

Do you hear what I hear? Neural correlates of thought disorder during listening to speech in schizophrenia

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Abstract

Thought disorder is a fundamental symptom of schizophrenia, observable as irregularities in speech. It has been associated with functional and structural abnormalities in brain regions involved in language processing, including left temporal regions, during language production tasks. We were interested in the neural correlates of thought disorder during receptive language processing, as this function is relatively preserved despite relying on the same brain regions as expressive language. Twelve patients with schizophrenia and 11 controls listened to 30-s speech samples while undergoing fMRI scanning. Thought disorder and global symptom ratings were obtained for each patient. Thought disorder but not global symptomatology correlated positively with the BOLD response in the left posterior superior temporal lobe while listening to comprehensible speech (cluster-level corrected $p = .023$). The pattern of brain activity associated with thought disorder during listening to comprehensible speech differs from that seen during language generation tasks, where a reduction of the leftward laterality of language has often been observed. As receptive language is spared in thought disorder, we propose that the increase in activation reflects compensatory processing allowing for normal performance.

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1. Introduction

Thought disorder is a fundamental symptom of schizophrenia, expressed as disturbance in the organization and coherence of speech. Functional brain imaging studies in thought disordered subjects have

found abnormal patterns of activity during the production of speech and performance of language-based tasks. These abnormalities suggest a deviation from the normal pattern of hemispheric lateralization of language functions. Specifically, severity of thought disorder has been observed to correlate negatively with activation in the left posterior superior temporal gyrus (McGuire et al., 1998; Kircher et al., 2001b, 2002) and positively with activation in the right superior and middle temporal gyri (Kircher et al., 2002) during continuous speech

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production. A similar reduction in the normal leftward functional lateralization of language has also been observed in schizophrenia during the performance semantic decision and verbal fluency tasks (Sommer et al., 2001; Weiss et al., 2004).

Abnormal lateralization in thought disorder is also reflected in the anatomy of the cortex. One of the more consistent morphological findings in schizophrenia is reduced posterior superior temporal lobe asymmetry, and severity of thought disorder is inversely related to the degree of grey matter volume reduction in this area (Shenton et al., 1992; Rossi et al., 1994). Posterior superior temporal lobe is one of the classic language processing regions, incorporating Wernicke's area, and is important for both speech comprehension and production (Binder et al., 1997, 2000; Moore and Price, 1999; Buchsbaum et al., 2001; Crinion et al., 2003). The linguistic nature of this symptom coupled with these and other findings have led to the proposal that thought disorder reflects abnormality in language function, marked by a decrease in the normal leftward structural and functional asymmetry of brain regions involved in language processing (Crow, 1997; Kircher et al., 2002).

Neuroimaging investigations of language and thought disorder have focused on productive language tasks as this is the domain in which disorder is observed. However, receptive and productive language functions rely largely but not entirely on the same brain regions, a key difference being a greater reliance of receptive language on the right hemisphere, particularly at the level of discourse comprehension (St George et al., 1999; Robertson et al., 2000). As both functions involve posterior superior temporal lobe processes, the same region in which grey matter density and activation during producing language correlate with severity of thought disorder, it is interesting that thought disorder is not also evident in receptive language. Working memory is also affected in schizophrenia. Increased brain activation has been observed to accompany normal performance on working memory tasks by subjects with schizophrenia; this is thought to reflect compensatory processing (Callicott et al., 2003; Manoach, 2003).

We hypothesized that a similar process may underlie the preservation of receptive language in thought disorder, that is, that compensatory processing allows for maintenance of this function. If this postulation is correct, severity of thought disorder should be associated with increased brain activation in receptive language processing regions. We imaged subjects as they listened to comprehensible speech to test this hypothesis; specifically, that activity in receptive language processing areas would be positively correlat-

ed with the severity of thought disorder in patients with schizophrenia.

2. Methods

2.1. Subjects

Eleven healthy control subjects and 12 patients with schizophrenia were recruited. Groups were matched for age, IQ as estimated with the Quick Test (Ammons and Ammons, 1962; Nelson, 1982), and parental socioeconomic status (SES) as determined with the Hollingshead Index (Hollingshead, 1957). Summary statistics for these and other sample characteristics are given in Table 1. All subjects were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971), and were native English speakers with no history of head injury, substance abuse or neurological disorder. Three patients were receiving typical and 8 atypical antipsychotic medication and all were stable outpatients with no recent changes to their medication. Patients with schizophrenia were recruited from the Schizophrenia Day Program at Vancouver Hospital or through their primary care physician. Diagnosis according to DSM-IV criteria was confirmed by one of the authors (E.N.). Control subjects were recruited via advertisement from the University of British Columbia campus. All subjects received 10 dollars per hour remuneration; subjects were screened for MRI compatibility and provided informed written consent before participating. Experimental procedures were approved by the University of British Columbia Clinical Research Ethics Board.

2.2. Procedure

Stimuli were thirty 30-s blocks of speech: 10 English (comprehensible), 10 Mandarin (non-comprehensible),

Table 1
Sample characteristics

	Control subjects (n=11)	Schizophrenic subjects (n=12)
Gender (male/female)	7:4	7:5
Age	34.0±12.0	35.9±12.6
IQ (Quick Test)	111.6±14.1	102.7±5.2
Education (years)	18.4±2.3	15.1±2.4*
Parental SES	3.0±1.6	3.1±1.7
Age of onset		24.3±6.3
SSPI (total score)		9.5±5.7
TLI (total score)		5.0±3.7
Chlorpromazine equivalent of antipsychotic dose (mg)		412.9±271.4

* $t(21)=3.35, p=.003$.

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