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ORIGINAL PAPER

Neuropsychological functioning in early-onset first-episode psychosis: comparison of diagnostic subgroups

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Abstract The aims of this study were to examine the nature and extent of cognitive impairment in first-episode early-onset psychosis (FE-EOP) soon after their stabilisation and to search for potential differences according to specific diagnostic sub-groups of patients. As part of a Spanish multicentre longitudinal study, 107 FE-EOP patients and 98 healthy controls were assessed on the following cognitive domains: attention, working memory, executive functioning, and verbal learning and memory. Three diagnostic categories were established in the patient sample: schizophrenia ($n = 36$), bipolar disorder ($n = 19$), and other psychosis ($n = 52$). Patients performed significantly worse than controls in all cognitive domains. The three diagnostic subgroups did not differ in terms of impaired/preserved cognitive functions or degree of impairment. FE-EOP patients show significant cognitive impairment that, during this early phase, seems to be non-specific to differential diagnosis.

Keywords Cognition · Early onset · First episode · Psychosis

Introduction

Cognitive deficits, considered as an inherent feature to psychosis, have been consistently described in adult-onset

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patients [10]. On the contrary, the search for a cognitive pattern of deficits in early-onset psychosis (EOP) (first psychotic symptoms before 18 years of age; [16]) is limited. Preliminary findings in early-onset schizophrenia patients have replicated deficits in the same cognitive domains as those described in adult-onset schizophrenia (attention, working memory, executive functioning, and learning and memory) [4, 6, 7, 17, 19, 22, 25]. However, it is unclear whether the nature (preserved vs. impaired functions) and extent of cognitive impairment is specific to schizophrenia or shared with other early-onset forms of psychosis [6, 7, 20, 23].

The Child and Adolescent First-Episode Psychosis Study (CAFEPS) is a Spanish multicentre, 2-year, longitudinal study. The main objectives of this project are to evaluate clinical, neuroimaging, biochemical, immunological, genetic, and neuropsychological variables in first-episode EOP [5]. This report describes the baseline neuropsychological results of the CAFEPS project. The primary aims in this area were: (1) to examine the nature (preserved vs. impaired functions) and extent of cognitive impairment in first-episode EOP patients soon after their stabilisation, and (2) to search for potential differences in the profile and severity of cognitive impairment according to differential diagnoses.

Method

This study is part of the CAFEPS. The methodology of the complete study has been comprehensively described elsewhere [5].

Subjects

Neuropsychological assessments were available for 107 of the 110 first-episode EOP patients who composed the original CAFEPS sample (three patients did not co-operate with the evaluation), and for all 98 recruited paired healthy controls.

Patients were recruited from child–adolescent psychiatry units at six university hospitals that cover a population of approximately 8 million people. All patients consecutively seen in those facilities between March 2003 and November 2005 who fulfilled the inclusion criteria described below were invited to participate in the study. The inclusion criteria for patients were age between 7 and 17 years at the time of first evaluation and presence of positive psychotic symptoms (within a psychotic episode) of less than 6 months' duration. Exclusion criteria were presence of a concomitant Axis I disorder, mental retardation if functioning was impaired prior to the onset of the disorder, pervasive developmental disorders, neurological diseases, history of head trauma with loss of consciousness, and pregnancy. Drug use was not an exclusion criterion if positive symptoms persisted for more than 2 weeks after a negative urine drug screening. The inclusion criteria for controls were age and gender similar to patients, coming from the same geographical area and schools, no presence of psychiatric disorders, and no neurological disorders, head trauma, pregnancy, or mental retardation (for more information on recruitment see [5]).

After receiving a full explanation of the study, all parents or legal guardians gave written informed consent before the patients were enrolled in the study, and patients gave their assent to participate. The study was approved by the Institutional Review Boards of all participating clinical centres.

Clinical assessment

All patients met DSM-IV criteria for a first episode of psychosis, assessed using the Kiddie-SADS-Present and Lifetime Version (K-SADS-PL). This scale was also used to rule out the presence of any Axis I or Axis II diagnosis in the healthy control sample. Clinical diagnostic interviews were performed by experienced child psychiatrists during the patient's first hospitalisation. The mean duration of illness, defined as the time between the onset of the first positive symptom and enrolment in the study, was 2.1 ± 1.7 months (range 1–6 months). Psychotic symptoms were assessed using the Positive and Negative Symptom Scale (PANSS), validated Spanish version [27]. Baseline diagnoses were confirmed or revised at a 1-year follow-up visit, based on DSM-IV criteria, in all patients with the exception of 10 who were lost to follow-up. For nine of those patients, diagnoses were confirmed or revised at a 6-month follow-up visit. For the remaining patient, the baseline clinical diagnosis—Psychosis Not Otherwise Specified (NOS)—was used. Three diagnostic categories were established: schizophrenia $n = 36$, bipolar disorder $n = 19$, and "other psychosis" $n = 52$. The latter group was composed as follows: 26 psychoses NOS, 9 schizophreniform disorders, 6 schizoaffective disorders, 6 major depressions with psychotic features, 3 brief reactive episodes, and 2 obsessive compulsive disorders with psychotic symptoms.

Before recruitment, $n = 27$ (27.3%) patients were on antipsychotic treatment. The mean duration of antipsychotic treatment at the time of enrolment was 5 ± 9.6 weeks (range 0–20 weeks). At the baseline assessment, 96.2% ($n = 103$) of the patients were receiving a second generation antipsychotic and 1.9% ($n = 2$) a first generation antipsychotic. The remaining 1.9% ($n = 2$) were not receiving any antipsychotic medication. Eighty per cent ($n = 84$) of patients in the treated sample ($n = 105$) were receiving only one antipsychotic, whereas 19% ($n = 20$) were receiving two antipsychotics simultaneously, and 1% ($n = 1$) a combination of three antipsychotics. The distribution of antipsychotic treatment was as follows: 64% ($n = 67$) risperidone, 25%

($n = 26$) quetiapine, 24% ($n = 25$) olanzapine, 3% ($n = 3$) ziprasidone, 2% ($n = 2$) aripiprazole, and 2% ($n = 2$) haloperidol. The mean daily antipsychotic dose in chlorpromazine equivalents was 312.98 ± 515.41 mg. Other medications administered were benzodiazepines (46.4%), antidepressants (17.3%), lithium (1.3%), mood stabilisers (6%), anticholinergics (7.3%), and others (1%).

Neuropsychological evaluation

The cognitive assessment was performed using a neuropsychological battery designed to assess four cognitive domains—attention, working memory, executive functioning, and verbal learning and memory—by combining selected individual measures from different tests (Table 1). Selection of these four domains was based on the MATRICS battery [11] and on a previous review of the literature [1, 12]. Decisions about grouping individual measurements into cognitive domains were based on the psychometric characteristics of the tests [21, 31]. All of the subjects included in this report completed at least 80% of the neuropsychological test battery designed for the CAFEPS.

Table 1 Neuropsychological assessment by cognitive domain

Cognitive domain	Neuropsychological variable
Attention	WAIS-III digits forward[a]
	Time to complete TMT-A
	Number of correct items Stroop 1 words
	Number of correct items Stroop 2 colours
	Number of correct responses CPT
	Mean hit reaction time CPT
Working memory	WAIS-III digits backward[a]
	WAIS-III number–letter sequencing[a]
Learning and memory	TAVEC total learning
	TAVEC short term free recall
	TAVEC long term free recall
	TAVEC discrimination
Executive functions	Derived score from TMT-B
	Number of words on the FAS
	Number of words on the COWAT (animals)
	Stroop interference score
	WCST number of perseverative errors
	WCST number of errors
	WCST conceptual level responses

WAIS-III Wechsler adult intelligence scale, 3rd edition, *TMT-A* trail making test, part A, *CPT* continuous performance test—II, *TAVEC* Spanish version of the California verbal learning test, *TMT-B* trail making test, part B. The score used in this study was: (time to complete TMT-B—time to complete TMT-A)/time to complete TMT-A, *FAS* verbal fluency test, *COWAT* control oral word association test, *WCST* Wisconsin card sorting test

[a] Number of longest series achieved

In order to obtain summary scores for each cognitive domain, raw scores were transformed to *z*-scores (mean 0; SD 1) based on the performance of the control group at baseline. The mean summary scores were calculated as the arithmetic means of the individual measurements that composed the specific cognitive domains (mean of the *z*-scores). The global cognitive score was calculated as the arithmetic mean of the four cognitive domains. This methodology is based on previous studies using similar procedures [7, 25]. In order to minimise the effect of age and schooling, when calculating the *z*-scores, the sample was divided into three age groups of similar size: 9–14, 15–16, and 17 year olds. We chose those age groups based on two criteria: grouping ages with similar reported cognitive function, and a minimum of 25–30 healthy subjects for each age group. The reason that minimum number of subjects is needed in the healthy group is that their performance was considered the "normal performance", similar to the way normative data is used for tests. If such groups were much smaller than 30, the performance of our healthy subjects could have not been considered representative of that age group.

All *z*-scores were calculated in such a way that higher scores always reflected better performance. The *z*-scores were truncated at −4.0 to prevent rarely occurring, extremely deviant scores.

All tests were administered and scored according to published standardised instructions, by six Master's level psychologists familiarised with the instruments. For those scales that required manual rating, an Intraclass Correlation Coefficient (ICC) was calculated (ICCs 0.95–1.00). Cognitive assessments were performed between weeks 4 and 8 after recruitment, either at the end of inpatient care or early in the course of outpatient treatment. Occasionally, when symptomatology had not properly resolved, evaluations were postponed in order not to interfere with the cognitive assessment. The mean duration of illness at the time of the neuropsychological assessment was approximately 3.6 ± 1.7 months. At this same visit, clinical symptoms were evaluated by means of the PANSS in order to ensure the reliability of associations with cognitive performance.

Statistical analysis

Mean and standard deviation are provided for continuous variables. Discrete variables are expressed as frequencies and/or percentages. For socio-demographic data, Student's *t* test for two independent samples (patients vs. control subjects) was used to compare means for continuous variables. When more than two groups were concerned (for socio-demographic and clinical data), a one-way analysis of variance (ANOVA) was performed, with the Bonferroni post hoc test where significant differences were detected. For the analysis of possible differences between subgroups

in the "mean daily medication dose", and due to the skewed distribution of this variable, the Kruskal–Wallis test was performed. The chi-square test was used for comparison of categorical measurements and the Mann–Whitney *U* test for parental socio-economic status (SES) as an ordinal variable. As control and patient groups differed in parental SES and patient subgroups differed in negative symptomatology, analyses of neuropsychological functioning were performed, controlling for these variables when required.

To investigate differences between the healthy control group and the patient group/diagnostic subgroups in neuropsychological functioning, the following models were used (with Pillai's criterion as the significance test, due to unequal size of groups): a full factorial multivariate analysis of covariance (MANCOVA) models, using group (patient/control) or diagnostic subgroups (schizophrenia, bipolar affective disorder, "other psychosis", and controls) as fixed factors, mean *z*-scores as dependent variables, parental SES and PANSS negative score as the co-variates when appropriate, and the Bonferroni post hoc test and Bonferroni correction for multiple comparisons. Possible associations between performance in cognitive domains and (a) severity of symptoms (PANSS total score) and (b) antipsychotic treatment (chlorpromazine equivalents) were analysed using a Pearson correlation test. All statistical tests were two-tailed and analyses were performed using SPSS for Windows software, version 11.5.1.

Results

Socio-demographic and clinical characteristics of the samples

The total sample of patients with first-episode EOP did not show significant differences from the healthy control group in socio-demographic variables (Table 2) with the exception of parental SES, which was lower in the patient group ($p = 0.001$). There was no difference in parental SES among the three diagnostic subgroups of patients; however, each had a lower parental SES compared to the healthy control group (Table 2). The clinical symptoms are summarised in Table 2. The schizophrenia subgroup scored significantly higher on the negative subscale of the PANSS than the bipolar disorder subgroup ($p = 0.012$).

Neuropsychological functioning

Comparison between first-episode early-onset psychosis patients and healthy controls

The mean raw scores and standard deviations for patients and controls on the cognitive tasks are presented in Table 3 for descriptive purposes. Overall, the MANCOVA controlling for parental SES revealed a significant difference in cognitive performance between patients and controls, with Pillai's Trace Criterion $F(4,198) = 51.596$, $p < 0.001$. The subsequent ANCOVA using the mean *z*-scores of both groups revealed significant differences in all cognitive domains evaluated: attention (patient mean −1.07 SD 0.68, $p < 0.001$), working memory (patient mean −0.87 SD 1.12, $p < 0.001$), executive functioning (patient mean −0.86 SD 0.81, $p < 0.001$), and verbal learning and memory (patient mean −1.93 SD 1.31, $p < 0.001$). A significant association was detected between PANSS total score and the mean *z*-score for attention ($r = -0.216$, $p = 0.028$). No significant associations were detected between PANSS total score and the mean *z*-score for working memory ($r = 0.135$, $p = 0.172$), executive functioning ($r = -0.159$, $p = 0.107$), or verbal learning and memory ($r = 0.002$, $p = 0.983$). No significant associations were found between the mean daily chlorpromazine-equivalent dose and patients' performance in any cognitive domain: attention ($r = -0.031$, $p = 0.752$); working memory ($r = -0.011$, $p = 0.909$); executive functioning ($r = -0.078$, $p = 0.425$); or learning and memory ($r = -0.072$, $p = 0.466$).

Comparison of diagnostic subgroups

The MANCOVA was performed again using the healthy control group and the three diagnostic subgroups of patients as the fixed factor. Differences in cognitive performance in the four groups were detected, with Pillai's Trace Criterion $F(12,594) = 10.781$, $p < 0.001$. Bonferroni-adjusted post hoc comparisons indicated that the differences lay between the healthy control group and each of the patient subgroups: attention (schizophrenia mean difference = −1.07, $p < 0.001$; bipolar disorder mean difference = −0.95, $p < 0.001$; other psychosis mean difference = −0.95, $p < 0.001$), working memory (schizophrenia mean difference = −0.82, $p < 0.001$; bipolar disorder mean difference = −0.84, $p = 0.005$; other psychosis mean difference = −0.69, $p = 0.001$), executive functioning (schizophrenia mean difference = −0.69, $p < 0.001$; bipolar disorder mean difference = −0.90, $p < 0.001$; other psychosis mean difference = −0.78, $p < 0.001$), and learning and memory (schizophrenia mean difference = −2.04, $p < 0.001$; bipolar disorder mean difference = −2.03, $p < 0.001$; other psychosis mean difference = −1.65, $p < 0.001$). No significant differences were found in cognitive domains among the patient subgroups, with Pillai's Trace $F(8,202) = 0.572$, $p = 0.800$. Results did not change when the analysis was re-conducted with negative symptoms as a co-variate [Pillai's Trace $F(8,194) = 0.750$, $p = 0.647$].

Table 2 Demographic and clinical information for first-episode early-onset psychosis patients and healthy controls

	Healthy controls	First episode psychosis	Analysis	Schizophrenia	Bipolar disorder	Other psychosis	Analysis[a]
N	98	107	–	36 (34%)	19 (18%)	52 (48%)	
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	Mean (SD)	
Age (years) (range 9–17)	15.17 (1.93)	15.50 (1.78)	t (203) = −1.277 p = 0.203	15. 61 (1.84)	15.74 (1.88)	15.35 (1.73)	F(3.201) = 0.804 p = 0.493
Education (years)	8.85 (1.86)	8.40 (1.80)	t (203) = 1.741 p = 0.083	8.36 (1.96)	8.89 (1.567)	8.25 (1.76)	F(3.201) = 1.595 p = 0.192
	n	*n*		*n*	*n*	*n*	
Gender							
Male	62 (63%)	71 (66%)	χ^2 (1) = 0.214 p = 0.643	28 (78%)	12 (63%)	31 (60%)	χ^2 (3) = 3.398
Female	36 (37%)	36 (34%)		8 (22%)	7 (37%)	21 (40%)	p = 0.334
Race							
Caucasian	92	92	χ^2 (4) = 6.952	32	18	42	χ^2 (12) = 13.814
African Black	1	1	p = 0.138	0	0	1	p = 0.313
Caribbean Black	0	1		0	0	1	
Hispanic	5	7		3	0	4	
Others	0	6		1	1	4	
Parental SES[b]							
1	10	22	U = 3830.5	6	3	14	[d]
2	23	34	p = 0.001	12	8	16	
3	27	21		8	5	10	
4	10	12		6	1	5	
5	28	12		4	2	7	
Clinical characteristics				Mean (SD)	Mean (SD)	Mean (SD)	
Daily medication dose[c]				273.24 (184.54)	278.47 (169.49)	357.31 (728.09)	χ^2 (2) = 0.270 p = 0.874
PANSS positive				16.29 (7.36)	14.89 (6.79)	14.02 (5.85)	F(2.101) = 1.231 p = 0.296
PANSS negative				19.65 (5.63)	14.47 (5.02)	16.59 (6.77)	F(2.101) = 4.853 p = 0.010[e]
PANSS general				35.21 (7.69)	34.53 (9.54)	32.45 (10.22)	F(2.101) = 0.972 p = 0.382

[a] Analysis comparing the four groups: healthy controls, schizophrenia, bipolar disorder, and other psychosis

[b] *SES* parental socio-economic status, assessed using the Hollingshead Scale [14] (ranging from 1 to 5). A rating of five corresponds to the highest SES and a rating of 1 means the lowest SES

[c] Chlorpromazine equivalents

[d] Mann–Whitney U test. Significant differences between Healthy Controls and Schizophrenia U = 1386.000, $p < 0.05$; Healthy Controls and Bipolar Disorder U = 652.500, $p < 0.034$; Healthy Controls and Other Psychosis U = 1792.000, $p < 0.002$. No significant differences among diagnostic subgroups

[e] Bonferroni post hoc test. Significant differences between Schizophrenia and Bipolar Disorder, p = 0.012

The *z*-score profiles for each diagnostic subgroup relative to the comparison sample are shown in Fig. 1. The mean *z*-scores and standard deviations for individual tests are presented in Table 4.

Mean global cognitive impairment was calculated for the three diagnostic subgroups (in *z*-score units, reflecting the number of standard deviations below the healthy control group mean). The overall profile means were as

Table 3 Mean raw scores on neuropsychological tests for first-episode early-onset psychosis patients and healthy controls

	Healthy controls $n = 98$ Mean (SD)	First episode psychosis $n = 107$ Mean (SD)
Attention/concentration		
Digits forward	6.48 (1.46)	5.37 (1.16)
TMT-A	30.17 (10.17)	42.20 (19.77)
Stroop-word	108.07 (17.61)	91.07 (15.56)
Stroop-colour	72.25 (12.85)	56.69 (11.37)
CPT-II correct R	318.15 (8.24)	307.67 (32.81)
CPT-II hit RT	0.402 (0.10)	0.487 (0.17)
Working memory		
Digits backwards	5.15 (1.34)	4.01 (1.39)
Letter-number seq.	5.77 (1.94)	4.48 (1.96)
Executive functioning		
WCST; errors	22.77 (14.64)	41.63 (23.50)
WCST; persev. errors	11.90 (8.49)	22.18 (16.03)
WCST; conceptual level	65.71 (10.37)	59.07 (18.53)
Stroop; interference	3.49 (9.18)	−1.76 (7.55)
TMT B-A/A	1.37 (0.84)	1.67 (1.38)
FAS	38.61 (10.55)	29.65 (11.33)
COWAT	22.06 (5.47)	15.69 (4.62)
Learning and memory		
Total learning	57.92 (7.85)	42.99 (12.08)
Short term memory	12.88 (2.11)	8.34 (3.36)
Long term memory	13.11 (2.29)	8.43 (3.63)
Discriminability	96.13 (10.50)	87.66 (16.25)

WAIS-III Wechsler adult intelligence scale, third edition, *TMT-A* trial making test, part A, *CPT-II* conners' continuous performance test II, *WCST* Wisconsin card sorting test, *TMT-B* trial making test, part B.; (time to complete TMT-B—time to complete TMT-A)/time to complete TMT-A, *FAS* verbal fluency test, *COWAT* control oral word association test, *TAVEC* Spanish version of the California verbal learning test

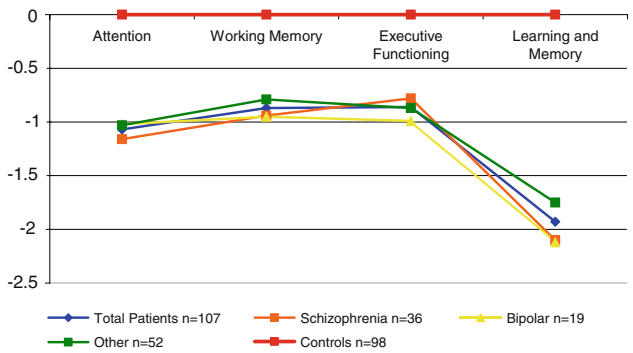

Fig. 1 Neuropsychological profile by diagnostic group

follows: schizophrenia mean −1.26, SD 0.67; bipolar disorder mean −1.27, SD 0.81; and other psychosis mean −1.11, SD 0.76. No significant differences were detected among the three diagnostic subgroups, with $F(2,100) = 0.575$, $p = 0.565$.

Discussion

Patients with a FE-EOP (first-episode EOP) showed deficits in attention, working memory, executive functioning, and verbal memory, the latter being the domain most affected, soon after their stabilisation. Impairment in the early course of psychotic illness affecting the aforesaid cognitive domains has been consistently reported in adult-onset psychosis [1, 3, 9, 24] and has been detected in antipsychotic-naïve adolescents with psychosis [4].

The effect of symptoms on cognitive performance in our sample of FE-EOP patients was significant only for the area of attention, with a minimal influence explaining only 4.7% of the variance. Other studies in early-onset psychosis have similarly reported neuropsychological profiles for which no influence of symptoms have been detected [19]. Additionally, no significant correlations were detected between the mean daily dose of antipsychotic medication and cognitive performance, in line with the result obtained by Kravariti et al. [19], derived from the Maudsley Early-Onset Schizophrenia Study. Overall, our results indicate that the cognitive profile reported in this study for our sample of FE-EOP patients is not secondary to clinical factors such as severity of symptoms or dosage of antipsychotic medication.

The deficits in attention, working memory, executive functioning, and verbal memory that characterised our FE-EOP group were likewise characteristic of all the patients, regardless of diagnosis. We were not able to detect differences among the diagnostic subgroups (i.e., schizophrenia, bipolar disorder, and "other psychosis") in the nature (preserved vs. impaired functions) or degree of the cognitive impairment described. Our results indicate a lack of specificity of cognitive impairment in FE-EOP patients.

The notion of an overlap in cognitive functions impaired across diagnostic categories in EOP has been previously described in the literature, both in chronic schizophrenia and psychosis NOS patients [20] and in first-episode patients when comparing schizophrenia and non-organic, non-affective psychotic disorders [6], and schizophrenia, affective psychosis, and substance-induced psychosis [7, 23]. Likewise, research in an adult-onset population has concluded that psychotic disorders comprise cognitive deficits that are qualitatively similar [30].

With respect to the severity of the cognitive deficits, our data show a similar degree of impairment across patient subgroups, in keeping with previous results in FE-EOP [23]. On the contrary, a prior study has reported that the severity of verbal memory deficits may be the specific

Table 4 Mean *z*-scores on neuropsychological tests by diagnostic group

	Schizophrenia $n = 36$ Mean (SD)	Bipolar disorder $n = 19$ Mean (SD)	Other psychosis $n = 52$ Mean (SD)	Analysis[a]		Post hoc
				F (DF)	*p*	
Attention/concentration	−1.16 (0.68)	−1.02 (0.68)	−1.03 (0.68)	42.12 (3,199)	<0.001	SZ, BD, OP < C
Digits forward	−0.72 (0.96)	−0.90 (0.92)	−0.93 (0.91)			
TMT-A	−2.09 (1.53)	−1.32 (1.59)	−1.61 (1.60)			
Stroop-word	−1.65 (1.06)	−1.14 (1.00)	−1.10 (1.22)			
Stroop-colour	−1.53 (1.03)	−1.59 (0.83)	−1.09 (0.89)			
CPT-II correct R	−0.61 (1.66)	−0.34 (0.65)	−0.88 (1.62)			
CPT-II hit RT	−0.71 (1.44)	−0.48 (1.16)	−1.09 (1.56)			
Working memory	−0.94 (0.89)	−0.95 (1.17)	−0.79 (1.26)	9.82 (3,199)	<0.001	SZ, BD, OP < C
Digits backwards	−0.85 (1.19)	−1.10 (1.27)	−0.95 (1.06)			
Letter–number seq.	−1.04 (0.8)	−0.80 (1.37)	−0.63 (1.73)			
Executive functioning	−0.78 (0.78)	−0.99 (0.88)	−0.87 (0.81)	46.62 (3,199)	<0.001	SZ, BD, OP < C
WCST; errors	−1.29 (1.31)	−0.93 (1.65)	−1.07 (1.57)			
WCST; persev. errors	−1.23 (1.31)	−0.88 (1.56)	−1.11 (1.48)			
WCST; conceptual level	−0.30 (1.68)	−0.98 (1.93)	−0.67 (1.55)			
Stroop; interference	−0.28 (0.87)	−0.96 (0.78)	−0.66 (0.81)			
TMT B-A/A	−0.17 (1.36)	−0.84 (1.55)	−0.33 (1.76)			
FAS	−1.10 (1.60)	−1.24 (1.33)	−1.14 (1.54)			
COWAT	−1.39 (0.74)	−1.32 (0.71)	−1.13 (1.16)			
Verbal learning and memory	−2.10 (1.35)	−2.12 (1.13)	−1.75 (1.35)	22.17 (3,199)	<0.001	SZ, BD, OP < C
Total learning	−2.03 (1.47)	−1.97 (1.23)	−1.64 (1.52)			
Short term memory	−2.54 (1.53)	−2.33 (1.50)	−2.13 (1.67)			
Long term memory	−2.27 (1.61)	−2.41 (1.29)	−1.86 (1.58)			
Discriminability	−1.31 (1.46)	−1.76 (1.60)	−1.35 (1.51)			

SZ schizophrenia, *BD* bipolar disorder, *OP* other psychosis, *C* control group

[a] MANCOVA. Fixed factor: diagnostic subgroups and healthy controls. Dependent variable: mean *z*-scores for cognitive domains. Covariate: Parental SES. Bonferroni correction for multiple comparisons

cognitive marker that differentiates those adolescents and young adults, during the first episode, with a diagnosis of schizophrenia from those with an affective psychosis, with the former group of patients achieving significantly poorer scores [7]. Additionally, more marked deficits in verbal learning have also been described for early-onset schizophrenia versus psychosis NOS in more chronic patients (with a mean of approximately 4 years of duration of illness) [20]. Overall, research in the adult-onset population indicates that cognitive deficits may be significantly more marked in schizophrenia patients than in other psychotic disorders [18]. However, it is not clear whether these differences are observable at the early stage of the disease or later in the course of the illness.

It must be considered that, even in studies finding no significant differences in the cognitive performance of EOP patients, there is a general tendency in results showing that schizophrenia patients generally present a more marked level of impairment, with lower neuropsychological test scores than the other psychotic subgroups of patients being assessed [6, 7, 23]. On the contrary, our bipolar disorder and "other psychosis" subgroups of patients performed as poorly as the schizophrenia subgroup in all cognitive domains. Comparison of overall cognitive functioning did not show significant differences across diagnostic subgroups, and a close examination of the individual *z*-scores does not support the notion of a generalised higher degree of cognitive impairment in our sample of schizophrenia patients. Hence, we found no support for the hypothesis that schizophrenia patients show a tendency towards greater cognitive impairment than other diagnoses, at least during the first episode of the illness.

One possible factor for the discrepancy across the studies is the variability of clinical characteristics of the samples and of the diagnostic composition of the subgroups that are being compared. Additionally, unlike some previous reports on first-episode patients, our study has the methodological strength that we followed our patients for

1 year (93% of the enrolled cases). This allowed us to prospectively categorise our first-episode patients in a more reliable way.

Based on the hypothesis that early-onset schizophrenia is a more severe manifestation than the adult-onset form [2, 13], it would be expected that our young sample would present a higher degree of impairment than that reported for the adult-onset form. The results of our study do not support more marked cognitive impairment in the early-onset form of schizophrenia when compared to the paediatric control group and may suggest a biological continuity between both clinical entities. Early-onset schizophrenia patients obtained general cognitive scores between 0.78 and 2.10 SD below the healthy control group. This finding is consistent with previous studies in early-onset schizophrenia [4, 17, 19, 26, 29]. The pattern and degree of impairment described are also similar to that reported in first-episode adult-onset schizophrenia patients, between −1 and −2 SD below the healthy controls [3, 28], although no direct comparisons can be made because we did not have a first-episode adult-onset psychosis control group. However, it must be considered that the early-onset form of the illness may be associated with a disruption in development, during a period of acquisition and consolidation of higher cognitive functions. Therefore, the functional impact of cognitive deficits may be more devastating in EOP. A longitudinal study of the assessed sample may help to clarify whether, along with the illness and compared to the normal developmental trajectory of cognition, EOP patients are more deviated from the healthy population and end up having more marked cognitive deficits than adult-onset patients.

The "other psychosis" subgroup showed a mixed profile, with a tendency towards less marked cognitive deficits than the schizophrenia or the bipolar group (i.e., more favourable mean domain scores than the other subgroups of patients or in between the two groups, but not presenting the more marked mean domain deficit). Due to the heterogeneity of the diagnoses included in this group, it is difficult to draw any conclusion. In addition, whereas the temporal stability and predictive value for the schizophrenia or bipolar disorder diagnoses is greater than 80% in EOP, it is much lower for other psychotic diagnoses [8, 15]. Consequently, it is very likely that, when longitudinally followed-up, some of the patients in this subgroup will be re-diagnosed with schizophrenia or bipolar disorder, whereas others will have a single episode with full recovery. In summary, the present configuration of the "other psychosis" subgroup is characterised by enormous clinical heterogeneity that prevents us from drawing reliable conclusions.

Although the cognitive assessment was performed using an extensive neuropsychological battery, there are cognitive domains, such as psychomotor speed, visuoconstructive abilities, visual learning and memory, or social cognition that have not been evaluated in this study. Another limitation is the small sample size of the patient subgroups, which could possibly explain the lack of significant differences across diagnoses. This fact may contribute to increasing the possibility of type II error due to low statistical power, limiting the study's ability to detect moderate to small differences between diagnostic subgroups. Finally, the absence of a non-psychotic psychiatric disorder group does not allow us to draw conclusions relative to the specificity of cognitive deficits for EOP.

Conclusion

Our results do not support either a differential profile of cognitive impairment or dissimilarities in the degree of deficit among the diagnostic subgroups of patients with first-episode EOP. During this early phase, cognitive impairment may constitute a non-specific marker for psychosis. A longitudinal study of this sample may help to elucidate whether the course of the cognitive deficits is similar for the different psychotic diagnoses or whether those entities with a better prognosis display better cognitive performance during remission.

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