Article

Neuropsychological Performance in Schizotypal Personality Disorder: Importance of Working Memory

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Background: Cognitive deficits consistently have been reported in schizophrenia patients and in patients with schizotypal personality disorder. For this study, the authors wanted to identify which of the domains of cognitive impairment represent "core" deficits of schizophrenia, comparing subjects with schizotypal personality disorder to two comparison groups: healthy volunteers and patients with personality disorders unrelated to schizophrenia.

Method: Three groups completed a neuropsychological battery: patients with DSM-III-R schizotypal personality disorder (N=82); patients with DSM-III-R personality disorders unrelated to schizophrenia (i.e., a personality disorder other than schizotypal, schizoid, or paranoid [N=44]); and healthy volunteers (N=63). The battery included the California Verbal Learning Test, Trailmaking Test parts A and B, the Dot test of working memory, the Stroop Color and Word Test, the Paced Auditory Serial Addition Test, the WMS visual reproduction test, and the WAIS-R vocabulary and block design.

Results: Normative standards for performance that controlled for age, gender, and education were created from the scores of the healthy volunteers. Overall, schizotypal personality disorder patients performed significantly worse than the healthy volunteers and those with personality disorders unrelated to schizophrenia. Specifically, patients with schizotypal personality disorder demonstrated impaired performance on the Paced Auditory Serial Addition Test, WMS visual reproduction test, Dot test, and California Verbal Learning Test. In addition, in a regression analysis, performance on the Paced Auditory Serial Addition Test demonstrated the largest effect size. Indeed, it accounted for unique variance above and beyond all other cognitive measures, since controlling for Paced Auditory Serial Addition Test performance abolished group differences across all other measures.

Conclusions: Patients with schizotypal personality disorder demonstrated moderate cognitive impairment compared with healthy volunteers (significant for seven out of 11 measures). These differences reached statistical significance for tasks of working memory, episodic memory, and delayed recall. Working memory performance accounted for the group differences. This study supports the view that working memory represents a core deficit of schizophrenia spectrum disorders.

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There is ample evidence that schizophrenia patients demonstrate cognitive impairment (1). Moreover, cognitive impairment is more predictive of long-term daily functioning than the severity of psychotic symptoms (2, 3). Extensive research has attempted to characterize the nature of cognitive impairment in schizophrenia to develop strategies to improve cognitive function in these patients. Indeed, cognitive impairment in schizophrenia has become not only a focus in the research arena but also a treatment target for the novel antipsychotic medications, which no longer focus on just ameliorating psychotic symptoms but also on improving cognitive function.

It appears that cognitive impairment represents a common factor that is shared across the schizophrenia spectrum disorders. Schizotypal personality disorder represents the best characterized of the schizophrenia-related personality disorders and shares with schizophrenia genetic, biological, and treatment response characteristics (4–9). Unlike schizophrenia patients, who exhibit severe cognitive impairment across most cognitive functions, patients with schizotypal personality disorder exhibit moderate impairment across a few cognitive domains (4, 10–16). The study of patients with schizotypal personality disorder offers a unique opportunity to disentangle the pathophysiological mechanisms implicated in schizophrenia without the confounds of institutionalization, neuroleptic exposure, and other consequences of illness seen in schizophrenia. Thus, the study of patients with schizotypal personality disorder provides the opportunity to identify the mechanisms that are central to disease susceptibility rather than a consequence of it.

Working memory (referred to by Baddeley [17] as a "system that is necessary for the storage and manipulation of information," a paradigm originally proposed in Baddeley

TABLE 1. Demographic and Clinical Characteristics of Personality Disorder Groups and Healthy Comparison Subjects

Characteristic	Patients With Schizotypal Personality Disorder (N=82)		Healthy Volunteers (N=63)		Patients With Personality Disorder Unrelated to Schizophrenia[a] (N=44)		Analysis		
	N	%	N	%	N	%	χ^2	df	p
Gender							10.3	2	0.01
Male	61	74	32	51	23	52			
Female	21	26	31	49	21	48			
	Mean	SD	Mean	SD	Mean	SD	F	df	p
Age (years)	37.9	10.7	31.4	10.6	33.6	10.5	7.0	2, 188	0.01[b]
Education (years)	14.3	2.9	16.5	2.9	15.4	2.2	13.1	2, 188	0.01[c]
Beck Depression Inventory score	15.7	11.6	3.8	2.6	12.1	8.4	30.1	2, 180	0.01[c]

[a] Any personality disorder other than schizotypal, schizoid, or paranoid.
[b] Both personality disorder groups significantly differed from the healthy volunteers, per Tukey-B post hoc tests.
[c] Patients with schizotypal personality disorder significantly differed from healthy volunteers and those with personality disorders unrelated to schizophrenia, who also significantly differed from healthy volunteers (Tukey-B post hoc tests).

and Hitch [18]) has been widely accepted as one of the key areas of cognitive impairment in schizophrenia patients (19, 20) (for review of working memory and schizophrenia see Goldman-Rakic [21]). However, there are several other key areas of cognitive impairment in schizophrenia spectrum disorders, such as attention (12, 22), executive function (23), or processing speed (24). While we should keep in mind that the possibility of a generalized deficit in schizophrenia may exist, there is the possibility that dysfunction in a key area may underlie dysfunctions in other related areas. It is logical to hypothesize that if an area of cognitive impairment represents such a "core" deficit, its effects should be observed across the entire schizophrenia spectrum but not in populations with psychopathology outside of the schizophrenia spectrum.

The goals of this study, which used the largest sample of patients with clinically diagnosed schizotypal personality disorder to date, were to 1) investigate whether these patients would demonstrate cognitive impairment relative to healthy comparison subjects, 2) examine whether this cognitive impairment would be specific to schizophrenia spectrum disorders, and 3) assess whether any of these cognitive domains represent a "core" area of neuropsychological dysfunction in the spectrum. In addition, we explored the relationship between these cognitive measures and the schizotypal symptom clusters (25), since there is evidence that cognitive deficits are related to deficits in social and other functional skills (3, 26).

Method

Subjects

The study group included 1) 82 subjects who met criteria for DSM-III-R schizotypal personality disorder, 2) 44 subjects who met criteria for a personality disorder unrelated to schizophrenia (i.e., a personality disorder other than schizotypal, schizoid, or paranoid) and met no more than two DSM-III-R schizotypal personality disorder criteria, and 3) 63 healthy comparison subjects, all recruited by advertisement and word of mouth. Clinical and demographic characteristics of the study group are displayed in Table 1. All were studied as outpatients. (We have previously published data on 48 of the subjects with schizotypal personality disorder, 22 of those with personality disorders unrelated to schizophrenia, and 32 of the healthy volunteers [10].)

Written informed consent was obtained according to institutional guidelines. Subjects then underwent a medical evaluation (laboratory analyses and physical examination) and were excluded if there was evidence of systemic medical illness or neurological abnormalities, a history of significant head trauma (with loss of consciousness), or positive toxicology screen results. All subjects were evaluated by doctoral-level clinical psychologists with the Structured Clinical Interview for DSM-III-R (27) for axis I disorders and the Structured Interview for DSM-III-R Personality, Revised (28) for axis II disorders (kappa=0.73 for schizotypal personality disorder diagnosis [range=0.68–0.84 for each criterion]). Diagnoses were reached in a consensus meeting with an expert diagnostician (J.M.S.) in which the clinical interviewer presented information gathered from all sources. Patients were excluded if they met criteria for a psychotic disorder or bipolar I disorder, had met lifetime criteria for substance dependence or abuse in the preceding 6 months, or were currently taking psychotropic medications. Healthy comparison subjects had no history of axis I or axis II disorders and had no first-degree relative with an axis I disorder. The Beck Depression Inventory (29) was also given to all subjects on the day of testing in order to assess the effect, if any, of depressive symptoms on performance.

Consistent with the nature of personality disorders and reports from other centers (16), patients who met criteria for schizotypal personality disorder also met criteria for other axis II diagnoses, including paranoid personality disorder (N=41 [50%]), avoidant personality disorder (N=26 [32%]), and borderline personality disorder (N=22 [27%]). The personality disorders unrelated to schizophrenia mainly were borderline personality disorder (N=21 [48%]), obsessive-compulsive personality disorder (N=8 [18%]), or avoidant personality disorder (N=7 [16%]). (We report here only personality disorder diagnoses with group prevalence greater than 15%.) Patients with schizotypal personality disorder met criteria for a mean of 1.81 other personality disorders (SD=1.50), whereas the patients with personality disorders unrelated to schizophrenia met criteria for a mean of 1.40 other personality disorders (SD=0.79).

Cognitive Testing

Eleven cognitive measures of five general cognitive domains were included for this report (Table 2). From each measure one task was selected on which abnormal performance had been con-

TABLE 2. Neuropsychological Battery Performance of Personality Disorder Groups and Healthy Comparison Subjects

	Score					
	Patients With Schizotypal Personality Disorder (N=82)		Healthy Volunteers (N=63)		Patients With Personality Disorder Unrelated to Schizophrenia[a] (N=44)	
Cognitive Domain and Measure	Mean	SD	Mean	SD	Mean	SD
Working memory						
Dot test (distance error [in cm] at 30 sec)[b, c]	1.01	0.96	0.53	0.60	0.60	0.71
Paced Auditory Serial Addition Test (correct responses)[b, c]	33.96	11.01	43.41	5.97	41.27	8.27
Episodic memory						
California Verbal Learning Test (total words recalled)[b, c]	49.87	9.96	58.69	10.08	57.18	8.47
WMS visual reproduction test (immediate recall score)[b, c]	32.07	7.33	36.19	3.38	35.61	7.17
Delayed recall						
California Verbal Learning Test (words recalled after 20 min)[b, c]	10.78	2.95	12.67	2.96	12.66	2.92
WMS visual reproduction test (delayed recall score after 30 min)[b]	28.62	8.45	34.08	4.58	32.14	7.77
Processing speed						
Trailmaking test (sec)						
Part A[b]	33.56	14.45	26.14	9.50	29.25	10.63
Part B	85.15	44.60	58.59	26.78	63.82	23.34
Stroop Color and Word Test (interference condition latency)	–1.84	8.08	2.15	7.49	1.29	10.35
Overall intellectual function (WAIS scores)						
Vocabulary	10.62	2.91	11.44	2.72	12.00	2.84
IQ equivalent for vocabulary	106.2	29.0	114.4	27.2	120.0	28.4
Block design	9.57	2.95	11.33	2.97	11.02	3.08
IQ equivalent for block design	95.7	29.5	113.3	29.7	110.2	30.7

[a] Any personality disorder other than schizotypal, schizoid, or paranoid.
[b] Significant impairment in schizotypal personality disorder subjects relative to healthy volunteers ($p<0.001$, analysis after Z transformation; overall repeated-measures ANOVA with post hoc tests).
[c] Significant impairment in schizotypal personality disorder patients relative to patients with personality disorders unrelated to schizophrenia ($p<0.001$, analysis after Z transformation; overall ANOVA with post hoc tests).

sistently demonstrated in numerous studies of schizophrenia patients as well as some previous studies of first-degree relatives and clinical subjects with schizotypal personality disorder.

Working memory assessments. The Dot test is a test of visuospatial working memory developed by Keefe et al. (30, 31). Subjects are presented a dot at a specific position on a standard size paper and then asked to reproduce it at the same location on a separate sheet after different periods of delay (no delay and after 10, 20, and 30 seconds). Performance is measured as the distance in cm between the drawn dot and the actual dot (distance error). The distance error at the 30-second delay (longest memory load of all three delays) minus the distance error at no delay is the dependent variable.

The Paced Auditory Serial Addition Test is a test of verbal (auditory) working memory that has been well described and validated (32). Briefly, subjects listen to a tape recorded voice presenting a series of numbers (50 numbers at a rate of one digit per 2 seconds) and are asked to add each adjacent pair of numbers and respond by verbalizing the sum. The total number of correct responses is the dependent variable.

Episodic memory assessments. The California Verbal Learning Test involves five presentations of a list of 16 words (four words from each of four semantic categories), with recall after each presentation (33). The total number of words recalled (trials 1 through 5) is the dependent variable.

The Wechsler Memory Scale (WMS) visual reproduction test is a test of memory for nonverbal stimuli. Four line drawings are presented one at a time for a 10-second exposure period. After the drawing is removed, the subject is asked to immediately draw the figure from memory. Performance is scored according to standardized criteria (34). The raw score is the dependent variable.

Delayed recall assessments. The California Verbal Learning Test contains multiple recall measures, with the number of free recalled words after a 20-minute delay the dependent variable used in this report.

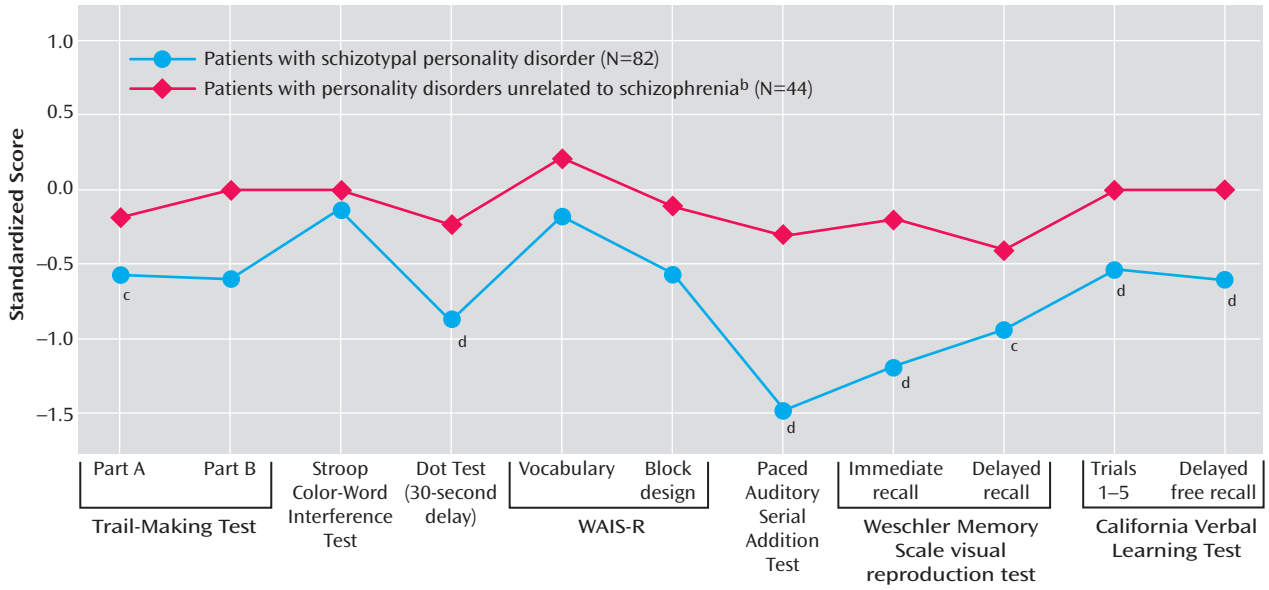
As part of the WMS visual reproduction test, subjects are asked to draw the four items from memory after a 30-minute delay, with no prompts or cues provided. The raw score of the visual reproduction of the four figures after this delay is the dependent variable.

Processing speed assessments. The Trailmaking Test has two conditions that combine to assess verbal/spatial perception and psychomotor speed (35). In part A the subject must connect numbers presented on a standard sheet of paper in ascending order (1–2–3). In part B the subject must alternate connecting numbers and letters (for example, 1-A, 2-B, 3-C, etc.). The amount of time it takes to complete part A and part B are the two dependent variables.

The Stroop Color and Word Test measures the subject's ability to shift perceptual sets in response to changing demand characteristics and to avoid interference from irrelevant aspects of the stimulus situation (36). The subject is asked first to read the names of colors written in black ink (first condition), then is asked to name the color of noncolor words written in colored ink (second condition). The third condition elicits what is called the Stroop interference effect, where the subject must name the color of the ink in which the names of various colors are written while ignoring the word. The dependent measure is the latency for naming all of the colors correctly in this third condition minus the score of the second condition.

Overall intellectual function assessments. The WAIS-R vocabulary and block design tests are standardized, well-validated measures assessing overall intelligence. These two measures were administered in order to estimate both verbal and nonverbal intellectual functions (37). The dependent measures are the age-corrected scaled scores.

FIGURE 1. Neuropsychological Performance Profiles of Personality Disorder Groups[a]



[a] Regression-based approach for normative standards with age, education, and gender controlled; performance of healthy volunteers (N=63) has been set to zero (SD=1). Repeated-measures analysis of variance showed an overall significant effect of diagnosis (F=6.9, df=2, 186, p<0.001); with post hoc tests revealing measures on which those with schizotypal personality disorder significantly differed from healthy volunteers (c) and both healthy volunteers and those with personality disorders unrelated to schizophrenia (d).
[b] Any personality disorder other than schizotypal, schizoid, or paranoid.

Data Analysis

Creation of normative standards. A regression-based approach was used to create normative standards. Age, education, and gender were regressed on each of the dependent variables in the healthy volunteer group. Scores were standardized on the basis of these regression results (see Heaton et al. [38] for a description of this procedure). In addition, the adjusted scores were then found to be uncorrelated with the demographic variables, suggesting that the standardization had actually controlled for the effect of these factors on performance. The same procedure was applied to the schizotypal personality disorder group, using these same norms to create standardized scores (i.e., z scores). The creation of normative standards across measures is used so that comparisons between cognitive measures can be made and represents a standard way of reporting results across a large cognitive battery (19).

Analyses between diagnostic groups. A repeated-measures analysis of variance (ANOVA) was conducted on the standardized scores, using the 11 measures as the dependent variables and group membership as the independent variable followed up by a Tukey-B post hoc test to reveal which groups were different. While age, education, and gender were controlled in the creation of normative standards for each test, the Beck depression score was controlled by an analysis of covariance.

Evaluation of cognitive domains implicated in schizophrenia spectrum disorders. A simultaneous entry for all 11 measures using the schizotypal personality disorder and the healthy comparison group (dependent measure) was conducted in order to examine which measures accounted for the variance. This procedure was repeated using both personality disorder groups as well as using the healthy volunteers and the group with personality disorders unrelated to schizophrenia. Moreover, in order to determine whether the Paced Auditory Serial Addition Test accounted for unique variance over and above the other cognitive measures, all the measures (except the Paced Auditory Serial Addition Test) were entered as a block in a regression analysis followed by the Paced Auditory Serial Addition Test (this analysis was performed in the patients with schizotypal personality disorder and healthy volunteers).

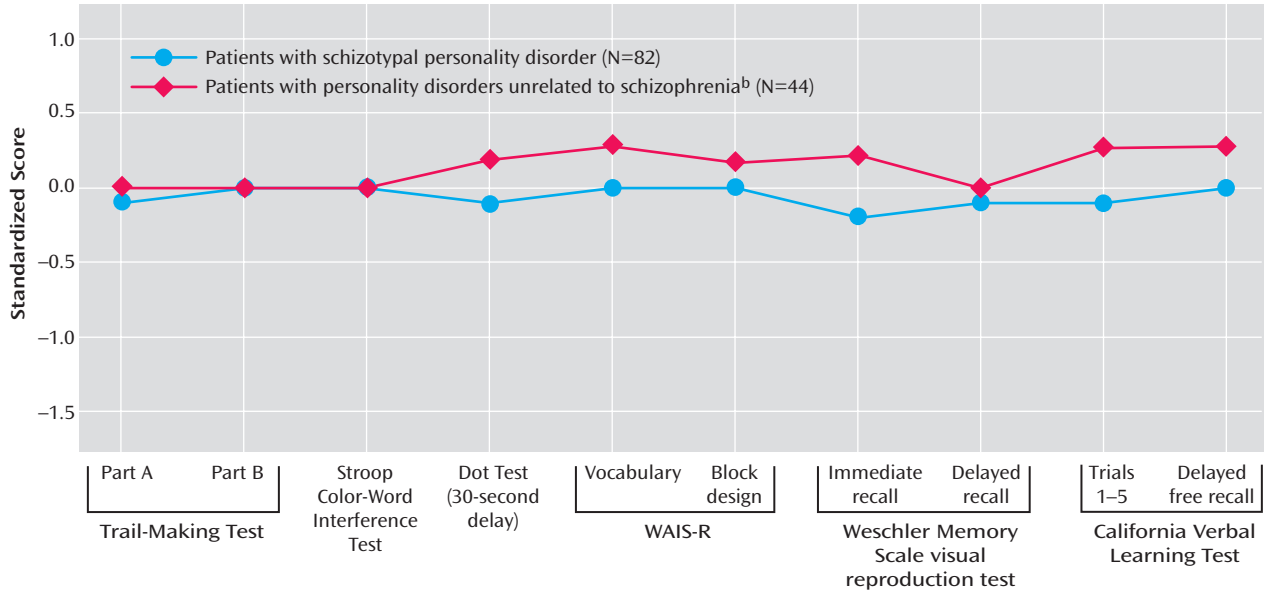
Correlational analyses. In order to investigate whether a particular group of symptoms was associated with cognitive impairment, DSM-III-R schizotypal personality disorder symptoms were grouped into three factors: interpersonal, paranoid, or cognitive/perceptual on the basis of previous work (25) and were correlated with the 11 cognitive measures for the total personality disorder cohort (N=126). For each of the five cognitive domains, we are reporting correlations that are significant at the p<0.005 level in the total patient cohort (so that they would remain significant if they were Bonferroni corrected for multiple correlations).

Results

Analyses of Clinical and Demographic Variables

Subjects in all three groups were studied in their 30s and had an average of a 2-year college education. The three groups were significantly different in age and education. These differences were controlled for statistically by the creation of standardized scores. Regarding the gender distribution, more patients with schizotypal personality disorder were men compared with the other two groups and, as expected, patients with schizotypal personality disorder demonstrated higher Beck Depression Inventory scores relative to comparison subjects and patients with personality disorders unrelated to schizophrenia (Table 1). (Similar results were obtained when the sample was restricted to the previously unreported subjects.)

FIGURE 2. Neuropsychological Performance Profiles of Personality Disorder Groups After Paced Auditory Serial Addition Test Performance Controlled[a]



[a] Regression-based approach for normative standards with age, education, gender, and Paced Auditory Serial Addition Test score controlled; performance of healthy volunteers (N=63) has been set to zero (SD=1). Repeated-measures analysis of variance showed no significant effect of diagnosis.
[b] Any personality disorder other than schizotypal, schizoid, or paranoid.

Analyses Between Diagnostic Groups

In order to evaluate our primary hypothesis that subjects with schizotypal personality disorder would demonstrate significant cognitive impairment specific to the schizophrenia spectrum, an ANOVA using the 11 standardized scores was conducted. An overall significant effect of diagnosis was found, with schizotypal personality disorder subjects demonstrating overall impairment relative to both healthy volunteers and those with personality disorders unrelated to schizophrenia (Figure 1). Healthy volunteers and patients with personality disorders unrelated to schizophrenia were not different per post hoc simple contrast (similar results were obtained when the sample was restricted to the previously unreported subjects). Entering the Beck Depression Inventory score as a covariate did not change these results (effect of Beck score: $F=0.3$, df=1, 177, $p=0.75$; effect of diagnosis: $F=5.9$, df=2, 177, $p<0.005$). An ANOVA with post hoc tests was then conducted in order to investigate which of the 11 measures contributed to the overall effect of diagnosis. Patients with schizotypal personality disorder demonstrated impairment when compared with both healthy volunteers and those with personality disorders unrelated to schizophrenia for the following individual measures (listed in order of effect size): Paced Auditory Serial Addition Test, WMS visual reproduction test (immediate recall), California Verbal Learning Test (total words recalled), Dot test, and California Verbal Learning Test (delayed recall). Moreover, patients with schizotypal personality disorder were impaired compared with healthy volunteers for the WMS visual reproduction test delayed recall condition and Trailmaking Test part A. (No statistically significant differences were observed for the Trailmaking Test part B, Stroop interference test, or WAIS vocabulary or block design; entering Beck Depression Inventory score as a covariate did not change the results.)

Regression Analysis

A simultaneous entry regression analysis conducted utilizing all 11 standardized measures in the schizotypal personality disorder group and healthy volunteers (dependent measure) was highly significant ($F=4.78$, df=11, 133, $p<0.0001$; $R^2=0.28$). A follow-up stepwise regression analysis revealed that the measure that entered the model first was the Paced Auditory Serial Addition Test score (explaining 15% of variance), while the WMS visual reproduction test immediate recall, California Verbal Learning Test total words recalled, and vocabulary scores entered the model next and accounted for an additional 10% (individually 5%, 3%, and 2%, respectively) (overall model: $F=11.9$, df=4, 144, $p<0.001$; $R^2=0.25$). In order to investigate whether the Paced Auditory Serial Addition Test contributed unique variance to the model we conducted a regression analysis two ways. First, we entered all 10 variables as a block (i.e., all variables except for the Paced Auditory Serial Addition Test) in the model, followed by the Paced Auditory Serial Addition Test. Second, we entered the Paced Auditory Serial Addition Test first and then the remaining variables in the second block. Regardless of whether the Paced Auditory Serial Addition Test was entered first or last it ac-

TABLE 3. Correlations Between Cognitive Measures in Patients With Schizotypal Personality Disorder (N=82)

Cognitive Domain and Measure	Correlation (r)										
	1	2	3	4	5	6	7	8	9	10	11
Working memory											
1: Dot test		–0.24	–0.10	–0.05	–0.08	–0.11	0.30	0.26	–0.30	–0.05	–0.21
2: Paced Auditory Serial Addition Test	–0.24		0.19	0.04	0.25	0.21	–0.17	–0.46*	0.09	0.36*	0.29
Episodic memory											
3: California Verbal Learning Test 1–5	–0.10	0.19		0.14	0.68*	0.21	–0.07	–0.29	0.13	0.20	0.01
4: Wechsler Memory Scale (WMS) visual reproduction test immediate recall	–0.05	0.04	0.14		0.26	0.71*	0.02	–0.18	–0.03	0.15	0.18
Delayed recall											
5: California Verbal Learning Test delayed recall	–0.08	0.25	0.68*	0.26		0.36*	–0.11	–0.32	0.17	0.06	0.08
6: WMS visual reproduction test delayed recall	–0.11	0.21	0.21	0.71[a]	0.36		0.00	–0.38*	0.04	0.17	0.34*
Processing											
7: Trailmaking, part A	0.03	–0.17	–0.07	0.02	–0.11	0.00		0.32	0.02	0.01	–0.13
8: Trailmaking, part B	0.26	–0.46*	–0.29	–0.18	–0.32	–0.38*	0.32		–0.13	–0.33	–0.28
9: Stroop Color and Word Test	–0.30	0.09	0.13	–0.03	0.17	0.04	0.02	–0.13		–0.07	0.08
Overall intellectual functioning (WAIS)											
10: Vocabulary	–0.05	0.36*	0.20	0.15	0.06	0.17	0.01	–0.33	–0.07		0.34
11: Block design	–0.21	0.29	0.01	0.18	0.08	0.34*	–0.13	–0.28	0.08	0.34	

*p<0.001.

counted for unique variance in the model (R^2=0.08 when last; R^2=0.15 when first, overall model R^2=0.28). Indeed, the Paced Auditory Serial Addition Test score as a covariate in the ANOVA above abolished the group differences across the three groups (Figure 2). The Paced Auditory Serial Addition Test also accounted for most of the variance (8%) in the discrimination of the schizotypal personality disorder and no schizophrenia groups, while the only other variable that entered the model was the California Verbal Learning Test total words recalled (4%) (F=8.3, df=2, 125, p<0.001). (No variable entered the model when the regression analysis looked at the healthy volunteers and those with personality disorders unrelated to schizophrenia.)

Correlational Analysis

In order to investigate whether any of the schizotypal personality disorder symptom dimensions were associated with cognitive impairment, the 11 individual tests were correlated with each of the three symptom clusters. These correlations performed for the entire sample of patients revealed that only the interpersonal factor had a significant inverse correlation (i.e., greater isolation associated with poorer performance) with cognitive measures: Paced Auditory Serial Addition Test, WMS visual reproduction test immediate recall, and California Verbal Learning Test delayed recall scores (all r≥0.26, df=124, p<0.005). Similar results were obtained between the Paced Auditory Serial Addition Test and the interpersonal factor when the study group was restricted to the schizotypal personality disorder subjects (r=–0.29, df=80, p<0.05), whereas no statistically significant association was seen between Paced Auditory Serial Addition Test performance and schizotypal symptoms in patients with personality disorders unrelated to schizophrenia. (Again the results are the same when the sample is restricted to the previously unpublished subjects.) The correlational matrix across all 11 measures within the schizotypal personality disorder group, the group of interest, is presented in Table 3. We have highlighted those that would remain significant after multiple comparisons (p<0.001). The directionality of the correlations remains the same if the entire sample is used.

Discussion

We have demonstrated, in the largest group of clinically identified subjects with schizotypal personality disorder to date, that patients with schizotypal personality disorder demonstrate modest cognitive impairment on a variety of cognitive measures. The areas of impairment are specific to domains of working memory, episodic memory, and delayed recall but not in processing speed, susceptibility to interference, or overall intellectual function. Thus, a generalized deficit in performance was clearly not detected. This impairment was specific to the schizotypal personality disorder group, since patients with psychopathology unrelated to schizophrenia did not demonstrate cognitive impairment relative to the healthy group but did differ from the schizotypal personality disorder group. Moreover, we have demonstrated that a measure of auditory working memory (the Paced Auditory Serial Addition Test) accounts for the observed group differences. These results are similar to the ones previously reported with a partially overlapping sample and do not change if we limit the current study group to previously unreported subjects. While patients with schizotypal personality disorder demonstrated impairment relative to healthy subjects in other domains, the Paced Auditory Serial Addition Test was the measure accounting for most of the variance. Indeed, the Paced Auditory Serial Addition Test accounted for unique variance over and above all the other cognitive measures combined. In addition, the same auditory working memory task accounted for most of the variance in the difference between the schizotypal personality disorder subjects and those with personality disorders unrelated to schizophrenia. These results support the notion that working memory

represents a core neuropsychological deficit in the schizophrenia spectrum that may have cascading effects leading to impairment in several other cognitive areas (39). Our results are consistent with a recent study (40) in which we reported that subjects with schizotypal personality disorder exhibited impairment relative to healthy subjects on a working memory task that required online maintenance of context. The auditory working memory task presented in this report (the Paced Auditory Serial Addition Test) is similar in that it places demands on context processing, since subjects have to actively update and discard information. While it is widely accepted that the dorsolateral prefrontal cortex is a key area associated with working memory (as reviewed by Levy and Goldman-Rakic [41]) and also an area of dysfunction in the schizophrenia spectrum (42), previous work has focused on trying to characterize the specific brain regions within the dorsolateral prefrontal cortex that are associated with different modalities of working memory (43, 44).

It is of interest that the cognitive task on which the patients with schizotypal personality disorder exhibited the most impairment (the Paced Auditory Serial Addition Test) was significantly associated with the interpersonal factor of the schizotypal symptoms (comprising the following four symptoms: odd/eccentric behavior/appearance, no close friends/confidants, odd speech, and inappropriate/constricted affect). This finding is consistent with findings previously reported in studies of patients with schizophrenia. In those studies, working memory deficits (as well as deficits in learning and vigilance) have been reported to be correlated with social functioning deficits. The association between working memory impairment and social deficit provides modest support for the hypothesis that deficits in information processing and the inability to titrate effort to situational demands could possibly lead to increases in social isolation, a core characteristic of the schizophrenia spectrum disorders (8, 9, 45). However, it is also possible that in early life poor social skills may impede interactions that improve cognitive performance.

Limitations of the study may include the fact that the healthy volunteers were screened to exclude any history of axis I or axis II disorders—leading this group to be "supernormal." This concern is partly obviated by the fact that we do have a nonschizophrenia personality disorder cohort and the finding that there was no overall group difference in IQs. Moreover, there are always drawbacks in defining a comparison group. We wanted to have a group that was not contaminated with psychopathology and in addition be free of schizophrenia spectrum pathology. In addition, studies in schizophrenia spectrum disorders by definition need rigorous screening of healthy volunteers, since there have been reports of group differences among normal healthy volunteer groups in sensorimotor gating based on psychosis proneness items (46). Another limitation may include the unmatched study group sizes, which means that differences between the subjects with personality disorders unrelated to schizophrenia and the healthy subjects cannot be detected with the same power as the differences between the patients with schizotypal personality disorder and healthy volunteers. This concern is partly obviated by the essential trivial magnitude of differences between healthy volunteers and those with personality disorders unrelated to schizophrenia, wherein even a very substantial sample size would not have found statistically significant differences. Even though we did not find any differences in cognitive function between the patients with personality disorders unrelated to schizophrenia and the healthy volunteer group on the 11 measures selected to compare impairment between schizotypal personality disorder subjects and healthy volunteers, it is possible that these two groups are different in other measures. While there is no agreed upon "perfect" battery to test for impairment in cognitive domains, we have included tests that have relatively consistently differentiated schizophrenia and healthy subjects.

In summary, we have found that patients with schizotypal personality disorder demonstrate moderate cognitive impairment, supporting the view that working memory may be a core deficit in schizophrenia spectrum disorders. The similar yet more circumscribed and specific impairments observed in patients with schizotypal personality disorder compared with schizophrenia patients make them a particularly attractive population for studies designed to clarify the etiology and design paradigms to evaluate potential treatment of this impairment.

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