Administration of Selective Serotonin Reuptake Inhibitors Changes Amygdala Activation During Facial Emotion Processing

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Introduction:

It has been demonstrated that patients suffering from anxiety disorders show hyperactivity in limbic brain areas including the amygdalae (Davidson et al., 1999) and treatment with selective serotonin reuptake inhibitors (SSRIs) is well known to reduce anxiety symptoms (Worthington et al. 2005). Accordingly, we have hypothesized that the anxiolytic effect of SSRIs is based on a medication-dependent change in responsivity to emotional stimuli in limbic areas. In this study we used fMRI at 3T to investigate whether SSRI administration may cause changes in brain activation during emotion processing.

Materials and Methods:

Ten healthy male subjects (25.3±3.7 yrs., mean age±SD) were investigated using a randomized, cross-over, placebo-controlled, double-blind design. Each participant underwent three fMRI scanning sessions with an interscan interval of ~30 days. Study medication (either 10mg escitalopram/d, or 20mg citalopram/d, or placebo p.o.) started 10 days prior to the fMRI scans. MR measurements were performed on a 3 Tesla Medspec scanner (Bruker Medical, Germany) using a high-resolution protocol (EPI inplane resolution 1.6*2.7mm, 10 axial slices with 3mm thickness oriented parallel to the AC-PC plane, TE/TR=31/1000ms) optimized for imaging of the amygdala region (Robinson et al, 2004). Subjects performed a facial emotion discrimination task (EDT) and a sensorimotor control task (matching geometrical objects) adapted from (Hariri et al, 2002). Preprocessing and analysis was performed in SPM2, including slice-timing correction, realignment, normalization to standard space and spatial smoothing (FWHM=9mm). For first-level analysis, a fixed-effects model was setup for each participant comprising all three scanning sessions. Using a regions-of-interest (ROI) approach, two ROIs (amygdala region, primary visual cortex) were defined. Parameter estimates for the contrast Task-Control were extracted in each subject and included in one-factorial ANOVAs (factor medication, contrast EDT vs. control task) and post-hoc t-tests were performed.

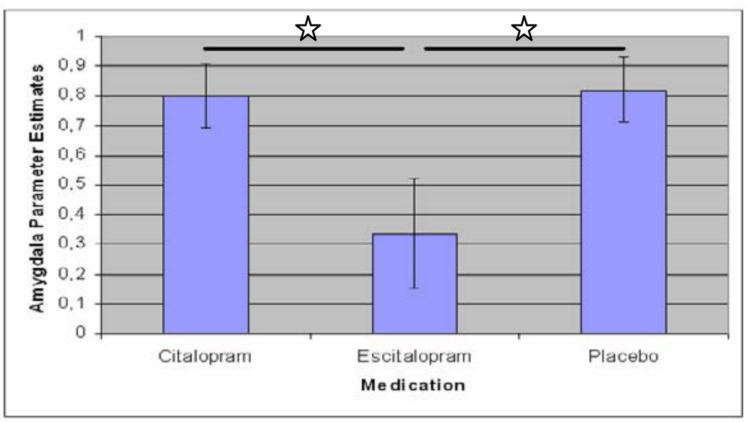

Fig. 1: Amygdala ROI parameter estimates for the three different medications given as mean and standard error. The star indicates significant differences at the p<0.05 level.

Results:

ANOVA revealed a significant effect of medication on amygdala activation (F=3.8, p=0.034). Post-hoc t-tests between medications (fig. 1) showed that escitalopram caused significantly decreased amygdala activation when compared to placebo (p=0.042) or citalopram (p=0.046). No significant activation differences were found between citalopram and placebo. There was no significant main effect of medication on activation in the primary visual cortex (F=0.2, p=0.80, ANOVA).

Discussion:

Escitalopram reduced amygdala activation in healthy subjects during processing of emotional stimuli. A similar task-specific effect was not found in the primary visual cortex arguing against medication-induced changes in attention or vigilance. These findings confirmed our hypothesis and are consistent with a change of responsivity in limbic areas due to escitalopram administration.

References:

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