

## Psychopathology in never-treated schizophrenia

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### Abstract

The effect of drug treatment and its adverse effects confound studies on symptoms and associated factors in schizophrenia. Knowledge of psychopathology in the untreated state would identify the natural state of the illness and is relevant to understand pathology underlying the illness. We report here symptoms of schizophrenia as measured by Positive and Negative Syndrome Scale in 143 patients with schizophrenia living in the community never treated with antipsychotic drugs. Positive symptoms were more frequent than negative ones. Negative subscale scores correlated negatively with positive subscale scores and positively with general psychopathology subscale scores. Age correlated negatively with negative and general psychopathology subscale scores independent of duration of illness. Duration of illness and the proportion of life spent in psychosis did not correlate with any Positive and Negative Syndrome Scale scores. The factors (*negative, positive, anxiety-depression, motor, and excitement*) extracted by a forced 5-factor analysis explained 56% of variance. This factor structure resembled that of treated patients reported in most studies except for the identification of a motor symptom cluster. Psychopathology in the never-treated schizophrenia varied in some aspects from descriptions in the treated state. The differences can be said to demarcate the natural features of the illness from medication effects on the relationship of symptoms with one another and to sex, age, duration of illness, and age at onset.

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### 1. Introduction

One of the greatest challenges for clinicians and researchers with schizophrenia is the heterogeneity of the clinical manifestation of the disorder. There is considerable variation in symptoms in patients given this diagnosis [1]. Factor analytical studies demonstrated that symptoms occurred together as several syndromes [2–4]. Pathophysiologic mechanisms have been proposed for the symptoms and their relationship to one another and to demographic and clinical characteristics [4–7]. Most of these studies were of patients who received drugs. One cannot be sure how far artifacts of drug treatment influenced these descriptions. A study of schizophrenia unmodified by drug treatment would describe the natural in situ manifestation of the illness. This would not merely be of clinical interest but of importance in understanding the neuropathology of the illness. The detailed descriptions of the illness in late 19th and early

20th centuries of the preneuroleptic era were of high clinical standards but could not directly be compared with current literature because of differences in mode of data collection and analysis.

Recent studies of untreated patients usually examined either first-episode patients ill for a short time or previously treated patients in a new untreated episode [3,8,9]. The phenomenology of schizophrenia present for many years without treatment was little studied in recent times. In developing countries, there are significant numbers of patients untreated for many years [10]. We described in this article clinical symptoms of schizophrenia that had lasted untreated for many years and explored their relationship to one another as well as to sex, age, age at onset, and duration of illness. The observations were compared with the reports in the literature on treated patients.

### 2. Methods

We conducted 3 studies in Chennai city in south India and the neighboring villages with never-treated schizophrenic patients. One examined the prevalence of dyskinesia and other extrapyramidal symptoms [11], the second studied

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the relationship between cognitive dysfunction and dyskinnesia [12], and the third was a magnetic resonance imaging (MRI) study of never-treated patients [13]. Psychopathology of a total of 143 patients recruited for these 3 studies were analyzed and presented here.

The studies were conducted at the Schizophrenia Research Foundation, India (SCARF), a nongovernmental organization involved in research and psychiatric rehabilitation work located in Chennai. Most patients were identified through rural outreach services of SCARF, whereas some were recruited from the urban outpatient center of SCARF. All patients fulfilled *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria for schizophrenia [14]. The diagnosis was made through mental state examination and history obtained from patients and relatives.

The Ethical Review Board of SCARF approved the study. Written consent was inappropriate because most subjects were illiterate. All patients gave informed oral consent witnessed by their next-of-kin and by a SCARF member of staff not involved in the research project, and recorded in the patient's case record. For the group that underwent MRI examination, a detailed oral explanation of the study and the procedures involved was presented to them before obtaining consent. They were provided travel facilities and compensated for any expenses incurred during their travel to the MRI facility. All patients were offered treatment irrespective of their consent to participate in the study.

The time of onset of illness was identified as the one at which psychotic symptoms were recognized by the patient and/or a family member. At least 1 informant living with the patient at the time of onset was available for this assessment. We used personal and public historical events as time anchors to increase the accuracy. History of possible exposure to antipsychotic medication was determined using multiple sources that included discussion with patients and their relatives. Examination of medical records and prescription sheets, wherever available, showed that they never received antipsychotic medication. We were also confirmed that patients did not receive any treatment from practitioners of indigenous systems of medicine. As we reported earlier [11], taking antipsychotic medication is an important and often expensive event in the lives of patients and their families in the region and would be easily recalled. We were therefore confident of the accuracy of the medication histories obtained.

### 2.1. Assessment

Symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS) [15]. Positive and Negative Syndrome Scale provides a standardized method of assessing 30 psychiatric symptoms on a 7-point scale. The items are grouped as positive (P) subscale, negative (N) subscale, and general psychopathology (GPP) subscale. The rating of items for each patient was made with reference to the previous month. Ratings were based on an interview with

the patient and at least 1 caregiver who had been living with the patient in the same household. The assessment was made by one of the authors (SNT, RT, RP) who have extensive experience in the use of the PANSS.

### 2.2. Data analysis

Data compilation and statistical analysis were carried out using the Statistical Package for Social Sciences, version 7.5 (SPSS Inc, Chicago, Ill).  $\chi^2$  Test and *t* tests were used to compare subgroups of patients and Pearson correlation analysis with study the relationship between variables. Interrelationship of symptoms was examined using factor analysis. For this, all 30 symptoms of the PANSS were analyzed using the ratings of individual symptoms. A forced 5-factor model was used. The interpretation of factors was based on item loadings higher than 0.5. Initial factors with eigenvalues greater than 1 were extracted by principal components method and subjected to varimax rotation.

## 3. Results

### 3.1. The study population

There were 71 men and 72 women. The mean age of the patients was  $47 \pm 16.3$  years. Fifteen patients (10%) were younger than 25 years, and 27 (19%) were older than 65 years. The illness was present for a mean duration of  $10.7 \pm 9.1$  years. It had lasted for less than 2 years in 14 (10%), 2 to 5 years in 46 (32%), and more than 5 years in 83 (58%). The mean age at onset was  $36.2 \pm 14.5$  years. The onset was early (before 45 years) in 102 (71%) and late (after 45 years) in 41 subjects.

### 3.2. Symptoms

The mean scores on the PANSS P, N, and GPP subscales were  $18.5 \pm 7.6$ ,  $16.8 \pm 9.9$ , and  $27.4 \pm 9.4$ , respectively. Of the 5 most frequently occurring symptoms (rated as present if scored 3 or more), 4 were positive symptoms (delusions, suspiciousness/persecution, hallucinatory behavior, and conceptual disorganization). These symptoms were present in more than 50% of patients. The 2 sexes did not differ significantly in their PANSS subscale scores (P subscale,  $19.0 \pm 7.3$  vs  $18.0 \pm 7.8$ ; N subscale,  $15.8 \pm 9.4$  vs  $17.8 \pm 10.3$ ; GPP subscale,  $27.7 \pm 9.0$  vs  $27.1 \pm 9.8$ ).

Partial correlations were measured for PANSS subscale scores with one another and with age, duration of illness, and age at onset. Controlling for age and duration of illness, P subscale correlated negatively with N subscale ( $r = -0.27$ ,  $P < .01$ ) and both P and N subscale scores correlated positively with GPP subscale scores ( $r = 0.22$ ,  $P = .01$ ; and  $r = 0.23$ ,  $P < .01$ , respectively). Age correlated negatively with N subscale ( $r = -0.25$ ,  $P < .01$ ) and GPP subscale scores ( $r = -0.22$ ,  $P < .01$ ) independent of duration of illness. Duration of illness did not correlate with any PANSS scores independent of age (P subscale,  $r = -.04$ ; N subscale,  $r = .07$ ; GPP subscale,

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