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Deficient visual sensitivity in schizotypal personality disorder☆

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ABSTRACT

Schizotypal personality disorder is a personality disorder in the schizophrenia spectrum, sharing genetic and neurobiologic characteristics with schizophrenia. Visual contrast detection, found to be abnormal in chronic schizophrenia, was investigated in schizotypal personality disorder (SPD). Since dopamine in the retina enhances visual contrast detection and SPD patients have relatively reduced dopaminergic activity in the brain compared to schizophrenia patients, it was hypothesized that SPD patients would have decreased to normal contrast sensitivity. Twenty-one subjects with DSM-IV diagnosed SPD, 18 healthy controls, and 12 subjects with a personality disorder unrelated to schizophrenia (OPD) were evaluated for contrast detection using a sinusoidal grating presented at varying temporal frequencies. Subjects also were evaluated neuropsychologically using several standardized neurocognitive tests. A significant effect of subject group was found on the contrast detection threshold ($p<0.01$) with a significant difference between the SPD group and the healthy control group but not between the OPD group and the healthy control group. The SPD group had higher contrast detection thresholds at all temporal frequencies tested. Correlations were found between contrast detection and performance on the Trail-Making, N-Back, and CPT tasks in SPD patients. These results, based upon a paradigm reflecting dopamine activity in the early visual system, highlight the differences as well as similarities between SPD and schizophrenia with regard to the dopamine system in schizophrenia spectrum (Siever and Davis, 2004).

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1. Introduction

Schizotypal personality disorder (SPD) represents a diagnostic phenotype in the schizophrenia spectrum between schizophrenia and healthy controls (HC), with genetic, biological and behavioral characteristics shared with chronic schizophrenia (Siever and Davis, 2004). The symptoms of SPD, while less severe, mirror those of schizophrenia, including psychotic-like symptoms, social deficits, and cognitive impairment. Since SPD patients share these underlying spectrum characteristics with typical schizophrenia, insights into the pathophysiology of SPD may improve our understanding not only of this disorder, but of schizophrenia itself (Siever and Davis, 2004). Another particularly important question is what biological characteristics protect the SPD patients from the emergence of severe psychosis. This phenotypic difference has been hypothesized to be related to a better regulated (less responsive) striatal dopaminergic system in SPD compared to schizophrenia (Kirrane and Siever, 2000; Siever and Davis, 2004).

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Hyperdopaminergic activity in the striatum is thought to be related to positive symptoms and hypodopaminergic activity in the prefrontal cortex to be related to negative ones (Davis et al., 1991; Siever, 1994). Dopamine activity can be measured both in imaging and pharmacological intervention studies. Imaging studies have shown that patients with schizotypal personality disorder have higher striatal dopamine release in response to amphetamine than healthy patients, but lower than schizophrenia patients (Abi-Dargham et al., 2004). In one study (Mitropoulou et al., 2004) SPDs evidenced a blunted cortisol and normal dopaminergic responses to 2-deoxyglucose (DG), in contrast to increased cortisol and dopamine responses to 2DG in schizophrenia patients.

Visual contrast detection reflects dopaminergic functioning in the early visual system (Harris et al., 1990; Masson et al., 1993). Dopamine enhances visual contrast detection by inhibiting the surrounding areas of the retinal neural unit's receptive field via the D_2 receptors (Djamgoz et al., 1997). Studies in Parkinson's Disease patients (Bodis-Wollner, 1990), patients with phenylketonuria (PKU) (Diamond and Herzberg, 1996), and animals and humans with dopaminergic intervention (Corbe et al., 1992; Boumghar et al., 1997) suggest these retinal dopamine activity may in some cases parallel dopamine activity in the brain. Although the cellular mechanisms of striatal dopamine release are incompletely understood, SPD patients demonstrate less subcortical hyperdopaminergia than patients with schizophrenia, consistent with the hypothesis that SPD patients have less subcortical dopaminergic hyper-responsiveness compared to patients with schizophrenia (Abi-Dargham et al., 2004; Siever and Davis, 2004). Furthermore, SPD patients are hypothesized to have reduced dopamine activity in the prefrontal cortex (Siever and Davis, 2004) and their abnormal working memory and cognitive performance (Mitropoulou et al, 2005) are inversely correlated with dopamine and memory (Siever et al., 1993) and can be partially normalized by dopaminergic agents (Siegel et al., 1996; Kirrane et al., 2000; McClure et al., 2009). If retinal D2 receptor activity mirrors that of the brain, reduced to normal visual contrast sensitivity might be expected in SPD, in contrast to the increased contrast sensitivity in schizophrenia (Kéri et al., 1998; Chen et al., 2003).

Disparate results have been reported for visual contrast detection in schizophrenia patients: Some studies show decreased contrast sensitivity (Slaghuis, 1998; Butler et al., 2001, Kéri et al., 2002; Chen et al., 2004), others describe excessive sensitivity (Kéri et al., 1998; Chen et al., 2003), and another reports no difference (Chen et al., 1999). One factor that may account for these disparate findings is the different antipsychotic drugs administered to these patients. One study hypothesized that the differences were due to the relative potency and the respective binding strength of the different classes of antipsychotic drugs (Chen et al., 2003). The typical antipsychotics, potent dopamine antagonists, were associated with the lowest visual contrast sensitivity. Atypical antipsychotics, on the other hand, are less potent dopamine antagonists and thus do not lower contrast sensitivity as dramatically. Thus, patients with schizophrenia on typical antipsychotic agents had lower contrast sensitivity than HC, while those on atypical agents had the same sensitivity as HC, and those who were not medicated had higher sensitivity (Chen et al., 2003). Indeed in the two studies that have tested unmedicated patients thus far, superior visual contrast detection was demonstrated in schizophrenia, even compared to HC.

Recent studies reported that SPD patients' performance was normal in visual contrast detection (O'Donnell et al., 2006) and abnormal in other visual tasks such as those requiring temporal integration or working memory (Cadenhead et al., 1999; Farmer et al., 2000; Mitropoulou et al., 2005). This pattern of results, while interesting, poses a question as to whether visual processing in SPD is still normal when basic temporal integration is involved. Temporal integration and storage is a fundamental aspect of visual functioning (Supèr et al., 2001) and the temporal dynamics of contrast detection is modulated by dopamine (Masson et al., 1993). In this study, we evaluated contrast detection of SPD patients under the conditions for which visual information is temporally integrated.

Moreover, in order to demonstrate whether the visual contrast detection in question is specifically related to a schizophrenia spectrum disorder or mainly due to personality disorders unrelated to schizophrenia, it is important to examine SPD patients in comparison to patients who have other personality disorders (OPDs), and thus are not hypothesized to have a dopamine abnormality affecting contrast detection. This study proposed to determine whether SPD patients differ from patients with other personality disorders and HCs in their ability to detect visual contrast.

2. Experimental/materials and methods

2.1. Subjects

Twenty-one subjects with DSM-IV diagnosed schizotypal personality disorder, eighteen healthy controls, and twelve subjects with a personality disorder unrelated to schizophrenia (with less than 2 schizotypal traits) were recruited for this study by advertisements and word of mouth. All participants were between the ages of 18 and 65 and were studied as outpatients. The subject groups had no significant differences in age, gender, or years of education (Table 1).

After informed consent was obtained, participants completed a medical evaluation and any participants with a history of systemic medical illnesses, serious eye disorders, a history of serious head trauma, or positive toxicology screens were excluded. The patients were evaluated for medical illnesses by a standard battery of blood tests, including an SMA-18. A medical history was also taken, where patients were asked about current or past eye problems. Patients were also excluded if they met criteria for a psychotic disorder or bipolar I, met lifetime criteria for substance dependence, had substance abuse in the last 6 months, or were currently taking psychiatric medication.

Diagnostic evaluations were conducted by doctoral-level clinical psychologists using the Structured Clinical Interview for DSM-IV for Axis I disorders and the Structured Interview for DSM-IV Personality for Axis II disorders (First et al., 1997). Diagnoses were given in a consensus meeting with an expert diagnostician in which the clinical interviewer presented all available information on each participant. Healthy control participants had no history of Axis I or Axis II disorders, and no first degree relatives with Axis I disorders. Those participants who had personality disorders unrelated to schizophrenia primarily consisted of patients with avoidant personality disorder, and all had less than 2 schizotypal traits. Patients with Schizotypal Personality Disorder met DSM-IV criteria according to the SIDP, all possessing at least 5 schizotypal traits.