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Heterogeneity and symptom structure of schizophrenia

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ABSTRACT

Previous studies failed to identify a consistent factor structure of the BPRS-24 in schizophrenia. Our aims were to examine the fit of all previously published factor models and then to explore unobserved population heterogeneity and identify salient latent classes. Two hundred thirty-nine patients with ICD-10 schizophrenia admitted to a random sample of all Italian public and private acute inpatient units during an index period were administered the BPRS-24. Confirmatory factor analysis (CFA) was used to test all factor models derived in previous studies. Then, factor mixture analysis (FMA) with heteroscedastic components was carried out to explore unobserved population heterogeneity. No previously reported factor solution showed adequate fit in CFA. FMA indicated the presence of three heterogeneous groups and yielded a 5-factor solution (Depression, Positive Symptoms, Disorganization, Negative Symptoms, Activation). Group 1 was characterized by higher Disorganization, lower Activation, lower psychosocial functioning, greater lifetime number of admissions, more frequent history of compulsory admission. Group 2 displayed lower Disorganization. Group 3 showed higher Activation and more frequent history of recent self-harming behavior. Our finding that a reliable factor structure for the BPRS-24 could be obtained only after assuming population heterogeneity suggests that the difficulty in identifying a consistent factor structure may be ascribed to the clinical heterogeneity of schizophrenia. As compared with clinical subtypes, the psychopathological dimensions displayed much greater discriminatory power between groups identified by FMA. Though preliminary, our findings corroborate that a dimensional approach to psychopathology can facilitate the assessment of the clinical heterogeneity of schizophrenia.

1. Introduction

Since the inception of the concept of schizophrenia, there has been debate about its exact clinical nature and whether it is a unitary disease entity or a heterogeneous disorder. Indeed, patients with schizophrenia vary widely in their symptomatology, course of illness and treatment response, to the point that the diagnosis may identify individuals who share few or no symptoms in common (Andreasen, 1999). Although different syndromes were noted in schizophrenia already one century ago (Bleuler, 1950), it has been difficult to develop a reliable clinical typology, despite many efforts to do so. The validity of the traditional clinical subtypes as nosological entities has often been questioned (Andreasen et al., 1997) and their prognostic value is limited (Kay and Sevy, 1990).

Some studies comparing categorical and dimensional models of psychosis suggested that symptoms and disease course are better explained in terms of continuous distributions (Peralta and Cuesta, 2007). A better understanding of the symptom structure of schizophrenia through the identification of distinct, well-defined symptom clusters would facilitate research aimed at identifying different clinical entities with specific neurobiological dysfunction, course of illness, and outcome (Tandon et al., 2009). Many studies examined the symptom structure of schizophrenia (Blanchard and Cohen, 2006), and a variety of dimensional models has been proposed to account for the whole range of schizophrenic symptoms (Peralta and Cuesta, 2001). The adequacy of the positive/negative dichotomy (Crow, 1980; Andreasen and Olsen, 1982) was challenged in favor of a subsequent three-dimensional model including positive and negative symptoms as well as disorganization (Liddle, 1987). In subsequent years, this model was questioned (Stuart et al., 1999) and more complex multidimensional solutions, with up to 11 factors (Peralta and Cuesta, 1999), were proposed to describe the varied expression of schizophrenic symptomatology (Peralta and Cuesta,

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2001). Despite these efforts, there is still no firm agreement about the precise symptom structure of schizophrenia, in terms of number of underlying dimensions and symptoms loading on each dimension.

Factor analytic studies of schizophrenia have relied on several different rating scales to assess psychopathology. Studies using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) usually yielded three-dimensional solutions (Andreasen et al., 1995), which have been criticized as being an artifact of a restrictive measure of psychotic symptoms (Stuart et al., 1999). Studies using more comprehensive rating scales often yielded solutions with a greater number of factors, including affective symptom dimensions. An instrument that proved particularly suitable for factor analytic studies is the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962), especially its expanded 24-item version (BPRS-E) (Lukoff et al., 1986; Ventura et al., 1993) that was designed to improve psychotic and affective symptom coverage and is commonly used in the assessment of patients with schizophrenia.

To our knowledge, there are 19 published factor analyses of the BPRS-E, which are summarized in Table 1. Most of these studies have limitations in sample size and composition. Most studies, with only few exceptions (Panos, 2004; Thomas et al., 2004; Velligan et al., 2005; Kopelowicz et al., 2008) were carried out on samples smaller than the recommended size of 200 (Comrey and Lee, 1992). Also, many studies were performed on diagnostically mixed groups of patients, which makes it difficult to attribute specifically to schizophrenia the factor structures identified by these studies.

Studies including 'general psychiatric' inpatients (Panos, 2004), outpatients with schizophrenia and unipolar and bipolar disorders (Velligan et al., 2005), patients with psychotic and affective disorders as well as substance abuse disorders (Thomas et al., 2004), and in- and outpatients with schizophrenia or schizoaffective disorder (Kopelowicz et al., 2008) did not yield consistent results. Four of them (Ventura et al., 2000; Thomas et al., 2004; Velligan et al., 2005) reported four-factor solutions with different structures, while three studies (Dingemans et al., 1995 'first sample'; Burger et al., 1997; Panos, 2004) reported different five-factor solutions.

Some studies were performed only on patients with schizophrenia. They include five analyses performed on the same small sample at different times (Van Der Does et al., 1993, 1995) and five simultaneous analyses on samples drawn from a collaborative project in Europe (Ruggeri et al., 2005). These studies yielded somewhat different 4-factor structures, with a positive symptoms factor, a negative symptoms factor, and either a disorganization factor and a depression factor (Van Der Does et al., 1993, 1995) or a mixed excitement/disorganization factor and an anxiety/depression factor (Ruggeri et al., 2005).

Taken together, although published factor analyses of the BPRS-E share some similarities in the number and composition of factors, they show several discrepancies between each factor structure, with differences in the number and interpretation of the factors and in the profile of factor loadings of the items on the factors. While small sample size and inclusion of patients with diagnoses other than schizophrenia may at least partly account for the conflicting findings, the failure to identify a consistent factor structure of the BPRS-E in schizophrenia may also be due to the clinical heterogeneity of the disorder, that may make it difficult to identify a factor solution that is sufficiently stable and independent from the clinical characteristics of the specific sample under study.

The present study is based on data collected during the PROGRES-Acute project, a national survey of psychiatric inpatient care in Italy (de Girolamo et al., 2007; Preti et al., 2009; Guzzetta et al., 2010). Its aim was to examine the fit of all previously published factor models of BPRS-E in a national sample of patients with schizophrenia admitted to acute inpatient units, and then to explore unobserved population heterogeneity through factor mixture analysis, which enables the identification of salient latent classes as it models the latent factors through a mixture of distributions that correspond to different subpopulations.

2. Methods

2.1. Sampling

All 21 Italian regions with the exception of Sicily took part in the study. Each region appointed a coordinator, who organized and supervised data collection. First, all inpatient facilities admitting acute patients with primary diagnosis of mental disorder were surveyed. Then, a 20% random sample of General Hospital Psychiatric Units (GHPUs), and all remaining public and private facilities were selected for further detailed study.

There were some exceptions to the sampling plan. Eight GHPUs, not originally sampled, asked to participate and were included. Also, organizational problems precluded participation of six 24-hour Community Mental Health Centers (24 h-CMHCs), three University Psychiatric Clinics (UPCs), and 18 private facilities. Furthermore, in the Lazio region participation was on voluntary basis due to financial constraints. Therefore, the facility sample included 130 public (107 GHPUs, 13 UPCs, 10 24 h-CMHCs) and 36 private facilities.

The patient sample included all patients admitted to public and private facilities during an index period of 12 and 3 days, respectively. It comprised 1577 patients, of whom 261 received a diagnosis of schizophrenia and were considered for inclusion in the study.

2.2. Assessment

All regional coordinators took part in a centrally held training session on the study instruments. In larger regions they, in turn, trained additional researchers. Each facility was visited by a researcher who completed the assessment of each patient included in the study within 3 days from admission. Socio-demographic information was retrieved from patient records. The primary diagnosis was made by the psychiatrist who had the patient in charge, according to ICD-10 criteria.

The assessment included the 24-item Brief Psychiatric Rating Scale (BPRS) and the Personal and Social Performance scale (PSP). The 24-item BPRS (Ventura et al., 1993) is an expanded standardized version of the 18-item BPRS (Overall, 1972) with defined scale points and probe questions. The PSP is a version of the Global Assessment of Functioning scale that includes detailed instructions and was found to have high reliability (Morosini et al., 2000). The BPRS items are scored on a 7-point scale ranging from 1 to 7, while the PSP provides a summary score reflecting the level of functioning in psychological, social, and occupational domains on a scale from 1 (extremely poor functioning) to 100 (superior functioning). The inter-rater reliability, as measured by the intraclass correlation coefficient between raters, was tested during the training session and was found to be 0.81 and 0.88 for the BPRS and PSP, respectively.

2.3. Patients

Of 261 patients who received a diagnosis of schizophrenia, 202 with a complete BPRS and 37 who were rated on most items were included in the study. Missing item values were substituted with the variable mean. Twenty-two patients had a severely incomplete or blank BPRS and were excluded from the study. They did not significantly differ in any sociodemographic variable from the included patients.

Among the 239 patients included in the study, the most common subtype was paranoid ($N=134$, 56.1%), followed by hebephrenic (corresponding to the DSM-IV Disorganized subtype) ($N=23$, 9.6%), residual ($N=20$, 8.4%), undifferentiated ($N=10$, 4.2%), unspecified ($N=7$, 2.9%), catatonic ($N=4$, 1.7%), and simple ($N=1$, 0.4%), whereas the subtype was not reported for 40 (16.7%) patients. Eighty-nine (37.2%) were females, and 150 males (62.8%), while their mean age was 43.2 ± 13.7 years. The majority (89.1%) were admitted in public facilities, mostly GHPUs (80.7%). Fifteen (6.3%) patients were at their first admission. Patients' sociodemographic characteristics are summarized in Table 2. The mean BPRS total score was 60.7 ± 17.9.

2.4. Statistical analysis

After descriptive analysis, confirmatory factor analysis (CFA), which allows to test hypotheses on the relationships between the observed variables and their underlying latent constructs, was performed on BPRS items. On the collected data we tested several factor model specification derived in previous works (Van Der Does et al., 1993; Van Der Does et al., 1995; Dingemans et al., 1995; Burger et al., 1997; Ventura et al., 2000; Panos, 2004; Ruggeri et al., 2005; Thomas et al., 2004; Velligan et al., 2005; Kopelowicz et al., 2008) by using the LISREL 8.52 package (Jöreskog and Sörbom, 2001) under the structural equation modeling approach (Jöreskog and Sörbom, 1979). CFA relies on several goodness of fit indicators to determine the adequacy of model fit to the data. The Comparative Fit Index (CFI) measures the discrepancy function between the estimated and the theoretical model adjusted for sample size. It ranges from 0 to 1 with a larger value indicating better model fit: an acceptable model fit should have a CFI value greater than 0.90. The Goodness-of-Fit Index (GFI) is a measure of the adequacy of the fit based on the model variances and covariances.