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Is perseveration uniquely characteristic of schizophrenia?

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ABSTRACT

Evidence for the existence of categorically distinct disorders such as schizophrenia, bipolar disorder, and major depression is mixed: neuropsychological impairments may be similar in schizophrenia and bipolar disorder; schizophrenia and major depression show similar neuropsychological and frontal lobe disturbances; and overlap in biochemical anomalies among the disorders has also been reported. Interestingly, there are very few studies that directly compare all diagnoses. The present study compares cognitive perseveration in these three diagnostic groups using the Wisconsin Card Sorting Task (WCST) to examine performance across patients with schizophrenia ($n=143$), bipolar disorder ($n=25$) and major depression ($n=21$). Individuals used in this sample were 18–45 years old at time of testing to eliminate confounds of aging. Sex ratios within each diagnostic group are comparable to those of the national population. Univariate analyses examining diagnostic group and percent perseverative error revealed no significant differences in WCST performance across the diagnostic groups. Examination of clinical variables in the sample of individuals with schizophrenia revealed that perseveration is related to negative symptoms and depressive symptoms in young adults.

1. Introduction

Individuals with schizophrenia experience a host of different symptoms that can impact daily functioning. Cognitive impairments are particularly important because such deficits are trait-like, core features of the disorder and may show more robust relationships with functional outcome than negative or positive symptoms alone (Tuulio-Henriksson, 2004; Elvevag and Goldberg, 2000; Addington and Addington, 1999). Cognitive impairments are often pervasive and present before the onset of any other symptoms (Tuulio-Henriksson, 2004), and are associated with social problem solving, skill acquisition, and community outcome (Koren et al., 2006; Tuulio-Henriksson, 2004).

Cognitive flexibility describes the ability to organize and restructure knowledge based on an evaluation of situational demands. Perseveration, a measure of cognitive flexibility impairment and an element of executive function, characterizes behaviors that are unintentionally repeated in the presence of feedback indicating the response is incorrect or inappropriate, despite situations in which novel responses are required. Perseveration is a consistently replicated deficit in schizophrenia and therefore warrants continued examination in an attempt to understand the characteristics of this deficit in schizophrenia and other psychiatric disorders.

The Wisconsin Card Sorting Task (WCST; Heaton et al., 1993) has been widely used to assess executive function in a variety of psychiatric (especially schizophrenia) and neurologic samples via measures of set-shifting ability, conceptual reasoning, response inhibition, and goal-directed searching and planning. In particular, WCST Percent Perseverative Error (PPE) is consistently greater in schizophrenia patients than in individuals with schizoaffective disorder (Szoke et al., 2008), individuals with psychosis (Reed et al., 2002), and healthy controls (see

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Appendix A) (Morice, 1990; Perry and Braff, 1998; Rossi et al., 2000; Saoud et al., 2000; Keri et al., 2001; Liu et al., 2003; Szoke et al., 2008). Moreover, Liu et al. (2003) and Saoud et al. (2000) provided evidence for perseveration as a biomarker of schizophrenia: unaffected siblings of those with the disorder committed significantly more perseveration errors on the WCST than healthy controls, (unaffected siblings of individuals with schizophrenia = 22.8, healthy controls = 14.8; unaffected siblings of individuals with schizophrenia = 42.24, healthy controls = 28.16, respectively). It is not clear, however, how unique perseveration is among psychiatric disorders.

Evidence for the existence of categorically distinct disorders such as schizophrenia, bipolar disorder, and major depression is mixed: neuropsychological (Schretlen et al., 2007; Dickerson et al., 2004), and cognitive and social (Dickerson et al., 2001) impairments may be similar in schizophrenia and bipolar disorder; schizophrenia and major depression show similar neuropsychological and frontal lobe disturbances (Franke et al., 1993); overlap in biochemical anomalies among the disorders has been reported (Cotter et al., 2005; Torrey et al., 2005); and insight appears to exist on a continuum across the three disorders (Yen et al., 2008). Interestingly, there are very few studies that directly compare all diagnoses, particularly with regard to measures of neuropsychological functioning. At best, the literature supports a continuum of schizophrenia, schizoaffective, and affective disorders (Szoke et al., 2008), but few studies directly compare schizophrenia, bipolar disorder, and major depression on measures of executive function (Brown et al., 2008; Rempfer et al., 2006; Mojtabai et al., 2000). A form of perseveration, rumination, does occur in affective disorders, specifically major depression and is described as focusing *perseveratively* about one's own thoughts and problems (Nolen-Hoeksema et al., 2008). In fact, rumination was identified as the "form most strongly and consistently related to depressive symptoms" (Nolen-Hoeksema et al., 2008, p. 400).

Originally developed to "assess abstract reasoning ability and the ability to shift cognitive strategies in response to changing environmental contingencies," (Heaton et al., 1993, p. 1) the WCST is a valuable tool to assess cognitive inflexibility, specifically perseveration, as it is an impairment directly related to poor community outcome and poor social and occupational functioning in individuals with schizophrenia (Addington and Addington, 1999; Green, 1996; Lysaker et al., 2005). Examining perseveration across these three diagnostic groups will provide additional evidence that addresses whether perseveration is a characteristic unique to schizophrenia or is common to other psychiatric disorders as well.

It was hypothesized that WCST PPE, at clinically impaired levels, would be significantly greater and occur more often in schizophrenia than in individuals with bipolar disorder and major depression. In addition, we expected strong associations between perseveration and core clinical symptoms of schizophrenia.

2. Methods

2.1. Participants

The data for the present study were taken from a larger database consisting of 664 patients recruited or referred to participate in an investigation of sex differences in neuropsychological functioning (see Lewine et al., 1996 for full recruitment procedure; Thurston-Snoha and Lewine, 2007). The present study examined perseveration in individuals with schizophrenia ($N = 143$), bipolar disorder, ($N = 25$) and major depression ($N = 21$). Only individuals with complete neuropsychological data and clinical data (for the schizophrenia group only) were retained for this study. Furthermore, individuals >45 years of age were excluded to control for aging effects. Finally, only individuals with complete WCST and clinical data (for schizophrenia patients only) were retained, yielding a final full sample size of 189 patients.

2.2. Procedure

Participation included a 13-hour neuropsychological battery completed over the course of several sessions, an MRI, and a battery of clinical measures (for schizophrenia patients only). For the schizophrenia patients only, the range of sample sizes for the clinical measures was 82–143. Missing data occurred largely due to fatigue and missed appointments.

2.3. Measures

2.3.1. Clinical assessment

The Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L; Spitzer and Endicott, 1975) was administered to determine psychiatric diagnoses. SADS-L scores and a weekly consensus diagnostic meeting were used to determine final diagnoses.

Patients in the schizophrenia study completed a large battery of clinical assessments including the Andreasen's Scale for Assessment for Negative Symptoms (SANS; Andreasen, 1983), Andreasen's Scale for Assessment for Positive Symptoms (SAPS; Andreasen, 1984), Hamilton Depression Rating Scale (HDRS; Hamilton, 1960), Beck Depression Inventory (BDI; Beck et al., 1961), and Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962).

2.3.2. Neuropsychological assessment

For a complete list of neuropsychological assessments administered in the larger study, see Lewine et al., 1996. The focus of the current study is performance on the WCST, the measure chosen to evaluate perseveration. The data were collected using the card version of the assessment. Because our interest is in perseveration, we chose to focus on PPE because of its direct measure of the phenomenon, its frequent use in the field as a measure of perseveration, and its frequent use and replication in schizophrenia research.

2.4. Analyses

The first set of analyses examined perseveration across the three diagnostic groups. A one-way ANOVA was conducted for PPE for the three groups (independent variable) to examine a cross-diagnosis comparison of perseveration. Participants within each diagnostic group were then classified as either *clinically impaired* or *not impaired* using the clinical metric identified by Heaton et al. (1993, p. 31). Individuals with PPE Standard Scores ranging from ≤54 to 84 were classified as *impaired* while those with Standard Scores ranging from 85 to ≥107 were classified as *not impaired*. The