Chronic SSRI Treatment Modifies BOLD Responses To Emotional Face Expressions

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Background

- Selective serotonin reuptake inhibitor (SSRI) antidepressants typically require 10-14 days of administration before clinically beneficial effects are seen
- The biological mechanisms that mediate antidepressant action are not well understood
- Therapeutic effect may be the result of adaptive changes in the 5-HT system to sustained reuptake inhibition
- Previous research in controls has found BOLD signal changes when observing emotional faces after 7 days of SSRI treatment (Harmer et al., 2006)
- Unclear whether increased duration of SSRI usage will lead to greater changes in 5-HT systems that are recruited during emotional processing
- We aim to explore adaptive changes in 5-HT signalling following 11 days of reuptake inhibition during the processing of emotional faces

Methods

- 24 healthy right handed, age and sex matched volunteers (mean age=21.1, sd=1.7 years)
- Randomised, balanced order, single blind design, with either 20mg daily citalopram or placebo for 11 days, 3 day washout and tested after 14 days from first dosage
- Participants underwent fMRI scanning while completing an 8 minute implicit face processing task
- Whole brain images were acquired on a Philips Intera 1.5T scanner using single-shot echo-planar 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)
- Data were compared to resting blocks using a random-effects multiple regression model in SPM5
- Brain responses adapted by citalopram pre-treatment were assessed by inclusively masking (p<0.05 uncorrected) the difference between groups by brain areas activated for face processing (all emotions) in the placebo control group

Results

**BOLD Increases Following SSRI Treatment**
- Citalopram increased BOLD responses compared to placebo, in the left insula, right thalamus, posterior cingulate (PCC) and supramarginal gyrus. These prior hypothesised areas were significant following small volume correction at p<0.05 (Family Wise Error)

**BOLD Decreases Following Treatment**
- BOLD reductions were observed following citalopram treatment in the left hippocampus, prefrontal cortex (BA 10), anterior cingulate and visual cortex (BA 19)

**Amygdala Response**
- There were no significant differences in amygdala responses to emotional or fearful faces following citalopram treatment

Discussion

- Chronic (11 days) 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 prefrontal response in emotional face processing
- Sustained SSRI treatment does not appear to alter the function of the amygdala in response to emotional stimuli, unlike acute challenges
- The response in posterior cingulate and BA40 may be due to the alteration of default mode network processes following SSRI 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
- The modified BOLD response indicates an adaptation of the 5-HT system to therapeutic doses of citalopram. These findings suggest that chronic SSRI use modifies 5-HT pathways involved in low level processes which may be involved in treatment response

References

- Harmer et al., Antidepressant drug treatment modifies the neural processing of nonconscious threat cues. Biol Psychiatry. 2006, May 1; 59(9): 816-20

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