

**Understanding others as a mediator between verbal memory and negative symptoms in schizophrenia-spectrum disorder**

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## **Abstract**

From the onset of schizophrenia, verbal memory (VM) deficits and negative symptoms are strongly associated, and both additively predict functional outcomes. Emotion recognition (ER) and theory of mind (ToM; the ability to infer others' mental states), two components of social cognition, are also particularly affected in schizophrenia. Explanatory models of negative symptoms have integrated these cognitive impairments as potential precursors and previous studies revealed relationships between ER and/or ToM and VM, as well as with negative symptoms, but the organization of these associations remains unclear. We aimed to determine whether impairments in VM and social cognition sequentially pave the way for negative symptoms in schizophrenia. To this end, we used mediation analyses. One hundred and forty participants with a diagnosis of schizophrenia or schizoaffective disorder were recruited. First, correlational analyses were conducted between our variables of interest. The mediating effect of social cognition between VM and negative symptoms was then examined using the PROCESS macro. Variables of interest were significantly correlated ( $r = |.166|$  to  $|.391|$ ), except for ER and negative symptoms. Only the serial multiple mediation model with 2 mediators (ER followed by ToM) revealed a significant indirect effect of VM on negative symptoms ( $\beta = -.160$ , 95% CI =  $-.370$  to  $-.004$ ). This relationship was selective for expressive negative symptoms (e.g., blunted affect and alogia). This study illustrates the richness of the relationship between cognitive deficits and negative symptoms and provides additional information for the involvement of social cognition in negative symptoms' etiology.

**Keywords:** psychosis; social cognition; emotion processing; theory of mind; neurocognition.

## Introduction

During the last decade, there has been a growing interest in understanding the etiology of negative symptoms in schizophrenia-spectrum disorder (SSD) (Correll and Schooler, 2020; Dollfus and Lyne, 2017; Galderisi et al., 2018; Galderisi et al., 2021). These prevalent symptoms appear early in the disease course and can increase in severity as a function of the duration of illness (Savé et al., 2019). A robust relationship between negative symptoms' severity and worse functional outcome has been observed across different stages of SSD (Foussias et al., 2014; Jordan et al., 2018), which could be partially due to a lack of effective pharmacological treatment (Bucci et al., 2020). Negative symptoms are difficult to treat especially because relatively little is known about their etiology (Correll and Schooler, 2020). A better understanding of their underpinnings might inform treatment development at both pharmacological (Correll et al., 2020) and psychosocial levels (Lutgens et al., 2017).

Negative symptoms are also strongly correlated with neurocognition (Hovington and Lepage, 2012; İnce and Üçok, 2018) and social cognition, the mental processes underlying social interactions (Bell et al., 2013; Green, 2020), which are particularly affected in SSD (Bora et al., 2017; Savla et al., 2013). Some studies suggest that negative symptoms mediate the relationship between these aspects of cognition and functioning (Griffiths et al., 2020; Lin et al., 2013). A recent study by Oliver et al. (2019) demonstrated that neurocognition is related to negative symptoms through social cognition and that a 2-factor social cognitive model was the best fit to observe this relationship. However, neurocognition and social cognition are umbrella terms each encompassing several constructs. Among the neurocognitive domains, verbal memory (VM) is particularly impaired in SSD. From the onset of schizophrenia, negative symptoms are strongly associated with VM deficits (Duan et al., 2020; Hovington et al., 2013; Hovington and Lepage, 2012; Thomas et al., 2017) and both additively predict functioning and quality of life (Jordan et al., 2014; Jordan et al., 2018; Karambelas et al., 2019). Compared to other cognitive domains, VM is disproportionately impaired in SSD (Heinrichs and Zakzanis, 1998), even after controlling for impairments in other cognitive domains (e.g., executive functions, working memory, and IQ) (Egeland et al., 2003; Kopald et al., 2012; Leeson et al., 2009).

Social cognition also comprises several subdomains: emotional processing, social perception and knowledge, theory of mind (ToM), and attributional style (Green et al., 2008; Pinkham, 2014). Emotion processing and ToM have been extensively explored in SSD (Bora and Pantelis, 2016), notably in relation to symptomatology (Peyroux et al., 2018). Emotion processing represents the ability to identify and recognize emotions through facial expressions, gestures, and tone of voice but also, at a more complex level, to use this information to manage and regulate emotions (Green et al.,

2008). Impaired performance in emotion recognition (ER) has been correlated to VM difficulties in early and enduring psychosis (Lysaker et al., 2021). This relationship between verbal and visual domains might be explained by the integrative role of the hippocampus that is involved in both memory recollection and spatial navigation. Indeed, this latter requires the active exploration of the environment and integration of visual representations to lead to action (Rubin et al., 2014). ER has also been associated with negative symptoms in meta-analytic studies conducted on patients with schizophrenia (Chan et al., 2010; Kohler et al., 2010). ToM refers to the ability to interpret others' speech and actions in terms of their intentions, knowledge, and beliefs (Corcoran et al., 1995) and is the most impaired social cognitive domain in schizophrenia (Beland and Lepage, 2017; Bertrand et al., 2008; Bertrand et al., 2007). ToM tasks requiring the attribution of intentions, such as the Hinting task (Corcoran et al., 1995), are strongly related to episodic memory (Thibaut et al., 2020). Hence, Laurita and Spreng (2017) proposed that our relational memory capacity influences how we perceive, construct, interact and ultimately connect with our social world. The recognition of emotions is traditionally considered as a first step when interacting with others, and a prerequisite to ToM (Achim et al., 2020; Baron-Cohen et al., 2001). Therefore, assessing others' intentions involves the appraisal of their emotional status and conceptual models of psychosis have proposed a serial organization in social information-processing with ER followed by ToM (Couture, 2006).

Most of the studies exploring cognitive domains and negative symptoms considered these symptoms as a whole. Whether negative symptoms represent a unified or multidimensional construct is still under debate (Galderisi et al., 2018). Five domains of symptoms were initially described by the NIMH-MATRICES consensus statement on negative symptoms: avolition (a reduction in the initiation and persistence of goal-directed activities), anhedonia (a reduction in the experience of pleasure), asociality (reduced social interactions and initiative due to decreased interest in relationships with others), blunted affect (decreased expression of emotion), and alogia (a reduction in the number of words spoken and amount of spontaneous elaboration) (Kirkpatrick et al., 2006). Subsequent factor analyses conducted on first-generation (e.g., the Scale for the Assessment of Negative Symptoms) and more recent rating scales (e.g., the Brief Negative Symptom Scale) support two core dimensions of negative symptoms (Galderisi et al., 2021); the *Motivation and Pleasure* factor (MAP), including avolition, asociality, and anhedonia and the *Expressive* factor (EXP) combining restricted affect, diminished emotional range, and poverty of speech (i.e., alogia and blunted affect) (Galderisi et al., 2018; Liemburg et al., 2013; Messinger et al., 2011; Strauss et al., 2013). These two dimensions of symptomatology might have different predictors and outcomes (Strauss et al., 2013) with discrepant results on cognitive impairments (Chang et al., 2017; Liemburg et al., 2020).

Therefore, we aimed to refine the understanding of the relationships between neurocognition, social cognition, and negative symptoms in a relatively large sample of patients with schizophrenia or schizoaffective disorder. We specifically examined whether VM is related to negative symptoms' factors (i.e., EXP and MAP) via specific constructs of social cognition (i.e., ER and ToM). We opted for the two-factor approach of the negative symptoms to have sufficient statistical power for our analyses and as the growing literature confirms the validity of the construct, with relationships to cognitive dimensions, as well as functional outcomes (Duan et al., 2020; Liemburg et al., 2013; Messinger et al., 2011; Pelletier-Baldelli and Holt, 2020; Thomas et al., 2017). ER and ToM are two representative subdomains of social cognition that have been extensively studied in SSD with robust findings (Bora and Pantelis, 2016) and with validated therapeutic options (Bordon et al., 2017; Yeh et al., 2019). To this end, we first conducted correlational analyses between these variables to determine their relationships, and second, we used mediation analyses to probe the process by which VM predicts negative symptoms through ER and/or ToM. We then further examined whether this process was unique to either EXP or MAP negative symptoms' dimension. We hypothesized that 1) both ER and ToM would individually partially mediate the relationship between VM and negative symptoms (Harvey et al., 2019), and 2) following the results from Liemburg et al. (2020), that the relationship between VM and the EXP factor would be significantly mediated by social cognition. For the inclusion of both mediators (ER and ToM) in the model, our approach was exploratory and different models were tested (parallel and serial mediation models) following proposed conceptual frameworks (Achim et al., 2020; Couture, 2006).

## **Methods**

### *Participants*

One hundred and forty patients were recruited from inpatient and outpatient units of a mental health institute and affiliated community centres, 103 with a diagnosis of schizophrenia and 30 with schizoaffective disorder, according to the DSM-IV criteria (APA, 2000). They were aged between 18 and 50 years old and were part of a larger cohort described in Beland et al. (2017). Non-inclusion criteria were: low estimated IQ score (< 70) measured with the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) (mean IQ score of SSD participants=94.26, SD=14.24), personal or familial history of neurological conditions (neurodegenerative disorders), head trauma with loss of consciousness, or diagnosis of substance dependence (except tobacco). The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study procedures were

approved by the Douglas Institute Research Ethics Board. All patients provided written informed consent after the nature of the procedures had been fully explained and received compensation for their participation. Seventy-three healthy controls group-matched for age and sex with no personal or familial history of psychotic illness were recruited through online advertisements for an add-on neuroimaging part of this project and used here to provide normative data for the cognitive measures. The Structured Clinical Interview for DSM-IV-TR Axis 1 Disorders, Non-patient Edition (Spitzer et al., 2002), was administered to all healthy participants to rule out the presence of any current mental illness.

### *Clinical and cognitive assessment*

Socio-demographic data, clinical information (through semi-structured interview and questionnaires), and cognitive performance were assessed during a face-to-face interview. Duration of illness and antipsychotic dosage (converted to chlorpromazine equivalent) (Woods, 2011) were collected by medical chart review, or directly confirmed by medical teams.

The SANS was used to assess negative symptoms and scores were computed following the recent recommendations of the European Psychiatric Association (Galderisi et al., 2021); items 6 (“appropriate affect”) and 10 (“poverty of speech content”) were excluded, as well as the attention subscore. Hence, these items include aspects that are closer to disorganization symptoms (items 6 and 10) or cognitive symptoms (attention subscore) and that do not cluster in the negative symptom factors (Galderisi et al., 2021). A total score was calculated accordingly, as well as two subscores corresponding to the EXP factor (combining blunted affect and alogia) and the MAP factor (combining avolition, asociality, and anhedonia) (Blanchard and Cohen, 2006; Liemburg et al., 2013; Lyne et al., 2017). Positive symptoms were assessed with the Scale for the Assessment of the Positive Symptoms (SAPS; Andreasen, 1984) and depressive symptoms with the Calgary Depression Scale (CDS; Addington et al., 1993).

VM was assessed by the CogState Schizophrenia Battery (Pietrzak et al., 2009) which consists of computerized tasks exploring general domains of cognition with minimal language complexity. VM was measured by the immediate and delayed recall version of the International Shopping List (Lim et al., 2009). ER was assessed through the Ekman 60 Faces (EK-60F) Test which uses a range of photographs from the Ekman and Friesen series of Pictures of Facial Affect (Ekman and Friesen, 1976) depicting the faces of 10 actors (6 female, 4 male). Each series displays six basic emotions (i.e., happiness, sadness, anger, fear, surprise, disgust) and neutral faces. The average accuracy score was used for all six emotions. For ToM, we used the Hinting Task which assesses one’s capacity to infer

other people's intentions through indirect speech (Corcoran et al., 1995). It comprises 10 stories containing a dialogue between two or more characters that are read out loud to participants. Participants are asked to identify the hidden meaning behind characters' remarks, producing a total score out of 20, with higher scores indicating better ToM. All cognitive scores (VM, ER, and ToM) were transformed into control-normative z-scores by subtracting healthy controls' mean score from the patient's raw score and dividing by the controls' standard deviation.

### *Statistical analyses*

Spearman correlations were used to examine expected associations between our variables of interest (SANS, VM, ER, and Hinting scores; see Supplementary Figure S1 for the distribution of all relevant variables). In line with the literature, sex (Buck et al., 2020; Navarra-Ventura et al., 2018) and duration of illness (Liemburg et al., 2020) were added as covariates. We also tested in our SSD sample their relationship to the variables of interest by conducting one-way ANOVAs and Spearman correlations respectively. The mediating effect of social cognition between VM and negative symptoms was examined using the PROCESS macro V3.4 for SPSS (Hayes, 2017) which uses a regression-based model. Assumptions of regression were met (see supplementary material for details and Figure S2 for the scatter plot between standardized predicted values and standardized residuals). Two single mediation models (VM-ER-NS and VM-ToM-NS), a parallel mediation model (including ER and ToM) and four serial multiple mediation models (two main models: VM-ER-ToM-NS and VM-ToM-ER-NS; two validity models: NS-ER-ToM-VM and VM-ToM-ER-SAPS) were tested. The selection of the models was based on the literature rather than on the correlational values. According to Hayes (2009), the direct effect does not need to be significant because conceptually we want to see if VM and SANS could be related via ER and ToM.

## **Results**

Sample characteristics for patients and controls are displayed in Table 1 as mean scores on each variable of interest.

### *Correlational analyses*

In the SSD group, VM was positively correlated with both ER ( $r_s=.280$ ;  $p=.001$ ) and ToM ( $r_s=.196$ ;  $p=.022$ ). ER and ToM were also positively correlated ( $r_s=.391$ ;  $p<.001$ ). The total negative symptoms

score was negatively correlated with VM ( $r_s = -.178$ ;  $p = .038$ ) and ToM ( $r_s = -.214$ ;  $p = .012$ ). Only the EXP factor was negatively correlated with ToM ( $r_s = -.232$ ;  $p = .007$ ) and a trend toward significance was observed between the MAP factor and VM ( $r_s = -.166$ ;  $p = 0.053$ ). Correlations between the variables of interest are displayed in Table 2. Additionally, VM was significantly more impaired in male than in female (male:  $-1.86$  and female:  $-1.17$ ;  $F(138,1) = 8.15$ ;  $p = .005$ ) and duration of illness was negatively correlated to ER ( $r_s = -.224$ ;  $p = .008$ ). In the HC group, VM was positively correlated with ER ( $r_s = .383$ ;  $p = .001$ ) and ER and ToM were positively correlated ( $r_s = .284$ ;  $p = .016$ ). VM was not significantly correlated to ToM ( $r_s = .201$ ;  $p = .092$ ).

### *Mediation analyses*

Simple mediation models exploring whether VM influenced negative symptoms through a single variable (ER or ToM) were not significant (direct effect:  $\beta = -1.36$ , 95% CI =  $-2.790$  to  $.061$ ; effect size =  $-.16$ ; indirect effect:  $\beta = -.159$ , 95% CI =  $-.633$  to  $.263$ ; effect size =  $.03$  and direct effect:  $\beta = -1.28$ , 95% CI =  $-2.585$  to  $.017$ ; effect size =  $-.18$ ; indirect effect:  $\beta = -.267$ , 95% CI =  $-.738$  to  $.033$ ; effect size =  $-.03$ , respectively), nor was the parallel mediation model with ER and ToM (direct effect:  $\beta = -1.23$ , 95% CI =  $-2.590$  to  $.127$ ; effect size =  $-.16$ ; indirect effect:  $\beta = -.292$ , 95% CI =  $-.889$  to  $.239$ ; effect size =  $-.04$ ), the multiple mediation model with ToM followed by ER ( $\beta = .001$ , 95% CI =  $-.102$  to  $.105$ ), or the validity models exploring whether negative symptoms influences VM through ER and ToM (direct effect:  $\beta = -.19$ , 95% CI =  $-.038$  to  $.000$ ; effect size =  $-.15$ ; indirect effect:  $\beta = -.001$ , 95% CI =  $-.002$  to  $.001$ ; effect size =  $-.01$ ) or the model replacing SANS by SAPS (direct effect:  $\beta = -2.11$ , 95% CI =  $-4.447$  to  $.227$ ; effect size =  $-.16$ ; indirect effect:  $\beta = .09$ , 95% CI =  $-.173$  to  $.376$ ; effect size =  $.01$ ). However, the serial multiple mediation model with ER followed by ToM revealed a significant indirect effect of VM on negative symptoms (direct effect:  $\beta = -1.23$ , 95% CI =  $-2.590$  to  $.127$ ; effect size =  $-.16$ ; indirect effect:  $\beta = -.160$ , 95% CI =  $-.370$  to  $-.004$ ; effect size =  $-.02$ ). Thus, both mediators in this order were necessary to explain a significant portion of VM's variance. This model remained significant when considering the EXP factor (direct effect:  $\beta = -.35$ , 95% CI =  $-1.35$  to  $.65$ ; effect size =  $-.06$ ; indirect effect:  $\beta = -.151$ , 95% CI =  $-.342$  to  $-.030$ ; effect size =  $-.03$ ) but not the MAP factor (direct effect:  $\beta = -.88$ , 95% CI =  $-1.92$  to  $.16$ ; effect size =  $-.16$ ; indirect effect:  $\beta = -.009$ , 95% CI =  $-.128$  to  $.140$ ; effect size =  $-.01$ ). These three models are represented in Figure 1. Additional serial models including sex and duration of illness as covariates displayed similar results; only the addition of IQ scores removed significance of the indirect effect in the serial mediation model (see detailed results in the supplementary material).



## Discussion

With the current study conducted on a large sample of SSD patients, we gathered further support for the hypothesis that social cognition mediates the relationship between VM and negative symptoms. It provided a finer-grained depiction of the association between those constructs by identifying a link from VM, to the two components of social cognition (ER first and ToM second), which affected negative symptoms. This path was selectively significant for the expressive component.

The expected positive association between VM and social cognition was confirmed in our sample of SSD participants. It is worth noting that most of the existing literature on this relationship in severe psychiatric disorders was specifically between VM and ToM (Dalkner et al., 2019; Navarra-Ventura et al., 2021; Thibaut et al., 2020). These previous publications suggest that ToM tasks, such as the Hinting task, require verbal abilities but cannot be reduced to VM performance alone. The addition of IQ scores removed the significance of our model but the use of IQ as a covariate might produce overcorrected findings in clinical populations (Dennis et al., 2009). In the current study, we also highlighted a relationship between VM and ER. This less-intuitive link, already reported in different psychiatric populations (Buitelaar et al., 1999; Lysaker et al., 2021; Martino et al., 2011), can be thought of in relation to the neuroanatomical correlates of both domains; indeed, besides the specific role of the hippocampus, at a brain network level, the medial temporal lobe may modulate the activity of the superior temporal sulcus (central to ER) and alter the ability to decode facial expressions (Åhs et al., 2014). These interesting findings were not specific to psychosis (i.e., resulting from anterior temporal lobe resection in epileptic patients) and would require further exploration in the SSD population.

The key role of social cognition on negative symptomatology should be considered in light of current explanatory models. Some previous mediation studies used structural equation modeling to test the influence of social cognition on negative symptoms and functioning. In the study by Lin et al. (2013), in which 302 patients were recruited, social cognition was combined with other cognitive domains to predict functioning through negative symptomatology. More recently, in a study conducted on 164 patients with SSD, Oliver et al. (2019) showed that a 2-factor model fit the social cognitive data with a low-level simulation factor (i.e., including ER and empathy tasks) and a high-level mentalizing factor (i.e., including more complex inference states, such as ToM). Interestingly, only the mentalizing factor was significantly associated with negative symptoms and functional outcomes. In our work, the serial association of ER and ToM is of particular interest as these two social cognitive subdomains are interrelated but distinct constructs. ER, which can be included in low-level non-specific simulation processes, would precede ToM, a higher level mentalizing process (Alcalá-López et al., 2019) and

both would be required to explain, at least in part, the relationship between VM and negative symptoms.

Moreover, recent models have been proposed to account for the interplay between social cognition and negative symptoms, and integrated brain imaging findings. A first integrated model proposed by Pelletier-Baldelli and Holt (2019) suggested that both higher-order (i.e., cognitive changes) and lower-level (i.e., perceptual changes) domains are impaired in SSD and that these wide-ranging impairments may interact to bring about impaired social cognition and negative symptoms. By dividing the constructs of social cognition and negative symptoms, a second “non-unitary” model has emerged; in this model, ToM deficits have a strong relationship with the EXP factor only, whereas deficits in facial affect recognition are linked to all five negative symptoms (Pelletier-Baldelli and Holt, 2020). Our results on EXP and MAP factors are partially in line with this model, with the EXP factor driving the significant mediation results through ER and ToM. The proximity of social cognition and negative symptoms even questions how much these two domains overlap and whether negative symptoms could represent the daily functioning consequences of social cognitive impairment (Pelletier-Baldelli and Holt, 2020).

This study also illustrates the richness of the relationship between cognitive deficits and negative symptoms and proposes a cognitive pathway to understand negative symptoms. The size of our sample was sufficiently large to provide adequate power to our analyses, however, it is necessary to be cautious about the generalisability of our findings due to the small effect sizes associated with our main results and the small portion of variance accounted by the models. Nevertheless, new approaches are mandatory to explore new therapeutic options and additional relevant therapeutic targets for negative symptoms could then be tested. For now, general cognitive remediation interventions only have a small beneficial effect on negative symptoms (Cella et al., 2017; Vita et al., 2021). More focused interventions targeting social cognitive domains might help to partially alleviate negative symptoms and ultimately improve functional outcomes (Kurtz et al., 2016). Some interventions targeting multiple social cognitive domains, such as the Social Cognition and Interaction Training (SCIT) (Penn et al., 2007), have been shown to improve functional outcomes and clinical symptoms (Javed and Charles, 2018). More focused programs on a specific domain are also proposed to SSD patients; a meta-analysis published in 2017 on psychosocial interventions targeting facial ER showed significant positive effects on social functioning, but not on the symptomatology itself (Bordon et al., 2017). Interestingly, a more recent randomized controlled trial using the Training of Affect Recognition showed durability effects of the training on ToM over a three-month period (Vaskinn et al., 2019). These results support our findings suggesting a path between ER and negative

symptoms through ToM. Programs that combine ER and ToM, like the Emotion and ToM Imitation Training (Mazza and et al., 2010) could be further explored in relation to the negative symptoms and, if effective, would add clinical value to the current results.

### *Limitations*

The present study has some limitations that need to be considered. First, we conducted mediation analyses on cross-sectional data. Hence, our results do not reflect causality and future longitudinal studies would provide a better test of our findings and assess the predictive value of such cognitive impairments. Second, our sample consisted primarily of male participants, which limits the generalization of our results to both biological sexes. Nevertheless, this proportion is typical of research samples in psychosis research and sex was controlled for while conducting the correlational analyses. Further studies on female participants and incorporating gender identity should help to delineate the potential sex and/or gender specificities. Third, our sample size was at the lower limit to detect the expected results. Given that we have observed significant effects, we can assume that we had enough power to detect them. The question of adequate power was more related to type I error, hence we applied a correction for multiple comparisons to our results in order to limit its potential inflation. Fourth, we focused our mediation model on VM because of the robust literature linking this cognitive domain to negative symptoms, but some previous studies have chosen to explore neurocognition more broadly in relation to negative symptoms. It remains to be determined whether these findings are specific to VM or are more generally characteristic of neurocognition. From a clinical perspective and if confirmed with longitudinal data, our results could contribute to the development of an easily implementable cognitive assessment focused on VM, ER, and ToM in the context of negative symptoms to propose adjusted interventions.

### *Conclusion*

By using cognitive and clinical data of a large sample of SSD patients, the current study provided evidence that the relationship between VM and negative symptoms can be partially attributed to ER through ToM. This result can contribute to advance existing theoretical models, notably by exploring the two main negative symptoms factors, the EXP and MAP dimensions, and providing additional justifications for potential different etiologies, and consequently different therapeutic targets. Hence, the symptoms of the EXP factor might be more related to social cognitive impairments and improved by psychosocial interventions, whereas the MAP factor might be more sensitive to the effects of medication (Strauss et al., 2021).

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**Table 1. Sociodemographic and clinical characteristics of the participants**

	SSD (n = 140)	HC (n = 73)	Statistic (df)	p-value
	Mean (SD)	Mean (SD)		
Age (years)	35.66 (7.94)	34.34 (9.03)	t(211) = 1.05	0.296
Male, n (%)	103 (73.6)	52 (71.23)	$\chi^2(1) = 0.13$	0.716
Education (years)	11.29 (2.55)	13.42 (2.35)	t(211) = -5.95	<0.001
Age of onset (years)	22.01 (6.57)	-		
Duration of illness (years)	13.64 (7.90)	-		
CDS	2.82 (2.94)	-		
SAPS	18.64 (17)	-		
SANS:				
Total	22.26 (10.01)	-		
EXP factor	9.61 (7.16)	-		
MAP factor	12.66 (7.11)	-		
CPZ equivalent (mg) [n]	793.21 (845.74) [133]	-		
VM performance [n]	-1.68 (1.29)	0 [72]	t(210) = -7.37	<0.001
EK-60F accuracy [n]	-1.16 (1.80) [138]	0	t(209) = -4.72	<0.001
Hinting task score [n]	-1.70 (2.36)	0 [72]	t(210) = -5.69	<0.001

*Note.* CDS: Calgary Depression Scale; CPZ: chlorpromazine; EK-60F: Ekman 60 Faces Test; EXP: Expressive; HC: healthy controls; MAP: Motivation and Pleasure; SANS: Scale for the Assessment of Negative Symptoms; SAPS: Scale for the Assessment of the Positive Symptoms; SD: standard deviation; SSD: schizophrenia-spectrum disorder; VM: Verbal Memory.

**Table 2. Correlational results between our variables of interest, controlled for sex and duration of illness.**

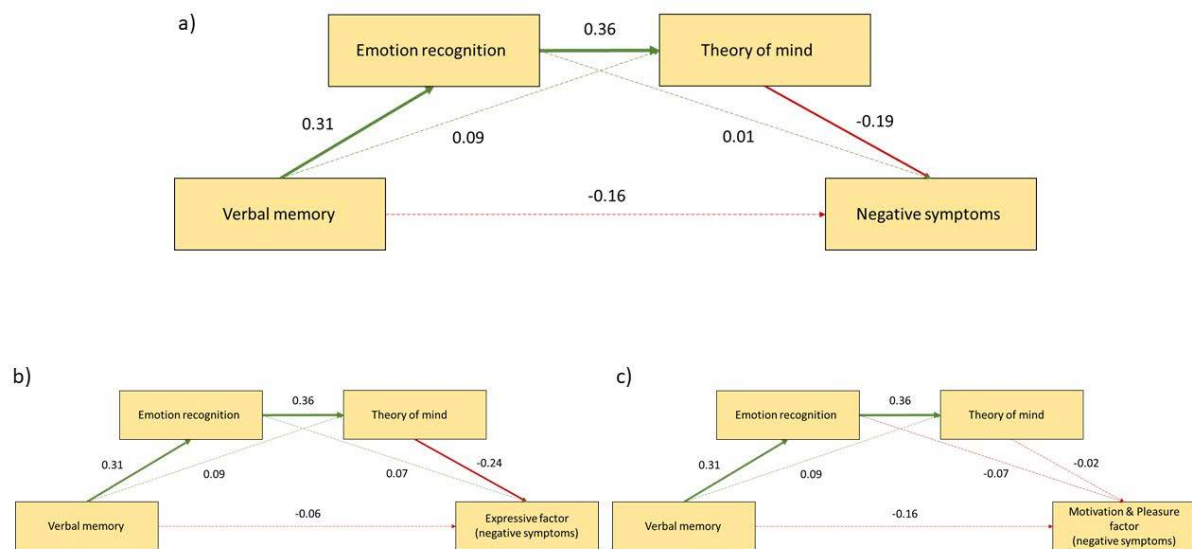
	VM	ER	ToM
VM	-		
ER	0.280*	-	
ToM	0.196*	0.391*	-
SANS total	-0.178*	-0.107	-0.214*
SANS - EXP factor	-0.086	-0.066	-0.232*
SANS - MAP factor	-0.166*	-0.086	-0.070

*Note.* ER: Emotion Recognition; EXP: Expressive; MAP: Motivation and Pleasure; SANS: Scale for the Assessment of Negative Symptoms; ToM: Theory of Mind; VM: Verbal Memory; \*:  $p < 0.05$ .

**Table 3. Significant Variables Within Serial Mediation Model**

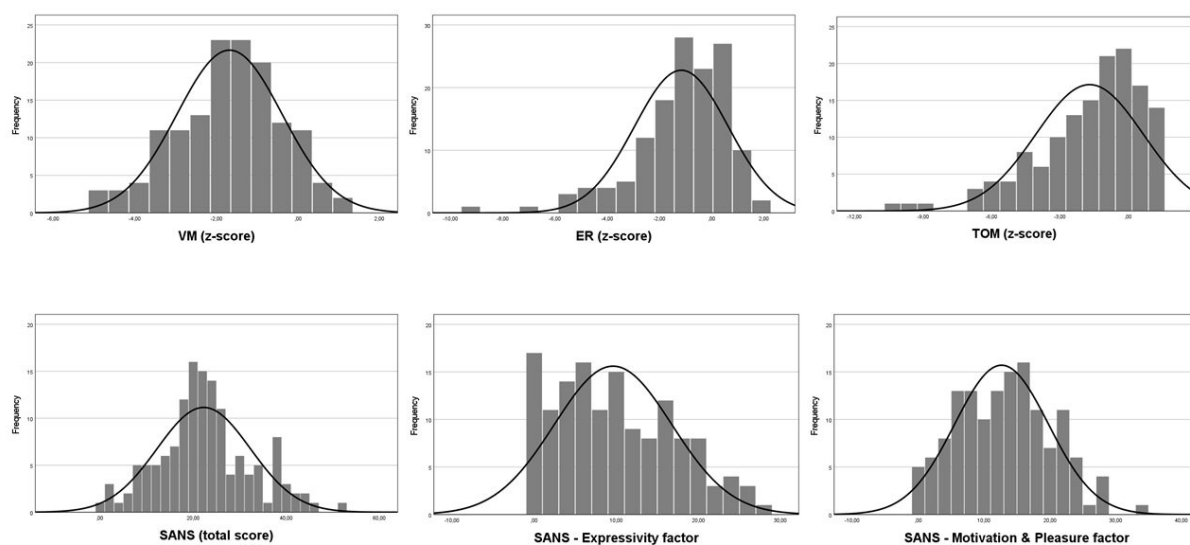
Outcome	Variable	Path	Unstandardized coefficient	SE	<i>p</i>	Model R <sup>2</sup>
ER	VM	a <sub>1</sub>	.43	.12	<b>&lt;.01<sup>a</sup></b>	.09
ToM	VM	a <sub>2</sub>	.17	.19	.38	.16
	ER	d <sub>21</sub>	.47	.11	<b>&lt;.01<sup>a</sup></b>	
SANS	VM	c'	-1.23	.69	.07	.07
	ER	b <sub>1</sub>	.01	.47	.99	
	ToM	b <sub>2</sub>	-.79	.38	<b>.04</b>	
EXP factor	VM	c'	-.35	.98	.49	.06
	ER	b <sub>1</sub>	.30	.50	.43	
	ToM	b <sub>2</sub>	-.74	.38	<b>&lt;.01<sup>a</sup></b>	
MAP factor	VM	c'	-.88	.5	.09	.04
	ER	b <sub>1</sub>	-.30	.42	.48	
	ToM	b <sub>2</sub>	-.05	.32	.89	

*Note.* ER: Emotion Recognition; SANS: Scale for the Assessment of Negative Symptoms; ToM: Theory of Mind; VM: Verbal Memory; <sup>a</sup>: survived to Bonferonni-Holms correction.



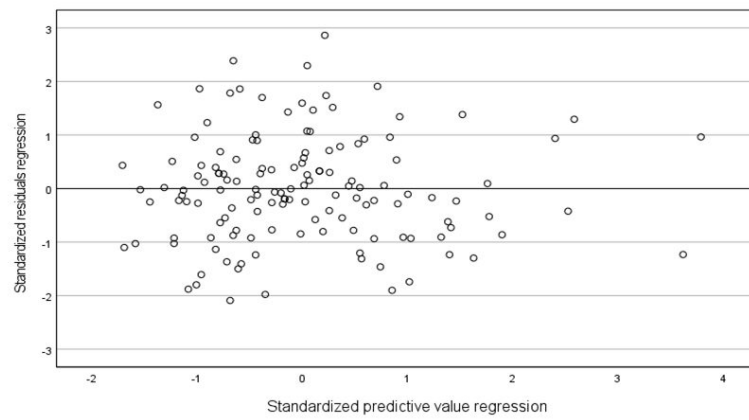
**Figure 1.** Serial multiple mediation models.

The association between verbal memory and (a) the total score of the Scale for the Assessment of Negative Symptoms (SANS), (b) the Expressive factor, and (c) the Motivation and Pleasure factor, mediated by emotion recognition followed by theory of mind . Values indicate regression coefficients. Dashed black lines indicate that the mediation pathway was not significant in the serial mediation analysis.



**Figure S1.** Distribution of the variables of interest.

ER: Emotion Recognition; SANS: Scale for the Assessment of Negative Symptoms; ToM: Theory of Mind; VM: Verbal Memory.



**Figure S2.** Scatter plot between standardized predicted values and standardized residuals

## **Understanding others as a mediator between verbal memory and negative symptoms in schizophrenia-spectrum disorder**

### Supplementary Material

#### *Assumptions required for mediation analyses*

First, in our study, the assumption of linearity between the outcome variables and the predictors called for a linear relationship between negative symptoms and/or VM, and/or ER, and/or ToM, but there is no consensus in the literature as to whether the direct effect needs to be significant or not in order to run a mediation analysis and Hayes (2009) suggested it is not necessary. Second, to verify that residual terms were uncorrelated, we used the Durbin-Watson test. The statistic was 1.84 meaning that the data were not autocorrelated. Third, the scatter plot between standardized predicted values and standardized residuals showed that the homoscedasticity assumption was met. Fourth, there was no perfect linear relationship between two or more predictors since all correlation coefficients were below 0.4. Other assumptions were irrelevant since we were using bootstrapping.

#### *Serial Mediation analyses with covariates*

By adding *sex and duration of illness* as covariates, the serial multiple mediation model with ER followed by ToM revealed a significant indirect effect of VM on negative symptoms (direct effect:  $\beta = -1.15$ , 95% CI = -2.581 to .279; effect size = -.15; indirect effect:  $\beta = .155$ , 95% CI = -.347 to -.005; effect size = -.02). This model remained significant when considering the EXP factor (direct effect:  $\beta = .21$ , 95% CI = -1.35 to .73; effect size = -.05; indirect effect:  $\beta = .140$ , 95% CI = -.314 to -.024; effect size = -.03) but not with the MAP factor (direct effect:  $\beta = -.86$ , 95% CI = -1.89 to .163; effect size = -.16; indirect effect:  $\beta = .015$ , 95% CI = -.126 to .124; effect size = -.01).

Without *a priori* hypotheses, other potential covariates (positive symptoms score, depression score, chlorpromazine-equivalent dosage, diagnosis, age, education level, and IQ) were selected through correlational analyses conducted with the variable of interest. Spearman correlations were used and corrected for multiple comparison (Bonferroni-Holms correction). Only IQ scores and the education level remained significant: the IQ score was positively correlated to VM ( $r_s = .40$ ;  $p < .001$ ), ER ( $r_s = .45$ ;  $p < .001$ ), and ToM ( $r_s = .39$ ;  $p < .001$ ) and the education level was positively correlated to ToM ( $r_s = .28$ ;  $p = .001$ ).

When *IQ scores* was added as covariates, there was no significant effect in the main serial mediation model (direct effect:  $\beta = -1.08$ , 95% CI = -2.496 to .344; effect size = -.14; indirect effect:  $\beta = .06$ , 95% CI = -.214 to .026; effect size = -.01, respectively). By adding the *education level*, the significant indirect effect of VM on negative symptoms was maintained in the main serial multiple mediation model (direct effect:  $\beta = -1.26$ , 95% CI = -2.636 to .123; effect size = -.16; indirect effect:  $\beta = .145$ , 95% CI = -.363 to -.003; effect size = -.02).