Effects of Citalopram on Effective Connectivity during the Go/No-Go task

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Introduction

Serotonin (5-HT) is implicated in the aetiology and treatment of a variety of psychiatric conditions including impulse control disorders. To further investigate the role of 5-HT in impulsivity we used the selective serotonin reuptake inhibitor (SSRI), citalopram which has been shown to modulate BOLD responses to the behavioural inhibition task (Go/No-Go) [1]. In this study, we use effective connectivity to further investigate the neuronal basis of citalopram's effects during the Go/No-Go task. Understanding the basis of such processes will provide useful insight into abnormal processes characterising psychiatric disorders.

Methods

12 healthy, right handed male volunteers, age 19-36 years were recruited from the students, staff and general public. Subjects visited on two occasions receiving saline (placebo) or citalopram (7.5 mg over 7.5 minutes), 20 minutes before the undertaking the task, in a randomised, balanced order, single-blind fashion. Subjects were asked to respond, via a button press, to a sequence of rapidly presented letters except when they saw a 'V'. Two conditions were presented in which a response was required for all stimuli (Go) or 50% of the stimuli (No-Go).

Images were acquired on a 1.5T Philips scanner with a multi-slice, single-shot EPI sequence to achieve whole brain coverage and analysed using Statistical Parametric Mapping (SPM5, www.fil.ion.ucl.ac.uk/spm). Time series were extracted from each individual's fixed effects analysis in the following brain regions: Inferior Frontal Gyrus (IFG), Inferior Parietal Lobe (IPL), the Anterior Cingulate (AC) and the Supplementary Motor Area (SMA). For each brain region, the time series for each subject were combined into a scan*subject matrix. We then performed principal component analysis on each matrix and used the first principal component as an input for Structural Equation Modelling (SEM) which was implemented using AMOS (www.spss.com/amos).

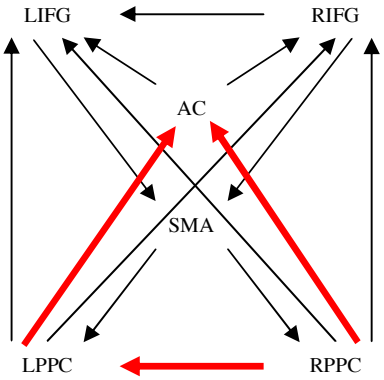

Figure 1: Model Tested

Results

There were no differences between placebo and citalopram conditions in the number of omission errors or commission errors. Responses were slightly slower during the citalopram condition (387±28ms for placebo, 406±24ms for citalopram, p=0.05).

The effective connectivity model that we specified is shown in Figure 1, where the connections which are significantly different between placebo and citalopram conditions are shown as red arrows. The model fitted the data well with χ^2=0.824 (P=0.662). There was a significant difference between the placebo condition and the citalopram condition, with χ^2_{diff}=37.297 (P=0.001). The connections which were significantly different between the placebo and citalopram conditions were: LPPC → AC (χ^2_{diff}=4.505, P=0.034), RPPC → AC (χ^2_{diff}=9.670, P=0.002) and RPPC → LPPC (χ^2_{diff}=18.108, P<0.001). The changes in connection strength between placebo and citalopram condition are: LPPC → AC changes from -0.058 to 0.425, RPPC → AC changes from 0.580 to -0.146 and RPPC → LPPC changes from 0.597 to -0.320.

Conclusions

Citalopram makes subjects respond more slowly to the No-Go targets, suggesting that citalopram makes them less impulsive. Citalopram also modulates the connections from the parietal cortices to the anterior cingulate with anterior cingulate being influenced by the right parietal cortex during placebo and the left parietal cortex during citalopram administration. These results support the role of 5-HT in impulsive disorders and have implications for the further understanding and treatment of disorders characterised by serotonergic dysfunction.

References

[1] Del-Ben CM, Deakin JF, McKie S, Delvai NA, Williams SR, Elliott R, et al. The effect of citalopram pretreatment on neuronal responses to neuropsychological tasks in normal volunteers: an FMRI study. Neuropsychopharmacology. 2005 Sep;30(9):1724-34.