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ORIGINAL ARTICLE

Medium-term course and outcome of schizophrenia depicted by the sixth-month subtype after an acute episode

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Background/Purpose: The intermediate course of schizophrenia is a complex intertwined with the heterogeneity of the illness. This article attempts to simplify this complexity using a hypothetical tripartite based on the profile of symptoms at 6 months after acute treatment.
Methods: This is a prospective 5-year follow-up study including 163 schizophrenic inpatients in northern Taiwan comparing patients' demographic data at index admission, scores on the Positive and Negative Syndrome Scale (PANSS) for schizophrenia and social function scale measured at admission, 6-month follow-up, and annually, and scores on a neuropsychologic test battery measured approximately 5 years after recruitment.
Results: Patients were grouped into three subtypes based on their sixth-month symptomatology by Generalized Association Plots, designated as remitted (RM), persistent delusion/hallucination (PDH), and markedly blunting (MB) groups. These three subtypes presented with similar positive symptom profiles at recruitment, yet during follow-up, the PDH group tended to maintain the highest risk of having worse clinical symptomatology, social functioning, and neuropsychologic functioning, and the RM was the best outcome group.

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Conclusion: This three-subtype model provides a practical reference to predict medium-term outcomes by the subject's response to acute treatment and serves as a model to sort out part of the heterogeneous nature of schizophrenia that still should be examined by further psychopharmacological, neurobiological, and genetic studies.
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Introduction

The course and outcome of schizophrenia are hard to predict despite long-term study.[1–3] Researchers tried to examine clinical and psychosocial variables to yield better prognostic power for course and outcomes,[4–6] or attempted to classify subtypes of schizophrenia according to outcome and severity.[7,8] The heterogeneity of the clinical entity, the differences in diagnostic criteria, treatment modalities, and the stage of illness, the measurement of clinical severity and outcomes, and the differential outcomes between the dropouts and the follow-up groups all contribute to the inconclusiveness.[9] Studies require broad symptom profiles to characterize the courses of schizophrenia and to better understand its intermediate course.[10]

The timing of symptom assessment is important for subtyping of schizophrenia. In our previous study, we used a new technique, the generalized association plot (GAP) analysis,[11] to subtype schizophrenia based on symptom profiles at the time of admission and stratified a group with negative symptoms and the other without marked negative symptoms.[12] However, the florid psychotic symptoms at admission usually regress somewhat after treatment and therefore do not provide enough information about long-term outcome,[9] and a substantial proportion of patients in the subgroups with acute symptoms would be categorized into other subgroups when symptoms are not acute.[13] Symptomatology at discharge from the hospital is also a poor predictor because the time of discharge is biased by service availability.[14] Although the nature of schizophrenia subtypes and their correlations to outcomes are complex,[12,15–17] the symptom profile assessed 3 to 6 months after acute treatment was a better reference to predict future course and outcome.[18,19] In the current study, we attempt to depict the 2- to 5-years course and outcomes of schizophrenia in terms of clinical symptom profile, social functioning, and neurocognitive functioning, using the subtypes identified by GAP analyses of symptomatology 6 months after acute treatment. We also examine whether this subtyping approach can reciprocally differentiate clinical variables at recruitment.

Methods

Participants

Participants were schizophrenic patients in northern Taiwan who have been followed annually for up to 5 years in the Multidimensional Psychopathological Group Research Project from August 1993 to June 1998. The recruitment procedures have been described in detail in earlier reports of this project.[12,20] Briefly, all patients met the criteria for schizophrenia set forth by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Revision (DSM-IV, American Psychiatric Association, 1994) and were consecutively admitted to the acute wards of three hospitals, National Taiwan University Hospital and the university-affiliated Taipei City Psychiatric Center and Taoyuan Psychiatric Center with written informed consent. All participants received a standard set of clinical management, including psychopharmacologic treatment, family and psychosocial intervention, and occupational therapy. The diagnoses were confirmed at discharge by consensus among three senior psychiatrists using data available from the Chinese version of the Diagnostic Interview for Genetic Study (DIGS),[21] clinical observations, medical records, and key informants.

A total of 225 patients completed a Mandarin version of the Positive and Negative Syndrome Scale (PANSS) for schizophrenia assessments at admission and were recruited. Of these patients, 181 were reassessed at 6-month follow-up, 172 at 1-year, 156 at 2-year, 133 at 3-year, 149 at 4-year, and 100 at 5-year follow-ups, respectively. The 163 patients with complete PANSS data at recruitment and at 6months were subtyped based on 6-month PANSS scores.

Measurements

Patients were assessed by PANSS; a clinical data book recording the participants' demographic features, previous psychiatric history, treatment history, and social functioning; and a neuropsychologic test battery composed of Continuous Performance Test (CPT), the Wisconsin Card Sorting Test (WCST), the Mandarin version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), Trail Making Test, and the Wechsler Memory Scale-Revised (WMS-R). These tools have been applied in our previous studies with good reliability.[12,21–23]

Demographic and clinical variables used for analyses included age at recruitment, sex, years of education, employment status at recruitment, age at onset of initial nonspecific symptoms, age at onset of psychotic symptoms, age at onset of severe function impairment, mode of onset, duration of illness from onset of any psychotic symptom to the index admission of the study, length of stay for the index admission, and the highest antipsychotic dosage converted to chlorpromazine equivalent dosage (CPZE; mg/day) of the index admission and at discharge. Patients' social functioning was measured using a seven-point Likert scale to evaluate four dimensions in their daily lives: interpersonal relationships, achievements, time arrangement of daily activities, and family-life functioning.[24]

Individual subtests of the neuropsychologic tests were recategorized into constructs of eight cognitive functional

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