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Overlap between individual differences in cognition and symptoms of schizophrenia

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ABSTRACT

Background: Neurocognitive impairment is a core feature of schizophrenia spectrum disorders (SSDs), and the relationship between cognition and symptoms in SSDs has been widely researched. Negative symptoms are related to a wide range of cognitive impairments; however, the aspects of negative symptoms that underpin this relationship have yet to be specified.

Study design: We used iterative Constrained Principal Component Analysis (iCPCA) to explore the relationship between 18 cognitive measures (including processing speed, attention, working, spatial and verbal memory and executive functions) and 46 symptoms in schizophrenia at the individual item level while minimizing the risk of Type I errors. ICPCA was conducted on a sample of SSD patients in the early stages of psychiatric treatment (n = 121) to determine the components of cognition overlapping with symptoms measured by the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS).

Results: We found that a verbal memory component was associated with items from SANS and SAPS related to impoverished and disorganized emotional communication, language, and thought. In contrast, a working memory component was associated with SANS items related to motor system impoverishment.

Conclusions: The iCPCA allowed us to explore the associations between individual items, optimized to understand the overlap between symptoms and cognition. The specific symptoms linked to verbal and working memory impairments imply distinct brain networks, which further investigation may lead to our deeper understanding of the illness and the development of treatment methods.

1. Introduction

Schizophrenia spectrum disorders (SSDs) are a group of psychiatric disorders characterized by hallucinations and delusions, disorganized speech and actions, and negative symptoms (American Psychiatric Association, 2013). Cognitive deficits are a core aspect of schizophrenia

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and related psychoses, particularly in attention, processing speed, verbal learning, and working memory (Heinrichs, 2001; Heinrichs and Zakzanis, 1998; Kahn and Keefe, 2013). The overlap between psychotic symptoms and cognition in schizophrenia is of interest to the field in that elucidating both the biological and the psychological underpinnings responsible for this overlap. Importantly, further exploration of the relationship between symptoms and cognition can potentially provide new symptom-specific treatment targets for psychotherapies (Garety et al., 2000; Wykes et al., 2011), medication (Goff et al., 2017) and neuromodulation (Tseng et al., 2022).

Reviews of studies investigating the overlap between individual differences in cognitive impairment and psychotic symptoms indicate that hallucinations and delusions are not correlated with performance on standard neurocognitive tests (Dominguez et al., 2009; Harvey et al., 2006; Pillny et al., 2022; Ventura et al., 2009; Ventura et al., 2010) but please see (Siddi et al., 2017; Toh et al., 2020). In contrast, negative symptoms (e.g., alogia, flattening affect, apathy) and disorganization (e.g., derailment, the illogicality of speech) have been associated with many neurocognitive domains, primarily verbal/visual memory and working memory (Aleman et al., 1999; Bagney et al., 2015; Dominguez et al., 2009; Lepage et al., 2021; O'Leary et al., 2000; Pillny et al., 2022; Ventura et al., 2009; Ventura et al., 2010). It should be pointed out that some studies showed a lack of significant association between negative symptoms and cognition (Au-Yeung et al., 2023; Berna et al., 2016; de Gracia Dominguez et al., 2009; Harvey et al., 2006), and results are often mixed concerning the specificity of negative versus disorganization symptoms in their relationship with cognition (Bagney et al., 2015; Harvey et al., 2006; Ventura et al., 2009; Yolland et al., 2021). A recent meta-analysis of the relationship between negative symptoms and neurocognitive domains (Au-Yeung et al., 2023) as specified by Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus (Nuechterlein et al., 2008) concluded that the global negative symptoms score was weakly to moderately correlated with all the domains: processing speed, attention, working memory, verbal learning and memory, visual learning and memory, and reasoning and problem-solving. While promising, this result raises questions about which specific symptoms (or items representing them) relate to selected cognitive impairment domains.

The primary purpose of the current study is to explore the dimensions of cognition and how they relate to positive and negative symptoms. In a study examining the dimensions of a set of variables, such as cognition, it is essential to optimize these dimensions to be the overlapping set of variables, such as psychotic symptoms. For instance, in the analysis of cognitive test batteries, the first step is typically principal component analysis (PCA), used to determine the dominant dimensions of the cognitive test battery. Alternatively, summary scores are computed based on the assumed dimensions (August et al., 2012; Bagney et al., 2015; Good et al., 2004; Kern et al., 2008; McDowd et al., 2011; Yolland et al., 2021). These components (or summary scores) would be optimized to index the primary dimensions in the cognitive test scores without consideration of any other set of overlapping variables. They would not, however, be optimized to index the primary dimensions in the portion of the variance of the cognitive test scores that overlaps with ratings of symptom severity, or any other set of variables measured on the same sample. The latter always differs from the former, sometimes substantially (Hunter and Takane, 2002; Takane and Hunter, 2001). Two steps must be employed to index the primary dimensions in the cognitive test scores that are optimized to overlap with symptom severity ratings. Namely, multivariate multiple regression is used in step one to constrain the variance in cognitive test scores to that coinciding with symptom severity ratings, and PCA is used in step two, carried out on the variance-constrained cognitive test scores.

To illustrate, consider the work by Bagney and colleagues (Bagney et al., 2015), which reported on the overlap between cognition and symptom severity using the summary score methodology. Based on the recommendations of the MATRICS Consensus Cognitive Battery (MCCB; Kern et al., 2008; Nuechterlein et al., 2008), they computed summary scores for seven neurocognitive domains: Speed of Processing, Attention/Vigilance, Working Memory, Verbal Learning, Visual learning, Reasoning and Problem-solving, and Social Cognition. They also used the Positive and Negative Symptom Scale (PANSS; Kay et al., 1987) to measure symptoms by computing summary scores based on the five-factor NIMH consensus model for symptom domains (i.e., Positive, Negative, Cognitive, Excited and Depressed factors Wallwork et al., 2012). The authors concluded that there is a small to moderate significant association between the PANSS Cognitive factor and MCCB neurocognitive domains of Processing Speed, Working Memory, and Verbal Learning (Bagney et al., 2015). Although using summary scores in this way is common (Lepage et al., 2021; Ventura et al., 2009; Ventura et al., 2010) and valid, it restricts analyses to the variance common to all aggregated variables, neglecting the specific variance independently measured by each scale item (Chinchani et al., 2021). Individual cognitive tests or individual symptom items underlying statistically borderline correlations, if optimized to cognition/symptom overlapping variance, may have shown a stronger relationship and a finer-grained description of the cognition/symptom overlap could be derived. This tradition of using summed aggregate scores when studying associations between symptoms and cognition is likely rooted in concerns regarding Type I errors, which would increase with multiple tests of statistical significance if each variable were individually analyzed (Chinchani et al., 2021).

The methodology introduced here allows the study of the overlap between cognition and symptoms at the level of individual items without an increase in Type I errors. We have also added additional measures to increase the reliability of our results. We analyzed a subset of already published data (Lepage et al., 2021), and instead of using summary scores, components of cognition were optimized to overlap with items from the SANS and SAPS symptom rating scales (Andreasen, 1984a, 1984b) To achieve this, we applied an iterative application of Constrained Principal Component Analysis (CPCA; Chinchani et al., 2021; Hunter and Takane, 2002; Takane and Hunter, 2001) This approach combines multivariate multiple regression and principal component analysis (PCA) into a unified framework and uses the iterative methodology to determine the reliability of the conclusion regarding overlap between sets of variables. This method allowed us to perform an exploratory study of the relationship between symptoms and cognition at the individual item level; therefore, we did not propose any specific hypotheses but rather let the data reveal significant patterns using restrictive multiple comparison correction solutions.

We applied the analysis to a cohort of patients in the early intervention program, Prevention and Early Intervention Program for Psychoses in Montreal, Canada (PEPP-Montreal). First Episode Psychosis (FEP) patients are characterized by heterogeneity of cognitive impairment severity (Tan et al., 2022) similar to chronic patients (Lewandowski et al., 2018). However, FEP patients are at an early stage of illness and treatment, and therefore, it is possible to study the relationship between symptoms relatively free of therapeutical effects and psychosocial factors that may affect the cognitive decline in later stages of the illness (Zanelli et al., 2019).

2. Methods

2.1. Participants

This analysis involved 121 participants (Mean age = 23.24, *SD* = 3.93, 87 males and 34 females) who were a subset of an already published data set (n = 434) described in detail elsewhere (Lepage et al., 2021). Patients received treatment at PEPP-Montreal, a comprehensive early intervention service that combines clinical care, research, and education, located at the Douglas Mental Health University Institute in Montreal, Canada. The prerequisites for admission were an IQ above 70, minimal or no previous antipsychotic treatment (maximum of one

month), and no diagnosed organic brain conditions or pervasive developmental disorders. However, contrary to previous research with this cohort (Lepage et al., 2021), we only selected participants diagnosed with schizophrenia ($n = 89$), schizoaffective ($n = 24$) or schizophreniform (n = 8) disorders. The main reason for such step was to be able to relate our results more closely to other reports investigating similar population of SSD patients. Moreover, due to the multivariate nature of the analysis, we could only include participants who completed a full set of cognitive measures (18 cognitive measures listed in Table 4) and symptom rating scales (46 items from SANS and SAPS, see Tables 5 and 6). Therefore, only 121 participants out of 230 diagnosed with these three disorders were analyzed in the current study. The difference between excluded and included participants on demographic, intelligence and symptoms summary scores are presented in Table 2 and further reviewed in the results section. The Research Ethics Boards of the Douglas Mental Health University Institute and the McGill University Faculty of Medicine approved the research protocols.

2.2. Symptom rating scales: Items included in the analysis

The Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a) consists of 20 items grouped into five global categories (subscales): flat affect, alogia, apathy, anhedonia, and attention. Additionally, each subscale has one Global Rating (GR) item (five total). The Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b) consists of 30 items (plus 4 GR items) grouped into four global categories: hallucinations, delusions, bizarre behavior, and formal thought disorder. Items on both instruments are rated on a six-point scale from absent (0) to severe (5). The ratings are based on a semi-structured interview covering the preceding month. Table 2 shows both total scores and subscale total scores for the patients included in the current analyses.

We used 17 items from SANS and 29 from SAPS in the present study. We did not include Global Rating items from each scale, commonly excluded from the two scales when calculating total summary and subscales scores (presented in Table 2) (Andreasen, 1984a, 1984b; Grot et al., 2021; Preda et al., 2018). Additionally, we excluded the SAPS item *Clanging* due to a lack of response to this item in the sample. We also excluded two attention items from SANS (*Social Inattentiveness* and *Inattentiveness During Mental Status Testing*). These items do not seem specific for negative symptoms. They are instead related to thought disorder (measured by SAPS), as shown by earlier studies of symptom dimensions measured by SANS and SAPS scales (Miller et al., 1993; Minas et al., 1992). We also expected these items to strongly correlate with cognitive measures and dropped them from our set of predictors.

2.3. Cognitive measures

In the current study, we included 17 neurocognitive tests reported by Lepage and colleagues (Lepage et al., 2021) and described in Table 1, plus a measure of participant performance in the Stroop task, *Stroop Interference*. Therefore, the total number of cognitive measures was 18. We exclusively utilized raw scores, avoiding standardization or correction for demographic variables. This is because the iCPCA depends on the original variance, and standardization could potentially obscure it. We used the number of correct trials for most of the cognitive measures. However, we used the completion time for Trail Making Test Part A (TMT-A) and Trail Making Test Part B (TMT-B). Therefore, a lower score on these two measures reflects better performance.

Table 1
Measures of cognition included in the current analysis.

Cognitive domains	Name of test	Description of the main task
Processing speed	Stroop Neutral[a]	Naming the colour of ink patches for 45 s
Processing speed	Stroop Congruent[a]	Reading words written in the congruent ink colour from a list for 45 s
Processing speed	Trial Making Test Part A[b]	Connecting numbered dots in ascending order as quickly as possible
Selective attention	Stroop Incongruent[a]	Naming the ink colour of colour words written in the incongruent ink colour for 45 s
Executive functions Processing speed	Trail Making Test Part B[b]	Connecting numbered and lettered dots in an alternating sequence as quickly as possible
Sustained attention Processing speed	Digit Symbol[c]	Drawing the symbol that is matched to nine numbers as quickly as possible for a series of numbers
Sustained attention	D2 Sustained Attention[d]	Identifying a target letter (letter d with two marks of any kind, such as lines or dots) surrounded by distractors and crossing it out
Executive functions Motor operations	Block Design[c]	Copying a pattern formed by coloured blocks (full white, full red, half red and half white)
Verbal working memory	Digit Span[c] backward and forward	Recalling the digits' names in both forward and backward orders in which they were presented aloud. Both forward and backward trials were included in the analysis.
Verbal memory and learning	Logical Memory[c] immediate, delayed and recognition trials	Repeating words from a story immediately (Immediate), and with a 20–30 min delay (Delayed), and recognizing them (Recognition)
Visual working memory	Spatial Span[c] backward and forward	Recalling the colour and position of squares in both forward and backward orders.
Visual working memory	Visual Reproduction[c] immediate and delayed trials	Reproducing (drawing) figures from a test page immediately (Immediate), and with a 20–30 min delay (Delayed).

[a] (Stroop, 1935)
[b] (Reitan, 1986)
[c] (Wechsler, 1997)
[d] (Brickenkamp and Zilmer, 1998).

2.4. Data analysis

2.4.1. Iterative constrained principal component analysis (iCPCA)

Constrained Principal Component Analysis (CPCA) is a supervised dimensionality reduction technique that combines multivariate multiple regression's variance constraints and PCA's dimensionality reduction into a unified framework (Takane and Hunter, 2001; Takane and Shibayama, 1991). In other words, the CPCA technique relies on a specific set of predictor variables to guide the dimensionality reduction process. CPCA provides a set of component and predictor loadings that link the low-dimensional component scores to the original criterion and predictor variables, respectively.

In the current study, we introduced an iterative CPCA (iCPCA) method using split halves and permutation methods to determine consistency and reliability in the overlap of criterion and predictor variables. More specifically, to assess the reliability of the predictor loadings across all the iterations, we used a metric termed the predictor loading reliability proportion (PLRP). This metric is computed as the proportion of iterations (here expressed as a percentage) that showed predictor loadings above a certain threshold in both split-half solutions for 1000 random permutations. We only interpreted PLRP values that passed the $p \leq .05$ after correcting for multiple comparisons using the Benjamini-Hochberg correction (Benjamini and Hochberg, 1995). Full details are provided in the supplementary material.

Predictor loadings and component loadings are used to interpret the results of a CPCA. The component loadings indicate the importance of

each criterion variable (i.e., cognitive measure) to each component, and predictor loadings indicate the association between each predictor variable (symptom) and each component of cognition. Component loadings and predictor loadings must be interpreted in conjunction because they are different pieces of information about the same components. Specifically, they are computed as correlations of component scores with the variance-constrained criterion variables (cognition in this case) for component loadings and the predictor variables (symptoms in this case) for predictor loadings. We selected the number of component loadings (cognitive measures) for each component based on average predictor loading reliability proportions (*PLRPs)* obtained by regressing each criterion variable out of the remaining criterion variables. The details are presented in Fig. 1. ICPCA component scores were also used to study the association with other variables, such as age, education years, WAIS Full, Verbal and Performance IQ.

2.4.2. Software and scripts

The data were analyzed using MATLAB (The MathWorks, Natick, MA) and IBM SPSS (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp). The iCPCA MATLAB script is available on our GitHub website: https://github.com/CNoS-Lab/Iterative_CPCA.

3. Results

The results presented in Table 2 illustrate the characteristics of the included sample and a comparison with patients excluded from the current study due to missing data. There were significant differences between groups on two variables. The excluded group had a higher WAIS Performance IQ score ($M = 97.05$, $SD = 17.05$) than the included group ($M = 92.23$, $SD = 18.07$) as measured by an independent samples t-test, $t(226) = -2.09$, $p \leq .05$, $d = 0.27$. The included group had a higher score on the SANS Apathy subscale ($M = 5.81$, $SD = 3.84$) than the excluded group ($M = 4.95$, $SD = 3.24$), $t(217) = 1.99$, $p \leq .05$, $d = 0.27$. Overall, the included and excluded groups were relatively young ($M = 23.24$, $SD = 3.24$ and $M = 23.95$, $SD = 4.70$, respectively) and had approximately 12 years of education ($M = 11.61$, $SD = 2.73$ and $M = 12.02$, $SD = 2.83$). In the included group, there were 87 males (72 %) and 34 females (28 %), while the excluded group comprised 83 males (77 %) and 25 females (23 %). A chi-square test revealed that these differences were not statistically significant, $\chi^2(1) = 0.73$, $p = .39$. Both groups scored relatively high on the Alogia and Flat Affect subscales of SANS but low on SAPS subscales assessing positive symptoms (Delusions and Hallucinations) and disorganization (Positive Formal Thought Disorder).

The multivariate overlap between cognitive measures and symptom rating scale items was 79.53 %, averaged across all 1000 iterations. We extracted three components from PCA (determined by the scree plot Cattell and Vogelmann, 1977). The components were varimax rotated. Only two of these three components were significantly predicted by specific predictor loadings. Therefore, we disregard the third one for further interpretation. These two components accounted for 42.96 % of the symptom-constrained cognitive score variance averaged over all iterations (C1 = 24.50 %, C2 = 18.43 %).

We selected four component loadings for C1 and five for C2, as shown in Fig. 1. The figure illustrates the component loadings selection process based on the average predictor reliability proportion**.** Fig. 2 summarizes the method of component interpretation, highlighting the selected criterion variables and their associated reliable predictor variables for each component. Additionally, all 18 component loadings are listed in Table 4, while all 46 predictor loadings are presented in Tables 5 and 6. Supplementary Tables S1 and S2 display the frequencies of symptom occurrence used as predictor loadings in the included group. The included participants under-performed the control group (described in Lepage et al., 2021) on all cognitive measures used here as component loadings (see Table S3 for details).

Component 1 (C1) was dominated by four variables: *Logical Memory recognition* ($r = 0.78$), *immediate recall* ($r = 0.76$), *delayed recall* ($r = 0.74$), and *Stroop Neutral* condition of Stroop task ($r = 0.53$). The three Logical Memory test trials assess verbal memory and, short-term/working memory and long-term/episodic memory. Participants are asked to recall a story read to them in three trials (immediate: immediately recall any words from the story; and recognition: recognition of immediate and delayed recall, and recognition of story elements). The Stroop Neutral condition measures how quickly participants can read a matching ink word. We labelled it as C1 Verbal Memory. This component overlapped with two symptoms. We grouped these overlapping symptoms into one category, Improvised and Disorganized

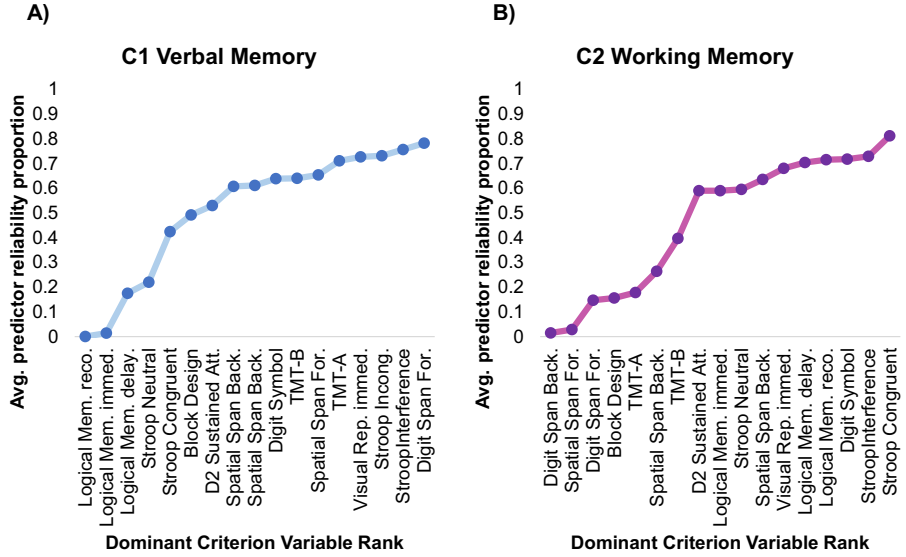

Fig. 1. Average predictor loading reliability proportions (*PLRPs)* were obtained by regressing each criterion variable out of the remaining criterion variables for Components 1 (subpanel A) and 2 (B) separately. For example, in the case of Component 1, regressing *Logical Memory recognition* out of all other criterion variables resulted in a reduction in *PLRP* value averaged over all predictor loadings (the ones reliable in the primary analysis) to essentially zero, suggesting that this variable is essential to the dimensional structure of the results. Using a criterion like component selection in a scree plot, we retained the first four variables as dominant component loadings for Component 1. In the case of Component 2, we retained the first five variables.

Table 2
Descriptive statistics of neurocognitive measures, independent Samples *t*-test (two-tailed, α = 0.05), and Cohen's d effect size for Included and Excluded participants in the iCPCA.

Variable name	Included Group			Excluded Group			t-test and Cohen's d	
	n	*M*	*SD*	*n*	*M*	*SD*	*t*	*d*
Age years	121	23.24	3.93	108	23.68	4.70	−0.78	0.10
Education years	119	11.61	2.73	109	12.02	2.83	−1.10	0.15
WAIS Full IQ	121	93.37	16.34	107	97.35	15.43	−1.88	0.25
WAIS Verbal IQ	121	94.64	15.31	107	96.95	15.92	−1.12	0.15
WAIS Performance IQ	121	92.23	18.07	107	97.05	17.05	**−2.06***	**0.27**
SANS Total	121	25.73	12.70	98	23.15	14.50	1.40	0.19
Flat affect	121	8.12	5.96	98	7.33	6.65	0.93	0.13
Alogia	121	2.31	2.70	98	2.70	3.07	−1.02	0.14
Apathy	121	5.81	3.13	98	4.95	3.24	**1.99***	**0.27**
Anhedonia	121	7.58	3.84	97	6.57	4.48	1.80	0.25
Attention	121	1.92	2.02	96	1.71	1.91	0.78	0.11
SAPS Total	121	7.87	9.75	98	9.14	10.50	−0.93	0.13
Hallucinations	121	2.46	4.33	98	2.04	3.67	0.77	0.10
Delusions	121	2.86	4.11	98	4.03	5.17	−1.87	0.25
Bizarre Behaviours	121	0.98	1.72	98	1.44	2.13	−1.75	0.24
Positive Form Thought Dis.	121	1.44	2.67	98	1.57	2.82	−0.36	0.05

* $p \leq .05$.

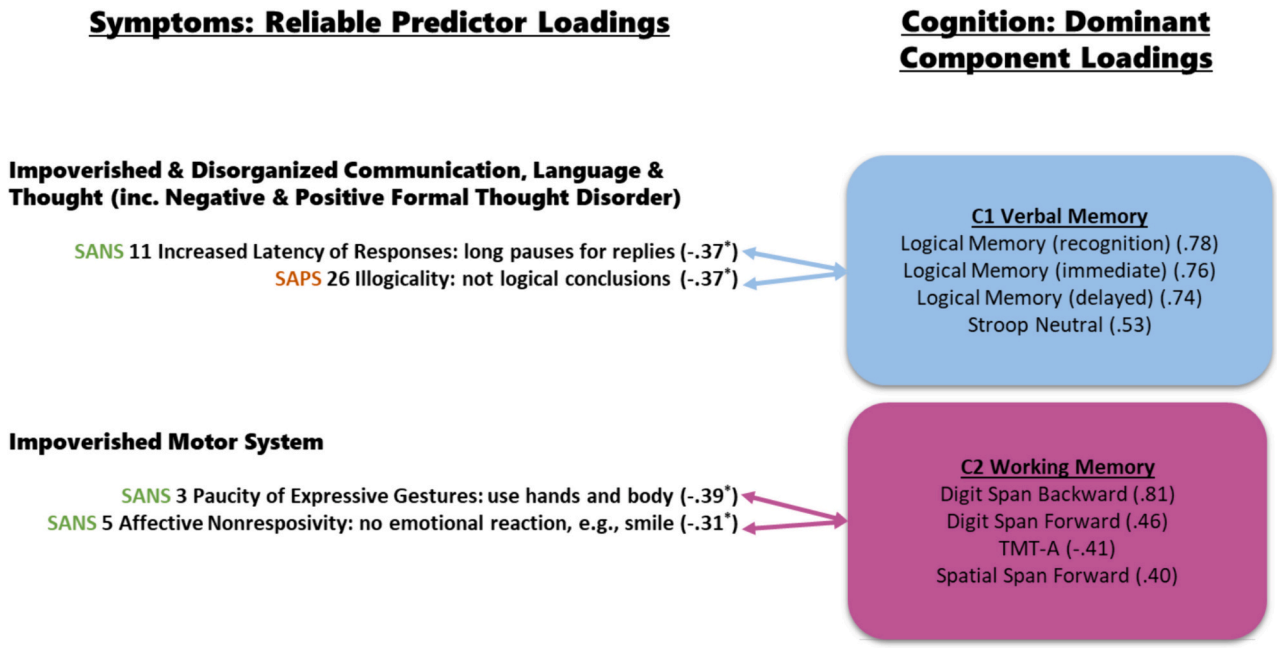

Fig. 2. On the left side are reliable predictor loadings grouped into symptom types. All symptom names include scale names (SANS in green or SAPS in orange). On the right side are components (C) and their dominant component loadings grouped by two colours: light blue is C1, and dark pink is C2. The light blue and dark pink connect symptoms with C1 and C2, respectively. The component and predictor loading values (in parenthesis) measure effect size; a minus sign precedes negative values. * $p \leq .05$ from the Benjamini-Hochberg multiple comparison correction test. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Communication, Language, & Thought (including Positive & Negative Formal Thought Disorder), with one SANS item: *Increased Latency of Responses* ($r = -0.37$, *PLRP* = 91 %, $p \leq .05$) and one SAPS item: *Illogicality* ($r = -0.37$, *PLRP* = 91 %, $p \leq .05$).

Component 2 (C2) consisted of working memory measures: *Digit Span Forward* ($r = 0.83$) and *Backward* ($r = 0.81$), and *Spatial Span Forward* ($r = 0.46$). *Digit Span* is a verbal analog of the *Spatial Span* task measuring working memory performance by recalling digits or geometrical shapes (forward-span) or reversing order (backward-span). This component also included the *Block Design* task ($r = 0.40$), which measures the visual-spatial processing of information and manual interaction with objects. Finally, C2 had *TMT-A* ($r = -0.41$); this test measures processing speed and working memory. We labelled this component as C2 Working Memory. C2 overlapped with two SANS items related to the Impoverished Motor System: *Paucity of Expressive Gestures* ($r = -0.39$, 100 %, $p \leq .01$) and *Affective Nonresposivity* ($r = -0.31$, 85 %, $p \leq .05$).

3.1. Relationship of CPCA components to other measures

A comparison of the component scores (averaged over 1000 iterations) revealed that there is no difference between females ($M = 0.24$, $SD = 0.94$) and males ($M = -0.11$, $SD = 0.90$) on C1 (Verbal Memory), $t(119) = -1.92$, $p = .06$ and on C2 (Working Memory), $t(119) = -0.27$, $p = .78$.

The years of education variable was significantly correlated with C1

($r = 0.31$, $p \leq .01$) but not with C2 ($p = .68$). Finally, the two CPCA components were significantly correlated with three measures of WAIS IQ: Full, Verbal, and Performance. Table 3 provides the complete set of results.

4. Discussion

In this study, we investigated components of cognition that optimally overlap with psychotic symptoms in the early stages of psychosis treatment. Our analysis allowed a focus on individual items while avoiding spurious results using variance constraints, dimension reduction, iterative bootstrapping, and permutation. We observed two components of cognitive functions, Verbal Memory (C1) and the second was Working Memory (C2), that were optimally predictable from symptoms. Symptoms related to impoverished *(Increased Latency of Responses) and* disorganized (*Illogicality*) communication, language and thought overlapped with the Verbal Memory component. The symptoms of *Paucity of Expressive Gestures and Affective Nonresposivity* related to motor impoverishment coincided with the Working Memory component.

A correlation between formal thought disorder (FTD) and verbal memory has been noted in past work (Oeztuerk et al., 2021; Tan and Rossell, 2017; Tan et al., 2014). In this study, we observed that components of both Positive (*Illogicality*) and Negative (*Increased Latency of Responses*) FTD (Jerónimo et al., 2018) were related to semantic processing deficit measured by the three trials of the Logical Memory test (mainly focused on assessing episodic memory). Positive FTD means disorganization of semantic knowledge, which may result in difficulties accessing items of semantic knowledge and logically applying them to proper syntax structure (Bora et al., 2019; Goldberg et al., 1998). Negative FTD in C1 might enhance difficulties in accessing semantic information from the memory system (Docherty et al., 2011), which points to cognitive deficits (Joyce et al., 1996) and lack of cognitive resources needed for verbal task performance (Cohen et al., 2014). These results stress the importance of the neural mechanisms of the language system (fronto-temporal network) for both Positive and Negative FTD (Gur et al., 2006; Kircher et al., 2018; Palaniyappan, 2022; Palaniyappan et al., 2023; Sumner et al., 2018). Additionally, C1 component scores were positively and moderately correlated with years of education in our sample (Tan et al., 2022). This supports the proposition that better verbal learning and memory support better academic performance; this is widely observed in the general population (Davis et al., 2017).

In contrast to the overlap with communication, language and thought noted in C1, C2 (Working Memory) overlapped with the impoverished motor system, suggesting a distinct brain network related to expressive gestures and working memory performance. A reduction in expressive gesture use is a common finding in SSD, which may arise from negative symptoms (which include psychomotor impoverishment) and specific deficits in gesture control (Walther et al., 2020; Walther et al., 2015; Walther et al., 2013). At least 50 % of patients with SSD are impaired in decoding and producing nonverbal cues such as hand gestures. These gesture deficits have been linked to negative symptoms, psychomotor abnormalities, poor working memory, and, to a lesser extent, disorganized thought (Straube et al., 2014; Walther et al., 2015; Wüthrich et al., 2020). Conceptual knowledge must be associated with current spatial and contextual semantic information to plan and execute meaningful hand gestures, which requires working memory (Goldenberg, 2009). Already early in the course of schizophrenia, patients use and decode gestures incorrectly, which is linked to poor visual working memory and negative symptoms (Gupta et al., 2021; Millman et al., 2014). Prefrontal mechanisms crucial for performance in working memory tasks, such as the dorsolateral prefrontal cortex and the anterior cingulate cortex, are often impaired in the SSD population (Glahn et al., 2005; Smucny et al., 2022). It is important to note that the relationship between motor impoverishment and working memory reported here is unlikely due to antipsychotic use in this young cohort. While some analyses suggest antipsychotics can negatively impact patients' quality of life, particularly concerning motor movements (Bebbington et al., 2009), there is no evidence of a systematic negative effect on cognitive performance (Goff et al., 2017; Peralta and Cuesta, 2010) In fact, some studies suggest the opposite (Clissold and Crowe, 2019; but please see Husa et al., 2017).

This study showed that negative symptoms associated with expressive (both non-verbal and verbal) and emotional behaviours appear to influence cognitive processes, explicitly working and verbal memory systems. An examination of Table 5 highlights similar negative

Table 4
Component loadings for the predicted solution.

Component loadings Cognitive measures:	Component		
	1 Verbal Memory	2 Working Memory	3 Non-significant loadings
Digit Symbol	0.44	0.11	0.44
Trail Making Test Part A	−0.23	**−0.41**	−0.38
Trail Making Test Part B	−0.37	−0.42	−0.39
D2 Sustained Attention	0.45	0.15	0.50
Digit Span Forward	0.03	**0.83**	0.07
Digit Span Backward	−0.06	**0.81**	−0.02
Spatial Span Forward	0.24	**0.46**	0.26
Spatial Span Backward	0.34	0.46	0.15
Visual Reproduction (immediate)	0.29	0.06	0.36
Visual Reproduction (delayed)	0.35	0.30	0.43
Logical Memory (immediate)	**0.76**	0.14	0.15
Logical Memory (delayed)	**0.74**	0.05	0.12
Logical Memory (recognition)	**0.78**	0.04	0.07
Block Design	0.41	**0.40**	0.44
Stroop Neutral	**0.53**	0.22	0.27
Stroop Congruent	0.51	0.33	0.28
Stroop Incongruent	0.27	0.19	0.74
Stroop Inference	−0.11	0.00	0.76

Note. Dominant component loadings are set in bold font. Fig. 1 specifies the selection of the component loadings based on the average predictor reliability proportion. Please also see Supplementary Material for a complete description of determining dominant component loadings.

Table 3
Descriptive of education, age, and IQ measures. Correlations between education years, age of participants, IQ measures, and iCPCA components.

Measure	M	SD	1. Edu.	2. Age	3. FSIQ	4. VIQ	5. PIQ	6. C1
1. Education years[#]	11.60	2.73						
2. Age years	23.24	3.93	0.43**					
3. WAIS Full IQ	93.37	16.34	0.28**	0.14				
4. WAIS Verbal IQ	94.64	15.31	0.38**	0.10	0.91**			
5. WAIS Performance IQ	92.23	18.07	0.12	0.12	0.90**	0.65**		
6. C1 Verbal Memory [##]	–	–	0.31**	0.13	0.51**	0.50**	0.41**	
7. C2 Working Memory[##]	–	–	0.04	0.08	0.45**	0.43**	0.38**	−0.02

** $p \leq .01$ (2-tailed)
[#] $n = 121$ for all measures but Education years $n = 119$
[##] for CPCA component measures (6, 7 and 8) all scores were standardized and their Means = approx. 0, and SDs = approx. 1.

Table 5
Mean predictor loadings from the Scale for Assessment of Negative Symptoms (SANS) for the predicted solution in three components.

Predictor loadings Part 1 SANS Items:	Component		
	1	2	3
1 Unchanging Facial Expression	−0.27	−0.14	0.06
2 Decreased Spontaneous Movements	−0.11	−0.27	−0.11
3 Paucity of Expressive Gestures	−0.12	**−0.39***	0.02
4 Poor Eye Contact	−0.26	−0.29	−0.05
5 Affective Nonresposivity	−0.17	**−0.31***	0.13
6 Lack of Vocal Inflections	−0.04	−0.04	0.02
7 Inappropriate Affect	−0.18	−0.09	0.12
8 Poverty of Speech	−0.26	−0.21	0.11
9 Poverty of Content of Speech	−0.22	−0.01	−0.02
10 Blocking	−0.28	−0.09	−0.10
11 Increased Latency of Response	**−0.37***	−0.06	−0.03
12 Grooming and Hygiene	−0.22	0.02	0.04
13 Impersistence at Work or School	−0.07	0.16	0.00
14 Physical Anergia	−0.06	−0.06	−0.01
15 Recreational Interests and Activities	0.01	−0.09	0.01
16 Sexual Activity	0.15	−0.07	−0.08
17 Ability to Feel Intimacy and Closeness	0.15	−0.06	0.09
18 Relationships with Friends and Peers	0.11	−0.04	0.05

Note. The values are Person *r* coefficients. Significant predictor loadings are set in bold font.
* $p \leq .05$ from the Benjamini-Hochberg multiple comparison correction test.

Table 6
Mean predictor loadings from the Scale for Assessment of Positive Symptoms (SAPS) for the predicted solution in three components.

Predictor loadings Part 2 SAPS items:	Component		
	1	2	3
1 Auditory Hallucinations	−0.17	−0.14	−0.11
2 Voices Commenting	−0.10	−0.03	−0.16
3 Voices Conversing	−0.03	−0.05	−0.20
4 Somatic or Tactile Hallucinations	0.03	−0.15	−0.08
5 Olfactory Hallucinations	0.19	−0.12	−0.08
6 Visual Hallucinations	−0.14	−0.01	−0.01
7 Persecutory Delusions	−0.02	−0.10	0.05
8 Delusions of Jealousy	0.04	−0.04	−0.02
9 Delusions of Guilt or Sin	0.02	−0.19	0.04
10 Grandiose Delusions	−0.15	−0.01	−0.17
11 Religious Delusions	−0.04	−0.20	−0.16
12 Somatic Delusions	0.04	−0.07	0.01
13 Delusions of Reference	0.02	−0.11	−0.18
14 Delusions of Being Controlled	0.00	−0.19	−0.09
15 Delusions of Mind Reading	−0.04	−0.15	−0.07
16 Thought Broadcasting	−0.07	−0.09	0.00
17 Thought Insertion	0.03	−0.09	−0.05
18 Thought Withdrawal	−0.05	−0.08	−0.14
19 Clothing and Appearance	0.08	−0.15	−0.04
20 Social and Sexual Behavior	−0.07	−0.08	0.01
21 Aggressive and Agitated Behavior	−0.03	−0.05	−0.08
22 Repetitive or Stereotyped Behavior	0.05	−0.11	−0.17
23 Derailment	−0.26	0.05	0.03
24 Tangentiality	−0.24	−0.07	−0.06
25 Incoherence	−0.26	−0.04	−0.15
26 Illogicality	**−0.37***	−0.11	0.12
27 Circumstantiality	0.06	0.11	−0.09
28 Pressure of Speech	0.28	0.07	0.00
29 Distractible Speech	−0.07	−0.10	−0.12

Note. The values are Person *r* coefficients. Significant predictor loadings are set in bold font.
* $p \leq .05$ from the Benjamini-Hochberg multiple comparison correction test.

symptoms potentially associated with cognitive impairment, such as *Unchanging Facial Expression* in C1 and *Poor Eye Contact* in C2. Future studies should investigate whether these symptoms and others related to flat affect, may represent a distinct category of negative symptoms predictive of cognitive deficits. In fact, previous research (Bègue et al., 2020; Blanchard and Cohen, 2006; Galderisi et al., 2018; Marder and Galderisi, 2017) has repeatedly shown that negative symptoms can be categorized into two groups: one related to diminished expression (flat affect and alogia) and another related to motivation (avolition and anhedonia). Our results indicate that only the diminished expression group has a significant relationship with verbal and working memory systems. Future studies may also be interested in exploring whether the symptoms of diminished expression that show a relationship with cognition are more primary, relating directly to the deficit, rather than being secondary consequences of other symptoms (mainly positive), medication, or external environmental factors (Correll and Schooler, 2020).

Lepage and colleagues (Lepage et al., 2021) and our investigation shed light on the association between neurocognitive impairments in early psychosis patients, albeit with different methodological approaches. Lepage et al. (Lepage et al., 2021) categorized patients into three groups based on persistent negative symptoms (PNS), secondary PNS (sPNS), and non-PNS (Addington et al., 1990). They examined the neurocognitive functions of these groups and found that FEP patients grouped on negative symptom summary scores showed impairment in verbal and working memory. Our findings elucidate which symptoms are differentially associated with these two memory systems. This, in turn, can facilitate designing and administrating treatments focused on rehabilitating specific cognitive functions such as working and verbal memory using psychotherapies such as Metacognitive Training (Moritz and Woodward, 2007), Cognitive Remediation Therapy (Barlati et al., 2013; Vianin et al., 2014; Wykes et al., 2011). Variations of Cognitive Remediation Therapies designed specifically to help patients practice verbal memory skills have already been developed and applied (Harvey et al., 2009; Vianin et al., 2014).

Our study has several limitations. First, our sample had more participants with prominent negative symptoms and fewer with positive symptoms (please refer to Table 2, Table S1 and S2). Notably, the number of patients with prominent hallucinations and delusions is much smaller than in other symptom groups, as measured by both rating scales. Therefore, the associations between cognition and positive symptoms might be limited due to the restricted range in the sample. This exploratory study requires replication with other samples and potentially different symptom rating scales. Second, due to the requirement that all subjects completed all tests and symptom ratings, the sample size was relatively small, considering the high number of predictors used in the analysis. However, iCPCA computed reliable predictor loading scores, which reduces the chances of Type 1 errors even in smaller samples. Third, our cognitive assessment battery did not include any social cognition tasks deemed necessary for symptom overlap in the past work (Hagiya et al., 2015; Yolland et al., 2021). Therefore, future research could apply our method to study the relationship between symptoms and cognition in larger samples, including social cognition. Finally, we observed that all our component scores are correlated with general intelligence scores. Therefore, we cannot rule out that the variance of general cognitive impairment impacts components and their relationships with overlapping psychotic symptoms.

In conclusion, the iCPCA allowed us to explore the associations between individual items, optimized to understand the overlap between symptoms and cognition. While summary scores and univariate analyses are commonly used due to the constraints of small datasets, multivariate analysis is better suited for large datasets, allowing for a deeper exploration of relationships at the level of individual items. This analysis revealed two distinct symptom clusters: disorganized and impoverished communication, language and thought associated with verbal memory, and motor impoverishment overlapping with working memory. These novel findings can inform future therapeutic interventions to increase verbal and nonverbal communication skills in patients diagnosed with SSD through psychotherapeutic approaches and neuromodulation targeting specific brain networks related to cognitive functions.

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CRediT authorship contribution statement

Rafal M. Skiba: Methodology, Investigation, Formal analysis, Conceptualization, Writing – review & editing, Writing – original draft. **Abhijit M. Chinchani:** Methodology, Investigation, Formal analysis, Conceptualization, Writing – review & editing, Writing – original draft. **Mahesh Menon:** Investigation, Conceptualization, Writing – review & editing. **Martin Lepage:** Investigation, Writing – review & editing. **Katie M. Lavigne:** Investigation. **Ashok Malla:** Investigation, Conceptualization, Writing – review & editing. **Ridha Joober:** Investigation. **Joel O. Goldberg:** Investigation, Writing – review & editing. **R. Walter Heinrichs:** Investigation, Writing – review & editing. **David J. Castle:** Investigation, Writing – review & editing. **Amy Burns:** Investigation, Writing – review & editing. **Michael W. Best:** Investigation, Writing – review & editing. **Susan L. Rossell:** Investigation, Writing – review & editing. **Sebastian Walther:** Investigation, Writing – review & editing, Writing – original draft. **Todd S. Woodward:** Supervision, Methodology, Investigation, Conceptualization, Writing – review & editing, Writing – original draft.

Declaration of competing interest

There are no financial or other conflicts of interest.

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Appendix A. Supplementary data

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