

Relationship between cognitive reserve (education), social cognition and negative symptoms

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ABSTRACT

Background: Negative symptoms (NS) are a core feature of schizophrenia spectrum disorders, yet their relationship with cognitive reserve (defined by educational attainment) and social cognition remains underexplored. This study examined whether education predicts NS and whether this relationship is mediated by social cognition, specifically emotional or inferential theory of mind Reading the Mind in the Eyes Test (RMET) vs. the Hinting Test.

Methods: A mediation model and multiple regression analysis were conducted within an ex-post-facto, cross-sectional design. The sample included 144 participants: 69 diagnosed with schizophrenia spectrum disorders and 75 healthy controls. Women comprised 52.8 % of the sample, with a mean age of 42.67 years ($SD = 15.88$). The average years of formal education were 8.37 ($SD = 2.77$) in the patient group and 8.62 ($SD = 3.66$) in the control group.

Results: The mediation model explained 67.57 % of the variance in NS, with age as a covariate. RMET showed a significant indirect effect ($d = -0.22$) in predicting NS, while HT did not ($d = -0.12$). In the patient group, multiple regression analysis explained 69.2 % of the variance, with education emerging as a significant predictor of NS.

Conclusions: Education, as an indicator of cognitive reserve, significantly predicts NS. This relationship is mediated by social cognition, with differential effects depending on the specific type of social cognition, either within the patient group or across the entire sample. These findings highlight the importance of cognitive reserve and social cognition in understanding and potentially mitigating NS in schizophrenia.

1. Introduction

Schizophrenia is a complex, early-onset, long-term, high-prevalence mental disorder with a significant functional impact, constituting one of the main causes of disability (Jauhar et al., 2022). Psychotic symptoms have received more attention in the literature than other psychotic manifestations, primarily due to their responsiveness to pharmacological treatments (Roche et al., 2015). Disorganization and negative and cognitive symptoms pose a greater challenge, due to their significant impact on prognosis and global functioning.

Negative symptoms (NS) represent one of the central and usual characteristics of the schizophrenia spectrum (Correll and Schooler,

2020; Galderisi et al., 2021b). The importance of studying NS is related to the worse course of illness, the association with cognitive and functional deterioration, and the significant impact on the quality of life of people with these symptoms (Bugarski-Kirola et al., 2022; Catalan et al., 2021; Galderisi et al., 2021a; Strauss et al., 2021; Yang et al., 2021).

However, there is no clear and established explanation for the origin and maintenance of NS, which is also hindered by the limited benefits of pharmacological and psychological interventions (Galderisi and Mucci, 2023; Sabe et al., 2023; Strauss et al., 2020). Among NS, it is worth highlighting altered social capacity and functioning, which is manifested as the loss of social interest and initiative (avolition), the loss of the capacity to enjoy social contact and interactions (anhedonia), and

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the tendency to social isolation (asociality). In this sense, cognitive processes such as social cognition may be relevant to progress in the knowledge and approach of NS (Pelletier-Baldelli and Holt, 2020). In fact, some studies have pointed out the relationship between NS, particularly those that involve experiential alterations (avolition, anhedonia, asociality), and social cognition (Lewandowski et al., 2024; Lincoln et al., 2011; Yolland et al., 2021).

Social cognition refers to the ability to process information relevant to social interactions, encompassing emotional processing, social perception, attributional bias, and theory of mind (Eslinger et al., 2021). *Emotional processing* involves the recognition and discrimination of emotions expressed through facial expressions, prosody, and body language (Lewandowski et al., 2024; Pinkham et al., 2016). *Social perception* entails the capacity to decode and contextualize social cues (Le Gall and Iakimova, 2018; Peyroux et al., 2019). *Attributional bias* refers to the ways individuals assign causes and meanings to social events or interactions (Bentall, 2013). *Theory of mind* (ToM) enables individuals to represent the hidden mental states of themselves and others, allowing them to infer intentions, emotions, and beliefs (mentalization), which in turn facilitates the prediction of behavior and/or the sharing of experiences (empathy) (Lewandowski et al., 2024).

Social cognition is considered a relevant process particularly in schizophrenia, standing out in the different stages of the disorder (Lewandowski et al., 2024). Several studies have shown that chronicity in schizophrenia is associated with greater impairment in social cognition compared to healthy individuals. However, no consistent differences have been observed based on diagnostic subtypes within the spectrum (García-Fernández et al., 2020). A study with different profiles of first episodes of psychosis did not identify differences in social cognition (e.g., ToM), neither in men nor in women (Ferrer-Quintero et al., 2022).

Nevertheless, the role of social cognition as a predictor of symptomatology, as well as the variables associated with it, remains unclear. Previous research has already established the relationship of ToM with positive symptoms (De Rossi and Georgiades, 2022), and that between social cognition and NS in first psychotic episodes (Pelletizza et al., 2020). In a different study, ToM mediated the relationship between adversities in childhood and NS, although only in men (Giordano et al., 2024). Although several studies report deficits in social cognition during first-episode psychosis—particularly in emotional processing and complex theory of mind (e.g., inferring beliefs), while more basic abilities remain preserved—methodological and clinical heterogeneity appear to account for many of these inconsistencies (Joseph Fortuny et al., 2023; Montaner-Ferrer et al., 2023).

Beyond first-episode psychosis, a relationship between neurocognition and the mediating role of social cognition in what Green et al. (2018) termed “social disconnection” had already been proposed. The mediating role of social cognition in the relationship between neurocognition and negative symptoms is well supported in the literature. Kharawala et al. (2022) and Mansueto et al. (2019) suggest that social cognition not only influences negative symptoms but may also be modulated by them, highlighting a bidirectional relationship. Montaner-Ferrer et al. (2023) further reinforce this mediating role, emphasizing the complex interaction between cognitive domains such as social cognition and negative symptomatology.

Some studies on first-episode psychosis report that social cognition mediates the relationship between cognitive reserve (e.g., education level) and cognitive domains (e.g., working memory), which were evaluated throughout a follow-up period of two years (Bora, 2015). The concept of cognitive reserve emerges in the context of dementias and can be defined as the brain's capacity to optimize its resources to tolerate or compensate for the effects of brain pathology or aging (Stern, 2002). It is determined by genetic and structural factors, but also by their interaction with environmental influences, represented by various indicators such as IQ, educational attainment, years of training, social engagement, and occupational status (González-Ortega et al., 2020). It is considered a

possible protective factor of cognitive functioning in people with schizophrenia (Barnett et al., 2006), and it is related to functional efficiency and flexibility through different cognitive strategies (or alternative neural networks) (Barulli and Stern, 2013).

In this way, cognitive reserve could be a start or predictive variable of the models that aim to explain not only functional capacity, but also the presence of NS. In this sense, although this finding has not been replicated, previous research has referred to a cognitive reserve for NS as a protective factor for schizophrenia (Lyne et al., 2018). This shows the plasticity of the nervous system from some genetically determined conditions (e.g., IQ), as well as environmental conditions (e.g., education, lifestyles and habits, physical activity) (Amoretti et al., 2024; de la Serna et al., 2013; Nithianantharajah and Hannan, 2009).

Recent studies have attempted to establish the polygenic risk to develop schizophrenia. Educational level—specifically, the number of years of completed education (i.e., cognitive reserve)—has been considered a relevant polygenic risk or protective factor (Escott-Price et al., 2020), particularly in contexts where access to education is equitable. Clougher et al. (2024) corroborated the polygenic risk associated with educational level in first-episode psychosis, considering social cognition and both positive and, particularly, negative symptoms as mediating variables that predicted functional decline in a serial mediation model.

Given that negative symptoms (NS) are observed in up to 90 % of individuals with schizophrenia spectrum disorders, that these indicators emerge as early as the prodromal phase, and that they often precede the onset of positive symptoms (Correll and Schooler, 2020; Galderisi et al., 2018; Mezquida et al., 2018; Strauss et al., 2021), the general aim of the present study was to develop a predictive model of NS from a dimensional perspective, including participants from the general population and considering these indicators as variants of normal mental processes. This exploratory perspective is relevant due to its clinical and scientific utility (Kaiser et al., 2011; Rodríguez-Testal et al., 2019).

It therefore seems relevant to consider the potential relationship between formal education and the development of social cognition, as sustained participation in structured educational contexts provides opportunities for the development of complex cognitive skills such as perspective-taking, understanding others' intentions, and emotional regulation (Peterson et al., 2016; Wang and Eccles, 2012). Furthermore, as some findings suggest, social cognition may play a mediating role in negative symptoms (NS), since impairments in the ability to infer others' behavior or intentions, or to understand others' emotional states (i.e., the inferential and emotional components of theory of mind, respectively), may manifest as NS related to reduced initiative and social withdrawal (Ferrer-Quintero et al., 2022; Giordano et al., 2024; Pelletizza et al., 2020).

The following specific objectives were also set:

1) Analyze the relationship between education (years of formal education, cognitive reserve) as a relevant predictor of NS.

Hypothesis 1. a direct and statistically significant relationship will be detected between education and NS (PANSS-N).

2) Analyze social cognition as a mediator variable based on its relationship with NS from ToM (both emotional processing [RMET] and inferential or intentional processing [HT]).

Hypothesis 2. statistically significant relationships will be identified between education and the hypothesized mediator variables of social cognition (RMET, HT).

Hypothesis 3. statistically significant relationships will be obtained between the mediator variables of social cognition (RMET, HT) and NS (PANSS-N).

3) Test whether the effect of education on NS is mediated by social cognition (RMET, HT).

Hypothesis 4. an indirect relationship will be identified between

Education and NS (PANSS-N), mediated by the variables of social cognition (RMET, HT).

4) Establish the specific predictors of the group of patients, including clinical variables such as course of illness and chlorpromazine-equivalent prescription.

Hypothesis 5. a significant prediction of NS (PANSS-N) will be obtained from education, social cognition (RMET, HT), course of illness (months) and chlorpromazine-equivalent prescription.

2. Methods

2.1. Participants

The sample of the present study was constituted by a total of 154 participants, 79 of whom belonged to the group of patients and 75 to the comparison group (control). Of the total sample, 82 were women (53.2 %). In the group of patients, there was a greater proportion of men (51.9 %), whereas the comparison group was mostly constituted by women (58.7 %). The mean age of the total sample was 41.60 years ($SD = 15.99$), with that of the comparison group being greater (45.84 years, $SD = 17.02$) than that of the patient's group (37.58 years, $SD = 13.91$). Regarding education (years of formal education, attendance and persistence in academic settings, regardless of whether a specific educational level was completed), 6.9 % of the total sample did not complete primary education, 31.9 % completed primary education, 41 % did not complete secondary education, 6.3 % completed secondary education, and 13.9 % did not complete higher education. The participants of the control group showed a similar average education (8.62 years, $SD = 3.66$) with respect to the patients (8.63 years, $SD = 2.85$).

The study design was ex-post-facto and cross-sectional (one measurement), taking all participants in a group in the statistical analyses, using covariances. The participants were recruited through non-random sampling by accessibility, from a group of patients during the follow-ups of Hospital de Clínicas, Maciel Hospital, Pasteur Hospital, and Vilardebó Hospital (Republic of Uruguay), and a comparison group constituted by staff of the health service where the study was conducted. In the group of patients, the diagnoses were: schizophrenia ($N = 63$), and schizophreniform disorder ($N = 6$) (according to [American Psychiatric Association, 2022](#)). The results section presents the corresponding descriptive analyses ([Table 1](#)).

Table 1
Descriptive data of the sample variables and according to groups of participants.

	Full sample ($N = 144$)	Patient sample ($n = 69$)	Control sample ($n = 75$)
Variables	$M((SD))$	$M((SD))$	$M((SD))$
Age	42.67 (15.88)	39.23 (13.85)	45.84 (17.02)
Education	8.50 (3.26)	8.37 (2.77)	8.62 (3.66)
PANSS-P	10.58 (4.80)	13.92 (5.10)	7.50 (0.81)
PANSS-N	13.98 (8.05)	20.87 (6.58)	7.65 (0.89)
PANSS-G	23.57 (8.61)	29.65 (8.98)	17.98 (1.72)
HINTING TASK	15.11 (4.27)	12.58 (4.66)	17.45 (1.93)
READING MIND	20.18 (5.63)	17.36 (5.26)	22.77 (4.65)
course of illness (months)	–	157.81 (118.33)	–
Chlorpromazine (mg/d)	–	360.73 (212.72)	–
Sex			
Woman	76 (52.8 %)	32 (46.4 %)	44 (58.7 %)
Man	68 (47.2 %)	37 (53.6 %)	31 (41.3 %)
Chronicity			
Brief	–	6 (8.7 %)	–
Chronic	–	63 (91.3 %)	–
Current Rehabilitation			
No	–	54 (78.3 %)	75 (100 %)
Yes	–	15 (21.7 %)	0 (0 %)
Current Psychotherapy			
No	133 (92.4 %)	65 (94.2 %)	68 (90.7 %)
Yes	24 (16.7 %)	4 (5.8 %)	7 (9.3 %)

2.2. Procedure

All participants were informed about the purpose of the study and signed the written consent to participate in the evaluation. The study was registered in the General Health Management–Sanitary Evaluation Unit- of the Ministry of Public Health of Uruguay (No. 807530), and it was approved by the Ethics Committee of Research Projects (Resolution of the Council of the Faculty of Medicine, File: 070153-000400-20).

The patients were called in the follow-up sessions and evaluated by an expert (SLS) in 40–60 min. The measurements were recorded in two different time points ([Baron and Kenny, 1986](#)). The control participants were recruited by accessibility among the members of the healthcare personnel with different degrees of specialization.

The following inclusion criteria were established: 1) being over 18 years of age; 2) active symptoms in the case of the patients; 3) full expression and comprehension capacity of the Spanish language, as well as full or corrected visual capacity; and 4) written informed consent. The following exclusion criteria were considered: 1) refusal to participate; 2) intellectual disability; 3) disorder by severe substance use (presence of 6 or more symptoms according to DSM-5 [[American Psychiatric Association, 2022](#)] that are not in initial or continued remission); 4) neurological diseases of the central nervous system; and 5) history of craniocerebral trauma with loss of consciousness.

For the characterization of the variable education, the years of formal education completed by the participants were considered.

2.3. Statistical design

Descriptive analyses (means, standard deviations, and percentages), Pearson's correlation analyses, chi-square tests, and Student's *t*-tests for mean comparisons between the two participant groups were conducted. The mediation analysis was performed with Model 4 of PROCESS software, v3.4 macro for SPSS by [Hayes \(2013\)](#), with 95 % confidence interval (CI) and bootstrapping with 5000 resamples. Education was considered as independent variable (X), the two measures of social cognition (HT, RMET) were considered as mediator variables (M), and the variable of NS (PANSS-N) was considered as the dependent variable (Y). The results were considered significant for the indirect effect when “0” was not in the CI. The effect sizes were calculated from the standardized β to obtain the *d* values ([Lenhard and Lenhard, 2016](#)): No effect (below 0.2), small effect (between 0.2 and 0.5), moderate effect (between 0.5 and 0.8), and large effect (greater than 0.8). Lastly, a multiple regression analysis (insert) was conducted on NS exclusively for the patient group, considering the β coefficients, standard errors (*SE*), *t*-tests, and the change in R^2 . The analyses were considered statistically significant at a probability level of $p < .05$.

2.4. Instruments

2.4.1. Basic socio-demographic information record sheet

These records were used to collect information about sex, date of birth, education (years of formal education completed), course of illness (months), chlorpromazine equivalent (mg/d), chronicity (brief/chronic), current rehabilitation (no/yes), and current psychotherapy (no/yes).

2.4.2. The Hinting Task (HT) ([Corcoran et al., 1995](#)) (Spanish version [Gil et al., 2012](#))

This instrument was designed to evaluate the theory of inferential mind, particularly the capacity of people to infer the intentions and beliefs of others from indirect hints or insinuations. It consists of 10 brief stories in which a character gives a hint or insinuation about his/her intentions, and the participant must deduce the intention of the character. In this study, a consistency of $\alpha = 0.799$ for the entire sample, $\alpha = 0.807$ for the patient sample, and $\alpha = 0.785$ for the control sample were obtained.

2.4.3. Reading the Mind in the Eyes Test (RMET) (Baron-Cohen et al., 2001) (Spanish version Redondo and Herrero-Fernández, 2018)

RMET is one of the most widely used instruments for the measurement of the capacity to understand the emotional state of other people (ToM) through the observation of facial expressions. It consists of 36 images that show the eye region of different people. Each image is accompanied by four response options that describe different emotions or feelings that could be represented in the image. The participants must select the word that best describes the emotion or feeling they believe is represented in each image. Each correct answer is scored with one point, whereas the incorrect answers do not receive any points, with the total score ranging between 0 and 36 points. The RMET evaluates the theory of emotional mind (Pavlova and Sokolov, 2022), which is relevant for effective social interaction. In the present study, it obtained $\alpha = 0.718$ for the entire sample, $\alpha = 0.748$ for the sample of patients, and $\alpha = 0.677$ for the control sample.

2.4.4. Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) (Spanish version Peralta and Cuesta, 1994)

This instrument evaluates the symptoms of schizophrenia. It consists of 30 items: 7 items for the positive dimension, 7 items for the negative dimension, and 16 items related to general psychopathology, with a Likert scale of 1 to 7 points (severity). In the Spanish validation of the instrument, the internal consistency for the positive scale, negative scale and general scale was 0.62, 0.92 and 0.55, respectively.

3. Results

3.1. Descriptive statistics and correlation analyses

Table 1 presents the main descriptive statistics of the sample. Significant differences were found between groups for age ($t(142) = 2.563$, $d.f. = 139.968$, $p < .05$; $F_{Levene} = 4.788$, $p < .05$), but not for education ($t(142) = -0.012$, $d.f. = 142$, $p > .05$; $F_{Levene} = 3.277$, $p > .05$). No significant differences were observed in sex distribution ($\chi^2(1, N = 144) = 2.178$, $d.f. = 1$, $p > .05$) or in the proportion of participants undergoing psychotherapy at the time of the study ($\chi^2(1, N = 144) = 0.637$, $d.f. = 1$, $p > .05$).

Table 2 presents the correlations among the variables. A significant negative relationship between education and participants' age was observed when considering the entire sample, as well as a significant positive relationship between age and negative symptoms (PANSS-N) within the patient sample. These findings may be related to the age differences reported in the previous paragraph. Education was significantly correlated, especially within the patient group, with NS ($r = -0.288$). Measures of social cognition (HT, RMET) also showed relevant correlations with the set of variables, particularly in the total sample.

Table 2

Pearson's correlations between the study variables for the whole sample (N = 144) and the group of patients (n = 69).

	1	2	3	4	5	6	7
1. Age	–	–0.390**	0.134	–0.132	–0.092	–0.065	–0.079
2. Education	–0.187	–	0.036	0.343**	–0.024	–0.135	–0.092
3. HT	–0.097	0.120	–	0.512**	–0.500**	–0.769**	–0.512**
4. RMET	–0.178	0.176	0.500**	–	–0.354**	–0.642**	–0.392**
5. PANSSP	0.102	0.038	–0.197	–0.028	–	0.674**	0.706**
6. PANSSN	0.325**	–0.292*	–0.684**	–0.673**	–0.296**	–	0.747**
7. PANSSG	0.165	–0.182	–0.233	–0.151	0.472**	0.467**	–
8. Course of illness†	0.734**	–0.263*	–0.278*	–0.232	0.195	0.435**	0.098
9. Chlorprm†	0.161	–0.140	–0.022	–0.242*	0.017	0.217	0.090

Note: The correlations above and below the diagonals correspond to the full sample and patient sample, respectively. 1. Age. 2. Education: years of formal education. 3. Hinting Task (HT). 4. Reading the Mind (RMET). 5. PANSSP: positive symptoms. 6. PANSSN: negative symptoms. 7. PANSSG: general psychopathology. 8. Course of illness (months), 9. Chlorprm: chlorpromazine equivalent mg/day.

† Patients group.

* $p < .05$.

** $p < .01$.

Notably, the relationship with NS was observed both in the entire sample and within the patient group.

The mediation analysis for the entire sample revealed a statistically significant relationship among the variables considered (see Table 3). Age was included as a covariate in the model, while PANSS-P and PANSS-G were previously excluded due to their collinearity with NS (PANSS-N). There was a significant association between Education and RMET performance, supported by a confidence interval of adequate width that excluded zero, and a large, standardized effect size ($d = 1.15$). The HT measure of social cognition was not statistically significant but reached a small effect size: $d = 0.36$.

The relationship between the social cognition measures (HT, RMET) and the negative symptoms measure (PANSS-N) was significant. In both cases, the confidence intervals were of appropriate width and did not include zero, and the negative t -values indicated an association between lower social cognition scores and higher levels of negative symptoms. The effect size for NS was large for both HT ($d = -1.31$) and RMET ($d = -0.72$).

The direct effect (non-significant effect size, $d = -0.04$) and the total

Table 3

Summary of the model of multiple mediation on negative symptoms (PANSS-N), with age as covariance (N = 154).

Variable: PANSS-N	B	SE	t	p	LLCI	ULCI
Direct and total effects						
X-M effect (a): Education on HT	0.13	0.11	1.14	0.25	–0.09	0.36
X-M effect (a): Education on RMET	0.59	0.14	4.00	0.00	0.30	0.88
M-Y effect adjusted for X (b): HT on PANSS-N	–1.10	0.10	–10.12	0.00	–1.32	–0.89
M-Y effect adjusted for X (b): RMET on PANSS-N	–0.48	0.08	–5.60	0.00	–0.66	–0.31
c' X-Y direct effect considering HT, RMET	–0.02	0.13	–0.18	0.85	–0.29	0.24
c' X-Y total effect: Education on PANSS-N	–0.46	0.22	–2.10	0.03	–0.90	–0.02
Bootstrap for the overall indirect effect	–0.44	0.15			–0.73	–0.12
Bootstrap for the indirect effect HT	–0.15	0.11			–0.38	0.07
Bootstrap for the indirect effect RMET	–0.29	0.08			–0.45	–0.13

Note: Education: years of formal education; Hinting Task (HT); Reading the Mind (RMET); PANSS-N: negative symptoms. PANSS-P (positive symptoms) and PANSS-G (general psychopathology) were excluded from the model due to collinearity with the considered variables. Unstandardized β coefficients based on bootstrapping with 5000 resamples. SE = standard error; LLCI = Lower limit of the confidence interval; ULCI = upper limit of the confidence interval (confidence intervals of bias-corrected bootstrap: 95 %).

effect (small effect size, $d = -0.36$) indicated that the relationship between education and NS was fully mediated by social cognition, particularly RMET. This set of variables explained 67.57 % of the variance in NS, including the contribution of age as a covariate ($\beta = -0.01$, $SE = 0.02$, $t = -0.655$, $p = .513$, $CI [-0.071, 0.035]$).

The indirect effects were significant based on the interpretation of the confidence intervals, with greater clarity in the case of RMET (small effect, $d = -0.22$) on NS (PANSS-N) than in the case of HT (null effect, $d = -0.12$) (see Fig. 1).

The patient group was selected for a multiple regression analysis on negative symptoms (NS) as measured by the PANSS-N (see Table 4). Age and chlorpromazine-equivalent dosage (mg) were excluded due to collinearity. The stepwise inclusion of variables demonstrated the significant predictive value of education (9.4 %), along with two social cognition variables. Among these, social cognition measures were particularly relevant to NS, with HT accounting for 41.7 % of the variance and RMET explaining 11.7 %. In the final step, the course of illness variable reached significance, although it accounted for only 2.5 % of the variance in NS, with collinearity indicators showing lower values. The final model explained 69.2 % of the adjusted variance. Residual analysis confirmed the adequacy of the model: Durbin-Watson = 1.77.

4. Discussion

Evidence of variables that mediate the processes involved in psychosis is crucial, as it enables the development of more precise interventions based on factors influencing the onset and persistence of symptoms. Notably, research on the origin and treatment of negative symptoms has not developed to the same extent as the extensive literature on positive symptoms. The dimensional approach adopted in this study proposes a model encompassing both the general and clinical populations regarding NS (Kaiser et al., 2011; Rodríguez-Testal et al., 2019), including cases with short illness duration as well as chronic cases. This perspective is essential for a comprehensive understanding of the scope, implicit temporal progression, and severity determination of NS responses.

The primary objective was to examine the role of cognitive reserve, specifically education (i.e., years of formal schooling completed). The first hypothesis was confirmed, as a direct and statistically significant relationship was identified between education and the presence of NS, after controlling for the effect of age. Education may serve as a protective and adaptive factor in relation to environmental conditions, as previously reported in the literature (Amoretti et al., 2024; de la Serna

Table 4

Multiple regression analysis (insert) on negative symptoms (PANSSN) in the patient group (n = 69).

Variables	R ² change	B	SE	t	CI 95 %	
					LLCI	ULCI
Sex	0.046	2.807	1.564	1.795	-0.315	5.929
Sex		3.060	1.499	2.041*	0.066	6.054
Education	0.094	-0.729	0.272	-2.683**	-1.272	-0.187
Sex		2.751	1.085	2.535*	0.583	4.918
Education		-0.539	0.198	-2.723**	-0.935	-0.144
HT	0.417	-0.919	0.117	-7.821**	-1.153	-0.684
Sex		2.165	0.956	-2.265*	0.255	4.076
Education		-0.423	0.175	-2.420*	-0.772	-0.074
HT		-0.653	0.118	-5.552**	-0.888	-0.418
RMET	0.110	-0.489	0.106	-4.608**	-0.701	-0.277
Sex		1.826	0.939	1.944	-0.051	3.703
Education		-0.298	0.175	-1.873	-0.677	0.022
HT		-0.602	0.116	-5.172**	-0.834	-0.369
RMET		-0.475	0.103	-4.605**	-0.681	-0.269
course of illness	0.025	0.010	0.004	2.350*	0.001	0.018

Note: Unstandardized β . Education: education level; Hinting Task (HT); Reading the Mind (RMET); course of illness (months).

* $p < .05$.

** $p < .01$.

et al., 2013; Nithianantharajah and Hannan, 2009) and further supported by prospective studies (Ayesa-Arriola et al., 2013; Norman et al., 2015; Torgalsbøen et al., 2015).

The study of social cognition in schizophrenia is particularly notable for its ability to predict positive symptoms (Ferrer-Quintero et al., 2022), with a large effect size observed in theory of mind (ToM) and social perception. In individuals with high-risk mental states, the effect size is small, but it becomes substantial during the first psychotic episode, especially in ToM.

Given these findings, social cognition should be considered a mediating factor in the proposed model for NS. Years of formal education may support the development of social cognition by providing opportunities for social interaction, learning social norms, and practicing social skills (García-López et al., 2022; Giordano et al., 2024). This enhanced competence in social cognition may influence the likelihood of developing or maintaining negative symptoms, as it strengthens the processes involved in understanding and adapting to social and functional contexts (Lincoln et al., 2011). Prior research suggests that social cognition can predict up to 39 % of the variance in NS, even after

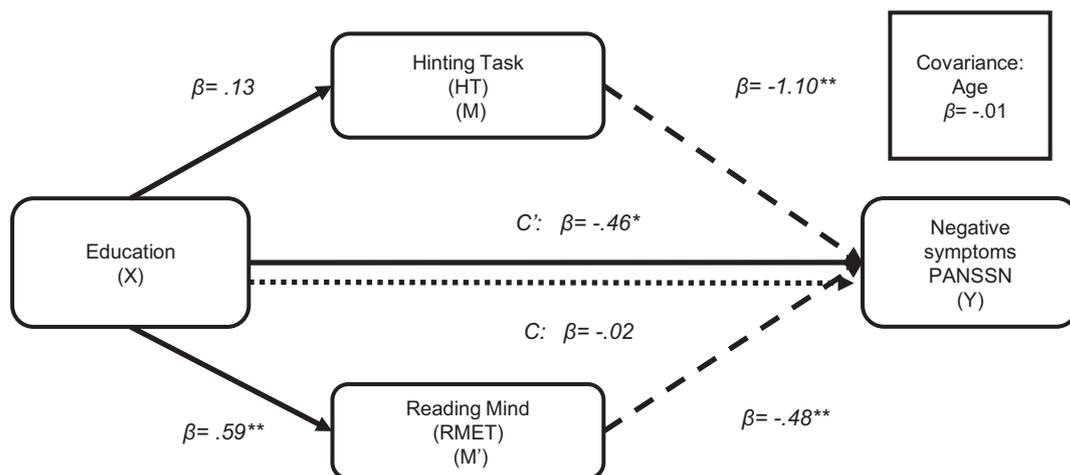


Fig. 1. Final model about negative symptoms (PANSSN).

Note: Unstandardized β coefficients. Solid line: direct relationship. Dashed line, indirect relationship. Dotted line, total effect. (X) independent variable, (M) mediators, (Y) dependent variable.

* $p < .05$. ** $p < .01$.

accounting for neurocognitive function and depression (Lincoln et al., 2011). Additional studies have provided evidence supporting the mediating role of social cognition in NS (Pelletizza et al., 2020), highlighting difficulties in evaluating and anticipating social interactions (e.g., ToM) (Ferrer-Quintero et al., 2022), which may contribute to social withdrawal or disinterest in social relationships. Therefore, the second objective of this study was to examine social cognition as a mediator of NS, specifically the theory of emotional mind (measured by RMET) (Pinkham et al., 2016) and the theory of inferential mind (measured by HT).

Hypothesis 2 was partially confirmed. A statistically significant relationship was found between education and the theory of emotional mind (RMET), but not with the theory of inferential mind (HT). **Hypothesis 3** was confirmed, demonstrating a significant relationship between both measures of social cognition (RMET and HT) and negative symptoms (NS). This finding aligns with previous research that also suggests a potential feedback effect of NS on social cognition itself, although this was not analyzed in the present study. The observed mediation was complete, although additional mediator or moderator variables—unexamined in this study—cannot be ruled out as potential influences on the proposed model.

The third objective was to examine the indirect relationship between education and NS through the mediation of social cognition (see Fig. 1). Confidence interval analysis partially confirmed **Hypothesis 4**, as inferential mind (HT) was not significant. Both measures of social cognition demonstrated a small effect size, with the theory of emotional mind (RMET) playing a more prominent role. Thus, while the mediating role of social cognition was supported, further research is needed to refine the understanding of this indirect effect and to identify additional contributing variables.

The fourth objective focused on the patient group, considering variables such as illness duration (months) and chlorpromazine-equivalent dosage (mg). **Hypothesis 5** was partially confirmed, as certain variables—such as age, illness duration, and chlorpromazine-equivalent dosage—exhibited collinearity. To minimize its impact on the model, illness duration (months) was selected, as it had a lower effect on model conditions, although its contribution to the explained variance was relatively low. In contrast, education played a significant role, with the two measures of social cognition accounting for more than half of the explained variance in the prediction of negative symptoms. When separating the effects of the two forms of social cognition assessment, it was evident that both the inferential mind (HT) and the emotional mind (RMET) contributed to the prediction of negative symptoms, without diminishing the effect of education—particularly the former.

Thus, social cognition (e.g., ToM) plays a crucial mediating role in NS. The social cognition deficits observed in schizophrenia are thought to result from neural network alterations, impairing the low-level detection of pre-reflective (implicit) intention and potentially reducing connectivity between this network and those involved in high-level (explicit) processing (Csulak et al., 2022). Prefrontal activation may serve as a compensatory mechanism, reflecting efforts to regulate negative emotions, which emerge in individuals at risk of psychosis, while temporal region activation may indicate executive control and the monitoring of processing errors (Kozuharova et al., 2020).

This study included both first-episode patients and those with chronic schizophrenia. While this could introduce bias, evidence suggests that once schizophrenia is established, factors such as age, education, sex, severity, or medication do not significantly affect social cognition (Lewandowski et al., 2024). This approach enabled the integration of all patient cases and general population participants to develop a model based on a dimensional perspective encompassing time, severity, and disease progression.

Characterizing social cognition is crucial for assessing cognitive and interpersonal abilities in individuals with schizophrenia, as it provides valuable insights for developing intervention and rehabilitation strategies. These strategies, in turn, enhance quality of life and social

functioning for those affected by the disorder (Lee et al., 2015). Thus, beyond targeting social skills, maladaptive beliefs, and the reinforcement of self-concept and self-esteem, interventions focusing on social cognition may also contribute to improving specific NS (Lee et al., 2015; Hotte-Meunier et al., 2024).

Studies evaluating interventions have reported moderate-to-large effect sizes for improvements in emotion recognition and social perception, although effect sizes were smaller for mentalization (Lewandowski et al., 2024). A recent meta-cognitive approach yielded significant improvements in social cognition (e.g., ToM) but not in emotional processing (Hotte-Meunier et al., 2024).

The present study has several limitations that should be acknowledged. Firstly, its cross-sectional design limits the extrapolation of the findings. However, the sample includes a relatively broad population with diverse psychotic disorders and varying stages of illness progression, along with a control group from the general population. Participant recruitment was based on accessibility, which also constrains the generalizability of conclusions. A more stringent selection process could help control for such heterogeneity. Nevertheless, a study comparing social cognition between chronic patients and healthy controls found no consistent diagnosis-related differences, suggesting that outcomes depend more on the measures used (e.g., cohort-by-diagnosis differences were detected with the Hinting Test but not with the Reading the Mind in the Eyes Test) (García-Fernández et al., 2020).

Indeed, another potential limitation of the measures used is that, while no relationship was observed between the inferential mind (HT) and education in the full sample—despite evidence of full mediation by social cognition—when focusing solely on the patient group, this measure showed the highest predictive value (41.7 %), with education maintaining its predictive role. Some references suggest that the inferential mind (HT) is a distinctly clinical instrument, which may explain why its role becomes less apparent in the general population (Gil et al., 2012).

Additionally, differences in years of formal education between patients and control participants should be considered. Selecting control participants with similar education levels would be ideal. However, in the final objective, the focus remained on key variables such as education and social cognition within the patient group. Some studies have explored various cognitive reserve indicators (de la Serna et al., 2013), which could provide a more comprehensive perspective. Indeed, considering cognitive reserve may help clarify unexplained variance and contribute to a more complete assessment. Nonetheless, this study opted for a single, easily verifiable variable—education—given its implications for neural plasticity and its non-fixed nature.

Other limitations include differences in illness duration and treatment regimens between first-episode and chronic patients (Lewandowski et al., 2024). To mitigate these, analyses were conducted within a single patient group (providing a broader perspective), and collinearity among variables was considered. Furthermore, social cognition test performance may have been influenced by intelligence, education level, and cultural background. However, two different tests assessing the same social cognition process (e.g., ToM) were used, and both joint and separate analyses of the patient group yielded similar predictive roles for social cognition. Finally, participant motivation during testing may have also affected the results (Moritz et al., 2017).

5. Conclusions

In this study, considering both patients and general population participants, education—an indicator of cognitive reserve—emerged as a significant predictor of NS. Notably, this relationship was mediated by social cognition (e.g., ToM). When analyzing only the patient group, social cognition remained a predictor of NS, with illness duration (measured in months) also contributing as a significant factor.

This perspective is innovative, since it highlights cognitive reserve (operationalized as years of formal education) as a dynamic variable

linked to modifiable conditions such as lifestyle, occupational engagement, task complexity, physical and leisure activities, and even educational quality (González-Ortega et al., 2020). This underscores the importance of developing targeted programs and interventions that enhance these protective factors, reinforcing the beneficial role of education (Clougher et al., 2024) in cognitive resilience and in cognitive processes that may remain amenable to stimulation later in life.

Moreover, the findings emphasize the need for a nuanced analysis of social cognition-related processes, particularly ToM given its mediating y predictor role in NS. This reinforces the value of interventions designed to strengthen social cognition as a strategy for mitigating NS.

CRedit authorship contribution statement

Sebastián Lema Spinelli: Writing – review & editing, Writing – original draft, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Juan Francisco Rodríguez-Testal:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Álvaro Cabana:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Sandra Romano:** Validation, Conceptualization. **Leonel Gómez-Sena:** Validation, Conceptualization.

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Declaration of competing interest

The authors declare that they have no conflicts of interest.

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