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A continuous emotional task activates the left amygdala in healthy volunteers: ^{18}FDG PET study

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Abstract

Human amygdalar activation has been reported during facial emotion recognition (FER) studies, mostly using fast temporal resolution techniques (fMRI, $H_2^{15}O$ PET or MEG). The ^{18}FDG PET technique has never been previously applied to FER studies. We decided to test whether amygdala response during FER tasks could be assessed with this technique. The study was conducted in 10 healthy right-handed volunteers who underwent two scans on different days in random order. Content of the tasks was either emotional (ET) or neutral (CT) and lasted for 17 ½ min. Three SPM2 analyses were completed. The first, an ET-CT contrast, showed left amygdalar activation. The second ruled out order effect as a confounder factor. Finally, the whole brain contrast showed activation of the emotional recognition-related areas. Time responses and errors indicated high rates of accuracy in both tasks. We discuss the results and the role of habituation phenomena and the possibility of applying this technique to samples of patients with psychiatric disorders. In conclusion, our study reveals left amygdalar activation assessed with FDG PET, as well as other major emotion recognition-related brain areas during FER tasks.

Keywords: Positron emission tomography; Nuclear medicine; Limbic system; Hemispheric specialization

1. Introduction

The functional neuroimaging era has seen the progressive inclusion of different activation paradigms in the emotional perception circuit (Reiman et al., 1997; Zald and Pardo, 1997; Buchanan et al., 2000; Zalla et al., 2000), and helped to define the brain structures that play a role in the neurobiology of emotion. These brain areas include the amygdala, hippocampus, insula, anterior cingulate cortex, ventral striatum and orbitofrontal cortex (Dolan, 2002; Gur et al., 2002b; Phillips et al., 2003a; Calder and Young, 2005), as well as other areas that play more minor roles. A summary of the activation paradigms published reveals a general consensus that facial emotion recognition (FER)

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tasks act as the most powerful trigger for activation of the emotion network (Hariri et al., 2002). Some studies have also focused on which brain structure shows the greatest activation during FER paradigms, and the amygdala has been identified (Gur et al., 2002b; Williams et al., 2004). Indeed, during recent years, several studies have limited their analysis of FER effects to the amygdala (Fitzgerald et al., 2006), although reliance on a region of interest (ROI) approach in neuroimaging studies remains controversial (Friston et al., 2006; Saxe et al., 2006).

Researchers have summarized the functions of the human amygdala in emotion and vigilance (Davis and Whalen, 2001), on the basis of its role in automatic evaluation of danger (Zald and Pardo, 1997), emotion recognition (Adolphs et al., 1994) and novelty detection (Wright et al., 2003). A lateralized specialization has also been suggested, where novelty awareness would be entrusted to the right side and emotion recognition to the left (Tulving et al., 1994; Martin, 1999). Specificity of the amygdala in fear emotion recognition was initially suggested (Adolphs et al., 1994), despite current research supporting reactivity of the amygdala, as well as the above-mentioned limbic and extra-limbic structures, in response to multiple expressions of facial affect (Gur et al., 2002b; Phan et al., 2002; Yang et al., 2002; Fitzgerald et al., 2006). As part of this emotional-vigilance network, the amygdala presents extensive bidirectional connections with the other limbic and extra-limbic structures (Minzenberg et al., 2007).

Despite the wealth of research published in this area, there are no studies reporting amygdalar activation with low time resolution techniques. All FER studies with functional brain imaging have been performed with high temporal resolution techniques, such as fMRI (Gur et al., 2002c; Abel et al., 2003; Takahashi et al., 2004), MEG (Streit et al., 2003) or $H_2^{15}O$ positron emission tomography (PET) (Phan et al., 2002), which allow the detection of rapid changes in amygdala activity. The other major functional neuroimaging technique, ^{18}[F]fluorodeoxyglucose (FDG) PET, has not been used for FER studies so far. The pharmacokinetics of FDG distinguish it from other faster time resolution brain imaging techniques, such as fMRI, MEG or $H_2^{15}O$ PET. FDG includes a 30-min uptake period and continuous emission for almost 120 min after administration. The metabolism of the tracer stops during the glycolytic pathway and essentially remains trapped in the area of active metabolism, thus allowing evaluation of the degree of accumulative activation of brain areas for a period of almost 30 min and obtaining a single image per scan. The FDG technique would be more useful than high temporal resolution techniques for emotion tasks that require practice, and the judgment of emotions has an emotional concomitant that builds over minutes. It would represent sustained brain activation and would be directly proportional to brain work. Some reports in non-emotional tasks suggest that the amygdala can be assessed by FDG PET (Grant et al., 1996; London et al., 1996; Bonson et al., 2002; Rilling et al., 2004) and that the amygdala may respond in a sustained manner (Zald, 2003).

Thus, the specific aim of this study is to assess whether, in a sample of healthy volunteers and using FDG PET technology, it is feasible to study amygdalar activation during a continuous FER task.

2. Methods

2.1. Subjects

Ten right-handed young men (age range = 23–31), without current or past history of any psychiatric (including substance abuse) neurological or major medical conditions, participated in the study. Subjects were evaluated with the Spanish versions of both the SCID-I for DSM-IV psychiatric disorders and the Calgary Depression Scale (Sarro et al., 2004), Spanish version. All volunteers provided written consent as approved by the local Institutional Review Board.

2.2. Facial stimuli

Face pictures were selected from a set of 175 black and white pictures of amateur actors in an evoked-emotion performance. These pictures were created by the *Brain Behavior Laboratory* (University of Pennsylvania) and have been validated for this type of study (Gur et al., 2002a). Selected pictures included male/female faces with neutral, sad or happy expressions. All of them have the same size, luminosity and visual characteristics.

2.3. Procedure

Participants were seated comfortably 1 m in front of a 15-inch screen laptop (Samsung X15plus). SuperLab Pro® (Cedrus, version 2.0.4) displayed the pictures and collected the behavioral data (responses and response times, in ms). Subjects held an optical two-button mouse (Logitec®) with both hands, using either the left or the right thumb for answering.

2.3.1. Tasks

Participants performed two different tasks on two different days. Each task consisted on rating 300 pictures (displayed for 3.5 s) during a total of 1050 s of continuous task. Subjects were instructed to be sure about their