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# Cognitive Profiles in Persons with Chronic Schizophrenia

**Sharron E. Dawes**[1], **Dilip V. Jeste**[1], and **Barton W. Palmer**[1]
[1]University of California, San Diego, Department of Psychiatry, La Jolla, CA

## Abstract

Cognitive heterogeneity has been a key barrier to clarifying the neuropathologic underpinnings of schizophrenia. We used an idiographic method for cluster analysis of neuropsychological data from 144 middle-aged and older people with schizophrenia to characterize and group the patterns of relative (within-person) profiles of cognitive strength and weakness. Results indicated a 5-cluster solution as most appropriate, with relatively even distribution across the five clusters in terms of the proportion of patients in each cluster. Cognitive subtyping may be useful in imaging and genetic research on schizophrenia, as well as having practical utility in treatment planning and cognitive rehabilitation.

## INTRODUCTION

There has been considerable research within the schizophrenia literature focused on describing the configuration of neuropsychological impairment (reviewed in Palmer, Dawes, & Heaton, 2009). However, the considerable heterogeneity among persons with schizophrenia in overall severity of cognitive deficits has hampered efforts to identify specific differential or “core” cognitive deficits (Dickinson, Ragland, Gold, & Gur, 2008; Dickinson, Ramsey, & Gold, 2007). There have been numerous attempts to identify more homogeneous cognitive subtypes using cluster analyses (e.g., Allen et al., 1998; Goldstein, Allen, & Seaton, 1998; Heinrichs & Awad, 1993; Hill, Ragland, Gur, & Gur, 2002; Horan & Goldstein, 2003; Seaton, Allen, Goldstein, Kelley, & van Kammen, 1999). Such studies generally reveal four to five clusters of schizophrenia patients, including a high functioning (neuropsychologically normal) cluster, a severely impaired cluster, and two or three intermediate clusters of patients with schizophrenia (reviewed in Palmer et al., 2009). However, the nature of the cluster analytic methods employed is such that they yield clusters for which the most reliable-consistent differences across studies are those emphasizing level of impairment, rather than specific profiles among those in the intermediate range. Many of these studies use analytic measures such as Ward’s to determine the cluster groupings (e.g., Allen et al., 1998; Heinrichs & Awad, 1993; Hill et al., 2002). Although differences in level of performance may simply reflect general severity of illness, they are helpful for some practitioners evaluating abilities, for example, ability to work (Green, Kern, Braff, & Mintz, 2000; Kurtz, 2006). However, clusters based on within-person patterns of deficits may be more helpful in identifying “differences in kind” and thereby help elucidate meaningful neurobiologic subtypes of schizophrenia (Lange, Iverson, Senior, & Chelune, 2002).

An alternative to the standard way of applying cluster analytic methods is an idiographic approach whereby an individual’s performance on each test is expressed in reference to his or her overall test performance (Lange et al., 2002). Doing so permits an evaluation focused on differences in pattern, rather than differences in level or magnitude, and thereby provides

Address correspondence to: Barton W. Palmer, Professor of Psychiatry, University of California, San Diego, 9500 Gilman Drive 0603V, La Jolla, CA 92093 - 0603, bpalmer@ucsd.edu, Telephone: 858-642-3907, Fax: 858-642-3425.

a complementary form of information to that yielded from the more common cluster analytic methods. This idiographic approach levels all people's performances and allows the cluster analysis to develop clusters based on specific relative strengths and relative weakness based on the derived test scores of each individual. One of the well documented neuropsychological aspects of schizophrenia is the considerable inter-patient heterogeneity in terms of level of cognitive functioning (Palmer et al., 2009). The degree to which specific cognitive domains have been affected by schizophrenia in any two patients could conceivably be identical, reflecting the same pattern of spared versus affected brain systems underlying those domains, but if the overall level of functioning is not the same, then the similarity of the two patients could be readily overlooked. The idiographic approach permits identification of patients with similar patterns of relative strength and weakness. This method has proven useful in identifying cognitive subgroups among people with HIV-related cognitive impairment (Dawes et al., 2008), but to our knowledge there have been no published studies applying this method in schizophrenia research.

In the present study we applied a two-step cluster procedure to neuropsychological data from middle-aged and older patients with schizophrenia to determine if there were subgroups of persons with schizophrenia with more homogenous profiles of cognitive impairment based on relative strengths and weaknesses. Our research group has previously reported factor analyses of a larger neurocognitive battery in schizophrenia (Gladsjo et al., 2004), as well as a more recent study focused on the factor structure of a large battery of tests specifically within the domain of executive functions (Savla, Twamley, Delis, et al., 2010). However, those studies were focused on identifying meaningful groupings of cognitive tests; the present study (based on a sample independent from the other studies) is focused on identifying cognitive groupings patients. We also examined differences among identified clusters in terms of demographic characteristics and severity and type of psychopathologic symptoms, to assess for other causes of these neuropsychological profiles. As there were no a priori hypotheses about the number or type of neuropsychological patterns of performance that would be determined, the main aims of this study were to explore the nature of neuropsychological patterns of relative strengths and weaknesses in performance within a group of people with schizophrenia and then to ascertain how much the patterns differed with regard to demographic and psychiatric markers.

## METHOD

### Participants

Participants were 144 outpatient middle-aged and older (current age > 40 years) patients with schizophrenia or schizoaffective disorder. The issue of cognitive heterogeneity is not limited to middle-aged and older patients, but these data were originally collected through the University of California, San Diego (UCSD) Advanced Center for Innovation in Services and Interventions Research (ACISIR) as part of studies on capacity to consent to treatment or research among middle-aged and older persons with psychotic disorders. Although some of the subjects have provided neurocognitive data in prior reports (Palmer, Dunn, Appelbaum, & Jeste, 2004; Palmer, Dunn, Depp, Eyler, & Jeste, 2007; Palmer & Jeste, 2006), the focus of those reports was on the association of level of cognitive scores to decisional capacity, whereas the present analyses are focused on the identification of cognitive profile subtypes.

Participants were recruited from a number of outpatient settings including UCSD Psychiatry Services, the Veterans Affairs San Diego Healthcare System Psychiatry Service, referrals from individual psychiatrists and physicians, and direct recruitment at San Diego–area assisted living facilities ("board-and-care" homes). Sixty-three percent of the participants were living in Board and Care homes at the time of evaluation. Inclusion criteria were (a)

DSM-IV diagnosis of schizophrenia or schizoaffective disorder (as determined by the participant's clinical care providers), (b) current age > 40 years, (c) fluency in English, (d) currently prescribed an FDA-approved "atypical" antipsychotic medication, and (e) written informed consent for participation (with the consent form reviewed and approved by the UCSD IRB). Exclusion criteria were: (a) known DSM-IV diagnosis of dementia or other medical conditions likely to influence neurocognitive functioning and (b) any medical or physical ailmentspreventing completion of the study assessments. As the analyses used in the present study require complete data for each case, we excluded 58 potential participants from the larger database who were missing more than one of the measures in the neuropsychological test battery. Imputation of scores was therefore minimized to less than 5% of scores while allowing an increased number of available participants for the study. This 5% rule is recommended for scales that are part of a multiscale battery (DiLalla & Dollinger, 2006). There were no significant differences between the 58 excluded versus 144 included participants in terms of age (included: Mean =51.6, SD=6.8; excluded : Mean=53.4, SD=8.6, p=.13), education (included: Mean =12.1, SD=2.5; excluded : Mean =12.1, SD=2.4, p=.87), gender (Mann-Whitney U = 3733, p=.28), ethnicity (Mann-Whitney U = 3978, p=.78), type of medication (Mann-Whitney U = 4463, p=.38) or severity of psychiatric symptoms (measured with the scales described below, all ps>.05 ).

## Demographics and Psychiatric Measures

Participant's age, education, sex, and ethnicity were determined via self-report and/or (with participant authorization) via review of available records. Severity of participants' psychiatric symptoms was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). Severity of depressive symptoms was evaluated in a subset of participants (n=95) with the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1967).

## Neuropsychological Measures

Subjects completed a comprehensive neuropsychological test battery that included the following measures and ability areas (for those tests which yield multiple scores, the scores used in present analyses are indicated parenthetically):

1. Verbal Comprehension: Vocabulary, Similarities, and Information subtests from the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 1997b)
2. Perceptual Organization: WAIS-III Picture Completion, Block Design, and Matrix Reasoning subtests
3. Attention/Working Memory: WAIS-III Arithmetic, Digit Span, and Letter-Number Sequencing subtests
4. Processing Speed: WAIS-III Digit Symbol and Symbol Search subtests, Trail Making Test Part A (seconds to complete; Reitan & Wolfson, 1993), Letter and Category Fluency (total correct FAS and total correct animals; Heaton, Miller, Taylor, & Grant, 2004)
5. Abstraction/Cognitive Flexibility: Wisconsin Card Sorting Test–64 Card Version (WCST-64, conceptual level responses; Kongs, Thompson, Iverson, & Heaton, 2000), Stroop Color Word Interference Test (Color Word Interference Trial, total correct; Golden & Freshwater, 2002) and Trail-Making Test Part B (seconds to complete)
6. Auditory Learning and Memory: Story Memory Test (learning and memory scores; Heaton et al., 2004), Hopkins Verbal Learning Test–Revised (HVLT-R, total

correct learning trials 1-3, and total correct delayed recall; Brandt & Benedict, 2001)

7. Visual Learning and Memory: Brief Visual-Spatial Memory Test–Revised (BVMT-R, total correct trials 1-3, and total correct delayed recall; Benedict (BVMT-R, total correct trials 1-3, and total correct delayed recall; Benedict, 1997), and Family Pictures subtests (immediate and delayed recall) from the Wechsler Memory Scale–Third Edition (WMS-III; Wechsler, 1997a).

The tests were split into the seven cognitive ability areas based on prior factor analyses of these or similar tests (Gladsjo et al., 2004; Tulsky & Price, 2003), and largely overlap with those identified by an expert consensus panel, convened as part of the NIH-sponsored MATRICS project, to be relevant to characterizing the cognitive deficits associated with schizophrenia (Nuechterlein et al., 2008).

## Statistics

Cluster analysis becomes increasingly vulnerable to producing clusters with questionable origins with increasing numbers of dependent variables (Everitt, 1974). Therefore, to reduce the number of scores used, domain scores were calculated based on the seven predetermined cognitive ability areas listed above. We did this by converting all raw scores from the tests to demographically corrected T-scores (mean = 50, SD = 10) using the standard published normative data for each test. [The standard published normative data for the HVLT-R and BVMT-R adjust only for age (Benedict, 1997; Brandt & Benedict, 2001), those for the other tests adjust for age, education, and in some cases gender and ethnicity (Heaton et al., 2004; Kongs et al., 2000; Taylor & Heaton, 2001).]

We imputed missing test scores (<5% of test scores or equivalent to no more than one missing score per participant) using regression equations based on the other scores in the domain for the current sample (i.e., the participant's available demographically adjusted T-scores were used to impute missing T-scores.) Imputation by regression is a common way of handling randomly occurring missing data (Allison, 2002). The Mean Overall T-score was then calculated based on averaging the T-scores across all of the seven domains for that particular individual. We then computed deviation scores for each of the individual subtests (Test deviation score = individual Test T- score - Mean Overall T-score) for each participant. Then we calculated the average domain deviation score by summing all of the individual test deviation scores in a given domain and dividing that sum by the number of tests in the domain for each individual. We used these domain deviation scores as the basis for the analyses.

The domain deviation scores were submitted to a 2-part cluster analysis using MATLAB R2007b. The first part is a hierarchical cluster analysis used to determine the number of clusters, and the second K-means is an iterative cluster analysis used to determine cluster membership. We used the hierarchical cluster analysis (similarity metric: Pearson correlation; distance metric: squared Euclidean distance) to determine the number of clusters by appraising the inverse scree plot and the dendrogram. According to Lange et al. (2002), hierarchical analysis is the best method for determining the number of clusters present in a data set, but because it does not allow movement of cases between clusters once they are allocated, it is not good at determining final membership. The inverse scree plot is interpreted like the scree plot in factor analysis, where a change in slope indicates the number of clusters, with the dendrogram indicating the likely number of clusters, shown as a natural "break" in the graph. The final likely number of clusters was then entered into the K-Means analysis method because K-means is better at determining final cluster membership, as it allows movement of cases between clusters throughout the iterative process. These clusters should therefore be more stable and cohesive (Lange et al., 2002). Using the

Statistical Package for Social Sciences (SPSS) version 12.0.1, we examined the clusters for differences in demographic composition, measures of psychopathology, and overall level of neuropsychological functioning. For continuous variables these comparisons were conducted with a series of one-way analyses of variance (ANOVAs) with Sheffe post-hoc comparisons for those tests in which the omnibus comparison was significant). Categorical variables were compared with Pearson Chi-square tests with post-hoc pairwise comparisons using Ryan's procedure (Linton & Gallo, 1975). Significance was defined as $p<.05$ (two-tailed).

## RESULTS

### Demographic and clinical characteristics

The mean age of the sample was 51.6 (SD = 6.8; range = 40 to 70) years, and mean education was 12.2 (SD=2.4; range = 4 to 18 years). Ethnic background included 62% Caucasian, 21% African American, 12% Hispanic/Latino, 2% Asian-American, and 3% other ethnic backgrounds. Psychopathological symptoms were generally mild in nature (HAM-D: mean = 8.9, SD = 6.1; PANNS-Positive: mean = 13.6, SD = 5.5; PANNS-Negative mean = 13.3, SD = 5.2; PANNS-General: mean = 26.2, SD = 6.6). Using the categories for describing T-score ranges suggested by Heaton et al. (2004), T-scores generally fell within the "mild to moderately" impaired range (mean = 38.3, SD = 6.7) but among the individual participants the mean T-scores ranged from T=25 ("moderately impaired") to T=62 ("above average"). Age of onset was not available for all subjects, but for those (N=119) for whom it was available either via self-report or records review, the mean age of onset was 27.1 years (SD = 9.9), and duration of illness ranged from 4 to 54 years.

### Cognitive clusters

After calculating and submitting the domain scores to the hierarchical cluster analysis, two- to twelve-cluster solutions were plausible based on inspection of the inverse scree plot and dendrogram (i.e. tree diagram indicating the arrangement of clusters). However, a five-cluster solution was determined to be most appropriate and was sought with random seed points (i.e., random points in space from where the clusters start to be grouped) from the K-Means analysis. Although the silhouette plot (i.e., a plot showing how independent the clusters are) indicated some cluster overlap based on their centroids (i.e., the mean scores for the cluster; see Table 1 for mean domain T-scores for each cluster), there were no significant positive correlations between the clusters (all ps >.05, not reported here), indicating relative independence between cluster outcomes. The centroids presented in Table 1 are mean domain T-scores, with relative strengths and weaknesses (being more than five points above or below the overall mean T-score across all seven domains) being highlighted.

As shown in Table 1, Profile 1 (n=19) showed relative weakness in the area of Visual Learning and Memory. Profile 2 (n=38) showed relative strengths in Verbal Comprehension and Processing Speed but relatively poor Auditory and Visual Learning and Memory, and Abstraction/Cognitive Flexibility, whereas participants with Profile 3 (n=40) presented with only relative weaknesses in Abstraction/Cognitive Flexibility. The remaining two profiles indicate that both Profile 4 (n=17) and Profile 5 (n=30) have a relative strength in Verbal Comprehension and Visual Learning & Memory with a relative weakness in Abstraction/ Cognitive Flexibility, but whereas Profile 4 has an additional relative weakness in Auditory Learning & Memory, Profile 5 has a relative weaknesses in Visual Learning & Memory.

We also completed a series of ANOVAs and Chi-square analyses to assess if the clusters differed with respect to demographics or severity of depressive, positive, negative, or

general psychiatric symptoms (shown in Table 2). No significant cluster group differences were found on age, gender, or severity of positive, negative, or general psychiatric symptoms. The only significant differences among the clusters were in reported level of education and ethnicity (percent Caucasian) distribution (both p values ≤ .001). Participants in K5 were more educated than participants in K1, K2 and K3, and there was a larger proportion of Caucasians K1, K3, and K4. The HAM-D scores indicated that there was a main difference between the clusters on the number of depressive symptoms endorsed, but post-hoc analyses did not show any differences between the clusters when evaluated on a pair-wise basis.

## DISCUSSION

We found five relatively independent cognitive clusters (or profiles) of patients with schizophrenia. In addition, the solution was reasonably replicated using the two cluster methods (i.e., we found positive correlations between the cluster solutions found by the two differing methods of analysis). These ideographic cognitive profiles did not appear to have any major associations related to age, gender, or level of positive, negative, or general psychiatric symptoms, but Profile 5 (relative strength in verbal abilities and relative weaknesses in abstraction/cognitive flexibility executive functions and visual learning and memory) contained a larger percentage of Caucasians and was better educated than the other clusters. Profile 5 contained approximately 21% of the sample. To our knowledge, this is the first study to assess the patterns of neuropsychological performance in people with schizophrenia based on relative strengths and weaknesses rather than the magnitude of their performance, and thus gives a complementary perspective to the cognitive subtyping in schizophrenia relative to those observed with the more common cluster analytic approaches (focused on absolute magnitude of deficits relative to normative values).

Given the long standing interest in impaired executive functions in schizophrenia (Zec, 1995), it was notable that the one domain that emerged as the most consistent relative weakness across clusters was Abstraction/Cognitive Flexibility, which was a relative weakness in four of the five clusters. Executive functioning deficits are often touted as one of the main neuropsychological deficits in schizophrenia (Palmer & Heaton, 2000; Velligan & Bow-Thomas, 1999; Wobrock et al., 2008). On the other hand, there was one cluster, consisting of 14% of the sample, that did not display a relative weakness in Abstraction/ Cognitive Flexibility. Indeed, for this particular cluster (Profile 1), the average T- score for Abstraction/Cognitive Flexibility (T=41) was one of the higher scores in this profile and fell within what Heaton et al. (2004) label the “average range” of functioning. So, even with these abilities as representatives of “executive functions,” it cannot be said that they are invariably differentially impaired in schizophrenia.

Of the other abilities, none of the profiles was characterized by relative weaknesses in Verbal Comprehension, Perceptual Organization, Attention/Working Memory, and Processing Speed. The finding in regard to Verbal Comprehension is expected given the heavy emphasis on crystallized verbal knowledge among the tests in this domain. (Indeed, almost one third of the sample [Profiles 4 and 5] had a relative strength in Verbal Comprehension.) However, the lack of relative weakness in Attention/Working Memory and in Processing Speed is noteworthy given suggestions that these abilities may contribute to deficits in other domains (Dickinson et al., 2007; Goldman-Rakic, 1994; Kern et al., 2011). On the other hand, a deficit in a particular domain may be more central/important without necessarily being more impaired, i.e., depending on where the ability falls within a causal chain among various dimensions of the disorder (Palmer et al., 2010).

Because the focus of the original studies from which these data were drawn was on middle-aged and older outpatients, it is possible that the present findings would not readily generalize to younger adults with schizophrenia. On the other hand, the present analyses were based on scores that had been adjusted for normal age-effects using standard published norms, and neither age nor duration of illness have been found to be correlated with severity of cognitive impairment among non-institutionalized persons with schizophrenia (Heaton et al., 2001; Kurtz, 2005). Therefore, it seems unlikely that age alone would strongly bias the present findings.

Another potential limitation of the present study is that diagnostic status was determined through the participants' treating clinical care providers, rather than being confirmed with the Structured Clinical Interview for the DSM-IV (First, Spitzer, & Gibbon, 2002) or similar standardized method. Thus it is possible that some of the participants would have met criteria for another schizophrenia-spectrum or psychotic disorder. We also had no systematic data on clinical subtypes, so the degree to which the cognitive profiles may co-vary with clinical subtypes was not empirically evaluated. On the other hand, the limited validity of traditional clinical subtypes is well documented (Carpenter & Stephens, 1979), and these subtypes are to be eliminated in the forthcoming DSM-V (Miller & Holden, 2010).

Another consideration is that the clusters identified may be affected by the specific tests used to operationalize the cognitive domains. For instance, recent findings from our research group based on an independent sample (Savla, Twamley, Delis, et al., 2010; Savla, Twamley, Thompson, et al., 2010) suggest that the mental flexibility and abstraction components of executive function may be at least partially independent, and that severity of deficits on some mental flexibility tasks may be more common than among others. Those findings were based on a large battery of executive function tests designed to permit distinguishing different aspects of executive function, whereas the present battery did not include sufficient numbers of tests of each type of executive function to examine those two types separately.

It is also noted that there were no chronically institutionalized patients in the study, but 63% were in assisted living (i.e., Board and Care homes) at the time of evaluation. Prior data from our research center has shown that chronically institutionalized patients have worse cognitive functioning than community dwelling patients (Evans et al., 1999), but among community dwelling patients, those in assisted living/Board and Care homes tend to have worse cognitive deficits than those living independently (Auslander et al., 2001). The focus of the present study was on patterns/profiles of cognitive strengths and weaknesses, rather than level, but further research with larger subsamples of persons living in various levels of care would be helpful to determine if the present patterns replicate equally across the full range of such settings.

The present study is based on cross-sectional data, but in future research it would also be useful to determine the natural stability of these subtype groupings as well as clinical and intervention factors that may affect that stability. The finding that the patients in the fifth cluster (Profile 5) had higher levels of education and were more likely to be Caucasian raises the possibility that patterns of relative impairment could be affected by non-biologic factors. Future studies should consider use of imaging or EEG to determine the degree to which the subtype patterns correspond to differences in other indicators of brain function, as well as exploring the degree to which these patterns predict specific deficits or strengths in various aspects of everyday functioning. For example, the first cluster (Profile 1) was characterized by a relative weakness in Visual Learning & Memory. The mean T-score for Auditory Learning & Memory in Profile 1 did not meet our *a priori* criterion for identification as relative weakness, but it was the second (relative) lowest cognitive domain in the cluster.

There was no indication in Profile 1 of a relative weakness in Abstraction/Cognitive Flexibility, but the latter did emerge as at least one of the relative weaknesses in the other four clusters. It would be interesting to use EEG and neuroimaging to explore whether the pattern of temporal/hippocampal versus prefrontal function or structure for patients in this cluster differs systematically from that of patients in the other four clusters. Through such follow-up research, the approach employed in the present study, focused on relative (within-person) cognitive strengths and weaknesses, may prove helpful in identifying subgroups of patients with more neurobiologic homogeneity than has been observed when defined solely by absolute level of performance.

In short, although future research would be helpful to replicate and extend the present findings, our results establishing five relatively independent clusters of neuropsychological performance in those with schizophrenia are important in demonstrating the possibility of more homogenous cognitive subgroups, and are an alternative to other methods which focus on absolutely level of performance. If replicated, use of such subtypes may prove useful in tailoring rehabilitation efforts to the person's strengths to gain more benefit to the person, guiding neuroimaging studies by pinpointing particular areas to focus on in the search for a neurobiological underpinning of the disease, or even assisting in identifying biological subtypes of schizophrenia.

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## References

Allen DN, Huegel SG, Seaton BE, Goldstein G, Gurklis JA Jr, van Kammen DP. Confirmatory factor analysis of the wais-r in patients with schizophrenia. Schizophrenia Research. 1998; 34(1–2):87–94. [PubMed: 9824880]

Allison, PD. Missing data. Thousand Oaks, CA: Sage Publications Inc; 2002.

Auslander LA, Lindamer LL, Delapena J, Harless K, Polichar D, Patterson TL, Jeste DV. A comparison of community-dwelling older schizophrenia patients by residential status. Acta Psychiatrica Scandinavica. 2001; 103(5):380–386. [PubMed: 11380308]

Benedict, R. Brief visuospatial memory test-revised. Professional manual. Odessa, FL: Psychological Assessment Resources, Inc; 1997.

Brandt, J.; Benedict, RH. Hopkins verbal learning test-revised. Professional manual. Lutz, FL: Psychological Assessment Resources, Inc; 2001.

Carpenter WT Jr, Stephens JH. An attempted integration of information relevant to schizophrenic subtypes. Schizophrenia Bulletin. 1979; 5(3):490–506. [PubMed: 482882]

Dawes S, Suarez P, Casey CY, Cherner M, Marcotte TD, Letendre S, Heaton RK. Variable patterns of neuropsychological performance in hiv-1 infection. Journal of Clinical and Experimental Neuropsychology. 2008; 30(6):613–626. [PubMed: 18608689]

Dickinson D, Ragland JD, Gold JM, Gur RC. General and specific cognitive deficits in schizophrenia: Goliath defeats david? Biological Psychiatry. 2008; 64(9):823–827. [PubMed: 18472089]

Dickinson D, Ramsey ME, Gold JM. Overlooking the obvious: A meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. Archives of General Psychiatry. 2007; 64(5):532–542. [PubMed: 17485605]

DiLalla, DL.; Dollinger, SJ. Cleaning up data and running preliminary analyses. In: Leong, FTL.; Austin, JT., editors. The psychology research handbook: A guide for graduate students and research assistants. 2. Thousand Oaks, CA: Sage Publications, Inc; 2006.

Evans JD, Negron AE, Palmer BW, Paulsen JS, Heaton RK, Jeste DV. Cognitive deficits and psychopathology in institutionalized versus community-dwelling elderly schizophrenia patients. Journal of Geriatric Psychiatry and Neurology. 1999; 12(1):11–15. [PubMed: 10447149]

Everitt, B. Cluster analysis. New York: Wiley; 1974.

First, MB.; Spitzer, RL.; Gibbon, M. Structured clinical interview for dsm-iv-tr axis i disorders, research version, patient edition with psychotic screen (scid-i/p w/psy screen). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

Gladsjo JA, McAdams LA, Palmer BW, Moore DJ, Jeste DV, Heaton RK. A six-factor model of cognition in schizophrenia and related psychotic disorders: Relationships with clinical symptoms and functional capacity. Schizophrenia Bulletin. 2004; 30(4):739–754. [PubMed: 15957196]

Golden, CJ.; Freshwater, SM. Stroop color and word test: A manual for clinical and experimental uses. 2. Wood Dale, IL: Stoelting Co; 2002.

Goldman-Rakic PS. Working memory dysfunction in schizophrenia. Journal of Neuropsychiatry and Clinical Neurosciences. 1994; 6(4):348–357. [PubMed: 7841806]

Goldstein G, Allen DN, Seaton BE. A comparison of clustering solutions for cognitive heterogeneity in schizophrenia. Journal of the International Neuropsychological Society. 1998; 4(4):353–362. [PubMed: 9656609]

Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the “right stuff”? Schizophrenia Bulletin. 2000; 26(1):119–136. [PubMed: 10755673]

Hamilton M. Development of a rating scale for primary depressive illness. British Journal of Social and Clinical Psychology. 1967; 6(4):278–296. [PubMed: 6080235]

Heaton RK, Gladsjo JA, Palmer BW, Kuck J, Marcotte TD, Jeste DV. The stability and course of neuropsychological deficits in schizophrenia. Archives of General Psychiatry. 2001; 58(1):24–32. [PubMed: 11146755]

Heaton, RK.; Miller, W.; Taylor, MJ.; Grant, I. Professional manual. Lutz, FL: Psychological Assessment Resources, Inc; 2004. Revised comprehensive norms for an expanded halstead-reitan battery: Demographically adjusted norms for african american and caucasian adults.

Heinrichs RW, Awad AG. Neurocognitive subtypes of chronic schizophrenia. Schizophrenia Research. 1993; 9(1):49–58. [PubMed: 8096391]

Hill SK, Ragland JD, Gur RC, Gur RE. Neuropsychological profiles delineate distinct profiles of schizophrenia, an interaction between memory and executive function, and uneven distribution of clinical subtypes. Journal of Clinical and Experimental Neuropsychology. 2002; 24(6):765–780. [Article]. [PubMed: 12424651]

Horan WP, Goldstein G. A retrospective study of premorbid ability and aging differences in cognitive clusters of schizophrenia. Psychiatry Research. 2003; 118(3):209–221. [PubMed: 12834815]

Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (panss) for schizophrenia. Schizophrenia Bulletin. 1987; 13(2):261–276. [PubMed: 3616518]

Kern RS, Gold JM, Dickinson D, Green MF, Nuechterlein KH, Baade LE, Marder SR. The mccb impairment profile for schizophrenia outpatients: Results from the matrics psychometric and standardization study. Schizophrenia Research. 2011; 126(1–3):124–131. [PubMed: 21159492]

Kongs, SK.; Thompson, LL.; Iverson, GL.; Heaton, RK. Professional manual. Odessa, FL: Psychological Assessment Resources, Inc; 2000. Wisconsin card sorting test-64 card version.

Kurtz MM. Neurocognitive impairment across the lifespan in schizophrenia: An update. Schizophrenia Research. 2005; 74(1):15–26. [PubMed: 15694750]

Kurtz MM. Symptoms versus neurocognitive skills as correlates of everyday functioning in severe mental illness. Expert Review of Neurotherapeutics. 2006; 6(1):47–56. [PubMed: 16466311]

Lange RT, Iverson GL, Senior GJ, Chelune GJ. A primer on cluster analysis applications to cognitive rehabilitation research. Journal of Cognitive Rehabilitation. 2002; 20(1):16–33.

Linton, M.; Gallo, PS, Jr. The practical statistician: Simplified handbook of statistics. Monterey, CA: Brooks/Cole Publishing Company; 1975.

Miller G, Holden C. Proposed revisions to psychiatry's canon unveiled: Dsm-v at a glance. Science. 2010 February 12.327:770–771. [PubMed: 20150459]

Nuechterlein KH, Green MF, Kern RS, Baade LE, Barch DM, Cohen JD, Marder SR. The matrics consensus cognitive battery, part 1: Test selection, reliability, and validity. American Journal of Psychiatry. 2008; 165(2):203–213. [PubMed: 18172019]

Palmer BW, Dawes SE, Heaton RK. What do we know about neuropsychological aspects of schizophrenia? Neuropsychology Review. 2009; 19(3):365–384. [PubMed: 19639412]

Palmer BW, Dunn LB, Appelbaum PS, Jeste DV. Correlates of treatment-related decision-making capacity among middle-aged and older patients with schizophrenia. Archives of General Psychiatry. 2004; 61(3):230–236. [PubMed: 14993110]

Palmer BW, Dunn LB, Depp CA, Eyler LT, Jeste DV. Decisional capacity to consent to research among patients with bipolar disorder: Comparison with schizophrenia patients and healthy subjects. The Journal of Clinical Psychiatry. 2007; 68(5):689–696. [PubMed: 17503977]

Palmer, BW.; Heaton, RK. Executive dysfunction in schizophrenia. In: Sharma, T.; Harvey, P., editors. Cognition in schizophrenia: Impairments, importance and treatment strategies. New York: Oxford University Press; 2000. p. 52-72.

Palmer BW, Jeste DV. Relationship of individual cognitive abilities to specific components of decisional capacity among middle-aged and older patients with schizophrenia. Schizophrenia Bulletin. 2006; 32(1):98–106. [PubMed: 16192412]

Palmer BW, Savla GN, Fellows IE, Twamley EW, Jeste DV, Lacro JP. Do people with schizophrenia have differential impairment in episodic memory and/or working memory relative to other cognitive abilities? Schizophrenia Research. 2010; 116(2–3):259–265. [PubMed: 19945256]

Reitan, RM.; Wolfson, D. The halstead-reitan neuropsychological test battery: Theory and clinical interpretation. 2. Tucson, Ariz: Neuropsychology Press; 1993.

Savla GN, Twamley EW, Delis DC, Roesch SC, Jeste DV, Palmer BW. Dimensions of executive functioning in schizophrenia and their relationship with processing speed. Schizophrenia Bulletin. 2010

Savla GN, Twamley EW, Thompson WK, Delis DC, Jeste DV, Palmer BW. Evaluation of specific executive functioning skills and the processes underlying executive control in schizophrenia. Journal of the International Neuropsychological Society. 2010:1–10.

Seaton BE, Allen DN, Goldstein G, Kelley ME, van Kammen DP. Relations between cognitive and symptom profile heterogeneity in schizophrenia. Journal of Nervous and Mental Disease. 1999; 187(7):414–419. [PubMed: 10426461]

Taylor MJ, Heaton RK. Sensitivity and specificity of wais-iii/wms-iii demographically corrected factor scores in neuropsychological assessment. Journal of the International Neuropsychological Society. 2001; 7(7):867–874. [PubMed: 11771630]

Tulsky DS, Price LR. The joint wais-iii and wms-iii factor structure: Development and cross-validation of a six-factor model of cognitive functioning. Psychological Assessment. 2003; 15(2): 149–162. [PubMed: 12847775]

Velligan DI, Bow-Thomas CC. Executive function in schizophrenia. Seminars in Clinical Neuropsychiatry. 1999; 4(1):24–33. [PubMed: 10229790]

Wechsler, D. Administration and scoring manual. San Antonio: The Psychological Corporation; 1997a. Wechsler memory scale - third edition (wms-iii).

Wechsler, D. Weschler adult intelligence scale. 3. San Antonio, TX: The Psychological Association; 1997b. (wais-iii)

Wobrock T, Ecker UK, Scherk H, Schneider-Axmann T, Falkai P, Gruber O. Cognitive impairment of executive function as a core symptom of schizophrenia. World Journal of Biological Psychiatry. 2008:1–10.

Zec RF. Neuropsychology of schizophrenia according to kraepelin: Disorders of volition and executive functioning. European Archives of Psychiatry and Clinical Neuroscience. 1995; 245(4–5):216–223. [PubMed: 7578284]

**Table 1**

Mean Composite T-Scores for the K-Means (KMA) Solutions

| Factor | K1 (n=19) | K2 (n=38) | K3 (n=40) | K4 (n=17) | K5 (n=30) |
|---|---|---|---|---|---|
| Verbal Comprehension | 37.5 | 44.1 S | 38.3 | 47.6 S | 52.3 S |
| Perceptual Organization | 39.2 | 41.2 | 38.0 | 43.4 | 42.9 |
| Attention/Working Memory | 37.1 | 40.9 | 38.8 | 41.8 | 43.7 |
| Processing Speed | 38.7 | 41.6 S | 41.1 | 39.3 | 40.0 |
| Abstraction/Cognitive Flexibility | 39.2 | 30.0 W | 31.6 W | 32.9 W | 31.8 W |
| Auditory Learning & Memory | 33.8 | 28.9 W | 40.6 | 34.8W | 42.4 |
| Visual Learning & Memory | 29.3 W | 29.6 W | 36.1 | 46.9 S | 34.0 W |
| Mean T-score | 37.4 | 36.5 | 38.1 | 39.9 | 40.4 |

S = Relative strength; W = Relative Weakness; Strengths & Weaknesses = five points above or below the overall mean T-score across all seven domains.

**Table 2**

Demographic, Cognitive and Psychiatric Characteristics of Individual Clusters

| | K1 (n=19) | K2 (n=38) | K3 (n=40) | K4 (n=17) | K5 (n=30) | F or $X^2$ | df | p |
|---|---|---|---|---|---|---|---|---|
| Age (years) | 52.2 (7.9) | 51.8 (6.1) | 49.3 (6.1) | 51.9 (7.6) | 54.1 (7.0) | 2.24 | 4,139 | 0.068 |
| Education (years) | 11.2 (3.4) | 11.8 (2.3) | 11.5 (2.0) | 12.7 (1.5) | 13.7 (2.3) | 5.75 | 4,138 | <0.001[a] |
| Sex (% men) | 73.7% | 73.7% | 60.0% | 47.1% | 46.7% | 7.84 | 4 | 0.097 |
| Ethnicity (%Caucasian) | 47.4% | 68.4% | 45.0% | 52.9% | 90.0% | 17.8 | 4 | 0.001[b] |
| Age of Onset (years) | 30.9 (10.7) | 27.5 (11.3) | 25.6 (8.8) | 24.8 (9.2) | 27.3 (9.3) | 0.99 | 4,114 | 0.415 |
| Duration of illness (years) | 22.1 (11.1) | 24.8 (11.8) | 23.9 (9.7) | 27.3 (11.2) | 27.2 (10.5) | 0.78 | 4,114 | 0.540 |
| PANSS | | | | | | | | |
| Positive | 14.9 (5.2) | 12.6 (4.4) | 14.3 (5.1) | 12.8 (5.2) | 14.2 (6.6) | 0.94 | 4,132 | 0.440 |
| Negative | 13.2 (5.9) | 13.3 (6.0) | 13.8 (4.9) | 13.7 (5.8) | 12.7 (4.5) | 0.18 | 4,131 | 0.949 |
| General | 26.7 (8.6) | 24.7 (4.5) | 25.8 (6.1) | 28.2 (7.7) | 27.5 (7.3) | 1.22 | 4,132 | 0.307 |
| HAM-D | 7.3 (5.5) | 7.8 (5.5) | 7.6 (4.5) | 13.4 (8.7) | 11.3 (6.7) | 3.06 | 4,90 | 0.021[c] |

Note: Values for Sex and Ethnicity represent proportions; all others represent group means (and SDs)

Key to abbreviations: K = cluster, M = Mean, SD = Standard Deviation, PANSS = Positive and Negative Syndrome Scale; HAM-D = Hamilton Rating Scale for Depression

[a] K5 > K1, K3 & K4

[b] Percent Caucasians K5 > K1, K3, & K4

[c] No significant pairwise group differences