

# Neurocognition in Bipolar and Depressive Schizoaffective Disorder: A Comparison with Schizophrenia

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## Keywords

Neurocognition · Psychosis · Psychotic disorders · Affective disorders · Neuropsychology

## Abstract

**Introduction:** Schizoaffective disorder (SA) is classified into bipolar (bSA) and depressive (dSA) subtypes. Although clinical differences between both have been reported, there is no clear information regarding their specific cognitive profile. **Objective:** To compare neurocognition between SA subtypes and schizophrenia (SC). **Methods:** A total of 61 patients were assessed and divided into 3 groups: 35 SC, 16 bSA, and 10 dSA. All participants signed an informed consent letter. The MATRICS Consensus Cognitive Battery, Central and South American version was used to assess neurocognition. The study was performed at the Instituto Nacional de Psiquiatría “Ramón de la Fuente”. Participants were identified by specialized psychiatrists. Trained neuropsychologists carried out the clinical and cognitive assessment, which lasted 2 h approximately. **Results:** The cognitive assessment showed a significant difference in Trail Making Test part A subtest ( $F_{[2,58]} = 4.043$ ;  $p = 0.023$ ). Post hoc analyses indicated that dSA obtained a significantly higher score than SC ( $MD =$

$-11.523$ ;  $p = 0.018$ ). The  $f$  test showed a large effect size ( $f = 0.401$ ). No statistical differences were observed regarding other cognitive variables. **Conclusions:** The cognitive profile of SA subtypes and SC is similar since no differences were found in most subtests. However, dSA may be less impaired than SC in measures of processing speed. Further research with larger samples must be conducted.

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## Introduction

Schizophrenia (SC) is a chronic psychotic disorder that includes behavioral disturbances as well as affective and cognitive impairment. SC cardinal symptomatology is classified into negative (i.e., emotional flattening, apathy, and social withdrawal) and positive (i.e., hallucinations, delusions, and disorganized behavior/speech) symptoms [1]. Schizoaffective disorder (SA) is defined as the presence of cardinal symptoms of SC in addition to major depressive or manic affective episodes. SA is classified into bipolar and depressive subtypes. The bipolar subtype (bSA) is diagnosed if the patient fulfills criteria for a manic episode, although major depressive episodes

had been present; the depressive subtype (dSA) is considered if the patient meets for major depression, but no mania has been developed [1, 2].

There still is controversy regarding the clinical and cognitive features which may differentiate SA from SC since the clinical diagnostic criteria for SA lack clear boundaries between SC and bipolar disorder [3, 4]. A recent meta-analysis by Rink et al. [5] suggested that SA includes distinct clinical features that fall between SC and affective disorders, supporting the notion that SA is a clinical entity by itself, as part of a continuum of psychotic spectrum disorders. However, little has been explored about the clinical features of SA subtypes. Marneros [6] reported that bSA and dSA differ from each other regarding demographic and clinical variables (i.e., course, treatment), in which bSA implies a worse outcome.

Regarding cognition, consistent evidence has pointed out that SC patients show cognitive dysfunction, particularly in attention, memory, executive functions, and social cognition [7–9]. Conversely, the cognitive profile of SA has been poorly described since research on this population is scarce, probably due to the complexity of the diagnosis and the heterogeneity of its clinical symptomatology. Most studies which have assessed and compared cognition between SA and healthy controls have included SC and SA in the same clinical group, thus blurring the cognitive profile of SA. Few studies focused on neurocognition have assessed SA as a separate clinical entity from SC. A meta-analysis performed by Bora et al. [10] and a recent systematic review by Madre et al. [11] suggest that cognitive deficits observed in SA are similar to those found in SC and that the differences between both disorders are minimal. Moreover, a study by Van Rheenen et al. [12] could not discriminate the neuropsychological performance of SA subjects from the one obtained by SC or bipolar disorder patients. However, to our knowledge, no studies have explored the cognitive profile of SA subtypes.

Since there is evidence about putative clinical differences between SA subtypes, the comparison of their cognitive profile could bring specific information about the disorder, which may represent a potential tool to support SA diagnosis and treatment. Thus, the purpose of the study was to assess and compare neurocognition in patients with SC and SA subtypes using the MATRICS Consensus Cognitive Battery, Central and South American version (MCCB) [13] in a sample of Mexican patients. We hypothesized statistical differences in cognitive performance would be observed between SA subtypes and SC, as well as among bSA and dSA.

## Materials and Methods

### Participants

The study was approved by the Research Ethics Committee of the Instituto Nacional de Psiquiatría “Ramón de la Fuente” (IN-PRF) and the Ethics Committee of the Facultad de Estudios Superiores Iztacala (FESI). A total of 61 subjects were assessed and divided into 3 groups: 35 SC patients, 16 bSA patients, and 10 dSA patients. All participants were over 18 years old, which is the legal age of consent in Mexico, and signed an informed consent letter. Patients were recruited if they fulfilled DSM-5 criteria for SC or SA [1]. Additional inclusion criteria were being under pharmacological treatment and clinically stable. Psychiatrists considered the patient was clinically stable if they scored between 60 and 90 points in the Positive and Negative Syndrome Scale (PANSS) [14]. Exclusion criteria included the presence of neurological or comorbid mental disorders and a history of alcohol or drug abuse.

### Materials

Demographic data were obtained with a structured interview. The identification of the clinical groups – SC, bSA, and dSA subtypes – was based on DSM-5 criteria [1]. The PANSS, Spanish version [14], was used to obtain clinical data measurements.

The MCCB Central and South American version [13] was used to assess cognitive functions. The MCCB measures the following cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning, and problem-solving, and social cognition. It comprises the following tests.

#### Speed of Processing

*Brief Assessment of Cognition in Schizophrenia: Symbol Coding (BACS-SC).* The participant is instructed to write as fast as possible a series of numbers that correspond to specific symbols in a time lapse of 90 s. The score is obtained with the number of hits.

*Category Fluency: Animal Naming (CF).* The participant is asked to name as many animals as possible in a 60-second period. The total score corresponds to the number of animals named.

*Trail Making Test: Part A (TMT-A).* Participants are instructed to draw a line connecting consecutive numbers, which are irregularly located in a sheet of paper. The score corresponds to the time – in seconds – it takes the participant to achieve the task successfully.

#### Attention/Vigilance

*Continuous Performance Test: Identical Pairs (CPT-IP).* It is a computerized task in which the participant has to push a button every time two identical consecutive numbers appear on the screen. These targets are embedded in a random sequence of numbers. The score corresponds to the ratio of hits and misses (d-prime) provided by the software.

#### Working Memory

*Wechsler Memory Scale: Spatial Span (WMS-SS).* It includes a board with ten embedded cubes. The examiner touches the cubes following a specific sequence and asks the participant to touch them in the same order. This exercise corresponds to the progression condition. After that, the reverse condition is administered: the examiner touches the cubes following a specific sequence and asks the participant to touch them in reverse order. The total score comprises the sum of both conditions' hits.

**Table 1.** Demographic and clinical data of SC, bSA, and dSA

	SC	bSA	dSA	$\chi^2$	<i>p</i>
Gender (male/female)	21/14	6/10	5/5	2.258	0.323
Marital status (single/married)	34/1	13/3	8/2	4.886	0.087
Occupation (work, school/non)	16/19	8/8	5/5	5.032	0.540
Antipsychotic medication (atypical/typical)	29/6	13/3	10/0	2.093	0.351
Pharmacotherapy (antipsychotic/antipsychotic + antidepressant or anxiolytic/polytherapy)	10/15/10	3/4/9	2/2/6	5.381	0.250
	M (SD)			$F_{[2,58]}$	
Age, years [range]	37.1 (7.7) [26–59]	37.9 (9.8) [23–54]	34.6 (9.2) [28–59]	0.481	0.620
Years of education	12.8 (2.6)	14.5 (4)	13.1 (2.5)	1.753	0.182
Chronicity in years	14.3 (9.6)	12.1 (8.2)	14.2 (8.1)	0.287	0.752
Number of hospitalizations	1.3 (1.1)	3.2 (1.5)	1.1 (1.4)	12.047	0.000***
PANSS positive symptoms	23.2 (5.5)	21.9 (6.7)	25.2 (5.4)	0.911	0.408
PANSS negative symptoms	21.9 (5)	21.1 (4.4)	21.4 (5.1)	0.131	0.877
PANSS total score	83.4 (16)	77 (8.8)	85.2 (15.6)	1.140	0.327

SC, schizophrenia group; bSA, bipolar schizoaffective disorder group; dSA, depressive schizoaffective disorder group; PANSS, Positive and Negative Syndrome Scale. \*\*\* $p < 0.001$ .

**Letter-Number Span (LNS).** The examiner pronounces a series of mixed numbers and letters. The participant must separate both categories mentally, sorting numbers in ascendant order and letters according to the alphabet. He/she has to name the sorted numbers and letters as instructed. The score is the number of hits.

#### Verbal Learning

**Hopkins Verbal Memory Test-Revised (HVLT-R).** It includes a list of 12 words, which are recited by the examiner. The participant is asked to name all the words he/she remembers. The test includes 3 trials containing the same words. The total score comprises the sum of the words remembered in all trials.

#### Visual Learning

**Brief Visuospatial Memory Test-Revised (BVMT-R).** A sheet with 6 geometric figures is presented for 10 s. Next, the examiner asks the participant to draw the shapes he/she remembers as similar as possible. The test includes 3 trials with the same figures. The total score is the sum of the remembered shapes in all trials.

#### Reasoning and Problem-Solving

**Neuropsychological Assessment Battery: Mazes (NAB-M).** The participant is instructed to solve 7 mazes. The scoring depends on the time the participant takes to solve each one successfully. The total score is the sum of all solved mazes.

#### Social Cognition

**Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions (MSCEIT-ME).** The participant is instructed to assess the efficacy of different alternative actions that may be useful to cope with emotion-related situations in which self-regulation is needed. A computerized software calculates the total score.

#### Procedure

Clinical diagnosis of the patients was performed at the INPRF by specialized psychiatrists using DSM-5 criteria [1]. After verifying inclusion/exclusion criteria, volunteers signed an informed consent letter. Trained neuropsychologists carried out the clinical and neuropsychological assessment, which lasted 2 h approximately. If the patient was not available for the evaluation at the moment, an appointment was scheduled.

#### Statistical Analyses

Statistical analyses were performed using SPSS software (IBM, version 18). Descriptive statistics were used to analyze demographic and clinical data. One-way ANOVA was used to compare SC and SA subtypes. Bonferroni's post hoc analyses were computed to identify those groups that were statistically different. The effect size was estimated with Cohen's *f* test. Small effect sizes ranged from 0.10 to 0.24, medium effect sizes corresponded to scores between 0.25 and 0.39, and large effect sizes were considered from 0.40 [15]. Finally, Pearson correlations were performed to assess the association between clinical and cognitive variables.

## Results

Demographic and clinical comparisons are shown in Table 1. Statistical differences were found among groups in number of hospitalizations ( $F_{[2,58]} = 12.047$ ;  $p = 0.001$ ). Post hoc analyses indicated that bSA patients had been hospitalized more times than dSA and SC. PANSS mean scores did not differ between groups.

**Table 2.** Neuropsychological performance comparison between groups (T-scores)

Domains and tests	M (SD)			$F_{[2,58]}$	$p$	$f$ test	1 – B
	SC	bSA	dSA				
<i>Speed of processing</i>	28.1 (9.5)	31.7 (10.1)	33.4 (13.2)	1.333	0.272	0.210	0.277
BACS-SC	34.6 (9.5)	35.2 (9.1)	34 (15.6)	0.043	0.958	0.047	0.056
CF	40.4 (7.8)	45.7 (10.5)	41.7 (7.9)	2.037	0.140	0.246	0.403
TMT-A	24.5 (10.5)	27 (11.8)	36.1 (12.9)	4.043	0.023*	0.401	0.699
<i>Attention/vigilance</i>	32.9 (11.7)	32 (11.9)	35.6 (9.9)	0.309	0.736	0.130	0.097
CPT-IP 2 digits	2.6 (1)	2.7 (1.1)	3.2 (0.7)	1.284	0.285	0.245	0.267
CPT-IP 3 digits	1.9 (0.9)	1.7 (0.9)	2.1 (0.7)	0.554	0.577	0.181	0.137
CPT-IP 4 digits	0.8 (0.6)	0.9 (0.6)	0.6 (0.6)	0.703	0.499	0.204	0.163
CPT-IP total	32.9 (11.7)	32 (11.9)	35.6 (9.9)	0.309	0.736	0.130	0.097
<i>Working memory</i>	39.2 (9.1)	36.5 (10.3)	40.4 (12.4)	0.589	0.558	0.049	0.143
WMS-SS	44 (9.3)	40 (9)	45.4 (9.8)	1.346	0.268	0.235	0.261
LNS	38.2 (8.3)	37.3 (10.2)	38.6 (12.4)	0.072	0.931	0.056	0.060
<i>Verbal learning</i>	33.9 (7.8)	36.8 (7.1)	33.7 (6.9)	0.923	0.403	0.169	0.202
HVLT-R	33.9 (7.8)	36.1 (8.7)	34.4 (7.8)	0.437	0.648	0.115	0.118
<i>Visual learning</i>	46.7 (11.6)	48.8 (10.6)	44.1 (6.1)	0.600	0.552	0.181	0.145
BVMT-R	46.7 (11.6)	48.8 (10.6)	44.1 (6.1)	0.600	0.552	0.181	0.145
<i>Reasoning and problem-solving</i>	39.4 (12.4)	40.5 (8)	42.1 (9.8)	0.510	0.603	0.141	0.130
NAB-M	39.3 (7.2)	40.5 (8)	42.1 (9.8)	0.510	0.603	0.147	0.130
<i>Social cognition</i>	39.4 (12.4)	39.1 (11.9)	34.7 (7.1)	0.666	0.518	0.167	0.157
MSCEIT-ME	40.8 (14.8)	39.1 (11.9)	34.7 (7.1)	0.846	0.434	0.190	0.188
Total score	29.1 (10.8)	31.5 (11.4)	30.4 (11.6)	0.243	0.785	0.090	0.086

SC, schizophrenia group; bSA, bipolar schizoaffective disorder group; dSA, depressive schizoaffective disorder group; M, mean; SD, standard deviation; BACS-SC, Brief Assessment of Cognition in Schizophrenia: Symbol Coding; CF, Category Fluency; TMT-A, Trail Making Test: A version; CPT-IP, Continuous Performance Test: Identical Pairs; WMS-SS, Wechsler Memory Scale: Spatial Span; LNS, Letter-Number Span; HVLT-R: Hopkins Verbal Memory Test-Revised; BVMT-R, Brief Visuospatial Memory Test-Revised; NAB-M, Neuropsychological Assessment Battery: Mazes; MSCEIT-ME, Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions. \* $p < 0.05$ .

The comparison between groups regarding their performance at the neuropsychological assessment is displayed in Table 2. A significant difference was observed in TMT-A score ( $F_{[2,58]} = 4.043$ ;  $p = 0.023$ ). Post hoc analyses indicated that dSA obtained a significant higher score than SC (MD =  $-11.523$ ;  $p = 0.018$ ). The  $f$  test showed a large effect size ( $f = 0.401$ ). No statistical differences were observed in other cognitive variables.

Correlation analyses between clinical data and cognitive domains are shown in Table 3. For SC, number of hospitalizations negatively correlated with speed of processing ( $r = -0.404$ ,  $p = 0.040$ ), attention/vigilance ( $r = -0.423$ ,  $p = 0.031$ ), and total MCCB score ( $r = -0.441$ ,  $p = 0.024$ ); positive symptoms inversely correlated with social cognition ( $r = -0.462$ ,  $p = 0.007$ ); negative symptoms and PANSS total score inversely correlated with speed of processing ( $r = -0.374$ ,  $p = 0.032$ ;  $r = -0.454$ ,  $p = 0.008$ , re-

spectively) and social cognition ( $r = -0.365$ ,  $p = 0.037$ ;  $r = -0.447$ ,  $p = 0.009$ , respectively). The bSA group showed significant inverse associations between negative symptoms and speed of processing ( $r = -0.817$ ,  $p < 0.001$ ), attention/vigilance ( $r = -0.713$ ,  $p = 0.006$ ), verbal ( $r = -0.548$ ,  $p = 0.042$ ) and visual learning ( $r = -0.719$ ,  $p = 0.004$ ), and total MCCB score ( $r = -0.684$ ,  $p = 0.010$ ). For dSA, only a negative correlation was found between chronicity and reasoning and problem-solving ( $r = -0.458$ ,  $p = 0.048$ ).

## Discussion

Evidence about a differential cognitive profile between SC and SA is inconsistent. While some studies have reported that SA patients show better general cognitive per-



**Table 3.** Correlations between clinical data and cognitive domains

	SP	AV	WM	VL	ViL	RPS	SoC	MCCB total score
Chronicity in years								
SC	−0.295	−0.164	0.148	−0.131	−0.217	−0.055	−0.327	−0.234
bSA	−0.507	−0.256	−0.281	−0.367	−0.604*	−0.194	0.191	−0.337
dSA	−0.414	−0.708	−0.614	0.152	−0.079	−0.758*	−0.042	−0.507
Number of hospitalizations								
SC	−0.404*	−0.423*	−0.379	−0.374	−0.359	−0.387	0.027	−0.441*
bSA	−0.008	0.133	−0.340	−0.148	−0.235	−0.059	−0.132	−0.151
dSA	0.319	0.151	0.478	0.276	0.255	0.353	0.645	0.427
PANSS positive symptoms								
SC	−0.157	0.015	−0.136	−0.127	0.061	0.129	−0.462**	−0.186
bSA	0.352	0.342	−0.149	0.243	0.357	0.484	−0.089	0.184
dSA	0.057	0.172	0.067	0.368	0.049	−0.145	−0.337	0.061
PANSS negative symptoms								
SC	−0.374*	−0.294	0.111	−0.095	−0.194	−0.224	−0.365*	−0.318
bSA	−0.817***	−0.713**	−0.261	−0.548*	−0.719**	−0.484	−0.333	−0.684
dSA	−0.180	0.262	0.292	−0.189	−0.044	0.070	0.001	0.062
PANSS total score								
SC	−0.454**	−0.160	−0.060	−0.082	−0.101	−0.075	−0.447**	−0.344
bSA	−0.145	−0.087	−0.405	0.058	−0.006	−0.004	−0.403	−0.224
dSA	−0.213	0.064	0.010	0.060	−0.035	−0.150	−0.422	−0.110

SC, schizophrenia group; bSA, bipolar schizoaffective disorder group; dSA, depressive schizoaffective disorder group; SP, speed of processing; AV, attention/vigilance; WM, working memory; VL, verbal learning; ViL, visual learning; RPS, reasoning and problem-solving; SoC, social cognition; MCCB, MATRICS Consensus Cognitive Battery; PANSS, Positive and Negative Syndrome Scale. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

formance than SC, suggesting SA should be considered as a midpoint between SC and bipolar disorder along the psychotic continuum, others have failed to discriminate between such conditions [12, 16, 17]. To address such inconsistencies, we aimed to focus on SA subtypes by comparing their cognitive performance with SC patients using the MCCB.

The findings of the present study indicate a subtle yet significant difference regarding the cognitive profile of the comparison groups: dSA significantly outperformed SC in TMT-A, a standard speed of processing task. To achieve a successful performance of TMT-A, some other subprocesses, like adequate visual tracking and sequenced follow-up abilities as well as psychomotor speed low latencies, are required [18, 19]. SC patients achieved a lower performance than dSA, probably due to the psychomotor speed dysfunction consistently reported in SC [20]. Furthermore, a study by Chen et al. [17] highlighted that SC patients are particularly impaired in the psychomotor speed domain, which could be a specific cognitive feature that may discriminate between SC and other psychotic disorders. The fact that bSA did not show a significantly

different performance among any cognitive domain concerning SC, supports the notion that both SA subtypes may implicate different clinical and cognitive features. Our findings support the study of Marneros [6], who found clinical differences among SA subtypes, whereas bSA implied a poorer prognosis. It is possible that previous studies which have failed to differentiate the cognitive profile between both SC and SA, have assumed that SA involves a unique clinical entity irrespective of its subtypes. This assumption may have blurred the underlying subtle cognitive differences among them.

It has been widely documented that cognitive disturbances are a core feature of psychotic disorders. However, the analyses of the differences among specific cognitive domains may be more relevant than the mere comparison of the severity of the deficits. For instance, Owoso et al. [21] suggest that the significant cognitive differences between SC and SA relay on the error type throughout the task execution. These authors found that both SC and SA obtained low scores at information representation and maintenance tasks. However, those with SA diagnosis committed consistent errors related to goal maintenance,

while SC patients displayed more errors in relational encoding and retrieval tasks. These findings indicate that specific processes may be disturbed in the psychotic spectrum, so a profound analysis of the execution of the task is mandatory to delineate the differences between such disorders.

It is noteworthy that the cognitive specific domain differences along the psychotic spectrum may not only represent essential implications for the diagnostic characterization of the patients, but the non-pharmacological treatments available as well. Caponnetto et al. [22] reported that the implementation of cognitive remediation therapy with the inclusion of cognitive specific domain components had a positive effect on general cognitive and functioning measures. Thus, considering the subtle cognitive differences among the psychotic spectrum may not only provide an efficient directed individual treatment but a reduction on the costs of long-term interventions that imply a positive impact on the patient's functioning.

Interestingly, the correlation analysis showed that associations between symptomatology, number of hospitalizations, and cognition were stronger for SC and bSA than for dSA, suggesting the latter implies different interactions between variables. These findings bring evidence about the importance of analyzing SA in function of its subtypes, which may be a useful strategy to differentiate SA from SC. SC and bSA may be closer entities along the psychotic spectrum than dSA so that it may be more accurately discriminable [23]. The results of the present study bring alternative approaches with useful clinical implications that must be explored; further research is necessary.

### Limitations

It must be noted that the present study has some methodological limitations. The sample we worked with was small, and larger samples must be studied to obtain certain information regarding the cognitive profile of SA subtypes. Another limitation that must be noted is the clinical stability of the patients we recruited. As part of the inclusion criteria, participants of the study had to be clinically stable, as assessed by the physician. It allowed us to obtain reliable assessments since the patients were in adequate conditions to be examined. However, this criterion did not let us appreciate differences regarding the clinical profile that could differentiate both psychotic disorders (i.e., SC and SA) as well as SA subtypes. Maybe the recruitment of acute SA in patients or antipsychotic-na-

ive patients could bring more information about the symptomatology of SA. Finally, this was a cross-sectional study; clinical and cognitive evolution should be addressed to clarify the course of SA subtypes.

### Conclusions

The cognitive profile of SA subtypes and SC is similar since no differences were found in most subtests. However, dSA significantly outperformed SC in measures of processing speed, indicating that dSA may be less impaired in such a domain than SC and bSA. The domain-specific approach could be more useful for discriminating SA from SC. Furthermore, exploring SA characteristics by its subtypes could bring valuable information that could support accurate diagnosis and treatment. Further research with larger samples must be conducted to support our findings.

### Acknowledgements

The authors thank Lorena Guadalupe Rodríguez Carrillo, Martha Aida Rocha García, Miriam Tatiana Serment Azuara, Alejandra Itzel Solís Flores, Heroldo Palomares Guzmán, Susana Medina Loera, Mónica Arienti González, Rafael Campuzano De García, Areli López Alvarado, and Marlon Saavedra Delgado for their support in recruiting the study sample.

### Statement of Ethics

The study was approved by the Research Ethics Committee of the INPRF (record number: CEI/C/030/2016) and the Ethics Committee of the FESI (record number: CE/FESI/012016/1061).

### Disclosure Statement

The authors have no conflicts of interest to declare.

### Funding Sources

This work was supported by Programa UNAM-DGAPA-PA-PIIT under grant IA205516. The grant support contributed to the acquisition of the materials used to obtain and analyze the clinical and cognitive data reported in the present study (i.e., neuropsychological and clinical tests, computer equipment, software, etc.).

## Author Contributions

A.M.-M. designed the study, wrote the protocol, recruited and assessed participants, performed the data analysis, and wrote the manuscript since the first draft. Y.F.-M. designed the study, performed the data analysis, and wrote the manuscript since the first draft. J.S.-P. performed the data analysis and wrote the manuscript since the first draft. D.R.-M. recruited the sample, performed the

clinical and cognitive assessments, and worked with the database. G.Y.-T. designed the study, wrote the protocol, supervised the study, and reviewed the manuscript. R.E.-O. recruited the sample, supervised the study, and reviewed the manuscript. R.S.-Á. designed the study, wrote the protocol, recruited the sample, and wrote the manuscript since the first draft. All authors contributed to and have approved the final manuscript.

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