Amygdala Hypersensitivity in Tourette's Patients

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Introduction: Perception of emotional facial expressions is a hallmark of daily social interaction. In an event-related fMRI study at 1.5T we studied the implicit discrimination of six emotional facial expressions (happy, sad, anger, fearful, disgusted, neutral) in Tourette's patients and control subjects. Tourette's syndrome is characterised by motor and vocal tics as well as a high level of impulsivity and emotional dysregulation. Neuroimaging studies point to structural changes of the basal ganglia, frontal areas and parts of the limbic system (Peterson et al. 1998, 2003, Stern et al. 2000).

Methods: 34 patients (11 female, 23 male, aged 18-55 years) fulfilling DSM-IV-TR criteria for Tourette's syndrome (TS) participated in this fMRI-study. For data analysis we included 19 patients (5 women, 14 men) aged 18-55 (mean 29.7 years) and a healthy control group (n=19, 5 women, 14 men, aged 18-51 years, mean age 29.8 years). Tics were assessed with the Yale Global Tic Severity Scale (YGTSS, mean 52.7, SD 17.8) (Leckman et al. 1989). Six patients had a co-morbid obsessive-compulsive disorder and 3 patients ADHD, as assessed according to DSM-IV-TR criteria. 8 of the included 19 TS patients were unmedicated.
In an event-related design, we presented six emotional facial expressions (neutral, happy, sad, angry, fearful, disgusted) of 10 identities from the stimulus set Pictures of Facial Affect (Ekman and Freisen, 1975). Order and timing of the events was calculated using Optseq (http://surfer.nmr.mgh.harvard.edu/optseq) for 180 stimuli with an interstimulus interval of 1000ms and a stimulus duration of 2000ms. Subjects were instructed to judge whether the displayed face was male or female and to respond by pressing a button to each of the stimuli. For functional imaging, a T2*-weighted, echo planar imaging sequence with slice dependent echo times (TE 40-60ms) optimised for BOLD sensitivity in subcortical regions such as the amygdala (Stoecker et al., 2006) was used. The following parameters were applied: repetition time per volume (TR) = 3000ms, TE = 40-60 ms, FOV = 200 x 200 mm^2, flip angle = 90° matrix size = 64 x 64, voxel size = 3.125 x 3.125 x 3 mm^3. Using a mid-sagittal scout image, 32 axial slices (0.3 mm inter-slice gap) were positioned along the anteriorposterior commisure (AC-PC).

Results: The gender judgments were correct in 92.5% in the patient group in comparison to 95% in the control group. In the fMRI analysis we focus on the amygdala activation. Using SPM2 (www.fil.ion.ucl.ak.uk/spm\spm2) we extracted data from a sphere, radius 3mm at MNI coordinates -26 -10 -12 and 26 -10 -12. Statistical analysis shows a significant difference for the effect group and emotion ($P=0.008$, $F=3.2_{\text{numDF 5, denDF 360}}$). The activation pattern is depicted in Figure 1. The results of the patients are drawn in red, the ones of the comparison subjects in black. For each emotion the activation level is shown for the left and the right amygdale separately (left amygdala corresponds to left bar in the figure). On the x-axis the six emotional facial expressions are depicted as H for happy, S for sad, F for fear, A for Anger, D for disgust and N for neutral.

Discussion: For the most facial expressions Tourette's patients show a higher amygdala activation than the control subjects. Most prominent is the reaction for fearful, angry and neutral facial expressions. Since expressions as anger and fear are salient social signals, the overshooting activation to neutral faces in Tourette's patients however, is an unexpected finding. It points to an inadequate and high sensitivity of amygdala activation in Tourette's patients. One might speculate whether this inadequate level of activity gives rise to bouts of motor and vocal tics in situations observers would judge as nothing unusual and patients cannot name a trigger source. The highly activated amygdala may match the clinically described high impulsivity in Tourette's patients. Because of the downsampling of the patients group due to motion artefacts and data quality, possible effects of sex and medication could not be assessed separately.

Conclusion: Deficient inhibition in Tourette's syndrome has, to date, been closely associated with the motor system. However, in a group spanning different severity of symptoms, comorbidities and medication, this deficient inhibition applies to emotional processing also and mirrors well clinical observations and results from neuropsychological evaluation.

References: 1) Peterson BS et a. (1998): Arch Gen Psychiatry 55:326-333 2) Peterson BS et al. (2003): Arch Gen Psychiatry 60:415-424. 3) Stern E et al. (2000): Arch Gen Psychiatry 57:741-748. 4) Leckman JF et al. (1989): J Am Acad Child Adolesc Psychiatry 28:566-573. 5) Ekman P and Freisen W (1975): Pictures of facial affect. 6) Stoecker T et al. (2006): NeuroImage 30:151-159.

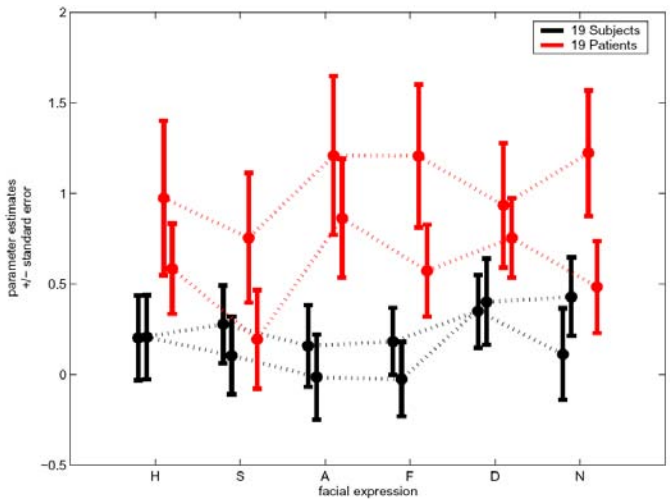

Figure 1: Amygdala activation in Tourette's patients (red) and control subjects (black)