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Memory Profiles in Schizophrenia: Categorization Validity and Stability

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Abstract

Background—Memory profiles corresponding to nearly normal (NN), Subcortical impairment (Sub) and Cortical impairment (Cort) have been identified in schizophrenia by several investigators using cluster analytic techniques. Specific aims of the current study were to (1) perform a K mean cluster analysis using Hopkins Verbal Learning Test –R scores (2) create classification rules based upon cluster distributions and expected memory profiles and to determine their concordance with cluster analysis; (3) explore differences among classified groups on demographic, neurocognitive and social cognitive domains; and (4) determine the stability of the classifications 12 months later.

Methods—Clinical and neuropsychological assessments were obtained at intake and 12 months from 151 outpatients with schizophrenia or schizoaffective disorder from an urban community mental health center.

Results—Clusters corresponded to those of the three expected subgroups. Using simple decision rules, rationally-derived groups were created and had 90% classification agreement with cluster groups. Groups did not differ on illness characteristics. Groups differed significantly in neurocognitive and social cognitive domains with NN>Cort and NN> Sub in all domains except visual/motor speed. Sub>Cort in verbal working memory. NN>Cort in social cognition. Rationally derived groupings showed fair stability at 12 month follow-up with 65% classification agreement. Specificity was good for NN (82.4%),

Discussion—Results support validity of memory profiles and offer some support for their stability at 12 months. The simple rules for classification can be used by other investigators for neuroimaging and other studies. Findings support the hypothesis that verbal memory may be an important source of heterogeneity in schizophrenia.

Keywords

Schizophrenia; neuropsychology; verbal memory; neurocognition; social cognition

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1. Introduction

As the cognitive deficits of schizophrenia become better characterized and understood, it is hoped that these will provide insights into their neuroanatomical correlates and into the heterogeneity of the disorder. Using neurocognitive test batteries, studies have identified distinct patterns including a relatively unimpaired group (Brazo et al. 2002; Bryson et al. 1993; Heinrichs and Awad 1993; Palmer et al. 1997). In a recent study, Wexler and colleagues (2009) used structural MRI to compare schizophrenia subjects who had nearly normal cognitive profiles to those with cognitive impairments and to healthy controls. Grey matter volumes were similar for the two schizophrenia groups, and they were significantly different from healthy controls. However, white matter volumes were not significantly different between the cognitively nearly normal schizophrenia group and healthy controls while significantly discriminating the schizophrenia group with cognitive impairment.

In pursuit of greater specificity regarding cognitive impairment, several recent articles have focused on verbal memory identifying verbal memory deficits in schizophrenia that appear to correspond to Cortical, Subcortical (some may prefer the term “fronto-striatal”) or unimpaired profiles. For example, using the California Verbal Learning Test (CVLT), a list learning task that also tests delayed recall and recognition memory, Paulsen and colleagues (1995) found that 35% had a normal profile, 50% had a Subcortical profile in which free recall was impaired but recognition was preserved, and 15% had a Cortical profile with impaired recall and recognition. Turetsky and colleagues (2002) also found these three groups and related structural MRI differences between them. They reported decreased grey matter in the frontal and temporal lobes for the Cortical group and decreased grey matter only in the frontal lobe for the Subcortical group.

In 2005, our research group reported finding these three memory profile groups using a K means cluster analysis of the Hopkins Verbal Learning Test scores of 151 subjects participating in a VA vocational work rehabilitation program (Abi-Saab et al. 2005). Proportions were generally similar to those found in the CVLT studies with 42% identified as nearly normal, 38% as having Subcortical profiles and 20% as having Cortical profiles. The nearly normal group had scores on other neuropsychological tests which were generally in the normal range and which were significantly better than the other two groups on most measures. The Subcortical and Cortical groups did not differ significantly from each other but showed different profiles of neurocognitive deficit relative to the nearly normal group, with selective visuospatial/sensori-motor and verbal deficits observed in Subcortical, attentional deficits observed in Cortical, and deficits in executive function and memory common to both groups. There were no significant PANSS score difference or differences in illness characteristics, but both the nearly normal and Subcortical group significantly increased their hours of work activity during the active rehabilitation intervention while the Cortical group did not. This finding suggested that there may be important differences between memory profile groups in their response to a work intervention and that being able to identify membership in these groups based on memory profiles could be useful in rehabilitation planning as well as in furthering our understanding of the heterogeneity of the disorder.

One limitation of studies that identify subgroups through cluster analysis is that it is impractical to use this empirical classification in other studies or in clinical research. However, such cluster analyses could potentially be used as a basis for deriving decision rules for membership, which if simple enough could have general applicability for classifying individuals. Moreover, if these decision rules conform to theoretical requirements for membership, such rules would have the convergent force of both empirical and rational support.

In the present study we undertook to create such decision rules using the HVLT-R scores from an entirely new sample of participants. Unlike our previous study within the VA, the current study recruited outpatients with schizophrenia or schizoaffective disorder from an urban community mental health center which led to greater balance in terms of gender and a greater range of age of onset. We undertook a replication of our earlier K mean cluster findings and, given a successful replication, to derive rules for membership in nearly normal, Subcortical and Cortical memory profile groupings that would also conform to theoretical expectations of those profiles. Namely, membership in the nearly normal group should require having scores within the normal range on key HVLT-R variables including Trial 3 total, delayed recall and recognition discrimination; membership in the Cortical group should require having abnormal scores on all three variables; and membership in the Subcortical group should require that the individual has an abnormal delayed recall score but a normal recognition discrimination score. The validity of these rationally-derived groups could be tested with other neuropsychological measures. Their relative independence from other illness characteristics such as symptoms would add support to their unique contribution to explaining heterogeneity in schizophrenia.

Another important issue in judging the value of this categorization method would be to test its stability over an extended period of time. This is different than test-retest reliability, which is a psychometric property of the instrument. Stability has to do with whether membership in a memory profile group is a trait-like characteristic. The more stable, the more likely it is that it may reflect an enduring feature of brain functioning. Long term stability is of course affected by the test-retest reliability of the instrument, but HVLT-R has passed the rigorous requirements for test-retest reliability for inclusion in the MATRICS battery, and in previous work, we have also found it to be highly reliable (Greig et al. 2004c). It may also be affected over time by deterioration as a consequence of progressive illness, particularly in elderly samples where decline tends to be more rapid.

There have been two previous studies regarding the stability of memory classification in elderly samples. Harvey et al. (2002) used a 10 word list learning task with 239 elderly people with schizophrenia (about 70 years of age) and used theoretically derived criteria to assign them to group membership. In this older population, Cortical classification was most common (37%), 28% were identified as unimpaired, 21% as Subcortical and 7% were unclassified. A word fluency task was also used as a theoretical basis for classification but yielded very different rates with 19% unclassified. There was poor agreement between the memory based and word fluency approaches. One year follow-up indicated that the Cortical group had the best stability (86% same) with good stability for the unimpaired group (72% same), and poor stability for the Subcortical group (50% same). In a second study, the same group (Bowie et al. 2004) used their memory classification procedure with 589 elderly patients (about 76 years of age) and in this study nearly half the patients were classified as Cortical (49%), 35% were Subcortical, and only 5.4% were unimpaired; 10% were unclassified. Follow-up for 243 subjects was between 1 and 8 years (averaged about 3.5 years) and found poorest stability for the Subcortical group with changes consistently in the direction of being reclassified as Cortical. It appears from these two studies that the more elderly the sample, the higher the rates of Cortical classification, and that stability of classification may be affected by decline in performance over time.

The specific aims of the current study were to (1) repeat the cluster analysis in an entirely new sample of subjects recruited from an urban population served by a community mental health center (2) create decision rules for classification based on cluster distributions and expected memory profiles for nearly normal, Subcortical and Cortical memory profiles and determine the concordance between the observed clusters and the rational classification; (3) explore differences among classified groups on demographic features and illness

characteristics and in neurocognitive and social cognitive domains; and (4) determine the stability of the classifications 12 months later.

2. Methods

2.1 Participants

Participants were recruited for a study of vocational rehabilitation and cognitive training and its extension. This is a registered clinical trial (NCT00339170). The inclusion and exclusion criteria and length of intervention were the same for the original study and its extension but there were changes to the vocational services provided and to the cognitive training software, which was updated. In addition the neuropsychological assessment battery was altered in the extension to accommodate the introduction of the MATRICS battery. Participants were outpatients at an urban community mental health center referred by their clinicians because they expressed a desire to receive work services and cognitive training. Inclusion criteria were SCID confirmed diagnosis of schizophrenia or schizoaffective disorder and exclusion criteria were clinical instability defined as hospitalization or emergency room visit within 30 days, homelessness within 30 days, active substance abuse or dependence within 30 days or a history of developmental disability, traumatic brain injury or current neurological disease. The period of recruitment began in 2001 and the extension began in 2007, with 77 participants assessed at intake during the first period and 76 assessed at intake during the second. Two participants had incomplete HVLТ data and were excluded leaving a total of 151. Of these participants, 48 did not have follow-up data either because they had refused the cognitive assessment or had not reached 12 month follow-up at the time of this analysis. Thus, 103 had complete HVLТ data at 12 month follow-up. Demographic and illness characteristics of all participants are presented in Table 1.

2.2 Measures

All participants were administered an extensive neuropsychological assessment that focused on common areas of impairment in schizophrenia spectrum disorders including attention, working memory, visuospatial organization, processing speed, executive function and social cognition. Tests were selected because they had been found to be stable at test and retest (10 week interval) in a schizophrenia population (Greig et al. 2004c). Since some tests used in the original study were replaced by other tests measuring similar constructs in the MATRICS battery, the current analysis was limited to tests that were used in both the original study and its extension.

In addition to the neuropsychological battery, all participants were assessed using the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1989). Total PANSS scores were calculated along with 5 factor derived composite scores: Positive, Negative, Cognitive, Hostility and Emotional Discomfort (Bell et al. 1994).

2.3 Neuropsychological measures

The Hopkins Verbal Learning Test-Revised (HVLТ-R) is a list learning test comprised of 12 words that are orally presented over three immediate recall trials followed by a delayed recall trial at 20 to 30 minutes and a yes/no recognition trial that includes semantically related and unrelated false targets (Brandt and Benedict 2001). Several variables from the HVLТ-R were used including raw scores for trials 1, 2 and 3, delayed recall total and recognition discrimination (recognition minus false positives). These indices are important for distinguishing between impairment in retrieval (with poor free recall but good recognition discrimination) and a primary encoding impairment (with poor free recall and poor recognition discrimination). Published norms for mean age 40 (mean age of the current sample) were used to determine normal performance on these indices.

Neurocognition and social cognition were assessed using a number of instruments. The Wisconsin Card Sorting Test (WCST; Heaton 1981) was used to measure executive functioning. The Digit Span and Letter Number Sequencing subscales of the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler 1997a) were used to assess verbal working memory. Visual motor speed was assessed using the Digit Symbol subscale of the WAIS-III and Trails A time (Reitan and Wolfson 1985). Perceptual Reasoning was measured using the WAIS-III Block Design and WAIS-III Matrix Reasoning scaled scores. Structured verbal memory was measured using Logical Memory I & II scaled scores of the Wechsler Memory Scales-III (WMS-III; Wechsler 1997b). The mental control subscale of the WMS-III was used to measure mental alertness. Verbal fluency was measured by the Animals total raw score of the Controlled Oral Word Association Test (COWAT; Luria 1980). Social cognition was assessed with the North American version (Greig et al. 2004b) of The Hinting Task (Corcoran et al. 1995), the Bell-Lysaker Emotion Recognition Task (BLERT; Bell et al. 1997) and the Egocentricity subscale score of the Bell Object Relation and Reality Testing Inventory (Bell 1995). These three measures have previously been shown to represent a single latent construct of social cognition (Bell et al. 2008a).

2.4 Conditions

After completing intake assessments, participants were randomly assigned to vocational services (VOC) or Neurocognitive Enhancement Therapy (NET) + VOC conditions. Participants in both conditions received identical vocational services (Greig et al. 2004a) but participants in NET + VOC received computer-based cognitive remediation in addition to vocational services. Published reports showing favorable cognitive and vocational outcomes for NET+VOC in the original study are available elsewhere (Bell et al. 2008b; Greig et al. 2007). The extension of the study has involved some changes in the vocational services, an update of the cognitive training software and the introduction of the MATRICS battery, and is on-going. Treatment condition was not considered as a covariate in this analysis of memory profiles because most analyses are performed on intake data before randomization occurred and because there were no significant differences between conditions on HVLT scores in the original study.

2.5 Procedures

After obtaining written informed consent approved by the institutional review board, psychologists and/or master's level research assistants collected demographic information, conducted clinical interviews, and administered neuropsychological tests (at intake and at one year follow-up). Testing was typically completed over the course of several weeks in sixty-minute sessions. Participants were randomly assigned to condition following this complete assessment and were engaged in active rehabilitation activities for 12 months. At 12 months, clinical and neuropsychological assessment procedures were repeated.

2.6 Analysis

HVLT-R scores were checked for their distributional properties using the box-plot function of SPSS (16.0). No cases were identified as extreme outliers based on criteria used in SPSS (i.e. twice the inter-quartile range), thus all data were retained. For aim (1), K means cluster analysis (SPSS 16.0) for three clusters were performed on HVLT variables (Delayed Recall, Recognition Discrimination). The K means cluster algorithm was chosen for three reasons. First, it is simple to implement and interpret. Second, this is the approach used in a previous study, which we sought to replicate (Abi-Saab et al. 2005). Third, the K means algorithm is the most appropriate for our purpose. It is the most commonly used method in data for which the desired number of clusters (K) is decided a priori and extreme groups are desired. For aim (2), rational decision rules were determined based on cluster distributions and expected memory profiles in reference to the norm tables for HVLT. The sensitivity and

specificity of the concordance between cluster membership and the rationally-derived classification was assessed. Overall agreement was measured by Cramer's V and Gamma for ordinal to ordinal comparisons. For aim (3) rationally-derived subgroups were examined for differences in demographic and illness characteristics using chi-square tests for categorical variables and analyses of variance for continuous variables. Neurocognitive and social cognitive variables were grouped by domains and MANOVA's were conducted on these grouped variables. For aim (4), the rationally-derived classification method was applied to HVLT-R data collected at 12 month follow-up and concordance with baseline classification was assessed. All tests were two-tailed with alpha set at .05. Bonferonni post-hoc comparisons were used for all between-groups analyses.

3. Results

3.1 Aim 1: K means cluster

The three groups derived by K means cluster analysis aligned with expected Cortical, Subcortical, and nearly normal memory profiles. The largest cluster ($n = 68$) had a cluster center at 5 for delayed recall and 10 for recognition discrimination. These values are raw scores meaning that 5 out 12 possible words were recalled after 30 minute delay and 10 were recognized after adjusting for false positives. This cluster was labeled Subcortical because these values indicate a pattern of impaired recall but preserved recognition. The second largest cluster ($n = 52$) had a cluster center at 9 for delayed recall and 11 for recognition discrimination. This cluster was labeled Nearly Normal because these values are within the expected range for normal performance. The smallest cluster ($n = 31$) had a cluster center at 4 for delayed recall and 6 for recognition discrimination. This cluster was labeled Cortical because both these values indicate impaired performance. Figure 1 illustrates the performance of these clusters across the three learning trials, at delayed recall and their recognition discrimination score. ANOVA with Bonferonni post-hoc comparisons reveals that the Nearly Normal cluster differs significantly from the other clusters on each HVLT-R variable. The Subcortical cluster differs significantly from the Cortical cluster on Trial 3, delayed recall and recognition discrimination.

3.2 Aim 2: Cluster Group Concordance with rationally-derived groups

The criteria for the decision rules were that they needed to be easy to apply, that they had to be in accord with expected memory profiles, and that they should allow classification of most of the participants. Various combinations and cut-off scores were attempted. The final rules were that the Nearly Normal group must have a) trial 3 score of 8 to 12, b) a delayed recall score of 7 to 12 and c) a recognition discrimination score of 9 to 12. The Cortical group must fail to meet all three rules. Those who do not meet the rules for Nearly Normal or Cortical and have a Delayed Recall score of 0 to 6 and a Recognition score of 9 to 12 would be classified as Subcortical. Application of these rules resulted in 137 of 151 subjects (91%) being classified. Most that were not classified just missed the cut-off, an inevitable occurrence when using decision rules. However, some showed unusual patterns. For example, one subject had a 10 on Trial 3, a 5 on delayed recall and a 7 on recognition. Concordance between clusters and rationally-derived subgroups is presented in Table 2, and shows 90% agreement with good to excellent rates of sensitivity and specificity. Cramer's V was .86 ($p < .000$) and Gamma, which compares the ordinal relationship among the groups, was .99 ($p < .000$). HVLT Profiles are presented in Figure 2. ANOVA with Bonferonni post-hoc comparisons reveals that the Nearly Normal rationally-derived groups differ significantly from the other groups on each HVLT-R variable. The Subcortical group differed significantly from the Cortical group on Trials 1 and Trial 3, and on delayed recall and recognition discrimination. The pattern of means is very similar to that of the cluster groups.

3.3 Aim 3: Differences among rationally-derived groups

Rationally-derived groups were compared on demographic and illness characteristics (Table 1). Education was the only variable that was significantly different with post-hoc comparison showing Nearly Normal>Cortical. Age of onset and the cognitive component of the PANSS showed non-significant trend differences with Nearly Normal>Cortical. Comparisons between groups on neuropsychological variables are presented in Table 3. Nearly Normal>Cortical on all variables except Trails A. Subcortical differed from Cortical only on Verbal Working Memory (Digit Span and Letter Number Sequencing). Nearly Normal>Subcortical on most WCST variables, Letter Number Sequencing, Digit Symbol, Perceptual Reasoning, Story Memory, and Mental Control.

3.4 Aim 4: Stability of classification at 12 month follow-up

Of the 107 participants with follow-up data, 95 were classified at intake into rationally-derived groups. At follow-up 81 of those were successfully classified. Classification stability is presented in Table 4. Specificity for the Nearly Normal group was good; it was fair for the Cortical group and poor for the Subcortical groups. Sensitivity for Nearly Normal and Subcortical groups was fair, and it was poor for Cortical. Total agreement was 65.4%. Cramer's V was .49 ($p < .000$) and Gamma for ordinal by ordinal was .769 ($p < .000$).

4. Discussion

Results replicated the presence of three distinct profiles using cluster analysis. These clusters had HVLT-R mean scores across trials and on delayed recall and recognition discrimination that were very similar to those reported by us previously (Abi-Saab et al. 2005) and that met the definition of Nearly Normal, Subcortical and Cortical memory profiles. Simple decision rules were created using the cluster distributions and the theoretical description of these categories, which produced groupings that showed excellent agreement with cluster membership. Both the sensitivity and specificity of categorization were very good to excellent. Notably, no participant in the Nearly Normal cluster was labeled as Cortical and no participant in the Cortical cluster was labeled as Nearly Normal. Thus the Gamma measure of ordinal association was very high.

One limitation of K means cluster analysis is that it tends to produce high, medium and low groupings, and to some extent the Subcortical group might be seen as the medium group. However, an examination of its HVLT-R profile in Figure 1 shows that the Subcortical group scored comparably to the Cortical group on most variables with a large divergence from the Cortical group on recognition discrimination. Thus, the distinctiveness of this classification relied on a specific pattern of scores rather than just having medium scores across all HVLT-R variables. Still, because it is the in-between group, its members are the most vulnerable to being reclassified in either direction. Thus, the rationally-derived classification rules for the Subcortical group were relatively less sensitive at identifying members of the Subcortical cluster group than was the case for the other rationally-derived groups.

The HVLT-R profile of the rationally-derived groups (Figure 2) is very similar to that of the cluster groups, although the Subcortical group shows slightly more similarity to the Cortical group on all variables except the recognition discrimination score, where it shows even greater divergence from the Cortical group and greater similarity to the Nearly Normal group. These findings strongly suggest that the simple rules created for group membership succeeded in creating groupings that closely matched the cluster groupings and that conform to theoretical expectations on the HVLT-R. Therefore, these simple rules may be useful to other investigators who wish to classify participants for neuroimaging and other studies.

When the rationally-derived groups were compared on demographic and illness characteristics, few differences were found. Education was the only significant variable with Nearly Normal>Cortical. This is a finding in keeping with the theoretical expectation that Nearly Normal members should be generally normal on cognitively related variables, and their educational achievement was consistent with that of their non-mentally ill peers. The significantly lower level of education in the Cortical group is suggestive of greater premorbid cognitive impairment in this group that may have affected school achievement, even though age of illness onset did not differ by group. It is also possible that education may serve as a protective factor against cortical impairment, although this may be less likely.

On the other hand, symptoms did not distinguish groups, except for a trend in the expected direction on the cognitive component of the PANSS. The lack of differences on symptoms is in keeping with many other studies that suggest that symptoms and cognition tend to be semi-autonomous within the range of function covered by our sample, which is one of the reasons to explore neurocognition as a basis for explaining heterogeneity in this disorder. Neurocognitive and social cognitive findings generally supported the validity of the classifications. The Nearly Normal group had scores in the normal range on most variables for which scaled scores were provided, with the notable exception of the Digit Symbol Substitution task. This task is usually regarded as the best general measure of cognitive compromise involving visual-motor ability and processing speed. On the other visual motor task, Trails A (more purely a measure of visual motor speed, involving no memory at all), Nearly Normal does as poorly as the other groups. Thus, as other researchers of this topic have suggested (Wilk et al. 2005), the Nearly Normal group should not be viewed as being without any important cognitive impairment, even if the group performs well on most measures. The Cortical group had the poorest performance on all measures, in keeping with expectations. The Subcortical group did not significantly differ from the Cortical group except on verbal working memory. This finding suggests some greater verbal memory capacity for the Subcortical group, which was reflected in their nearly normal recognition discrimination on the HVLT-R and adds convergent validity to the distinction between this group and the Cortical group, if perhaps uniquely in verbal memory. The social cognitive variables followed the general pattern of Nearly Normal>Cortical with no significant differences between Nearly Normal and Subcortical or between Subcortical and Cortical.

This is the first study to investigate the stability of memory profile membership in a non-elderly sample and found mixed results with best stability in the nearly normal group. Possible sources of variance that reduced stability for Subcortical and Cortical groups include marginal cases, particularly for the Subcortical group, and performance issues such as motivation that may affect performance differentially at two points in time. Nevertheless the specificity at 12 months for the Nearly Normal group is good, indicating that an individual who is so classified at 12 months was very likely to have been in that group at intake. The weaker agreement at 12 months for the other two groups leaves open the possibility that these classifications do not represent a trait-like characteristic and that a simpler classification into nearly normal and impaired may be better for certain types of studies. The two previous studies in elderly samples (Harvey et al. 2002, Bowie et al. 2004) found much higher rates of Cortical classification and found poor stability for the Subcortical group. This was explained by many of the Subcortical patients being reclassified into the Cortical group. We did not find a clear direction of change in our younger sample, but we did find that the Subcortical group was the least stable. Further research is needed into the stability of these memory profiles, since this study is the first to report any findings on this important question in a non-elderly sample.

Overall, results from the current study should encourage other investigators to use HVLT-R scores in the categorical way proposed here. Particularly with the inclusion of HVLT-R in the MATRICS battery, many more investigators may have access to data which could allow for such classifications. In so doing, we may learn whether these categories have neuroanatomical relationships and whether verbal memory profiles characterize an important source of heterogeneity in schizophrenia.

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NN = Nearly Normal, Sub = Subcortical, Cort = Cortical, Norms = T Score of 50 for ages 35 to 44.

Figure 1.

Mean HVLT-R Raw Scores for Cluster Groups Across Trials

NN = Nearly Normal, Sub = Subcortical, Cort = Cortical, Norms = T Score of 50 for ages 35 to 44.

NN = Nearly Normal, Sub = Subcortical, Cort = Cortical, Norms = T Score of 50 for ages 35 to 44.

Figure 2.

Mean HVLt-R Raw Scores for Rationally Derived Groups

NN = Nearly Normal, Sub = Subcortical, Cort = Cortical, Norms = T Score of 50 for ages 35 to 44.

Table 1

Participants Characteristics

	All Subjects In Cluster (n=151)	NN (n=54)	Sub (n=55)	Cort (n=28)
	n (%)	n (%)	n (%)	n (%)
GENDER				
Male	89 (58.9)	32 (59.3)	29 (52.7)	18 (64.3)
Female	62 (41.1)	22 (40.7)	26 (47.3)	10 (35.7)
ETHNICITY				
African American	82 (54.3)	25 (46.3)	32 (58.2)	20 (71.4)
Asian	1 (0.7)	1 (1.9)	0 (0)	0 (0)
Caucasian	63 (41.7)	26 (48.1)	21 (38.2)	7 (25.0)
Hispanic	2 (1.4)	1 (1.9)	1 (1.8)	0 (0)
Other	3 (2.0)	1 (1.9)	1 (1.8)	1 (3.6)
SCHIZOPHRENIA DIAGNOSIS				
Disorganized	6 (4.0)	2 (3.7)	3 (5.5)	1 (3.6)
Paranoid	77 (51.0)	26 (48.1)	27 (49.1)	19 (67.9)
Residual	15 (9.9)	3 (5.6)	7 (12.7)	1 (3.6)
Undifferentiated	16 (10.6)	6 (11.1)	5 (9.1)	3 (10.7)
Schizoaffective	36 (23.8)	17 (31.5)	12 (21.8)	4 (14.3)
<i>Psychosis Disorder NOS</i>	1 (0.7)	0 (0)	1 (1.8)	0 (0)
MEDICATIONS				
Atypical	97 (64.2)	34 (63.0)	34 (61.8)	18 (64.3)
Conventional	25 (16.6)	10 (18.5)	10 (18.2)	3 (10.7)
Both	19 (12.6)	6 (11.1)	7 (12.7)	6 (21.4)
None	10 (6.6)	4 (7.4)	4 (7.3)	1 (3.6)

	All Subjects	NN	Sub	Cort
	MEAN (SD)	MEAN (SD)	MEAN (SD)	MEAN (SD)
AGE	40.95 (9.8)	41.20 (9.0)	41.24 (9.8)	39.43 (10.4)
EDUCATION	12.70 (2.4)	13.28 (2.9) *	12.49 (2.0)	11.86 (1.6) *
AGE AT 1st HOSP	22.96 (9.3)	24.37 (9.6)	23.02 (6.5)	19.68 (10.2)
LIFETIME # HOSP	8.70 (10.0)	9.75 (12.2)	8.65 (8.6)	8.63 (10.4)
PANSS				
Total	70.85 (16.3)	68.74 (16.0)	71.62 (17.4)	74.25 (13.3)
Positive	16.55 (5.3)	16.49 (5.9)	17.04 (4.9)	16.46 (4.9)
Negative	17.77 (7.0)	16.58 (6.7)	17.40 (6.9)	19.96 (7.3)
Cognitive	17.56 (4.8)	16.32 (4.5)	18.00 (5.6)	18.68 (3.5)
Hostility	7.56 (3.0)	7.45 (2.9)	8.11 (3.4)	7.61 (2.6)
Emotional Discomfort	9.97 (3.7)	10.49 (4.1)	9.56 (3.3)	10.07 (3.4)

* .05 significance in Education NN vs Cort

Table 2

Concordance between Cluster Groups and Rationally-derived groups

Cluster Groups				
Rationally-derived	Nearly Normal	Subcortical	Cortical	Specificity
Nearly Normal	47	7	0	87%
Subcortical	3	51	1	93%
Cortical	0	3	25	89%
Sensitivity	94%	84%	89%	Total Agreement 90%

Table 3

Neurocognitive and social cognitive differences between rationally-derived groups

	Nearly Normal (n = 54)	Subcortical (n = 55)	Cortical (n = 28)	F	P	Bonferroni Post-Hoc Comparisons
<i>Executive Functioning</i>						
WCST				1.81	.046	
# Items	108.3 (23.3)	118.0 (17.1)	120.5 (15.7)	4.93	.009	NN>Sub; NN>Cor
%Errors Scaled	90.8 (18.0)	80.4 (17.1)	76.4 (17.1)	7.52	.001	NN>Sub; NN>Cor
% Persev Resp Scaled	93.2 (21.1)	82.0 (19.6)	77.9 (18.7)	6.87	.001	NN>Sub; NN>Cor
% Non-persev Err Scaled	91.2 (16.3)	89.6 (17.7)	87.4 (18.0)	.478	.621	ns
% Concept Level Scaled	90.6 (18.1)	80.0 (16.9)	76.0 (17.9)	8.0	.001	NN>Sub; NN>Cor
Trials to First Category	22.3 (23.8)	39.5 (44.8)	57.6 (52.2)	7.5	.001	NN>Cor;
<i>Verbal Working Mem</i>				7.4	.000	
Dig Span Scaled	9.5 (2.4)	8.6 (2.8)	7.1 (2.0)	8.6	.000	NN>Cor; Sub>Cor
Let/Num Seq Scaled	9.1 (2.84)	7.3 (3.1)	5.4 (2.5)	15.5	.000	NN>Cor; NN>Sub; Sub>Cor
<i>Visual Motor Speed</i>				2.3	.052	
Dig Symbol Coding Scaled	6.8 (2.4)	5.8 (1.9)	5.8 (2.4)	3.6	.03	NN>Sub
Trails A Time	38.4 (15.2)	43.6 (21.6)	48.7 (25.6)	2.5	.09	ns
<i>Perceptual Reasoning</i>				6.5	.000	
Block Design Scaled	9.4 (2.7)	7.9 (2.9)	7.3 (2.6)	5.5	.005	NN>Sub; NN>Cor
Matrix Reasoning Scaled	10.6 (3.3)	8.0 (2.9)	7.3 (2.6)	14.4	.000	NN>Sub; NN>Cor
<i>Structured Verbal Memory</i>				7.8	.000	
WMS Logical Mem 1 Scaled	9.1 (2.8)	7.1 (2.9)	5.6 (3.1)	15.2	.000	NN>Sub; NN>Cor
WMS Logical Mem 2 Scaled	10.2 (2.6)	8.1 (2.7)	7.0 (3.1)	15.4	.000	NN>Sub; NN>Cor
<i>Verbal Fluency</i>						
VF 1 Animals	17.6 (4.7)	16.4 (4.7)	14.6 (5.0)	3.6	.029	NN>Cor
<i>Mental Control</i>						
Mental Control Scaled	8.9 (3.1)	7.09 (2.9)	6.3 (2.0)	.68	.509	NN>Sub; NN>Cor
<i>Social Cognition</i>				2.9	.009	
Hinting	17.22 (2.1)	16.2 (3.6)	15.4 (3.2)	3.6	.029	NN>Cor
BORRTI Egocentricity	.35 (.92)	.53 (.94)	.93 (.85)	3.7	.028	NN>Cor

	Nearly Normal (n = 54)	Subcortical (n = 55)	Cortical (n = 28)	F	P	Bonferroni Post-Hoc Comparisons
BLERT	14.8 (3.5)	13.3 (4.2)	12.1 (3.0)	5.7	.004	NN>Cor

Table 4

Concordance of rationally-derived group membership at Intake and 12-month follow-up

Intake Group Membership				
Follow-up Group Membership	Nearly Normal	Subcortical	Cortical	Specificity
Nearly Normal	28	4	2	82.4%
Subcortical	11	15	7	45.5%
Cortical	2	2	10	71.4%
Sensitivity	68.3%	71.4%	52.6%	Total Agreement 65.4%