Differences in mCPP-induced BOLD signal response between Anti-social personality disorder individuals (ASPD) and healthy volunteers

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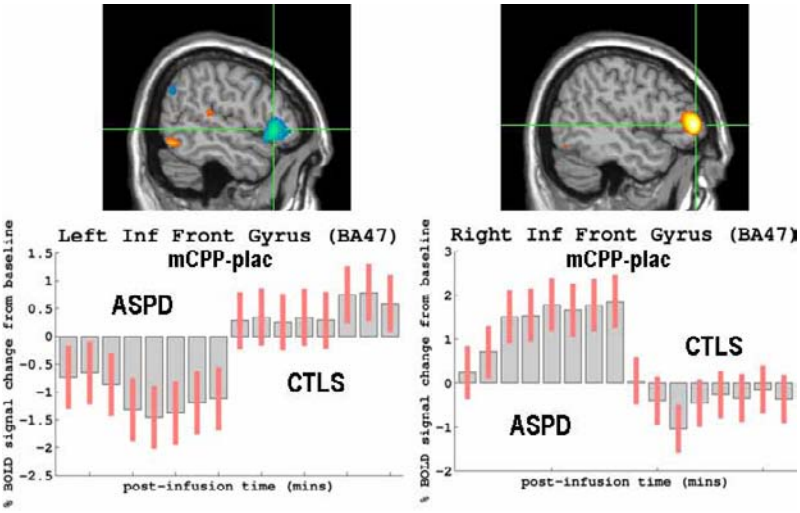
Introduction

The pathogenesis of a number of psychiatric disorders, such as anti-social personality (ASPD), can be linked to serotonin and its receptors. Using a serotonergic agonist (m-chlorophenylpiperazine, mCPP) in conjunction with fMRI (pharmacoMRI; phMRI), we aimed to investigate the role of serotonin in making ASPDs more impulsive than healthy individuals. It has been shown that mCPP infusion in healthy volunteers modulates the BOLD response during a behavioural inhibition task[1], designed to test impulsivity. We hypothesised that differences in the mCPP-induced BOLD signal between ASPDs and healthy volunteers would be found in regions implicated in impulsivity, such as the inferior frontal gyrus.

Methods

29 ASPDs (aged between 22 and 58) and 31 healthy volunteers (aged between 19 and 62) were recruited into a randomised, single-blind study. Each subject was given an infusion of either placebo or mCPP (0.08 mg/kg) in saline. This created 4 groups: ASPD-mCPP (11 subjects), ASPD-plac (18), CTL-mCPP (15) and CTL-plac (16).

Each subject underwent a 16 minute fMRI scan, 8 minutes into which they received the infusion. Images were acquired on a 1.5T Philips scanner with a multi-slice, single shot EPI sequence to achieve whole-brain coverage. Data were analysed using SPM2 (Friston, The Wellcome Department of Cognitive Neurology, London, UK). Data analysis identified voxels showing significant changes in successive 1 minute time-bins compared to pre-infusion baseline and compared to saline infusion responses across the groups.



Results

Group differences in mCPP-induced BOLD signal were observed in several areas including inferior frontal gyrus (BA47) (Figure 1), insula (BA13), middle temporal gyrus (BA21), fornix, parahippocampal gyrus (BA35), inferior frontal gyrus (BA20), thalamus, caudate and posterior cingulate gyrus (BA29/30). In most of these areas, the ASPDs showed a BOLD signal increase (or decrease) due to mCPP infusion whereas the BOLD signal in healthy controls remained close to baseline.

Figure 1: The mCPP-induced BOLD signal changes observed in the inferior frontal gyri (BA47) are different between the two groups.

Conclusions

mCPP-induced BOLD responses were observed in ASPDs, but not in healthy volunteers, in areas implicated in impulsivity, such as the inferior frontal gyrus (BA47). We hypothesise that this imbalance in serotonergic function makes individuals more impulsive and that this result acts as a biomarker for individuals suffering from impulsive control disorders. This study demonstrates that direct infusion of mCPP combined with fMRI (phMRI) can be used as a powerful tool for localising and pharmacologically dissecting the differences in serotonin receptor function between a personality group and healthy individuals.

References

[1]Anderson IM et al. 5-HT_{2c} receptor activation by m-chlorophenylpiperazine detected in humans with fMRI. Neuroreport 2002; 13: 1547