



Avoidant personality disorder symptoms in first-degree relatives of schizophrenia patients predict performance on neurocognitive measures: The UCLA family study

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ABSTRACT

Whether avoidant personality disorder symptoms are related to neurocognitive impairments that aggregate in relatives of schizophrenics is unknown. We report the relationship between avoidant personality disorder symptoms and neurocognitive performance in the first-degree relatives of probands with schizophrenia.

367 first-degree relatives of probands with schizophrenia and 245 relatives of community controls were interviewed for the presence of avoidant personality symptoms and symptoms of paranoid and schizotypal personality disorders and administered neurocognitive measures. Relationships between neurocognitive measures and avoidant symptoms were analyzed using linear mixed models.

Avoidant dimensional scores predicted performance on the span of apprehension (SPAN), 3–7 Continuous Performance Test (3–7 CPT), and Trail Making Test (TMT-B) in schizophrenia relatives. These relationships remained significant on the SPAN even after adjustment for paranoid or schizotypal dimensional scores and on the TMT-B after adjustment for paranoid dimensional scores. Moreover, in a second set of analyses comparing schizophrenia relatives to controls there were significant or trending differences in the degree of the relationship between avoidant symptoms and each of these neurocognitive measures even after adjustments for paranoid and schizotypal dimensional scores. The substantial correlation between avoidant and schizotypal symptoms suggests that these personality disorders are not independent.

Avoidant and in some cases schizotypal dimensional scores are significant predictors of variability in these neurocognitive measures. In all analyses, higher levels of avoidant symptoms were associated with worse performance on the neurocognitive measures in relatives of schizophrenia probands. These results support the hypothesis that avoidant personality disorder may be a schizophrenia spectrum phenotype.

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1. Introduction

Cognitive deficits aggregate in first-degree relatives of schizophrenia probands unaffected by schizophrenia and therefore reflect liability to schizophrenia (Snitz et al., 2006; Touloupoulou et al., 2007). Some of these cognitive deficits may be related to schizophrenia spectrum personality disorders. There is some direct evidence that spectrum personality disorders aggregate in relatives of schizophrenics suggesting that they also index a liability to schizophrenia (Kendler et al., 1995). In a previous study we found that first-degree relatives of probands with childhood-onset or adult-onset schizophrenia are at increased risk for avoidant personality disorder even when controlling for the presence of paranoid and schizotypal personality disorders (Fogelson et al., 2007). We concluded that avoidant personality disorder is a schizophrenia spectrum personality disorder and that symptoms of avoidant personality may represent a core expression of vulnerability to schizophrenia. In this study we extend our prior findings by determining whether avoidant personality symptoms in first-degree relatives are associated with performance on cognitive tests that index a liability to schizophrenia (namely, the Degraded Stimulus Continuous Performance Test (DS-CPT) (Nuechterlein, 1991; Nuechterlein et al., 1983), the 3–7 Continuous Performance Test (3–7 CPT) (Nuechterlein et al., 1986), the Trail Making Test B (TMT-B) (Reitan, 1958), the Span of Apprehension Test (SPAN) (Asarnow et al., 1991), and the Wechsler adult intelligence Vocabulary Subscale (WAIS Vocab) (Wechsler, 1955).

Many studies have demonstrated that poor performance on the CPT, TMT-B, SPAN, and WAIS Vocab aggregate in first-degree relatives of probands with schizophrenia, reflecting a liability to schizophrenia. A meta-analysis of 43 cognitive test scores in the unaffected adult relatives of probands with schizophrenia examined the magnitude of the effect size for the CPT-X (d') (Cohen's $d = .43$), TMT-B ($d = .41$), SPAN ($d = .23$), and WAIS Vocab ($d = .21$). (Snitz et al., 2006) All effect sizes were positive, indicating poorer performance for relatives of schizophrenics than controls, where a " d " of .20 to .40 was considered small and a $d > .40$ was considered medium. When studies controlled for age, the effect size increased for the CPT-X (d') ($d = .56$), TMT-B ($d = .50$), and WAIS Vocab ($d = .44$) and decreased for the SPAN ($d = .17$). Samples not matched on education were not excluded from the meta-analysis because controlling for education may over-control for liability to schizophrenia.

Far fewer studies have examined neurocognitive/neurophysiologic measures in relatives or individuals affected by schizotypal personality disorder or other schizophrenia spectrum personality disorders. Relatives with DSM-III-R schizophrenia spectrum personality symptoms have antisaccade eye movement abnormalities, higher error rates and longer antisaccade latency than unaffected relatives (American Psychiatric Association, 1987; Thaker et al., 1999). Patients with schizotypal personality disorder have poorer eye tracking and mean tracking accuracy (Siever et al., 1990). A measure of disorganization schizotypy derived from the Structured Interview for Schizotypy-Revised was correlated with the CPT37 false alarm variable in 63 relatives of schizophrenia patients (Kendler et al., 1989) (Vollema and Postma, 2002). Some studies have examined neurophysiologic measures and avoidant symptoms

in patients with schizotypy. Poorer quality eye tracking is associated with the deficit-like symptoms of social isolation, inadequate rapport, social anxiety, and odd speech in patients with schizotypal symptoms and schizotypal personality disorder (Siever et al., 1994). In this study there was no differentiation made between the contribution of avoidant and schizotypal symptoms. Eye tracking accuracy is correlated with the presence of social isolation and limited desire for social contact (Bergman et al., 1996). We could find no studies that have examined neurocognitive or neurophysiologic correlates of avoidant personality disorder. Herein we determine the relationship between avoidant personality disorder symptoms in the first-degree relatives of probands with schizophrenia and their performance on the DS-CPT, 3–7 CPT, TMT-B, SPAN, and the WAIS Vocab. If symptoms of avoidant personality disorder are correlated with neurocognitive deficits shown in prior studies to be associated with liability to schizophrenia this would provide additional support for the hypothesis that avoidant personality disorder is a schizophrenia spectrum personality disorder and that symptoms of avoidant personality may represent a core expression of vulnerability to schizophrenia (Fogelson et al., 2007).

2. Methods

2.1. Diagnosis of first-degree relatives

Three-hundred sixty-seven first-degree relatives, age 18 and older, of probands with adult-onset schizophrenia (AOSz, $n = 275$ relatives of 11 probands) and with childhood-onset schizophrenia (COSz, $n = 92$ relatives of 51 probands) and 245 relatives of adult and child community control (CC) probands ($n = 48$ adult probands; $n = 71$ child probands) were blindly and directly interviewed for the presence of selected DSM-III-R axis I and II disorders. All adult participants in this study provided written informed consent. Minor participants provided assent and their parents provided written consent for the minors study participation. Demographics of these participants are presented in Table 1.

Best estimate diagnoses, derived from an integration of direct interview, family history, and medical records, were used for the analyses (4, 18). Nine family interviewers were doctorate or master's degree-level clinicians, while one had a bachelor's degree and four years of experience in clinical interviewing. Training procedures and reliability of the interviewers has been described in prior publications of the UCLA Family Study (Asarnow et al., 2001; Fogelson et al., 1991). The best estimate diagnoses were reviewed and confirmed by the study investigators at a weekly research meeting.

2.2. Direct interview

Axis I diagnoses were assessed with the Diagnostic Interview Schedule (DIS) (Robins et al., 1981) augmented with the Present State Exam (PSE) psychosis section (Wing et al., 1974) and a timeline of psychotic and affective symptoms. We have modified the DIS with supplemental items from the Expanded PSE to allow for in-depth probing of possible psychotic symptoms after the standard DIS is completed. The time line of affective and psychotic episodes allows temporal judgments that are critical for diagnostic decisions. These modifications

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