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ORIGINAL ARTICLE

Relationship of negative symptom severity with cognitive symptoms and functioning in subjects at ultra-high risk for psychosis

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Abstract

Aim: Negative symptoms and cognition are related with functioning in schizophrenia. However, it is not clear whether they have a similar effect in individuals at ultra-high risk (UHR) for psychosis. In this study, we aimed to explore relationship of negative symptoms with cognition and functioning cross-sectionally in people with UHR for psychosis.

Methods: In total, 107 people participated in this study. We assessed negative symptoms with Scale for Negative Symptoms (SANS). We applied a cognitive battery including seven tests. We evaluated functioning by using Global Assessment of Functioning Scale and work/study status as an indicator of role functioning.

Results: SANS scores were correlated to global functioning cross-sectionally. SANS total score was correlated to cognitive test scores related to cognitive flexibility and attention. Only Trail Making Test B (TMT B) was negatively correlated to global functioning. SANS-affective blunting and SANS-avolition scores were independently related to global functioning. There was a significant indirect effect of the TMT B and composite attention scores on global functioning through negative symptoms indicating a complete mediation.

Conclusion: Our findings suggest that negative symptoms, particularly avolition have an impact on functioning and the association of cognition with functioning was mediated by negative symptoms in UHR.

KEYWORDS

cognition, functioning, negative symptoms, ultra-high risk for psychosis

1 | INTRODUCTION

Negative symptoms and cognitive deficits are related to functional outcomes of schizophrenia (Foussias & Remington, 2010; Green, Kern, Braff, & Mintz, 2000). They may present in early stages of psychosis spectrum (Azar et al., 2016; Bora & Murray, 2014; Carrión et al., 2016; Carrión, Correll, Auther, & Cornblatt, 2017; Meyer et al., 2014; Piskulic et al., 2012; Salokangas et al., 2014; Sauvé, Brodeur, Shah, & Lepage, 2019; Üçok et al., 2013).

There are several studies exploring the relationship of negative symptoms with functional outcome in individuals at ultra-high-risk (UHR) for psychosis. It was shown that negative symptoms were associated with poor global, social, role and occupational functioning (Chang et al., 2018; Corcoran et al., 2011; Cotter et al., 2017; Glenthøj, Kristensen, Wenneberg, Hjorthøj, & Nordentoft, 2020; Gur et al., 2015; Kim et al., 2013; Kim et al., 2019; Meyer et al., 2014; Pelizza et al., 2020; Schlosser et al., 2015; Svirskis et al., 2007) in people at UHR for psychosis. Particularly, avolition and anhedonia (Glenthøj

et al., 2020; Shim et al., 2008) and longer duration of negative symptoms (Carrión et al., 2016) were related to poor social functioning in UHR group whereas these results were not confirmed by other studies (Chang et al., 2018; Shim et al., 2008). In a recent study, persistent negative symptoms in UHR group were associated with poor psychosocial functioning at follow-up (Yung, Nelson, McGorry, Wood, & Lin, 2019).

Relationship between cognitive functions and functional impairment in UHR groups has been explored in a few studies. Different aspects of cognitive functions such as processing speed, verbal learning, memory performance, reasoning and problem solving were related to functional outcomes in people at UHR for psychosis (Carrión et al., 2011; Niendam et al., 2006).

A possible relationship between negative symptoms, cognitive functions and functioning in individuals at UHR for psychosis was investigated in a few studies. In two recent studies, negative symptoms were related to cognitive deficits and functional impairment in individuals at UHR for psychosis (Gur et al., 2015; Ohmuro et al., 2015). On the other hand, there were two studies which found no relationship between negative symptoms and cognitive performance in UHR groups (Niendam et al., 2006; Therman et al., 2009).

It was shown that negative symptoms mediate the association between cognitive impairment and functioning in patients with schizophrenia (Ventura, Hellemann, Thames, Koellner, & Nuechterlein, 2009). These studies led researchers and clinicians to discuss and develop new treatment models focusing on cognitive functions and negative symptoms together to improve functional outcomes. Despite several studies in schizophrenia, there are few studies exploring whether the impact of cognition on functioning is mediated by negative symptoms in individuals at UHR for psychosis (Glenthøj et al., 2017; Meyer et al., 2014). Meyer et al. (2014) reported that negative symptoms mediated the relationship between composite neurocognition scores and social and role functioning in people at UHR for psychosis (Meyer et al., 2014). Similarly, Glenthøj et al. (2017) reported that negative symptoms mediated the relationship between cognition and role and social functioning. However, it is noteworthy that 45% of their sample (n = 84) were under antipsychotic treatment that may affect the results. Antipsychotic medication status of the participants was not reported in their study by Meyer et al. (2014) study.

As we summarized above, the number of the studies designed to search the relationship among negative symptoms, cognition and functioning are limited. The aim of the current study was to explore the relationship of negative symptoms with cognition and functioning cross-sectionally in antipsychotic naïve individuals at UHR for psychosis. Since antipsychotics may cause secondary negative symptoms, including antipsychotic-naïve individuals would eliminate this effect. We also explored whether cognition has an indirect effect on functioning through negative symptoms.

2 | MATERIALS AND METHODS

2.1 | Study participants

This cross-sectional study was conducted at the Psychotic Disorders Research Program, Istanbul University, Istanbul Faculty of Medicine between June 2004 and September 2019. People, who were literate, without mental retardation, present alcohol or substance use, antipsychotic use, severe medical condition and psychosis that lasted more than a week, were eligible to participate to the study. In total, 127 individuals, who were at UHR for psychosis, were consecutively recruited. Our sample comprised help-seeking persons who came directly or were referred by other psychiatrists for further evaluation. Among 127 individuals at UHR for psychosis, 14 (11%) had no information on global functioning. Of the remaining 113 participants, 6 (5.3%) had no information on negative symptom scores. Final study sample was consisted of 107 participants. There were no significant differences between participants and non-participants in terms of age and gender. Non-participants had significantly higher duration of education when compared to participants (mean = 12.1 vs 10.5 years, P = .007). In total, 76.4% (n = 81) of the individuals were in the attenuated psychotic symptoms subgroup, 15.1% (n = 16) were in the Brief Limited Intermittent Psychotic Symptoms (BLIPS) subgroup, and the remaining 8.5% (n = 9) were in the high familial risk with reduced function subgroup. Seven individuals in the attenuated psychosis group and one individual in the BLIPS group also had a family history of schizophrenia in their first-degree relatives.

All participants provided written informed consent after complete description of the study. This study was approved by local ethical committee of the Istanbul University.

2.2 | Clinical assessments

We used the previously defined criteria to identify individuals at UHR for psychosis (Yung et al., 1998). The individuals were defined as at UHR if they met the criteria of at least one of the following conditions: (a) BLIPS, (b) attenuated psychotic symptoms and (c) family risk with reduced function.

The BLIPS and attenuated symptom groups were operationally defined using the Brief Psychiatric Rating Scale-Expanded (BPRS-E) (Lukoff, Liberman, & Nuechterlein, 1986). The BPRS-E contains 24 items using a 1 to 7-Likert-type scale. Although assessment of the first 14 items depends on the interview, the last 10 items are evaluated on the basis of observation and interview. The BLIPS were operationally defined as a score of 4 or more in the hallucination item, a score of 5 or more in the unusual thought content item or a score of 4 or more in the suspiciousness item that were present for less than a week. The operational criteria for attenuated psychotic symptoms was defined as a score of 2 or 3 in the hallucination item, a score of 3 or 4 in the unusual thought content item, or 3 or 4 in the suspiciousness item. These symptoms should occur with a frequency of at least several times per week and the change in mental state should have been present for at least 1 month. The third group consisted of individuals who had a first-degree family member with a psychotic or schizotypal personality disorder with functional impairment. Functional impairment was characterized as a decrease of at least 30 points on the Global Assessment of Functioning (GAF) scale within the last 12 months (American Psychiatric Association, 2000). All individuals were evaluated by a senior psychiatrist (A. U.).

Besides above-mentioned inclusion criteria, we also applied Comprehensive Assessment of at Risk Mental States (CAARMS, Yung et al., 2005) to the last 29 participants. Unusual Thought Content-Severity score of CAARMS was correlated to Unusual Thought Content item of BPRS (rho = 0.81, $P < .001$), Non-bizarre Ideas-Severity score of CAARMS was correlated to Suspiciousness item of BPRS (rho = 0.77, $P < 0{,}001$),Perceptual Abnormalities-Severity score was correlated to Hallucinations item of BPRS (rho = 0.75, $P = 0.002$) and Disorganized Speech Severity score of CAARMS was correlated to Conceptual Disorganization item of BPRS (rho = 0.39, $P = .04$).

Negative symptoms were evaluated with the Scale for Negative Symptoms (SANS) and positive symptoms were measured with SAPS (Andreasen, 1984, 1995; Andreasen, 1989). Inter-rater reliabilities for the BPRS, SANS and SAPS total scores were acceptable ($\kappa = 0.78$, $\kappa = 0.76$ and $\kappa = 0.83$, respectively) at the beginning of the study.

We selected cognitive tests according to their reliability, validity, positive predictive value, lack of ceiling and floor effects in an UHR population, as well as usefulness in younger populations. Cognitive domains and related tests were selected based on previous studies (Gur et al., 2015; Meyer et al., 2014). Performance measures of each cognitive test are the same as we selected for our previous studies on individuals at UHR for psychosis (Üçok et al., 2013).

The Rey Auditory Verbal Learning Test (AVLT) is a list-learning paradigm (Rey, 1964) and we used the total number of correctly recalled words in trials I to V (verbal learning) and in the delayed recall trial (secondary verbal memory) as performance measures. The Stroop test measures selective attention, interference inhibition, processing speed, cognitive flexibility and executive functions (Golden, 1978). In accordance with our previous publications, we used number of commission errors and time difference between colour and word reading tasks as performance measures. In the computer version of the Wisconsin Card Sorting Test (WCST), we evaluated the number of correct answers and categories (Heaton, Chelune, Talley, Kay, & Curtiss, 1993). This test is used to measure executive function and working memory. Short-term auditory recall was assessed with the Digit Span-Forward Test (Wechsler, 1987). The Digit Span-Backward Test was used for the evaluation of working memory. Trail Making Test (TMT) A and B measure processing speed, sequencing, mental flexibility and working memory (Reitan, 1955). The N-back test is again used to assess working memory. Subjects perform the two-back version of the task. The reaction time of correct trials and accuracies are explored.

We evaluated role functioning with work/study status. Occupational status was rated based on direct interviews with the patient and relatives. Patients' occupational status was evaluated for 1 month before the admission. Full-time students and paid workers were regarded as occupied. We used the GAF scale to evaluate global functioning (American Psychiatric Association, 2000).

Depression may overlap with negative symptoms and may have an impact both on functioning and cognition in individuals at UHR (Glenthøj et al., 2020). We assessed depressive symptoms with the Calgary Depression Scale for Schizophrenia (CDSS) (Addington, Addington, Maticka-Tyndale, & Joyce, 1992). The validity and the reliability of the Turkish version of the CDSS was performed (Aydemir, Esen Danaci, Deveci, & Icelli, 2000). In a recent study, a score of 7 on the CDSS yielded the highest sensitivity and specificity in detecting depression in UHR individuals (Rekhi, Ng, & Lee, 2018). We used this cut-off score to detect depression in our sample.

2.3 | Statistical methods

We excluded SANS-attention subscale items because inattention was not considered in the negative symptom construct in recent reviews (Blanchard & Cohen, 2006; Kirkpatrick, Fenton, Carpenter, Marder, & Marder, 2006). This approach has been used in previous studies (Ergül & Üçok, 2015; Malla et al., 2002; Strauss et al., 2013).

First, we performed Spearman's correlation analysis as variables were not normally distributed. Second, a linear regression analysis was conducted to test the associations of SANS total and subdomain scores with GAF scores. All analyses were adjusted for age, gender and duration of education. Third, a logistic regression analysis was used to explore the relationships between SANS total and subdomain scores and working status. We adjusted these analyses for age, gender and duration of education. Finally, we tested the possible mediation of the association between cognition and global functioning by negative symptoms.

We performed a mediation analysis to evaluate whether the relationship of cognition with functional outcomes were mediated by negative symptom severity. To establish mediation, there are four steps: (a) exposure is related to the outcome (direct effect), (b) exposure is related to mediator, (c) mediator is related to the outcome when it is controlled for exposure, and (d) there is no direct effect (for complete mediation) or a weaker direct effect (for partial mediation) of exposure on outcome when the analysis controlled for mediator. Bootstrapping in mediation analysis is used for generating an empirically derived representation of the sampling distribution of the indirect effect which provide more accurate results with higher power. Therefore, the indirect effect was tested with a percentile bootstrap estimation method with 5000 samples in the current study. We used an SPSS macro developed by Andrew Hayes for mediation analyses (Hayes & Rockwood, 2017).

Additionally, we compared GAF scores between participants with and without depression using Mann-Whitney *U* test. A series of comparisons by work/study status was performed for cognitive tests using Mann-Whitney *U* test.

A Bonferroni correction was used for multiple comparisons in the correlation analyses that were done for separate cognitive domains ($\alpha = .05/23 = .002$).

We used IBM SPSS version 21 for the analyses. A *P*-value threshold of .05 was used for the statistical significance.

3 | RESULTS

Sociodemographic and clinical characteristics of the UHR sample are presented in Table 1.

TABLE 1 Characteristics of study sample[a]

	UHR (n = 107)
Age (y), mean (SD)	20.47 (4.62)
Male, n (%)	78 (72.9)
Education (y), mean (SD)	10.50 (2.33)
SANS total score, mean (SD)	39.88 (17.02)
SANS-affective score, mean (SD)	9.25 (7.09)
SANS-alogia score, mean (SD)	3.73 (4.12)
SANS-avolition score, mean (SD)	8.89 (3.68)
SANS-anhedonia score, mean (SD)	12.99 (5.25)
SAPS total score, mean (SD)	17.61 (8.51)
Rey AVLT, mean (SD)	
Learning	49.91 (11.26)
Memory	10.62 (3.03)
Digit Span Test, mean (SD)	
Backward	6.70 (2.48)
Forward	6.73 (2.48)
The Stroop Test, mean (SD)	
The Stroop Test (time difference)	44.28 (24.85)
The Stroop Test (colour errors)	2.42 (5.87)
TMT	
Trail Making A time (s), mean (SD)	44.80 (20.37)
Trail Making B time (s), mean (SD)	106.38 (52.19)
WCST, mean (SD)	
Correct answers	84.75 (21.27)
Categories	5.21 (2.91)
Two-back hit %	84.73 (5.14)
CDSS, mean (SD)	6.06 (3.81)
Depression[b], n (%)	34 (32.1)
GAF score, mean (SD)	62.01 (9.89)
Work/study status, no, n (%)	49 (47.1)

Abbreviations: AVLT, Auditory Verbal Learning Test; CDSS, Calgary Depression Scale for Schizophrenia; GAF, Global Assessment of Functioning; SANS, Scale for the Assessment of Negative Symptoms; TMT, Trail Making Test; UHR, ultra-high risk; WCST, Wisconsin Card Sorting Test.
[a]Percentages were given on the basis of non-missing data for each item.
[b]Number of people scored 7 or above in CDSS is considered as depressed.

3.1 | Relationship between negative symptoms, cognition and functioning

SANS total score and SANS subdomain scores were negatively correlated with GAF score. Among cognitive tests, TMT A and B (time) were negatively and number of correct answers on WCST, composite scores for attention and executive functions were positively correlated with GAF score. However, only the correlation of TMT B with GAF remained significant after Bonferroni correction. The CDSS score was negatively correlated to GAF score, again this association was not significant after Bonferroni correction (Table 2).

TMT A (time) and SANS-alogia score was positively correlated. TMT B (time) was positively correlated with SANS total and subdomain scores. WCST number of correct answers and WCST categories score were negatively correlated with SANS total, SANS-affective and SANS-alogia. After Bonferroni correction, correlation of TMT B test remained correlated with SANS total, SANS-affective and SANS-alogia scores.

In linear regression analysis, we found that total and all subdomain SANS scores were inversely related with GAF score (Table 3). Among all subdomain scores, the highest effect size was observed for avolition (r^2 for affective .19, for alogia .11, for avolition .23 and for anhedonia .16). All analyses were adjusted for age, sex and level of education. Logistic regression analysis, in which work/study status was used as a dependent variable, showed that SANS total and subdomain scores were related to likelihood of lack of role functioning. All analyses were adjusted for age, sex and level of education.

3.2 | Negative symptoms as a mediator between neurocognition and functioning

We tested the hypothesis that the association between TMT B (time) and global functioning was mediated by negative symptoms. TMT B (time) was not a significant predictor after controlling for total SANS score (regression coefficient = −.03, 95% CI = −0.07; 0.003, P = .07). The indirect effect was tested using a percentile bootstrap estimation approach with 5000 samples and the results indicated a significant indirect effect (regression coefficient = −.03, 95% CI [bootstrapped] = −0.06; −0.01). Overall, these results are consistent with a full mediation. Approximately 13% of the variance in GAF was accounted for by the predictors. We performed the same analysis using the attention composite score as exposure. In this analysis, attention composite score was not related with GAF after controlling for total SANS score (regression coefficient = 1.68, 95% CI = -1.36; 4.71, P = .27). We detected a significant indirect effect of total SANS score on the association between attention composite score and GAF score (regression coefficient = 2.23, 95% CI [bootstrapped] = 0.53; 4.36). Approximately 1% of the variance in GAF was accounted for by the predictors (Figure 1).

In the secondary analyses, we found that those who work/study at first contact had better Digit Span-Forward Test (7.6 ± 2.4 vs 5.9±, Z = 2.91, P = .001) and TMT B test scores (89.2 ± 43.7 vs 120.6 ± 56.1, Z = 2.91, P = .04). After Bonferroni correction, only significant difference was observed for Digit Span-Forward Test score.

According to the cut-off score of seven in CDSS, 32.1% (n = 34) of the patients had depression. There was no difference between those with and without depression in terms of GAF score (60.5 ± 7.1 vs 63.1 ± 11.4, df = 98, P = .2). SANS-avolition (r = .43, P < .001) and SANS-anhedonia (r = .29, P = .005) subscale scores were correlated with CDSS scores whereas there were no correlations of alogia and affective bluntness scores with CDSS score. We did not find any correlations between cognitive variables and CDSS score (results not shown).

TABLE 2 Correlations among negative symptoms scores, cognition scores and GAF scores

	SANS total	SANS affective	SANS alogia	SANS avolition	SANS anhedonia	GAF score
Rey AVLT—Learning	.16	.11	.09	.97	.16	−.06
Rey AVLT—Memory	.03	.11	.04	−.09	.03	.06
Digit Span—Backward Test	−.01	−.04	−.13	.05	.03	−.06
Digit Span—Forward Test	−.18	−.19	−.23*	−.16	−.04	.13
The Stroop Test (time difference)	.05	.04	.12	−.04	.11	−.07
The Stroop Test (colour errors)	−.15	−.09	−.12	−.14	−.18	.03
Trail Making A (time)	.17	.12	.26*	.17	.15	−.20*
Trail Making B (time)	.40***	.35***	.42***	.29**	.30**	−.36***
WCST (correct answers)	−.22*	−.23*	−.20*	−.13	−.10	.19*
WCST (categories)	−.24*	−.21*	−.26*	−.13	−0.9	.15
Two-back hit %	−.15	−.73	−.28*	−.24	.08	.12
Learning/memory composite score	.07	.09	.08	−.03	.08	.02
Executive functions composite score	−.21*	−.20*	−.23*	−.12	−.07	.16
Attention composite score	−.26**	−.25*	−.29**	−.19	−.16*	.23*
Global composite score	−.19*	−.18	−.19	−.17	−.06	.21*
SAPS score	−.01	−.11	−.08	.04	−.04	.11
CDSS score	.29**	.17	.09	.44***	.27**	−.24*
GAF Score	−.51***	−.41***	−.31***	−.48***	−.38***	—

Abbreviations: AVLT, Auditory Verbal Learning Test; CDSS, Calgary Depression Scale for Schizophrenia; GAF, Global Assessment of Functioning; SANS, Scale for the Assessment of Negative Symptoms; WCST, Wisconsin Card Sorting Test.
*Correlation is significant at the .05 level (one-tailed).
**Correlation is significant at the .01 level (one-tailed).
***Correlation is significant at the .001 level (one-tailed).

TABLE 3 Association between SANS scores and GAF scores and working status[a]

	GAF at baseline			Working status at baseline		
	B	95% CI	*P*	*B*	95% CI	*P*
SANS total	−0.29	−0.39; −0.18	<.001	1.05	1.02; 1.08	.001
SANS affective	−0.57	−0.83; −0.30	<.001	1.08	1.01; 1.15	.02
SANS alogia	−0.68	−1.19; −0.16	.01	1.13	1.02; 1.28	.03
SANS avolition	−1.19	−1.67; −0.70	<.001	1.29	1.13; 1.47	<.001
SANS anhedonia	−0.61	−0.96; −0.26	.001	1.11	1.02; 1.20	.01

[a]Analyses were adjusted for age, gender and duration of education.
Abbreviations: GAF, Global Assessment of Functioning; SANS, Scale for the Assessment of Negative Symptoms.

4 | DISCUSSION

In this study, we investigated the relationships of the negative symptoms and cognitive functions with global and role functioning in individuals at high risk for psychosis. We found that negative symptoms were associated with deficits in cognitive performance, and global and role functioning.

We found that negative symptoms mediated the relationship between cognitive flexibility and global functioning. Two previous studies reported that negative symptoms mediated the relationship between composite neurocognition and both social and role functioning (Glenthøj et al., 2017; Meyer et al., 2014). Similar findings were also reported for patients with chronic schizophrenia (Lin et al., 2013). It is possible that people with diminished cognitive functioning have worse functional outcome as negative symptoms impair cognition most likely through lowered motivation to attend the tasks. As a result, they may have decreased motivation to participate in daily activities with directly influence functional outcome. When we comment on this finding, we should keep in mind that a content overlap on the measures of negative symptoms and global functioning) which may increase the association between the constructs. Although we did not test it, Meyer et al. (2014) addressed this issue and found that negative symptoms remained a significant mediator when the overlapping items were removed.

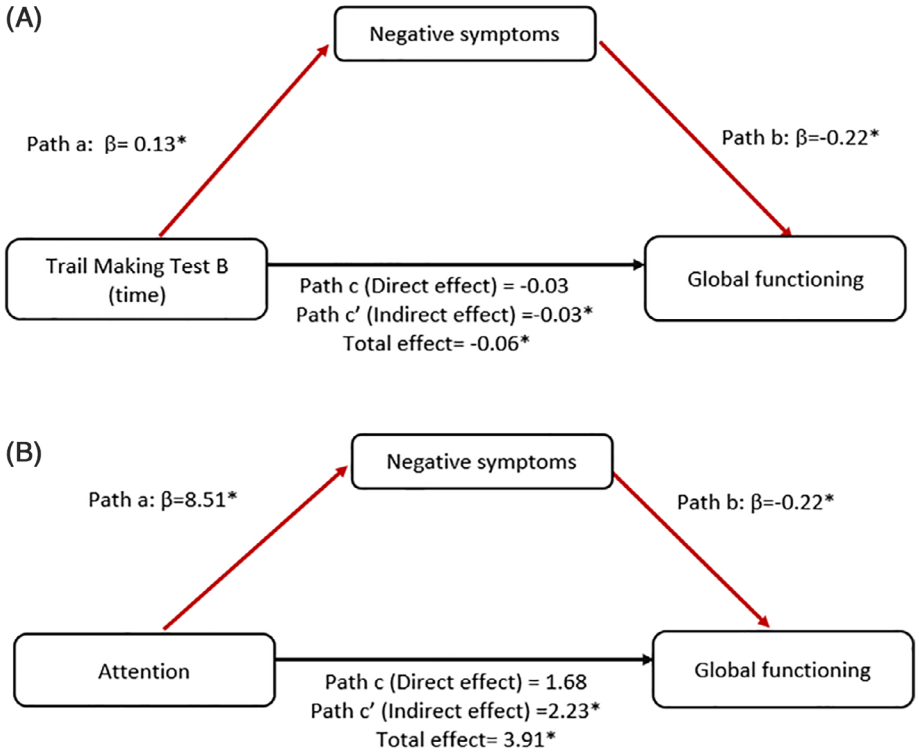

FIGURE 1 DAG representations of mediation analyses. A, Trail Making Test B (time) was positively associated with negative symptom score (path a). Negative symptom score was negatively related with global functioning (path b). Trail making test-B (time) was not a significant predictor (regression coefficient = −.03, 95% CI = −0.07; 0.003, *P* = .07) (path c or direct effect). The indirect effect (path c′) was tested using a percentile bootstrap estimation approach with 5000 samples and the results indicated a significant indirect effect (regression coefficient = −.03, 95% CI [bootstrapped] = −0.06; −0.01). Total effect is the sum of the direct and indirect effect. B, Attention composite score was related with negative symptoms (path a). Negative symptoms were related with global functioning (path b). Attention composite score was not a significant predictor of global functioning (regression coefficient = 1.68, 95% CI = −1.36; 4.71, *P* = .27) (path c or direct effect). We detected a significant indirect effect (path c′) of total SANS score on the association between attention composite score and GAF score at baseline (regression coefficient = 2.23, 95% CI [bootstrapped] = 0.53; 4.36). Total effect is the sum of the direct and indirect effect

We found that negative symptoms were correlated with global functioning whereas there was no significant association of the severity of positive symptoms and global functioning which is consistent with previous UHR (Gur et al., 2015; Kim et al., 2013; Meyer et al., 2014) and first-episode schizophrenia (Ergül & Üçok, 2015) studies. Although all subscale scores of SANS were related to global functioning, the effect size of these associations was the largest for avolition subdomain. Studies focusing on neurobiology of negative symptoms in schizophrenia reported that avolition has related to specific brain regions and independent from anhedonia (Mucci et al., 2015; Vignapiano et al., 2016). Foussias and Remington (2010) reported that avolition may be the key contributor to the relationship between negative symptoms and functioning in patients with schizophrenia (Foussias & Remington, 2010).

Our findings suggest that deficit of motivation has more impact on functioning compared to other negative symptoms in individuals at UHR for psychosis as well.

Additionally, we found that avolition is independently contributed to role functioning. Avolition was associated with poor role functioning in individuals at UHR (Azis et al., 2019). Similarly, Glenthøj et al. (2020) found that experiential negative symptoms were more related to real life functioning than expressive negative symptoms. Our findings are in line with these findings.

We found that depression scores were correlated with GAF scores. In our sample, we found that 32.1% of the participants had depression according to the CDSS scores, which is very similar to the prevalence of depression (34%) reported by Salokangas et al. (2012). We did not detect any significant differences between participants with and without depression in terms of GAF. Continuous correlation of CDSS score and GAF might stem from an overlap of negative symptoms with subtle depressive symptoms. In a recent UHR study, those with major depressive disorder had higher negative symptoms and poor cognitive performance than those without any depressive disorders (Mallawaarachchi et al., 2020). In our study, the CDSS score was correlated with experiential (avolition and anhedonia) but not with expressive negative symptoms. It is not surprising as there is an overlap between experiential negative symptoms and depressive symptoms. On the other hand, there was no relationship between CDSS score and cognition. We can speculate that relationship between depression and functioning comes from an overlap between depression and experiential negative symptoms. Findings of a recent study (Glenthøj et al., 2020) reporting that experiential negative

symptoms were more related to real life functioning than expressive negative symptoms may supports our explanation.

Our study has some limitations. First, we enrolled participants from a tertiary centre, which may limit the generalizability of our results because the participants were more likely comprised help-seeking people. Second, we evaluated participants according to BPRS-based UHR criteria instead of a well-validated interview assessment for UHR status like CAARMS or SIPS. Third, there might be a selection bias as some participants were not able to attend to cognitive tests. However, participants and non-participants did not differ in terms of age, education, gender, work/study status, GAF score, BPRS, SANS and SAPS scores and cognitive test performances at baseline. Fourth, we used GAF score as a measure of global functioning. GAF score also reflects the severity of symptoms and may not be the best tool to measure the functioning. When we started to collect data 15 years ago, it seemed as optimal option available. Finally, assessing mediation in cross-sectional data is ill-advised as it is assumed that the order of the causality is correct, and an alternative temporal order is not likely. However, it is also possible that the association of negative symptoms with functional outcomes might be mediated by cognitive functions even though it is not commonly accepted in previous studies of schizophrenia. Therefore, results of the mediation analysis in the current study should be interpreted carefully.

In conclusion, the present study found that negative symptoms, particularly avolition in individuals at UHR for psychosis has an impact on both global and role functioning. These findings imply that, for better functioning, psychosocial and pharmacological interventions should be comprehensive, considering negative symptoms in treating patients, rather than managing positive symptoms alone.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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