# Auditory processing of different stimuli in depressed patients vs. healthy subjects as assessed by fMRI

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## Introduction

Clinically, not only depressed mood, somatic symptoms and cognitive impairment, but also disturbances of sensory perception for example for visual and auditory stimuli (Michael et al., 2004; Töllkötter et al., 2005) can occur with depression. The goal of this study was to assess auditory cortical processing by fMRI of patients with major depression vs. healthy controls pre and after antidepressant treatment (electroconvulsive therapy, ECT). Responses to positive emotional stimuli (music) were compared with responses to neutral stimuli (sine tones). Major depression is accompanied by alterations in brain cortical networks compared to controls, depending on the auditory stimuli. We tested the hypothesis that depression should be accompanied by alterations in brain cortical networking compared to controls, depending on the auditory stimuli. Further, we assessed if successful treatment normalizes auditory processing.

## Methods

***Subjects:*** Twenty patients (10 female; age: 53.1 ±10.8 years; unipolar n = 14, bipolar n = 6; Hamilton Depression Rating Scale, HAMD: 27.5 ±7.2, 17 right handed) and 20 healthy controls (7 females; 19 right-handed; age: 29.5 ±11.3 years) participated in this study. All patients had been off psychiatric medication for 2.8 ±0.83 days at the time of the exam. Patients were assigned to two groups according to the severity of depression (medium depressed (n = 13), severely depressed (n = 7)) according to the mean split level of HAMD-scores (differences between groups: Mann-Whitney: $p<0.0001$). The number of episodes also differed (Mann-Whitney $p< 0.005$), other clinical parameter did not. Patients were reexamined after they had completed ECT.

***fMRI measurements, paradigm and data analysis:*** For each subject, 62 functional image volumes (3T Gyroscan, Intera, Philips, Best, NL) were acquired: single shot EPI sequence (TE = 55 ms, TR = 11500 ms (sparse imaging), flip angle 90°, slice thickness 3.6 mm matrix 64 x 64, FOV 230 mm, in-plane resolution 3.6 x 3.6 mm, 36 transversal slices orientated parallel to the AC-PC line). Auditory stimulation: A1- music: recording of a piano piece of Alkan/Barcarole and A2- sine tones (digitally generated pulsed (ν= 5 Hz) 800 Hz) of 115 sec duration each (ON), alternating with rest periods R1-R3 of 69 sec min duration (OFF). Auditory stimulation was presented binaurally via pneumatic headphones and the same sound pressure level of 85 dB above the individual hearing threshold. Image Processing and statistical analysis of the fMRI images were done by SPM2 first and second level standard routines and templates (www.fil.ion.ucl.ac.uk/spm) and SPSS 12.0.

## Results and discussion

Compared to healthy subjects, patients with major depression presented less activation to music (second level analysis, 2 sample t-test) of the left hippocampus, left BA 21, right BA 32 (limbic), right temporal pole (BA 38) und right BA 40 (processing of sensoric stimuli). Patients generally revealed a reduced response to these emotional stimuli, which may correlate with the symptom of "non-feeling". In patients there was a positive correlation between HAMD (second level, SPM2); p = 0.001) and right BA 22 (secondary auditory cortex) and left BA 24 (limbic). After ECT patients and controls showed comparable activations. When presenting neutral sine tones, no differences in activation levels between both groups were seen. However, medium depressed patients activated a compensatory network (right BA 17/18 (cuneus), right BA 7 (precuneus) and left BA 39: part of the associative visual network) when processing tones (figure 1). For all patients there was a negative correlation between HAMD and right/left BA 17 as well as left BA 18 (figure 2). This is in line with the observation that severely depressed patients were no longer capable of recruiting a compensatory network. When comparing severely depressed with medium depressed, severely depressed patients showed stronger activation in right the right BA 25 (limbic), left, right BA 32 (limbic), left, right BA 6 (medium frontal), right BA 9 (medium frontal), and left BA 47 (orbitofrontal) (figure 3), indicating that these patients may present hyperactivation mainly of frontal brain areas and show an emotional response to neutral tones. Again, these additional activations disappeared after successful therapy. In summary, depressives prior to ECT reveal altered auditory processing, which normalizes after successful ECT.

**Figure 1:** **Figure 2:** **Figure 3:**

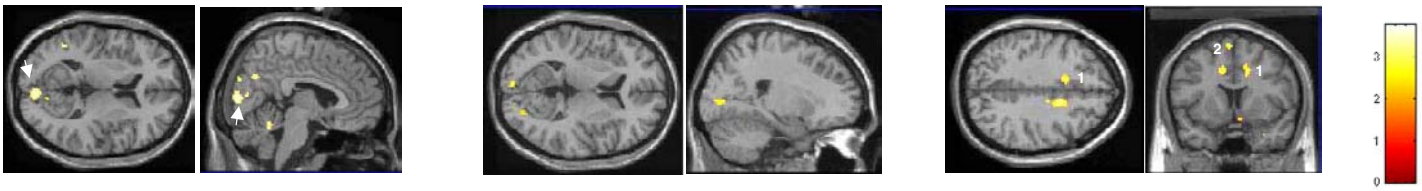


*Fig.1: Medium depressed patients (prior to ECT) > controls (2-sample T-test, second level, p = 0.005, 5 voxels). BA17 (arrow). Fig. 2: Negative correlation with HAMD in patients (n = 20) prior to ECT, second level, p = 0.005, 5 voxel).association with BA 17/18. Fig. 3: Severely > medium depressed patients. 1=BA 32 (limbic), 2 = BA 6 (frontal cortex; 2-sample T-test, second level, p = 0.001, 5 voxels).*

1. Michael N, Ostermann J, Sörös P, Schwindt W, Pfleiderer B. Neuropsychobiology 2004; 49: 5-9.
2. Töllkötter M, Pfleiderer B, Sörös P, Michael N. Journal of Psychiatric Research 2005; in press.