Event Related fMRI of successfully implicitly encoded negative and neutral words in Major Depressive Disorder. Preliminary results from the NESDA neuroimaging-study.

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Introduction

Neuropsychological studies have reported verbal memory abnormalities in depression. Functional MRI and EEG studies exploring these abnormalities have found abnormal activation patterns in prefrontal and temporal areas during explicit encoding and emotional processing of verbal stimuli in depression (1-4). The neural correlates of the implicit encoding of negative verbal stimuli using fMRI has not been studied before in depression. Implicit encoding of verbal stimuli may be relevant for the investigation of the postulated 'mood-congruent' cognitive bias in depression. In the present study we used an event related fMRI paradigm to compare left-frontal and temporal activation during an implicit emotional encoding paradigm in patients with depression and healthy controls.

Methods

Eleven healthy subjects (HC) and eleven subjects with a primary diagnosis of Major Depression Disorder (MDD), no other axis I or II disorder and a MADRS-score of more than 21 participated in the study. The present pilot study is part of the larger neuroimaging-study within the Netherlands Study on Depression and Anxiety (NESDA), involving 250 patients. Subjects were group wise matched for age (range 24-45), gender and education level. In the encoding phase of the subject-paced task, 120 study words were presented (40 negative, 40 neutral and 40 positive words) and 40 baseline items (press left, right, middle). Subjects had to indicate with a button press whether they evaluated the word as negative, neutral of positive. No reference to the later recognition phase was made. After an eight minute interval, in which a high resolution T1-3D image was acquired, subjects were tested for recognition: 120 previously seen words, 120 new words and 40 baseline items. Subject had to indicate whether they had seen the word before, probably seen before or not seen before. The recognition was tested under the same circumstances as the encoding. The dynamic scans acquired during recognition were not taken into analysis for this report.

Gradient echo, echo planar imaging was applied (TE=30 ms, TR=2.3 sec, voxel size = 2.29 x 2.29 x 3 mm, 35 slices, matrix size: 96 x 96, Philips Intera 3T system). Data were analyzed with SPM5 (4). For this report only negative and neutral words were considered. Correctly recognized negative and neutral words were analyzed and classified as retrieval success (CR). Data analysis included reorientation, slice-timing, realignment, coregistration of the mean-EPI with the structural image, normalization and spatial smoothing (8 mm FWHM). Hemodynamic responses to each stimulus onset were modeled with a delta function convolved with a synthetic hemodynamic response function.

Contrasts between 1)correctly recognized negative words and baseline items and 2)between correctly recognized neutral and baseline items were calculated (threshold $p<0.001$). We also calculated the percentage of correctly recognized (CR) and correctly rejected (CRej) words and differences in reaction times (threshold $p<0.001$).

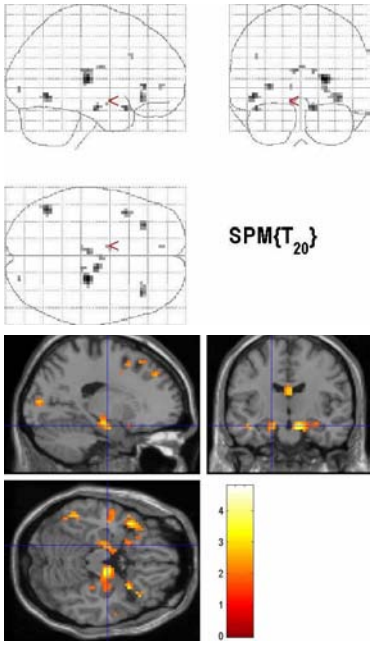

Fig. 1: glass brain (top), sagittal, coronal en transversal projections of all regions showing significant activations resulting from the interaction MDD>HC for the contrast baseline<successfully encoded neutral words ($p<0.001$).

Results

Depressive subjects showed no difference in overall performance (percentage CR and CRej) (68%), compared to healthy controls (66%). There were also no differences between groups in reaction times during encoding and recognition.

Main-effect: Baseline vs successfully encoded words: MDD and HC-subjects showed more activation in the left frontal areas and anterior cingulate during successful encoding of items. An uncorrected two-sample t-test showed slightly more activation in prefrontal cortex and medial temporal lobe for MDD-subject compared to healthy controls.

Baseline vs successfully encoded neutral words: MDD-subjects showed increased activation in left prefrontal cortex, medial temporal lobe and inferior frontal gyrus, compared to healthy controls. The opposite contrast (HC>MDD) revealed no significant differences in activations.

Baseline vs successfully encoded negative words: No signal increase was found for any comparison.

Discussion

In this pilot study depressive subjects showed an increased activation in the left prefrontal cortex, medial temporal lobe and inferior frontal gyrus while evaluating and implicitly encoding neutral words, even in the absence of any performal differences. Interestingly, we did not found an increased activation in these regions during the encoding of negative words. A possible interpretation is that depressive patients need more effort to evaluate and encode neutral stimuli, in contrast to the less demanding "mood-congruent" evaluation and encoding of negative words.

References

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