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ORIGINAL PAPER

Alexander Jatzko · Andrea Schmitt · Traute Demirakca · Erik Weimer · Dieter F. Braus

Disturbance in the neural circuitry underlying positive emotional processing in post-traumatic stress disorder (PTSD)

An fMRI study

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Abstract This study was designed to investigate the circuitry underlying movie-induced positive emotional processing in subjects with chronic PTSD. Ten male subjects with chronic PTSD and ten matched controls were studied. In an fMRI-paradigm a sequence of a well-known Walt Disney cartoon with positive emotional valence was shown. PTSD subjects showed an increased activation in the right posterior temporal, precentral and superior frontal cortex. Controls recruited more emotion-related regions bilateral in the temporal pole and areas of the left fusiform and parahippocampal gyrus. This pilot study is the first to reveal alterations in the processing of positive emotions in PTSD possibly reflecting a neuronal correlate of the symptom of emotional numbness in PTSD.

Key words fMRI · post-traumatic stress disorder · PTSD · emotional processing

A. Jatzko, M.D. · A. Schmitt, M.D. · T. Demirakca, M.Sc. · E. Weimer, M.D. · D. F. Braus, M.D.
Central Institute of Mental Health (ZI)
NMR-Research
P. O. Box 122120
68072 Mannheim, Germany

D. F. Braus, M.D.
NeuroImage Nord
Martinistr. 52
20246 Hamburg, Germany

D. F. Braus, M.D. (✉)
Clinic for Psychiatry and Psychotherapy
University of Hamburg
Martinistrasse 52
20246 Hamburg, Germany
Tel.: +49-40/42803-7549
Fax: +49-40/42803-7666
E-Mail: dbraus@uke.uni-hamburg.de

Drs. Jatzko and Schmitt contributed equally to the work.

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Introduction

One of the core symptoms of chronic PTSD is emotional numbness. PTSD subjects report less positive emotions and describe restrictions in their emotional experience that were not present before the traumatic event [2]. This limits patients' quality of life, especially with regard to pleasure gained from positive stimuli, such as reading books or watching movies. So far, however, studies have only investigated exposure to personal trauma cues or negative or neutral emotional stimuli in PTSD patients [11].

It has been hypothesized that in healthy subjects especially the right hemisphere is involved in emotional processing [3]. Aalto et al. for example have described anterior temporal pole activity in positive and negative emotions and inferior frontal gyrus activity in the right hemisphere for negative emotions while watching emotional film clips [1]. Underlying these findings, Surguladze et al. found that the emotional valence of visual cues modulate the activity of the ventral pathway of visual information processing [19].

Considering these earlier findings, we expected to find less activation in areas of the ventral pathway of visual information processing and emotion-related regions and more activation in areas of the dorsal pathway in PTSD subjects compared to controls when exposing subjects to a film clip with positive emotional valence.

Method

Our study included ten well-characterized right-handed male subjects who had developed PTSD according to the DSM–IV criteria after the 1988 Ramstein air show crash (mean age 50 years, SD 13). Trauma intensity was comparable for all PTSD subjects, because all had participated in the same event. Mean scores for Clinician-Administered Post-Traumatic Stress Disorder Scale (CAPS) in patients were 47 (SD 21), Impact of Event Scale (IES) 48 (SD 21). These were compared with ten healthy male control subjects carefully selected

with respect to a lack of relevant traumata in the history without any sign of PTSD according to DSM-IV and matched to the PTSD subjects with regard to age (mean 51 years, SD 11) and handedness. None of the participants had taken any psychoactive substance for at least 2 weeks prior to entry into the study, or had a history of substance abuse, significant medical or neurological disorder. Two PTSD subjects had experienced a depressive episode in the past and two subjects had suffered burns from the crash. Four PTSD subjects have taken antidepressants in the past; 4 did not.

The study had been approved by the ethics committee of the Faculty of Clinical Medicine Mannheim, University of Heidelberg and written informed consent was obtained from all subjects.

The MRI study was performed on a 1.5-T whole body Siemens Vision. For functional imaging, a 2D echo planar imaging sequence with T2* contrast, TR 2.475 s., FOV 220 mm, matrix size 64×64, TE 60 ms, 24 slices with thickness of 4 mm and 1 mm gap (covered the whole brain) was used. For exclusion of major brain abnormalities and for visualization purposes a 3D T1 MPRAGE was performed.

The fMRI-paradigm was shown in block design, with 19.8 seconds of a baseline condition (fixation cross) followed by 19.8 seconds of a positive-emotion-eliciting film-clip (singing and dancing bear from Walt Disney's Jungle Book). Each condition was shown eight times. The film clip shown was the same in each film condition. The film or fixation cross was presented on a screen in front of the scanner with the subject looking at the screen over a mirror on the head coil. Sound was presented over MRI headphones. All subjects had seen the film Jungle Book in the past. Directly after data acquisition all subjects reported subjectively neutral or positive feelings but no negative emotional experiences when seeing the film clip within the magnet.

Functional data was processed with SPM2 (Wellcome Department of Neurology, London, U. K.) [8]. The images were preprocessed by discharging the first 4 images, realigning, performing slice time correction, normalization and smoothing (10 mm). We used a second level analysis (random effect) in the context of the general linear model. The regions of interest were defined on the basis of T1-weighted images and MNI coordinates (Montreal Neurobiological Institute). Based on our a priori hypothesis regarding the differential brain response, a statistical threshold of $P < 0.05$ with a volume of interest (VOI) correction for multiple comparisons was used to identify significant responses for all group comparisons.

Results

Only within 16 subjects (8 patients and 8 controls), movement corrections were below 1 mm in all directions, making it necessary to exclude the data sets of 4 participants. Positions of activation are given in MNI and Brodman area (BA) coordinates. In a between group comparison activation differences were seen in the following areas: for the contrast PTSD > controls in right precentral (BA 6, MNI: 33, –15, 51, t-score: 3.21, $P < 0.02$), right superior frontal (BA 10, MNI: 21, 57, 18, t-score: 3.21, $P < 0.02$) and right posterior middle temporal (BA 39, MNI: 48, –51, 3, t-score: 3.83, $P < 0.007$) regions. For the contrast controls > PTSD in the left parahippocampal/fusiform gyrus (BA 20, BA 36, MNI: –36, –33, –24, t-score: 5.3, $P < 0.001$), right temporal pole/right superior temporal region (BA 38, MNI: 36, 15, –27, t-score: 4.93, $P < 0.002$) and the left temporal pole/left superior temporal region (BA 38, MNI: –36, 9, –24, t-score: 3.6, $P < 0.006$) (Fig. 1).

Conclusion

The major finding of this pilot study reveals profound differences in brain regions mediating positive information processing in chronic PTSD subjects compared to controls. PTSD subjects showed an increase in posterior middle temporal, precentral and prefrontal areas on the right hemisphere, while in controls increased activation was found in bilateral temporopolar regions as well as in left fusiform/parahippocampal gyrus (Fig. 1), areas with major input from and to the limbic system.

The activation increase in the posterior middle temporal area is near the junction between BA 39, 37 and 19 and therefore near to area MT/MST. This area is important in detecting biological motion and is part of the dorsal visual stream [20]. The observed increase in this area noted in PTSD patients during the film clip may reflect more effort on dorsal visuospatial information processing [20] when compared to controls, even in positive emotional visual stimulation. In this context our results correspond to a PET study by Bremner et al. [4] with exposure of trauma pictures and sounds, and a PET study by Clark et al. [6] with a verbal working memory paradigm, both showing an increased neuronal correlated of visuospatial processing in PTSD. The increase activation seen in PTSD in the precentral area corresponds also to two studies by Bremner et al., one mentioned above [4] and the other study with exposure of emotionally valenced words in sexually abused woman [5]. The frontal increased activation in PTSD compared to controls may reflect neural substrates of altered emotional processing and experience [13, 16].

In comparison to PTSD patients, control subjects re-

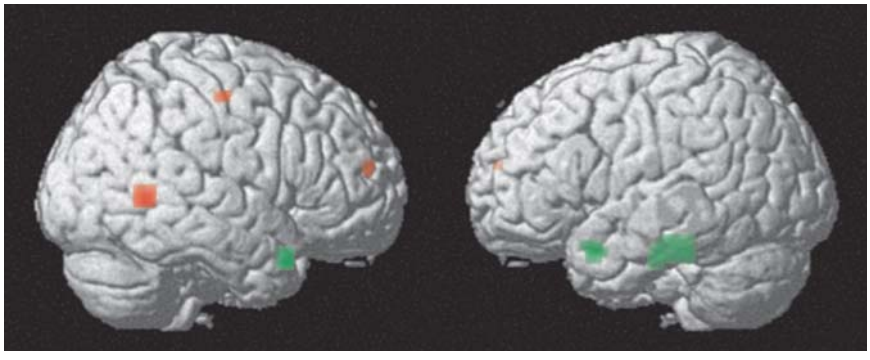

Fig. 1 Increased BOLD activity in PTSD subjects shown in red compared to increased activity in controls (green) (SPM 2, group interaction, $p < 0.005$)

cruited more bilateral temporopolar areas (BA 38), consistently described as associated with emotional and mnemonic processing and gating input to the amygdala [14] as well as involved in the processing of emotion-eliciting film clips [12]. In addition, the left-sided fusiform and parahippocampal gyrus showed greater activation in controls compared to PTSD. Both areas are known to be involved in face and object identification [10] and have been shown to be modulated by context-dependent enhancement during early processing of an emotional visual input [7].

Interestingly PTSD patients showed less activation in areas generally activated by positive emotional film clips [12], but showed more activation in those areas which had been described within the context of trauma exposition [15, 17].

As a major limitation of this study, we had only examined male subjects with the intention to reduce heterogeneity and to exclude gender effects [18]. Furthermore, no direct quantification of the positive subjective experience or attention in the magnet was performed as an additional performance control and no extra neutral movie as baseline had been scanned. However, the recently documented startling tendency of healthy brains to synchronize a widespread cortical activation pattern in correlation with emotionally arousing movie scenes would argue against this as a possible explanation for our results [9].

In summary, our results reveal first evidence for disturbed affect modulation even for trauma-unrelated positive information processing in PTSD. Therefore these results may reflect an underlying neuronal correlative of emotional numbness. However, replication in a larger sample (including female subjects) is needed before our results can be generalized.

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