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Research report

Amygdala subregions differentially respond and rapidly adapt to threatening voices

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ABSTRACT

Emotional states can influence the human voice during speech utterances. Here, we tested the sensitivity and signal adaptation of functional activity located in amygdala subregions to threatening voices during high-resolution functional magnetic resonance imaging. Bilateral superficial (SF) complex and the right laterobasal (LB) complex of the amygdala were generally sensitive to emotional cues from speech prosody. Activity was stronger, however, when listeners directly focused on the emotional prosody of the voice instead of attending to a nonemotional feature. Explicit attention to prosody especially elicited activity in the right LB complex. Furthermore, the right SF specifically showed an effect of sensitization indicated by a significant signal increase in response to emotional voices which were preceded by neutral events. The bilateral SF showed signal habituation to repeated emotional voices indicated by a significant signal decrease for an emotional event preceded by another emotional event. The right SF and LB finally showed an effect of desensitization after the processing of emotional voices indicated by a signal decrease for neutral events that followed emotional events. Thus, different amygdala subregions are sensitive to threatening emotional voices, and their activity depends on the attentional focus as well as on the proximal temporal context of other neutral and emotional events.

1. Introduction

The amygdala is an important brain structure for detecting the affective information (Zald, 2003) that is most relevant for the current context of behavior (Sander et al., 2003). The amygdala is responsive to different kinds of visual affective stimuli (Pessoa and Adolphs, 2010; Zald, 2003), but was also shown to decode the affective value from auditory information such as affective environmental sounds (Anders et al., 2008) or emotions expressed by the human voice during verbal (Bach et al., 2008; Frühholz et al., 2012; Grandjean et al., 2005; Sander et al., 2005a; Wiethoff et al., 2009) or nonverbal utterances (Fecteau et al., 2007; Morris et al., 1999). However, evidence for the role of the amygdala during the decoding of emotions from voices is not consistent. Some studies report activations of the amygdala (Leitman et al., 2010; Scott et al., 1997; Sprengelmeyer et al., 1999; Wiethoff et al., 2009), whereas the results from other studies do not support its involvement in processing emotional voices (Adolphs and Tranel, 1999; Anderson and Phelps, 2002; Belin et al., 2008).

Several factors could contribute to these inconsistent findings in previous studies, such as different tasks used

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across studies, which imply different levels of attentional orientation or different levels of processing vocal expressions. These are known to affect amygdala responses to emotional stimuli (Bach et al., 2008; Grandjean et al., 2005; Sander et al., 2005a). Signal adaptation effects in the amygdala to the repeated presentation of emotional stimuli (Fischer et al., 2003; Ishai et al., 2004; Phillips et al., 2001; Wiethoff et al., 2009) could also contribute to previous inconsistent findings. Finally, functional activity in amygdala might be restricted to amygdalar subnuclei rather than the amygdala as a whole, and the response pattern in amygdala subnuclei is not consistent in response to emotional stimuli (see for example, Davis et al., 2010). This inconsistent response might cancel out when using standard scanning procedures or a standard whole brain analysis of functional data. The present study therefore sought to investigate amygdala responses to angry intonated pseudo-speech by using an experimental approach including three important experimental factors and questions.

First, using high-resolution brain imaging, we tried to localize functional activations in amygdalar subregions rather than examining the functional responses of the amygdala as a whole. The amygdala is composed of several nuclei that can be organized into different subregions on the basis of cytoarchitectonic differentiation as well as on structural (Bach et al., 2011; Sah et al., 2003) and functional connectivity patterns (Roy et al., 2009). On a general level, the amygdala can be subdivided into a laterobasal (LB), superficial (SF), and centromedial (CM) complex of amygdaloid nuclei on the basis of cytoarchitectonic probability maps (Amunts et al., 2005). Recent studies in nonhuman primates have shown that besides some possible involvement of the CM complex (Kuraoka and Nakamura, 2007) the LB complex seems to be most important for decoding the emotional value of stimuli (Gothard et al., 2007; Hoffman et al., 2007; Kuraoka and Nakamura, 2007), given its widespread connectivity to sensory processing regions (McDonald, 1998). Recent functional magnetic resonance imaging studies in humans partly confirmed these findings for the LB complex (Davis et al., 2010; Gamer et al., 2010; Kukolja et al., 2008), but found more consistent activation in the SF complex (Davis et al., 2010; Goossens et al., 2009; Hurlemann et al., 2008; Kukolja et al., 2008) or the CM complex (Boll et al., 2011; Gamer et al., 2010), especially in response to negative stimuli.

Our second question concerned signal habituation as well as sensitization and desensitization in the amygdala and its subregions to the successive presentation of emotional and neutral stimuli. Repeated auditory stimulation leads to signal habituation in primate and nonprimate amygdala, especially in the LB complex (e.g., Bordi and LeDoux, 1992; Herry et al., 2007). More specifically, the processing of emotional stimuli can lead to a signal decrease in the amygdala when preceded by other emotional stimuli (Fischer et al., 2003; Ishai et al., 2004; Phillips et al., 2001; Wiethoff et al., 2009). This effect is also known as repetition suppression (Grill-Spector et al., 2006), which is thought to sharpen the brain representation of emotional stimuli (Ishai et al., 2004). However, many questions remain, especially for the repeated processing of emotional sounds and voices. Recent studies have mainly investigated long-term habituation, including stimulus repetitions separated for up to several minutes across experimental blocks. Angry and erotic sounds revealed amygdala habituations (Wiethoff et al., 2009), but these results were not consistent across studies (Ethofer et al., 2009; Wiethoff et al., 2008). The functional pattern of short-term habituation on a trial-by-trial basis is however still unknown. This short-term habituation is crucial, given the proposed functional role of the amygdala for the fast detection of emotional stimuli (Dolan and Vuilleumier, 2003; Ohman, 2002; Vuilleumier, 2005).

In addition to this habituation for repeated emotional voices, the amygdala might also show sensitization in response to an emotional voice as a relevant and novel stimulus in the context of preceding neutral events. This novel emotional event after neutral events might lead to general changes in the brain system, such as increasing the alertness to support stimulus detection (e.g., Anderson and Phelps, 2001) or attentional focusing (e.g., Fenske and Eastwood, 2003). This might make the involved brain system more sensitive for information which is currently most important for adaptive behavior. This sensitization should be indicated by an increased functional activation of the amygdala for emotional events preceded by neutral events. Similarly to this sensitization, the amygdala might show desensitization to neutral stimuli when they follow the presentation of emotional voices. A signal decrease for these neutral events might indicate the end of an emotional event and its related emotional processing. This might allow the organism to recover and to return to a nonemotional processing state. Though this process of desensitization has yet not been widely investigated in healthy populations, data from clinical populations such as patients with social anxiety disorder provide evidence for a severe disturbance in this mechanism (e.g., Brozovich and Heimberg, 2008). Together, both mechanisms of sensitization and of desensitization might help to enhance the detection, processing and recovery from the processing of emotional stimuli when embedded in a series of neutral events. We thus explored habituation, sensitization, and desensitization to emotional voices in subregions of the amygdala (see Fig. 1).

Our third question concerned the level of processing as manipulated by the orientation of the attentional focus. While some studies found amygdala activity in response to vocal expressions to be independent of the focus of spatial (Grandjean et al., 2005; Sander et al., 2005a) or feature based attention (Bach et al., 2008; Ethofer et al., 2009), we recently only found amygdala activity when the emotional value of voices was inside the focus of attention (Frühholz et al., 2012). These inconsistencies might be due to standard scanning protocols which might obscure intra-amygdalar difference in response to emotional voices depending on the attentional focus. However, using high-resolution scanning techniques different amygdala subregions studies have recently shown that different amygdala subregions such as the LB and the SF complex might be responsive to the emotional value of stimuli when it was presented inside (Gamer et al., 2010; Kukolja et al., 2008) or outside the focus of attention (Davis et al., 2010; Goossens et al., 2009; Hurlemann et al., 2008). To determine the differential sensitive of amygdala subregions depending on the attentional focus toward vocal expressions, we