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Subtyping First-Episode No affective Psychosis Using Four Early-Course Features: Potentially Useful Prognostic Information at Initial Presentation

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Abstract

Aim—Heterogeneity of symptoms, course, and outcomes in primary psychotic disorders complicates prognosis, treatment, and diverse aspects of research. This study aimed to identify interpretable subtypes of first-episode nonaffective psychosis based on four early-course features (premorbid academic functioning, premorbid social functioning, duration of the prodrome, and age at onset of psychosis).

Methods—Data from 200 well-characterized patients hospitalized in public-sector inpatient units for first-episode nonaffective psychosis were used in latent profile analyses. Derived subtypes were then compared along a number of clinical dimensions using analyses of variance.

Results—Using four early-course features, three classes were derived. A *good premorbid/short prodrome* subtype was characterized by a lower severity of positive symptoms, better social/occupational/global functioning, and a shorter duration of untreated psychosis; a *poor premorbid/early onset* subtype demonstrated greater negative and preoccupation symptoms, as well as greater psychosocial problems; and a *long prodrome/late onset* subtype was characterized by greater dysphoric symptoms.

Conclusions—Findings indicate a need for further research with first-episode samples on the utility of subtyping based on early-course (premorbid, prodromal, and onset-related) characteristics. Such efforts could enhance the parsing of heterogeneity, thereby advancing clinical practice and research.

Keywords

Age at onset; First-episode psychosis; Heterogeneity; Premorbid functioning; Prodrome; Schizophrenia

1. Introduction

Schizophrenia and related psychotic disorders represent a set of highly heterogeneous clinical syndromes in terms of symptomatology, course, outcomes, and likely etiology and pathophysiology. Heterogeneity complicates clinical evaluation and treatment (e.g., prognostication and the tailoring of somatic and psychosocial therapies), and impedes research by obscuring potentially discrete subtypes. Given the recognized heterogeneity, parsing the syndrome into subtypes that are useful for clinical and research purposes is a crucial goal.¹ Initial attempts to divide the syndrome into useful groups relied on diagnostic categories,² most notably the paranoid/non-paranoid distinction. At present, the various diagnostic categories are based on features such as current or recent symptoms and the longitudinal course of those symptoms and impaired functioning. However, phenomenological similarity of patients within diagnostic categories is modest at best,¹ and the validity of such categories is highly debated.³

The most studied subtypes within schizophrenia research appear to be those based on illness presentation or symptomatology, originating with the positive-negative distinction proposed by Crow,⁴ which was then amended to include a third, disorganized, subtype.^{5,6} However, further research into these classifications showed considerable fluctuation in classes over time.⁷⁻⁹ Since the most common indicator of a more severe course of illness was consistently related to negative symptoms, additional classifications based on longitudinal course of negative symptoms¹⁰ were proposed to identify “deficit syndrome” patients who may require different treatment modalities.¹¹ More recent developments have used multiple symptom dimensions¹² as well as a combination of symptom dimensions and neurodevelopmental risk factors¹³ in an attempt to improve upon the current diagnostic classification of psychotic disorders. However, the deficit syndrome and other symptom-based subtypes are difficult to identify early in the disorder,¹⁴ which makes that approach less attractive as a method of parsing heterogeneity that may be relevant for early intervention. Subtyping early in the course of illness might best be accomplished using features of the very early, pre-treatment course of the disorder (*the premorbid phase, the prodromal period, and the onset of psychosis*). These features are best defined in a first-episode sample, unobscured by: (1) the accumulated psychosocial disability that is commonly associated with chronicity, (2) the impact of psychosocial treatments on the early course, (3) the beneficial and adverse effects of medications, and (4) the known effects of chronic substance abuse on symptoms and course (though some first-episode patients may have chronic substance abuse problems prior to psychosis onset).

Regarding *the premorbid phase*, numerous studies have shown that deficits in overall premorbid functioning predict multiple adverse illness-related variables, such as neurocognitive deficits and more severe positive and negative symptoms.¹⁵⁻¹⁷ Premorbid functioning also has been studied as a predictor of treatment outcome, with the general pattern indicating that good premorbid functioning is predictive of better response to treatment.^{15,18-23} Within the premorbid phase, the distinction between academic and social dimensions has been shown to be more useful for illustrating differential associations with important clinical and biological variables.^{21,24,25} In terms of *the prodromal period*, there are some indications that the duration of untreated illness (which represents the time from prodrome onset to initiation of adequate treatment) is more strongly associated with functional outcomes than duration of untreated psychosis (DUP) in first-episode patients;²⁶ thus the duration of the prodromal phase may be critical to parsing heterogeneity. The duration of the prodrome was chosen as a key early-course variable in this study because it may be considered an inherent aspect of the illness, whereas DUP is largely a function of factors external to the illness such as financial/insurance status, family functioning, and the characteristics of the local healthcare system,²⁷⁻²⁹ making DUP less attractive as a primary

aspect of the early illness for subtyping, though clearly a target for early intervention strategies. Finally, regarding *the onset of psychosis*, age at onset is known to be a key prognostic factor in schizophrenia. An earlier age at onset is associated with a higher degree of cognitive impairment,^{30–32} more severe psychopathology,^{33,34} and remission status.³⁵ Similarly, early, adolescent-onset schizophrenia is consistently associated with poorer outcomes in multiple domains than later-onset illness.^{36–39}

We utilized pre-treatment features of first-episode patients (including premorbid functioning, duration of the prodrome, and age at onset), which are not affected by treatment (or lack of treatment) in the way that symptoms are, in an attempt to identify subgroups of potential relevance to clinicians and researchers. Subgroups defined by these pre-treatment features could be useful for prognostication and treatment planning. The goal of the current study was to identify homogenous subgroups that can be used in other studies, including those designed to uncover genetic underpinnings.

2. Methods

2.1. Setting, sample, and general procedures

Following approval by all relevant human subjects research review committees, participants were recruited between July 2004 and April 2010 from public-sector hospital settings: 142 (71.0%) were admitted to a unit with a relatively long average length of stay (14.4 ± 8.4 days);⁴⁰ 28 (14.0%) to a shorter-stay (6.8 ± 3.0 days)⁴⁰ crisis-stabilization unit in the same hospital, five (2.5%) from the psychiatric emergency receiving service of that hospital, and 25 (12.5%) to a crisis stabilization unit in an adjacent suburban county. These units are general psychiatric settings (rather than specialty first-episode treatment settings) that provide evaluation and treatment services to an urban population with no insurance or with only public-sector insurance (i.e., Medicaid). This population, and thus the present sample, is low-income and socially disadvantaged in other ways (e.g., high rates of school drop out,⁴¹ prior incarceration,⁴² and unemployment⁴³), and is predominantly African American.

Consecutively admitted first-episode patients were eligible if they were between the ages of 18 and 40 years and spoke English. Those with prior outpatient treatment for psychosis lasting >3 months, or prior hospitalization for psychosis more than three months before the index hospitalization, were considered to have had prior treatment for psychosis and were therefore ineligible. Other exclusion criteria included known or suspected mental retardation, a Mini-Mental State Examination^{44,45} score of <24, a significant medical condition that could compromise ability to participate, or inability for any reason to provide written informed consent.

This analysis was performed using a combined dataset ($n=200$) that included data collected during six years as part of two research studies—one focused on predictors of treatment delay and DUP,^{27–29,46–48} and the other being an ongoing study of the impact of premorbid cannabis use on the early course of psychotic disorders.^{49,50} The two studies had identical eligibility criteria, recruitment processes, and data collection procedures. Referred patients were invited to participate in the study after they had sufficient time to acclimate to the inpatient treatment setting. Detailed clinical research assessments were conducted once psychotic symptoms were stabilized enough to allow for informed consent, typically between hospital day four and 10. Research diagnoses of nonaffective psychotic disorders (and substance use disorders) were made using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID).⁵¹ All patients gave written informed consent prior to participation.

2.2. Measurement of key early-course variables for latent profile analysis

Premorbid functioning was measured with the *Premorbid Adjustment Scale* (PAS), for which reliability, validity, and predictive utility have been reported.⁵² Functioning was assessed in two domains—academic and social—across three age periods: childhood (11 years), early adolescence (12–15 years), and late adolescence (16–18 years). Premorbid functioning was not assessed in any age period that would have included the year before onset of prodromal symptoms, as a conservative measure to safeguard against inadvertently assessing prodromal functioning during the rating of premorbid functioning.⁵³ Two overall indices of premorbid functioning—in an academic domain (e.g., adaptation to school and grades) and a social domain (e.g., sociability and peer relationships)—were computed by averaging childhood, early adolescence, and late adolescence scores, as applicable. Higher scores indicate poorer premorbid functioning.

Onset of the prodrome was operationalized as the date of the first prodromal symptom(s), from among 14 provided in the *Symptom Onset in Schizophrenia* inventory (SOS).⁵⁴ Such symptoms were contiguous (without clearly discernible periods of wellness intervening) with subsequent onset of psychosis.²⁶ The end-point of the prodrome was the date at onset of positive psychotic symptoms, which was also measured in a systematic manner using the SOS inventory. Standardized methods were used to resolve ambiguities in obtaining exact dates for the onset of prodromal and psychotic symptoms, and interview questions were cross-referenced with milestones and memorable events. In-depth SOS interviews were conducted by trained research assessors. Consensus-based best estimates of dates of onset of both prodromal and psychotic symptoms were then derived in a meeting involving the lead investigator and the 1–3 assessors involved in collecting all data, based on all available information, including informant/family member data when available. From these dates, duration of prodrome, age at onset of psychosis, and DUP (weeks from onset of positive symptoms to first hospital admission) were derived.

2.3. Measurement of dependent variables

Positive and negative symptoms during the month prior to, and at the time of hospitalization were assessed with the *Positive and Negative Syndrome Scale* (PANSS).⁵⁵ The PANSS was completed by clinically trained research staff using data gathered from a chart review and an in-depth, semi-structured interview. In addition to the positive and negative syndrome scores, activation, dysphoric, and preoccupation domains were examined, based on a prior confirmatory factor analysis.⁵⁶ The *Proxy for the Deficit Syndrome* (PDS)⁵⁷ score was also derived, using PANSS scores based on the following formula to quantify deficit-like features: negative symptoms (blunted affect + poverty of speech) – emotionality (hostility + guilt + anxiety + depressed mood).

Insight was measured using the *Birchwood Insight Scale* (BIS)⁵⁸, an 8-item, self-report questionnaire. The participant indicates whether he or she “agrees,” “disagrees,” or is “unsure” about each of the statements provided (e.g., “My stay in the hospital is necessary.”) A total score is derived based on established scoring conventions, with higher scores indicating better insight. Satisfactory internal consistency ($\alpha=0.75$) and test-retest reliability ($r=0.90$) have been reported,⁵⁸ and the internal consistency in the present sample of 200 first-episode patients was good ($\alpha=0.82$).

The total number of current DSM-IV-TR-defined Axis IV psychosocial problems² was recorded upon completion of the entire clinical research assessment, during which time extensive information about the patient's current psychosocial functioning was gathered. Functioning was measured with the widely used, reliable, and valid *Global Assessment of Functioning* scale (GAF),^{2,59,60} and the Social and Occupational Functioning Assessment

Scale (SOFAS).⁵⁹ Both the GAF and SOFAS consist of a 100-point range that indicates overall current psychosocial functioning, and the scales are divided into 10 intervals with anchoring descriptions for each.² The GAF and SOFAS were rated by the research assessor upon completion of the entire clinical research assessment (SCID, PAS, SOS, PANSS, etc).

2.4. Data analyses

Latent profile analysis (Gaussian mixture modeling) was used to classify all subjects into groups (or classes) based on the values of the four markers of interest: premorbid academic functioning, premorbid social functioning, duration of the prodrome, and age at onset of psychosis. The data were first rank-transformed in order to: (1) ensure an equal metric across variables and thus meaningful distance measures, (2) reduce the effect of some extreme outliers in duration of prodrome, and (3) take into account the non-interval nature of the PAS scores.⁶¹ Solutions for 2, 3, and 4 classes were each estimated and then validated using post-hoc analyses of variance (ANOVAs) to determine successful and optimal separation of the derived subgroups. They were then examined for face validity. Various clinical features of interest (dependent variables) were then compared across the derived classes using univariate ANOVAs for each variable separately. Descriptive statistics were computed using IBM SPSS Statistics 19, and the main analyses were conducted with gllamm (generalized linear latent and mixed models), an add-on to Stata.⁶² Our criterion for establishing statistical significance was $p < 0.05$, and post-hoc Bonferroni tests were used.

3. Results

3.1. Sample characteristics

Sociodemographic characteristics of the study sample are shown in **Table 1**. The majority of participants were male (145, 72.5%); African American (178, 89.0%); single and never married (182, 91.0%); living with parents, siblings, or other family members prior to hospitalization (132, 66.0%); and unemployed in the month prior to hospitalization (132, 66.0%). Although all participants were considered to have first-episode nonaffective psychosis based on our eligibility criteria given above, for 50.5% the current hospitalization represented their first professional help-seeking contact and for 38.0% it was the second or third help-seeking contact (the remaining 11.5% had had more than three help-seeking contacts). Diagnoses included: schizophrenia (115, 57.5%; 88 with paranoid type, 13 with disorganized type, 12 with undifferentiated type, and two with residual type), schizophreniform disorder (30, 15.0%), schizoaffective disorder (18, 9.0%; nine with bipolar type and nine with depressive type), brief psychotic disorder (6, 3.0%), delusional disorder (3, 1.5%), and psychotic disorder not otherwise specified (28, 14.0%). Some 55.5% of participants met SCID criteria for cannabis abuse or dependence at present or within the past five years; this percentage was 27.0% for alcohol use disorders, 9.0% for cocaine use disorders, and 3.5% for abuse or dependence involving another substance. As documented in a prior report on 155 of these first-episode patients recruited between July 2004 and September 2009⁶³ (the present study included patients through April 2010), 78% were prescribed the atypical antipsychotic risperidone, with a mean daily risperidone dosage at hospital discharge of 4.26 mg (minimum=1, maximum=10, median=4, mode=4). The remaining received other atypical agents, and a very small minority received conventional antipsychotics.

3.2. Latent profile analysis

Analyses fit 2-, 3-, and 4-class solutions. Rather than using overall measures of fit such as likelihood or Bayesian information criterion, which are not well-defined for latent variable models,⁶⁴ post-hoc comparisons of the derived classes were examined with correction for multiple tests to determine whether the classes were uniquely defined by all four variables of

interest. The 3-class solution was the only solution in which all groups were statistically significantly distinguishable from the others on all four measures. As shown in **Table 2**, the first derived subgroup (termed *poor premorbid/early onset*) had poor premorbid functioning in both academic and social domains and a relatively early age at onset of psychosis (17.3 ± 3.8 years). The second class (called *long prodrome/late onset*) had a very long prodrome (291.6 ± 209.5 weeks) and a later age at onset of psychosis (24.9 ± 4.0 years). The third subgroup (termed *good premorbid/short prodrome*) was characterized by good premorbid functioning in both academic and social domains, as well as a short prodrome (35.3 ± 58.3 weeks).

3.3. Clinical characteristics of the derived subgroups

The derived classes differentiated patients on both positive and negative symptoms; dysphoric, preoccupation, and deficit symptoms; psychosocial functioning; and DUP (**Table 3**). Examination of the post-hoc comparisons indicated that some salient features of the *poor premorbid/early onset* group (Class 1) are: greater severity of negative symptoms, more preoccupation symptoms, and a greater number of Axis IV psychosocial problems. The *good premorbid/short prodrome* group (Class 3) had: a lesser severity of positive symptoms, dysphoric symptoms, and preoccupation symptoms; higher global and social/occupational functioning; fewer Axis IV psychosocial problems; and a shorter DUP. The *long prodrome/late onset* group (Class 2) seemed to be differentiated from the other two groups only by the fact that patients in this class had more mood symptoms, as indicated by the PANSS dysphoric symptoms domain and the PDS score. The subgroups were not simply proxies for diagnosis given the spread of diagnoses in each group and the spread across groups; for example, paranoid type schizophrenia, the most common diagnosis within the overall sample (88, 44%), was present in 43% of those in class 1, 54% of those in class 2, and 39% of those in class 3.

4. Discussion

Some of the present findings are consistent with prior observations from attempts at subtyping. Farmer and colleagues⁶⁵ applied cluster analysis to 42 course and symptom items in 76 patients, documenting two groups, one of which was characterized by *poor premorbid adjustment* and *earlier onset*, as well as bizarre behavior and “third person” auditory hallucinations. However, feasibility of translating and disseminating a subtyping approach is far greater when a few key variables are examined rather than dozens, and the present study focused on four variables that can be ascertained as early as the first treatment contact, irrespective of the nature or course of symptoms displayed. Lieberman and associates⁶⁶ identified two subtypes in a sample of 70 first-episode patients using latent class analysis based on four dichotomous variables: presence or absence of magnetic resonance imaging brain morphology abnormalities, deficit versus non-deficit status, remitted versus partially or not remitted status, and gender. One subtype in that study was characterized by *poor premorbid adjustment* and *earlier onset*, as well as *greater negative symptom severity*, as in the present study. In a larger sample of more than 400 patients, Sham and coworkers⁶⁷ identified three subtypes of first-contact, nonaffective psychosis patients using latent class analysis relying on eight variables. Again, one subtype was characterized by *poor premorbid social adjustment* and *earlier onset*, and, as in the present study, that group had significantly *greater negative symptom severity* than the two other groups.

Historically important subtypes, such as process versus reactive psychoses,⁶⁸ and more recent attempts at subtyping based on the presence of the deficit syndrome,¹⁰ have informed understandings of heterogeneity but have not been incorporated into formal diagnostic classification systems. Subtyping efforts could be advanced through further research aimed

at identifying subtypes that are meaningfully separable in terms of symptomatology and functioning. Early-course features may facilitate such subtyping efforts; Haas and Sweeney⁶⁹ noted that systematic characterization of the earliest manifestations of schizophrenia (i.e., before or during illness onset) may be important in identifying subtypes with similar course, thus facilitating treatment and advancing understandings of etiology and pathophysiology. From a clinical perspective, prognostication and tailoring of treatment for first-episode patients, perhaps regardless of the specific psychotic disorder diagnosis, would be easier if valid subtypes could be identified even at the initial contact with treatment services. Furthermore, clinicians already typically assess the features used in our subtyping approach (e.g., premorbid functioning), though in a less systematic way, as part of their regular history-taking with recent-onset patients.

Several methodological limitations should be recognized. First, results may not be generalizable to other samples drawn from different settings, given the particular sociodemographic and clinical characteristics of the study sample. Namely, the sample was predominantly male, African American, and socially disadvantaged, characteristics tied to the fact that the study was conducted in urban, public-sector treatment settings. Furthermore, the sample had a level of clinical severity necessitating hospitalization. Given our convenience sample drawn from relatively homogenous public-sector settings, the present analysis was unable to address the extent to which characteristics inherent to the sample (e.g., predominantly African American patients, all inpatients) may have influenced study results. However, the relative homogeneity of the study sample enhances internal validity and may facilitate attempts at subtyping by reducing excessive sociodemographic and clinical heterogeneity. Second, although dependent variables included several important clinical measures—such as positive symptoms, negative symptoms, insight, psychosocial functioning, and DUP—other outcome domains were not addressed, such as neurocognitive deficits, which are well-established impairments associated with schizophrenia. Neurocognitive domains and other endophenotypes may serve as signposts to a biological subtyping of schizophrenia,¹ potentially facilitating less ambiguous methods of classification.⁷⁰ Third, the cross sectional study design limits conclusions that can be drawn about prognosis beyond initial presentation. Although symptoms, psychosocial problems, and functioning at initial hospitalization were deemed appropriate outcome domains for this analysis, other prognostic factors, assessed longitudinally, such as response to treatment, would help in confirming predictive validity of the reported subtypes. Fourth, PAS ratings (of premorbid functioning) and SOS ratings (to collect data for the consensus-based approach of determining duration of the prodrome and age at onset of psychosis) were completed by the same research assessors who collected data on the dependent variables (e.g., symptom severity, insight, SOFAS and GAF); however, data were collected for the two overarching studies without the present analysis yet being planned or known to the assessors. Fifth, although data on the four early-course features were obtained based on patient/informant report whereas most dependent variables were based on the research assessors' standardized ratings after an in-depth clinical research interview (e.g., PANSS symptom severity scores), other dependent variables (e.g., SOFAS and GAF) were based on all available information. For the latter, we cannot exclude the possibility that recall bias among informants could have influenced those findings.

For the purposes of deriving classes, the present analysis focused on four continuous variables. To become useful for subtyping in a clinical or research setting, cut-points of such variables would likely be needed, and clinically implementable approaches to assessment would be required (rather than using relatively complex research instruments). The four variables were selected to provide a representation of three key epochs of evolving psychotic disorders—the premorbid phase, the prodromal period, and the onset of psychosis—though other early-course variables may be equally important (e.g., the level or rate of decline in

premorbid functioning, the age at onset of prodromal symptoms, the qualitative nature of prodromal symptoms experienced, the pattern of emergence of positive symptoms). Additional research is necessary to determine whether subtyping based on combinations of various early-course features is predictive of longer-term course in addition to cross-sectional symptoms and psychosocial functioning at the time of initial hospitalization. Yet, this study demonstrates that parsing the heterogeneity of schizophrenia may be advanced by attention to select early-course features, and that such subtypes may provide potentially useful prognostic information even at the time of initial presentation.

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Table 1Sociodemographic characteristics of the study sample ($n=200$)

Age at hospitalization, years	23.6±4.9
Gender, male	145 (72.5%)
Race, African American	178 (89.0%)
Years of education	11.8±2.3
Relationship status	
<i>Single and never married</i>	182 (91.0%)
<i>Married or living with a partner</i>	8 (4.0%)
<i>Separated, divorced, or widowed</i>	10 (5.0%)
Who the patient lived with in the month prior to hospitalization	
<i>Parents, siblings, or other family members</i>	132 (66.0%)
<i>Alone</i>	21 (10.5%)
<i>Friends or roommate</i>	11 (5.5%)
<i>Boyfriend, girlfriend, spouse, or partner</i>	11 (5.5%)
<i>Homeless</i>	11 (5.5%)
<i>Other</i>	12 (6.0%)
Employment status prior to hospitalization, unemployed	132 (66.0%)

Table 2Latent profile analysis: Raw means (SD) and post-hoc Bonferonni test *p* values based on ranked data

Class	PAS academic [†]	PAS social [†]	Duration of the prodrome	Age at onset of psychosis
1 (<i>n</i> =61, 30.8%)	3.05 (1.03)	2.32 (0.90)	82.9 (102.9)	17.3 (3.8)
2 (<i>n</i> =55, 27.8%)	2.50 (1.02)	1.62 (0.96)	291.6 (209.5)	24.9 (4.0)
3 (<i>n</i> =82, 41.4%)	1.66 (0.96)	0.76 (0.61)	35.3 (58.3)	22.2 (4.4)
<i>p</i> value, 1 vs 2	0.045	< 0.0005	< 0.0005	< 0.0005
<i>p</i> value, 2 vs 3	< 0.0005	< 0.0005	< 0.0005	< 0.0005
<i>p</i> value, 1 vs 3	< 0.0005	< 0.0005	0.023	< 0.0005

Class 1 – *poor premorbid/early onset*Class 2 – *long prodrome/late onset*Class 3 – *good premorbid/shortprodrome*

[†] These two indices of premorbid functioning represent averages of childhood, early adolescence, and late adolescence (as applicable) Premorbid Adjustment Scale scores. Higher scores indicate poorer premorbid adjustment.

Table 3

Comparison of classes: Raw means (SD), group test *p* values, and post-hoc Bonferroni test *p* values. Some of the most salient features (based on 2-group comparisons) are shown in bold.

Variable	Class 1	Class 2	Class 3	<i>p</i> value, group test	<i>p</i> value, 1 vs 2	<i>p</i> value, 1 vs 3	<i>p</i> value, 2 vs 3
Male, %	80.3	76.4	64.6	0.088	---	---	---
Employed, %	24.6	40.7	36.6	0.154	---	---	---
PANSS positive symptoms [†]	3.57 (0.78)	3.57 (0.88)	3.16 (0.80)	0.003	1.000	0.011	0.014
PANSS negative symptoms [†]	2.93 (0.59)	2.54 (0.75)	2.55 (0.97)	0.009	0.029	0.016	1.000
PANSS activation symptoms [†]	2.49 (0.86)	2.46 (0.84)	2.41 (0.99)	0.903	---	---	---
PANSS dysphoric symptoms [†]	2.76 (1.01)	2.82 (0.87)	2.44 (0.84)	0.030	1.000	0.113	0.056
PANSS preoccupation symptoms [†]	3.18 (0.62)	2.98 (0.74)	2.77 (0.87)	0.008	0.515	0.006	0.339
Birchwood Insight Scale	6.25 (3.70)	6.22 (3.50)	5.06 (3.18)	0.083	---	---	---
SOFAS	37.3 (10.6)	37.7 (12.9)	42.9 (12.8)	0.011	1.000	0.023	0.055
GAF	32.5 (10.3)	32.9 (11.3)	37.1 (12.0)	0.032	1.000	0.059	0.112
Total number of Axis IV problems	5.00 (1.87)	4.52 (1.87)	3.61 (2.02)	<0.0005	0.587	<0.0005	0.029
Proxy for the Deficit Syndrome	-4.48 (3.21)	-6.44 (3.11)	-5.04 (3.16)	0.003	0.003	0.886	0.036
DUP (weeks) [‡]	41.0	40.0	13.0	0.002			

Class 1 – *poor premorbid/early onset*

Class 2 – *long prodrome/late onset*

Class 3 – *good premorbid/shortprodrome*

[†] subscales of the pentagonal model of White et al., 1997

[‡] nonparametric test of medians