Explaining individual differences in cognition from symptoms of schizophrenia

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Introduction

- Neurocognitive impairment is recognized as a critical feature of schizophrenia spectrum disorder (SSD)¹.
- A plethora of studies have investigated individual differences in cognitive impairments by studying differences in symptomology through global scores, for example, positive, negative and general global symptom scores². Unfortunately, these attempts led to mixed results ^{2,3}.
- In the present study, we decided to verify individual symptoms' influence on cognitive outcomes in a large sample of SSD patients in the early stages of psychiatric treatment.

Methods

- We used a subset (n = 206) of published data from Lepage et al. (2021)⁴.
- We employed 58 items from Scale for the Assessment for Negative Symptoms (SANS)⁵ and Scale for the Assessment for Positive Symptoms (SAPS)⁶ rating scales as predictors of 17 cognitive measures of attention, executive functions, processing speed, verbal and nonverbal memory and learning, visual working and spatial memory ⁴.
- We conducted Constrained Principal Component Analysis (CPCA)^{7,8}. CPCA combines the variance constraints of multivariate multiple regression and principal component analysis into a unified framework. The method constrains the variance in the criterion variables (cognition tests) to that explained by the predictor variables (symptoms) and extracts components that summarize the overlap between these two sets of variables.
- In the final stage of the analysis, the method detects which specific individual variables are responsible for this overlap. In this last stage, we introduced an iterative analysis method (I-CPCA), ensuring improved results' reliability verification.

Sample demographics				
Total	N	206		
Age	Mean (SD)	23.03 (4.00)		
Gender	Male	140 (68.6%)		
	Female	66 (31.4%)		
Education years	Mean (SD)	11.70 (2.60)		
Schizophrenia or				
Schizophreniform	N (%)	125 (60%)		
Affective Disorder	N (%)	57 (28%)		
Delusional Disorder				
or Psychosis	N (%)	24 (12%)		

Symptom rating scale summary scores				
Factor	Mean	SD		
Scale for the Assessment				
for Negative Symptoms				
Total	33.05	17.01		
Flat affect	8.59	7.33		
Alogia	3.11	3.63		
Apathy	8.50	4.39		
Anhedonia	10.02	5.07		
Attention	2.84	3.05		
Scale for the Assessment				
for Positive Symptoms				
Total	8.96	11.16		
Hallucinations	2.69	7.33		
Delusions	2.12	3.63		
Bizarre Behavior	1.72	4.39		
Positive Formal	1.16	5.07		
Thought Disorder				

Detailed Results of I-CPCA

Component loadings	Component		
Cognitive measures	1 Sustained Attention	2 Verbal Memory	3 Visual Working Memory
Digit Symbol	.50	.34	.07
Trail Making Test Part A	49	08	23
Trail Making Test Part B	50	23	27
D2 Test	.42	.34	.23
Digit Span	.27	.06	.43
Spatial Span forward	.22	.09	.56
Spatial Span backward	.08	.25	.55
Visual Reprod. (immediate)	.06	.13	.52
Visual Reprod. (delayed)	.24	.19	.47
Logical Memory (immediate)	.16	.64	.27
Logical Memory (delayed)	.12	.61	.24
Logical Memory (recognition)	.13	.70	.17
Block design	.32	.22	.49
Congruent Stroop Word Reading	.45	.41	.00
Neutral Stroop Colour Naming	.49	.36	.14
Incongruent Stroop Colour Naming	.65	.16	.22
Stroop Inference	.47	13	.24

t loadings, determined to be reliable in I-CPCA (please check supplementary materials for more details), are highlighted in bold.

SANS Items	1
1 Unchanging Facial Expression	.07
2 Decreased Spontaneous Movements	03
3 Paucity of Expressive Gestures	.03
4 Poor Eye Contact	04
5 Affective Nonresponsivity	.11
6 Inappropriate Affect	15
7 Lack of Vocal Inflections	.04
8 Global Rating of Affective Flattening	01
9 Poverty of Speech	.08
10 Poverty of Content of Speech	05
11 Blocking	08
12 Increased Latency of Response	03
13 Global Rating of Alogia	01 ·
14 Grooming and Hygiene	.15
15 Inpersistence at Work or School	.18
16 Physical Anergia	.07
17 Global Rating of Avolition/Apathy	.12
18 Recreational Interests and Activities	.04
19 Sexual Activity	.02
20 Ability to Feel Intimacy and Closeness	.11
21 Relationships with Friends and Peers	.04
22 Global Rating of Anhedonia/Asociality	.02
23 Social Inattentiveness	01
24 Inattentiveness During Mental Status Test	30*
25 Global Rating of Attention	16

are Person r coefficients. Bolded are these predictor.

Summary of the results

Symptoms as reliable predictors

Formal Thought Disorder/Disorganized Speech SANS 13 Global Rating of Alogia (impoverished thinking) (-.33**) SAPS 26 Derailment (speech incomprehensible) (-.37**) SAPS 29 Illogicality (not logical conclusions) (-.28*) SAPS 27 Tangentiality (oblique answers) (-.25) SANS 11 Blocking (-.24)

Disengagement

SANS 12 Increased Latency of Responses (long pauses for replies) (-.31*),

- SANS 23 Social Inattentiveness (seems spacy) (-.26*)
- SANS 1 Unchanging Facial Expression (wooden) (-.26*)
- SANS 8 Global Rating of Affective Flattening (not responsive) (-.26*)
 - SANS 9 Poverty of Speech (-.25*)

Working Memory Impairment

SANS 24 Inattentive During Mental Status Testing (spell "world" backwards) (-.30* & -.32*)

Inattentive

SANS 25 Global Rating of Attention (clinical and cognitive) (-.25 & -.31*)

Impoverished Motor System

SANS 3 Paucity of Expressive Gestures (use hands and body) (-.28*) SANS 2 Decreased Spontaneous Movements (shift hands and body) (-.26*) -SANS 5 Affective Nonresponsivity (smile, laugh) (-.26)



Component 2 3 **-.27*** -.17 -.12 **-.26*** -.12 -.28* -.23 -.21 -.17 **-.26*** -.14 -.01 -.22 -.08 **-.26*** -.17 **-.25*** -.14 -.21 -.10 -.24 -.22 -.31* -.16 **-.33**** -.14 -.14 -.15 -.16 -.03 -.11 .00 -.14 -.06 .00 .02 .14 -.16 .13 -.04 .05 -.05 .10 .00 **-.26*** -.22 -.11 **-.32*** -.25 -.31*

Predictor loadings	Со	mponer	nt
SAPS Items	1	2	3
1 Auditory Hallucinations	20	19	08
2 Voices Commenting	17	14	03
3 Voices Conversing	13	05	11
4 Somatic or Tactile Hallucinations	05	.03	12
5 Olfactory Hallucinations	.02	02	.08
6 Visual Hallucinations	02	20	04
7 Global Rating of Hallucinations	16	19	08
8 Persecutory Delusions	.03	08	.01
9 Delusions of Jealousy	.06	01	04
10 Delusions of Guilt or Sin	.04	14	08
11 Grandiose Delusions	13	12	16
12 Religious Delusions	06	.00	30*
13 Somatic Delusions	.04	.00	04
14 Delusions of Reference	13	.02	07
15 Delusions of Being Controlled	09	.03	08
16 Delusions of Mind Reading	07	.00	14
17 Thought Broadcasting	03	09	.02
18 Thought Insertion	05	.04	.00
19 Thought Withdrawal	05	03	13
20 Global Rating of Delusions	05	06	06
21 Clothing and Appearance	03	.05	06
22 Social and Sexual Behavior	09	13	07
23 Aggressive and Agitated Behavior	.06	.02	07
24 Repetitive or Stereotyped Behavior	09	.05	18
25 Global Rating of Bizzare Behavior	11	05	15
26 Derailment	06	28*	.03
27 Tangentiality	14	25	07
28 Incoherence	10	22	.02
29 Illogicality	05	37**	.04
30 Circumstantiality	07	.03	.05
31 Pressure of Speech	.03	.19	04
33 Clanging	01	10	15
34 Global Rating of Positive Formal Though			
Disorder	09	21	02

Components and dominant <u>component loadings of</u> <u>cognitive functions</u>

C1 Sustained Attention & Processing **Speed** Stroop Incongruent Naming (.65) Stroop Neutral Naming (0.49) Stroop Congruent Naming (.45) Trail Making Test Part B (-.51) Trail Making Test Part A (-.49) D2 Selective Attention Test (.42) Block Design (.32)

C2 Verbal Memory

Logical Memory (recognition) (.70) Logical Memory (Immediate) (.64) Logical Memory (delayed) (.61)

C3 Visual & Working Memory[#] Spatial Span Forward (.56) Spatial Span Backward (.55) Visual Reproduction (delayed) (.47) Block Design (.49) Digit Span (.43)

- from
- motor system and inattention.
- education (r = .3, p < .001).

- comparison tests.

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Summary

• We discovered three components of cognitive functions that were optimally predictable from symptoms. The first was dominated by cognitive measures reflecting Sustained Attention and Processing Speed (C1). Verbal Memory (C2) tests characterized the second component. The third component was described as Visual and Working Memory (C3).

• C1 was dominated by cognitive measures of sustained attention and processing speed and was predicted by one SANS question item: *Inattentive during mental status testing*.

• C2 was characterized by three measures of verbal memory. This component was predicted by the largest group of symptoms SANS and SAPS related to thought form disorder/disorganized speech, disengagement, and inattention.

• C3 was focused on visual and working memory affected by a separate group of impairments related to an impoverished

• We observed that females had greater verbal memory (C2) component scores than males (t(204) = 2.77, p = .006, Cohen's)d = .41). The C2 scores were also correlated with years of

Conclusion

• I-CPCA allowed us to focus on individual items while avoiding spurious results using variance constraints, dimension reduction, iterative bootstrapping, permutation, and multiple

• The results showed that inattention predicts impairments across all three components. However, verbal memory was specifically associated with items from both SANS and SAPS related to disorganized speech. In contrast, visual and working memory was associated exclusively with SANS items related to motor system impoverishment.

• These novel findings can direct future therapeutical interventions to increase verbal and nonverbal communication skills in high-risk individuals and patients diagnosed with SSD through psychotherapeutic approaches and neuromodulation targeting specific brain networks.

References