

Cognitive profile in recent-onset schizophrenia

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Abstract: The aim of this study was to compare WAIS-IV and WMS-IV performance in recent-onset schizophrenia (ROS) with performance in a demographically matched healthy comparison group. Forty-three ROS inpatients were compared with 43 healthy individuals drawn from the Croatian standardization samples for the WAIS-IV and WMS-IV and matched to patients on age, sex and years of education. Primary analyses used separate MANCOVAs (Pillai's Trace) on WAIS-IV and WMS-IV index scores with Group as the between-subjects factor and years of education as a covariate. Significant multivariate effects were followed by univariate ANCOVAs on each index, with Holm correction across the nine index tests. Clinical interpretability was summarized by the proportion of participants falling below -1 SD and -1.5 SD relative to the control-group distribution. Large deficits were observed on WAIS-IV Processing Speed and Working Memory, with sizable effects on Perceptual Reasoning and Verbal Comprehension. WMS-IV showed very large decrements in Immediate and Delayed Memory and large reductions in Visual Memory and Visual Working Memory. These findings suggest that broad cognitive impairment is already evident near illness onset, with slowed processing and episodic-memory dysfunction being prominent targets for early assessment and remediation.

Keywords: schizophrenia, cognition, WAIS-IV, WMS-IV, processing speed, episodic memory

Introduction

Cognitive problems are present in schizophrenia, even before the psychotic symptoms of the disease develop (Dickinson et al., 2012). They are stable over time and remain so even after antipsychotic therapy (Keefe & Fenton, 2007; Keefe et al. 2011). Cognitive problems such as difficulties with attention,

working memory, perceptual reasoning, verbal memory, executive functions, and information processing are common in patients with schizophrenia (Keefe & Fenton, 2007; Michel et al., 2013). In studies, such patients have up to 1.5 standard deviations of lower scores (Keefe & Fenton, 2007; Michel et al., 2013) on standardized tests. Furthermore, impediments in neurocognition have impor-

tant clinical implications. Cognitive deficits are associated with poor quality of life and social functioning (Williams et al., 2008). For more than four decades, the WAIS has been used extensively to test cognitive abilities in schizophrenia (Allen et al., 1998). There is research on clinical groups of schizophrenia on earlier versions of WAIS. In these studies, earlier versions of the WAIS showed a specific pattern of cognitive dysfunction on tasks involving processing speed, early memory, and perceptual reasoning, while the results on verbal tasks were similar to the averages of comparative samples. However, several changes have taken place in the last revision of WAIS-IV (Wechsler, 2008). Whereas the WAIS-IV measures general cognitive functioning, it does not provide a comprehensive assessment of episodic memory. Therefore, to investigate potential memory problems in detail we also used the WMS-IV, which assesses auditory, visual, immediate and delayed memory as well as visual working memory (Cirillo & Seidman, 2003). Prior research has documented episodic-memory deficits in schizophrenia involving encoding and retrieval processes across both verbal and visual modalities. Clinical studies consistently demonstrate that individuals with schizophrenia show poorer performance than healthy controls on WMS-IV indices.

The mentioned studies involving the WAIS-IV and WMS-IV have had samples of people with chronic schizophrenia, with a wide range of disease durations, from 10 to 20 years. These studies therefore could not provide an answer to the question of how much cognitive changes are present at the very beginning of the disease, that is, in patients with recent onset of schizophrenia (ROS). In addition, testing the same individuals with the WAIS-IV and WMS-IV allows an accurate as-

essment of the correlation between the tests and the underlying values of the differences between the results obtained based on the WAIS-IV and WMS-a-IV.

The aim of this study was to compare cognitive performance measured by the WAIS-IV and WMS-IV between patients suffering from schizophrenia and healthy participants comprising the control group.

We tested whether patients with ROS show deficits on WAIS-IV and WMS-IV subtests and index scores compared with matched control sample. All confirmatory analyses adjusted for years of education, with age and sex addressed by matching. No additional sensitivity analyses are reported in this version.

Prior work consistently indicates robust impairments in processing speed and episodic memory near illness onset, with additional but sometimes smaller group differences in working memory and reasoning. However, many studies assess only selected domains or rely on a single instrument, which limits cross-battery inferences. Moreover, few investigations use locally normed versions of both WAIS-IV and WMS-IV within the same recent-onset sample, even though local norms can materially affect clinical classification (e.g., proportions falling below conventional cutoffs) and improve the interpretability of group differences.

The present study addresses this gap by providing a cross-battery profile of WAIS-IV and WMS-IV performance in patients with recent-onset schizophrenia compared with demographically comparable healthy controls, using country-specific norms. Beyond group mean differences, we also quantify the clinical salience of findings by reporting the proportion of participants who fall below conventional thresholds (e.g., -1 SD and -1.5 SD) on key indices.

Methods

Participants and setting

We assessed 43 inpatients with ROS diagnosed with schizophrenia within two years before enrolment. Each had at least one psychiatric hospitalization in the preceding 12 months. Diagnoses were established by a trained psychiatrist using a structured clinical interview for DSM-5 disorders (SCID-5). Data were collected at the University Hospital Centre Sestre milosrdnice between January 2018 and September 2019.

During that period, 361 patients with schizophrenia were hospitalized. We excluded 64 individuals due to comorbid physical or neurologic illness, 157 due to illness duration longer than two years, 48 due to additional psychiatric diagnoses and 49 because of substance abuse. The final sample comprised 43 patients who completed the study (Figure 1).

Patients were stabilized for at least one month before cognitive testing. Antipsychotic regimens included risperidone, aripiprazole,

amisulpride, haloperidol, olanzapine, fluphenazine, ziprasidone, quetiapine and clozapine, with several patients on combinations.

The control group comprised 43 individuals selected from the Croatian standardization samples for the WAIS-IV and WMS-IV. Controls were matched to patients on age, sex and years of education. Because these data were archival, control participants did not undergo the same testing procedure or clinical assessments; only WAIS-IV and WMS-IV scores were available. Exclusion criteria for the normative samples are specified in the WAIS-IV-HR and WMS-IV-HR manuals (Wechsler, 2019a; 2019b).

Clinical measures

We obtained Clinical Global Impression–Severity (CGI-S) and Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) scores on the day before cognitive testing. CGI-S rates overall illness severity from 1 (normal) to 7 (among the most severely ill). The improvement scale (CGI-I) ranges from 1 (very much improved) to 7 (very much worse). CRDPSS is an 8-item clinician-rated scale that captures the severity of delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, negative symptoms, impaired cognition, depression and mania over the past seven days (Barch et al., 2013; Heckers et al., 2013; Rabinowitz et al., 2006; Rabinowitz et al., 2010).

Cognitive measures

WAIS-IV. Ten core and five supplemental subtests yield four indices: VCI (Similarities, Vocabulary, Information), PRI (Block Design, Matrix Reasoning, Visual Puzzles), WMI (Digit Span, Arithmetic) and PSI (Symbol Search, Coding). Scores are corrected and standardized.

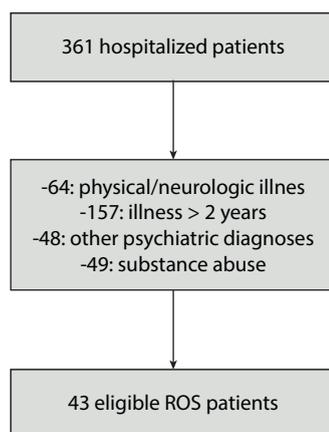


Figure 1. Flowchart of patient selection.

WMS-IV. Primary subtests include Logical Memory (LM I/II), Verbal Paired Associates (VPA I/II), Designs (DE I/II), Visual Reproduction (VR I/II), Spatial Addition and Symbol Span. Index scores are Auditory Memory (AMI), Visual Memory (VMI), Visual Working Memory (VWMI), Immediate Memory (IMI) and Delayed Memory (DMI), standardized to mean 100 and SD 15.

Procedure

Patients were tested in two sessions to reduce fatigue. The first session included the clinical assessments (CGI-S/CRDPSS) and WAIS-IV. The second session included WMS-IV. Each battery typically requires more than 90 minutes. Control data were drawn from the standardization samples; control participants were not assessed in our study.

Statistical analysis

Analyses were conducted in SPSS 27. Continuous variables are reported as mean \pm SD. Group differences in demographics/clinical used t-tests or χ^2 as appropriate.

Primary cognitive analyses. We ran two MANCOVAs on WAIS-IV and WMS-IV index sets, respectively, with Group (ROS vs. control) as the between-subjects factor and years of education as a covariate. We report Pillai's Trace (robust to covariance violations), associated F, df, p, and partial η^2 . Follow-up univariate ANCOVAs were run for each index (same covariate). Multiplicity across the 9 index tests (4 WAIS + 5 WMS) was controlled using the Holm method. Tables report unadjusted p-values, and the Holm correction does not change the conclusions. Subtests are presented descriptively (effect sizes, p-values without multiplicity correction) to aid clinical interpretation.

For each index we computed observed proportions of participants scoring ≤ -1 SD and ≤ -1.5 SD relative to the control-group distribution (m and SD from the matched control sample), and compared groups using Fisher's exact test.

We tested the assumptions of the model by inspecting residuals (normality), Levene's test (homoscedasticity) and Box's M. We also screened Group \times covariate terms to verify the homogeneity of regression slopes assumption for ANCOVA/MANCOVA; no material violations were detected. For each subtest and index comparison we report Cohen's d (pooled SD) with the conventional interpretation (≈ 0.20 small, ≈ 0.50 medium, ≥ 0.80 large).

Results

Sociodemographic and clinical characteristics

Patients and controls were matched on age (32.6 ± 8.5 years in both groups), sex (31 men and 12 women per group) and years of education. ROS patients had a mean illness duration of 1.6 ± 0.3 years and averaged 1.1 ± 2.3 prior hospitalisations. The mean CGI-S was 3.2 ± 0.8 (moderately ill), and the mean CRDPSS was 12.8 ± 4.3 . Table 1 provides descriptive statistics.

WAIS-IV indices and subtests

The MANCOVA on WAIS-IV index scores (VCI, PRI, WMI, PSI) revealed a highly significant main effect of Group (Pillai's Trace = 0.71, $F(4, 78) = 9.4$, $p < .001$, partial $\eta^2 = .38$) after adjusting for education, indicating a multivariate deficit in ROS patients. Years of education was a significant covariate

Table 1. Sociodemographic and clinical characteristics of the recent-onset schizophrenia and control groups

	Schizophrenia (N=43)	Control group (N=43)
Age, in years (mean ± SD)	32.6 ± 8.5	32.6 ± 8.5
Duration of illness, in years (mean ± SD)	1.6 ± 0.3	—
Sex N (%)		
Male	31 (72.1)	31 (72.1)
Female	12 (28.9)	12 (28.9)
Education level N (%)		
Elementary school	4 (9.3)	4 (9.3)
High school	29 (67.4)	29 (67.4)
University	10 (23.3)	10 (23.3)
Marital status N (%)		
Married	7 (16.3)	—
Unmarried	32 (74.4)	
Divorced	4 (9.3)	
Number of hospitalizations (mean ± SD)	1.1 ± 2.3	—
CGI (mean ± SD)	3.2 ± 0.8	—
CRDPSS (mean ± SD)	12.8 ± 4.3	—

($p = .02$). Follow-up ANCOVAs confirmed significant impairments in all indices (all $p < .001$). Effect sizes ranged from $d = 1.12$ for WMI (working memory) to $d = 1.78$ for PSI (processing speed).

Table 2 summarizes means, SDs, F statistics, and effect sizes for each WAIS-IV index and subtest. Patients scored approximately 0.9–1.8 SD below controls on subtests; the largest deficits were on Coding, Symbol Search, and Letter–Number Sequencing, reflecting slowed processing speed and working-memory limitations. Even for crystallized abilities (Vocabulary, Similarities, Comprehension), which are often relatively preserved in chronic schizophrenia, patients scored ≈ 1.3 SD below controls (note: subtest results are descriptive/exploratory).

Proportion of patients below normative cut-offs

Using control means and SDs as normative reference, 58 % of patients scored below 1 SD and 34 % below 1.5 SD of the normative mean on the VCI. Corresponding proportions were 57 % and 38 % for PRI, 51 % and 28 % for WMI, 77 % and 59 % for PSI and 75 % and 58 % for FSIQ. Thus, processing speed and overall IQ were most severely affected.

WMS-IV indices and subtests

A second MANCOVA conducted on WMS-IV index scores (AMI, VMI, VWMI, IMI, DMI) also showed a significant main effect of Group (Pillai's Trace = 0.82, $F(5, 80) = 18.5$, $p < 0.001$, partial $\eta^2 = 0.54$) after

Table 2. WAIS-IV indices and selected subtests in the recent-onset schizophrenia and control groups

WAIS-IV measure	ROS <i>M (SD)</i>	Control <i>M (SD)</i>	<i>F</i>	<i>p</i>	Cohen's <i>d</i>
Indices					
Verbal Comprehension (VCI)	80.91 ± 12.56	98.88 ± 15.42	35.11	< 0.001	1.30
Perceptual Reasoning (PRI)	82.16 ± 15.12	100.21 ± 15.11	30.64	< 0.001	1.21
Working Memory (WMI)	86.74 ± 13.33	102.84 ± 15.81	26.04	< 0.001	1.12
Processing Speed (PSI)	79.05 ± 13.40	102.95 ± 13.92	65.82	< 0.001	1.78
Full-Scale IQ (FSIQ)	79.88 ± 13.15	101.95 ± 13.02	61.15	< 0.001	1.72
Selected subtests					
Block Design	7.74 ± 3.24	10.19 ± 2.56	15.03	< 0.001	0.97
Similarities	6.67 ± 2.45	9.67 ± 2.72	28.88	< 0.001	1.41
Digit Span	7.53 ± 2.48	10.81 ± 2.80	33.07	< 0.001	1.49
Matrix Reasoning	7.26 ± 3.16	11.02 ± 3.05	31.68	< 0.001	1.38
Vocabulary	7.33 ± 2.49	10.53 ± 3.02	28.97	< 0.001	1.37
Arithmetic	7.51 ± 2.91	10.14 ± 3.69	13.44	< 0.001	0.89
Symbol Search	6.26 ± 2.41	10.60 ± 3.21	50.49	< 0.001	1.80
Visual Puzzles	7.07 ± 2.62	9.91 ± 3.42	18.63	< 0.001	1.07
Coding	6.30 ± 2.80	10.53 ± 2.71	50.73	< 0.001	1.82
Letter–Number Sequencing	6.73 ± 2.95	11.42 ± 3.55	42.58	< 0.001	1.62
Figure Weights	6.73 ± 3.19	10.81 ± 3.05	35.59	< 0.001	1.49
Comprehension	6.23 ± 2.48	10.44 ± 2.96	49.13	< 0.001	1.84
Cancellation	6.40 ± 3.04	10.60 ± 3.42	34.84	< 0.001	1.47
Picture Completion	7.20 ± 3.01	10.37 ± 2.79	24.82	< 0.001	1.27

adjusting for education. The covariate was non-significant in this model. Patients showed marked impairments across auditory, visual and working-memory domains. Table 3 sum-

marizes subtest and index results. Cohen's *d* values ranged from 1.32 to 2.75, reflecting very large impairments.

Table 3. WMS-IV indices and selected subtests in the recent-onset schizophrenia and control groups

WMS-IV measure	ROS mean (SD)	Control mean (SD)	<i>F</i>	<i>p</i>	Cohen's <i>d</i>
Indices					
Auditory Memory (AMI)	70.63 ± 16.39	100.56 ± 13.89	83.46	< 0.001	2.00
Visual Memory (VMI)	69.95 ± 18.04	101.63 ± 11.50	94.27	< 0.001	2.13
Visual Working Memory (VWMI)	75.84 ± 15.69	102.28 ± 14.21	67.09	< 0.001	1.80
Immediate Memory (IMI)	68.56 ± 15.43	101.53 ± 11.18	128.81	< 0.001	2.49
Delayed Memory (DMI)	66.12 ± 16.77	101.28 ± 13.34	115.74	< 0.001	2.36
Selected subtests					
Logical Memory I	4.58 ± 1.91	9.74 ± 2.97	92.10	< 0.001	2.56
Spatial Addition	6.77 ± 2.69	10.60 ± 2.46	47.66	< 0.001	1.81
Logical Memory II	4.49 ± 2.00	9.95 ± 2.86	105.22	< 0.001	2.75
Verbal Paired Associates I	5.95 ± 3.26	10.40 ± 2.83	45.56	< 0.001	1.67
Designs I	4.86 ± 2.88	9.58 ± 2.69	61.77	< 0.001	2.00
Symbol Span	5.70 ± 2.90	10.70 ± 3.16	58.47	< 0.001	1.89
Verbal Paired Associates II	6.30 ± 3.76	10.47 ± 3.20	30.57	< 0.001	1.32
Designs II	4.07 ± 3.51	10.14 ± 2.23	91.40	< 0.001	2.39
Visual Reproduction I	6.93 ± 3.97	11.81 ± 2.39	47.79	< 0.001	1.68
Visual Reproduction II	6.30 ± 3.99	11.14 ± 3.09	39.56	< 0.001	1.50

Proportion of patients below normative cut-offs

Below 1 SD scored 84 % of patients and 71 % below 1.5 SD of the normative mean on Auditory Memory. For Visual Memory these proportions were 87 % and 79 %, for VWMI 78 % and 63 %, for Immediate Memory 92 % and 85 % and for Delayed Memory 90 % and 82 %, respectively. These findings underscore the severity of early episodic-memory impairment in schizophrenia.

Discussion

The results of this study found that cognitive impairment is present early in schizophrenia and may not be solely attributable to illness duration or repeated hospitalizations. Medication effects could not be assessed in this study, and future work should consider antipsychotic dosages and other treatment variables (Heinrichs et al., 2013; Dickinson et al., 2012).

To closely examine specific cognitive functions, it seems prudent to take a closer look into the instruments used: first WAIS-IV, then WMS-IV. Verbal Comprehension is a WAIS-IV index; it measures verbal concept formation, abstract verbal reasoning, categorical thinking, word knowledge, verbal comprehension, and crystallized intelligence (Wechsler, 2008). In our sample, patients with ROS scored significantly lower on this index, which contrasts with previously reported findings by Michel et al. (2013) and the results of Fuentes-Durá et al. (2019), whose clinical schizophrenia sample had the same results as the control group. The authors of those studies point out that the VCI is a measure of general knowledge that builds up with time. However, patient samples differed between that study and ours. Furthermore, the paucity of available data specifically regarding Verbal Comprehension in schizophrenia limits the interpretation of this finding while directing us to the previously proposed global cognitive deficit in early schizophrenia (Addington & Addington, 2002).

The results on all the WAIS-IV indices were significantly lower compared to the control. These results are consistent with several studies that have found that short-term maintenance and manipulation of information in memory is problematic for people with schizophrenia (Gold et al., 1997; Lee & Park, 2005; Michel et al., 2013; Fuentes-Durá et al., 2019; Dickinson et al., 2007).

The WMS-IV is not constructed to diagnose a specific condition, such as traumatic brain injury, but to measure memory functions that are impaired in a variety of clinical conditions. Deficits in patients with schizophrenia have been identified on spatial span (Glahn et al., 2003), spatial working memory (Park, Püschel, Sauter, Rentsch, & Hell, 1999), and visual working memory (Coleman et al., 2002). The Visual Memory Index (VMI) is

measured by subtests that require recalling designs from memory and drawing them or replicating the placement of designs in a grid (Wechsler, 2019a). Visual memory on the WMS-IV assesses both memory for visual details and for spatial location. Poor memory for spatial location or visual details may result in a lower score on VMI. The results on this index that are given on a sample of the schizophrenia group in the Technical and Interpretive Manual for the WMS-IV are similar to those in this study. The results from 70 to 85 are associated, among others, with schizophrenia. The average VMI was, in our study, significantly lower than that in the control sample.

The WAIS-IV and WMS-IV profiles in our ROS sample support cognitive models of schizophrenia emphasizing that cognitive deficits are core features of the disorder rather than mere consequences of chronicity (Barch & Ceaser, 2012; Kahn & Keefe, 2013).

Limitations

Our research has several limitations to keep in mind. Although we included a homogenous sample of ROS patients, they were not treated with the same antipsychotic medication (or a combination of antipsychotics), raising the question of different mechanisms of action, as well as potential adverse events (in terms of cognition). Future studies should focus on the effects of psychopharmacotherapy, as well as of other therapeutic interventions, on cognitive functions in schizophrenia. Furthermore, this research was not longitudinal. Because of that fact, we are not able to speculate about the progress – deterioration of cognitive functions, or their recovery. Finally, we did not measure cognitive functions from day one of illness onset.

The present study demonstrates and confirms that a considerable impairment of cognitive functions, measured by both WAIS-IV and WMS-IV, exists in patients suffering from schizophrenia, even in its early course. Mild to severe cognitive impairments were evident in domains of visual memory, visual working memory, immediate memory, delayed memory, verbal comprehension, perceptual reasoning, working memory, and processing speed.

Ethics approval and consent to participate

All procedures were approved by the Ethics Committee of the University Hospital Centre Sestre milosrdnice. Written informed consent was obtained from all participants.

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Kognitivni profil u shizofreniji recentnog početka

Sažetak: Cilj ovog istraživanja bio je usporediti izvedbu na WAIS-IV i WMS-IV u bolesnika sa shizofrenijom recentnog početka (ROS) s izvedbom demografski uparene zdrave kontrolne skupine. Četrdeset i tri hospitalizirana bolesnika s ROS-om uspoređena su s 43 zdrava sudionika iz hrvatskih standardizacijskih uzoraka za WAIS-IV i WMS-IV, uparenih prema dobi, spolu i godinama obrazovanja. Primarne analize provedene su zasebnim MANCOVA-ama (Pillai's Trace) na indeksnim rezultatima WAIS-IV i WMS-IV, pri čemu je skupina bila međuispitanički faktor, a godine obrazovanja kovarijata. Nakon značajnih multivarijatnih učinaka provedene su univarijatne ANCOVA-e za svaki indeks, uz Holm korekciju kroz devet indeksnih testova. Klinička interpretabilnost prikazana je udjelom sudionika s rezultatima nižima od -1 SD i $-1,5$ SD u odnosu na distribuciju kontrolne skupine. Utvrđeni su veliki deficiti u brzini procesiranja i radnom pamćenju na WAIS-IV, uz izražene učinke i u perceptivnom rasuđivanju te verbalnom razumijevanju. Na WMS-IV zabilježena su vrlo velika sniženja u neposrednom i odgođenom pamćenju te velika sniženja u vizualnom pamćenju i vizualnom radnom pamćenju. Nalazi upućuju na to da je široko kognitivno oštećenje prisutno već u ranoj fazi bolesti, pri čemu su usporena obrada informacija i disfunkcija epizodičkog pamćenja osobito važni ciljevi rane procjene i rehabilitacije.

Ključne riječi: shizofrenija, kognicija, WAIS-IV, WMS-IV, brzina procesiranja, epizodičko pamćenje

