Schizophrenia Research 211 (2019) 88–92

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

MCCB cognitive profile in Spanish first episode schizophrenia patients

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ARTICLE INFO

Article history:
Received 20 February 2019
Received in revised form 19 June 2019
Accepted 7 July 2019
Available online 22 July 2019

Keywords:
Schizophrenia
Cognition
MATRICS
First episode
MCCB

ABSTRACT

The objective of the study was to examine the cognitive profile of Spanish patients with a first episode of schizophrenia (FESz) and to compare that to the profile of patients with a chronic schizophrenia (CSz) and non-psychiatric (NP) control subjects. The study included 106 FESz, 293 CSz, and 210 NP, assessed with the Spanish version of the MATRICS Consensus Cognitive Battery (MCCB). The MCCB cognitive profile in a Spanish sample of FESz was similar to the cognitive profile of CSz with some discrepancies in select domains. The scores of both patient samples were about 1–2 SD below the scores of non-psychiatric control subjects.

1. Introduction

Cognitive dysfunction has been considered a core symptom of the schizophrenia since the first descriptions of the disorder (Kraepelin, 1919; Bleuler, 1950). Cognitive deficits have been described in patients with a chronic schizophrenia (CSz) (Reichenberg, 2010), and in patients with a first episode of schizophrenia (FESz) (Addington et al., 2003; Galderisi et al., 2009; Mesholam-Gately et al., 2009; Barder et al., 2013). There have been contradictory results regarding the comparison of cognitive profiles in FESz and CSz. Specifically, some authors have found a similar deficit (Hoff et al., 1992), but others have found less impairment in FESz than in CSz (Saykin et al., 1994; Albus et al., 1996; Addington and Addington, 2002; Townsend and Norman, 2004; Braw et al., 2008). A meta-analysis by Mesholam-Gately et al. (2009) included 47 cognition studies (43 separate samples) in FESz and found cognitive deficits with mean effect sizes from −0.64 to −1.20, similar to that described in CSz (i.e., from −0.46 to −1.41) in the meta-analysis by Heinrichs and Zakzanis (1998). Among the limitations of the meta-analysis in FESz is that the studies used a wide variety of neuropsychological measures, and it was suggested that future studies use the MATRICS Consensus Cognitive Battery (MCCB) to ensure a common core cognitive battery across studies.

McCleery et al. (2014) conducted the first study with a sample of FESz using the MCCB and found that the pattern and overall magnitude of cognitive impairment in FESz were similar to those observed in CSz. Both FESz and CSz showed marked impairment across MCCB domains compared to healthy participants. The MCCB domain scores were similar in FESz and CSz, with the exception of relative preservation of Working Memory and Social Cognition in FESz.

The MCCB was developed by the *Measurement and Treatment Research to Improve Cognition in Schizophrenia* (MATRICS) initiative of the U.S. National Institute of Mental Health. It is comprised of 10 tasks (Nuechterlein et al., 2008; Kern et al., 2008) which evaluate seven separable cognitive domains that are impaired in schizophrenia

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https://doi.org/10.1016/j.schres.2019.07.011
0920-9964/

(Nuechterlein et al., 2004). Our group developed the co-norming and standardization of the MCCB in Spain in collaboration with developers of the MCCB (Rodriguez-Jimenez et al., 2012). We previously described the profile of MCCB impairment for a Spanish CSz sample (Rodriguez-Jimenez et al., 2015), finding that CSz patients were impaired compared with healthy participants across all MCCB domains, similar to the results previously reported with a U.S. sample by Kern et al. (2011). Hence, the objective of the present study was to examine the cognitive profile of Spanish FESz patients and to compare that between FESz and CSz and healthy participants, similar to what McCleery et al. (2014) did with a U.S. sample. We also examined the differences in the distribution of severity of cognitive impairment between these samples, based on the criteria outlined by Heaton et al. (1991).

2. Materials and methods

2.1. Sample

The present cross-sectional study was carried out with 106 Caucasian FESz outpatients, who were consecutively included in the First Episode Program of the San Juan Hospital (Alicante, Spain). The assessment of the FESz patients was completed. The inclusion criteria were: 1) diagnosis of schizophrenia or schizophreniform disorder according to DSM-IV criteria, using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1995), 2) at least eight weeks of stabilization on their antipsychotic medication after discharge from the hospitalization unit, 3) age of 18 to 45 years, and 4) sufficient fluency in Spanish to allow the completion of the protocol. Exclusion criteria were: 1) substance abuse/dependence in the past eight weeks, 2) neurological or somatic diseases that could interfere the performance of the tasks, and 3) traumatic head injury. The study was approved by the Clinical Research Ethics Committee. The 210 non-psychiatric (NP) control subjects were the same sample of community residents used in the standardization process of the MCCB in Spain (Rodriguez-Jimenez et al., 2012). The 293 CSz subjects were the same sample as in our previous study (Rodriguez-Jimenez et al., 2015). The demographic and clinical characteristics of the FESz, CSz patients and NP groups are presented in Table 1.

Table 1
Demographic and clinical characteristics.

Characteristic	FESz (N = 106)	CSz (N = 293)	NP (N = 210)
Age-years mean (SD)	26.1 (7.1)[a,b]	41.2 (9.4)	42.7 (11.3)
Gender n (% men)	77 (72.6)[b]	206 (70.3)[c]	105 (50.0)
Education-years mean (SD)	10.5 (2.7)[a]	11.8 (3.6)[c]	10.7 (3.8)
Illness chronicity (years) mean (SD)	0.7 (0.6)[a]	17.1 (9.6)	
Antipsychotic treatment			
Second Generation n (%)	105 (99.1)[a]	228 (77.8)	
First Generation n (%)	1 (0.9)[a]	30 (10.2)	
Mixed n (%)	0 (0)[a]	35 (12.0)	
Chlorpromazine equivalents mean (SD)	707.2 (359.3)[a]	531.6 (415.0)	
PANSS			
Positive mean (SD)	28.0 (6.4)[a]	13.0 (4.8)	
Negative mean (SD)	26.0 (6.2)[a]	18.1 (7.7)	
General Psychopathology mean (SD)	52.8 (8.4)[a]	30.2 (10.4)	
Total mean (SD)	106.9 (14.1)[a]	61.3 (20.2)	

FESz: first-episode schizophrenia. CSz: chronic schizophrenia. NP: non-psychiatric control subjects.
[a] FESz differs from CSz, $p < 0.05$.
[b] FESz differs from NP, $p < 0.05$.
[c] CSz differs from NP, $p < 0.05$.

2.2. Instruments

2.2.1. MATRICS Consensus Cognitive Battery (MCCB)

The MCCB assesses seven cognitive domains: Speed of Processing, Attention/Vigilance, Working Memory, Verbal Learning, Visual Learning, Reasoning and Problem Solving, and Social Cognition (Nuechterlein et al., 2008; Kern et al., 2008). This study used the published and approved translation of the MCCB for Spain and the Spanish normative and standardized data correction. The MCCB testers had extensive experience in the administration of the battery, and they trained with the group that normed the MCCB in Spain. The training included didactic instruction, hands-on practice, and then certification by an experienced MCCB tester.

2.3. Statistical analysis

Data were managed and analyzed with SPSS v.19. For the MCCB impairment profile, the raw scores from each of the 10 MCCB tests were entered into the MCCB Computer Scoring Program, using the option to produce age- and gender-corrected T-scores for the seven cognitive domains and an Overall Composite (normative mean = 50; standard deviation = 10) based on a Spanish normative sample. To compare the MCCB profiles of the groups, a three (group) by seven (MCCB domain) mixed model analysis was conducted.

To compare the degree of impairment between the FESz, CSz patients and NP groups, the MCCB Overall Composite T-scores were grouped by degree of impairment based on criteria outlined by Heaton et al. (1991): "unimpaired" ($T \geq 45$), "below average" ($T = 40–44$), "mild impairment" ($T = 35–39$), "moderate impairment" ($T = 20–34$), and "severe impairment" ($T < 20$). Differences in the distribution of severity of cognitive impairment in the groups were assessed using Chi-square tests.

3. Results

3.1. Descriptive statistics

Age and gender corrected T-scores for each MCCB domain and the Overall Composite score by group are presented in Table 2. Missing data were minimal (0.9% of data points). The mixed model analyses used all available data.

3.2. Mixed model analysis

The MCCB profiles for each group are presented in Fig. 1. A mixed model was fit to the data, with diagnostic group (n = 3), MCCB domain (n = 7) entered as fixed effects.

There was a significant main effect of group [$F(2, 4236) = 633.59$, $p < 0.001$], a significant main effect of MCCB domain [$F(6, 4236) = 14.14$, $p < 0.001$], and a significant group by MCCB domain interaction [$F(12, 4236) = 9.84$, $p < 0.001$].

Pairwise comparisons to decompose the main effect of group demonstrated that the average score across the seven MCCB domains for the NP group was significantly higher than for FESz [$t(1224.38) = -22.46$, $p < 0.01$; mean difference = −11.83, 95% CI: −12.86, −10.79] and CSz [$t(3478.67) = -35.48$, $p < 0.01$, mean difference = −13.42, 95% CI: −14.16, −12.68]. Thus, the FESz and CSz samples showed significant impairment across MCCB domains compared to NP. The significant interaction indicated that the MCCB profile of the two patient groups significantly differed from that of the control group.

To evaluate the MCCB performance profiles of the patient groups, a mixed model analysis was conducted comparing only the two patient groups. There was no main effect of group [$F(1,2771) = 0.86$, $p = 0.35$], indicating similar magnitude of impairment averaged across the seven MCCB domains in the patient groups. There was a significant main effect of MCCB domains [$F(6,2771) = 18.60$, $p < 0.001$] and a

Table 2
Mean MCCB domains, age and gender corrected T-scores, by group.

	FESz (n = 106)	CSz (n = 293)	NP (n = 210)
	Mean (SD)	Mean (SD)	Mean (SD)
Speed of Processing	35.0 (9.4)	35.9 (10.5)	50.0 (9.9)[b]
BACS SC	33.0 (10.0)	36.2 (10.7)	50.0 (10.0)
Fluency	42.8 (8.6)	41.5 (9.2)	50.1 (9.9)
TMT-A	38.0 (10.1)	38.1 (11.0)	50.0 (10.0)
Attention/Vigilance (CPT-IP)	34.8 (9.9)[a]	38.4 (9.6)	50.1 (9.9)[b]
Working Memory	39.9 (12.3)	38.3 (11.3)	50.0 (9.9)[b]
WMS-III SS	41.9 (12.0)	41.4 (11.0)	50.1 (10.0)
LNS	40.9 (12.1)	38.3 (11.6)	50.0 (10.0)
Verbal Learning (HVLT-R)	38.6 (13.9)[a]	30.3 (13.6)	50.1 (9.9)[b]
Visual Learning (BVMT-R)	36.0 (14.6)[a]	32.8 (14.1)	49.9 (10.0)[b]
Reasoning and Problem Solving (NAB-mazes)	41.2 (10.6)	40.6 (11.6)	50.0 (9.9)[b]
Social Cognition (MSCEIT-ME)	41.8 (13.7)	39.9 (12.6)	49.9 (9.6)[b]
MCCB Overall Composite	32.8 (11.8)	30.8 (12.6)	50.0 (9.9)[b]

BACS SC: Brief Assessment of Cognition in Schizophrenia Symbol Coding; TMT-A: Trail Making Test A; CPT-IP: Continuous Performance Test- Identical Pairs; WMS-III SS: Wechsler Memory Scale 3rd Edition, Spatial Span; LNS: Letter-Number Span; HVLT-R: Hopkins Verbal Learning Test-Revised; BVMT-R: Brief Visuospatial Memory Test-Revised; NAB: Neuropsychological Assessment Battery; MSCEIT-ME: Mayer-Salovey-Caruso Emotional Intelligence Test- Managing Emotions.
Note: Group contrasts conducted at MCCB domain level only, rather than for individual subtests.
FESz: first-episode schizophrenia. CSz: chronic schizophrenia. NP: non-psychiatric control subjects sample.
[a] FESz differs from CSz. $p < 0.05$.
[b] NP differs from both patient groups. $p < 0.05$.

significant group by MCCB domain interaction [$F(6,2771) = 8.01$, $p < 0.001$]. Follow-up contrasts demonstrated a significant difference between the FESz and CSz groups on Attention/Vigilance [$F(1,394) = -3.69$, $p < 0.01$], Verbal Learning[$F(1,397) = 8.36$, $p < 0.01$] and Visual Learning [$F(1,397) = 3.22$, $p = 0.046$], with the FESz group achieving higher scores on the two learning domains and lower on Attention/Vigilance.

Next, within each patient group, we examined the pattern of relative strengths and weaknesses in the MCCB profiles. Within each group, performance on each MCCB domain was compared to the average score of the six remaining domains. FESz patients exhibited relative weakness in Speed of Processing [$t(105) = -4.04$, $p < 0.01$, mean difference = −3.71, 95% CI: −5.53, −1.89], Attention/Vigilance [$t(105) = -4.15$, $p < 0.01$, mean difference = −3.99, 95% CI: −5.90, −2.09] and relative strength in Reasoning and Problem Solving [$t(105) = 3.41$, $p < 0.01$, mean difference = 3.53, 95% CI: 1.48, 5.57] and Social Cognition [$t(105) = 3.51$, $p < 0.01$, mean difference = 3.62, 95% CI: 1.58, 5.67].

CSz patients exhibited relative weakness in Verbal Learning [$t(292) = -9.29$, $p < 0.01$, mean difference = −7.39, 95% CI: −8.96, −5.83], Visual Learning [$t(292) = -5.39$, $p < 0.01$, mean difference = −4.43, 95% CI: −6.05,-2.82] and relative strength in Attention/Vigilance [$t(289) = 3.85$, $p < 0.01$, mean difference = 2.17, 95% CI: 1.06, 3.27], Working Memory [$t(292) = 3.05$, $p < 0.01$, mean difference = 2.02, 95% CI: 0.72, 3.32], Reasoning and Problem Solving [$t(292) = 6.83$, $p < 0.01$, mean difference = 4.63, 95% CI: 3.30, 5.97] and Social Cognition [$t(292) = 6.67$, $p < 0.01$, mean difference = 4.52, 95% CI: 3.19, 5.86].

3.3. Distribution of cognitive impairment between samples

The distribution of the Overall Composite scores in the NP group is significantly different from that of the FESz group and CSz group. FESz and CSz patients were much more likely than NP individuals to have a greater degree of cognitive impairment ($\chi 2(8) = 222.6$; $p < 0.001$). Thus, while most NP participants fell into the "unimpaired" category, the largest proportion of FESz and CSz patients fell into the "moderate impairment" category. The distribution pattern for the FESz and CSz groups was similar (see Table 3).

4. Discussion

We found that the MCCB cognitive profile in a Spanish sample of FESz is generally similar in overall deficit severity to the cognitive profile of CSz. The data from the present study also revealed some significant differences in the MCCB profiles for FESz and CSz: although both patient groups show significant impairment across MCCB domains compared to NP, FESz patients show poorer performance in Attention/Vigilance and better scores in Verbal and Visual Learning compared to CSz patients. There were no substantial changes in the results if PANSS_scores and antipsychotic medication dosing (chlorpromazine equivalents) were included as covariates in the mixed models analyses.

These results are consistent with those of McCleery et al. (2014) with U.S. patients for overall severity of FESz and CSz deficits, but differ

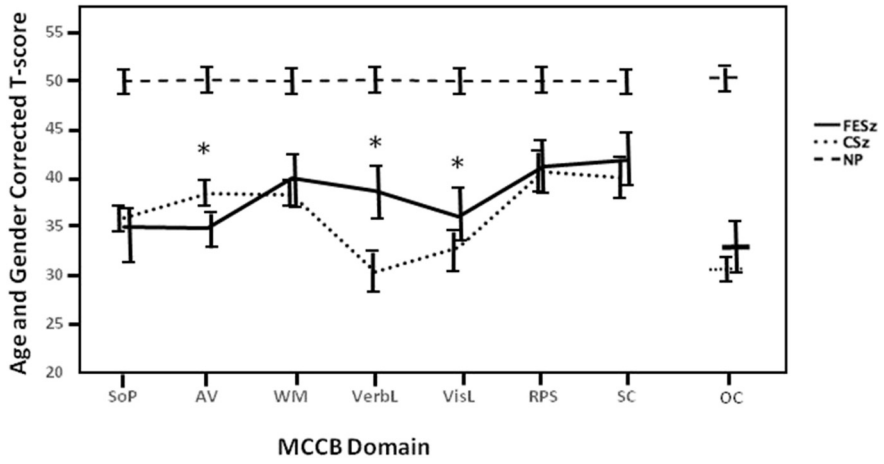

Fig. 1. MCCB profile for FESz, CSz, and NP (mean age and gender corrected T-score, 95% confidence interval). SoP: Speed of Processing, AV: Attention/Vigilance, WM: Working Memory, VerbL: Verbal Learning, VisL: Visual Learning, RPS: Reasoning and Problem Solving, SC: Social Cognition, OC: Overall Composite score. FESz: first-episode schizophrenia, CSz: chronic schizophrenia, NP: non-psychiatric community comparison sample. * Significant difference between FESz and CSz.

Table 3
Distribution of severity of impairment on MCCB Overall Composite score across groups.

MCCB Overall Composite score Level of impairment	FESz (n = 106)	CSz (n = 293)	NP (n = 210)	Total (n = 603)
	n	n	n	n
Severe impairment (T ≤ 20)	15[a]	57[b]	1	71
Moderate impairment (T = 20–34)	42[a]	124[b]	16	179
Mild impairment (T = 35–39)	16[a]	41[b]	15	72
Below average (T = 40–44)	16	27	27	69
Unimpaired (T ≥ 45)	17[a]	44[b]	151	212
$\chi^2(8) = 222.6$, p ≤ 0.001				

FESz: first-episode schizophrenia. CSz: chronic schizophrenia. NP: non-psychiatric control subjects sample.
The two patient groups did not differ from each other.
[a] FESz differs from NP, p < 0.05.
[b] CSz differs from NP, p < 0.05.

in the patterns across cognitive domains. McCleery et al. (2014) found that FESz showed better performance in Working Memory and in Social Cognition than CSz. In the Spanish sample of FESz we found poorer performance in Attention/Vigilance and better scores in Verbal and Visual Learning compared to CSz. The very low scores of the Spanish CSz in the Learning domains appear to contribute to these differences. The Differences between the national samples could be explained by differences in the MCCB scores between CSz samples of the two studies, but not by differences in FESz (with the exception of Attention/Vigilance). The MCCB scores in Working Memory, Verbal Learning, Visual Learning, and Social Cognition are poorer in the Spanish CSz sample than in U.S. sample. These cross-national differences could be due to the composition of the patient samples: the U.S. CSz sample had 14% with schizoaffective disorder and the Spanish CSz sample was limited to those with a diagnosis of schizophrenia. Further, the U.S. CSz sample had one more year of education on average; and a somewhat higher proportion were prescribed second-generation antipsychotic medications compared with the Spanish sample. Nonetheless, the profiles were very similar between the more clinically homogenous FESz samples from U.S. and Spain. The Spanish FESz exhibited relative strengths in Reasoning and Problem Solving and in Social Cognition, and the U.S. sample in Working Memory and Social Cognition. The Spanish FESz exhibited relative weaknesses in Speed of Processing and Attention/Vigilance, similar to the U.S. FESz sample. It should be noted that the U.S. and Spanish FESz samples were not in the exactly same stage of the disorder because the Spanish FESz sample was assessed nearer the onset of psychotic episode than the U.S sample. This may explain the higher doses of antipsychotics and the higher scores in symptom assessments in the Spanish sample. This discrepancy could contribute to the minor differences between the U.S. and Spain MCCB cognitive profiles in FESz.

Regarding the degree of cognitive impairment between the groups based on the Overall Composite, we found that FESz and CSz patients were different from NP, but there were no differences between FESz and CSz groups. In the present sample of FESz 53.8% were classified as having “moderate” or “severe” levels of cognitive impairment, and only 16.0% classified as “unimpaired”. These results are very similar to those obtained in the U.S sample of McCleery et al. (2014) (59% and 17%, respectively), and highlight the fact that cognitive impairment is present from the first stages of the disorder.

This study has some strengths and limitations. The main strengths are the large sample sizes for the patients and non-psychiatric controls samples, and the use of the MCCB as the instrument to assess cognition. Regarding its limitations, the cross-sectional design of this study cannot avoid potential biases, such as cohort effects.

In conclusion, this is the first study with a large sample of Spanish FESz compared with a CSz sample and with NP control subjects. The profiles found in the two patient samples were similar in overall severity, 1–2 SD below that of control subjects. The differences found between the profiles in our results and those of McCleery et al. (2014) in U.S., appear to be due to differences in CSz sample performance.

Contributors

RRJ, KHN, MFG, RSK, TP and LGF designed the study. RO, JLS, MD, JS, ESM, AL and EJL managed the literature searches and analyses. RLA, AIA, MD, ESM, EJL, AL and JLS selected the sample, evaluated patients and contributed in some aspects of the study design and in the interpretation of results. JS, RO and RRJ undertook the statistical analysis. RRJ, TP, KHN, MFG, RSK and LGF wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Role of the funding source

This research was supported in part by the by the Instituto de Salud Carlos III (grant PI16/00359; Fondo de Investigaciones Sanitarias/FEDER), by the European Development Regional Fund “A way to achieve Europe” (ERDF), by Madrid Regional Government (R&D activities in Biomedicine S2017/BMD-3740 (AGES-CM 2-CM)) and Structural Funds of the European Union.

Declaration of Competing Interest

Dr. Rodriguez-Jimenez has been a consultant for, spoken in activities of, or received grants from: Instituto de Salud Carlos III, Fondo de Investigación Sanitaria (FIS), Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Madrid Regional Government (S2010/BMD-2422 AGES; B2017/BMD-3740 AGES CM 2-CM), JanssenCilag, Lundbeck, Otsuka, Pfizer, Ferrer, Juste, Takeda.

Although not related to this work, Dr. Nuechterlein has consulted for Astellas, Biogen, Genentech, Janssen, Medincell, Takeda, and Teva and has had research grants from Janssen and PositScience. Dr. Green has been a paid consultant for AiCure, Biogen, Lundbeck, and Rosche, a member of the Scientific Board of Cadent, and has received research funds from Forum. Dr. Nuechterlein and Dr. Green are officers in the non-profit MATRICS Assessment, Inc., but receive no financial compensation.

All other authors declare that they have no conflicts of interest.

Acknowledgements

Instituto de Salud Carlos III (grant PI16/00359; Fondo de Investigaciones Sanitarias/FEDER), the European Development Regional Fund “A way to achieve Europe” (ERDF), Madrid Regional Government (R&D activities in Biomedicine S2017/BMD-3740 (AGES-CM 2-CM)) and Structural Funds of the European Union, and the Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM) of the Instituto de Salud Carlos III.

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