Face Processing and 5-HT: Chronic citalopram treatment on BOLD responses

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Introduction

Understanding facial expression and emotion identification are important in mediating social functioning. Serotonin (5-HT) is involved in many normal psychological processes, including face emotion recognition (Anderson et al., 2008). Modifying 5-HT availability through depletion or reuptake inhibition has been shown to differentially affect brain responses to specific emotional stimuli, especially emotionally valanced faces (Anderson et al., 2007). Citalopram, a standard serotonin specific reuptake inhibitor (SSRI) has been used both as an acute 5-HT challenge (by intravenous injection) and through daily administration as a sustained inhibitor of 5-HT reuptake. Clinically significant effects of SSRIs are typically observed 10-14 days after starting treatment and so there may be adaptive changes to 5-HT signalling pathways resulting from sustained drug administration. Previous research in controls has found BOLD signal changes when observing emotional faces after 7 days of treatment (Harmer et al., 2006). It remains unclear whether increased duration of SSRI usage will lead to greater changes in 5-HT systems that are recruited during emotional processing. We explored adaptive changes in 5-HT signalling following sub-chronic reuptake inhibition during the processing of emotional faces.

Methods

24 healthy, right handed, age and sex matched volunteers were recruited (mean age=21.1, sd=1.7 years). Participants were provided, in a randomised, balanced order, single blind design, with either 20mg citalopram or placebo for 11 days and tested after 14 days from first dosage. They then underwent an 8 minute implicit face emotion fMRI task using 19 blocks of 6 faces with different emotional valence (10 neutral (N), 3 happy (H), 3 sad (S) 3 fearful (F)) and 3 rest blocks. The emotional face blocks were presented in a pseudorandom order, and interleaved with neutral blocks. Faces were presented for 3000ms and followed by a fixation cross for 500ms. Participants were required to identify the gender of the face not the emotion presented. Data were analysed and compared to resting blocks using a random-effects multiple regression model in SPM5. Whole brain images were acquired on a Philips *Intera* 1.5T scanner using single-shot echo-planar (EPI) pulse sequence. Each volume comprised 29 ascending axial slices (TR=2s, TE=40ms, 4.5mm thickness with 0.5mm slice gap, in-plane resolution of 3.5x3.5mm).

Results

Group differences were assessed by contrasting BOLD signal changes between placebo and citalopram treatment groups for face processing regardless of emotion. Brain areas attenuated by citalopram treatment were assessed by inclusively masking ($p<0.05$ uncorrected) the difference between groups for face processing (all emotions) by brain areas activated in the placebo control group.

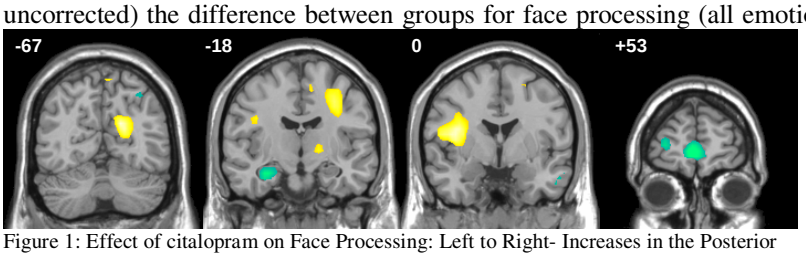

Figure 1: Effect of citalopram on Face Processing: Left to Right- Increases in the Posterior Cingulate, Supramarginal Gyrus, Thalamus and Insula. Decreases in Hippocampus, Prefrontal and Anterior Cingulate Cortex.

Significant BOLD reductions were observed following sub-chronic citalopram in the left hippocampus, prefrontal cortex (BA 10), anterior cingulate and occipital cortex (BA 19) ($p<0.001$ uncorrected). Citalopram augmented the BOLD response in the left insula, right thalamus, right posterior cingulate and supramarginal gyrus (BA 40) ($p<0.001$ uncorrected). These prior hypothesised areas survived small volume correction at $p<0.05$ (FWE).

Discussion

Sub-chronic SSRI treatment in healthy controls was associated with modulation of brain areas involved in emotional and cognitive control. Citalopram appears to blunt the normal hippocampal and anterior cingulate response in face processing. In addition, the response in posterior cingulate and BA40 may be due to a reduction in the default mode network following drug treatment. These findings may be due to enhanced post synaptic signalling or down regulation of 5-HT receptors following chronic increases in central 5-HT availability.

Conclusion

SSRI treatment in healthy volunteers causes adaptive changes in 5-HT signalling compared to placebo when viewing faces regardless of emotion. Different face emotions may highlight further changes in response to specific cues. These findings suggest that chronic SSRI use modifies 5-HT pathways involved in low level processes which may be involved in treatment response.

References

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