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The evolution of illness phases in schizophrenia: A non-parametric item response analysis of the Positive and Negative Syndrome Scale

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ABSTRACT

Background: The Positive and Negative Syndrome Scale (PANSS) assesses multiple domains of schizophrenia. Evaluation of each of these domains was conducted to assess differences in the characteristics of psychopathology and their relative predominance in sub-populations.
Method: Subjects (N = 1,832) with *DSM-IV* schizophrenia were represented in three sub-populations: First Episodes, n = 305, Chronic Inpatients, n = 694, and Ambulatory Outpatients, n = 833. Nonparametric Item Response Analysis (IRT) was performed with Option Characteristic Curves (OCC), Item Characteristic Curves (ICC), slopes and item biserial correlation. Items were characterized as Very Good, Good, or Weak based on specified operational criteria for item selection.
Results: First episode patients were represented by negative, disorganized hostility and anxiety. Some negative domain items (Poor Rapport, Passive/Apathetic Social Withdrawal) and most positive domain items were scored as Weak. For chronic inpatients, all items of the anxiety domain and some items of the positive domain (Suspiciousness/Persecution, Stereotyped Thinking, Somatic Concerns) were Weak; for all other domains, items were Very Good or Good. For ambulatory outpatients, most items in the anxiety and hostility domain were scored as Weak. The majority of PANSS items were either Very Good or Good at assessing the overall illness severity: chronic inpatients (73.33%, 22 items), first episodes (60.00%, 18 items), and only 46.67% (14 items) in the ambulatory group.
Conclusion: Findings confirm differences in symptom presentation and predominance of particular domains in subpopulations of schizophrenia. Identifying symptom domains characteristic of subpopulations may be more useful in assessing efficacy endpoints than total or subscale scores.

1. Introduction

Schizophrenia has marked heterogeneity in symptoms. The current symptom domains contained in the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-V*) are psychosis, negative symptoms, disorganization, abnormal motor behavior and social/occupational dysfunction (American Psychiatric Association, 2013). Although not part of the formal diagnostic criteria for the illness, mood symptoms including depression and anxiety are common in many patients (Green et al., 2003; Moller, 2005), hostility and belligerence are present in some cases (Chen et al., 2001), and cognitive impairments are present in nearly all patients (Green et al., 2004; Keefe, 2008). Symptoms as domains or dimensions have been examined in detail with factor analytic procedures (e.g., White et al., 1997a, 1997b), including factor analyses of the current dataset (Kelley et al., 2013), and the domains examined by the PANSS have been widely validated.

Different subsets of patients, defined by their stage or course of illness or their overall outcome, have different predominant symptoms (Bengston, 2006). For example, at an acute phase, patients with schizophrenia routinely come to clinical attention because of the emergence of psychosis, often accompanied by social withdrawal. Since these experiences are new and unsettling, anxiety and depression would be expected to be substantially present as well. A clear case of a subgroup defined by long term outcome is

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difficult to discharge patients, who have been found to have elevated levels of hostility, aggression, and positive psychotic symptoms (Bartels et al., 1991; White et al., 1997b). High levels of disorganization and communication disorders are also associated with this particular poor outcome subgroup (Davidson et al., 1995). Conversely, successful adaption to living in the community may be contingent on lower levels of disorganization, aggressiveness, and flagrant psychosis and patients with sustained community tenure are also likely not to manifest substantial aggressive and hostile behavior, which would bring them into contact with the legal system or induce readmissions.

The long term course of schizophrenia suggests longitudinal changes in patients with different outcomes developing (e.g., Chronic inpatients vs. stable outpatients) and finding similarities within a disorder may help in the expansion of models to explain stages or the course of the disorder. While the Positive and Negative Syndrome Scale (PANSS) assesses multiple dimensions of schizophrenia, evaluation of each of its individual domains has not been systematically targeted at differences in the characteristics of psychopathology in subpopulations. There is considerable interest in identifying the course and treatment needs across different stages of illness. One symptom domain that seems likely to be present across all of the different subgroups of patients is negative symptoms (see prevalence review in Buchanan, 2007). These symptoms are temporally stable in follow-up studies (Putnam et al., 1996) and are associated with impairments in functional outcomes in both community dwelling and institutionalized patients (see Chemerinski et al., 2006; and Harvey et al., 2006 for a review). They are found to be present in many patients when other symptoms are in relative remission (particularly in cases of the deficit syndrome). Negative symptoms are also present at the time of the first episode (Lindenmayer et al., 1986; Milev et al., 2005) and have been reported to be moderate or greater in severity in a substantial proportion of community dwelling patients (Kurtz, 2005). Studies of older patients have reported even higher levels of negative symptoms (Harris, 1991; Roseman et al., 2008), although the longitudinal detection of change over the lifespan is challenging. In a cross-sectional study comparing symptom severity in chronic patients across 8 decades (Davidson et al., 1995), negative symptoms were more severe in older patients and manifested a greater age-associated difference than positive symptoms. That said, studies of older patients discharged from long-stay psychiatric care found greater improvements in negative symptoms than cognitive deficits post-discharge (Leff and Trieman, 2000), implicating environmental factors to an extent.

In this paper, we present the results of an analysis of assessment data from a large collated sample of people with schizophrenia, including data from studies of first episode patients, community dwelling patients, and long-stay patients from two New York State Psychiatric facilities. These patients were all examined with a clinical psychiatric rating instrument, the Positive and Negative Syndrome Scale (PANSS) and for this paper we examined several features of their clinical symptoms. Our hypotheses were that various domains of symptoms would be differentially prominent in different subgroups, as described above. Prominence was defined in terms of symptom severity. Using Item Response Theory (IRT) models, we examined the extent to which an individual item contributed to the overall severity scores for each domain and the extent to which items were consistently sensitive to differing levels of severity for each separate subgroup.

We hypothesized primarily that negative symptoms would be found to be consistently validly measured and similarly prominent in all three subgroups. We also hypothesized that institutionalized patients would have more severe and validly measured symptoms of hostility and disorganization, and psychosis, compared to the other two groups. First episode patients were hypothesized to have greater severity and measurement validity for anxiety/depression and psychosis. Community dwelling patients were hypothesized to be less impaired in other symptom domains (such as Anxiety and Disorganized domains), with resulting alterations in the patterns of domain structure and IRT findings.

2. Methods

2.1. Data source

This study uses data from 5 different observational studies (see Table 1) aimed at cognition, functioning, and the course of illness in people with schizophrenia. Subjects (N = 1,832) were all diagnosed with *DSM-IV* schizophrenia or schizoaffective disorder, and were combined into three groups: First Episodes, n = 305, Chronic Inpatients, n = 694, and Ambulatory Outpatients, n = 833. Studies were carried out in accordance with the latest version of the Declaration of Helsinki. Study procedures were reviewed by appropriate ethics committees and informed consent (with specific exceptions as seen below) was obtained after the procedures were fully explained.

The First Episode group was defined as: consenting 18–45-year-old patients who met *DSM-IV* criteria for schizophrenia, or schizoaffective disorder for no more than 1 year prior to the assessment and during which period they had no more than two psychiatric hospitalizations for psychosis; and who did not have another axis I diagnosis, including substance dependence or abuse (Compton et al., 2009; Compton et al., 2011). Diagnoses were determined using the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I; First et al., 1998). Patients with first episode were not determined by age but rather the course of symptom presentation and to ensure that all courses during first episode (illness onset, episode onset, end of episode, relapse of episode) were covered. The Chronic Inpatient group was defined as: 18–85-year-old patients who met the *DSM-IV* criteria for schizophrenia or schizoaffective disorder and staying in a chronic psychiatric ward for >6 months. This group was examined with a waiver of signed informed consent because all patients in the hospital received the assessment and information was

Table 1
Clinical description of data used in the investigation.

	Chronic Patient Sample							First Episode Sample
Series	Kay & Sevy, 1990	Caton et al., 1994, 1995	Bell et al., 1994	Davidson et al., 1995	Bowie et al., 2008	Harvey et al., 2010	Total	
Setting	Inpatient	Urban Community	Veterans Hospital Rehabilitation	Geriatric inpatient	Outpatient	Outpatient		
n	239	400	150	305	238	195	1527	305
Age Mean (sd)	33.1 (10.2)	38.8 (10.6)	40.2 (8.6)	75.7 (7.0)	56.6 (9.7)	44.0 (5.2)	48.9 (15.1)	23.6 (4.9)
% Male	77	50	95	44	73	69	64	73