 2010). The role of the FG in processing of facial expressions in SAD is therefore not yet clearly understood. Importantly, due to the low temporal resolution of fMRI, these studies cannot offer temporal information regarding the timing of the limbic over-activity or the FG activation.

Second, using EEG, a similarly inconclusive pattern emerged with the face-specific N170 component found as weaker, stronger or equally powerful in participants with SAD as compared to HCs (Kolassa and Miltner, 2006; Mueller et al., 2009; Muhlberger et al., 2009). These discrepancies may stem from the focus of participants' attention in the different tasks: Kolassa et al. (2006) found *stronger* N170 amplitudes in participants with SAD (compared to HCs), but only on tasks in which emotional expression was task-relevant (emotion categorization task), but not when it was task-irrelevant (gender categorization). A *weaker* N170 in participants with SAD (compared to HCs) was found using another variant of an emotion-irrelevant task (dot-probe, in which two faces are presented, Mueller et al., 2009). Another factor which may have affected the N170 is the type of facial stimuli: all studies which found no effects of SA on the N170 used artificial faces, whether exclusively (Kolassa, 2009; Kolassa et al., 2007), or alongside natural faces (Muhlberger et al., 2009). Due to the diverse findings, it is thus still unclear whether SA affects the amplitude of the N170/M170, but it seems that relevant variables which may modulate this component are the type of task, type of faces (artificial or natural) and whether a single face or multiple faces are presented.

In addition to these functional findings, recent studies also suggest the existence of structural brain abnormalities in SAD as compared to HCs. Differences in gray matter morphometry and cortical thickness have been observed in various brain areas of individuals with SAD (although results are somewhat mixed, see review by Bruhl et al., 2014). Interestingly, studies also point to abnormalities in the connectivity or interaction of different brain areas in SAD. As compared to HCs, individuals with SAD show reduced volume of the left uncinate fasciculus, which connects frontal and temporal areas, including the amygdala (Baur et al., 2013); and show reduced connectivity between limbic areas (anterior insula) and prefrontal regions (dorsal anterior cingulate cortex) (Klumpp et al., 2012).

The processing of EFEs in SAD has also been studied using behavioral methods. These studies consistently suggest that individuals with SAD experience difficulty disengaging from threatening stimuli (Amir et al., 2003), as well as ignoring irrelevant emotional information from faces (Gilboa-Schechtman et al., 2004) or words (Grant & Beck, 2006; Mattia et al., 1993). Eye tracking studies also revealed that people with SAD exhibit disengagement difficulties from EFEs (Buckner et al., 2010; Schofield et al., 2012). As compared to HCs, individuals with SAD also show longer fixation duration at EFEs during the first 1000 ms of stimulus exposure (Wieser et al., 2009). In addition, individuals with SAD initially direct their gaze more frequently at angry faces rather than neutral faces when shown angry–neutral face pairs (Gamble and Rapee, 2010; Schofield et al., 2012). While behavioral and eye-tracking studies depict a unique pattern of EFE processing in SA, these methodologies have not enabled a clear understanding of the moment-by-moment unfolding of these processes.

In summary, research efforts spanning a variety of methodologies have been aimed at uncovering the EFE processing patterns in individuals with SAD. Specifically, the main questions have been whether, as compared to HCs, individuals with SAD (a) show greater early sensitivity to facial display of threat; and (b) do they show later elaborate processing or avoidance of threatening expressions. An examination of the temporal course of face processing is likely to shed light on these questions. This is the main focus of the present study.

1.1. Overview of the present study

We chose to use MEG technology, which provides excellent temporal resolution (in the order of milliseconds) and good spatial resolution with source modeling methods. Despite these advantages, MEG has never been used in the study of SA before.

Participants diagnosed with SAD and HCs were presented with photographs of facial displays and asked to categorize the faces according to gender. Our decision to use a task in which emotional expression is task irrelevant was driven by two considerations. First, we believe that gender categorization tasks are ecologically valid, as in many interactions