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Cognitive and brain function in schizotypal personality disorder

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Abstract

Schizotypal personality disorder, a diagnosis defined partially in terms of a genetic relatedness to schizophrenia, has begun to receive extensive investigative study. While the exact etiologic relationship between schizotypal personality disorder and schizophrenia remains to be determined, three models have been considered: (1) the two may be distinct disorders, (2) they may be essentially identical disorders but expressed with different degrees of severity, or (3) they may be related disorders with a partially overlapping etiology that might account for the many similarities yet the lack of psychosis or severe deficits in schizotypal individuals. Some of the recent research in the structural and functional neuroanatomy, neurochemistry, cognitive function, and pharmacology of schizotypal personality disorder is reviewed with citation of the most recent findings from our laboratory and others. Both schizotypal and schizophrenic subjects appear to show abnormalities in temporal lobe volume, but schizotypal subjects do not appear to show the volumetric decreases in frontal cortex that schizophrenic patients evidence. Abnormalities in thalamic nuclei parallel these findings-the pulvinar, which projects to temporal association and sensory cortices, is reduced in both disorders, but the mediodorsal nucleus, which projects extensively to the frontal cortex, is reduced in schizophrenic patients but not in schizotypal patients. Functional imaging studies suggest that there may be abnormalities in frontal activation in both disorders, but that schizotypal individuals can recruit alternative regions to accomplish tasks requiring frontal lobe activation that may help compensate. Imaging studies of the subcortex including FDG/PET imaging of metabolic activity during a verbal learning task, SPECT imaging studies which measure binding of IBZM and its displacement following amphetamine administration, and plasma HVA determinations following 2-deoxyglucose administration all suggest the possibility of relatively reduced dopaminergic subcortical activity in schizotypal individuals compared to schizophrenic patients. Cognitive function is also impaired in the areas of working memory, verbal learning, and attention in schizotypal patients, as in schizophrenic patients, and they may be particularly susceptible to cognitive tasks with high context dependence, as in schizophrenia. Preliminary trials of catecholaminergic agents suggest that these agents may be able to improve these impaired cognitive functions. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Schizotypal personality disorder; Schizophrenia; Cognitive function

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1. Introduction

Although schizotypal personality disorder shares an extensive array of similarities with schizophrenia in terms of genetics, phenomenology, neurochemistry, structural anatomy, and functional anatomy, patients with schizotypal personality disorder are spared overt psychotic symptoms and have less severe cognitive disturbances than patients with schizophrenia. Several possibilities may be hypothesized regarding the relationship between schizotypal personality disorder and schizophrenia. One is that schizophrenia and schizotypal personality disorders are truly distinct and only have superficial similarities. This hypothesis is unlikely given the common genetic factors shared between the two disorders, but could still apply to many schizotypal personality disorder subjects drawn from clinical or volunteer populations. While difficult to disprove definitively, this hypothesis would imply that an in-depth examination of genetic susceptibility factors, structural and functional neuroanatomy, and cognitive impairment would yield distinct differences and few similarities in the patterns of abnormalities of subjects with the schizotypal and schizophrenia disorders. A second hypothesis is that the two disorders are identical and differ only in severity, predicting that specific abnormalities in these domains would be identical in character and differ only in the extent of the abnormality. Finally, a third hypothesis posits that the disorders are partially overlapping in etiology and genetics with both similarities, i.e., common risk or susceptibility factors that they share as part of the schizophrenia spectrum and differences, that account for the sparing of schizotypal patients from frank psychosis and cognitive deterioration.

If this third hypothesis proves true, a better understanding of these differences would enable us to approach schizotypal personality disorder as an experiment of nature, and an opportunity to better understand the basis of psychosis and the cognitive impairments of schizophrenia can be afforded. It may also help us to disentangle the contributions of genetic and environmental factors in the development of schizophrenia. Recent findings of neurobiological differences between schizotypal personality disorder and schizophrenia are beginning to suggest specific factors that may be protective against overt psychotic symptoms in the schizophrenia spectrum and that explain the more circumscribed cognitive impairments in schizotypal personality disorder. We will first review the broad similarities between schizotypal personality disorder and schizophrenia and then

examine the differences emerging in the more recent studies. These differences provide important clues to risk for "core" cognitive and social deficits and protective factors against psychosis and severe functional deterioration in the schizophrenia spectrum.

2. Commonalties between schizotypal personality disorder and schizophrenia

2.1. Phenomenology, course, and genetics

Both schizotypal personality disorder patients and schizophrenic patients display psychopathology that is characterized by deficit-like symptoms, psychoticlike cognitive and perceptual symptoms, and cognitive disorganization (Siever et al., 1993b; Bergman et al., 1996, 2000; Raine et al., 1994). An extensive body of research has identified similarities in key cognitive impairments in both disorders, although the impairments in schizophrenia tend to be quantitatively more severe. Another indication of the similarity between schizotypal personality disorder and schizophrenia is reflected in the outcome. Schizotypal patients have a long-term outcome more similar to schizophrenic patients than to patients with another severe personality disorder, borderline personality disorder (McGlashan, 1986). Genetic/family: Family, twin, and adoptive studies have demonstrated a genetic relationship between schizotypal personality disorder and schizophrenia, with an increased incidence of schizotypal personality disorder in relatives of schizotypal probands (Baron et al., 1983; Gunderson et al., 1983; Kendler et al., 1981; Siever et al., 1990b) and an increase in schizophrenia-related disorders (Siever et al., 1990b) and schizophrenia itself in the families of patients with schizotypal personality disorder (Schulz et al., 1986; Battaglia et al., 1995). The likelihood of having a schizophrenic relative is comparable for probands diagnosed with either schizotypal personality disorder or schizophrenia (6.9% vs. 6.5%) (Kendler et al., 1993). These observations suggest that schizotypal personality disorder and schizophrenia may share one or more genotypes. Both the deficit-like symptoms, which are associated with attentional dysfunction and psychotic-like symptoms seem to be independently heritable (Kendler et al., 1991).

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