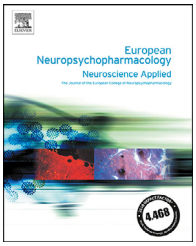
European Neuropsychopharmacology (2020) 33, 36–44



www.elsevier.com/locate/euroneuro

REVIEW

The brief negative symptom scale in translation: A review of psychometric properties and beyond

Kazunori Tatsumi[a,*], **Brian Kirkpatrick**[b], **Gregory P. Strauss**[c], **Mark Opler**[a]

[a] *WCG MedAvante-Prophase, LLC, New York, NY, United States*
[b] *Department of Psychiatry and Behavioral Sciences, University of Nevada, Reno School of Medicine, Reno, NV, United States*
[c] *Department of Psychology, University of Georgia, Athens, GA, United States*

Received 14 November 2019; received in revised form 26 January 2020; accepted 31 January 2020

KEYWORDS
BNSS;
Cross-culture;
Negative symptoms;
Psychometrics;
Schizophrenia;
Translation

Abstract
Negative symptoms are a core feature of schizophrenia and associated with social and occupational impairment. To encourage treatment development and address the limitations of existing rating instruments in this area across culture, the Brief Negative Symptoms Scale (BNSS) was developed. The authors reviewed studies published since the BNSS was published in 2010 that examined the psychometric properties of the instrument in translation and compared for consistency, psychometric performance and related features. Eleven published cross-cultural validation studies demonstrated the translated versions of the BNSS have strong psychometric properties, similar to the original English version. The internal consistency ranged from 0.88 to 0.98 and the inter-rater reliability ranged from 0.81 to 0.98 for the total score. The BNSS exhibited good convergent validity with existing measures of similar constructs and function, and good discriminant validity relative to other constructs. Recent research also reported that the BNSS is sensitive to drug effects, with effect sizes comparable to established scales. The results of confirmatory factor analyses revealed that the 5-factor structure of negative symptoms in schizophrenia (blunted affect, anhedonia, avolition, asociality, and alogia) crosses cultures. This psychometric evidence suggests that the BNSS is a valid and reliable instrument for assessing pathological mechanism underlying the negative symptoms of schizophrenia across cultures and can be a useful instrument in global clinical trials.
© 2020 Elsevier B.V. and ECNP. All rights reserved.

1. Introduction

It has been a decade since the Brief Negative Symptom Scale (BNSS) was developed and published first online in 2010

* Corresponding author.
E-mail address: kt2393@tc.columbia.edu (K. Tatsumi).

https://doi.org/10.1016/j.euroneuro.2020.01.018
0924-977X/© 2020 Elsevier B.V. and ECNP. All rights reserved.

(Kirkpatrick et al., 2011). The BNSS originally grew out of work done at the U.S. National Institute of Mental Health (NIMH) sponsored Consensus Development Conference on Negative Symptoms held in 20,005 (Kirkpatrick et al., 2006). The conference recognized five commonly accepted domains of negative symptoms including anhedonia, asocialty, avolition, blunted affect and alogia, and necessity of developing new assessments that measure these five constructs per modern conceptualizations.

As the BNSS is designed to assess the presence and severity of the five consensus domains of negative symptoms of schizophrenia, it is a second-generation negative symptom scale. The first-generation scales included negative symptoms as one of the elements of the overall evaluation of schizophrenia. Such scales include the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) and the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). The Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982, 1989) had more detailed evaluations and were intended to assess negative symptoms only, though it includes inappropriate affect and impaired attention items that are no longer considered as negative symptoms. The BNSS and Clinical Assessment Interview for Negative Symptoms (CAINS) (Kring et al., 2013) reflect the consensus points stated by the Consensus Development Conference.

The BNSS consists of 13 items which are organized into six subscales, consisting of the five consensus domains and an item that measures a decrease in normal distress. It is concise and can be rated following a 10–15 min interview. A manual with a semi-structured interview guide, a worksheet, and scoresheet are part of the scale and they were developed to standardize the scale administration and to achieve higher inter-rater reliability. Initial psychometric studies of the original English version of the BNSS demonstrated excellent psychometric properties, including inter rater reliability, test-retest reliability, internal consistency, convergent validity, discriminant validity, and construct validity (Strauss et al., 2012a, b).

To be applicable for use in clinical trials, newly developed scales require extensive validation across languages and cultures. When clinical trials are conducted internationally, it is imperative to attend to cultural influences on clinical assessment tools to help ensure that data can be properly interpreted across regions and be reasonably pooled for analysis. Cross-cultural literature has consistently shown that the expression of the same phenomena in psychiatry can differ substantially across cultures (Kirmayer, 2001). In schizophrenia specifically, prior studies demonstrate comparisons between populations on the same rating scale can reveal meaningful differences--including perceived importance by both patients and clinicians--on phenomena such as social withdrawal (Aggarwal et al., 2012). However, while expression and perceived clinical importance of symptoms may differ, some studies demonstrate that certain phenomenological structures are highly conserved, such as the relatively robust findings on factor analyses across cultures, particularly with respect to negative symptoms (Emsley et al., 2001).

In order to further these goals and to advance the assessment of negative symptoms, research studies have been focused on translating and testing the BNSS across languages and cultures. On the verge of the tenth anniversary, the present paper reviews the currently available translations and the reliability and validity results of cross-cultural studies that have used the BNSS in translation in populations in different countries are compared for consistency, psychometric performance, and related features. Qualitative comparisons and inquires, including clinician perceptions of the relative ease of use of the BNSS, the relevance of BNSS probes and items, most frequently asked questions and performance of the BNSS in the field will be also discussed.

2. Experimental procedures

2.1. Materials and method

All studies described in this report were either provided by authors or obtained from library sources and online databases, including Science Direct, PubMed, and Google Scholar. The identification of relevant studies was performed by the first author who has previous clinical and research experiences in psychometric assessments. The search terms used were: BNSS, psychometrics, validation, cross-cultural, validity, reliability, sensitivity, and specific language. After relevant articles were collected, the reference sections of the articles were carefully examined to identify additional studies for inclusion. The studies reviewed in this paper are limited to peer-reviewed professional articles (a) published during the last ten years, from June 2010 to November 2019, and (b) reported any one of the following data related to the psychometric properties of the BNSS: validity analysis such as convergent and/or discriminant validity; reliability analysis, including internal consistency, test-retest reliability and/or inter-rater reliability; factor analysis, and sensitivity. To evaluate the sensitivity to change of the BNSS, we included non-psychometric articles on neuroscience, interventional study, and randomized-controlled clinical trial in addition to the traditional psychometric research study.

2.2. Linguistic validation

The demand for translation has sharply risen as the BNSS is more frequently used in global clinical trials in addition to its use in academic research studies. To ensure the content and cultural validity of the clinical instrument, all BNSS translations produced to date and reviewed here underwent a state-of-the-art linguistic validation process including forward translation(s), backward translation, reconciliation of backward translation, clinician review(s), and final approval from the authors of the BNSS (BK and GPS). The BNSS has been translated into 29 languages (see Table 1) and of those, nine translated BNSS were psychometrically validated with the local population. In addition to the official language, common minority language(s) was developed for multilinguistic countries such as Latvia and Ukraine.

3. Results

3.1. Internal consistency

A total of 13 studies evaluated the internal consistency of the BNSS using the Cronbach's alpha test. The Cronbach's α coefficient for the entire scale ranged from 0.88 to 0.98, suggesting the 13-item BNSS had good to excellent internal consistency (see Table 2).

Table 1 Translations.

North/South America		Western Europe		Eastern Europe		Asia and Pacific	
Country	Language	Country	Language	Country	Language	Country	Language
US	English*	Czech	Czech	Bulgaria	Bulgarian	China	Chinese Simplified
US	Spanish	Denmark	Danish	Estonia	Estonian	Hong Kong	Chinese Traditional
Brazil	Portuguese	Netherland	Dutch	Estonia	Russian	Japan	Japanese
		France	French	Greece	Greek	South Korea	Korean
		Germany	German	Hungary	Hungarian		
		Italy	Italian	Latvia	Latvian		
		Norway	Norwegian	Latvia	Russian		
		Portugal	Portuguese	Poland	Polish		
		Spain	Spanish	Romania	Romanian		
				Russia	Russian		
				Serbia	Serbian		
				Turkey	Turkish		
				Ukraine	Ukrainian		
				Ukraine	Russian		

* English (US) can be used in United Kingdom.

3.2. Reliability

The inter-rater reliability of the BNSS has proven to be strong and quite consistent across languages, with statistics ranging from 0.81-0.98 for the total score. Only four studies reported test-retest reliability coefficients. English, Spanish and Chinese BNSS demonstrated good stability ($r = 0.81$-0.95).

3.3. Convergent and discriminant validity

US and Non-US studies reported that the BNSS total score was significantly correlated, but were not in effect redundant, with the BPRS negative symptom factor ($r = 0.68$ to 0.83), the PANSS negative subscale ($r = 0.42$ to 0.86), the PANSS Marder negative factor ($r = 0.87$), the PANSS negative factor described by Wallwork et al. (2012) ($r = 0.89$), and the SANS total score ($r = 0.68$ to 0.88), suggesting good convergent validity with existing measures of negative symptoms (see Table 3).

Concerning discriminant validity, low to null correlations between the BNSS total and the BPRS positive ($r = -0.11$ to -0.15), the PANSS positive subscale ($r = 0.09$ to 0.55), the PANSS Positive factor (r=−0.02), and the PANSS general ($r = 0.13$ to 0.63) were reported. The BNSS total scores were also not strongly correlated with the Calgary Depression Scale for Schizophrenia (CDSS: Addington et al., 1990) ($r = -0.01$ to -0.31), the Extrapyramidal Symptom Rating Scale (ESRS: Chouinard and Margolese, 2005) ($r = 0.22$), and the Simpson-Angus Extrapyramidal Side Effects Scale (SAS: Simpson and Angus, 1970) ($r = 0.30$), suggesting that these scores are not reflective of mood or extrapyramidal symptoms and the scale largely captures primary rather than secondary negative symptoms.

The BNSS total score also had a high inverse correlation with the Level of Function Scale (LOF: Hawk et al., 1975) total score (r= −0.68 to −0.71), the Global Assessment of Functioning (GAF: Frances et al., 1994) total score ($r = -0.69$), and the Personal and Social Performance Scale (PSP: Morosini et al., 2000) total score ($r = -0.70$), suggesting negative symptoms hinder daily life functioning in individuals with Schizophrenia. These functional assessments are not designed to assess psychiatric symptomatology or cognitive dysfunctions per se, thereby they are categorized as others in Table 3.

3.4. Construct validity

To understand the factor structure of BNSS, principle component analysis, exploratory- and confirmatory-factor analysis have been conducted. Table 4 lists 12 studies reporting the factor structure of the BNSS. Kirkpatrick et al. (2011) originally demonstrated construct validity of the BNSS using principal components analysis (PCA), which indicated the presence of two factors reflecting: (a) emotional expressivity and (b) motivation and pleasure that accounted for 71% of variance. Strauss et al. (2012b) carried out an exploratory factor analysis (EFA) and provided further evidence for the existence of two negative symptom factors. Furthermore, using other language versions of the BNSS and the exploratory factor analysis, a similar two-dimensional structure was found in non-US psychiatric populations. However, some researchers reached a different result, with more than two dimensions (Garcia et al., 2015) and item 4: Lack of normal distress had a high load on avolition factor (0.61), including items 1,-8 (Mucci et al., 2015). These discrepancies suggested the existence of alternative structural models.

Although these exploratory factor analyses are important for generating hypotheses about dimensions in negative symptoms, confirmatory factor analysis (CFA) is required to test competing models and evaluate the underlying latent structure of BNSS rated negative symptoms (Ahmed et al., 2019). Recent CFA studies have revealed that the five-factor

Table 2 Internal consistency and reliability.

Study	Language	Country	n	Sample	%M	Average Age (SD)	BNSS Average values (SD)	Alpha	Inter-rater reliability	Test-retest	
										Interval	r
Kirkpatrick et al. (2011) (1)	English	US	20	Schizophrenia	80	48 (6.6)	26.8 (±16.8)	0.93	ICC: 0.89-0.95 Total 0.96	1 week	0.81
Strauss et al. (2012a) (2)	English	US	100	Schizophrenia or Schizoaffective disorder	74	42.2 (11.1)	24.1 (17.0)	0.94	NR	214 days on average apart	0.93
Strauss et al. (2016a) (3)	English	US	50	Schizophrenia	54	40.8 (12.5)	15.4 (14.1)	0.91	NR		NR
Strauss (2016b) (4)	English	US	65	Schizophrenia or Schizoaffective disorder	73.8	40.1 (11.2)	23.93 (15.2)	0.94	NR		NR
Mane et al. (2014) (5)	Spanish	Spain	20	Schizophrenia	70	37.3 (11.7)	19.79 (12.6)	0.98	ICC: 0.86-0.96	1 week	0.95
Yao et al. (2014) (6)	Chinese	China	163	Schizophrenia	54.6	45.0 (7.0)	18.25 (12.7)	0.93	ICC: 0.90	2-week	0.82
Mucci et al. (2015) (7)	Italian	Italy	912	Schizophrenia	69.8	40.1 (10.7)	35.91 (17.6)	NR	ICC: 0.81-0.98		NR
Bischof et al. (2016) (8)	German	Switzerland	75	Schizophrenia or Schizoaffective disorder	74.7	31.5 (10.9)	26.3 (14.7)	0.93	ICC: 0.87-0.97		NR
Nazli (2016) (9)	Turkish	Turkey	75	Schizophrenia	76	34.6 (8.3)	29.4 (17.6)	0.96	$r = 0.98$		NR
Jang et al. (2016) (10)	Korean	Korea	78	Schizophrenia, Schizoaffective disorder, or Psychotic disorder not otherwise specified	NR	NR	NR	0.94	α=0.83		NR
Mederios (2018) (11)	Portuguese	Brazil	111	Schizophrenia	NR	39.5 (12)	32.5 (15.6)	0.94	ICC: 0.92		NR
Mederios (2019) (12)	Portuguese	Brazil	30	Schizophrenia	66.7	41.9 (13.1)	28.3 (11.4)	0.88	NR		NR
Wójciak et al. (2019) (13)	Polish	Poland	40	Paranoid Schizophrenia	50	44.0 (13.0)	17.4 (15.3)	0.97	NR		NR
Gehr et al. (2019) (14)	Danish	Denmark	19	Schizophrenia or Schizoaffective disorder	65	33.1 (10.8)	NR	NR	ICC: 0.95		NR
Ang et al. (2019) (15)	English	Singapore	274	Schizophrenia	55.5	40.42 (10.17)	24.9 (11.88)	0.88	NR		NR

Note: NR=not reported.

Table 3 Convergent and discriminant validity.

		BNSS total			
		US		Non-US	
		r (range)	*r* (study)	*r* (range)	*r* (study)
Convergent validity	BPRS negative factor	0.68-0.83	0.68***(2) 0.83***(3) 0.82***(4)		
	PANSS negative subscale	0.80	0.80*** (1)	0.42-0.86	0.74***(5) 0.42***(6) 0.76***(7) 0.85** (9) 0.86*** (13) 0.81*** (rs;14) 0.79** (rs;15)
	PANSS negative factor			0.89	0.89**(8)
	Marder negative factor			0.87	0.87***(11)
	SANS total	0.80-0.88	0.84***(1) 0.80***(2) 0.88***(4)	0.68-0.89	0.68** (5) 0.77*** (6) 0.89** (8) 0.85*** (rs;14) 0.88** (rs;15)
Discriminant validity	BPRS positive/psychosis	−0.11-0.15	−0.06 (2) −0.11 (3) 0.15 (4)		
	PANSS positive subscale	0.09	0.09 (1)	0.11-0.55	0.16 (5) 0.11 (6) 0.29* (9) 0.23 (7) 0.29 (10) 0.55*** (rs;14) 0.13* (14)
	PANSS positive factor			−0.02	−0.02 (8)
	PANSS general	0.40	0.40***(1)	0.13-0.63	0.30 (5) 0.13 (6) 0.63*** (rs;14)
	CDSS			−0.01-0.31	0.28 (7) 0.16 (8) −0.01 (9) 0.31* (rs;14) 0.04 (15)
	ESRS			0.22	0.22 (9)
	SAS			0.30	0.30** (rs;15)
Others	PANSS total	0.58	0.58*** (1)	0.24-0.86	0.46* (5) 0.24***(6) 0.64***(7) 0.69***(9) 0.86*** (13) 0.74*** (rs;14)
	LOF total	−0.68--0.71	−0.71***(2) −0.68***(4)		
	GAF			−0.69	−0.69*** (8)
	PSP			−0.48--0.73	−0.73*** (8) −0.48*** (rs;14)

Notes: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$; rs=Spearman's correlations. Studies: (1)=Kirkpatrick et al. (2011); (2)=Strauss et al. (2012a); (3)=Strauss et al. (2016a); (4)=Strauss (2016b); (5)=Mane et al. (2014); (6)=Yao et al. (2014); (7)=Mucci et al. (2015); (8)=Bischof et al. (2016); (9)=Nazli (2016); (10)=Jang et al. (2016); (11)=Mederios (2018); (12)=Mederios (2019); (13)=Wójciak et al. (2019); (14)=Gehr et al. (2019); (15)=Ang et al. (2019).

Table 4 Construct validity.

Study	Language	Method	#Factors	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Kirkpatrick et al. (2011)	English	PCA	2	Anhedonia/ avolition/ asociality	Emotional expressivity			
Strauss et al. (2012b)	English	EFA	2	Motivation and pleasure	Emotional expressivity			
Garcia-Portilla et al. (2015)	Spanish	PCA	3	External world	Inner world	Alogia		
Mucci et al. (2015)	Italian	EFA	2	Avolition	Poor emotional expression			
Yao et al. (2014)	Chinese	EFA	2	Impairment of observable behavior	Impairment of subjective experience			
Nazli (2016)	Turkish	PCA	2	Motivation and pleasure	Emotional expressivity			
Mederios (2018)	Portuguese (Brazil)	EFA	2	Motivation and Pleasure	Emotional Expressivity			
Ahmed et al. (2019)	Multiple languages*	CFA	5	Blunted affect	Anhedonia	Alogia	Avolition	Asociality
Strauss et al. (2018)	English	CFA	5	Blunted affect	Anhedonia	Alogia	Avolition	Asociality
Ang et al. (2019)	English (Singapore)	CFA	5	Blunted affect	Anhedonia	Alogia	Avolition	Asociality
Mucci et al. (2019)	Multiple languages	CFA	5	Blunted affect	Anhedonia	Alogia	Avolition	Asociality
Strauss et al. (2019)	Multiple languages	Network Analysis	5	Blunted affect	Anhedonia	Alogia	Avolition	Asociality

Notes: PCA=principal components analysis; EFA=exploratory factor analysis; CFA=confirmatory factor analysis.
* The datasets used for CFA were drawn from Mucci et al. (2015), Mane et al. (2014), Yao et al. (2014), Bischof et al. (2016), and Strauss et al. (2012b).

model with separate factors reflecting the five consensus domains and hierarchical models fit the data better than the two-factor model; these findings have been replicated across diverse languages and cultures (Ahmed et al., 2019; Ang et al., 2019; Mucci et al., 2019; Strauss et al., 2018). Strauss et al. (2019) also replicated these findings using an alternate mathematical approach, network analysis, suggesting that the 5-factor solution is not limited to a singular mathematical approach. These findings suggest that the underlying construct of negative symptoms should no longer be considered a simple 2-dimentional construct, but rather as 5 distinct domains that serve as distinct treatment targets.

3.5. Sensitivity to change

The BNSS has shown sensitivity to change by demonstrating strong correlation with the PANSS negative symptom factor in a psychosocial intervention trial (Choi et al., 2016), moderate to high correlations in the expected directions across time between the SANS and BNSS scores in a neurological study (Eisenstein et al., 2017), and factor-specific correlations (using the two-factor structure) to regional brain activation (Kirschner et al., 2016).

Recent findings suggested that the BNSS is sensitive to drug effects, with effect sizes comparable to established scales. The PANSS and BNSS were administered to 244 stable patients with high negative symptoms and minimal positive psychotic symptoms to investigate the efficacy and safety of MIN-101 (Davidson et al., 2017). In this 12-week, randomized, double-blind, placebo-controlled parallel clinical trial, improvement in the PANSS negative scale score for both doses (32 mg and 64 mg) of MIN-101 was superior to that of placebo ($p \leq 0.01$ for both doses, effect size[ES], 0.45 and 0.57, respectively). There were also statistically significant changes in the BNSS total ($P < 0.01$; ES, 0.56) for MIN-101 64 mg compared to placebo at the end of 12-weeks. A trend toward superiority was also found in the BNSS scores for MIN-101 32 mg over placebo (Kirkpatrick et al., 2018).

The BNSS was also used in a study investigating efficacy and safety of SEP-363856, a novel psychotropic agent with a non-D2 mechanism of action (Koblan et al., 2019). In this 4-week study, 245 patients with schizophrenia experiencing an acute exacerbation of psychotic symptoms (PANSS total $\geq$ 80; item score $\geq$4) were randomized to the treatment groups (50 or 75 mg) or placebo. Least-square (LS) mean score reduction from baseline to Week 4 was significantly greater for the treatment group when compared to placebo on the PANSS negative subscale score

(−3.1 vs. −1.6; $P = 0.008$; ES, 0.32), the BNSS total score (−7.1 vs. −2.7; $P<0.001$; ES; 0.48) and the CGI-Severity score (−1.0 vs. −0.5; $P<0.001$; ES, 0.52).

4. Discussion

The present study reviewed linguistic and psychometric validation studies of the BNSS in the original English version and in translations, the results of which were all published over the last decade. These studies demonstrated that the BNSS is a multidimensional measure of negative symptoms with good to excellent internal, inter-rater and test-retest reliability and evidence of validity and sensitivity to change. Efforts are underway with linguistic and psychometric validations to further evaluate the performance of the BNSS globally (e.g. Japanese, Greek, Portuguese).

Although the BNSS demonstrated satisfactory reliability across cultures, the Brazilian BNSS yielded a relatively smaller Cronbach's alpha when compared to other language versions. The difference in value seem to be due to the smaller sample size since the larger value was found when the sample size increased. Similarly, the reliability of the English BNSS was weaker when it was administered in the English-speaking Asian population, compared to the US population (Ang et al., 2019). This may be attributable to the lager sample size or cultural differences.

It is also worth noting that the Danish BNSS had moderate relationships with PANSS positive and general subscales ($r = 0.55$ and 0.63, respectively), in contrast to the other versions of the BNSS. The author suggested that this is mostly likely due to the inclusion of acutely psychotic patients, and this stems from negative symptom secondary to positive symptoms (Gehr et al., 2019). The other validation studies reviewed in this report only included in- and outpatients whose symptoms were mild to moderate and clinically stable.

The latent structure of the BNSS can be best described as multi-dimensional, consisting of the five domains identified in the NIMH consensus conference: anhedonia, avolition, asociality, alogia, and blunted affect. This structure appears consistent across diverse cultures and languages. Those who train raters in the BNSS should emphasize the need to be careful to rate each BNSS item separately without being unduly influenced by other item scores to avoid a halo effect. Each subscale as well as internal experience and external behavior of avolition and asociality items may have different correlates, and may impact on a person's function in different ways. Furthermore, new treatments may need to target and focus each domain separately rather than the two broader factors identified be EFA.

In addition to quantitative results from the included studies, we collected qualitative reports from the field. The brevity and simplicity of the interview language and structure was perceived as valuable by both clinicians and patients. Qualitative reports also revealed subtle differences in ratings across languages and cultures, specifically when evaluating scores for training patient videos utilized in the network. Italian BNSS raters reported "cultural differences (for) ratings attributed to US patients on the anhedonia subscale and on items 10 and 11 (vocal expression and expressive gestures)" with average differences of approximately 1 point from the consensus scores that were established by US clinicians. Such a difference might become important in a multicultural trial, but the presence of control subjects (for instance patients taking a placebo rather than an active drug in a randomized trial) should mitigate any impact on validity.

There are a few common inquiries raised by the raters of the BNSS. For example, the manual states that Item 1 is rated based on the *most* intense pleasure the subject experienced, not on the most representative pleasure. This does not mean the rater should rate the item based on a single activity that the patient immensely enjoyed. The procedure for item 1 involves considering the intensity of pleasure reported over the past week for the four domains: physical, social, recreational, work/school. Each domain is considered when making the rating.

While the quantitative results showed that the raters from different countries demonstrated good to excellent inter-rater reliability, the rater training is pivotal to clinicians' understanding of administration procedures and scoring convention. The authors of this study constructed a frequently asked questions document. Along with the manual, this document may further help standardize the use of the BNSS in cross-cultural studies.

Limitations to this study were the inclusion of a relatively small number of studies and the majority of studies reviewed in this paper are designed to examine psychometric or other properties of the BNSS on a selected population - clinically stable patients. These limitations restrict the applicability and generalizability of their reliability findings to the whole population of schizophrenia patients and to ordinary and cross-cultural clinical settings. Conducting the BNSS validation study on acute psychosis and treatment-resistant schizophrenia patients may reveal undiscovered aspects of the BNSS and help understand the relationship between positive and negative symptoms. As more data on the reliability of the BNSS becomes available, the reliability generalization meta-analysis on reliability including internal consistency, inter-rater and test-retest reliability should be conducted to examine the variability of reported estimates and estimate the average reliability of the scores of the BNSS. Furthermore, the minimal clinically important difference (MCID) in the BNSS has not been investigated. This is another area that should be addressed. It would be also helpful for the interpretation of future cross-cultural studies to have normative data, in both people with psychotic disorders and those without such a disorder. This would be an expensive and formidable undertaking.

To date, the results from research studies conducted in different part of the world demonstrated that the BNSS is suitable to assess negative symptoms of schizophrenia in cross-cultural contexts. The BNSS is well positioned to capture change in negative symptoms for both psychosocial and pharmacologic intervention trials.

Role of the funding source

This study is not funded.

Conflict of interest

Kazunori Tatsumi and Dr. Mark Opler are employees of WCG MedAvante-ProPhase LLC, New York, NY, which is licensed to provide the BNSS and provides training on its use. Dr. Kirkpatrick and Dr. Strauss receive licensing royalties and travel support from WCG MedAvante-ProPhase for use of the Brief Negative Symptom Scale (BNSS) by for-profit groups; these fees are donated the Brain and behavior Research Foundation. Dr. Kirkpatrick has also received consulting fees and travel support from Genentech/Roche, from WCG MedAvante-ProPhase LLC, consulting fees from anonymized pharmaceutical companies through Decision Resources, Inc. and from an investment capital company through Guideposts. Dr. Kirkpatrick also receives fees from Walsh Medical Media for editorial services, and received fees for editorial services from Physicians Postgraduate Press, Inc. Dr. Strauss has consulted or received speaking honorarium from Minerva Neurosciences, Lundbeck, and Acadia. There are no other conflicts of interest to report.

CRediT authorship contribution statement

Kazunori Tatsumi: Writing - review & editing. **Gregory P. Strauss:** Writing - review & editing. **Mark Opler:** Conceptualization, Writing - review & editing.

Acknowledgements

The authors would like to thank Ms. Gianna Capodilupo and Ms. Vanitha Krishna for their operational assistance in the translation of the BNSS.

References

Addington, D., Addington, J., Schissel, B., 1990. A depression rating scale for schizophrenics. Schizophr. Res. 3, 247–251.

Ahmed, A.O., Kirkpatrick, B., Galderisi, S., Mucci, A., Rossi, A., Bertolino, A., Rocca, P., Maj, M., Kaiser, S., Bischof, M., Hartmann-Riemer, M.N., Kirschner, M., Schneider, K., Garcia-Portilla, M.P., Mane, A., Bernardo, M., Fernandez-Egea, E., Jiefeng, C., Jing, Y., Shuping, T., Gold, J.M., Allen, D.N., Strauss, G.P., 2019. Cross-cultural validation of the 5-factor structure of negative symptoms in schizophrenia. Schizophr. Bull. 45 (2), 305–314.

Aggarwal, N.K., Zhang, X.Y., Stefanovics, E., Chen, D.C., Xiu, M.H., Xu, K., Rosenheck, R.A., 2012. Rater evaluations for psychiatric instruments and cultural differences: the positive and negative syndrome scale in China and the United States. J. Nerv. Ment. Dis. 200 (9), 814–820.

Andreasen, N.C., 1982. Negative symptoms in schizophrenia. definition and reliability. Arch. Gen. Psychiatry 39 (7), 784–788.

Andreasen, N.C., 1989. The scale for the assessment of negative symptoms (SANS): conceptual and theoretical foundations. Br. J. Psychiatry Suppl. 7, 49–58.

Ang, M.S., Rekhi, G., Lee, J., 2019. Validation of the brief negative symptom scale in its association with functioning. Schizophr. Res. 208, 97–104.

Bischof, M., Obermann, C., Hartmann, M.N., Hager, O.M., Kirschner, M., Kluge, A., Strauss, G.P., Kaiser, S., 2016. The brief negative symptom scale: validation of the German translation and convergent validity with self-rated anhedonia and observer-rated apathy. BMC Psychiatry 16, 415.

Choi, K.H., Jaekal, E., Lee, G.Y., 2016. Motivational and behavioral activation as an adjunct to psychiatric rehabilitation for mild to moderate negative symptoms in individuals with schizophrenia: a proof-of-concept pilot study. Front Psychol. 14 (7), 1759.

Chouinard, G., Margolese, H.C., 2005. Manual for the extrapyramidal symptom rating scale (ESRS). Schizophr. Res. 76, 247–265.

Davidson, M., Saoud, J., Staner, C., Noel, N., Luthringer, E., Werner, S., Reilly, J., 2017. Efficacy and safety of MIN-101: a 12-Week randomized, double-blind, placebo-controlled trial of a new drug in development for the treatment of negative symptoms in schizophrenia. Am. J. Psychiatry 174, 1195–1202.

Emsley, R.A., Niehaus, D.J., Mbanga, N.I., Oosthuizen, P.P., Stein, D.J., Maritz, J.S., Pimstone, S.N., Hayden, M.R., Laurent, C., Deleuze, J.F., Mallet, J., 2001. The factor structure for positive and negative symptoms in South African Xhosa patients with schizophrenia. Schizophr. Res. 47 (2–3), 149–157.

Eisenstein, S.A., Bogdan, R., Chen, L., Moerlein, S.M., Black, K.J., Perlmutter, J.S., Hershey, T., Barch, D.M., 2017. Preliminary evidence that negative symptom severity relates to multi locus genetic profile for dopamine signaling capacity and D2 receptor binding in healthy controls and in schizophrenia. J. Psychiatr. Res. 86, 9–17.

Frances, A., Pincus, H.A., First, M.B., 1994. Global assessment of functioning scale (GAF). Diagnostic and Statistical Manual of Mental Disorders, fourth ed. American Psychiatric Association, Washington.

Garcia-Portilla, M.P., Garcia-Alvarez, L.G., Mane, A., Garcia-Rizo, C., Sugranyes, G., Berge, D., Bernardo, M., Fernandez-Egea, E., Bobes, J., 2015. The negative syndrome of schizophrenia: three-underlying components are better than two. Schizophr. Res. 166, 115–118.

Gehr, J., Glenthøj, B., Ødegaard Nielsen, M., 2019. Validation of the Danish version of the brief negative symptom scale. Nord. J. Psychiatry 73 (7), 425–432.

Hawk, A.B., Carpenter, W.T., Strauss, J.S., 1975. Diagnostic criteria and five-year outcome in schizophrenia: a report from the international pilot study of schizophrenia. Arch. Gen. Psychiatry 32, 343–347.

Jang, S., Choi, H., Park, S., Jaekal, E., Lee, G., Cho, Y., Choi, K., 2016. A two-factor model better explains heterogeneity in negative symptoms: evidence from the positive and negative syndrome scale. Front. Psychol. 7, 707.

Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13 (2), 261–276.

Kirkpatrick, B., Fenton, W.S., Carpenter Jr., W.T., Marder, S.R., 2006. The Nimh-Matrics consensus statement on negative symptoms. Schizophr. Bull. 32 (2), 214–219.

Kirkpatrick, B., Strauss, G.P., Nguyen, L., Fischer, B.A., Daniel, D.G., Cienfuegos, A., Marder, S.R., 2011. The brief negative symptom scale: psychometric properties. Schizophr. Bull. 37, 300–305.

Kirkpatrick, B., Saoud, J.B., Strauss, G.P., Ahmed, A.O., Tatsumi, K., Opler, M., Luthringer, R., Davidson, D., 2018. The brief negative symptom scale (BNSS): sensitivity to treatment effects. Schizophr. Res. 197, 269–273.

Kirmayer, L.J., 2001. Cultural variations in the clinical presentation of depression and anxiety: implications for diagnosis and treatment. J. Clin. Psychiatry 62 (Supp 13), 22–28 discussion 29-30.

Kirschner, M., Hager, O.M., Bischof, M., Hartmann, M.N., Kluge, A., Seifritz, E., Tobler, P.N., Kaiser, S., 2016. Ventral striatal hypoactivation is associated with apathy but not diminished expression in patients with schizophrenia. J. Psychiatry Neurosci. 41 (3), 152–161.

Koblan, K., Hopkins, S., Justine, K., Cheng, H., Goldman, R., Loebel, A., 2019. Efficacy and Safety of SEP-363856, a Novel Psychotropic Agent With a Non-D2 Mechanism of Action, in the Treatment of Schizophrenia: A 4-Week, Randomized, Placebo-

Controlled Trial. Poster Present: Schizophrenia International Research Society (SIRS), Orland, FL, USA.

Kring, A.M., Gur, R.E., Blanchard, J.J., Horan, W.P., Reise, S.P., 2013. The clinical assessment interview for negative symptoms (CAINS): final development and validation. Am. J. Psychiatry 170, 165–172.

Medeiros, H.L.V., Vasconcelos, S.C., Elkis, H., Martins, D.R., Leite, R.M.A., Albuquerque, A.C.L., Freitas, P.R., Scardoelli, M.A., Di-Sarno, E., Napolitano, I., Oliveira, G.M., Vizzotto, A., da-Silva, A.M.P., da-Costa, Lima, M.D., 2018. The brief negative symptom scale: validation in a multicenter Brazilian study. Compr. Psychiatry 85, 42–47.

Medeiros, H.L.V., Silva, A.M.P., Rodig, R.M.E., Souza, S.L., Sougey, E.B., Vasconcelos, S.C., Lima, M.D.C., 2019. Cross-cultural adaptation, reliability, and content validity of the brief negative symptom scale (BNSS) for use in Brazil. Arch. Clin. 46 (5), 132–136.

Mane, A., Garcia-Rizo, C., Garcia-Portilla, M.P., Berge, D., Sugranyes, G., Garcia-Alvarez, L., Bernardo, M., Bobes, J., Fernandez-Egea, E., 2014. Spanish adaptation and validation of the brief negative symptoms scale. Compr. Psychiatry 55, 1726–1729.

Morosini, P.L., Magliano, L., Brambilla, L., Ugolini, S., Pioli, R., 2000. Development, reliability and acceptability of a new version of the DSM-iv social and occupational functioning assessment scale (SOFAS) to assess routine social functioning. Acta. Psychiatr. Scand. 101, 323–329.

Mucci, A., Galderisi, S., Merlotti, E., Rossi, A., Rocca, P., Bucci, P., Piegari, G., Chieffi, M., Vignapiano, A., Maj, M.Italian Network for Research on Psychoses, 2015. The brief negative symptom scale (BNSS): independent validation in a large sample of Italian patients with schizophrenia. Eur. Psychiatry 30, 641–647.

Mucci, A., Vignapiano, A., Bitter, I., Austin, S.F., Delouche, C., Dollfus, S., Erfurth, A., Fleischhacker, W.W., Giordano, G.M., Gladyshev, I., Glenthøj, B., 2019. A large European, multicenter, multinational validation study of the brief negative symptom scale. Eur. Neuropsychopharm. 29 (8), 947–959.

Nazlı, I.P., Ergül, C., Aydemir, Ö., Chandhoke, S., Üçok, A., Gönül, A.S., 2016. Validation of Turkish version of brief negative symptom scale. Int. J. Psychiatry Clin. Pract. 20 (4), 265–271.

Overall, J.E., Gorham, D.R., 1962. The brief psychiatric rating scale. Psychol. Rep. 10 (3), 799–812.

Simpson, G.M., Angus, J.W.S., 1970. A rating scale for extrapyramidal side effects. Acta. Psychiatr. Scand. Suppl. 212, 11–19.

Strauss, G.P., Keller, W.R., Buchanan, R.W., Gold, J.M., Fischer, B.A., McMahon, R.P., Catalano, L.T., Culbreth, A.J., Carpenter, W.T., Kirkpatrick, B., 2012a. Next-generation negative symptom assessment for clinical trials: validation of the brief negative symptom scale. Schizophr. Res. 142, 88–92.

Strauss, G.P., Hong, L.E., Gold, J.M., Buchanan, R.W., McMahon, R.P., Keller, W.R., Fischer, B.A., Catalano, L.T., Culbreth, A.J., Carpenter, W.T., Kirkpatrick, B., 2012b. Factor structure of the brief negative symptom scale. Schizophr. Res. 142, 96–98.

Strauss, G.P., Vertinski, M., Vogel, S.J., Ringdahl, E.N., Allen, D.N., 2016a. Negative symptoms in bipolar disorder and schizophrenia: a psychometric evaluation of the brief negative symptom scale across diagnostic categories. Schizophr. Res. 170, 285–289.

Strauss, G.P., Gold, J.M., 2016b. A psychometric comparison of the clinical assessment interview for negative symptoms and the brief negative symptom scale. Schizophr. Bull. 42 (6), 1384–1394.

Strauss, G.P., Nunez, A., Ahmed, A.O., Barchard, K.A., Granholm, E., Kirkpatrick, B., Gold, J.M., Allen, D.N., 2018. The latent structure of negative symptoms in schizophrenia. JAMA Psychiatry 75 (12), 1271–1279.

Strauss, G.P., Esfahlani, F.Z., Galderisi, S., Mucci, A., Rossi, A., Bucci, P., Rocca, P., Maj, M., Kirkpatrick, B., Ruiz, I., Sayama, H., 2019. Network analysis reveals the latent structure of negative symptoms in schizophrenia. Schizophr. Bull. 45 (5), 1033–1041.

Yao, J., Cui, J.F., Chen, N., Fan, H.Z., Wang, Y.H., Li, Y.J., Tan, S.P., Li, Y.I., 2014. Reliability and validity of the Chinese version of brief negative symptom scale. Chin. Ment. Health J. 28 (4), 302–307.

Wallwork, R.S., Fortgang, R., Hashimoto, R., Weinberger, D.R., Dickinson, D., 2012. Searching for a consensus five-factor model of the positive and negative syndrome scale for schizophrenia. Schizophr. Res. 137, 246–250.

Wójciak, P., Górna, K., Domowicz, K., Jaracz, K., Gołębiewska, K., Michalak, M., Rybakowski, J., 2019. Polish version of the brief negative symptom scale (BNSS). Psychiatr. Pol. 53 (3), 541–549.