

Differential activation of temporal cortex during sentence completion in schizophrenic patients with and without formal thought disorder

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Abstract

The neural correlates of processing linguistic context in schizophrenic patients with formal thought disorder (FTD) were examined. Six right-handed male patients with prominent 'positive' FTD were compared with six schizophrenic patients without FTD and seven volunteers, matched for cognitive and demographic variables. Functional magnetic resonance imaging (fMRI) was used to measure cerebral activation while subjects read and completed sentence stems out loud. During a GENERATION condition, subjects were required to generate a word which completed the sentence stem appropriately. During a DECISION condition, subjects selected and articulated one of two presented terminal words. A READING condition served as baseline. The three conditions were compared with each other. Regions activated were identified in each group, and between-group differences were detected using an ANCOVA. When GENERATION was compared with READING, FTD patients showed less activation in the right superior temporal gyrus than patients without FTD or controls, but greater activation in the left inferior frontal, inferior temporal and fusiform gyri. FTD patients also showed an attenuated right temporal response when GENERATION was compared with DECISION. This differential engagement of the right temporal cortex was independent of differences in the speed or accuracy of responses, whereas the left fronto-temporal differences in activation were not evident after covarying for task errors. The attenuated engagement of right temporal cortex, which is implicated in language comprehension at the discourse level, is consistent with neuropsychological evidence linking thought disorder with deficits in processing linguistic context. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

Clinical experience, event-related potential (ERP) studies and discourse analysis suggest that patients with schizophrenia have difficulty in extracting contextual information from sentences (Chapman and Chapman, 1973; Rochester and Martin, 1979;

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Strandburg et al., 1997) These deficits are particularly evident in patients with ‘positive’ formal thought disorder (Kuperberg et al., 1998). Lesion studies indicate that the interpretation of phrases (Kaplan et al., 1990) or stories (Weylman et al., 1989), and the integration of elements of discourse (Brownell et al., 1986; Moya et al., 1986; Beeman, 1993) are impaired in patients with right lateral temporal pathology, while functional neuroimaging implicates the right temporal cortex in the normal processing of sentences (Muller et al., 1997), metaphors (Bottini et al., 1994) and reading paragraphs (St George et al., 1999). These data thus suggest that the processing of context at the sentence level involves the right temporal cortex.

Most functional imaging studies in schizophrenia have examined the brain regions associated with the processing of single words, as opposed to sentences, and have investigated this in relation to the disorder of schizophrenia, rather than specifically to thought disorder. Verbal fluency in schizophrenia has been associated with an attenuated left prefrontal activation (‘hypofrontality’; Yurgelun Todd et al., 1996; Curtis et al., 1998), and with abnormal correlations between frontal and temporal activation (‘functional dysconnectivity’; Frith et al., 1995; Fletcher et al., 1996). However, these findings have been inconsistent (Spence et al., 1998; Curtis et al., 1999), perhaps because of the potentially confounding effects of poorer task performance in patients than controls (Fletcher et al., 1998). Functional imaging studies of thought disorder have correlated the trait for this symptom with resting activity in the inferior frontal, cingulate (Liddle et al., 1992) and temporal cortex (Ebmeier et al., 1993; Kaplan et al., 1993) while articulation of thought disordered speech ‘on-line’ has been associated with relatively reduced activity in inferior frontal, cingulate and superior temporal cortex, but increased activity in the fusiform region (McGuire et al., 1998). Structural imaging studies have linked thought disorder with reduced left superior temporal volume (Shenton et al., 1992) and abnormal symmetry of the planum temporale (Rossi et al., 1994; Petty et al., 1995; Vita et al., 1995) although these findings have not been consistently replicated (Kleinschmidt et al., 1994).

The present study used functional magnetic resonance imaging (fMRI) to examine brain activity in schizophrenic patients with and without formal

thought disorder, while they were performing two sentence-completion tasks designed to engage the processing of linguistic context. Sentences were used, because more-word utterances are usually the basis of verbal communication. One of our tasks required subjects to generate a word appropriate to complete a sentence stem, while in the other, subjects selected the terminal word from two possible responses. In order to assess the relationship between cerebral activation and behavioral performance, we measured the speed and accuracy with which subjects executed the tasks, and examined the imaging data after covarying for these variables. We predicted that in healthy controls and non-FTD patients the tasks would be associated with activation in the right lateral temporal cortex, but that thought disordered patients would show a relatively attenuated activation in this region. We expected that this differential activation would be more pronounced when subjects had to generate the final word *de novo*, as this appeared to place greater demands on contextual processing than when the response was selected from extrinsic cues.

2. Method

2.1. Subjects

Six acutely psychotic male patients with schizophrenia (DSM-IV) were recruited from the Maudsley and Bethlem Royal Hospitals, London, UK. Patients were carefully selected if they were currently exhibiting prominent symptoms of ‘positive’ formal thought disorder. Two comparison groups, consisting of six non-thought-disordered schizophrenic patients (DSM-IV) and seven healthy male volunteers, were selected to match the patients on demographic variables. In order to minimize the risk of excessive head movement during scanning, patients who were agitated or distractible were excluded. There were no significant differences between the groups in cognitive (Table 1) and socio-demographic variables, which were taken from the hospital chart notes and the patients’ self reports (Spitzer and Endicott, 1979). All subjects were right handed (Annett, 1970). All the patients were on stable doses of antipsychotic medication.

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