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Negative Symptom Domains in Children and Adolescents at Ultra-High Risk for Psychosis: Association With Real-Life Functioning

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Background: **Negative symptoms (NS) appear early in subjects at ultra-high risk (UHR) for psychosis and may increase the risk of conversion to psychotic disorders and poor outcome. Contrary to schizophrenia, there is no consensus on the conceptualization and factor structure of NS in UHR subjects. This study aims to explore NS prevalence, factor structure, and impact on the outcome of UHR state in children and adolescents.** ***Methods:*** **71 UHR were recruited at the Neuropsychiatry Unit of the Hospital Bambino Gesù in Rome. We examined the prevalence of NS of at least moderate severity, the factor structure of NS by Principal Component Analysis (PCA) and Confirmatory Factor Analysis (CFA), and correlations between extracted factors and functioning. We also evaluated the severity of baseline NS in subjects who converted to psychosis (converters) and in those who did not convert (nonconverters) at 1-year follow-up.** ***Results:*** **At baseline, all participants showed at least one NS of at least moderate severity. PCA and CFA yielded a two-factor solution: an "Expressive" and an "Experiential" factor. Only the Experiential factor was associated with functioning. At baseline, severity of NS did not differ between converters (*N* = 16) and nonconverters (*N* = 55).** ***Conclusions:*** **In UHR children and adolescents NS have a high prevalence, a significant impact on functioning, and cluster in two-factors. Replications by independent studies, with state-of-the-art instruments and longer duration of follow-up, are needed to improve the characterization of NS in this population, clarify their impact on the outcome and enhance their early identification, prevention, and treatment.**

Key words: at risk mental state/schizophrenia/conversion to psychosis/avolition/experiential factor/expressive factor

Introduction

The identification of subjects at Ultra-High Risk (UHR) for psychosis is an opportunity to improve prevention and early intervention in psychosis. Currently, the identification of UHR subjects is mainly based on the presence of subthreshold positive symptoms.[1–5] However, also negative subthreshold symptoms and impaired cognitive functioning have been reported in UHR subjects.[6–9]

According to current evidence, in UHR subjects the rate of conversion to frank psychosis ranges from 23% to 36% within 2-years of follow-up,[10–12] it tends to increase in studies with a longer follow-up[11–13] and is significantly lower in 12 to 18-year-old subjects (9.5%).[13]

In the light of these findings, research is increasingly focusing on the variables that enhance the risk of conversion and interfere with functional outcome.[10, 14]

Several studies highlighted the role played by negative symptoms in the conversion to psychosis of UHR subjects and in poor social functioning.[15–32] However, most studies carried out so far have methodological pitfalls, mainly due to the lack of consensus in conceptualization and assessment of negative symptoms in UHR subjects.[26, 27, 33, 34]

Current Conceptualization of Negative Symptoms in Schizophrenia

According to the current conceptualization provided by the consensus conference of the National Institute of Mental Health - Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Initiative, negative symptoms in subjects with schizophrenia include five symptoms: blunted affect (reduced intensity and range of emotional expression), alogia (reduced spontaneous speech and loss of conversational

fluency), avolition (reduced interest and motivation for productive activities, or sense of purpose), asociality (diminished interest in social drive or interest and desire for affiliation), and anhedonia (consummatory anhedonia, ie the reduced ability to experience pleasure, and anticipatory anhedonia, ie the reduced ability to anticipate pleasure).[26, 34] Two second-generation clinician-rated scales were developed after the NIMH-MATRICS Initiative, and are now regarded as the gold standard instruments in evaluating negative symptoms in subjects with schizophrenia: the Brief Negative Symptom Scale (BNSS)[35, 36] and the Clinical Assessment Interview for Negative Symptoms (CAINS).[37]

Several factor analytic studies showed that negative symptoms cluster in two factors: the Experiential factor (avolition, anhedonia, and asociality) and the Expressive factor (blunted affect and alogia).[26, 38, 39] The two-factor solution is supported by the evidence that the two negative symptom factors are associated with different behavioral and neurobiological features, as well as with different psychopathological and functional outcomes.[38–47]

More recently, a five-factor model, reflecting the five individual negative symptoms, or a hierarchical model (five individual negative symptoms as first-order factors and the two factors, Experiential and Expressive domains, as second-order factors) are regarded as the most robust models, as they provide a better fit as compared to the two-factor solution. However, these results need replications.[26, 48–51]

Frequency and Severity of Negative Symptoms in the Ultra-High Risk Syndrome

Negative symptoms have been reported in a significant proportion of UHR individuals. They emerge before the attenuated positive symptoms[30, 52–54] and have a higher prevalence than the positive ones, especially asociality.[4, 18, 54] Severity of negative symptoms at baseline seems to predict conversion to psychosis[16, 18, 23, 25, 30, 31]. Velthorst et al[18] in 73 UHR subjects found that social anhedonia and withdrawal, bizarre thinking, and impairment in functioning were associated with subsequent transition to psychosis.

Demjaha et al[23] examined psychopathological dimensions in 122 UHR subjects (aged 16–35 years) and found that disorganization, cognitive, and negative dimensions were associated with subsequent transition to psychosis. Similar results were reported by Piskulic et al who, in a sample of 138 UHR individuals, observed a 15% rate of conversion to psychosis after 12 months and reported that, at baseline, converters had more severe negative symptoms (which persisted over time) than nonconverters.[30]

Recently, Zhang et al[31] found that in UHR adolescents the conversion was predicted by negative symptoms, while in UHR adults it was predicted by positive symptoms, suggesting that predictors of conversion may differ between adolescent and adult UHR subjects.

In addition, in UHR subjects negative symptoms have a direct impact on functioning and seem to mediate the association between cognition and functioning.[19, 20, 22–29, 55] Demjaha et al[23] reported a strong negative correlation between the total score of negative and anxiety domains of the Comprehensive Assessment of the At-Risk Mental State (CAARMS) and the level of functioning measured by the Global Assessment of functioning (GAF).[23] Lee et al[19] found that social and role functioning was primarily and independently associated with negative symptoms but not with positive or depressive symptoms[19]; in particular, the avolition-apathy item of the Scale for the Assessment of Negative Symptoms (SANS)[56] was correlated with both social and role functioning, while blunted affect was correlated with social functioning only.[9] Yung et al[29] investigated the presence of persistent negative symptoms (PNS) in 363 UHR individuals and showed that UHR subjects with PNS had a worse premorbid social adjustment than those without PNS (noPNS). This difference was larger in early (aged 12–15) and late adolescents (aged 16–18) than in adult UHR subjects. The PNS group also showed a poorer psychosocial functioning than the no-PNS one at one-year follow-up.[29]

Negative Symptoms in the Ultra-High Risk Syndrome – Assessment Tools

Unlike the adult psychosis population, there is no consensus on clinician-rated scales for evaluating negative symptoms in UHR individuals.[26, 27] Actually, in this population, negative symptoms are often evaluated with scales developed for the adult psychosis population (eg, SANS or the Positive and Negative Syndrome Scale, PANSS),[56, 57] which might not be sensitive enough to capture subtle negative symptoms of children, adolescents, and young adults, and often are not in line with the current conceptualization of negative symptoms.[26] Other scales, such as the Structured Interview for Psychosis-Risk Syndromes (SIPS)[58] or the CAARMS[17], developed primarily for the assessment of attenuated psychotic symptoms, have also been used for the assessment of negative symptoms in UHR population. Unfortunately, also these tools are not in line with the current conceptualization of negative symptoms.[26]

Finally, the BNSS[59] and the CAINS[60] were adapted and the Prodromal Inventory of Negative symptoms (PINS)[61] was developed for the use in UHR population. However, despite the strengths of the adapted versions of BNSS and CAINS and of the PINS, some authors have questioned the use of these scales, since it is possible that they are not sensitive enough to capture attenuated negative symptoms occurring in UHR states.[26, 27]

Negative Symptoms in the Ultra-High-Risk Syndrome – Factor Structure

Studies investigating the factor structure of negative symptoms in UHR population reported conflicting findings.

Some studies using either the CAARMS or SIPS analyzed the scale as a whole and reported a unidimensional structure of negative symptoms.[23, 30, 62, 63] However, the inclusion of dimensions other than negative symptoms might have influenced the findings.[26] Very few studies examining the factor structure of negative symptoms in UHR populations focused on the negative symptom scale or subscale only.[30, 64–67]

Lam et al[65] examined the factor structure of negative symptoms in a large cohort of schizophrenia subjects (n = 887; mean age: 49.1 years) and in a sample of UHR subjects (n = 173; mean age 21.3 years).[65] A confirmatory factor analysis, conducted on the PANSS negative items, showed a two-factor structure for both schizophrenia and UHR individuals: Social amotivation and Diminished expression.[65] Social amotivation predicted functioning in both groups at one-year follow-up. However, as stated above, the PANSS was developed for adult psychosis populations; in addition, in their factor analysis, the authors included motor retardation and active social avoidance, which currently are not conceptualized as negative symptoms.[26, 34, 68]

Azis et al[64] investigated the factor structure of negative symptoms assessed by the SIPS[58] in a large sample of UHR subjects (N = 214) performing both an exploratory and confirmatory factor analysis. The authors found that SIPS negative symptoms loaded on two factors: Volition (occupational functioning and avolition) and Emotion (expression of emotions, experience of emotions, and social anhedonia). The "Volition" factor was strongly correlated with role functioning while the "Emotion" factor showed a weak correlation. However, the inclusion of the occupational functioning in the factor analysis is questionable since this aspect is not conceptualized as a negative symptom.[26, 34, 68]

Finally, Chang et al adapted the BNSS to the UHR population to investigate digital social interactions (eg social media such as facebook, whatsapp, etc) and particular life situations of younger people (eg living in a dormitory with roommates).[66, 67] The authors performed an exploratory factor analysis and found that BNSS negative symptoms loaded on two factors named Amotivation (anhedonia, asociality, avolition) and Diminished expression (alogia and blunted affect). The Amotivation factor was correlated with the role functioning scale, while the Diminished expression had no association with the functioning. In a second study,[66] the same research group used a confirmatory factor analysis and, in line with other studies conducted in subjects affected by schizophrenia, showed that the 5-factor model provided a better fit as compared to the two-factor model.

In summary, in UHR subjects negative symptoms seem to contribute to conversion to psychosis and to poor functional outcome. Studies investigating their factor structure reported, as mentioned above, conflicting findings. In addition, most studies were conducted in young adults or adults. The few studies focusing on UHR adolescents (13–18 years) suggested that data relevant to negative symptoms are similar to those observed in adolescents in their first episode of psychosis[69] and in adult samples,[18,52] and highlighted the need to investigate frequency and severity of negative symptoms in UHR children and adolescents, and clarify the contribution of this psychopathological dimension to psychosis transition.

Aims

The present study aims to: (1) investigate the prevalence of negative symptoms in a group of UHR children and adolescents; (2) explore the factor structure of negative symptoms in this population; (3) evaluate their association with psychosocial functioning, and (4) compare the severity of negative symptoms at baseline between UHR individuals who show a transition to psychosis (converters) and those who do not convert (nonconverters) at 1-year follow-up.

Based on previous studies,[4, 5, 18, 30, 54, 64] we expected to find a high prevalence of negative symptoms in the UHR population, and a higher severity of baseline negative symptoms in converters than in nonconverters UHR subjects. In addition, we hypothesized that, according to the most robust finding in adult psychosis population,[26] negative symptoms assessed with the SIPS cluster in two factors that show different associations with functioning.

Methods

Study Participants

Seventy-one subjects, aged between 9 and 17-years, with suspected early-onset psychosis (EOP), consecutively seen from January 2017 to February 2018, were recruited for the study at the Child and Adolescent Neuropsychiatry Unit of the Children Hospital Bambino Gesù in Rome.

The inclusion criterion was the presence of any UHR syndrome,[70] ie, attenuated positive symptoms (APS), brief intermittent psychotic symptoms (BIPS), and/or genetic risk plus functional deterioration (GRFD). The exclusion criteria were past or present psychosis, traumatic brain injury, or any known neurological disorders, and current drug or alcohol abuse. A history of drug use was allowed if symptoms had also been present in drug-free periods. Participants were followed-up for 12 months.

The Ethics Committee of the Children Hospital Bambino Gesù approved the study.

All participants provided a written informed assent and their parents/legal guardians a written informed consent.

Psychopathological Assessment

All participants completed the SIPS[58] which includes a total of 19 items (five positive, six negative, four disorganized, and four general symptoms) that are evaluated based on the presence, duration, and severity of specific experiences and behavior. Each positive item (delusional ideas, persecutory ideas, hallucinations, grandiose ideas, disorganized communication) is rated on a scale from 0 (absent) to six (psychotic). Each negative item (social anhedonia, avolition, decreased expression of emotion, decreased experience of emotions and self, decreased ideational richness) is rated on a scale from 0 (absent) to 6 (extreme).

The SIPS contains diagnostic criteria for three "psychosis risk syndromes", ie, APS, BLIPS, and genetic risk and deterioration syndrome (GRD).

Transition to psychosis was monitored by applying the Presence of Psychotic Symptoms (POPS) criteria.[58] In particular, the transition was defined as presence of at least one of the 5 positive symptoms included in the Scale of Prodromal Symptoms (SOPS) with a score of at least 6 and a duration ≥1 h per day for at least 4 days per week during the past month, or as presence of symptoms with a serious impact on functioning (eg, severely disorganized, or dangerous to self or others).

All measures were collected at baseline and at 12 months follow-up.

Neurocognitive Functioning and Functional Outcome

Baseline total Intelligence Quotient (IQ) was assessed with the Wechsler Intelligence Scale for Children (WISC-IV).[71–73] The level of functioning was measured with the Children's Global Assessment Scale (C-GAS).[74] Furthermore, social and role functioning were assessed with the Global Functioning: Social Scale (GF: Social) and the Global Functioning: Role Scale (GF: Role),[75] respectively. These are clinician-rated, well-anchored scales, that take age and phase of illness into account and assess social and role functioning independently of clinical symptoms. GF: Social assesses quantity and quality of peer relationships, level of peer conflict, age-appropriate intimate relationships, and involvement with family members. GF: Role rates level of performance in vocational role (student, worker, or homemaker). For both scales, scores range from 1 to 10, with 1 indicating extreme dysfunction and 10 indicating superior functioning.

Statistical Analyses

All analyses were carried out using SPSS 24 (IBM Corp, Armonk, NY). Data distributions were evaluated for normality, homogeneity of variance, and presence of outliers (subjects whose scores exceeded the 75th or the 25th percentile by 1.5 times the interquartile range).

The demographic and clinical characteristics of the UHR sample, as well as of the Converter and Nonconverter subsamples, were summarized as means ± standard deviations (SDs) and percentages, as appropriate. Independent one-way analyses of variance (ANOVA) were used to test group differences at study inclusion between converters and nonconverters with respect to their demographic, psychopathological, and real-life functioning data. Group difference in gender distribution was assessed by the Pearson's chi-square test.

Frequency of Negative Symptoms of At Least Moderate Severity. In the whole UHR sample, we calculated the frequency of at least one SIPS core negative symptom (Social anhedonia-N1, Avolition-N2, Expression of emotions-N3, Experience of emotions and self-N4, and Ideational richness-N5) of at least moderate severity (≥3). In addition, we calculated both the frequency of at least one symptom rated 3 or 4 (moderate to moderately severe) and the frequency of at least one symptom rated 5 or 6 (severe to extremely severe).[76]

Factor Structure of the Negative Subscale of the Structured Interview for Psychosis-Risk Syndromes. A principal component analysis (PCA) was performed on the 5 items (N1–N5) of the negative subscale of the SIPS. A varimax rotation with Kaiser normalization was used, to take into account correlations among factors.

The optimal number of factors was determined via eigenvalue >1.0 and scree plot criteria.

The items with the highest loading (among those with robust loadings >0.50) after varimax rotation were used to interpret the extracted factors.[77]

Confirmatory Factor Analysis (CFA) using AMOS 24.0 was used to determine the fit of the generated models.

To assess the absolute fit of the models, the following indices were used: $\chi 2$ value, the comparative fit index (CFI), the Tucker Lewis index (TLI), the root mean square error of approximation (RMSEA). A good fit included a nonstatistically significant $\chi 2$ value, CFI, and TLI values of at least 0.95, RMSEA no greater than 0.08. Two information criteria, ie, the Akaike information criterion (AIC) and the Browne–Cudeck criterion (BCC), were used to compare relative fit indices of model parsimony. Lower values indicate better model fit.

Correlations Between Negative Symptom Factors and Functional Outcome. Correlations between factors extracted from negative SIPS items and real-life functioning scales (C-GAS, GF: Social and GF: Role scales) were explored by means of Pearson's correlation tests. A Bonferroni correction was applied to avoid type

1 error for multiple tests. Statistical significance level was set at $P \leq .05$ for all tests.

Results

Demographic and Clinical Characteristics of UHR Sample

Seventy-one subjects at ultra-high risk for psychosis were enrolled. All of them had a complete data set of the study measures and participated in the follow-up.

Demographic and clinic characteristics of the UHR enrolled subjects are shown in Table 1. They were predominantly males (59.2%), with a mean age of 14 years and a mean IQ of 95.

At baseline, all participants showed at least one negative symptom rated ≥3 on the SIPS; 23 (32.0%) participants had at least one symptom in the moderate to above moderate range (ie, SIPS ratings of 3 or 4), and 48 (68.0%) reported symptoms in the severe range (ie, SIPS ratings of 5 or 6) (Table 2).

Table 1. Demographic and Clinical Characteristics of the UHR Sample ($n = 71$)

Sex, *N*; *N* (%)	M 42 (59.2%) (mean ± SD)	F 29 (40.8%) min–max
Age, years	13.9 ± 2.1	9–17.6
Education, years	8.4 ± 2.1	3–12
Current IQ	98 ± 16.3	70–137
Total SIPS	47.5 ± 13.2	12–80
SIPS Positive Subscale	11.6 ± 4.2	3–24
SIPS Negative Subscale	17 ± 6.2	1–24
SIPS Disorganization Subscale	8.6 ± 4	1–19
SIPS General Psychopathology Subscale	10.3 ± 3.9	1–18
C-GAS	48.37 ± 3.93	35–55
GAF: Role	3.9 ± 0.5	3–5
GAF: Social	4 ± 0.5	3–5

Note: M, males; F, females; SIPS, Structured Interview for Psychosis-Risk Syndromes; C-GAS, Children's Global Assessment Scale; GAF: Role, Global Assessment of Functioning: Role; GAF: Social, Global Assessment of Functioning: Social.

Table 2. Frequency of Negative Symptoms of At Least Moderate Severity in the UHR Sample

Negative Symptoms	Frequency	%
At Least One Negative Symptom Rated ≥3	71	100
At Least One Symptom Rated 3 or 4	23	32
At Least One Symptom Rated 5 or 6	48	68

Factor Structure of the SIPS Negative Symptom Subscale

Principal Component Analysis. According to the PCA on the 5 items of the SIPS negative subscale a two-factor solution explained 69.42% of the total variance in the whole sample.

Table 3 shows the factor loadings after varimax rotation. The first factor was labeled "Expressive factor", and included expression of emotion (N3), experience of emotions and self (N4), and ideational richness (N5); the second factor was labeled "Experiential factor" and included social anhedonia (N1) and avolition (N2).

The communality was high for all items, except avolition, that showed a loading of 0.56 on the "Experiential factor".

Confirmatory Factor Analysis. CFA was used to determine the comparative fit of 3 models of the latent structure of negative symptoms, based on our PCA results and previous literature.[64] The first model (one-factor model) evaluated whether a unitary structure (general factor) reflected all core negative symptoms (N1, N2, N3, N4, N5); the second model (two-factor model) tested whether negative symptoms clustered in two factors, named "Expressive factor" (including N3, N4, and N5) and "Experiential factor" (including N1 and N2); and the third model tested the fit of a hierarchical model according to Azis et al[64] (the general factor and the 2 factors, Experiential and Expressive factors).

Results of the CFA analyses are reported in Table 4. None of the three models met all criteria of a good fit. In particular, the 1-factor model had the poorest fit, as shown by the statistically significant $\chi 2$ value, CFI, and

Table 3. Factor Loadings (After Varimax Rotation) of the 5 Negative Items of the Structured Interview for Prodromal Symptoms (SIPS)

	Principal Component Analysis with Varimax Rotation	
	Expressive Factor	Experiential Factor
SIPS N1 Social Anhedonia	0.02	0.93
SIPS N2 Avolition	0.45	0.56
SIPS N3 Decreased Expression of Emotion	0.82	0.32
SIPS N4 Decreased Experience Of Emotions And Self	0.83	0.13
SIPS N5 Decreased Ideational Richness	0.77	0.03

Note: SIPS, Structured Interview for Psychosis-Risk Syndromes.

Table 4. Model Fit Results From CFA on the 5 Negative Items of the Structured Interview for Prodromal Symptoms (SIPS)

Model	Number of Distinct Parameters to be Estimated	AIC	BCC	X^2 Value (df)	TLI	CFI	RMSEA
1 Factor	11	54.571	56.634	32.571 (9)*	0.716	0.744	0.193
2 Factor	16	43.447	46.447	11.447 (4)	0.798	0.919	0.163
Hierarchical	15	43.666	46.469	13.66 (5)	0.812	0.906	0.157

Note: CFA, confirmatory factor analysis; AIC, Akaike information criterion; BCC, Browne–Cudeck criterion; CFI, confirmatory fit index; RMSEA, root mean square error of approximation; TLI, Tucker Lewis index.
*$P < .01$.

Table 5. Correlations of the Functioning Scales With the Expressive and Experiential Factors

		Expressive Factor	Experiential Factor
C-GAS	Pearson's *r*	−.102	−.221
	P	.396	.064
GAF Role	Pearson's *r*	−.114	−.327
	P	.343	.005
GAF Social	Pearson's *r*	−.026	−.181
	P	.830	.132

Note: C-GAS, Children's Global Assessment Scale; GAF: Role, Global Assessment of Functioning: Role; GAF: Social, Global Assessment of Functioning: Social.

TLI values less than 0.95, RMSEA exceeding the 0.08 threshold and higher AIC and BCC values.

The 2-factor model and the hierarchical model provided a better fit than the 1-factor model with a small advantage of the 2-factor model.

Correlation Analysis

The "Experiential factor" was associated with GAF: Role score (r −.327; $P < .005$) (Table 5). The association remained significant when controlling for the severity of the positive symptomatology (r −.282; $P < .018$). No significant correlation was found between the "Expressive" factor and the functioning scales.

Transition to Psychosis at T1

Sixteen of the 71 participants (22.5%) made the transition to psychosis within the 12 months follow-up period.

Comparison between Converters and Nonconverters

No significant difference was identified between converters and nonconverters with respect to their demographic data (Table 6); a six-point difference was observed for the IQ (90.50 for converters and 96.25 for nonconverters), but it was not statistically significant ($P = .29$).

At study inclusion, converters showed significantly higher scores on the SIPS positive subscale ($P < .004$) and worse functioning on the C-GAS ($P < .03$) when compared with nonconverters. No difference was observed for the SIPS core negative symptoms (Table 7).

Discussion

Frequency of Negative Symptoms of At Least Moderate Severity

In this longitudinal, prospective study in UHR children and adolescents, we found that all participants showed at least one negative symptom of moderate or high severity.

These results confirm previous studies reporting a high prevalence of negative symptoms in mixed samples of young and adult UHR, in which negative symptoms were assessed with different tools.[4, 18, 54] They are also in line with previous studies using the SIPS/SOPS.[30, 64]

Factor Structure of the SIPS Negative Subscale and Association with Functioning

In line with previous factor analytic studies conducted in adults with psychotic disorders and in UHR subjects,[26, 39, 64, 65, 68, 78–80] our PCA yielded a two-factor solution explaining 69.42% of the total variance: the Expressive factor included the items Expression of emotion (N3), Experience of emotions and self (N4), and Ideational richness (N5), while the Experiential factor included the items Social anhedonia (N1) and Avolition (N2). The loading was high for all items (>0.75); avolition, while reaching the 0.50 loading criterion, had a rather low value (0.56).[77] A possible explanation of the reduced loading might be that, in the SIPS, Avolition (N2), and Experience of emotions and self (N4) include partially overlapping constructs. In fact, N4 rates a "sense of having no feelings: anhedonia, apathy, loss of interest, boredom", thus possibly leading to the evaluation of some aspects (eg, apathy) rated as avolition with other scales in the N4 item instead of N2.

The confirmatory factor analysis showed that, although none of the three models (one-factor, two-factor, and hierarchical models) met all criteria of a good fit, the 2-factor model and the hierarchical model had the best fit, with a small advantage of the 2-factor model.

In the UHR population, only one study investigated the factor structure of negative symptoms using the PANSS,[65] two studies used the adapted version of the BNSS[66, 67] and only one study used the SIPS.[64] Lam et al[65]

Table 6. Demographic and Clinical Characteristics of the UHR Nonconverters (N = 55) and Converters (N = 16) at Study Inclusion

	UHR Nonconverter (N = 55)	UHR Converter (N = 16)	F	P Value
Age, *y* (Mean ± SD)	13.99 ± 2.08	13.66 ± 2.09	0.31	.59
Education, *y* (mean ± SD)	8.45 ± 2.07	8.25 ± 2.08	0.12	.73
Sex, Male *N* (%)	33 (60)	9 (56.25)		.79
Current IQ (Mean ± SD)	96.25 ± 18.87	90.50 ± 19.24	1.14	.29
Total SIPS (Mean ± SD)	46.89 ± 13.28	49.75 ± 13.03	0.58	.45
Positive Subscale (SIPS-P; Mean ± SD)	11.04 ± 4.38	13.44 ± 2.94	4.22	.04
Negative Subscale (SIPS-N; Mean ± SD)	17.16 ± 6.24	16.63 ± 6.41	0.09	.76
Disorganization Subscale (SIPS-D; Mean ± SD)	8.51 ± 4.12	8.75 ± 3.53	0.04	.83
General Psychopathology Subscale (SIPS-G; Mean ± SD)	10.18 ± 3.94	10.94 ± 3.99	0.45	.50
C-GAS (Mean ± SD)	48.91 ± 3.48	46.50 ± 4.88	4.91	.03
GAF: Role (Mean ± SD)	3.98 ± 0.53	3.75 ± 0.44	2.56	.11
GAF: Social (Mean ± SD)	4.02 ± 0.53	3.81 ± 0.40	2.08	.15

Note: SD, Standard Deviations; SIPS, Structured Interview for Psychosis-Risk Syndromes; C-GAS, Children's Global Assessment Scale; GAF: Role, Global Assessment of Functioning: Role; GAF: Social, Global Assessment of Functioning: Social.

Table 7. Negative Symptoms in the UHR Nonconverter (N = 55) and UHR Converter (N = 16) Samples at Baseline

	UHR Nonconverter (N = 55)	UHR Converter (N = 16)	F	P Value
SIPS N1 Social Anhedonia	3.13 ± 1.55	3.25 ± 1.291	0.08	.77
SIPS N2 Avolition	2.87 ± 1.43	2.19 ± 1.328	2.94	.09
SIPS N3 Decreased Expression Of Emotion	2.73 ± 1.53	2.81 ± 1.682	0.04	.85
SIPS N4 Decreased Experience Of Emotion And Self	2.82 ± 1.56	2.94 ± 1.843	0.07	.80
SIPS N5 Decreased Ideational Richness	2.58 ± 1.58	2.31 ± 1.740	0.34	.56

Note: SIPS: Structured Interview for Psychosis-Risk Syndromes.

confirmed the two-factor solution of the PANSS in UHR population but included items that are not conceptualized as negative symptoms, such as motor retardation and active social avoidance.[26, 34, 68] The 5-factor model of the adapted version of the BNSS provided the best fit, thus suggesting that, similar to the chronic phase of schizophrenia, the latent structure of negative symptom is best conceptualized in relation to the 5 consensus domains in the UHR populations too.[66] Only Azis et al[64] examined the factor structure of the SIPS negative subscale and reported a two-factor structure[64]; however, the items loadings on each factor differ from our results, as in that study the Experiential factor included occupational functioning and avolition, and the Expressive factor included expression of emotion, experience of emotions, and self and social anhedonia. The discrepancy may be due to our choice of excluding the item "deterioration in role functioning (N6)" from the analysis because it is unrelated to negative symptoms and in overlap with functional outcome.

When controlling for the severity of the positive symptomatology, we found that only the Experiential factor was associated with role functioning. This is in line with several other studies in UHR subjects, in which role functioning was reported in association with the negative symptom factor "social amotivation"[65]/"volition"[64]/"amotivation"[67] but not, or only weakly, with the factor "Diminished Expression"/"Emotion".[65, 67]

Conversion Rate and Comparison between Converters and Nonconverters

In our study, at the end of the 12 months follow-up, 16 (22.5%) participants converted to psychosis. Converters did not differ significantly from nonconverters (N = 55; 77.5%) for demographic data or IQ, though nonconverters showed an IQ score about 6 points higher (96.25) than converters (90.50). Unlike other studies conducted in high-risk samples,[4, 5, 16, 18, 23, 25, 30, 31] in our study converters did not differ from nonconverters for the baseline severity of negative symptoms. The wide range of clinical presentations of the UHR population might account for this discrepancy[81]: our participants were recruited at a Children and Adolescents Neuropsychiatric Unit for suspected early-onset psychosis and, therefore, are likely to represent the severe spectrum of the UHR state with high rates of positive symptoms; also they are not affected by the risk-dilution effect described for samples recruited

from the community or mental health services.[82] In addition, we cannot rule out the possibility that the 1-year follow-up of our study is not enough to intercept the difference between converters and nonconverters in this psychopathological domain. It is reported that studies with a longer follow-up (2–3 years) reveal a significant difference at baseline between converters and nonconverters for negative symptoms.[17, 22]

In our sample, negative symptoms did not differ at baseline between converters and nonconverters, but were associated with a worse functional outcome. Considering that most UHR individuals do not convert to psychosis but do show poor long-term outcomes, including nonpsychotic disorders and poor psychosocial functioning,[18, 83, 84] we might speculate that our findings support a transdiagnostic conceptualization of the UHR status and of negative symptoms.[85]

Strengths and Limitations

The strengths of our data stem from the investigation of negative symptoms in a sample of UHR children and adolescents. The paucity of studies conducted in UHR children and adolescents[18, 52, 69] justifies research aimed to define the frequency and severity of negative symptoms in this population and the contribution of this psychopathological dimension to psychosis transition.

As to the factor structure of negative symptoms in UHR subjects, only one study has previously been conducted using the SIPS negative subscale.[64] Our data add to previous findings investigating exclusively core negative symptoms (thus excluding the item N6 which evaluates the functioning) in early at-risk stages.

Some limitations should be acknowledged. First, the sample size could limit the generalizability of our results and may lead to computational difficulties for the factor analysis. However, according to Everitt,[86] sample size for factor analysis requires a minimum of 10 subjects per item, and this requirement has been respected in our analysis. Second, the results of the CFA did not show a good fit, and, therefore, a replication in an independent sample is needed. Third, the 1-year follow-up period might not be sufficient to detect the real rate of conversion and have a clear-cut picture of the differences between converters and nonconverters, as the nonconverter group might still include several future converters. In addition, the SIPS, although developed for the UHR population, presents important limitations for the evaluation of negative symptoms. In particular, the scale does not cover the five negative symptom domains, as defined by the NIMH consensus statement, and therefore is not in line with the current conceptualization of negative symptoms, and contains an item N6 (deterioration in role functioning) that is in overlap with functioning.[26, 27] Actually, we tried to overcome the latter limitation by excluding the item from our analyses.

Conclusions

In conclusion, our study showed the presence of negative symptoms in all tested UHR subjects aged between 9 and 17 years. Negative symptoms clustered in two separate factors, the Experiential and the Expressive factors. Only the "Experiential" factor was associated with real-life functioning. At baseline, only positive symptoms significantly differed between converters and nonconverters UHR. Replications by independent studies, with larger sample size, state-of-the-art assessment tools, and a longer follow-up in young UHR subjects from different clinical and nonclinical contexts, are needed to improve the characterization of negative symptoms in this population, clarify their impact on clinical and functional outcome and enhance early identification, prevention and treatment of severe mental disorders.

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