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Evidence for a different role of the ventral and dorsal medial prefrontal cortex for social reactive aggression: An interactive fMRI study

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Interactive paradigms inducing reactive aggression are absent in the brain mapping literature. We used a competitive reaction time task to investigate brain regions involved in social interaction and reactive aggression in sixteen healthy male subjects with fMRI. Subjects were provoked by increasingly aversive stimuli and were given the opportunity to respond aggressively against their opponent by administering a stimulus as retaliation. fMRI revealed an increase of medial prefrontal cortex (mPFC) activity during retaliation. The dorsal mPFC was active when subjects had to select the intensity of the retaliation stimulus, and its activity correlated with the selected stimulus strength. In contrast, ventral mPFC was active during observing the opponent suffering but also during retaliation independent of the stimulus strength. Ventral mPFC activation, stronger in low callous subjects, correlated positively with skin conductance response during observation of the suffering opponent. In conclusion, dorsal mPFC activation seems to represent cognitive operations related to more intense social interaction processes whereas the ventral mPFC might be involved in affective processes associated with compassion to the suffering opponent.

Keywords: PFC; Social interaction; Imaging; Aggression; Emotion

Introduction

The experience of being unjustly assaulted evokes the impulse to defend oneself and to respond aggressively to the offender. This type of reactive aggression contrasts with instrumental aggression which is purposeful and goal-directed (Berkowitz, 1993). The cognitive control of reactive aggressive impulses, important for social interaction (Siegel, 2004), is motivated by the anticipation of negative consequences and leads to avoidance behavior (Gray, 1982) and the mobilization of empathic feelings (Ohbuchi et al., 1993).

The prefrontal cortex (PFC) plays a central role in many aspects of social cognition (Rilling et al., 2002), including perspective taking (Frith and Frith, 1999), and also in the regulation of emotions such as aggression (for a review, see Blair, 2004). In particular, studies with patients with lesions of the ventral prefrontal lobe demonstrated impairment in identifying emotional expression using face or voice stimuli (Hornak et al., 1996) and deficits in representing the mental states of others when performing verbal tasks based on theory of mind (Stone et al., 1998; Mah et al., 2005). Additionally, lesions of the ventromedial prefrontal cortex disturb the control of reactive aggressive behavior (Grafman et al., 1996; Anderson et al., 1999) which might result in a similar behavior as in other psychopathic individuals (Blair and Cipolotti, 2000). Increased reactive aggressive behavior in subjects without brain lesions is often associated with prefrontal dysfunction (Volkow et al., 1995).

Imaging studies on facial perception demonstrated an increase of activation in the lateral ventral prefrontal areas during observation of angry and fearful facial expressions (Blair et al., 1999) and social norm violations (Berthoz et al., 2002; together with the medial PFC (mPFC)). Imaging studies on social interaction and emotional control identified at least two distinct areas within the mPFC involved in aggression and its control. Activation of the dorsal mPFC has been observed during cognitive regulation of emotional behavior (Ochsner et al., 2004a) and when subjects made judgments about another person's emotional states (Ochsner et al., 2004b). In contrast, activity in the ventral mPFC has been associated with monitoring of one's own feelings (Lane et al., 1997; Phan et al., 2004) and physiological changes that accompany a particular emotional response (Damasio, 1996).

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The present study investigated the role of the PFC with functional magnetic resonance imaging (fMRI) in a paradigm provoking reactive aggression. We used a realistic, dynamic social interaction that involved being offended, retaliating and watching the opponent suffer. Subjects played a competitive reaction time task and, depending on the outcome, either received an aversive stimulus or administered one with an intensity of their choice to their opponent. Reactive aggression was induced by increasing the intensity of the aversive stimulus the subjects received over the course of the experiment. This paradigm was modified for usage in a social interactive imaging setting based on the experimental design from Taylor (1967), a design which reliably induces reactive aggressive behavior (Giancola and Zeichner, 1994). A modification in our paradigm was the reduction of number of winning trials during the course of the experiment. After each retaliation trial, subjects were shown a short video clip of the opponent receiving the aversive stimulus (see Fig. 1). By introducing a second person as a competitor and presenting his pain-related expressive behavior matching the intensity of the retaliation stimulus, we ensured that aggression control was induced. An event-related design that entailed anticipation of an offending aversive stimulation, retaliation and watching the opponent suffering was used to isolate functional brain activity associated with different aspects of aggression and its control. Specifically, we investigated the role of the mPFC during the interaction with an opponent. Additionally, we examined the relationship between brain activity during the different trial phases, skin conductance responses (SCR) as an indicator of autonomic arousal, and self-reported psychopathic personality traits. We hypothesized that the mPFC is critically involved in the regulation of reactive aggression (Taylor et al., 2003; Ochsner et al., 2004a) and that psychopathic personality traits correlating with a lack of peripheral physiological changes correspond with reduced activation within the mPFC. Lack of social affection in psychopathy was repeatedly found to be related to reduced processing of bodily signals during emotions (Damasio, 1996; Birbaumer et al., 2005; "somatic markers").

Material and methods

Subjects

Sixteen healthy male subjects (mean age 28.6 years, standard deviation (SD) 6.5 years), recruited by advertisement in the local newspaper, participated in the fMRI experiment. Two subjects who reported doubts about the veracity of the opponent's role were excluded from the analysis.

The study was approved by the Ethics Committee of the Medical Faculty of the University of Tübingen. Written informed consent was obtained according to the guidelines of the Declaration of Helsinki.

Experimental design

Before scanning, subjects were introduced to their opponent. Subjects were instructed about the competitive reaction time task to perform during scanning. They were told that, if they responded slower to a cue than their opponent, their opponent would be allowed to give them an aversive pneumatic pressure stimulus on the finger; if they responded faster, they would be allowed to administer a stimulus with an intensity of their choice to their opponent. The opponent was an instructed associate of the experimenter, and trial outcome and the intensity of painful stimuli were predefined and identical for all subjects.

Scanning consisted of four sessions with 20 trials each. Each trial started with a verbal cue followed by a visual signal prompting the subject to press a button with the right index finger as quickly as possible. A symbol indicated trial outcome. In the event the subject lost the trial, a visual five-point scale appeared indicating the intensity of the aversive stimulus the subject would receive. The adjustment of the intensity was shown in a dynamic way as if the opponent was adjusting at the same time. The intensity of the pain the subject received increased from an average of 2.33 points on a five-point scale during the first session to an average of 3.92 points during the last phase. This increase was performed over all subjects and was not dependent on the reaction of the subject. In the event the subject won the trial, the five-point scale appeared and this time the subject was allowed to adjust the intensity of the stimulus to be administered to his opponent by pressing a button with the right thumb. The time for adjustment was the same as during the losing trial (3 s). The numbers of "win" (36) and "lost" (44) trials were kept constant during the experiment. Subjects were presented a 3-second pre-recorded view of the opponent to allow observation of retaliation. Video clips were randomly chosen from 6 different pre-recorded video tapes for each stimulus intensity with the restriction that each video tape was shown only once (see Fig. 1 for the timing of the experiment).

The timing of the trials was selected in order to allow optimal modeling in a parametric statistical design and to allow realistic social interaction in the Taylor paradigm. In addition, the timing of the events was jittered (and therefore reducing the effective TR) to account for possible response overlaps in certain areas. For instance, the onsets of the pain stimuli were jittered 2.5 to 4.5 s relatively to the written cue ("you will be now punished") to disentangle anticipatory and pain-related responses, an approach often seen in conditioning paradigms. The inter-trial interval varied between 8 and 16 s, adequate to calculate a reliable implicit baseline. Aversive stimuli were applied using a pneumatic device containing a cylinder (diameter of 7 mm) which was moved by modulated air pressure (Dokoh-Pneu, Erlangen; velocities: 2 m/s to 20 m/s). Pain thresholds for each subject, ranging from 1 (only touch) over 3 (uncomfortable) to 5 (very painful), were determined in repetitive trials before the experiment started.

After each trial phase, subjects rated aggressive feelings, compassion and sympathy towards their opponent on five-point scale from no (0) to high (5) presented visually and answered verbally. Primary psychopathic traits were tested with the self-report psychopathy scale (SRPS; Levenson et al., 1995) after the fMRI investigation. This measure is a widely used instrument to assess psychopathic traits in healthy non-institutionalized individuals. The questionnaire contains 26 items and two derived factors (primary and secondary psychopathy), similar to the factor 1 and factor 2 of the PCL-SV (Hare, 1991). Brinkley et al. (2001) investigated prison inmates with the PCL-SV and the SRPS and found a good concordance between both instruments. The mean total score was 60.85 (SD 4.51; range 53–70), the mean score in factor 1 was 37.60 (SD 4.99; range 27–46) and the mean score in factor 2 was 23.27 (SD range 19–28). We used the median in factor 1 (primary psychopathy) to split the group into high and low callous participants. After completion of the questionnaires, subjects were verbally interviewed about the veracity of the experimental setting.