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The Brief Negative Symptom Scale (BNSS): Independent validation in a large sample of Italian patients with schizophrenia

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Abstract

Background

The Brief Negative Symptom Scale (BNSS) was developed to address the main limitations of the existing scales for the assessment of negative symptoms of schizophrenia. The initial validation of the scale by the group involved in its development demonstrated good convergent and discriminant validity, and a factor structure confirming the two domains of negative symptoms (reduced emotional/verbal expression and anhedonia/asociality/avolition). However, only relatively small samples of patients with schizophrenia were investigated. Further independent validation in large clinical samples might be instrumental to the broad diffusion of the scale in clinical research.

Methods

The present study aimed to examine the BNSS inter-rater reliability, convergent/discriminant validity and factor structure in a large Italian sample of outpatients with schizophrenia.

Results

Our results confirmed the excellent inter-rater reliability of the BNSS (the intraclass correlation coefficient ranged from 0.81 to 0.98 for individual items and was 0.98 for the total score). The convergent validity measures had r values from 0.62 to 0.77, while the divergent validity measures had r values from 0.20 to 0.28 in the main sample ($n = 912$) and in a subsample without clinically significant levels of depression and extrapyramidal symptoms ($n = 496$). The BNSS factor structure was supported in both groups.

Conclusions

The study confirms that the BNSS is a promising measure for quantifying negative symptoms of schizophrenia in large multicenter clinical studies.

Keywords

Schizophrenia; Negative symptoms; Primary negative symptoms; Poor emotion expression; Avolition

1. Introduction

Negative symptoms are a core feature of schizophrenia and account for much of the long-term morbidity and poor functional outcome of people with this disorder [7], [10], [12], [13], [23], [29] and [39]. However, there is a considerable debate as to which aspects of psychopathology should be considered as part of the negative symptom construct and whether this construct is a unitary one. These questions are important, since the accurate and consistent assessment of negative symptoms is crucial to determine the efficacy of new antipsychotic medications and non-pharmacological treatments [11], [24], [30], [31], [32] and [36].

The Scale for the Assessment of Negative Symptoms (SANS) [3] and the Positive and Negative Syndrome Scale (PANSS) [20] are currently the standard scales used to assess negative symptoms. For some experts, the SANS is preferable to the PANSS as it includes more items for each domain of negative symptoms and has clinically meaningful cut-off values which can be used in drug trials assessing negative symptoms improvement [32]. However, both the SANS and the PANSS do not cover the full range of negative symptoms, and include items that are not part of the negative symptoms construct, such as “attention” for the SANS and “abstract/stereotyped thinking” for the PANSS [2], [8], [18] and [24]. Factor analytic studies have suggested that these latter items do not cluster together with negative symptoms and do not reflect core aspects of the negative symptoms domain [17], [43] and [45].

A further problem with the above scales is that they explicitly instruct raters to only consider behavior even for the assessment of items referring to experiential deficits. This limitation is particularly problematic in the case of anhedonia, whose assessment should be focused on the subjective experience of pleasure, differentiating it from social functioning and other subjective experiences such as decreased interest, energy or will.

Furthermore, those scales fail to distinguish between consummatory and anticipatory anhedonia, a distinction which has important implications for the appropriate measurement of this domain, and may lead to more targeted treatments [4], [6], [14], [18] and [27].

These limitations are common to the Negative Symptom Assessment Scale (NSA) [2] and [8]. Furthermore, this scale also includes a rating of reduced emotional range encompassing both anhedonia and the lack of negative emotional experiences (such as anxiety, sadness, or anger). This rating may score high in individuals who have a generally healthy emotional functioning but experienced no negative emotional events during the observation period.

In all the above scales, negative symptoms that may be considered secondary to other factors (i.e., positive symptoms, depression or extrapyramidal side effects) are rated in a similar manner to primary negative symptoms. Another measure, the Schedule for the Deficit Syndrome (SDS) [22], allows to characterize negative symptoms according to their persistence and clinical stability, and to exclude that they are secondary to factors such as anxiety, effects of medications, suspiciousness and other psychotic symptoms, depression or mental retardation [12] and [22]. However, information about the longitudinal course of the symptoms, required to make the primary/secondary distinction, may not always be readily available. In addition, the differentiation between primary and secondary negative symptoms requires a level of sophistication beyond what is usually available in clinical settings. Furthermore, similarly to the NSA-16, the SDS includes a rating of reduced emotional range that encompasses both anhedonia and the lack of negative emotional experiences [12] and [18].

In 2006, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Development Conference on Negative Symptoms of the U.S. National Institute of Mental Health (NIMH) recommended the development of new negative symptom assessment instruments addressing the limitations of current scales, distinguishing between anticipatory and consummatory aspects of anhedonia, and evaluating the subject's desire for relationships [24]. In line with these recommendations, the Brief Negative Symptom Scale (BNSS) [26] was designed. This scale acknowledges that negative symptoms cluster in two factors, “reduced emotional/verbal expression” and “anhedonia/asociality/avolition”, as observed for the SDS [12], [21] and [40] and reported for BNSS by two factor analytic studies [26] and [41].

The initial validation of the BNSS demonstrated strong inter-rater reliability, internal consistency, stability, and convergent/discriminant validity [26] and [42]. However, only relatively small samples of patients with schizophrenia have been investigated to date by the group of researchers involved in the scale development. It remains to be proven that BNSS psychometric properties hold in large and representative clinical samples, and validation in non-English languages is needed. To date, only a Spanish version of the BNSS has been validated in a small sample of patients, providing evidence of adequate psychometric properties both in terms of reliability and validity, similarly to the original scale [35].

The current study aimed to explore the inter-rater reliability, convergent/discriminant validity and factor structure of the Italian version of the BNSS [37] in a large sample of stabilized outpatients with schizophrenia, recruited within an Italian multicenter study [13]. The assessment was conducted both in the whole sample of recruited subjects and in a subsample excluding subjects with confounding levels of depression and/or parkinsonism.

2. Methods

2.1. Study participants

The study subjects were recruited from those living in the community and attending the outpatient units of the 26 Italian university psychiatric clinics and/or community mental health departments composing the Italian Network for Research on Psychoses (details on the study procedures and assessed measures can be found elsewhere) [13]. Inclusion criteria were a clinical diagnosis of schizophrenia according to DSM-IV, confirmed by the Structured Clinical Interview for DSM-IV–Patient version (SCID-IP) [9], and an age range between 18 and 65 years. Exclusion criteria were: history of head trauma with loss of consciousness; history of moderate to severe mental retardation or neurological diseases; history of alcohol and/or substance abuse in the last six months; current pregnancy or lactation; inability to provide an informed consent; and treatment modifications and/or hospitalization due to symptom re-exacerbation in the last three months. All participants provided a written informed consent for participation after receiving a comprehensive explanation of the nature of the investigation. The study was approved by the ethics committees of the 26 university centers.

2.2. Instruments

2.2.1. Brief Negative Symptom Scale (BNSS)

The BNSS [26] has 13 items, organized into six subscales: anhedonia, distress, asociality, avolition, blunted affect and alogia. The scale includes a manual, a score sheet and a workbook. The manual defines the terms used in the scale, provides anchors for each item, and gives instructions for a semi-structured interview, including suggested questions. The workbook extracts the suggested questions and the anchors and is designed for rater's reference during administration.

For all items of the six subscales, higher scores are associated with greater impairment/presence of symptoms, with the exception of the distress item, for which the highest score is associated with the absence of negative emotions. A scale total score is calculated by summing the 13 individual items; subscale scores are calculated by summing the individual items within each subscale. The distress subscale has only one item, which quantifies the absence of distress, but this subscale is otherwise treated in the same manner as the other subscales. The BNSS has possible total scores ranging from 0 to 78.

The Italian version of the BNSS was developed using the translation–backtranslation method [37]. The manual, scoresheet and workbook were translated into Italian by two Italian psychiatrists (SG and AM). The translated version was then backtranslated into English by an English teacher. The backtranslated version was reviewed and approved by one of the original developers of the scale (Brian Kirkpatrick).

2.2.2. Other instruments

Two measures were considered to characterize the sample and for use in the convergent/discriminant validity analyses:

- the PANSS, to investigate general psychopathology, positive and negative symptoms;
- the Calgary Depression Scale for Schizophrenia (CDSS) [1], to assess depressive symptoms.

The PANSS is one of the most widely used instruments for the standardized measurement of psychopathology in schizophrenia. The scale includes seven positive symptom items (delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness, hostility); seven negative symptom items (blunted affect, emotional withdrawal, poor rapport, passive-apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotyped thinking); and 16 general psychopathology items (somatic concern, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation, active social avoidance). All 30 PANSS items are rated on a 7-point symptom severity scale, ranking from 1 (absent) to 7 (extremely severe). The PANSS is scored by summation of ratings across items, to yield the positive, negative and general psychopathology subscale scores, and a total score.

The CDSS includes nine items (depression, hopelessness, self depreciation, guilty ideas of reference, pathological guilt, morning depression, early wakening, suicide, observed depression), each rated from 0 (absent) to 3 (severe). Ratings > 6 on the total score indicate clinically significant depression [1]. The Italian translation of the CDSS is available on the official website (<http://www.ucalgary.ca/cdss/>) and has been validated [34].

An additional measure, the St. Hans Rating Scale (SHRS) [15], was used to investigate the presence of extrapyramidal symptoms, whose assessment is required to exclude that the observed negative symptoms are secondary to them. It is a multidimensional rating scale comprising four subscales: hyperkinesias, parkinsonism, akathisia and dystonia. Each subscale includes one or more items, with a score ranging from 0 (absent) to 6 (severe). Clinically significant extrapyramidal symptoms, which might confound the assessment of negative symptoms, were defined by a “mild” (2) rating on at least three items, or a “mild” rating for tremor or rigidity plus a “mild” rating on at least another item, or a “mild-moderate” (3 or more) rating on at least one item.

2.3. Training of the raters and inter-rater reliability assessment

For each instrument, the coordinating center (Department of Psychiatry, University of Naples SUN) recorded three interviews to patients with schizophrenia (who were not recruited for the study). These interviews were used for the inter-rater agreement evaluation. Raters were 26 research staff members, one from each of the 26 Italian university psychiatric clinics. None of them was aware of the ongoing validation of the Italian version of the BNSS as an add-on of the main study [13]. Although all raters had extensive prior experience in conducting research interviews, they participated in a training workshop on the instruments used in the study that focused on inter-rater reliability. The inter-rater reliability was evaluated by intraclass correlation coefficient (ICC). Details on the inter-rater reliability for PANSS and CDSS are reported elsewhere [13].

2.4. BNSS construct validity

The construct validity of the BNSS was assessed by evaluating its convergent and discriminant validity as well as its factor structure. Convergent validity was evaluated by examining the association of the BNSS total score with the PANSS negative subscale and total scores. Discriminant validity was assessed by examining correlations between the BNSS total score and PANSS positive subscale score and CDSS total

score, as well as between the BNSS anhedonia subscale and item scores with CDSS total score. The Pearson correlation coefficient was used for correlations with PANSS, while the Spearman rho was used for correlations with CDSS, as score distribution deviated from normality for the latter scale.

Given the large number of cases, correlations were interpreted taking into account the absolute value of the correlation coefficient rather than its significance. In fact, for sample sizes > 200, even a correlation coefficient of 0.10 is significant at $P < 0.01$ but has no clinical significance. Correlation coefficients (in absolute value) ≤ 0.35 are generally considered to represent low or weak correlations, those from 0.36 to 0.67 modest to moderate correlations, and those from 0.68 to 1.0 strong correlations.

Exploratory factor analysis was deemed appropriate as the two previous studies investigating BNSS factor structure were not independent [26] and [41]. A principal axis factoring (PAF) was used for factor extraction. PAF is an exploratory factor analysis, which takes into account the shared variance in a set of measured variables through a small set of latent variables (extracted factors). Although the optimal method of factor extraction is not consistently indicated by the relevant literature [26], [33] and [41], PAF is the method most commonly used to investigate whether a scale has a unitary or multifactor structure. An oblique rotation with Kaiser normalization was then used, to take into account the possible correlation among factors. The BNSS factor structure was investigated in both the main sample of recruited subjects and in the subsample of subjects without clinically relevant depression or extrapyramidal symptoms. 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 > 0.70) after promax rotation were used to interpret the extracted factors. The maximum number of iterations was set to 25 both for extraction and rotation.

The sampling adequacy was assessed by Kaiser-Meyer-Olkin (KMO) index. KMO varies between 0 and 1, and a value close to 1 indicates that the factor analysis should yield distinct and reliable factors. Values between 0.7 and 0.8 are good, those between 0.8 and 0.9 are very good and those above 0.9 are excellent. Furthermore, Bartlett's test of sphericity was carried out. The latter test is used to reject the null hypothesis that the correlation matrix is an identity matrix, which would not be suitable for factor analysis. A significant ($P < 0.05$) Bartlett's test rejects the null hypothesis. Taken together, these tests provide a minimum standard for factor analysis suitability.

The software used for all statistical analyses was SPSS 20 (IBM SPSS Statistics).

3. Results

Nine hundred thirty-seven patients with a diagnosis of schizophrenia were recruited for the main study [13]. Nine hundred twelve (i.e., 97.3% of the subjects) had a complete data set with respect to the considered measures and were included in the present investigation.

Patients' demographic and clinical characteristics are presented in **Table 1**. They were predominantly males, with a mean age of 40 years, with a mean education level of 11 years, mostly unmarried and unemployed, in a chronic phase of the illness. Almost all patients were treated with antipsychotics (97%), mostly with second-generation drugs (Table 1).

3.1. Inter-rater reliability

The ICC on the three recorded interviews was greater than 0.80 for each item and was 0.98 for the BNSS total, indicating an excellent inter-rater reliability among researchers from the 26 sites (**Table 2**).

3.2. Convergent validity

The analysis showed that the BNSS total score was highly correlated with the PANSS negative subscale score, in both the main sample of patients and in the subsample without clinically significant parkinsonism and/or depression (**Table 3A**). This correlation indicates good convergent validity, suggesting that both scales assessed a similar underlying construct of negative symptoms. The BNSS total score was moderately associated with PANSS total score (Table 3A), as the latter includes the negative subscale score.

3.3. Discriminant validity

The BNSS total score had weak correlations with positive symptoms, assessed by PANSS positive subscale ($r = 0.26$), and with CDSS total score ($r = 0.28$). The same correlations were found when excluding patients with clinically significant extrapyramidal side effects and depressive symptoms, as reported in Table 3A. The CDSS total score was weakly correlated with BNSS anhedonia subscale and item scores (Table 3B).

3.4. Factor structure

Sampling adequacy was found to be excellent for both the main sample ($n = 912$) and the subsample without clinical significant depression and/or parkinsonism ($n = 496$) ($KMO = 0.91$ for both samples; Bartlett's test: $\chi^2(78) = 13211.94$, $P < 0.0001$ for the main sample and $\chi^2(78) = 7473.73$, $P < 0.0001$ for the subsample).

PFA on BNSS scores extracted two factors, after three iterations, explaining 75.3% of the variance in the whole sample. Table 4 shows the factor loadings after normalized promax rotation. The first factor was interpreted as “avolition”, including intensity and frequency of pleasure during activities, intensity of expected pleasure from future activities, asociality behavior and inner experience, avolition behavior and inner experience; while the second factor was “poor emotional expression”, including facial and vocal expression, expressive gestures, quantity of speech and spontaneous elaboration. The item distress (measuring lack of normal distress) did not reach the 0.70 loading criterion but still had a high load on the first factor “avolition”.

4. Discussion

The present study sought to examine the inter-rater reliability, the convergent and discriminant validity as well as the factor structure of the BNSS within a multisite study including a large sample of patients with schizophrenia. Our results demonstrate that an excellent inter-rater reliability can be achieved among researchers even after a relatively brief specific training, making the instrument suitable for large clinical trials. The convergent validity of BNSS was supported by the strong correlation with PANSS negative factor,

and the moderate correlation with the PANSS total score. The discriminant validity was documented by the low correlations with PANSS positive subscale and CDSS total score. Furthermore, as depression might confound the assessment of anhedonia, the discriminant validity of BNSS anhedonia subscale and relevant items was explored versus CDSS, and demonstrated by the very low correlations with CDSS total score.

The low correlation between the BNSS anhedonia subscale and CDSS total score suggests that the experience of pleasure during an activity (with intensity and frequency rated separately) or the anticipated pleasure from a future activity measured by the subscale are separable from affective symptoms. These results are consistent with the previously reported evidence that negative symptoms are largely independent of other symptom domains [5]. The differentiation between depression and negative symptoms is difficult on the basis of both clinical phenomenology and rating scales, and therapeutic effects on depressive symptoms might be misinterpreted as successful treatment of negative symptoms and vice versa. The BNSS discriminant validity versus a rating scale commonly used to assess depression in schizophrenia is of particular importance in clinical trials assessing the effects of new medications or psychosocial interventions on negative symptoms.

Our results replicate the preliminary findings of Kirkpatrick et al. [26] and Strauss et al. [41] in a large sample of patients with schizophrenia. In our study, it was also possible to confirm the BNSS convergent and discriminant validity in a sample without clinically significant levels of parkinsonism or depression. We chose to validate BNSS psychometric properties in chronic, clinically stable patients with schizophrenia with and without clinically significant depression and parkinsonism, as they are the potential target of proof of concept and clinical trials for the development of innovative treatments for negative symptoms. As a matter of fact, our criteria for selection of a large sample of patients with schizophrenia are in line with European Medicines Agency (EMA) guidelines on drug approval for negative symptoms, requiring that major confounding factors, i.e. extrapyramidal symptoms and depression, be excluded.

The results of our factor analysis replicated, in the largest sample of patients examined so far, the two-factor structure reported in other studies [26] and [41], consistent with the underlying constructs of anhedonia/avolition and poor emotional expressivity. Other instruments have produced less clear factor loadings [19], [36] and [38]. Our results in patients without depression and extrapyramidal symptoms confirm the factor structure of primary and persistent negative symptoms as assessed in three studies using the SDS [12], [21] and [40]. The evaluation of these two endpoints separately might be important, because it is unknown whether they might respond to different treatment options [16], [24] and [36]. However, whether the BNSS factors can be described as multiple dimensions within the scale is still not proven, and in clinical trials the total sum of all BNSS items should be used as primary outcome measure [41]. Studies investigating external validators of the two factors are needed. The results of the main study [13] carried out by the Italian Network for Research on Psychoses clearly showed that the avolition factor had a strong direct effect and multiple indirect effects on real-life functioning of patients with schizophrenia, while the factor poor emotional expression had only a modest indirect effect on functioning through functional capacity. The independent confirmation of the factor structures and of their relationship with outcome and functional capacity might lead to the use of the two factors as secondary outcome measures. These factors include several items and might be preferable, in terms of psychometric properties, to the five negative symptoms domains, which only include two-three items each and might not be suitable for use as endpoints. Overall, the inclusion of only 13 items for six domains might represent a limitation of the scale, especially for clinical trials, unless it is confirmed that the inclusion of a reduced number of items has psychometric advantages, as it was demonstrated for both SANS [30] and the final version of the CAINS [28].

In our study, the distress item did not load clearly on either factor. Our communality data indicated that this item does not fit well with the factor solution, suggesting that it does not represent a domain of negative symptoms [26]. Some studies have reported that a measure of distress in combination with the negative symptom scores might help to delineate patient groups with and without primary negative symptoms [25], [38] and [44], and some authors have proposed this method to characterize deficit and nondeficit patients [26]. However, further studies will be needed to determine whether this item can serve this purpose or be useful in other ways. We cannot exclude that, in our sample of chronic stabilized patients, the distress item had a reduced variance, and for this reason did not load in either factor.

In conclusion, our findings indicate that the BNSS is a promising measure for quantifying negative symptoms of schizophrenia in large multicenter clinical studies. Future studies will need to provide data on the relative sensitivity to change and global suitability of the BNSS vs. earlier generation scales.

Disclosure of interest

A.M. received fees from the following companies, for the described activities: Amgen Dompè for advisory board and Janssen-Cilag for educational activity.

S.G. received honoraria from the following companies, for the described activities: Janssen-Cilag and Eli-Lilly for lectures; Amgen-Dompé and Gedeon-Richter for Advisory boards.

P.R. received honoraria from the following companies, for the described activities: Roche for lectures and Janssen-Cilag for Advisory boards.

All other authors declare that they have no conflicts of interest concerning this article.

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Table 1.

Patients' demographic and clinical characteristics (*n* = 912).

Males (%)	69.8
Age (years, mean±SD)	40.1±10.7
Unmarried (%)	86.1
Education (years, mean±SD)	11.7±3.4
Working (%)	29.4
Pension (%)	5.8
Duration of illness (years, mean±SD)	16.1±10.6
PANSS total (mean±SD)	75.2±22.9
PANSS positive subscale (mean±SD)	16.0±6.7
PANSS negative subscale (mean±SD)	21.9±8.6
PANSS general psychopathology (mean±SD)	37.3±11.7
CDSS total (mean±SD)	4.0±4.0
Antipsychotic treatment (%)	
First generation	14.1
Second generation	69.1
Both	13.8
None	3.0

PANSS: Positive and Negative Syndrome Scale; CDSS: Calgary Depression Scale for Schizophrenia.

Table 2.

Inter-rater reliability for the Brief Negative Symptom Scale (BNSS).

	ICC
Anhedonia	
1. Intensity of pleasure during activities	0.86
2. Frequency of pleasure during activities	0.81
3. Intensity of expected pleasure from future activities	0.92
Distress	
4. Distress	0.94
Asociality	
5. Asociality: behavior	0.82
6. Asociality: inner experience	0.88
Avolition	
7. Avolition: behavior	0.89
8. Avolition: inner experience	0.95
Blunted affect	
9. Facial expression	0.98
10. Vocal expression	0.97
11. Expressive gestures	0.96
Alogia	
12. Quantity of speech	0.92
13. Spontaneous elaboration	0.97
Total score	0.98

ICC: Intraclass correlation coefficient.

Table 3.

BNSS convergent and discriminant validity (*r*-values) in the main sample (*n* = 912) and in the subsample without clinically significant levels of depression and extrapyramidal symptoms (*n* = 496).

A				
	BNSS total score (main sample)	<i>P</i> value	BNSS total score (subsample without depression and extrapyramidal symptoms)	<i>P</i> value
Convergent validity				
PANSS negative subscale	0.76	<0.00001	0.77	<0.001
PANSS total score	0.64	<0.00001	0.62	<0.001
Discriminant validity				
PANSS positive subscale	0.23	<0.00001	0.24	<0.001
CDSS total score	0.28	<0.00001	0.24	<0.001
B				
	CDSS total score (main sample) ^a	<i>P</i> value [*]	CDSS total score (subsample without depression and extrapyramidal symptoms) ^a	<i>P</i> value [*]
Discriminant validity				
BNSS anhedonia subscale	0.27	<0.00001	0.21	<0.001
Item 1: intensity of pleasure during activities	0.26	<0.00001	0.20	<0.001
Item 2: frequency of pleasure during activities	0.28	<0.00001	0.22	<0.001
Item 3: intensity of expected pleasure from	0.25	<0.00001	0.20	<0.001

B				
	CDSS total score (main sample) ^a	<i>P</i> value [*]	CDSS total score (subsample without depression and extrapyramidal symptoms) ^a	<i>P</i> value [*]
future activities				

The Pearson's *r* is reported except when specified; BNSS: Brief Negative Symptom Scale; PANSS: Positive and Negative Syndrome Scale; CDSS: Calgary Depression Scale for Schizophrenia.

^a Spearman's rho.

^{*} Due to the large sample size, *P* values are generally highly significant even for very low correlation coefficients.

Table 4.

Severity ratings and factor loadings (after normalized promax rotation) for broadly defined negative symptoms as assessed by the Brief Negative Symptom Scale (BNSS) in the main sample of subjects with schizophrenia ($n = 912$).

	Mean severity (mean \pm SD)	Principal axis factoring with promax rotation	
		Factor 1 Avolition	Factor 2 Poor emotional expression
Item 1: intensity of pleasure during activities	2.85 \pm 1.57	0.89	0.65
Item 2: frequency of pleasure during activities	2.95 \pm 1.59	0.89	0.62
Item 3: intensity of expected pleasure from future activities	2.82 \pm 1.62	0.86	0.62
Item 4: distress	2.44 \pm 1.60	0.61	0.48
Item 5: asociality: behavior	3.30 \pm 1.60	0.79	0.61
Item 6: asociality: inner experience	3.03 \pm 1.61	0.78	0.59
Item 7: avolition: behavior	2.88 \pm 1.66	0.83	0.71
Item 8: avolition: inner experience	2.80 \pm 1.62	0.82	0.66
Item 9: facial expression	2.72 \pm 1.70	0.71	0.90
Item 10: vocal expression	2.64 \pm 1.80	0.71	0.92
Item 11: expressive gestures	2.70 \pm 1.79	0.70	0.91
Item 12: quantity of speech	2.26 \pm 1.77	0.60	0.85
Item 13: spontaneous elaboration	2.53 \pm 1.84	0.62	0.85
Eigenvalue		8.52	1.27
% Extracted variance		65.54	9.73

Table 5.

Severity ratings and factor loadings (after normalized promax rotation) for broadly defined negative symptoms as assessed by the Brief Negative Symptom Scale (BNSS) in the subsample of subjects with schizophrenia without clinically significant levels of depression and extrapyramidal symptoms ($n = 496$).

	Mean severity (mean \pm SD)	Principal axis factoring with promax rotation	
		Factor 1 Avolition	Factor 2 Poor emotional expression
Item 1: intensity of pleasure during activities	2.49 \pm 1.54	0.89	0.68
Item 2: frequency of pleasure during activities	2.56 \pm 1.56	0.88	0.66
Item 3: intensity of expected pleasure from future activities	2.46 \pm 1.58	0.87	0.67
Item 4: distress	2.07 \pm 1.56	0.61	0.46
Item 5: asociality: behavior	2.92 \pm 1.64	0.80	0.61
Item 6: asociality: inner experience	2.69 \pm 1.63	0.78	0.58
Item 7: avolition: behavior	2.40 \pm 1.63	0.84	0.70
Item 8: avolition: inner experience	2.39 \pm 1.59	0.82	0.65
Item 9: facial expression	2.28 \pm 1.69	0.73	0.90
Item 10: vocal expression	2.13 \pm 1.71	0.73	0.92
Item 11: expressive gestures	2.23 \pm 1.72	0.72	0.92
Item 12: quantity of speech	1.91 \pm 1.68	0.63	0.88
Item 13: spontaneous elaboration	2.18 \pm 1.75	0.64	0.88
Eigenvalue		8.46	1.23
% Extracted variance		67.03	9.45

References

[1] D. Addington, J. Addington, E. Maticka-Tyndale

Assessing depression in schizophrenia: the Calgary Depression Scale

Br J Psychiatry, 22 (Suppl.) (1993), pp. 39–44

[2] L.D. Alphs, A. Summerfelt, H. Lann, R.J. Muller

The negative symptom assessment: a new instrument to assess negative symptoms of schizophrenia

Psychopharmacol Bull, 25 (2) (1989), pp. 159–163

[3] N.C. Andreasen

The scale for the assessment of negative symptoms (SANS)

The University of Iowa, Iowa City, IA (1984)

[4] K.C. Berridge

The debate over dopamine's role in reward: the case for incentive salience

Psychopharmacology (Berl), 191 (3) (2007), pp. 391–431

[5] J.J. Blanchard, A.S. Cohen

The structure of negative symptoms within schizophrenia: implications for assessment

Schizophr Bull, 32 (2) (2006), pp. 238–245

[6] J.J. Blanchard, A.M. Kring, W.P. Horan, R. Gur

Toward the next generation of negative symptom assessments: the collaboration to advance negative symptom assessment in schizophrenia

Schizophr Bull, 37 (2) (2011), pp. 291–299

[7] W.C. Chang, C.L. Hui, S.K. Chan, E.H. Lee, G.H. Wong, E.Y. Chen

Relationship between diminished expression and cognitive impairment in first-episode schizophrenia: a prospective three-year follow-up study

Schizophr Res, 152 (1) (2014), pp. 146–151

[8] D.G. Daniel

Issues in selection of instruments to measure negative symptoms

Schizophr Res, 150 (2–3) (2013), pp. 343–345

[9] M.B. First, R.L. Spitzer, M. Gibbon, J.B. Williams

Structured clinical interview for DSM-IV axis I disorders, clinician version (SCID-CV)

American Psychiatric Press, Inc., Washington, DC (1996)

[10] G. Foussias, O. Agid, G. Fervaha, G. Remington

Negative symptoms of schizophrenia: clinical features, relevance to real world functioning and specificity versus other CNS disorders

Eur Neuropsychopharmacol, 24 (5) (2014), pp. 693–709

[11] S. Galderisi, M. Maj

Deficit schizophrenia: an overview of clinical, biological and treatment aspects

Eur Psychiatry, 24 (8) (2009), pp. 493–500

[12] S. Galderisi, P. Bucci, A. Mucci, B. Kirkpatrick, S. Pini, A. Rossi, et al.

Categorical and dimensional approaches to negative symptoms of schizophrenia: focus on long-term stability and functional outcome

Schizophr Res, 147 (1) (2013), pp. 157–162

[13] S. Galderisi, A. Rossi, P. Rocca, A. Bertolino, A. Mucci, P. Bucci, et al.

The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia

World Psychiatry, 13 (3) (2014), pp. 275–287

[14] D.E. Gard, A.M. Kring, M.G. Gard, W.P. Horan, M.F. Green

Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure

Schizophr Res, 93 (1–3) (2007), pp. 253–260

[15] J. Gerlach, S. Korsgaard, P. Clemmesen, A.M. Lauersen, G. Magelund, U. Noring, et al.

The St. Hans Rating Scale for extrapyramidal syndromes: reliability and validity

Acta Psychiatr Scand, 87 (4) (1993), pp. 244–252

[16] D.C. Goff

Future perspectives on the treatment of cognitive deficits and negative symptoms in schizophrenia

World Psychiatry, 12 (2) (2013), pp. 99–107

[17] P.D. Harvey, D. Koren, A. Reichenberg, C.R. Bowie

Negative symptoms and cognitive deficits: what is the nature of their relationship?

Schizophr Bull, 32 (2) (2006), pp. 250–258

[18] W.P. Horan, A.M. Kring, J.J. Blanchard

Anhedonia in schizophrenia: a review of assessment strategies

Schizophr Bull, 32 (2) (2006), pp. 259–263

[19] W.P. Horan, A.M. Kring, R.E. Gur, S.P. Reise, J.J. Blanchard

Development and psychometric validation of the Clinical Assessment Interview for Negative Symptoms (CAINS)

Schizophr Res, 132 (2–3) (2011), pp. 140–145

[20] S.R. Kay, A. Fizbein, L.A. Opler

The positive and negative syndrome scale (PANSS) for schizophrenia

Schizophr Bull, 13 (2) (1987), pp. 261–276

[21] D. Kimhy, S. Yale, R.R. Goetz, L.M. McFarr, D. Malaspina

The factorial structure of the schedule for the deficit syndrome in schizophrenia

Schizophr Bull, 32 (2) (2006), pp. 274–278

[22] B. Kirkpatrick, R.W. Buchanan, P.D. McKenney, L.D. Alphas, W.T. Carpenter Jr.

The Schedule for the Deficit Syndrome: an instrument for research in schizophrenia

Psychiatry Res, 30 (2) (1989), pp. 119–124

[23] B. Kirkpatrick, R.W. Buchanan, D.E. Ross, W.T. Carpenter Jr.

A separate disease within the syndrome of schizophrenia

Arch Gen Psychiatry, 58 (2) (2001), pp. 165–171

[24] B. Kirkpatrick, W.S. Fenton, W.T. Carpenter, S.R. Marder

The NIMH MATRICS consensus statement on negative symptoms

Schizophr Bull, 32 (2) (2006), pp. 214–219

[25] B. Kirkpatrick, E. Fernandez-Egea, C. Garcia-Rizo, M. Bernardo

Differences in glucose tolerance between deficit and nondeficit schizophrenia

Schizophr Res, 107 (2–3) (2009), pp. 122–127

[26] B. Kirkpatrick, G.P. Strauss, L. Nguyen, B.A. Fischer, D.G. Daniel, A. Cienfuegos, et al.

The Brief Negative Symptom Scale: psychometric properties

Schizophr Bull, 37 (2) (2011), pp. 300–305

[27] B. Knutson, G.W. Fong, C.M. Adams, J.L. Varner, D. Hommer

Dissociation of reward anticipation and outcome with event-related fMRI

Neuroreport, 12 (17) (2001), pp. 3683–3687

[28] A.M. Kring, R.E. Gur, J.J. Blanchard, W.P. Horan, S.P. Reise

The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation

Am J Psychiatry, 170 (2) (2013), pp. 165–172

[29] M.M. Kurtz, J.P. Moberg, J.D. Ragland, R.C. Gur, R.E. Gur

Symptoms versus neurocognitive test performance as predictors of psychosocial status in schizophrenia: a 1- and 4-year prospective study

Schizophr Bull, 31 (1) (2005), pp. 167–174

[30] S.Z. Levine, S. Leucht

Psychometric analysis in support of shortening the Scale for the Assessment of Negative Symptoms

Eur Neuropsychopharmacol, 23 (2013), pp. 1051–1056

[31] S.Z. Levine, S. Leucht

Attaining and sustaining remission of predominant negative symptoms

Schizophr Res, 143 (1) (2013), pp. 60–64

[32] S.Z. Levine, S. Leucht

Identifying clinically meaningful symptom response cut-off values on the SANS in predominant negative symptoms

Schizophr Res, 145 (1–3) (2013), pp. 125–127

[33] S.Z. Levine, J. Rabinowitz

Revisiting the 5 dimensions of the positive and negative syndrome scale

J Clin Psychopharmacol, 27 (5) (2007), pp. 431–436

[34] C. Maggini, A. Raballo

Exploring depression in schizophrenia

Eur Psychiatry, 21 (4) (2006), pp. 227–232

[35] A. Mané, C. García-Rizo, M.P. Garcia-Portilla, D. Bergé, G. Sugranyes, L. Garcia-Alvarez, et al.

Spanish adaptation and validation of the Brief Negative Symptoms Scale

Compr Psychiatry, 55 (7) (2014), pp. 1726–1729

[36] S.R. Marder, B. Kirkpatrick

Defining and measuring negative symptoms of schizophrenia in clinical trials

Eur Neuropsychopharmacol, 24 (5) (2014), pp. 737–743

[37] E. Merlotti, A. Mucci, P. Bucci, A. Nardi, S. Galderisi

Italian version of the “Brief Negative Symptom Scale”

J Psychopathol, 20 (2) (2014), pp. 199–215

[38] E. Messias, B. Kirkpatrick, E. Bromet, D. Ross, R.W. Buchanan, W.T. Carpenter Jr., et al.

Summer birth and deficit schizophrenia: a pooled analysis from 6 countries

Arch Gen Psychiatry, 61 (10) (2004), pp. 985–989

[39] P. Milev, B.C. Ho, S. Arndt, N.C. Andreasen

Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: a longitudinal first-episode study with 7-year follow-up

Am J Psychiatry, 162 (3) (2005), pp. 495–506

[40] M. Nakaya, K. Ohmori

A two-factor structure for the Schedule for the Deficit Syndrome in schizophrenia

Psychiatry Res, 158 (2) (2008), pp. 256–259

[41] G.P. Strauss, L.E. Hong, J.M. Gold, R.W. Buchanan, R.P. McMahon, W.R. Keller, et al.

Factor structure of the Brief Negative Symptom Scale

Schizophr Res, 142 (1–3) (2012), pp. 96–98

[42] G.P. Strauss, W.R. Keller, R.W. Buchanan, J.M. Gold, B.A. Fischer, R.P. McMahon, et al.

Next-generation negative symptom assessment for clinical trials: validation of the Brief Negative Symptom Scale

Schizophr Res, 142 (1–3) (2012), pp. 88–92

[43] M. van der Gaag, T. Hoffman, M. Remijnen, R. Hijman, L. de Haan, B. van Meijel, et al.

The five-factor model of the Positive and Negative Syndrome Scale II: a ten-fold cross-validation of a revised model

Schizophr Res, 85 (1–3) (2006), pp. 280–287

[44] X. Wang, S. Yao, B. Kirkpatrick, C. Shi, J. Yi

Psychopathology and neuropsychological impairments in deficit and nondéficit schizophrenia of Chinese origin

Psychiatry Res, 158 (2) (2008), pp. 195–205

[45] L. White, P.D. Harvey, L. Opler, J.P. Lindenmayer, The PANSS Study Group

Empirical assessment of the factorial structure of clinical symptoms in schizophrenia. A multisite, multimodel evaluation of the factorial structure of the Positive and Negative Syndrome Scale

Psychopathology, 30 (5) (1997), pp. 263–274