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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.

Keywords: Schizophrenia; Thought disorder; fMRI; Language; Speech comprehension

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 correlated 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

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

and 10 reversed English (control). The English and Mandarin speech was recorded from a bilingual male speaker fluent in both languages reading trivia about the physical world; the reversed English stimuli were created by reversing the English stimuli using conventional sound editing software. Stimuli were presented pseudorandomly, alternating with 30 s of silence and counterbalanced across three 10-min runs, through insert earphones contained within 30-dB sound attenuating MRI-compatible headphones. As the three conditions were likely to be differentially engaging–comprehensible commanding more attention than either non-comprehensible or reversed speech–a tone detection task was incorporated in an attempt to balance attention. Three or four 1000 Hz tones were embedded in each speech sample at random intervals and subjects were instructed to listen to the auditory stimuli and press a response button when they heard a tone. Although this task may have been distracting during the comprehensible speech, we hoped that it would increase attention during the other two conditions. As this task was simply intended to maintain attention across the three conditions, it was not included in analysis. We considered including a post-scan memory task to assess whether subjects were listening to the stimuli, but as this would be useful for only one of three conditions we chose not to. The difficulty in assessing memory of non-comprehensible speech reinforced our decision to use the tone task to maintain attention. Thought disorder was assessed with the Thought and Language Index (TLI) (Liddle et al., 2002a) and overall symptom severity with the Signs and Symptoms of Psychotic Illness (SSPI) rating scale (Liddle et al., 2002b).

2.3. Image acquisition

Echo-planar images were collected on a standard clinical GE 1.5 T system fitted with a Horizon Echospeed upgrade. Conventional spin-echo T_1-weighted sagittal localizers were used to view head position and to graphically prescribe the functional image volumes. Functional image volumes sensitive to the blood oxygen-level dependent (BOLD) contrast signal were collected with a gradient echo sequence (TR/TE 3000/40 ms, 90° flip angle, FOV 24 × 24 cm, 64 × 64 matrix, 62.5 kHz bandwidth, 3.75 × 3.75 mm in plane resolution, 5.00 mm slice thickness, 29 slices, 145 mm total brain coverage). The first 4 volumes (12 s) collected in each run were discarded to avoid T_1 saturation effects.

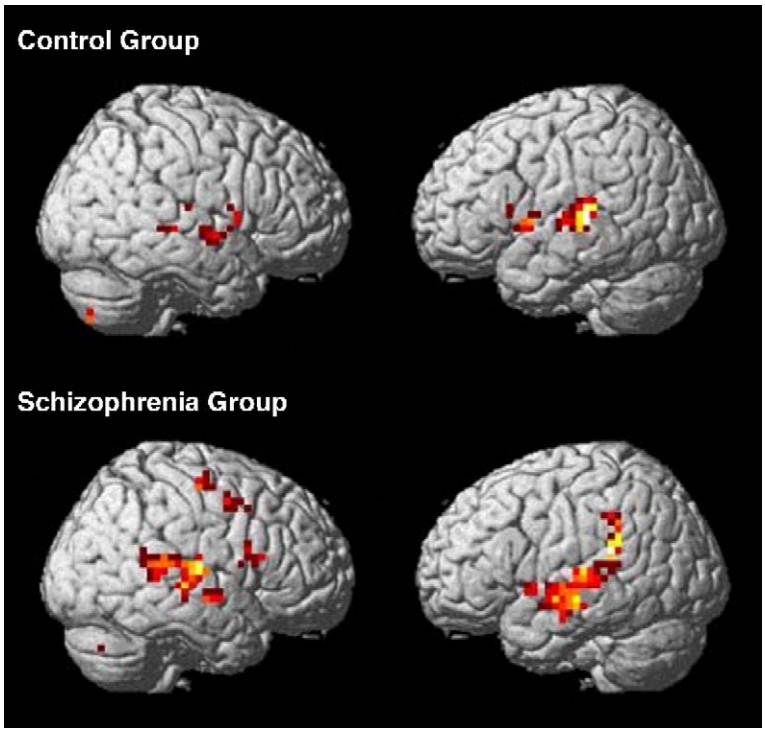

Fig. 1. Regions of activation observed during listening to English for the control group and patient group, corrected $p < 0.05$.

Table 2
Localization of activation during listening to English, $p<0.05$ corrected

Group	Region		MNI coordinates (x, y, z)	No. of voxels	p =
Controls	Left:	Superior temporal gyrus	−64, −28, 12	54	.000
		Inferior frontal gyrus and insula	−36, 12, 4	39	.000
		Cerebellum	−20, −76, −44	4	.005
	Right:	Superior temporal gyrus	52, −8, −4	35	.000
		Middle temporal gyrus	48, −28, 0	10	.000
		Cerebellum	24, −76, −52	5	.010
Patients	Left:	Superior and middle temporal gyri	−48, −24, 8	142	.000
		Hippocampus	−28, −32, 0	13	.000
		Inferior frontal gyrus	−32, 32, 4	3	.003
	Right:	Superior and middle temporal gyri	60, −16, 12	200	.000
		Precentral gyrus, inferior frontal gyrus	32, 8, 44	62	.001
		Mid cingulate gyrus	12, −28, 40	30	.000
		Caudate nucleus	20, 28, 0	17	.003
		Precentral gyrus	36, −12, 60	9	.003
		Cerebellum	32, −68, −36	7	.003
		Inferior temporal gyrus	40, −52, −8	3	.003

2.4. Image processing

Functional images were reconstructed offline. Statistical Parametric Mapping software (SPM2, Wellcome Institute of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm/) was used for image reorientation, realignment, normalization into Talairach stereotaxic anatomical space, and smoothing with a Gaussian kernel (8 mm FWHM) to compensate for inter-subject anatomical differences and optimize the signal to noise ratio. Maximum rotation and translation estimates from realignment, were 4 mm and 4°, respectively. The BOLD response for each block of auditory stimuli was modeled as the convolution of a 30 s box-car with a synthetic hemodynamic response function composed of two gamma functions. Beta weights associated with the modelled hemodynamic responses were computed to fit the observed BOLD-signal time course in each voxel using the General Linear Model as implemented in SPM2. Contrasts against baseline were calculated

Table 3
Localization of activation for English>Mandarin, $p<0.00001$ uncorrected

Group	Region		MNI coordinates (x, y, z)	No. of voxels	p =
Controls	Left:	Postcentral gyrus	−44, −12, 48	62	.001
		Middle temporal gyrus	−60, −56, 0	61	.004
		Superior temporal gyrus	−56, −16, 8	56	.001
		Insula	−28, 16, 4	12	.002
		Supramarginal gyrus	−48, −24, 32	10	.024
	Right:	Insula, superior temporal gyrus	32, −24, 12	219	.000
		Postcentral gyrus	36, −20, 44	126	.000
		Middle temporal gyrus	44, −40, −4	33	.008
		Paracentral lobule	8, −40, 68	19	.002
		Inferior temporal gyrus	52, −56, −12	15	.011
		Inferior frontal gyrus	48, 12, 32	3	.014
Patients	Left:	Middle temporal gyrus	−56, −28, 0	22	.030
		Hippocampus	−32, −32, −8	15	.002
		Thalamus	−20, −8, 8	8	.016
		Superior temporal gyrus	−52, 0, 0	4	.030
	Right:	Insula, middle temporal gyrus	36, −12, 4	80	.000
		Superior temporal gyrus	44, −40, 16	57	.006
		Thalamus	16, −8, 4	16	.003
		Middle frontal gyrus	32, 8, 44	10	.016
		Postcentral gyrus	48, −12, 32	8	.007
		Cerebellum	12, −48, −44	5	.002

separately for all three conditions in each subject. These contrasts were brought forward to a 2nd level analysis (random effects) to determine the regions of activation for each condition in the two groups.

3. Results

All three conditions produced similar patterns of activation relative to baseline in the patient and control groups: posterior superior and middle temporal gyri bilaterally, lateralized to the left. Fig. 1 shows the activation observed during listening to English relative to baseline for patients and controls, random effects $p<.05$ corrected for multiple comparisons; cerebral regions, MNI coordinates and voxel-level p-values are given in Table 2. English was associated with greater activation than Mandarin and reversed English for both groups at $p<0.00001$ uncorrected; cerebral regions, MNI coordinates and voxel-level p-values for the English–Mandarin and English–reversed English contrasts are given in Tables 3 and 4, respectively. Neither of the control conditions was associated with increased activity relative to English at this threshold. No significant differences between groups were observed for the baseline or between conditions contrasts.

A whole-brain regression analysis with TLI score entered as a covariate was conducted to identify regions active during listening to English that correlated with thought disorder in patients. This identified a single significant cluster of 54 voxels, spanning the left posterior superior temporal sulcus and middle temporal gyrus (maximum at $x\ y\ z$: −48 −12 −8, cluster-level corrected $p=0.023$; see Fig. 2). No other regions were found to correlate with TLI score, even when the threshold was lowered to $p<0.05$. The correlation between TLI score and activation (mean beta) in this region while listening to English was $r=.93$. The mean beta value in this region was 2.40 for the patients and 2.02 for the controls, a slight but not significant increase

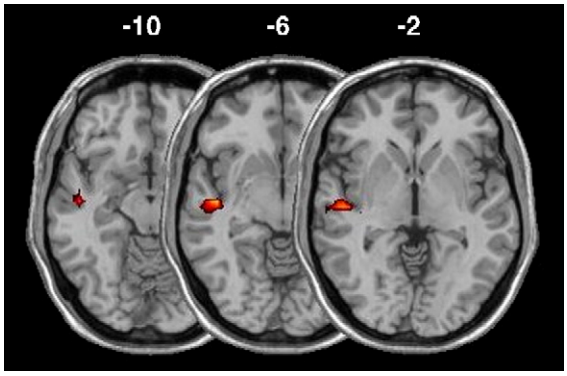

Fig. 2. Region of correlation between TLI score and brain activation in patients with schizophrenia during listening to English, cluster-level corrected $p<0.05$.

Table 4
Localization of activation for English>reversed English, $p<0.00001$ uncorrected

Group	Region		MNI coordinates (x, y, z)	No. of voxels	p =
Controls	Left:	Inferior parietal lobule	−48, −36, 40	28	.001
		Mid cingulate	−16, −28, 44	18	.001
		Postcentral gyrus	−40, −12, 48	11	.012
	Right:	Putamen, globus pallidus	28, −4, −8	65	.007
		Superior frontal gyrus	20, 24, 40	24	.000
		Precentral gyrus	36, 0, 52	23	.002
		Superior temporal gyrus	48, −28, 24	14	.001
		Inferior frontal gyrus	28, 20, 28	8	.026
		Middle temporal gyrus	40, −68, 16	8	.050
Patients	Left:	Superior temporal gyrus	−44, −24, 24	48	.002
		Parahippocampal gyrus	−32, −40, −8	41	.001
		Middle temporal gyrus	−60, −24, 0	27	.003
		Middle frontal gyrus	−20, 24, 48	10	.020
		Superior frontal gyrus	−16, 8, 48	7	.019
		Inferior frontal gyrus	−56, 16, 12	4	.043
	Right:	Parahippocampal gyrus	28, −32, −8	50	.001
		Precentral gyrus, inferior frontal gyrus	44, 8, 36	50	.007
		Superior temporal gyrus	32, −44, 16	40	.007
		Insula	36, −16, 12	31	.004
		Superior medial frontal gyrus	12, 44, 32	19	.010
		Angular gyrus	32, −60, 20	11	.000
		Caudate nucleus	24, 28, 8	6	.001

($p=0.16$). The regression analysis was repeated for the acoustic control conditions, Mandarin and reversed English, but identified no significant correlations. To test for an association between both overall symptom levels and positive symptom levels with activation during any of the three conditions, SSPI total and SSPI positive scores were separately entered as covariates in regression analyses; no correlations were found.

4. Discussion

In this study, while listening to comprehensible English speech, severity of thought disorder in patients with schizophrenia correlated with increased activation in left posterior superior temporal sulcus and middle temporal gyrus. Activation in this region was not associated with thought disorder when listening to either Mandarin or reversed English, or with overall symptomatology. This result contrasts with previous studies of language production, in which thought disorder was associated with decreased activation in this region (McGuire et al., 1998; Kircher et al., 2001b) or increased activation in the homologous right hemisphere region (Kircher et al., 2002) during continuous speech. A study of speech detection, however, found severity of thought disorder correlated positively with activation in the left temporo-parietal junction (Ngan et al., 2003), while a sentence completion paradigm showed reductions in right temporal and increases in left inferior frontal activation in thought disordered patients (Kircher et al., 2001a). This disparity suggests that a reduction in the functional laterality of language may not fully explain this symptom, and that patterns of language-related activation associated with thought disorder are likely task-dependent.

The concept of reduced efficiency in schizophrenia has been introduced in the working memory literature, where in low memory load conditions patients with schizophrenia show greater prefrontal activity than controls and normal performance, whereas at high load conditions patients show a reduction in prefrontal activity with impaired performance (Manoach et al., 1999; Cairo et al., in press). This is explained as a shift in the normal inverted-U relationship between memory load and prefrontal activation: in healthy subjects, activity increases commensurate with load until memory capacity is exceeded, at which time both activity and performance drop (Goldberg et al., 1998b; Callicott et al., 1999). In schizophrenia however, the memory system operates at a higher intensity to maintain normal performance at lower load levels and so reaches the capacity threshold earlier; increased activation observed at lower load levels reflects compensatory processing and is a sign of inefficiency in the system.

It is possible that a similar mechanism could explain the apparent preservation of comprehension in patients with thought disorder. Simple speech comprehension is a fundamental element of language, with lower cognitive demands than most productive language functions. An (in)efficiency model would predict that, for this relatively undemanding function, increased activation could compensate for processing deficits resulting in preserved comprehension, while for higher-demand generative language functions such as speech production capacity threshold would be exceeded resulting in reduced activation and impaired performance. Thus, increased left temporal activation in thought disordered subjects during speech comprehension may reflect the compensatory processing necessary to perform normally with an impaired language system. While this group of patients had a slightly higher mean activation than controls in the region correlating with thought disorder, the difference was not significant. This may reflect the symptomatic heterogeneity of this group. Under the inefficiency model, subjects who are not disordered would not be expected to show greater than normal activation-only those exhibiting the symptom would need to compensate for the underlying functional disturbance.

Our results suggest that thought disorder is associated with abnormal activity when listening to speech; however, these data do not allow direct assessment of between-group differences. The within-groups contrasts of English relative to the control conditions produced roughly similar patterns of activation with both groups showing activation in bilateral temporal cortices. This likely reflects semantic processing, and is consistent with previous findings contrasting speech and non-speech stimuli (Demonet et al., 1992; Binder et al., 1997, 2000). The common focus of activation for all three conditions was the left posterior superior temporal gyrus, a region known to be involved in acoustic and phonological processing (Demonet et al., 1992; Binder et al., 2000; Scott and Johnsrude, 2003). Previous research has found activation in posterior superior temporal gyrus for meaningless speech sounds comparable to that seen in response to comprehensible speech (Wise et al., 1991; Hirano et al., 1997; Binder et al., 2000). While reversed speech stimuli are intended to control for non-phonological acoustic features of speech, there is evidence of partial preservation of phonological information in the acoustic signal. It has been shown, for example, that subjects can phonologically transcribe reversed words with a notable degree of

intra-subject consistency (Binder et al., 2000), and that segment-reversed speech can be comprehensible (Saberi and Perrott, 1999).

If activity observed during the control conditions is primarily due to acoustic or phonological processing, the current correlation between thought disorder and activation when listening to English may reflect abnormal semantic processing. The region of correlation lies almost entirely within the section of left posterior superior temporal lobe implicated in semantic processing, lateral and inferior to the region involved in phonological processing. Both verbal and nonverbal semantic tasks have been found to activate cortex of the left posterior superior temporal sulcus and middle temporal gyrus (Vandenburghe et al., 1996; Binder et al., 1997). Increased semantic priming (Manschreck et al., 1988; Spitzer et al., 1993; Moritz et al., 2002; Quelen et al., 2005) suggests that semantic processing is abnormal in thought disorder, and there is evidence that the organization of the semantic network may be disturbed. Unlike healthy subjects, thought disordered subjects fail to use semantic category dimensions to generate words in a verbal fluency task (Aloia et al., 1996; Paulsen et al., 1996; Goldberg et al., 1998a).

It remains unclear whether temporal lobe functional abnormalities, including semantic processing deficits, are the source of thought disorder or whether they are both secondary to higher level dysfunction. Studies of semantic processing in schizophrenia have observed reduced inferior frontal activity in addition to overactivation of posterior temporal lobe (Kubicki et al., 2003), and there is evidence of a disconnection between frontal and temporal semantic processing regions (Kim et al., 2005). Recent behavioural studies suggest the strongest predictor of thought disorder is executive dysfunction (Kerns and Berenbaum, 2002; Barrera et al., 2005), but possible interactions between higher-level cognition and language have yet to be explored.

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References

Aloia, M.S., Gourovitch, M.L., Weinberger, D.R., Goldberg, T.E., 1996. An investigation of semantic space in patients with schizophrenia. J. Int. Neuropsychol. Soc. 2, 267–273.

Ammons, R.B., Ammons, C.H., 1962. The Quick Test (QT): provisional manual. Psychol. Rep. 11, 111–161.

Barrera, A., McKenna, P.J., Barrios, G.E., 2005. Formal thought disorder in schizophrenia: an executive or a semantic deficit? Psychol. Med. 35, 121–132.

Binder, J.R., Frost, J.A., Hammeke, T.A., Cox, R.W., Rao, S.M., Prieto, T., 1997. Human brain language areas identified by functional magnetic resonance imaging. J. Neurosci. 17, 353–362.

Binder, J.R., Frost, J.A., Hammeke, T.A., Bellgowan, P.S.F., Springer, J.A., Kaufman, J.N., Possing, E.T., 2000. Human temporal lobe activation by speech and nonspeech sounds. Cereb. Cortex 10, 512–528.

Buchsbaum, B.R., Hickok, G., Humphries, C., 2001. Role of left posterior superior temporal gyrus in phonological processing for speech perception and production. Cogn. Sci. 25, 663–678.

Cairo, T.A., Woodward, T.S., Ngan, E.T., in press. Decreased encoding efficiency in schizophrenia. Biol. Psychiatry.

Callicott, J.H., Mattay, V.S., Bertolino, A., Finn, K., Coppola, R., Frank, J.A., Goldberg, T.E., Weinberger, D.R., 1999. Physiological characteristics of capacity constraints in working memory as revealed by functional MRI. Cereb. Cortex 9, 20–26.

Callicott, J.H., Mattay, V.S., Verchinski, B.A., Marenko, S., Egan, M.F., Weinberger, D.R., 2003. Complexity of prefrontal cortical dysfunction in schizophrenia: more than up or down. Am. J. Psychiatry 160, 2209–2215.

Crinion, J.T., Lambon Ralph, M.A., Warburton, E.A., Howard, D., Wise, R.J.S., 2003. Temporal lobe regions engaged during normal speech comprehension. Brain 1193–1201.

Crow, T.J., 1997. Is schizophrenia the price that Homo sapiens pays for language? Schizophr. Res. 28, 127–141.

Demonet, J., Chollet, F., Ramsay, S., Cardebat, D., Nespoulous, J., Wise, R., Rascol, A., Frackowiak, R., 1992. The anatomy of phonological and semantic processing in normal subjects. Brain 115, 1753–1768.

Goldberg, T.E., Aloia, M.S., Gourovitch, M.L., Missar, D., Pickar, D., Weinberger, D.R., 1998a. Cognitive substrates of thought disorder, I: the semantic system. Am. J. Psychiatry 155, 1671–1676.

Goldberg, T.E., Berman, K.F., Fleming, K., Ostrem, J., Van Horn, J.D., Esposito, G., Mattay, V.S., Gold, J.M., Weinberger, D.R., 1998b. Uncoupling cognitive workload and prefrontal cortical physiology: a PET rCBF study. Neuroimage 7, 296–303.

Hirano, S., Naito, Y., Okazawa, H., Kojima, H., Honjo, I., Ishizu, K., Yenokura, Y., Nagahama, Y., Fukuyama, H., Konishi, J., 1997. Cortical activation by monaural speech sound stimulation demonstrated by positron emission tomography. Exp. Brain Res. 113, 75–80.

Hollingshead, A., 1957. Two Factor Index of Social Position. Yale University Press, New Haven, USA.

Kerns, J.G., Berenbaum, H., 2002. Cognitive impairments associated with formal thought disorder in people with schizophrenia. J. Abnorm. Psychology 111, 211–224.

Kim, J.J., Ho Seok, J., Park, H.J., Soo Lee, D., Chul Lee, M., Soo Kwon, J., 2005. Functional disconnection of the semantic networks in schizophrenia. NeuroReport 16, 355–359.

Kircher, T.T., Bulimore, E.T., Brammer, M.J., Williams, S.C., Broome, M.R., Murray, R.M., McGuire, P.K., 2001a. Differential activation of temporal cortex during sentence completion in schizophrenic patients with and without formal thought disorder. Schizophr. Res. 50, 27–40.

Kircher, T.T., Liddle, P.F., Brammer, M.J., Williams, S.C., Murray, R.M., McGuire, P.K., 2001b. Neural correlates of formal thought disorder in schizophrenia: preliminary findings from a functional magnetic resonance imaging study. Arch. Gen. Psychiatry 58, 769–774.

Kircher, T.T., Liddle, P.F., Brammer, M.J., Williams, S.C., Murray, R.M., McGuire, P.K., 2002. Reversed lateralization of temporal activation during speech production in thought disordered patients with schizophrenia. Psychol. Med. 32, 439–449.

Kubicki, M., McCarley, R.W., Nestor, P.G., Huh, T., Kikinis, R., Shenton, M.E., Wible, C.G., 2003. An fMRI study of semantic processing in men with schizophrenia. Neuroimage 20, 1923–1933.

Liddle, P.F., Ngan, E.T., Caissie, S.L., Anderson, C.M., Bates, A.T., Quested, D.J., White, R., Weg, R., 2002a. Thought and Language Index: an instrument for assessing thought and language in schizophrenia. Br. J. Psychiatry 181, 326–330.

Liddle, P.F., Ngan, E.T.N., Duffield, G., Kho, K., Warren, A.J., 2002b. The signs and symptoms of psychotic illness: a rating scale. Br. J. Psychiatry 180, 45–50.

Manoach, D.S., 2003. Prefrontal cortex dysfunction during working memory performance in schizophrenia: reconciling discrepant findings. Schizophr. Res. 60, 285–298.

Manoach, D.S., Press, D.Z., Thangaraj, V., Searl, M.M., Goff, D.C., Halpern, E., Saper, C.B., Warach, S., 1999. Schizophrenic subjects activate dorsolateral prefrontal cortex during a working memory task, as measured by fMRI. Biol. Psychiatry 45, 1128–1137.

Manschreck, T.C., Maher, B.A., Milavetz, J.J., Ames, D., Weisstein, C.C., Schneyer, M.L., 1988. Semantic priming in thought disordered schizophrenic patients. Schizophr. Res. 1, 61–66.

McGuire, P.K., Quested, D.J., Spence, S.A., Murray, R.M., Frith, C.D., Liddle, P.F., 1998. Pathophysiology of 'positive' thought disorder in schizophrenia. Br. J. Psychiatry 173, 231–235.

Moore, C.J., Price, C.J., 1999. Three distinct ventral occipitotemporal regions for reading and object naming. Neuroimage 10, 181–192.

Moritz, S., Woodward, T.S., Küppers, D., Lausen, A., Schickel, M., 2002. Increased automatic spreading of activation in thought disordered schizophrenic patients. Schizophr. Res. 59, 181–186.

Nelson, H.E., 1982. National Adult Reading Test: Test Manual. NFER, Windsor.

Ngan, E.T., Vouloumanos, A., Cairo, T.A., Laurens, K.R., Bates, A.T., Anderson, C.M., Werker, J.F., Liddle, P.F., 2003. Abnormal processing of speech during oddball target detection in schizophrenia. Neuroimage 20, 889–897.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Paulsen, J.S., Romero, R., Chan, A., Davis, A.V., Heaton, R.K., Jeste, D.V., 1996. Impairment of the semantic network in schizophrenia. Psychiatry Res. 63, 109–121.

Quelen, F., Grainger, A., Raymondet, P., 2005. An investigation of semantic priming in schizophrenia using a new priming paradigm. Schizophr. Res.

Robertson, D.A., Gernsbacher, M.A., Guidotti, S.J., Robertson, R.R., Irwin, W., Mock, B.J., Campana, M.E., 2000. Functional neuroanatomy of the cognitive process of mapping during discourse comprehension. Psychol. Sci. 11, 255–260.

Rossi, A., Serio, A., Stratta, P., Petruzzi, C., Schiazza, G., Mancini, F., Casacchia, M., 1994. Planum temporale asymmetry and thought disorder in schizophrenia. Schizophr. Res. 12, 1–7.

Saberi, K., Perrott, D.R., 1999. Cognitive restoration of reversed speech. Nature 398, 760.

Scott, K.S., Johnsrude, I.S., 2003. The neuroanatomical and functional organization of speech perception. Trends Neurosci. 26, 100–107.

Shenton, M.E., Kikinis, R., Jolesz, F.A., Pollak, S.D., LeMay, M., Wible, C.G., Hokama, H., Martin, J., Metcalf, D., Coleman, M., et al., 1992. Abnormalities of the left temporal lobe and thought disorder in schizophrenia. A quantitative magnetic resonance imaging study. N. Engl. J. Med. 327, 604–612.

Sommer, I.E., Ramsey, N.F., Kahn, R.S., 2001. Language lateralization in schizophrenia, an fMRI study. Schizophr. Res. 52, 57–67.

Spitzer, M., Braun, U., Hermle, L., Maier, S., 1993. Associative semantic network dysfunction in thought-disordered schizophrenic patients: direct evidence from indirect semantic priming. Biol. Psychiatry 34, 864–877.

St George, M., Kutas, M., Martinez, A., Sereno, M.I., 1999. Semantic integration in reading: engagement of the right hemisphere during discourse processing. Brain 122, 1317–1325.

Vandenburghe, R., Price, C.J., Wise, R., Josephs, O., Frackiowack, R.S.J., 1996. Functional anatomy of a common semantic system for words and pictures. Nature 383, 254–256.

Weiss, E.M., Hofer, A., Golaszewski, S., Siedentopf, C., Brinkhoff, C., Kremser, C., Felber, S., Fleischhacker, W.W., 2004. Brain activation patterns during a verbal fluency test—a functional MRI study in schizophrenia and healthy volunteers. Schizophr. Res. 70, 287–291.

Wise, R., Chollet, F., Hadar, U., Friston, K., Hoffner, E., Frackowiak, R., 1991. Distribution of cortical neural networks involved in word comprehension and word retrieval. Brain 114, 1803–1817.