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Using poverty of speech as a case study to explore the overlap between negative symptoms and cognitive dysfunction

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ABSTRACT

Background: Negative symptoms and cognitive impairment are both regarded as important prognostic markers in schizophrenia. Although these two domains are viewed as distinct and separable, conceptual overlap exists. We sought to illustrate this overlap using speech deficits among patients with schizophrenia.
Method: Reductions in verbal output were rated by a clinician following an interview, and these ratings were taken to represent negative symptoms (i.e., alogia). Patients were also asked to recount words from specific categories in a standardized manner, and the number of words was recorded as per standard protocol for verbal fluency tests. These scores were taken to represent cognitive impairment. The cross-sectional and longitudinal relationships between these two variables were then examined.
Results: Patients with more severe alogia produced significantly less words on the verbal fluency tests. This relationship was stronger than that observed with other negative symptoms, and also held after controlling for a number of sociodemographic and clinical variables (e.g., severity of illness). Prospective increases in the number of words produced during the verbal fluency test were associated with improvements in clinical alogia ratings, a longitudinal relationship that was not observed with other negative symptoms.
Conclusions: Some negative symptoms are conceptually related and therefore not fully distinct from cognitive impairments. Here, we demonstrate that clinical ratings of alogia and words produced during a cognitive test are tapping into a similar construct. Whether a specific deficit is classified as a negative versus cognitive symptom may be matter of semantics rather than reflective of divisible underlying processes.

1. Introduction

There is considerable conceptual overlap between the negative symptoms of schizophrenia and impairments in cognitive functioning. Negative symptoms have historically been defined as symptoms involving a loss or reduction of normal functioning, as opposed to positive symptoms which involve excess functioning (Berrios, 1985). Impairments in cognitive functioning, reflecting deficits in information processing (e.g., attention, memory), are as well documented in patients with schizophrenia (Heinrichs and Zakzanis, 1998). Deficits in neurocognition are ascribed to deficits in corresponding neural processes subserving these mental operations, and can therefore also be classified as a reduction in normal functioning. Based on these definitions, impairments in neural processing can be termed both as a negative symptom and as a cognitive deficit. Though these two domains are routinely found to be moderately related to one another, they are typically thought of as distinct and separable. This distinction is based on several sources of evidence including findings that indicators of negative symptoms and cognitive deficits differ in their clinical correlates, longitudinal course, and association with functional outcome (Harvey et al., 2006). We argue that at least some of the symptoms currently termed negative and others that fall under the umbrella of cognitive dysfunction are at least partially redundant, with differences emerging from the use of different sources of information as indicators.

The severity of negative symptoms is typically evaluated using clinical rating scales that include information (i.e., observations) from the interview itself, as well as information related to patient responses to interview questions. For example, ratings for anhedonia are based on patients' recall of a variety of past events and the pleasure derived from such encounters, as well as their ability and willingness to recall and recount this information. Cognitive impairments on the other hand are routinely measured using specific standardized performance-based tests. For example, verbal memory deficits can be assessed by evaluating patients' recall and recounting of a list of words that is delivered to them in a standardized manner. From these examples, it becomes apparent that both verbal memory tests and clinical ratings of anhedonia may be tapping into a similar construct, that is patients' ability and willingness to recall and recount information. The distinction between

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negative symptom and cognitive deficit in this case appears not as a conceptual distinction, but rather in the specific information being recalled, and in the manner in which this is being done.

In the present paper we use speech deficits to illustrate the conceptual overlap between negative symptoms and cognitive impairment. We specifically focus on poverty of speech (i.e., alogia). This symptom has a rich history of being classified as a negative symptom and is included as such in several negative symptom assessment tools (Foussias and Remington, 2010). Ratings of alogia are typically based on clinical observation during an interview and severity ratings reflect a clinician's impression of whether a patient demonstrates any reduction in spontaneous speech (e.g., replies) and, if so, the persistence of this speech pattern is taken into account; therefore, ratings of alogia are based on total speech output. There is also a parallel literature classifying a reduction in patients' speech, albeit in response to more standardized prompts, as reflecting deficits in language or cognition. Verbal fluency tests typically involve having patients recount the maximal number of words related to some criterion (e.g., animals) within a fixed duration; here too, total speech output is being measured. It is interesting to note that previous work has employed neuropsychological tests such as verbal fluency as potential correlates of clinical alogia, and reported significant overlap between the two measures (Stolar et al., 1994; Joyce et al., 1996; Bowie et al., 2004; Berenbaum et al., 2008).

Consistent with previous work, we hypothesized that clinical ratings of poverty of speech (i.e., alogia) would be significantly related to worse verbal fluency scores. This would be consistent with the notion that this association reflects, at least partially, a common source of variance, namely reduced speech output. We extend previous work by examining this relationship in a relatively large sample of patients experiencing a wide range of illness severity, and by statistically controlling for potentially confounding variables. For example, we hypothesized that the relationship between alogia ratings and verbal fluency scores would hold even after parsing variance related to other symptoms such as positive symptoms, overall illness severity or performance on other cognitive tests. We further hypothesized that changes in verbal fluency performance would be related to changes in clinical ratings of poverty of speech, but would not necessarily be related to changes in other negative symptoms. These findings would further support the specificity of the observed relationship between poverty of speech and verbal fluency, which does not simply reflect a general relationship between negative symptom severity and cognition in general.

2. Method

2.1. Study design

For the present study we were interested in examining a relatively large number of patients experiencing a wide range of clinical deficits including a range a speech deficits, which would allow us to confirm relationships among variables of interest while controlling for a number of potentially confounding variables. To establish inter-relationships between variables we sought to examine both cross-sectional associations, as well as longitudinal inter-relationships, the latter possibly representing a more robust form of evidence for a link between two variables. To this end, we utilized data collected as part of the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) schizophrenia study which included a large and heterogeneous patient sample representative of real-world patients with schizophrenia, and entailed prospective follow-up visits that included measurements of negative symptoms and cognition (Stroup et al., 2003). The CATIE project was designed to examine the effectiveness of atypical and typical antipsychotic medication for the treatment of persons with schizophrenia. The details of the study design and primary results are reported elsewhere (Stroup et al., 2003; Lieberman et al., 2005).

Participants were eligible to participate in the CATIE study if they were between the ages of 18 and 65 years and had a diagnosis of schizophrenia confirmed using the Structured Clinical Interview for DSM-IV Axis I Disorders (First, 1997). Participants were excluded from the study if they had a diagnosis of schizoaffective disorder, mental retardation, or other cognitive disorders; had a documented history of treatment refractory illness; or, had a serious and unstable medical condition. Eligible participants were initially randomized to one of five study medications under double-blind conditions and were followed up to 18 months or until treatment was discontinued for any reason (Stroup et al., 2003). Patients who discontinued their initially assigned treatment were eligible to receive other treatments and continue in the trial (Stroup et al., 2003).

The study was approved by the institutional ethics review board at each site, and written informed consent was obtained from the patients or their legal guardians.

2.2. Instruments and procedure

Poverty of speech (i.e., alogia) was evaluated using the Lack of Spontaneity and Flow of Conversation item from the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). This item is rated based on verbal output observed during a clinical interview, with higher scores denoting greater reductions in verbal output.

Verbal fluency was measured using the mean score from the Controlled Oral Word Association Test (letters: F, A, and S) and the Category Instances scale (categories: animals, fruits, and vegetables) (Benton and Hamscher, 1978; Keefe et al., 2006). For these tests, participants were asked to generate as many words as possible in the specified category (e.g., starting with a specific letter) within separate trials of 60 s each. The primary variable of interest was an average of the standardized scores from the 6 individual trials, with higher scores on this measure denoting more words produced during the tests.

To evaluate other cognitive domains we included two tests that do not require verbal responses on the part of the participant. Specifically, we used the total score from the Digit Symbol Test from the Revised Wechsler Adult Intelligence Scale and the mean score from the Mazes subtest of the Revised Wechsler Intelligence Scale for Children (Keefe et al., 2006). These scores were standardized before analysis.

Other measures of interest included the Clinical Global Impressions of illness Severity scale (CGI-S) to assess overall illness severity (Guy, 1976), the PANSS positive subscale to evaluate severity of positive psychotic symptoms (Kay et al., 1987), Calgary Depression Scale for Schizophrenia (CDSS) to assess depressive symptoms (Addington et al., 1992), Simpson-Angus Scale (SAS) to assess extrapyramidal symptoms (Simpson and Angus, 1970; Tracy et al., 1997), and the Heinrichs-Carpenter Quality of Life Scale (QLS), excluding the intrapsychic foundations subscale, to assess real-world community functioning (Heinrichs et al., 1984; Harvey et al., 2011). In addition, given our previous findings of an association between motivational deficits and cognitive test performance (Fervaha et al., 2014b), we also included this variable in the present study; motivational deficits were evaluated using the sense of purpose, goal-directed motivation, and curiosity items from the intrapsychic foundations subscale of the QLS (Heinrichs et al., 1984; Nakagami et al., 2008).

Participants were evaluated using the aforementioned measures at baseline, and again after 6-months of treatment, thus allowing for the examination of longitudinal inter-relationships.

2.3. Statistical analyses

Bivariate relationships between variables were quantified using Pearson product-moment correlation coefficients. Partial correlations were also computed to examine the relationship between poverty of speech ratings and performance on the verbal fluency measure while statistically controlling for various clinical and sociodemographic variables (e.g., severity of positive symptoms). The inter-relationship between change in clinical burden of alogia and change in verbal fluency

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