



Original article

Neural activity during the viewing of emotional pictures in veterans with pathological anger and aggression



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ABSTRACT

Anger and aggression are common mental health problems after military deployment. Anger and aggression have been associated with abnormalities in subcortical and cortical levels of the brain and their connectivity. Here, we tested brain activation during the processing of emotional stimuli in military veterans with and without anger and aggression problems. Thirty military veterans with anger and aggression problems and 29 veterans without a psychiatric diagnosis (all males) participated in this study. During an fMRI scan 32 negative, 32 positive and 32 neutral pictures from the International Affective Picture System were presented in intermixed order. The Aggression group showed heightened activity in brain areas including the supplementary motor area, the cingulum and the parietal cortex, in response to stimuli, regardless of category. Furthermore, the Aggression group showed stronger connectivity between the dorsal anterior cingulate cortex (dACC) and the amygdala during the viewing of negative stimuli, and weaker connectivity between dACC and medial prefrontal cortex during the viewing of positive stimuli. Veterans with anger and aggression problems showed enhanced brain response to all stimuli during the task, irrespective of valence and they rated the pictures more likely as negative. We take this to indicate enhanced preparation for action and attention to the presentation of stimuli that could prove to be threatening. Further, group differences in functional connectivity involving the dACC reveal abnormal processing of stimuli with negative and positive valence. In sum, the results point towards a bias towards an enhanced sensitivity to perceived or potential threat in aggression.

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1. Introduction

Military deployment is often a stressful period and regularly leads to mental and social difficulties after homecoming [1]. Frequently occurring problems, besides symptoms of posttraumatic stress disorder and depression, are anger and aggression [2,3]. Emotional and behavioral manifestations of these problems can be very disabling for the individual as well as their surroundings [4]. Problems regarding anger and aggression occur in many psychiatric disorders, the current study therefore takes a transdiagnostic approach [5,6]. Anger and aggression problems have been linked to disturbed emotional processing [7]. Stimuli are more easily

perceived as negative or threatening, which might lead to reactive or impulsive aggression.

An important brain area in emotional processing is the amygdala [8,9]. The amygdala consists of distinct subnuclei [9,10]. The basolateral amygdala (BLA) plays a role in differentiating responses to stimuli currently evaluated to have biologically significant outcomes [11–13]. The BLA is reciprocally connected with a wide range of brain areas, including medial and orbitofrontal prefrontal cortex and has projections to the central medial amygdala (CMA). The CMA in turn projects to areas such as the hypothalamus and brainstem, including the periaqueductal gray, thereby activating appropriate physiological responses such as freezing [14].

In patients diagnosed with Intermittent Explosive Disorder (IED) hyperactivity of the amygdala has been reported in response to angry faces [15,16]. Furthermore, the circuitry of the amygdala,

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including the orbitofrontal cortex and the anterior cingulate cortex, has been implicated in disorders characterized by aggressive behavior such as IED and borderline personality disorder [7,17,18].

Post-traumatic stress disorder (PTSD) is a common mental disorder after deployment and also associated with aggression [19,20]. Although in PTSD no evidence was found for amygdala dysfunction in relation to general, non-facial, emotional stimuli [21], it was found that patients with PTSD who did not respond to therapy show heightened amygdala activation to such stimuli before treatment [22]. Furthermore, stronger activation in the dorsal anterior cingulate cortex (ACC) is implicated in the processing of negative emotional stimuli in PTSD [21]. Increased attention to negative emotions has been related to dACC activity [23] and might therefore be of interest in aggression as well.

Differences in the processing of emotional stimuli in anger and aggression are mostly tested using facial stimuli [15,16], but general non-facial negative emotional stimuli also elicit amygdala activation [24]. However, whether such stimuli also result in enhanced responses in the amygdala related to anger and aggression is not yet known. Therefore, it is important to investigate the neural response to emotional stimuli in anger and aggression.

Here, we investigate brain responses to general, non-facial, emotional stimuli, in military veterans with and without anger and aggression problems. To this aim, 28 military veterans with anger and aggression problems and 28 veterans without a psychiatric diagnosis (all males) rated 32 negative, 32 positive and 32 neutral pictures from the IAPS while being scanned with fMRI. We studied both brain activity and the connectivity of the amygdala and the dACC with other areas of the brain in relation to the task. Based on previous studies in patients with aggressive behavior, we hypothesize that amygdala and dACC activation will be higher in the impulsive aggression group during the viewing of negative emotional pictures, in comparison to the control group. We expected that the functioning of the amygdala and dACC connectivity is also disturbed in aggression.

2. Methods

2.1. Participants

In this study, 30 male veterans with anger and aggression problems were included (Aggression group). They were recruited via their psychologists/psychiatrists at the Military Mental Health Care Institute and via advertisements in the waiting room and newsletters for veterans. Additionally, 29 male control veterans without anger and aggression problems were also included. It was attempted to include participants in the control group such that this group did not differ on age, education and number of deployments. These participants were recruited by advertisements in magazines for veterans or had participated in previous studies. Inclusion criteria for the Aggression group were based on the four research criteria for impulsive aggression described by Coccaro (2012):

- verbal or physical aggression towards other people occurring at least twice weekly on average for one month; or three episodes of physical assault over a one year period;
- the degree of aggressiveness is grossly out of proportion;
- the aggressive behaviour is impulsive (not premeditated);
- the aggressive behaviour causes either distress in the individual or impairment in occupational or interpersonal functioning (Coccaro, 2012 [25]).

Inclusion criteria for the Control group were:

- no current DSM-IV diagnosis;
- no history of pathological aggressive behaviour.

The Ethics Committee of the University Medical Center Utrecht, The Netherlands, approved this study and all participants signed an informed consent before participation after having received a complete written and verbal explanation of the study. This study was carried out in accordance with the Declaration of Helsinki.

2.2. Interview and questionnaires

The Dutch version of the International Neuropsychiatric Interview (MINI) was used in order to screen for the presence of comorbid psychiatric disorders [26]. The complete MINI was administered. In this interview the following current or life-time disorders were screened: depressive disorder, dysthymia, suicidal risk, (hypo)manic disorder, panic disorder, anxiety disorder, agoraphobia, social phobia, obsessive compulsive disorder, PTSD, alcohol or drug dependence and/or abuse, psychotic disorders, anorexia nervosa, bulimia nervosa, generalized anxiety disorder, antisocial personality disorder, somatization disorder, hypochondria, body dysmorphic disorder, pain disorder, attention deficit hyperactivity disorder (ADHD) and adjustment disorder. The interview was carried out by the research staff (psychologists with psychodiagnostic expertise).

To measure anger and aggression, the Dutch version of the State-Trait Anger Expression Inventory-revised (STAXI-2; Hovens, Rodenburg, & Lievaart, 2015, Spielberger, 1999 [27,28]) was used. The STAXI-2 consists of 57 items on a 4-point Likert scale and is divided into two subscales: State Anger and Trait Anger.

Furthermore, the Dutch translation of the Buss-Perry Aggression Questionnaire (AQ) [29,30] was administered. The AQ consists of 29 items on a 5-point Likert scale and is divided into 4 subscales: Physical Aggression, Verbal Aggression, Anger and Hostility.

2.3. Task

The task (Van Rooij et al., 2015; Vink, Derks, Hoogendam, Hillegers, & Kahn, 2014 [21,31]) consisted of 96 pictures from the IAPS [32]. These pictures elicit general emotional experience [32]. The pictures were categorized as neutral, positive, or negative based on the IAPS rating. The pictures were presented for 2 seconds, after which an evaluation screen was presented. By pressing a button with the thumb of their right hand, participants could give their rating (positive, negative or neutral) of the picture within 2 seconds. Immediately after giving the rating, a fixation cross appeared for the remaining trial duration. The task consisted of four blocks, each with 24 pictures in pseudo-randomized order (8 neutral, 8 positive, 8 negative). Between the blocks, a fixation cross was presented for 32 seconds. For a schematic overview of the task, see Fig. 1.

2.4. MRI acquisition

A 3.0-T whole-body magnetic resonance imaging scanner (Philips Medical System, The Netherlands) was used to acquire the functional images during the task, and a T1 weighted image for within-subject registration. An EPI-SENSE sequence scan acquired 322 functional images during the task, with the following parameters: repetition time (TR) = 1600 ms; echo time (TE) = 23 ms; flip angle = 72.5°; 64 × 51 matrix; 4 mm slice thickness; field of view (FOV) = 256 × 204 mm. For within subject registration, a T1 weighted image was used (200 slices, TR = 10 ms; TE = 3.8 ms; flip angle = 8°; FOV = 240 × 240 × 160 mm).

2.5. Preprocessing

Preprocessing and analyzing the data was done using SPM 12 (<http://www.fil.ion.ucl.ac.uk/spm>) and hiro3, a Matlab tool for

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