Brain and Cognition 69 (2009) 73–80

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Insular activity during passive viewing of aversive stimuli reflects individual differences in state negative affect

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ARTICLE INFO

Article history:
Accepted 20 May 2008
Available online 15 July 2008

Keywords:
fMRI
Psychophysiology
Salience
Female
Skin conductance
Interoception
Valence
Bodily state

ABSTRACT

People differ with regard to how they perceive, experience, and express negative affect. While trait negative affect reflects a stable, sustained personality trait, state negative affect represents a stimulus limited and temporally acute emotion. So far, little is known about the neural systems mediating the relationship between negative affect and acute emotion processing. To address this issue we investigated in a healthy female sample how individual differences in state negative affect are reflected in changes in blood oxygen level-dependent responses during passive viewing of emotional stimuli. To assess autonomic arousal we simultaneously recorded changes in skin conductance level. At the *psychophysiological* level we found increased skin conductance level in response to aversive relative to neutral pictures. However, there was no association of state negative affect with skin conductance level. At the *neural* level we found that high state negative affect was associated with increased left insular activity during passive viewing of aversive stimuli. The insula has been implicated in interoceptive processes and in the integration of sensory, visceral, and affective information thus contributing to subjective emotional experience. Greater recruitment of the insula in response to aversive relative to neutral stimuli in subjects with high state negative affect may represent increased processing of salient aversive stimuli.

1. Introduction

Perception, experience, and expression of emotions are subject to great interindividual variability. The identification of the neural correlates of these aspects of emotions may therefore crucially depend on the specific sample and their characteristics in emotion processing (Eugene et al., 2003; Friston et al., 1997). Accordingly, findings from neuroimaging studies concerning the neural correlates of emotions are often inconsistent. Relating individual differences in emotional reactivity or emotional experience to brain imaging data derived from group analyses will not only aid to clarify conflicting findings but may reveal the precise nature of neural mechanisms involved in emotion processing (Canli, 2004; Davidson & Irwin, 1999; Hamann & Canli, 2004; Meriau et al., 2006; Thompson-Schill, Braver, & Jonides, 2005).

When individuals are asked to report on their emotional states, negative affect emerges as a higher order factor in factorial analyses and generally reflects the extent to which a person reports feeling upset or unpleasantly aroused (Watson & Tellegen, 1985). Negative affect can be differentiated into trait and state negative affect and is a common factor of both anxiety and depression (Clark & Watson, 1991). *Trait* negative affect reflects a stable personality trait, that is, a negative emotional activation, which is sustained and not bound to discrete cues. In contrast, *state* negative affect is stimulus limited and a temporally acute emotion.

At the neural level individual differences in *trait* negative affect have been associated with increased cerebral blood flow during resting state in the bilateral ventromedial prefrontal cortex (Zald, Mattson, & Pardo, 2002) and in the amygdala (Abercrombie et al., 1998). Greater increases in amygdala response during active maintenance of a negative mood are associated with subjects' self-reported trait negative affect (Schaefer et al., 2002). Trait negative affect may be implemented by plastic changes of the brain, whereas a momentary change of mood (i.e., state negative affect) allowing for short-lived cognitive, behavioral and physiological adaptation may be differentially represented. However, so far it remains unclear how individual differences in *state* negative affect are instantiated at the neural level.

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doi:10.1016/j.bandc.2008.05.006

Moreover, negative affect is associated with increased *autonomic arousal* (Brown, Chorpita, & Barlow, 1998), which may influence the neural correlates of negative affect. Specifically, negative affect is strongly correlated with autonomic symptoms (Brown et al., 1998). For instance, self-reported high negative affect is associated with significantly greater skin conductance responses during error-related processing (Hajcak, McDonald, & Simons, 2004). Especially in women, negative emotions are related to physiological output: both *state* anxiety and *state* negative mood are associated with increased amplitudes of non-specific skin conductance responses and increases in heart rate in women (Carrillo et al., 2001). Thus, there is ample evidence that differences in state negative affect influence autonomic output.

As outlined above, feelings such as anxiety and sadness/depression can be subsumed under negative affect (Clark & Watson, 1991). Several imaging studies have reported insular activation to be modulated by negative affect. In healthy subjects, individual differences in *anxiety* modulate activity of the amygdala during unconscious processing of threat-related stimuli (Etkin et al., 2004), as well as during conscious processing of fearful faces (Bishop, Duncan, & Lawrence, 2004). It has recently been proposed that the insula plays a key role in anxiety proneness (Paulus & Stein, 2006). For instance, anxiety–prone healthy subjects show greater responses in the bilateral insulae during anticipation of aversive pictures compared to non-anxious subjects (Simmons, Strigo, Matthews, Paulus, & Stein, 2006).

Sadness, the other major constituent of negative affect, also modulates insular activity. Sadness induced by autobiographical memory scripts of past sad events in healthy female subjects activates the left insula, amongst other regions (Liotti et al., 2000). Moreover, individual differences in sadness correlate positively with activity in the right insula and the right temporal pole (Eugene et al., 2003). In females, transient sadness is associated with increased activation in the left insula and left amygdala (Levesque et al., 2003). Two PET studies also report on insular activation during self-induced sadness (George et al., 1995; Mayberg et al., 1999).

In sum, in healthy populations altered insula activation seems to play a crucial role in anxiety and sadness, that is, in negative affect. As outlined above, negative affect can be differentiated into state and trait negative affect. Thus, individual differences in state and trait negative affect may be differentially represented at the neural level and may result in different behavioral and psychophysiological outcomes. Therefore, the goal of the present study was to investigate how individual differences in state negative affect are represented at the neural level during exposition to aversive stimuli.

Based on the findings cited above we hypothesized that individual differences in state negative affect correlate positively with activity in limbic and paralimbic regions, such as the insular cortex and the amygdala during exposition to aversive stimuli. To address this issue we monitored blood oxygen level-dependent (BOLD) responses in a healthy female sample during passive viewing of aversive stimuli. To investigate changes in autonomic arousal we simultaneously measured skin conductance level. Individual differences in state negative affect were assessed using the Positive and Negative Affect Scale (PANAS) (Krohne, Egloff, Kohlmann, & Tausch, 1996).

2. Methods

2.1. Subjects

Gender differences in emotion processing have been reported at the psychophysiological level. Women show greater reactivity in response to aversive stimuli compared to men (Bradley, Codispoti, Sabatinelli, & Lang, 2001) and they also show differential activation patterns at the neural level (George, Ketter, Parekh, Herscovitch, & Post, 1996; Killgore & Yurgelun-Todd, 2001; Piefke, Weiss, Markowitsch, & Fink, 2005; for a review see Cahill, 2006). Therefore, only female subjects were included in the present study. Twenty-three healthy female subjects without any history of neurological or psychiatric disorders participated in the experiment (27.1 ± 4.7 years, mean ± SD). Nine percent completed 9 years of education (German "Hauptschule"), 74% completed 10 years of education (German "Realschule"), 17% completed 13 years of education qualifying for university entrance (German "Abitur"), in total subjects completed 10.43 years of education (±1.24). They were all right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The study was approved by the local ethics committee of the Charité University Medicine Berlin, and participants gave written informed consent prior to investigation.

2.2. Psychometric assessment

Before subjects went into the scanner we assessed individual differences in state and trait negative affect using the Positive and Negative Affect Scale (PANAS) (Krohne et al., 1996). The Negative Affect scale consists of 10 adjectives of mood states (e.g., nervous, afraid or upset). To assess state negative affect subjects rated their *current* affective state on the basis of these adjectives using a 5-point rating scale.

2.3. Stimuli

Neutral and aversive pictures were selected from the standardized International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 1999). Neutral stimuli consisted of pictures of household objects and scenes or abstract three-dimensional figures. Aversive pictures displayed threatening scenes, objects, animals or wounded people (73% of the aversive pictures were threat-related, 6% represented sad and 21% represented disgust pictures). Hence, the two sets of stimuli were not matched with regard to human faces, bodies, body parts or with regard to non-affective characteristics, such as color composition or pictorial complexity which may have affected our data in a systematic, however undesired manner. Mean normative ratings for pleasure, arousal and dominance, taken from the technical manual of the IAPS for selected neutral and aversive pictures, and results of *t*-test are provided in Table 1. The ratings differed significantly for neutral and aversive pictures (Lang et al., 1999).

Thirteen blocks of neutral pictures [A] and 12 blocks of aversive pictures [B] were presented in an ABA fashion. Within a block, four pictures of the same valence were presented. Each picture was shown only once, resulting in the presentation of 52 neutral and 48 aversive pictures. Each picture was approximately displayed for 4.3 s depending on scanner triggering resulting in a block duration of approximately 17.2 s. The whole experiment lasted 7.2 min. To allow the future application in clinical populations, we kept the experiment as short as possible, therefore no rest periods (fixation periods) were included in the experiment. Stimuli were displayed using the experimental control software Presentation (Neurobe-

Table 1
Mean normative ratings and standard deviations (±SD) for pleasure, arousal, and dominance for neutral ($N = 52$) and aversive ($N = 48$) pictures

	Neutral	Aversive	t, *p*
Pleasure	5.15 (±0.66)	2.49 (±0.86)	17.23, $p < 0.001$
Arousal	2.97 (±0.59)	6.27 (±0.81)	−23.06, $p < 0.001$
Dominance	5.95 (±0.58)	3.43 (±0.82)	17.58, $p < 0.001$