Psychological Medicine

cambridge.org/psm

Original Article

‡The online version of this article has been updated since original publication. A notice detailing the changes has also been published at: https://doi.org/10.1017/S0033291721003858

Cite this article: Czepielewski LS *et al* (2022). Effects of socioeconomic status in cognition of people with schizophrenia: results from a Latin American collaboration network with 1175 subjects. *Psychological Medicine* **52**, 2177–2188. https://doi.org/10.1017/S0033291721002403

Received: 10 December 2020
Revised: 26 May 2021
Accepted: 28 May 2021
First published online: 23 June 2021

Key words:
Cognition; low- and middle-income countries; schizophrenia; social factors

Author for correspondence:
Leticia Sanguinetti Czepielewski,
E-mail: leticia.czepielewski@ufrgs.br

© The Author(s), 2022. Published by Cambridge University Press

CAMBRIDGE UNIVERSITY PRESS

Effects of socioeconomic status in cognition of people with schizophrenia: results from a Latin American collaboration network with 1175 subjects

Letícia Sanguinetti Czepielewski[1,2], Luz Maria Alliende[3,4], Carmen Paz Castañeda[4], Mariana Castro[5,6], Salvador M. Guinjoan[7], Raffael Massuda[8], Arthur A. Berberian[9], Ana Olivia Fonseca[9], Ary Gadelha[10], Rodrigo Bressan[9], Marisa Crivelaro[11], Mario Louzã[11], Juan Undurraga[4,12], Alfonso González-Valderrama[4,13], Rubén Nachar[4,13], Rodrigo R. Nieto[14,15,16], Cristian Montes[14,15], Hernan Silva[14,15], Álvaro I. Langer[17,18,19,20], Carlos Schmidt[20,21], Rocío Mayol-Troncoso[14,15,19], Ana M. Díaz-Zuluaga[22], Johanna Valencia-Echeverry[22], Carlos López-Jaramillo[22], Rodolfo Solís-Vivanco[23], Francisco Reyes-Madrigal[24], Camilo de la Fuente-Sandoval[24,25], Nicolás A. Crossley[3,26,27], Clarissa S. Gama[1,28] and ANDES Network

Abstract

Background. Cognition heavily relies on social determinants and genetic background. Latin America comprises approximately 8% of the global population and faces unique challenges, many derived from specific demographic and socioeconomic variables, such as violence and inequality. While such factors have been described to influence mental health outcomes, no large-scale studies with Latin American population have been carried out. Therefore, we aim to describe the cognitive performance of a representative sample of Latin American individuals with schizophrenia and its relationship to clinical factors. Additionally, we aim to investigate how socioeconomic status (SES) relates to cognitive performance in patients and controls.

Methods. We included 1175 participants from five Latin American countries (Argentina, Brazil, Chile, Colombia, and Mexico): 864 individuals with schizophrenia and 311 unaffected subjects. All participants were part of projects that included cognitive evaluation with MATRICS Consensus Cognitive Battery and clinical assessments.

Results. Patients showed worse cognitive performance than controls across all domains. Age and diagnosis were independent predictors, indicating similar trajectories of cognitive aging for both patients and controls. The SES factors of education, parental education, and income were more related to cognition in patients than in controls. Cognition was also influenced by symptomatology.

Conclusions. Patients did not show evidence of accelerated cognitive aging; however, they were most impacted by a lower SES suggestive of deprived environment than controls. These findings highlight the vulnerability of cognitive capacity in individuals with psychosis in face of demographic and socioeconomic factors in low- and middle-income countries.

Introduction

Individuals with schizophrenia show reduced cognitive performance compared to unaffected subjects in a wide range of domains (Fioravanti, Bianchi, & Cinti, 2012), which is consistently associated with worse functional outcomes (Halverson et al., 2019), regardless of age, gender, or illness chronicity (Fett et al., 2011). These deficits are present since the early stages of the disease, even in drug-naïve patients (Fatouros-Bergman, Cervenka, Flyckt, Edman, & Farde, 2014), and there is evidence of cognitive compromise since before diagnosis (Mollon & Reichenberg, 2018). However, there is still controversy in the literature regarding the trajectory of cognitive change. Most studies report no further decline in cognition after the first episode (Szöke et al., 2008) even in never-medicated patients (Solís-Vivanco et al., 2020), while others have raised the possibility of a deteriorating trajectory with aging (Fett et al., 2020; Zanelli et al., 2019). There is also great heterogeneity in the cognitive deficits in schizophrenia (Shmukler,

Gurovich, Agius, & Zaytseva, 2015). Non-clinical studies show sex-differences in cognition; however, results for schizophrenia are inconsistent (Choleris, Galea, Sohrabji, & Frick, 2018; Mendrek & Mancini-Marïe, 2016). Recent literature has been trying to identify subgroups that might elucidate common mechanisms and risk factors, considering the variability within this population (Carruthers, Van Rheenen, Gurvich, Sumner, & Rossell, 2019). Studies using data-driven techniques revealed subgroups of cognitively spared, intermediate cognitive impairments, and deficit subtypes (Green, Girshkin, Kremerskothen, Watkeys, & Quidé, 2020). It is unclear, though, whether these findings result from diverse subgroups or only divisions in a linear continuum. Hence, adding evidence to this matter would have important implications for the clinical management of cognitive deficits in psychosis, in addition to broadening the understanding of the possible underlying mechanisms of psychopathology.

Schizophrenia and other psychotic disorders carry a genetic load related to cognitive performance and education attainment (Richards et al., 2020) that is shared across different populations (Lam et al., 2019). Nonetheless, a biocultural approach indicates that cultural patterns could influence neurobiology and inflammation in mental disorders (Shattuck, 2019). Specifically, an important focus should be given to the effects of the socioeconomic status (SES), which is 'a multidimensional construct comprising diverse socioeconomic factors' (Braveman et al., 2005, p. 2879), commonly operationalized through education, income, and/or occupation variables (Farah, 2017). SES is greatly predictive of several physical and mental health outcomes (Adler et al., 1994; Anderson & Armstead, 1995), and has been linked to risk for psychosis (Kwok, 2014; Luo et al., 2019). In non-clinical samples, SES is associated with cognitive ability and explains a significant proportion of shared environmental variance in twin-studies (Hanscombe et al., 2012; Hart, Petrill, Deater Deckard, & Thompson, 2007). In schizophrenia, SES has been shown to impact cognition (Goldberg et al., 2011). Interestingly, a study from USA found a group by parental SES interaction (based on occupation and education) in predicting executive functioning, indicating that low SES was related to worse performance in individuals with schizophrenia, but not in controls (Yeo et al., 2014). Curiously, only a few studies have investigated these effects in diverse settings. In this context, Latin America arises as an opportunity for studying the impact of SES on people with schizophrenia's cognitive performance, while at the same time looking into an understudied region of the world.

Latin America is a multiethnic and multicultural continent formed from a mixture of different pre-colonial indigenous cultures, European colonizers (mostly Spanish and Portuguese), and African ethnic groups brought as slaves during the colonization. It is home to almost 650 million people – around 8.45% of the world's population (World Bank, 2019), and has highly urbanized regions, with an estimated 80% of the population living in cities (United Nations, 2018). Because of its historical economic and political instability, there are over 36 million Latin American immigrants living abroad (Bayona-i-Carrasco & Avila-Tàpies, 2020), making the study of this population relevant beyond the continent's geographical limits. Latin America has significant and evident economic inequalities (World Bank, n.d.). The inequities experienced by its population go beyond income and lead to social discrimination and exclusion from exercise of rights, autonomy, and access to opportunities and education (Abramo, Cecchini, & Ullmann, 2020; Neidhöfer, Serrano, & Gasparini, 2018). These result in major health inequalities, both in access and outcomes (Abramo et al., 2020), implicating in factors such as a reduction in life expectancy at birth (Bilal et al., 2019). Furthermore, people in this region face challenges linked to extreme violence, such as reduced life expectancy due to homicide in young people (Canudas-Romo & Aburto, 2019). Such a different setting compared to highly industrialized western societies pose a valuable opportunity for the study of cognition, providing the opportunity to re-test previously known associations while also examining pending controversies under new light and different contexts, such as the effects of SES in cognition.

Therefore, we examined the cognitive performance of 1175 Latin American individuals with schizophrenia and healthy controls from five Latin American countries. We first focused on testing whether previously reported findings in schizophrenia and cognition, such as a global cognitive deficit, were replicated in such a different environment. We then sought to contribute to the discussions on the cognitive trajectory in schizophrenia by examining a possible differential association of age and cognition in our cross-sectional study. Additionally, we aimed to analyze how SES relates to cognitive performance in people with schizophrenia and healthy controls. Finally, we also explored whether patients clustered in different subgroups according to cognition.

Methods

Participants

This study is part of the ANDES network, which unites 15 groups from different countries across Latin America to promote science (Crossley et al., 2019). We included 1175 participants from five countries: Argentina, Brazil, Chile, Colombia, and Mexico, of which 864 were individuals diagnosed with schizophrenia or first-episode non-affective psychosis, and 311 were unaffected subjects. All participants were part of individual research projects that included cognitive and clinical assessments.

For a more complete description of sample features, we included in online Supplementary Table S1. each country's demographic characteristics, including population, Gross National Income (GNI) per capita, inequality measures (Gini coefficient), and Human Development Index (HDI) rating and rank. The per capita GNI (purchasing power parity) for the countries studied ranged from 12 896 to 219 722 011 USD, and Gini coefficients ranged from 40.6 to 53.3 (income distribution inequality). In terms of HDI (overall development), Chile and Argentina are ranked as 'Very High', while Mexico, Brazil, and Colombia are ranked 'High'.

All centers recruited patients with schizophrenia or an associated diagnosis from clinical centers. Some centers also included healthy controls. All patients and controls participated willingly and voluntarily, and proper consent forms were signed. Their local ethical committee approved each site's project. Table 1 describes the inclusion and exclusion criteria used for patients and controls in each center.

Assessments

Participants underwent a cognitive assessment through the MATRICS Consensus Cognitive Battery (MCCB). Because of differences in study design, some individuals completed only some of the battery subtests. We considered as SES the self-reported objective variables of personal education, parental education, and income, which are widely used in the neuroscience literature (Farah, 2017). We collected additional data related to

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

demographic (age, sex, and occupational status) and clinical factors (age of onset, illness duration, number of hospitalizations). Symptomatology in patients was assessed through the Positive and Negative Syndrome Scale (PANSS).

Data analysis

Statistical analyses were completed in R (version 4.0.2) and RStudio (version 1.3.1093). We transformed MCCB subtest raw scores into *z*-scores using the mean and standard deviation of the unaffected individuals. We used a reversed score of the Trail Making Test to maintain the direction of the other subtests. Then, we created a cognitive composite with the sum of *z*-scores divided by the number of subtests completed. Our first level of analysis was to compare patients and controls regarding demographic, socioeconomic, and cognitive data using independent samples *t* test and chi-square test when appropriate. We then investigated the relationship between cognitive performance and demographic, socioeconomic, and clinical data through linear regression models. Normality assumption was checked through visual inspections of histograms, qq-plots, and values of skew and kurtosis of the relevant variables. Skewed variables were log-transformed. Linear mixed-effects models with the site as a random effect were performed to confirm that linear models' findings were not due to site differences. Finally, we explored cognitive performance subgroups through hierarchical cluster analysis with the squared Euclidian distance and Ward linkage as the agglomeration procedure. The dendrogram's inspection was used as a criterion to establish the appropriate number of clusters to retain (Lima et al., 2019; Rabelo-Da-Ponte et al., 2020). We then compared the data-driven subgroups of cognitive performance regarding demographic, socioeconomic, and clinical variables using independent samples *t* test and χ^2 test. Descriptive data were expressed as mean and standard deviation, and significance was set at $p < 0.05$, two-tailed.

Results

Cognitive performance, clinical and demographic factors

Table 2 presents the demographic, socioeconomic, clinical, and cognitive data. Patients had similar age than unaffected participants. The patient's group included more males and had less working or studying individuals. Patients also had fewer years of education, parents' years of education, and family income than controls. Regarding cognition, as expected, we found a worse performance of patients compared to controls in the cognitive composite (Fig. 1*a*; $t(1128) = 18.588$, $p < 0.001$, Cohen's $d = 1.281$), and in each subtest individually (Table 2., Fig. 1b).

In patients, in linear models controlling for age, sex, and years of education, age of onset ($F(4,541) = 53.51$, $p < 0.001$, $t = 0.861$, $p = 0.390$, $\beta = 0.04$) and illness duration ($F(4,565) = 56.46$, $p < 0.001$, $t = -1.645$, $p = 0.101$, $\beta = -0.09$) were not related to the overall cognitive performance (online Supplementary Figure 1A–1B). Better cognitive performance was related to lower PANSS total score ($F(4,474) = 44.92$, $p < 0.001$, $t = -5.916$, $p < 0.001$, $\beta = -0.24$) and its subscales (Positive: $F(4,475) = 42.67$, $p < 0.001$, $t = -5.275$, $p < 0.001$, $\beta = -0.21$); Negative: $F(4,475) = 48.07$, $p < 0.001$, $t = -6.683$, $p < 0.001$, $\beta = -0.27$; General: $F(4,475) = 39.57$, $p < 0.001$, $t = -4.263$, $p < 0.001$, $\beta = -0.17$) (online Supplementary Figures S1C–S1F).

Effects of age and gender in patients and controls

We performed a linear regression model including the cognitive composite as the dependent variable, age, gender, and group as the independent predictors, and the interaction between age × group and gender × group ($F(51,049) = 118.3$, $p < 0.001$, Adj.$R^2 = .358$). We found that age ($t = -7.430$, $p < 0.001$, $\beta = -0.34$), gender ($t = -2.200$, $p = 0.028$, $\beta = -0.10$), and group ($t = -8.464$, $p < 0.001$, $\beta = -0.63$) were all independent predictors of cognitive performance, with no group by age ($t = 0.950$, $p = 0.342$, $\beta = 0.08$) or group by gender ($t = 0.859$, $p = 0.391$, $\beta = 0.04$) interactions. This indicated that aging was associated with a similar global cognitive decline in both patients and controls (Fig. 2*a*), and that male participants performed slightly better than females.

Exploring cognition in a relatively deprived setting: association with SES indicators of education, parental education, and income

We found a group by education interaction ($t = 5.333$, $p < 0.001$, $\beta = 0.49$) in a model with cognitive composite as the dependent variable, and the interaction between years of education and group as predictors, controlling for age and gender ($F(5,817) = 177.1$, $p < 0.001$, Adj.$R^2 = 0.517$), indicating that education was more important for the cognitive performance of patients than for controls (Fig. 2*b*). The same was found for parents' years of education ($F(5,444) = 112.1$, $p < 0.001$, Adj.$R^2 = 0.553$), where the interaction suggested a more significant effect for the patient's parents education ($t = 2.839$, $p = 0.0047$, $\beta = 0.26$), although in a less pronounced way than the patient's personal education (Fig. 2*c*).

Finally, a model with cognitive composite as the dependent variable, and income by group as predictors, controlling for age and gender ($F(5,239) = 66.85$, $p < 0.001$, Adj.$R^2 = 0.574$) found a group by income interaction ($t = 4.471$, $p < 0.001$, $\beta = 0.25$), indicating that patients with more income scored higher in cognitive performances, while income was not associated with cognitive performance in controls (Fig. 2*d*).

Investigating subgroups of cognitive performance

We conducted a hierarchical cluster analysis with only the patients with complete data considering the subtests *z*-scores of the MCCB. We identified two subgroups of cognitive performance: the first group had most patients ($n = 388$, 71.59%) and had lower middle performances than mean scores of healthy controls (*z*-scores between −1.05 and −0.19). The second subgroup ($n = 154$, 28.41%) showed performances considered as clinical deficits in all domains (*z*-scores below −1.5) (Fig. 3).

Patients from the first subgroup were younger, had more personal and parental education, and had fewer years of illness, psychiatric hospitalizations, and symptoms (lower PANSS scores) than the second subgroup. Additionally, the first group had an increased estimated IQ in relation to the other group. There were no differences regarding age at onset and family income (Supplementary Table S2).

Effects of site

Linear mixed-effects models with the site as a random factor were performed to ascertain that all results previously mentioned were not due to site differences. No differences were found between models' results.

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

Table 1. Sample characteristics by site

Site	Sample size	Inclusion criteria			Exclusion criteria	Healthy controls
		Diagnosis	Ages	Other		
Argentina Buenos Aires FLENI Institute Outpatient Unit	46 SZ 46 HC	DSM-IV-TR, SZ	18–65	Stable >2 weeks without change in medication or inpatient care	Substance abuse in the last 6 months. Intellectual disability	Included No current or previous history of psychiatric disorder. No ongoing psychotropic treatment.
Brazil Porto Alegre HCPA/UFRGS Outpatient Unit	42 SZ 45 HC	DSM-IV-TR, SZ	18–65	Stable >6 months		Included No current or previous history of psychiatric disorder. No first-degree family history of major psychiatric disorder
Brazil São Paulo UNIFESP Outpatient Unit	267 SZ 85 HC	DSM-IV-TR, SZ	>18	Stable >4 weeks without change in medication >4 years of education Estimated IQ >80.	Substance abuse in the last year History of traumatic brain injury or neurological disorder.	Included
Brazil São Paulo HCFMUSP Outpatient Unit	40 SZ	DSM-IV-TR, SZ	18–55	Stable >8 weeks No change in medication or inpatient care for the last 3 months >5 years of education.	Substance use disorders Comorbid axis I disorders Intellectual disability History of TBI or neurological disorder Suicide risk	Not included
Chile Santiago Horwitz Psychiatric Early Intervention Program Inpatient Unit	107 SZ 51 HC	ICD-10 F20-F29	16–25	Non-affective first-episode psychosis Estimated IQ >70		Included No current or previous history of psychiatric or neurological disorder No first-degree family history of major psychiatric disorder
Chile Santiago Horwitz Psychiatric Early Intervention Program Outpatient Unit	32 SZ	ICD-10 F20-F29	16–25	Diagnosis within the previous 5 years ⩽4 in PANSS positive and negative subscales Estimated IQ >70 Hamilton Depression's scale suicide item = 0.	Morbid obesity EEG abnormalities History of seizures	Not included
Chile Santiago Universidad de Chile Psychiatric Clinic	50 SZ	DSM-IV-TR, SZ	18–52	<15 years since onset of psychotic symptoms Treatment with ⩾1 atypical antipsychotic	Substance use disorder with recent substance use (<1 week) Neurological disorder	Not included
Chile Valdivia Outpatient Units	57 SZ	DSM-IV-TR, SZ schizoaffective or schizotypal	15–35	Clinically stable Early onset of the disorder.	Substance abuse in the last 6 months Suicide risk Intellectual disability.	Not included

Colombia Medellín San Vicente Foundation University Hospital	101 SZ	DSM-IV-TR, SZ	18–60	>6 and <16 years of education	Intellectual disability History of TBI or neurological disorder	Not included
Mexico Mexico City Instituto Nacional de Neurología y Neurocirugía	122 SZ 84 HC	DSM-IV-TR, SZ, schizophreniform disorder, brief psychotic disorder	18–50	Antipsychotic-naïve	Substance use disorders Comorbid axis I disorders	Included

Discussion

This is the first large and representative study to characterize the cognitive deficits of schizophrenia in a Latin American population. Using this sample from an under-reported region of the world, we were able to confirm certain associations frequently found in the literature, as well as shed light on new controversies. We found that patients had worse cognitive performance than healthy controls, which was generalized across all cognitive domains. Age was an independent predictor of cognitive performance, and we did not find any evidence suggesting that this association was different in patients and controls. When we looked at the SES variables, we found that a deprived environment was related to worse cognitive impairments mostly in patients. Personal education, parental education, and income were significantly related to both groups' cognitive performance, but higher SES variables were associated with larger cognitive function increases in schizophrenia. These results might indicate a vulnerability of individuals with psychosis that could prompt patients to be more impacted by chronic exposure to social factors, as we can observe in poor and developing countries such as in Latin America. Finally, not all patients showed severe deficits, and the gravity of impairments was related to demographic, socioeconomic, and clinical variables. These findings are discussed below.

First, as expected, patients performed worse than healthy controls in all subtests of the MCCB and the cognitive composite. Cognition was also related to symptomatology, particularly negative symptoms. These results were expected since these findings have been widely reported in different regions of the world and remained robust over the decades (Schaefer, Giangrande, Weinberger, & Dickinson, 2013). Nonetheless, there were no studies with representative data from Latin America reporting this outcome, which is why these results are important for a broader understanding of a diverse world. Further, as prior reports, we found high heterogeneity in the cognitive performance of individuals. Our data-driven clustering indicated that around 70% of patients presented performances considered as lower-middle compared to unaffected individuals. As indicated in the review by Green et al. (2020), a two-cluster solution has been found in previous studies. Our results suggest a smaller group for severe deficits (28.41% as opposed to 50% in other studies). A severe subtype appears to be common to all investigations of clusters, and several studies report differences in clinical and socioeconomic findings among groups (Green et al., 2020), which supports our results. Moreover, the subgroups of cognitive performance seem to be present in related diagnoses such as bipolar disorder, indicating that these cognitive subgroups might not imply distinct profiles but possibly different stages of the same cognitive trajectory (Karantonis et al., 2020).

Second, we observed in our sample that the SES variables of education, parental education, and income were all related to worse cognitive impairments mostly in patients, indicating that lower SES was associated to worse cognitive performance in schizophrenia, which is supported by the literature. A sample of individuals with schizophrenia from Australia (Wells et al., 2020) divided into preserved, deteriorated, and compromised groups based on estimated premorbid IQ and current cognitive performance showed a SES difference. Additionally, the compromised patients (e.g. individuals with a significant decline from estimated premorbid IQ) showed greater childhood adversities and lower SES than the deteriorated patients (e.g. those with both current and estimated premorbid impairments) (Wells

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

Table 2. Demographic, socioeconomic, clinical, and cognitive data

Variables	Individuals with schizophrenia or FEP ($n = 864$)	Healthy controls ($n = 311$)	Group comparisons
Demographic			
Age [mean (s.d.)]	30.39 (±10.90)	31.12 (±11.67)	$t(1153) = 1.0$, $p = 0.317$
Sex [*n*, male/female]	569/220	137/174	$\chi^2(1) = 76.43$, $p < 0.001$
Occupational status [*n* (%)]			$\chi^2(3) = 113.21$, $p < 0.001$
No work, no study	231 (60.47%)	5 (5.32%)	
Work	78 (20.42%)	34 (36.17%)	
Study	61 (15.97%)	55 (58.51%)	
Retirement or government aid	12 (3.14%)	0 (0%)	
Socioeconomic			
Personal years of education [mean (s.d.)]	11.26 (±3.07)	14.39 (±4.26)	$t(919) = 11.97$, $p < 0.001$
Parent's years of education [mean (s.d.)]	10.78 (±4.66)	14.29 (±4.33)	$t(478) = 8.134$, $p < 0.001$
Income [mean (s.d.)]	457.78 (±333.55)	1361.45 (±1755.32)	$t(243) = 6.312$, $p < 0.001$
Clinical			
Age at onset [mean (s.d.)]	21.95 (±6.61)	–	
Illness duration [mean (s.d.)]	9.10 (±9.67)	–	
Number of hospitalizations [mean (s.d.)]	1.78 (±2.87)	–	
PANSS positive [mean (s.d.)]	17.68 (±8.36)	–	
PANSS negative [mean (s.d.)]	21.38 (±8.05)	–	
PANSS general [mean (s.d.)]	37.40 (±13.57)	–	
PANSS total [mean (s.d.)]	76.33 (±26.80)	–	
Cognitive			
Trail Making Test (TMT): Part A [mean (s.d.)]	58.12 (±38.24)	35.45 (±14.63)	$t(1126) = -9.673$, $p < 0.001$
Brief Assessment of Cognition in Schizophrenia: Symbol Coding (BACS SC) [mean (s.d.)]	36.31 (±13.34)	55.53 (±14.80)	$t(955) = 19.616$, $p < 0.001$
Hopkins Verbal Learning Test – Revised (HVLT-R) Total Score [mean (s.d.)]	19.56 (±5.48)	26.25 (±4.35)	$t(1085) = 18.480$, $p < 0.001$
Wechsler Memory Scale-III (WMS-III): Spatial Span (SS) [mean (s.d.)]	13.49 (±4.30)	16.39 (±3.80)	$t(958) = 9.804$, $p < 0.001$
Letter-Number Span (LNS) [mean (s.d.)]	9.85 (±3.99)	13.89 (±3.43)	$t(955) = 14.798$, $p < 0.001$
Neuropsychological Assessment Battery (NAB): Mazes [mean (s.d.)]	12.26 (±6.94)	17.92 (±6.80)	$t(954) = 11.528$, $p < 0.001$
Brief Visuospatial Memory Test – Revised (BVMT-R) Total Score [mean (s.d.)]	17.60 (±8.70)	25.27 (±8.27)	$t(851) = 12.275$, $p < 0.001$
Category Fluency: Animal Naming (Fluency) [mean (s.d.)]	16.90 (±5.75)	23.26 (±5.75)	$t(1083) = 15.901$, $p < 0.001$
Continuous Performance Test – Identical Pairs (CPT-IP) Mean Score [mean (s.d.)]	1.56 (±0.79)	2.50 (±0.74)	$t(892) = 16.750$, $p < 0.001$
Estimated IQ [mean (s.d.)]	86.38 (±13.81)	104.85 (±12.14)	$t(483) = 13.742$, $p < 0.001$

et al., 2020), suggesting that social factors might impact both cognitive development and exposure to childhood adversity. Interestingly, there seems to be a difference between the observed and the expected global cognitive ability of patients, and even 'normal' performers (as indicated by normative data) might be impaired compared to their expected abilities (Hochberger et al., 2020). This might suggest that, in addition to biological neurodevelopmental abnormalities (Czepielewski, Wang, Gama, & Barch, 2017), individuals at risk of severe mental disorders may also be more vulnerable to social factors during development. A study of the Philadelphia Neurodevelopmental Cohort (USA) (Gur et al., 2019) found that lower SES was related to both reduced performances in different cognitive domains and lower volume across brain regions, including white and gray matter, that was related to an accelerated neurodevelopment. In patients from Latin America (Crossley et al., 2021), we recently showed that income was related to total gray matter volume in unaffected individuals but not in psychosis patients. This potentially

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

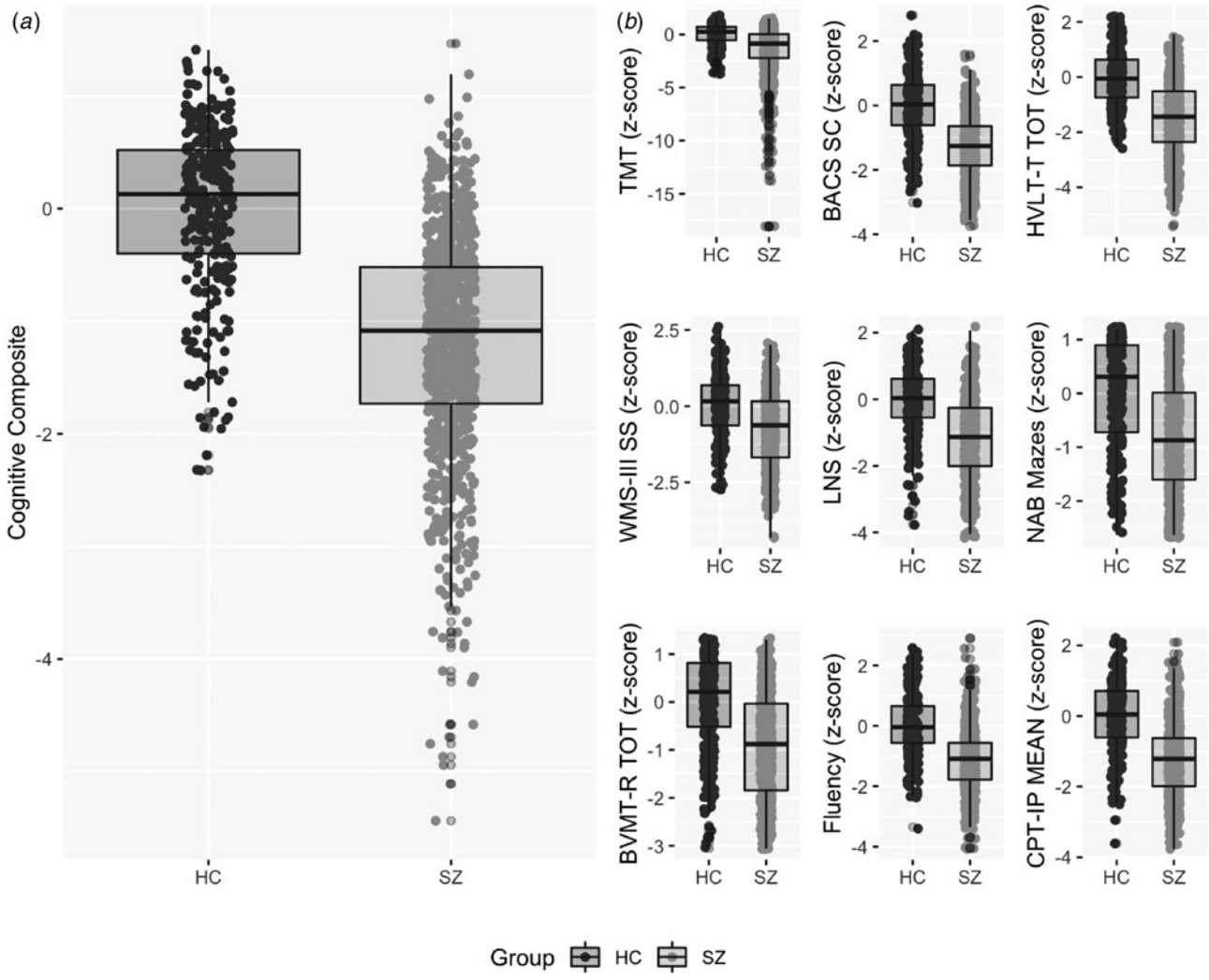

Fig. 1. (*a*) Comparison of the MCCB cognitive composite (*z*-score) between healthy controls (HC) and individuals with schizophrenia (SZ). (*b*) Comparison of each subtest of the MCCB (*z*-score) between healthy controls (HC) and individuals with schizophrenia (SZ).

indicated that less brain vulnerability in patients (e.g. less gray matter loss) would be sufficient to become unwell in adverse environments, and that considering the upbringing of patients is critical to understanding schizophrenia's anatomy (Crossley et al., 2021). Although this may seem contradictory to the present report, we believe that these two Latin American findings indicate that environmental variables might be key to explaining disease outcomes. The difference between patients and controls in the impact received by deprived environments was seen in our sample related to cognitive performances, specially where less income and parental education were more related to worse impairments in cognition for patients. While the unexpected findings for unaffected individuals might be different from other studies in the literature, a diagnosis by SES interaction has been described related to executive functions in a sample from the USA (Yeo et al., 2014). Further, we highlight that these relationships have not been extensively studied in non-WEIRD populations.

Third, we found that patients did not show a steeper cognitive decline in the cognitive composite than controls. Only longitudinal studies following participants through aging can actually confirm this association. Nonetheless, although our data is cross-sectional, we have a wide range of ages in our large sample (13–66 years), which might bring an idea of a longitudinal profile. The cognitive aging in schizophrenia and related disorders is still unestablished (Czepielewski et al., 2018). Some evidence suggests early deficits with stable trajectories after the first episode (Sheffield, Karcher, & Barch, 2018). A longitudinal study by the Genetic Risk and Outcome of Psychosis (GROUP, Netherlands and Belgium) (Islam et al., 2018) found five cognitive trajectories that remained stable after 3 and 6 years in individuals with SZ. However, others point to accelerated cognitive aging. The Suffolk County Mental Health Project (USA) (Fett et al., 2020) showed that patients with a first psychotic hospitalization, after 18 years, presented declines in some cognitive domains that were clinically significant and larger than expected due to normal aging. This was similar to the Aetiology and Ethnicity in Schizophrenia and Other Psychoses study (AESOP, UK) (Zanelli et al., 2019) that followed first-episode psychosis after 10 years and found a cognitive decline in specific domains after illness onset in patients with schizophrenia.

One possible argument for these inconsistencies may be related to the evidence that suggests that cognitive reserve might protect from accelerated cognitive aging declines (Van Rheenen

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

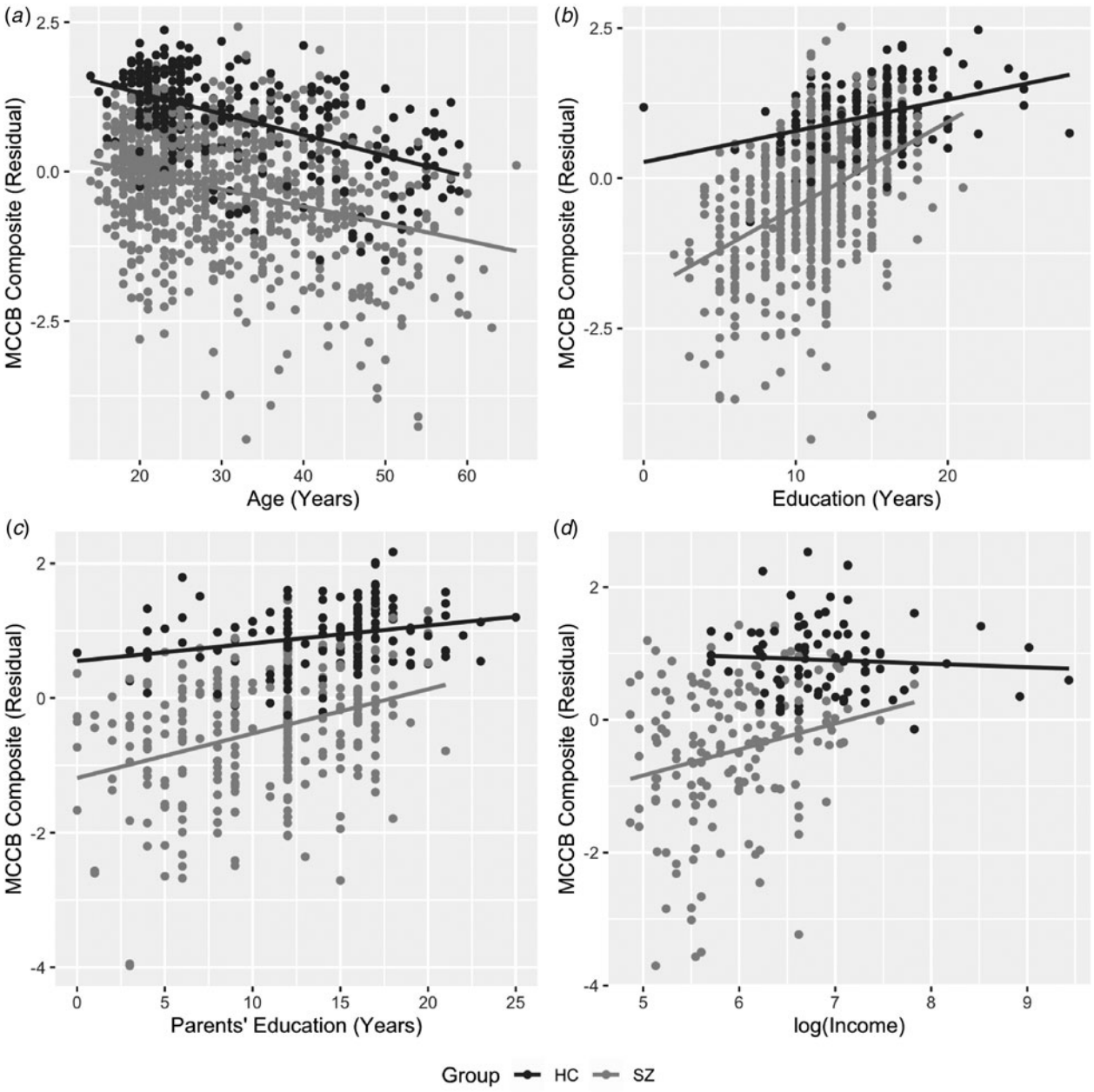

Fig. 2. Relationship between demographic and socioeconomic factors and MCCB cognitive composite (*z*-score) in healthy controls (HC) and individuals with schizophrenia (SZ), controlling for age and gender.

et al., 2020). Cognitive reserve refers to the brain's ability to reorganize itself to better cope with neuropathology, and is usually measured based on socio-behavioral proxies (e.g. IQ, education, and social activities) or other approaches (e.g. neuroimaging) (Stern, 2002). In our sample, we found that education was more important for cognitive performance in patients than in controls, supporting this hypothesis. Years involved in formal learning is one of the main components of cognitive reserve. Individuals with increased cognitive reserve might show better functional and cognitive performances, in addition to better clinical outcomes (Herrero et al., 2020). However, this process is greatly influenced by the fact that individuals who later develop schizophrenia show difficulties in acquisition of cognitive abilities during childhood and adolescence (Bora, 2015), which might also explain the shorter years of study compared to unaffected individuals. The interaction between neurodevelopmental and neuroprogressive processes could elucidate the heterogeneity and distinct cognitive trajectories of the disorder (Reckziegel et al., 2021).

Fourth, our results revealed that increased positive, negative, and general psychopathology symptoms were all associated with worse cognitive performance, even after controlling for the effects of age and education. This might indicate that patients with increased psychopathology have worse disease trajectories associated with poorer cognitive performances (Islam et al., 2018) since the overall symptomatology tend to persist over time (Haro et al., 2018). A previous meta-analysis of cross-sectional studies (Ventura, Hellemann, Thames, Koellner, & Nuechterlein, 2009) indicated that several cognitive domains were strongly related to negative symptoms, but not to positive symptoms, which was different to what we found in our study. However, the two different

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

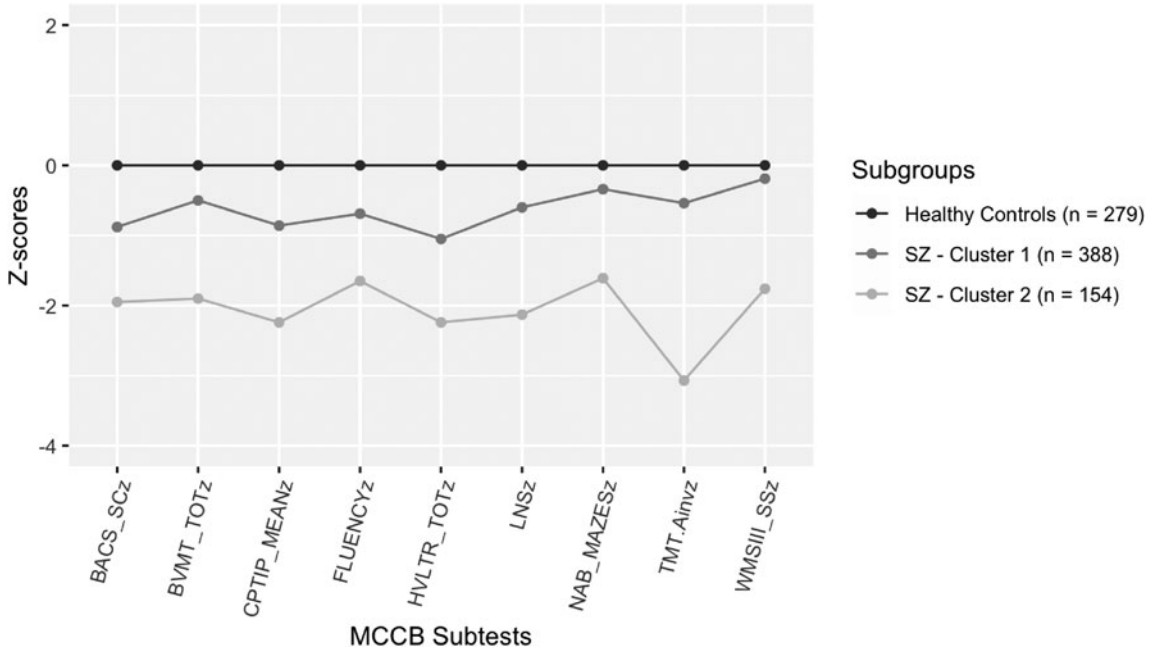

Fig. 3. Mean cognitive performance in each subtest *z*-scores between subgroups of individuals with schizophrenia (SZ) and healthy controls (HC).

dimensions within positive symptoms have been shown to be differently related to cognitive deficits in schizophrenia. Specifically, disorganization symptoms have a moderate effect, while reality distortion has a weak effect in relation to cognition (Ventura, Thames, Wood, Guzik, & Hellemann, 2010). Thus, the variability in symptom presentation might partially explain our findings regarding positive symptoms. Interestingly, these cognitive trajectories do not seem to be related to the age of onset (Islam et al., 2018), as seen in our sample. Therefore, the relationship between clinical variables and cognition was partially supported by previous literature.

Our study had some limitations. We presented cross-sectional data from several sites with different inclusion criteria and patient profiles. However, we used a mixed-model approach to manage inter-site differences. We also did not control for possible confounders, such as duration of untreated psychosis, medication use, and other lifestyle factors. Moreover, we did not present T-scores from the MCCB domains. It should be noted that there are different findings regarding the interpretation of cognitive data when comparing different cultures with the same normative scores, even in well-developed and high-income countries (HIC) (Raudeberg, Iverson, & Hammar, 2019). Therefore, comparing patients with unaffected individuals from the same cultural and socioeconomic background is preferred – as conducted in our study.

There are different findings in the literature between low- and middle-income countries (LMIC) and HIC. Individuals from LMIC report higher stress sensitivity and prevalence of psychotic experiences (DeVylder et al., 2016). Urbanicity does not seem to be related to increased risk for psychosis in developing countries, different from what has been described regarding HIC (DeVylder et al., 2018). Nonetheless, similarities have also been reported between LMIC and HIC findings, such as the generalized cognitive impairments in drug-naïve individuals with psychosis (Yang et al., 2020), and the relationship between a more prolonged duration of untreated psychosis and poorer clinical improvement and increased functional disability (Farooq, Large, Nielssen, & Waheed, 2009). However, even though several Latin American countries focused on expanding of universal health coverage to reduce health access inequalities during the last decades (Atun et al., 2015), there is still a significant concern regarding the treatment gap for mental disorders in LMIC (Kohn et al., 2018), which might prevent better outcomes for these patients.

LMIC publish fewer scientific reports related to mental disorders compared to HIC, although the number has increased in the last decades (Large, Nielssen, Farooq, & Glozier, 2010). Those that exist are usually underpowered, mainly because of a lack of government research funding and research capacity. Therefore, the scientific community could greatly benefit from the 'consolidation of more regional, interdisciplinary and international research networks' (Forero, Trujillo, González-Giraldo, & Barreto, 2020), since 'people working and living in LMICs are better placed to define issues of importance to their populations than are people living thousands of miles away in HICs – who often fund research based on their own interests' (Beran et al., 2017). Within this perspective, our study aimed to bring – from a collective effort – a contribution to the development of cognitive research in schizophrenia and related disorders in Latin American and other LMIC. Further research is needed combined with more practical measures from the scientific community, such as funding focused on LMIC and promoting the Schizophrenia International Research Society (SIRS) membership to represent the world's diversity (Gooding, Park, Dias, Goghari, & Chan, 2020).

In conclusion, this is the first large-scale study describing the cognitive characteristics of individuals with schizophrenia from Latin America and the possible impacts of SES on cognitive outcomes. As expected, patients showed general and heterogeneous cognitive deficits compared to unaffected individuals. Patients did not show evidence of accelerated cognitive aging; however, we found that they were most impacted compared to controls by a deprived environment as measured by SES variables. These findings indicate the need for public policy to protect children and youth from the effect of social

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

adversities, especially for those at risk or experiencing schizophrenia or other severe mental disorders. The ANDES Network brings a unique chance to study psychosis in disadvantaged settings, which are frequently less represented in research publications. Future studies from the ANDES Network will further explore the effects of the environment on cognition to understand better the mechanisms involved in this crucial dysfunction.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291721002403.

Acknowledgements. The authors thank all the patients and their families for inspiration, support, and participation. Alfonso González-Valderrama, Carmen Paz Castañeda and Rubén Nachar thank all senior leadership, professionals, and staff from Instituto Psiquiátrico José Horwitz and Universidad Finis Terrae who were involved in this project. Rodolfo Solís-Vivanco, Francisco Reyes-Madrigal and Camilo de la Fuente-Sandoval thank Felipe Rangel-Hassey and Pablo León-Ortiz (Instituto Nacional de Neurología y Neurocirugía), and Alejandra Mondragón-Maya (Universidad Nacional Autónoma de México) for their help in data acquisition, and Ricardo Mora-Durán (Hospital Fray Bernardino Álvarez) for his help in recruitment.

Author contributions. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Financial support. This project was supported by: *ARGENTINA* – Agencia de Promoción (PICT-2014-0633); *BRAZIL* – Fundação de Amparo à Pesquisa do Estado de São Paulo (Fapesp 2010/10788-6); *CHILE* – Agencia Nacional de Investigación y Desarrollo (ANID) Anillo ACT1414 and ACT192064, and FONDECYT 1180358 and 1200601; XII Concurso Nacional de Proyectos de Investigación y Desarrollo en Salud, FONIS 2015. Proyecto SA15I20058, Ministerio de Economia, Chile, Grant ICM P09-015F (Biomedical Neuroscience Institute); ANID FONDECYT 11150846, ANID - Millennium Science Initiative, grant 'Millennium Nucleus to Improve the Mental Health of Adolescents and Youths, Imhay,' and grant 'Millennium Institute for Research in Depression and Personality, Midap'; FONDECYT Postdoctoral 3190790; *COLOMBIA* – PRISMA UNION TEMPORAL (UNIVERSIDAD DE ANTIOQUIA / HOSPITAL SAN VICENTE FUNDACIÓN), Colciencias-INVITACIÓN 990 de 3 de agosto de 2017, Codigo 99059634; *MEXICO* – Instituto Nacional de Neurología y Neurocirugía: Consejo Nacional de Ciencia y Tecnología, Mexico, (CONACyT) Grants No. 261987 and 261895, National Institutes of Health Grant No. R21 MH102374, CONACyT's Sistema Nacional de Investigadores.

Conflicts of interest. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

[1]Laboratory of Molecular Psychiatry, Centro de Pesquisa Clínica, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil[2]Programa de Pós-Graduação em Psicologia, Instituto de Psicologia, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil[3]Department of Psychiatry, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile[4]Early Intervention Program, Instituto Psiquiátrico Dr J. Horwitz Barak, Santiago, Chile[5]Research Group on Neurosciences as applied to Abnormal Behaviour (INAAC Group), FLENI-CONICET Neurosciences Institute, Buenos Aires, Argentina[6]Department of Psychiatry and Mental Health (Fleni Teaching Unit) and Department of Physiology, University of Buenos Aires School of Medicine, Buenos Aires, Argentina[7]Department of Psychiatry and Mental Health (Fleni Teaching Unit), University of Buenos Aires School of Medicine. CONICET, Buenos Aires, Argentina[8]Departamento de Psiquiatria, Universidade Federal do Paraná (UFPR), Curitiba, Brazil[9]Universidade Federal de São Paulo, São Paulo, Brazil[10]Programa de Esquizofrenia, da Escola Paulista de Medicina Universidade Federal de São Paulo (PROESQ-EPM/UNIFESP). Laboratory of Integrative Neuroscience (LINC), Escola Paulista de Medicina Universidade Federal de São Paulo, São Paulo, Brazil[11]PROJESQ (Programa de Esquizofrenia), Instituto de Psiquiatria do HCFMUSP, São Paulo, Brazil[12]Department of Neurology and Psychiatry, Faculty of Medicine, Clínica Alemana Universidad del Desarrollo, Santiago, Chile[13]School of Medicine, Universidad Finis Terrae, Santiago, Chile[14]University Psychiatric Clinic, Clinical Hospital, Universidad de Chile, Santiago, Chile[15]Department of Psychiatry and Mental Health, Faculty of Medicine, Universidad de Chile, Santiago, Chile[16]Department of Neuroscience, Faculty of Medicine, Universidad de Chile, Santiago, Chile[17]Instituto de Estudios Psicológicos, Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile[18]Center for Interdisciplinary Studies on the Nervous System (CISNe), Universidad Austral de Chile, Valdivia, Chile[19]Millennium Nucleus to Improve the Mental Health of Adolescents and Youths (Imhay), Santiago, Chile[20]Millennium Institute for Research in Depression and Personality (MIDAP), Santiago, Chile[21]Brain, Cognition and Behavior PhD Program, University of Barcelona, Barcelona, Spain[22]Research Group in Psychiatry GIPSI, Department of Psychiatry, Faculty of Medicine, Universidad de Antioquia, Medellín, Colombia[23]Laboratory of Neuropsychology, Instituto Nacional de Neurología y Neurocirugía, Mexico City, Mexico[24]Laboratory of Experimental Psychiatry, Instituto Nacional de Neurología y Neurocirugía, Mexico City, Mexico[25]Neuropsychiatry Department, Instituto Nacional de Neurología y Neurocirugía, Mexico City, Mexico[26]Biomedical Imaging Center and Center for Integrative Neuroscience, Pontificia Universidad Católica de Chile, Santiago, Chile[27]Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neurosciences, King's College London, London, UK[28]Graduate Program in Psychiatry and Behavioral Sciences, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

References

Abramo, L., Cecchini, S., & Ullmann, H. (2020). Enfrentar las desigualdades en salud en América Latina: el rol de la protección social. *Ciência & Saúde Coletiva*, *25*(5), 1587–1598. https://doi.org/10.1590/1413-81232020255.32802019.

Adler, N. E., Boyce, T., Chesney, M. A., Cohen, S., Folkman, S., Kahn, R. L., & Syme, S. L. (1994). Socioeconomic status and health: The challenge of the gradient. *American Psychologist*, *49*(1), 15–24. https://doi.org/10.1037/0003-066X.49.1.15.

Anderson, N. B., & Armstead, C. A. (1995). Toward understanding the association of socioeconomic status and health. *Psychosomatic Medicine*, *57*(3), 213–225. https://doi.org/10.1097/00006842-199505000-00003.

Atun, R., de Andrade, L. O. M., Almeida, G., Cotlear, D., Dmytraczenko, T., Frenz, P., … Wagstaff, A. (2015). Health-system reform and universal health coverage in Latin America. *The Lancet*, *385*(9974), 1230–1247. https://doi.org/10.1016/S0140-6736(14)61646-9.

Bayona-i-Carrasco, J., & Avila-Tàpies, R. (2020). Latin Americans and Caribbeans in Europe: A cross-country analysis. *International Migration*, *58*(1), 198–218. https://doi.org/10.1111/imig.12565.

Beran, D., Byass, P., Gbakima, A., Kahn, K., Sankoh, O., Tollman, S., … Davies, J. (2017). Research capacity building—obligations for global health partners. *The Lancet Global Health*, *5*(6), e567–e568. https://doi.org/10.1016/S2214-109X(17)30180-8.

Bilal, U., Alazraqui, M., Caiaffa, W. T., Lopez-Olmedo, N., Martinez-Folgar, K., Miranda, J. J., … Diez-Roux, A. V. (2019). Inequalities in life expectancy in six large Latin American cities from the SALURBAL study: An ecological analysis. *The Lancet Planetary Health*, *3*(12), e503–e510. https://doi.org/10.1016/S2542-5196(19)30235-9.

Bora, E. (2015). Neurodevelopmental origin of cognitive impairment in schizophrenia. *Psychological Medicine*, *45*(1), 1–9. https://doi.org/10.1017/S0033291714001263.

Braveman, P. A., Cubbin, C., Egerter, S., Chideya, S., Marchi, K. S., Metzler, M., & Posner, S. (2005). Socioeconomic status in health research. *JAMA*, *294*(22), 2879. https://doi.org/10.1001/jama.294.22.2879.

Canudas-Romo, V., & Aburto, J. M. (2019). Youth lost to homicides: Disparities in survival in Latin America and the Caribbean. *BMJ Global Health*, *4*(2), e001275. https://doi.org/10.1136/bmjgh-2018-001275.

Carruthers, S. P., Van Rheenen, T. E., Gurvich, C., Sumner, P. J., & Rossell, S. L. (2019). Characterising the structure of cognitive heterogeneity in schizophrenia spectrum disorders. A systematic review and narrative synthesis.

Neuroscience & Biobehavioral Reviews, *107*, 252–278. https://doi.org/10.1016/j.neubiorev.2019.09.006.

Choleris, E., Galea, L. A. M., Sohrabji, F., & Frick, K. M. (2018). Sex differences in the brain: Implications for behavioral and biomedical research. *Neuroscience & Biobehavioral Reviews*, *85*, 126–145. https://doi.org/10.1016/j.neubiorev.2017.07.005.

Crossley, N., Guinjoan, S., Rivera, G., Jackowski, A., Gadelha, A., Elkis, H., … Bressan, R. (2019). S81. Andes network – studying early psychosis in Latin America. *Schizophrenia Bulletin*, *45* (Suppl 2), S338–S338. https://doi.org/10.1093/schbul/sbz020.626.

Crossley, N. A., Zugman, A., Reyes-Madrigal, F., Czepielewski, L. S., Castro, M. N., Diaz-Zuluaga, A. M., … Bressan, R. A. (2021). Structural brain abnormalities in schizophrenia in adverse environments: Examining the effect of poverty and violence in six Latin American cities. *The British Journal of Psychiatry*, *218*(2), 112–118. https://doi.org/10.1192/bjp.2020.143.

Czepielewski, L.S., Massuda, R., Panizzutti, B., Grun, L. K., Barbé-Tuana, F. M., Teixeira, A. L., … Gama, C. S. (2018). Telomere length and CCL11 levels are associated with gray matter volume and episodic memory performance in schizophrenia: Evidence of pathological accelerated aging. *Schizophrenia Bulletin*, *44*(1), 158–167. https://doi.org/10.1093/schbul/sbx015.

Czepielewski, L.S., Wang, L., Gama, C. S., & Barch, D. M. (2017). The relationship of intellectual functioning and cognitive performance to brain structure in schizophrenia. *Schizophrenia Bulletin*, *43*(2), 355–364. https://doi.org/10.1093/schbul/sbw090.

DeVylder, J. E., Kelleher, I., Lalane, M., Oh, H., Link, B. G., & Koyanagi, A. (2018). Association of urbanicity with psychosis in low- and middle-income countries. *JAMA Psychiatry*, *75*(7), 678. https://doi.org/10.1001/jamapsychiatry.2018.0577.

DeVylder, J. E., Koyanagi, A., Unick, J., Oh, H., Nam, B., & Stickley, A. (2016). Stress sensitivity and psychotic experiences in 39 low- and middle-income countries. *Schizophrenia Bulletin*, *42*(6), 1353–1362. https://doi.org/10.1093/schbul/sbw044.

Farah, M. J. (2017). The neuroscience of socioeconomic status: Correlates, causes, and consequences. *Neuron*, *96*(1), 56–71. https://doi.org/10.1016/j.neuron.2017.08.034.

Farooq, S., Large, M., Nielssen, O., & Waheed, W. (2009). The relationship between the duration of untreated psychosis and outcome in low- and middle-income countries: A systematic review and meta analysis. *Schizophrenia Research*, *109*(1–3), 15–23. https://doi.org/10.1016/j.schres.2009.01.008.

Fatouros-Bergman, H., Cervenka, S., Flyckt, L., Edman, G., & Farde, L. (2014). Meta-analysis of cognitive performance in drug-naïve patients with schizophrenia. *Schizophrenia Research*, *158*(1–3), 156–162. https://doi.org/10.1016/j.schres.2014.06.034.

Fett, A.-K. J., Velthorst, E., Reichenberg, A., Ruggero, C. J., Callahan, J. L., Fochtmann, L. J., … Kotov, R. (2020). Long-term changes in cognitive functioning in individuals with psychotic disorders. *JAMA Psychiatry*, *77*(4), 387. https://doi.org/10.1001/jamapsychiatry.2019.3993.

Fett, A.-K. J., Viechtbauer, W., Dominguez, M.-G., Penn, D. L., van Os, J., & Krabbendam, L. (2011). The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis. *Neuroscience & Biobehavioral Reviews*, *35*(3), 573–588. https://doi.org/10.1016/j.neubiorev.2010.07.001.

Fioravanti, M., Bianchi, V., & Cinti, M. E. (2012). Cognitive deficits in schizophrenia: An updated meta-analysis of the scientific evidence. *BMC Psychiatry*, *12*(1), 64. https://doi.org/10.1186/1471-244X-12-64.

Forero, D. A., Trujillo, M. L., González-Giraldo, Y., & Barreto, G. E. (2020). Scientific productivity in neurosciences in Latin America: A scientometrics perspective. *International Journal of Neuroscience*, *130*(4), 398–406. https://doi.org/10.1080/00207454.2019.1692837.

Goldberg, S., Fruchter, E., Davidson, M., Reichenberg, A., Yoffe, R., & Weiser, M. (2011). The relationship between risk of hospitalization for schizophrenia, SES, and cognitive functioning. *Schizophrenia Bulletin*, *37*(4), 664–670. https://doi.org/10.1093/schbul/sbr047.

Gooding, D. C., Park, S., Dias, E. C., Goghari, V. M., & Chan, R. R. C. K. (2020). Increasing diversity within scientific research organizations: A call to action. *Schizophrenia Research*, *216*, 7–9. https://doi.org/10.1016/j.schres.2019.12.033.

Green, M. J., Girshkin, L., Kremerskothen, K., Watkeys, O., & Quidé, Y. (2020). A systematic review of studies reporting data-driven cognitive subtypes across the psychosis Spectrum. *Neuropsychology Review*, *30*(4), 446–460. https://doi.org/10.1007/s11065-019-09422-7.

Gur, R. E., Moore, T. M., Rosen, A. F. G., Barzilay, R., Roalf, D. R., Calkins, M. E., … Gur, R. C. (2019). Burden of environmental adversity associated with psychopathology, maturation, and brain behavior parameters in youths. *JAMA Psychiatry*, *76*(9), 966. https://doi.org/10.1001/jamapsychiatry.2019.0943.

Halverson, T. F., Orleans-Pobee, M., Merritt, C., Sheeran, P., Fett, A.-K., & Penn, D. L. (2019). Pathways to functional outcomes in schizophrenia spectrum disorders: Meta-analysis of social cognitive and neurocognitive predictors. *Neuroscience & Biobehavioral Reviews*, *105*, 212–219. https://doi.org/10.1016/j.neubiorev.2019.07.020.

Hanscombe, K. B., Trzaskowski, M., Haworth, C. M. A., Davis, O. S. P., Dale, P. S., & Plomin, R. (2012). Socioeconomic status (SES) and Children's Intelligence (IQ): In a UK-representative sample SES moderates the environmental, not genetic, effect on IQ. *PLoS ONE*, *7*(2), e30320. https://doi.org/10.1371/journal.pone.0030320.

Haro, J. M., Altamura, C., Corral, R., Elkis, H., Evans, J., Krebs, M.-O., … Nordstroem, A.-L. (2018). Understanding the course of persistent symptoms in schizophrenia: Longitudinal findings from the pattern study. *Psychiatry Research*, *267*, 56–62. https://doi.org/10.1016/j.psychres.2018.04.005.

Hart, S. A., Petrill, S. A., Deater Deckard, K., & Thompson, L. A. (2007). SES and CHAOS as environmental mediators of cognitive ability: A longitudinal genetic analysis. *Intelligence*, *35*(3), 233–242. https://doi.org/10.1016/j.intell.2006.08.004.

Herrero, P., Contador, I., Stern, Y., Fernández-Calvo, B., Sánchez, A., & Ramos, F. (2020). Influence of cognitive reserve in schizophrenia: A systematic review. *Neuroscience & Biobehavioral Reviews*, *108*, 149–159. https://doi.org/10.1016/j.neubiorev.2019.10.019.

Hochberger, W. C., Thomas, M. L., Joshi, Y. B., Swerdlow, N. R., Braff, D. L., Gur, R. E., … Light, G. A. (2020). Deviation from expected cognitive ability is a core cognitive feature of schizophrenia related to neurophysiologic, clinical and psychosocial functioning. *Schizophrenia Research*, *215*, 300–307. https://doi.org/10.1016/j.schres.2019.10.011.

Islam, M. A., Habtewold, T. D., van Es, F. D., Quee, P. J., van den Heuvel, E. R., Alizadeh, B. Z., & Bruggeman, R. (2018). Long-term cognitive trajectories and heterogeneity in patients with schizophrenia and their unaffected siblings. *Acta Psychiatrica Scandinavica*, *138*(6), 591–604. https://doi.org/10.1111/acps.12961.

Karantonis, J. A., Rossell, S. L., Carruthers, S. P., Sumner, P., Hughes, M., Green, M. J., … Van Rheenen, T. E. (2020). Cognitive validation of cross-diagnostic cognitive subgroups on the schizophrenia-bipolar spectrum. *Journal of Affective Disorders*, *266*, 710–721. https://doi.org/10.1016/j.jad.2020.01.123.

Kohn, R., Ali, A. A., Puac-Polanco, V., Figueroa, C., López-Soto, V., Morgan, K., … Vicente, B. (2018). Mental health in the Americas: An overview of the treatment gap. *Revista Panamericana de Salud Pública*, *42*, e165. https://doi.org/10.26633/RPSP.2018.165.

Kwok, W. (2014). Is there evidence that social class at birth increases risk of psychosis? A systematic review. *International Journal of Social Psychiatry*, *60*(8), 801–808. https://doi.org/10.1177/0020764014524737.

Lam, M., Chen, C.-Y., Li, Z., Martin, A. R., Bryois, J., Ma, X., … Huang, H. (2019). Comparative genetic architectures of schizophrenia in East Asian and European populations. *Nature Genetics*, *51*(12), 1670–1678. https://doi.org/10.1038/s41588-019-0512-x.

Large, M., Nielssen, O., Farooq, S., & Glozier, N. (2010). Increasing rates of psychiatric publication from Low- and middle-income Countries. *International Journal of Social Psychiatry*, *56*(5), 497–506. https://doi.org/10.1177/0020764009102412.

Lima, F., Rabelo-da-Ponte, F. D., Bücker, J., Czepielewski, L., Hasse-Sousa, M., Telesca, R., … Rosa, A. R. (2019). Identifying cognitive subgroups in bipolar disorder: A cluster analysis. *Journal of Affective Disorders*, *246*, 252–261. https://doi.org/10.1016/j.jad.2018.12.044.

Luo, Y., Zhang, L., He, P., Pang, L., Guo, C., & Zheng, X. (2019). Individual-level and area-level socioeconomic status (SES) and schizophrenia: Cross-sectional analyses using the evidence from 1.9 million Chinese adults. *BMJ Open*, *9*(9), e026532. https://doi.org/10.1136/bmjopen-2018-026532.

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press

Mendrek, A., & Mancini-Marïe, A. (2016). Sex/gender differences in the brain and cognition in schizophrenia. *Neuroscience & Biobehavioral Reviews*, *67*, 57–78. https://doi.org/10.1016/j.neubiorev.2015.10.013.

Mollon, J., & Reichenberg, A. (2018). Cognitive development prior to onset of psychosis. *Psychological Medicine*, *48*(3), 392–403. https://doi.org/10.1017/S0033291717001970.

Neidhöfer, G., Serrano, J., & Gasparini, L. (2018). Educational inequality and intergenerational mobility in Latin America: A new database. *Journal of Development Economics*, *134*, 329–349. https://doi.org/10.1016/j.jdeveco.2018.05.016.

Rabelo-Da-Ponte, F. D., Lima, F. M., Martinez-Aran, A., Kapczinski, F., Vieta, E., Rosa, A. R., … Czepielewski, L. S. (2020). Data-driven cognitive phenotypes in subjects with bipolar disorder and their clinical markers of severity. *Psychological Medicine*, 1–8. https://doi.org/10.1017/S0033291720003499.

Raudeberg, R., L. Iverson, G., & Hammar, Å. (2019). Norms matter: U.S. Normative data under-estimate cognitive deficits in Norwegians with schizophrenia spectrum disorders. *The Clinical Neuropsychologist*, *33* (Suppl 1), 58–74. https://doi.org/10.1080/13854046.2019.1590641.

Reckziegel, R., Czepielewski, L. S., Hasse-Sousa, M., Martins, D. S., de Britto, M. J., de Lapa, C. O., … Gama, C. S. (2021). Heterogeneous trajectories in schizophrenia: Insights from neurodevelopment and neuroprogression models. *Brazilian Journal of Psychiatry*. https://doi.org/10.1590/1516-4446-2020-1670.

Richards, A. L., Pardiñas, A. F., Frizzati, A., Tansey, K. E., Lynham, A. J., Holmans, P., … Walters, J. T. R. (2020). The relationship between polygenic risk scores and cognition in schizophrenia. *Schizophrenia Bulletin*, *46*(2), 336–344. https://doi.org/10.1093/schbul/sbz061.

Schaefer, J., Giangrande, E., Weinberger, D. R., & Dickinson, D. (2013). The global cognitive impairment in schizophrenia: Consistent over decades and around the world. *Schizophrenia Research*, *150*(1), 42–50. https://doi.org/10.1016/j.schres.2013.07.009.

Shattuck, E. C. (2019). A biocultural approach to psychiatric illnesses. *Psychopharmacology*, *236*(10), 2923–2936. https://doi.org/10.1007/s00213-019-5178-7.

Sheffield, J. M., Karcher, N. R., & Barch, D. M. (2018). Cognitive deficits in psychotic disorders: A lifespan perspective. *Neuropsychology Review*, *28* (4), 509–533. https://doi.org/10.1007/s11065-018-9388-2.

Shmukler, A. B., Gurovich, I. Y., Agius, M., & Zaytseva, Y. (2015). Long-term trajectories of cognitive deficits in schizophrenia: A critical overview. *European Psychiatry*, *30*(8), 1002–1010. https://doi.org/10.1016/j.eurpsy.2015.08.005.

Solís-Vivanco, R., Rangel-Hassey, F., León-Ortiz, P., Mondragón-Maya, A., Reyes-Madrigal, F., & de la Fuente-Sandoval, C. (2020). Cognitive impairment in never-medicated individuals on the schizophrenia spectrum. *JAMA Psychiatry*, *77*(5), 543. https://doi.org/10.1001/jamapsychiatry.2020.0001.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society: JINS*, *8*(3), 448–460. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11939702.

Szöke, A., Trandafir, A., Dupont, M.-E., Méary, A., Schürhoff, F., & Leboyer, M. (2008). Longitudinal studies of cognition in schizophrenia: Meta-analysis. *British Journal of Psychiatry*, *192*(4), 248–257. https://doi.org/10.1192/bjp.bp.106.029009.

United Nations. (2018). 2018 Revision of World Urbanization Prospects. Retrieved 7 July 2020, from https://population.un.org/wup/.

Van Rheenen, T. E., Cropley, V., Fagerlund, B., Wannan, C., Bruggemann, J., Lenroot, R. K., … Pantelis, C. (2020). Cognitive reserve attenuates age-related cognitive decline in the context of putatively accelerated brain ageing in schizophrenia-spectrum disorders. *Psychological Medicine*, *50*(9), 1475–1489. https://doi.org/10.1017/S0033291719001417.

Ventura, J., Hellemann, G. S., Thames, A. D., Koellner, V., & Nuechterlein, K. H. (2009). Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: A meta-analysis. *Schizophrenia Research*, *113*(2–3), 189–199. https://doi.org/10.1016/j.schres.2009.03.035.

Ventura, J., Thames, A. D., Wood, R. C., Guzik, L. H., & Hellemann, G. S. (2010). Disorganization and reality distortion in schizophrenia: A meta-analysis of the relationship between positive symptoms and neurocognitive deficits. *Schizophrenia Research*, *121*(1–3), 1–14. https://doi.org/10.1016/j.schres.2010.05.033.

Wells, R., Jacomb, I., Swaminathan, V., Sundram, S., Weinberg, D., Bruggemann, J., … Weickert, T. W. (2020). The impact of childhood adversity on cognitive development in schizophrenia. *Schizophrenia Bulletin*, *46* (1), 140–153. https://doi.org/10.1093/schbul/sbz033.

World Bank. (2019). Population, total – Latin America & Caribbean, World.

World Bank. (n.d.). Poverty and Inequality. Retrieved 7 July 2020, from http://datatopics.worldbank.org/world-development-indicators/themes/poverty-and-inequality.html.

Yang, L. H., Ruiz, B., Mandavia, A. D., Grivel, M. M., Wong, L. Y., Phillips, M. R., … Stone, W. S. (2020). Advancing study of cognitive impairments for antipsychotic-naïve psychosis comparing high-income versus low- and middle-income countries with a focus on urban China: Systematic review of cognition and study methodology. *Schizophrenia Research*, *220*, 1–15. https://doi.org/10.1016/j.schres.2020.01.026.

Yeo, R. A., Martinez, D., Pommy, J., Ehrlich, S., Schulz, S. C., Ho, B.-C., … Calhoun, V. D. (2014). The impact of parent socio-economic status on executive functioning and cortical morphology in individuals with schizophrenia and healthy controls. *Psychological Medicine*, *44*(6), 1257–1265. https://doi.org/10.1017/S0033291713001608.

Zanelli, J., Mollon, J., Sandin, S., Morgan, C., Dazzan, P., Pilecka, I., … Reichenberg, A. (2019). Cognitive change in schizophrenia and other psychoses in the decade following the first episode. *American Journal of Psychiatry*, *176*(10), 811–819. https://doi.org/10.1176/appi.ajp.2019.18091088.

https://doi.org/10.1017/S0033291721002403 Published online by Cambridge University Press