BJPsych The British Journal of Psychiatry (2009) 194, 373–374. doi: 10.1192/bjp.bp.108.055459

Short report

Using the Stroop task to investigate the neural correlates of symptom change in schizophrenia

Lydia Krabbendam, Owen O'Daly, Lucy A. Morley, Jim van Os, Robin M. Murray and Sukhwinder S. Shergill

Summary

This study examined brain activation during a cognitive inhibition task in patients with schizophrenia following changes in their positive symptoms. A Stroop task was used during functional magnetic resonance imaging in 11 patients with schizophrenia (patient group) and 9 healthy volunteers (control group). At baseline, the patient group showed significantly attenuated activation within the anterior cingulate gyrus, left pre-/postcentral gyrus and inferior frontal junction. At follow-up, there was a significant increase in activation in the left inferior frontal junction associated with a decrease in positive symptoms, suggesting this region plays a role in the development of these symptoms.

Declaration of interest

None.

Reduced cognitive inhibition may contribute to the development of positive symptoms.[1] The Stroop task is a classic test of cognitive inhibition, in which the processing of an irrelevant dimension of the stimuli (words) conflicts with a competing stimulus dimension (colours).[2] Increased interference on the Stroop task has been demonstrated in patients with schizophrenia.[3]

The anterior cingulate cortex, left inferior frontal gyrus and left inferior frontal junction are the core processing areas for the Stroop interference effect in healthy individuals.[4] Both the anterior cingulate and prefrontal cortex have been implicated in the increased susceptibility to the Stroop effect in schizophrenia.[5,6]

If positive symptoms of psychosis arise as a consequence of reduced cognitive inhibition, then symptom change will be reflected in the activation of cortical regions associated with inhibition. We hypothesised that: (a) performance on the Stroop task would be associated with attenuated activation in the anterior cingulate cortex and the left inferior frontal gyrus/junction in schizophrenia; and (b) changes in positive symptoms would be correlated with activation in these areas.

Method

We studied 11 patients (9 males) with DSM–IV[7] schizophrenia: mean age, 35.4 years (s.d.=9.2); years in full-time education, 13.5 (s.d.=2.1); National Adult Reading Test (NART)[8] IQ, 106.9 (s.d.=11.0); duration of illness, 12.6 years (s.d.=9.1). All were receiving stable doses of antipsychotic medication (mean chlorpromazine equivalent, 523 mg/day (s.d.=455); eight patients treated with conventional and three patients with atypical antipsychotics). The interval between baseline and follow-up measurements was 6–8 weeks, sufficient to allow for change in positive symptoms, while antipsychotic medication was kept constant. Two patients failed to attend their second scan (one did not give a reason, the other felt uncomfortable in the scanner).

Symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS)[9] immediately prior to scanning on both occasions. The total score was 56.3 (s.d.=16.5) at baseline and 48.3 (s.d.=6.6) at follow-up with mean positive PANSS scores of 15.4 (s.d.=6.7) at baseline and 11.4 (s.d.=4.1) at follow-up. The difference between baseline and follow-up was significant for the positive symptoms ($t(8)=2.33$, $P=0.048$), but not for the total score ($t(8)=1.68$, $P=0.13$).

Nine healthy controls without a family history of psychosis were scanned once; complete data were not available for two people owing to technical problems in the recording of the behavioural data. Controls (four males) were comparable to patients for age (mean=33.3 years (s.d.=7.2), $t(16)=-0.50$, $P=0.62$) and education (mean=15.7 years (s.d.=3.1), $t(16)=1.78$, $P=0.09$). Mean NART score in the control group was 118.6 (s.d.=2.0) ($t(16)=2.6$, $P=0.02$).

Individuals were excluded if they had a history of drug or alcohol misuse, neurological illness, head injury, speech/hearing difficulty or any contraindication to magnetic resonance imaging (MRI) scanning such as metal implants. All participants provided informed consent; ethical approval was provided by the Institute of Psychiatry ethics committee.

The Stroop task consisted of congruent, incongruent, neutral and baseline (fixation cross) conditions. The analysis contrasted the incongruent condition (colour name printed in an incongruent colour) with the congruent condition (colour name printed in the congruent colour). Participants were presented with a stimulus every 6 s, named the colour of the word in a 4 s quiet period which was followed by 2 s of compressed sequence acquisition. There were 20 trials for each condition, resulting in a total of 80 trials, presented in random order suitable for an event-related analysis.

Data were acquired at 1.5 T and analysed using XBAM (www.brainmap.it) with protocols previously described[10] (see online supplement).

Results

A two × two ANOVA comparing error rates between groups (patients *v.* controls) and conditions (congruent *v.* incongruent) revealed a trend main effect of condition ($F(1,16)=3.59$, $P=0.07$; incongruent: 4.4% (s.d.=7.0); congruent: 1.1% (s.d.=2.1)). There was no significant main effect of group ($F(1,16)=0.06$, $P=0.80$; controls: 2.5% (s.d.=5.8); patients: 3.0% (s.d.=5.3)). At follow-up, the mean percentage error was 2.8% (s.d.=6.0).

Controls demonstrated a significant increase within the left pre-/postcentral gyrus, extending into the left inferior frontal gyrus, the anterior cingulate cortex and the left lingual gyrus during the incongruent compared with the congruent condition. The patient group showed significantly attenuated activation within the left pre-/postcentral gyrus extending into the left

inferior frontal junction, the anterior cingulate cortex and the right middle temporal gyrus (online Fig. DS1a) during the incongruent condition compared with controls.

Although there was increased activation in the bilateral pre-/postcentral gyrus extending into the left inferior frontal junction during both incongruent and congruent conditions at follow-up, only inferior frontal junction activation was specific to the incongruent condition (online Fig. DS1b) and correlated with reduced positive symptoms (Pearson's r=0.89, $P<0.01$) (online Fig. DS1c).

Discussion

In controls, the areas activated show substantial overlap with a recent meta-analysis of imaging findings in the Stroop task[4] for the left inferior frontal junction/gyrus and the anterior cingulate cortex. The finding of attenuated anterior cingulate cortex activation in patients replicates previous results[5,6] but our study suggests that the left inferior frontal junction is also implicated. Recent Stroop studies have suggested that inferior frontal junction/gyrus and anterior cingulate cortex are related to top-down control and conflict detection respectively.[11] The task-related attenuation in the inferior frontal junction/gyrus in patients suggests that prefrontally mediated implementation of top-down control is compromised in schizophrenia, consistent with a long tradition of studies reporting abnormal prefrontal functioning in this disorder.[12] The results suggest that normalisation of the task-related activity in this area may contribute to the reduction of positive symptoms of psychosis, possibly through a reduced susceptibility to interference.[1] As Stroop interference may be specifically related to symptoms of disorganisation,[3] future studies could test whether the observed association between signal change and decrease in positive symptoms can be accounted for by specific items within the positive symptom domain.

Methodological limitations include first, the issue of generalisability and specificity of the results from the analysis of a relatively small number of participants and experimental trials. However, we used established non-parametric image analysis software with stringent thresholds to minimise any Type I errors. Second, use of medication in the patient group may have influenced the between-group variability. Examining for medication effects within the patient group, we found no significant correlation of the activation maps with dosage equivalents of medication. Patients did not have any alterations in their antipsychotic medication between the two imaging sessions, thus findings are unlikely to be related to changes in medication.[13] Third, we did not examine reaction time differences in participants, as subtle variation in reaction time is unlikely to influence the rather slow blood oxygen level dependent response measured by functional MRI. However, it would be interesting to investigate the influence of reaction time in future studies.

Finally, repetition effects of the task may confound these findings; however, a passive auditory and visual stimulation experiment showed no changes between the two scans, excluding any non-specific repetition or session effects and we observed a significant correlation between the increased activation in the inferior frontal junction and the reduction in positive symptoms. It would be interesting to examine the effects on positive symptoms of increasing the inferior frontal junction, or prefrontal, activation on positive symptoms through specific interventions using either pharmacological, neurofeedback or psychological techniques.

Lydia Krabbendam, PhD, Institute of Psychiatry, King's College London, UK and School for Mental Health and Neuroscience, University of Maastricht, The Netherlands; **Owen O'Daly**, BSc, MSc, **Lucy A. Morley**, MBBS, PhD, MRCPsych, Institute of Psychiatry, King's College London, UK; **Jim van Os**, MD, PhD, Institute of Psychiatry, King's College London, UK and School for Mental Health and Neuroscience, University of Maastricht, The Netherlands; **Robin M. Murray**, MD, DSc, FRCPsych, Institute of Psychiatry, King's College London, UK; **Sukhwinder S. Shergill**, MBBS, PhD, FRCPsych, Institute of Psychiatry, King's College London, and Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College London, UK

Correspondence: Dr Lydia Krabbendam, Department of Psychiatry and Neuropsychology, Maastricht University, PO BOX 616 (location VIJV), 6200 MD Maastricht, The Netherlands. Email: l.krabbendam@sp.unimaas.nl

First received 28 May 2008, final revision 26 Aug 2008, accepted 8 Oct 2008

Funding

L.K. was funded by a VIDI Grant from the Netherlands Organisation for Scientific Research (NWO); S.S.S. was funded by the Wellcome Trust; and L.A.M. and O.O'D. were funded by the Psychiatry Research Trust.

References

1 Frith CD. Consciousness, information processing and schizophrenia. *Br J Psychiatry* 1979; **134**: 225–35.

2 MacLeod CM. Half a century of research on the Stroop effect: an integrative review. *Psychol Bull* 1991; **109**: 163–203.

3 Henik A, Salo R. Schizophrenia and the Stroop effect. *Behav Cogn Neurosci Rev* 2004; **3**: 42–59.

4 Laird AR, McMillan KM, Lancaster JL, Kochunov P, Turkeltaub PE, Pardo JV, et al. A comparison of label-based review and ALE meta-analysis in the Stroop task. *Hum Brain Mapp* 2005; **25**: 6–21.

5 Carter CS, Mintun M, Nichols T, Cohen JD. Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [15O]H2O PET study during single-trial Stroop task performance. *Am J Psychiatry* 1997; **154**: 1670–5.

6 Kerns JG, Cohen JD, MacDonald AW 3rd, Johnson MK, Stenger VA, Aizenstein H, et al. Decreased conflict- and error-related activity in the anterior cingulate cortex in subjects with schizophrenia. *Am J Psychiatry* 2005; **162**: 1833–9.

7 American Psychiatric Association. *Diagnotstic and Statistical Manual of Mental Disorders (4th edn) (DSM–IV)*. APA, 1994.

8 Nelson HE. *National Adult Reading Test Manual (2nd edn)*. nferNelson, 1991.

9 Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 1987; **13**: 261–76.

10 Shergill SS, Bullmore E, Simmons A, Murray R, McGuire P. Functional anatomy of auditory verbal imagery in schizophrenic patients with auditory hallucinations. *Am J Psychiatry* 2000; **157**: 1691–3.

11 MacDonald AW 3rd, Cohen JD, Stenger VA, Carter CS. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 2000; **288**: 1835–8.

12 Weinberger DR, Berman KF. Prefrontal function in schizophrenia: confounds and controversies. *Philos Trans R Soc Lond B Biol Sci* 1996; **351**: 1495–503.

13 Davidson LL, Heinrichs RW. Quantification of frontal and temporal lobe brain-imaging findings in schizophrenia: a meta-analysis. *Psychiatry Res* 2003; **122**: 69–87.

EXTRA CONTENT ONLINE