Journal of Neurolinguistics 23 (2010) 204–222

Contents lists available at ScienceDirect

Journal of Neurolinguistics

journal homepage: www.elsevier.com/locate/jneuroling

Semantic processing and thought disorder in childhood-onset schizophrenia: Insights from fMRI

L.A. Borofsky [a], K. McNealy [a,c,d], P. Siddarth [b], K.N. Wu [b], M. Dapretto [a,b,d,*], R. Caplan [b]

[a] Ahmanson-Lovelace Brain Mapping Center, University of California, Los Angeles, California, USA
[b] Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, California, USA
[c] Neuroscience Interdepartmental Program, University of California, Los Angeles, California, USA
[d] FPR-UCLA Center for Culture, Brain and Development, University of California, Los Angeles, California, USA

ARTICLE INFO

Article history:
Received 13 January 2009
Received in revised form 27 June 2009
Accepted 14 July 2009

Keywords:
fMRI
Neuroimaging
Schizophrenia
Language
Development
Syntax
Semantics

ABSTRACT

Impairments in language processing and thought disorder are core symptoms of schizophrenia. Here we used fMRI to investigate functional abnormalities in the neural networks subserving sentence-level language processing in childhood-onset schizophrenia (COS). Fourteen children with COS (mean age: 13.34; IQ: 95) and 14 healthy controls (HC; mean age: 12.37; IQ: 104) underwent fMRI while performing a semantic judgment task previously shown to differentially engage semantic and syntactic processes. We report four main results. First, different patterns of functional specialization for semantic and syntactic processing were observed within each group, despite similar level of task performance. Second, after regressing out IQ, significant between-group differences were observed in the neural correlates of semantic and, to a lesser extent, syntactic processing, with HC children showing overall greater activity than COS children. Third, while these group differences were not related to effects of medications, a significant negative correlation was observed in the COS group between neuroleptic dosage and activity in the left inferior frontal gyrus for the semantic condition. Finally, COS children's level of thought disorder was significantly correlated with task-related activity in

* Corresponding author. Ahmanson-Lovelace Brain Mapping Center, University of California, Los Angeles, California, USA.
E-mail address: mirella@loni.ucla.edu (M. Dapretto).

0911-6044/$ – see front matter
doi:10.1016/j.jneuroling.2009.07.004

language-relevant networks. Taken together, these findings suggest that children with COS exhibit aberrant patterns of neural activity during semantic, and to a lesser extent syntactic, processing and that these functional abnormalities in language-relevant networks are significantly related to severity of thought disorder.

1. Introduction

Language processing abnormalities and thought disorder are among the hallmark features of schizophrenia (e.g., DeLisi, 2001). Neuroimaging studies investigating the neural basis of these symptoms in schizophrenic adults have regularly identified both abnormal structural organization in language-related circuitry (DeLisi, Szulc, Bertisch, Majcher, & Brown, 2006; Walder et al., 2007; Weiss, Dewitt, Goff, Ditman, & Heckers, 2005) and aberrant patterns of neural activity in fronto-temporal networks in response to a broad range of tasks with linguistic demands (Kircher, Oh, Brammer, & McGuire, 2005; Kuperberg, Deckersbach, Holt, Goff, & West, 2007; Kuperberg, West, Lakshmanan, & Goff, 2008; Ngan et al., 2003; Ragland et al., 2008; Razafimandimby et al., 2007; Weinstein, Werker, Vouloumanos, Woodward, & Ngan, 2006; Weiss et al., 2006). For example, research has found that schizophrenic adults exhibit abnormal neural activity as compared to normal adults when assessing word meaning, with hypoactivation in some frontal regions and hyperactivation in others (Kubicki et al., 2003). Additionally, while normal adults are known to have left-lateralization of neural activity in fronto-temporal regions during language processing, individuals with schizophrenia have been found to exhibit more bilateral, or even right-lateralized activity during speech processing, verbal fluency, and lexical discrimination tasks (Li et al., 2007; Ngan et al., 2003; Weiss et al., 2005). Interestingly, this abnormal lateralization profile has also been observed in individuals at high genetic risk for schizophrenia, who have not yet manifested symptoms of the disease (Li et al., 2007).

Neuroimaging studies of adults with schizophrenia have also attempted to characterize the relationship between severity of thought disorder and brain activity in language-related networks. For instance, severity of thought disorder has been found to be associated with less activation in left temporal regions and with greater activation in the precentral gyrus, cerebellar vermis and caudate when participants were asked to generate verbal descriptions of pictures (Kircher, Bulimore, et al., 2001). Furthermore, adults with schizophrenia who have thought disorder showed decreased activity in the right inferior frontal gyrus and increased activity in the left fusiform gyrus, inferior frontal gyrus and inferior temporal gyrus while generating sentences (vs. reading sentences), as compared to adults with schizophrenia who did not have thought disorder (Kircher, Bulimore, et al., 2001). Severity of thought disorder has also been found to be positively related to increased activity in the left posterior superior temporal lobe (Weinstein et al., 2006) and posterior middle temporal gyrus (Weinstein, Woodward, & Ngan, 2007) while listening to speech. Taken together, these findings indicate that severity of thought disorder, a key feature of schizophrenia, is integrally related to the abnormal neural activity observed in language-related networks in adults with schizophrenia.

Substantially less is known about the neural underpinnings of language processing and thought disorder in childhood onset schizophrenia (COS). Despite onset by 13 years of age, these children have hallucinations, delusions, and thought disorder (Caplan, Guthrie, Tang, Komo, & Asarnow, 2000; Green et al., 1984; Kolvin, Ounsted, Humphrey, & McNay, 1971; McKenna et al., 1994; Russell, Bott, & Sammons, 1989), as well as a significant decrease in IQ around the onset of the illness (Gochman et al., 2005), just as observed in the adult disorder. However, cytogenetic abnormalities, found in 10% of the childhood onset cases and a higher rate of familial transmission imply that COS is a more severe form than the adult disease (Addington & Rapoport, 2009). Treatment with typical (Kumra et al., 1996; Spencer & Campbell, 1994) and atypical neuroleptics (Sikich et al., 2008) reduces symptom severity, and clozapine, more than high dose olanzepine, mitigates negative symptoms in treatment resistant subjects (Kumra et al., 2008; Shaw et al., 2006). Clinical predictors of outcome include premorbid impairment, baseline severity of the illness, and illness course in treatment resistant COS (Kumra et al., 2008; Shaw et al., 2006; Sporn et al.,