

ORIGINAL ARTICLE

Spanish validation of the Negative Symptom Assessment-16 (NSA-16) in patients with schizophrenia[☆]



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Abstract

Introduction: Negative symptoms are prevalent in schizophrenia and associated with a poorer outcome. Validated newer psychometric instruments could contribute to better assessment and improved treatment of negative symptoms. The Negative Symptom Assessment-16 (NSA-16) has been shown to have strong psychometric properties, but there is a need for validation in non-English languages. This study aimed to examine the psychometric properties of a Spanish version of the NSA-16 (Sp-NSA-16).

Material and method: Observational, cross-sectional validation study in a sample of 123 outpatients with schizophrenia. Assessments: NSA-16, PANSS, HDRS, CGI-SCH and PSP.

Results: The results indicate appropriate psychometric properties, high internal consistency (Cronbach's alpha=0.86), convergent validity (PANSS negative scale, PANSS Marder Negative Factor and CGI-negative symptoms r values between 0.81 and 0.94) and divergent validity

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PALABRAS CLAVE

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(PANSS positive scale and the HDRS r values between 0.10 and 0.34). In addition, the NSA-16 also exhibited discriminant validity (ROC curve=0.97, 95% CI=0.94 to 1.00; 94.3% sensitivity and 83.3% specificity).

Conclusions: The Sp-NSA-16 is reliable and valid for measuring negative symptoms in patients with schizophrenia. This provides Spanish clinicians with a new tool for clinical practice and research. However, it is necessary to provide further information about its inter-rater reliability. © 2018 SEP y SEPB. Published by Elsevier España, S.L.U. All rights reserved.

Validación española de la escala de evaluación de los síntomas negativos-16 (NSA-16) en pacientes con esquizofrenia

Resumen

Introducción: Los síntomas negativos prevalecen en la esquizofrenia y están asociados con un peor resultado. La validación de nuevos instrumentos psicométricos podría contribuir a una mejor evaluación de los síntomas negativos y a un avance en su tratamiento. La escala de evaluación de los síntomas negativos-16 (*Negative Symptom Assessment-16* [NSA-16]) ha demostrado adecuadas propiedades psicométricas, pero existe la necesidad de validarla en otros idiomas diferentes del inglés. Este estudio tiene como objetivo examinar las propiedades psicométricas de la versión española de la NSA-16 (Sp-NSA-16).

Material y método: Estudio observacional, transversal de validación en una muestra de 123 pacientes con diagnóstico de esquizofrenia en tratamiento ambulatorio. Evaluación: NSA-16, PANSS, HDRS, ICG-ESQ y PSP.

Resultados: Los resultados muestran unas adecuadas propiedades psicométricas, alta consistencia interna (alfa de Cronbach=0,86), validez convergente (escala negativa de la PANSS, factor negativo de Marder de la PANSS y escala de los síntomas negativos de la ICG: valores r entre 0,81 y 0,94) y validez divergente (escala positiva de la PANSS y HDRS: valores r entre 0,10 y 0,34). Además, la NSA-16 también muestra validez discriminante (curva ROC = 0,97; IC 95%=0,94 a 1,00; 94,3% de sensibilidad y 83,3% de especificidad).

Conclusiones: La Sp-NSA-16 es fiable y válida para medir los síntomas negativos en pacientes con esquizofrenia. Proveemos a los clínicos españoles con una nueva herramienta para la práctica clínica e investigación. Sin embargo, es necesario proporcionar más información sobre su fiabilidad interevaluadores.

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Introduction

The negative syndrome of schizophrenia, which includes social isolation, anhedonia, avolition, flat affect, and alogia,^{1,2} affects about 20% of patients with schizophrenia. Together with cognitive symptoms, it has a significant impact on functioning, especially in the social domain.³⁻⁶

These symptoms can occur at any stage of the illness. In fact, they can exist in a prodromal stage before the emergence of positive symptoms^{7,8} or co-exist with them, although they may be less impressive during acute psychosis because the clinical picture is dominated by positive symptoms.⁸ Furthermore, they can be present at subsequent follow-up points for up to 10 years⁹ and may become more prevalent over time.¹⁰ Negative symptoms are viewed as treatment-resistant, and only modest progress has been made in treating them effectively,¹¹⁻¹³ although some evidence suggests that secondary negative symptoms may respond to pharmacologic and psychosocial interventions.

Progress in these treatments is currently impeded by the limitations of available assessment instruments. For this reason, the development of instruments able to assess the severity of a patient's negative symptoms is the most important first step towards optimal treatment.¹ Moreover, the commonly used negative symptom assessment tools, like the Brief Psychiatric Rating Scale (BPRS),¹⁴ the Scale for the Assessment of Negative Symptoms (SANS),¹⁵ and the Positive and Negative Syndrome Scale, Negative Subscale (PANSS-NS)¹⁶ have been the subject of criticism.

The Negative Symptom Assessment (NSA) was initially developed by Alphas et al. in 1989.¹⁷ However, the most widely used version is the shortened 16-item version of the NSA developed by Axelrod et al. in 1993,¹⁸ which has a latent structure similar to the original instrument (five-factor dimensional structure: communication, social involvement, affect/emotion, motivation, and retardation). It was modified from 25 to 16 items to make it an easy-to-use instrument with strong psychometric properties and

good clinical utility.^{17,18} It has demonstrated high interrater and test-retest reliability as well as high concurrent validity with similar instruments when used by English-speaking raters.¹⁸⁻²⁰ At present, there is a need to validate the NSA-16 in different languages. Clinical trials for approval of new drugs involve various regions/countries. Spanish is the primary language of 20 countries, ranking as the second most widely spoken language in terms of native speakers.²¹ Therefore, this study aims to validate the Spanish version of the NSA-16. We hypothesise that the NSA-16 is a reliable and valid instrument for assessing negative symptoms in Spanish patients with schizophrenia. Furthermore, this new instrument could contribute to better understanding of negative symptoms and improved psychopharmacological research.

Materials and methods

Participants and study design

The number of participants included was 123 patients with stable schizophrenia. Stability was defined as those patients who were clinically stable and had not required any change in their current pharmacological treatment during the previous month. Patient inclusion criteria were¹ age ≥ 18 years²; ICD-10 diagnosis of schizophrenia³; currently on treatment for his/her illness; and⁴ written informed consent to participate in the study. Exclusion criteria were designed to be minimal, due to the nature of the study, and only individuals with intellectual developmental disorder or acquired brain injury, or who refused to participate in the study were excluded. Participants were recruited from two outpatient mental health centres in Spain. This was an observational, cross-sectional validation study. It was approved by the Clinical Research Ethics Committee of one of the centres (Hospital Universitario Central de Asturias, Oviedo, Spain) and it was in compliance with the 1975 Declaration of Helsinki, as revised in 1983. Written informed consent was obtained from all subjects before enrolment.

Measures

Demographic and clinical data were collected and assessments were done for all subjects. Severity of illness was assessed with the Clinical Global Impression-Schizophrenia scale (CGI-SCH).²² In addition to the Spanish validation of the NSA-16,¹⁸ psychopathology was evaluated using the Spanish versions of the Positive and Negative Syndrome Scale (PANSS)²³ and the Hamilton Depression Rating Scale (HDRS).²⁴⁻²⁶ Level of functioning was assessed using the Global Assessment of Functioning (GAF)²⁷ and the Spanish version of the Personal and Social Performance scale (PSP).²⁸

The *Negative Symptom Assessment - 16 items (NSA-16)*¹⁸ is a semi-structured interview containing 16 items that comprehensively assess the negative syndrome of schizophrenia, including the following five factors: communication, emotion/affect, social involvement, motivation, and retardation.¹⁸ It has been validated in inpatients and outpatients with schizophrenia.¹⁸ These five factors were extracted from the larger six-factor NSA-25.¹⁸ Each of the sixteen items and the overall global negative symptoms are rated on a 1 to 6-point scale where '1' represents no reduc-

tion from normal behaviours associated with the item and '6' represents a severe reduction in or absence of the behaviour, with markedly impaired functionality. The rating scale also includes a "Not Ratable" designation (denoted as "9"). Detailed anchoring criteria for the rating points are provided on the scale, along with a total score, sum of the scores on the 16 items, and scores in each of the five factors. Also, the NSA-16 has an "extra" item which provides a Global Negative Symptom Rating - Severity based on the global clinical impression of the patient's negative symptoms. The main limitation of the NSA is its high reliance on functioning or behaviours even for experiential symptoms such as reduced social drive whose severity is measured by type and frequency of social interactions.

The Spanish version of the NSA-16 (NSA-16-Sp) was developed using the translationback-translation method. The original developer accepted that we carried out the Spanish validation of the scale. The short-form scale, long-form scale, and interview were translated into Spanish by native Spanish-speaking clinicians. The translated version was back-translated into English by an English clinician fluent in Spanish. Finally, the back-translated version was reviewed and approved.

Statistical analysis

The statistical analysis was done using the SPSS 17.0. The two-tailed level of significance used was 0.05. Skewness and kurtosis were calculated to measure the shape of the distributions (skewness and kurtosis values ± 1 were considered good). Ceiling and floor effects were also determined (number of patients with scores greater than 95% and lower than 5%, respectively). The internal consistency of the Sp-NSA-16 and its factors was calculated using the Cronbach's alpha coefficient at the item level. Convergent validity was calculated using the Pearson correlation coefficient between the total Sp-NSA-16 score and total scores on the PANSS negative scale, PANSS Marder Negative Factor,²⁹ and CGI-negative symptoms with the hypothesis that a moderate r coefficient would be found as they are related but different constructs. Pearson correlation coefficients between the total Sp-NSA-16 score and scores on the PANSS positive scale and HDRS were determined to assess divergent validity. In this case, the hypothesis was that a low r coefficient would be found as they are different constructs.

For analysing discriminant validity, patients with schizophrenia were classified into four groups based on their CGI-SCH negative symptom severity scores: doubtfully ill (CGISCH=1-2), mildly ill (CGI-SCH=3), moderately ill (CGI-SCH=4), and severely ill (CGI-SCH=5-7). An ANOVA test (Duncan post hoc) was used to identify statistically significant differences in Sp-NSA-16 scores according to severity groups. The diagnostic performance of the Sp-NSA-16 for discriminating between patients with and without negative symptoms was analysed using the receiver operating characteristic (ROC) curve analysis.

Results

One hundred and twenty-three subjects were included with a mean age (standard deviation) of 40.7 (10.4) years and a

Table 1 Demographic and clinical characteristics.

Schizophrenia (n = 123)	
Mean age (sd)	40.7 (10.4)
Gender, males [n(%)]	83 (67.5)
Civil status [n (%)]	
Never married	82 (66.7)
Married/Living as married	29 (23.6)
Divorced/Separated	12 (9.8)
Educational level [n (%)]	
Primary school	45 (36.6)
Secondary school	54 (43.9)
University	24 (19.5)
Work status [n (%)]	
Working	9 (7.3)
Permanent disabled due to mental illness	65 (52.8)
Not working ^a	39 (32.7)
Housewife	4 (3.3)
Student	6 (4.9)
Length of illness [mean (sd)]	13.8 (10.9)
CGI-SCH [mean (sd)]	
Positive symptoms	3.1 (1.4)
Negative symptoms	3.8 (1.2)
Depressive symptoms	2.5 (1.3)
Cognitive symptoms	3.3 (1.8)
Total	4.2 (1.0)
PANSS [mean (sd)]	
Positive scale	13.5 (5.4)
Negative scale	18.9 (5.1)
Negative Marder factor	17.8 (5.8)
General Psychopathology scale	33.0 (8.5)
Total	65.6 (15.7)
HDRS total score [mean (sd)]	9.3 (7.1)
GAF [mean (sd)]	50.5 (14.7)
PSP total score [mean (sd)]	49.1 (16.2)

sd: standard deviation.

^a Not working included: temporary disabled for other health conditions than mental disorder, temporary disabled for schizophrenia, retired, and unemployed. CGI-SCH: Clinical Global Impression, Schizophrenia. PANSS: Positive and Negative Syndrome Scale. HDRS: Hamilton Depression Rating Scale. GAF: Global Assessment of Functioning. PSP: Personal and Social Performance scale.

mean illness duration of 13.8 (10.9) years; 67.5% were male. NSA-16-Sp demographic and clinical characteristics of the full sample of patients are presented in [Table 1](#).

Distribution characteristics of NSA-16 scores

The mean scores and the psychometric characteristics of the total Sp-NSA-16 and its factors are shown in [Table 2](#). For all global measures and factors, the scores show symmetrical and mesokurtic distribution, except the communication factor, which shows slightly right-skewed and leptokurtic distribution. There were no ceiling or floor effects in any of them.

Reliability (internal consistency)

The Sp-NSA-16 scale had good internal consistency (Cronbach's α of 0.86). Cronbach's α s for the Sp-NSA-16 factors were good with the exception of the social involvement factor (Cronbach's α : communication = 0.70; emotion/affect = 0.70; social involvement = 0.44; motivation = 0.78; retardation = 0.65).

Convergent validity

The Pearson correlation coefficient between the Sp-NSA-16 total score and the total score on the PANSS negative scale was 0.84 ($p < 0.0001$). When we used the PANSS negative factor described by Marder, the coefficient was 0.84 ($p < 0.0001$). With the CGI-negative symptoms, the Pearson coefficient was 0.91 ($p < 0.0001$). When we consider the global assessment provided by item 17 of the NSA-16 (Global Negative Symptom Rating – Severity), the Pearson correlation coefficients between this score and scores on the PANSS negative scale, PANSS Marder Negative Factor, and CGI-negative symptoms were 0.81, 0.82, and 0.94, respectively.

Divergent validity

Pearson correlation coefficients between the Sp-NSA-16 total score and total scores on the PANSS positive scale and the Hamilton Depression Rating Scale were low in magnitude ($r = 0.17$, $p = 0.061$, and $r = 0.32$, $p < 0.0001$, respectively). Similar results were obtained when we consider the Global Negative Symptom Rating – Severity provided by item 17 of the Sp-NSA-16 ($r = 0.10$, $p = 0.254$, and $r = 0.34$, $p < 0.0001$, respectively). Finally, Pearson correlation coefficients between the scores on the NSA-16 and the PSP total score were high (Sp-NSA-16 total score: $r = 0.73$, $p < 0.0001$; Sp-NSA-16 global negative symptom severity: $r = 0.75$, $p < 0.0001$, respectively).

Discriminant validity

The Sp-NSA-16 and its factors were able to discriminate between the different levels of negative symptom severity according to CGI-SCH negative symptom severity scores (see [Table 3](#)). We found similar results for the PANSS negative scale and PANSS Marder Negative Factor (see [Table 3](#)). The area under the ROC curve was 0.97 (95% $CI = 0.94-1.00$), indicating good accuracy of the test. A cut-off point of 31 provided excellent sensitivity (94.3%) and good specificity (83.3%) for separating patients without negative symptoms and patients with negative symptoms according to the CGI negative symptom scores (1 and 2 versus ≥ 3) (see [Fig. 1](#)).

Discussion

It is essential for clinicians to have effective instruments for measuring the severity of negative symptoms and changes in these symptoms over time. This study validated the Spanish version of the NSA-16 in a sample of patients with

Table 2 Distribution characteristics of Sp-NSA-16 scores.

Sp-NSA16	Score range	Mean (sd)	Skewness (se)	Kurtosis (se)	Ceiling effect ^a	Floor effect ^b
<i>Factor scores</i>						
Communication	4–24	6.7 (3.1)	1.34 (0.22)	1.66 (0.43)	5 (4.0)	0 (0.0)
Emotion/Affect	3–18	9.4 (3.1)	−0.10 (0.21)	−0.47 (0.43)	6 (4.8)	5 (4.0)
Social involvement	3–18	9.2 (3.1)	0.08 (0.22)	−0.76 (0.43)	4 (3.2)	3 (2.4)
Motivation	4–24	13.1 (4.7)	0.26 (0.22)	−0.79 (0.43)	3 (2.4)	5 (4.0)
Retardation	2–12	4.5 (2.3)	0.77 (0.22)	−0.30 (0.43)	5 (4.0)	0 (0.0)
NSA-16 Total score	16–96	42.9 (12.1)	−0.04 (0.22)	−0.37 (0.43)	6 (4.8)	4 (3.2)
NSA-16 Global rating	1–6	3.7 (1.2)	−0.12 (0.22)	−0.70 (0.43)	0 (0.0)	3 (2.4)

sd: standard deviation; se: standard error.

^a Number (%) of patients with scores greater than 95%.^b Number (%) of patients with scores smaller than 5%.**Table 3** Sp-NSA-16 and PANSS negative scale and factor scores according to severity of the negative symptoms as determined by CGI negative symptoms severity scores.

Sp-NSA-16 factors	Doubtfully ill (CGI-S = 1–2)	Mildly ill (CGI-S = 3)	Moderately ill (CGI-S = 4)	Severely ill (CGI-S = 5–7)	ANOVA, <i>F</i>	<i>p</i>
Communication [mean (sd)]	4.2 (0.5)	5.1 (1.5)	6.2 (2.1)	9.8 (3.5)	31.430 ^a	<0.0001
Emotion/Affect [mean (sd)]	6.2 (2.3)	8.0 (3.2)	9.7 (2.2)	11.7 (2.3)	22.925 ^b	<0.0001
Social involvement [mean (sd)]	5.8 (2.1)	7.9 (2.5)	10.3 (2.5)	10.7 (2.9)	18.772 ^c	<0.0001
Motivation [mean (sd)]	6.2 (2.5)	10.3 (3.1)	14.7 (2.8)	16.9 (3.1)	65.411 ^b	<0.0001
Retardation [mean (sd)]	2.4 (0.6)	3.5 (1.4)	4.0 (1.4)	7.0 (2.1)	45.892 ^d	<0.0001
Global negative symptoms [mean (sd)]	1.9 (0.5)	2.8 (0.4)	3.9 (0.5)	5.1 (0.5)	222.100 ^b	<0.0001
Total score [mean (sd)]	24.8 (5.4)	34.7 (5.1)	44.8 (5.7)	56.0 (6.5)	139.201 ^b	<0.0001
PANSS negative scale [mean (sd)] ^e	11.8 (3.0)	16.5 (2.3)	19.2 (3.0)	24.0 (3.7)	69.875 ^b	<0.0001
PANSS marder negative factor [mean (sd)] ^e	9.8 (2.7)	14.9 (3.1)	17.9 (2.9)	23.8 (4.7)	69.687 ^b	<0.0001

sd: standard deviation. CGI: Clinical Global Impression.

^a Duncan test showed that severely ill patients were different from those doubtfully, mildly and moderately ill, and moderately ill patients were different from those doubtfully ill.^b Duncan test showed that the 4 subgroups of patients were different from each other.^c Duncan test showed that severely and moderately ill patients were different from those mildly and doubtfully ill, and mildly ill patients were different from those doubtfully ill.^d Duncan test showed that severely ill patients were different from those doubtfully, mildly and moderately ill, and doubtfully ill patients were different from those mildly and moderately ill.^e Score range: 7–49.

schizophrenia. The mean age (40.7, SD = 10.4) of the sample was similar to the study that validated the original version of the NSA-16 (40.0, SD = 11.0).¹⁸

The internal consistency of the overall scale was adequate and similar to previous studies.^{18,30} Regarding convergent validity, as expected, there were highly significant correlations between the NSA-16 and the PANSS negative scale, Marder factor, and CGI-negative symptoms, indicating strong convergent validity. Similar results have been reported for the original NSA-16.³¹ On the contrary, divergent validity was supported by lower correlations with instruments assessing other psychopathological aspects, i.e. positive and depressive symptoms. It is worth noting the moderate correlation found between scores for negative symptoms and functioning in keeping with the results of Velligan et al. (2009). This may be related to the widely reported negative influence of negative symptoms on real-world functioning.^{6,32} In fact, it has been observed that improvements in negative symptoms correlate with

improvements in a global measure of functional outcome and functional capacity. However, the relationship between the two is complex.³³ On the one hand, it has been pointed out that the main limitation of the NSA is its high reliance on functioning or behaviours even for experiential symptoms such as reduced social drive whose severity is measured by type and frequency of social interactions.³⁴ This could explain the complexity of their relationship. On the other hand, this scale also includes a rating of reduced emotional range encompassing both anhedonia and lack of negative emotional experiences (such as anxiety, sadness, or anger). Thus, individuals who have healthy emotional functioning but experienced no negative emotional events during the observation period may score high, increasing their negative symptom severity.³⁵ Finally, the Sp-NSA-16 and its factors were able to discriminate between different levels of negative symptom severity according to CGI-SCH negative symptom scores. Our results show that the NSA total score increases by ten for each increased level on the CGI-SCH,

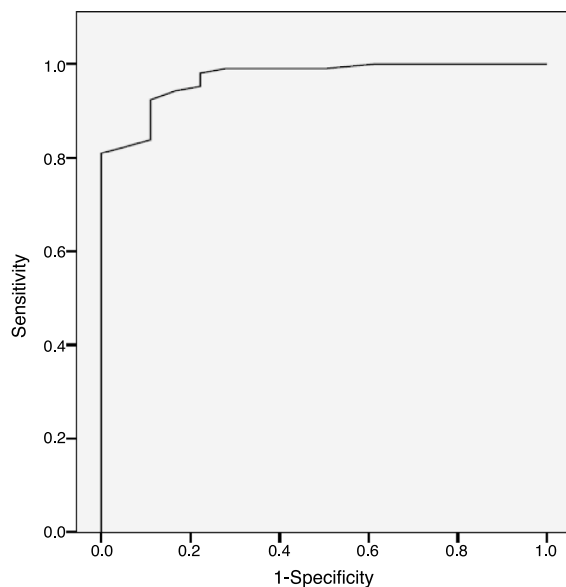


Figure 1 ROC curve of the total score of the Sp-NSA-16.

and the same happens in the NSA global negative symptoms, which increases by one.

One potential limitation of this study is that the inter-rater reliability was not estimated, as the assessments were conducted by the same rater, so it would be appropriate to investigate these relationships among instruments for assessments conducted by different raters. Another limitation was related to the generalizability of our results, since all patients were outpatients from the same region of Spain (Asturias), and there was a lack of patients with extremely severe negative symptoms, such as institutionalised individuals. The main strength of this study relies on the non-restrictive inclusion and exclusion criteria, so our patients are very similar to those seen in daily clinical practice.

In conclusion, we were able to demonstrate that the Spanish version of the NSA-16 (Sp-NSA-16) is an accurate and valid instrument for measuring negative symptoms in Spanish patients with schizophrenia. Furthermore, it seems to be appropriate for use in clinical trials and routine clinical practice as a means of measuring and monitoring changes in negative symptoms in these subjects. Moreover, the NSA-16 is easier to apply than other new scales such as the Clinical Assessment Interview for Negative Symptoms (CAINS)³⁶ or the Brief Negative Symptom Scale (BNSS)³⁷ since it includes the questions that should be asked to the patients and it is not necessary to make so many inferences (especially in regard to the observable signs). Moreover, nurses or non-psychiatrists doctors could obtain more reliable information assessing psychotic patients using this scale than others which require deeper training and knowledge, like CAINS or BNSS.

Conflict of interest

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References

- Kirkpatrick B, Fenton W, Carpenter W, Marder SR. The NIMH-MATRICES consensus statement on negative symptoms. *Schizophr Bull.* 2006;32:296–303.
- Blanchard JJ, Cohen AS. The structure of negative symptoms within schizophrenia: implications for assessment. *Schizophr Bull.* 2006;32:238–45.
- Bowie CR, Depp C, McGrath JA, Wolyniec P, Mausbach BT, Thornquist MH, et al. Prediction of real-world functional disability in chronic mental disorders: a comparison of schizophrenia and bipolar disorder. *Am J Psychiatry.* 2010;167:1116–24.
- Bowie CR, Reichenberg A, Patterson TL, Heaton RK, Harvey PD. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am J Psychiatry.* 2006;163:418–25.
- Harvey PD, Heaton RK, Carpenter WT, Green MF, Gold JM, Schoenbaum M. Functional impairment in people with schizophrenia: focus on employability and eligibility for disability compensation. *Schizophr Res.* 2012;140:1–8.
- Rocca P, Montemagni C, Zappia S, Piterà R, Sigauco M, Bogetto F. Negative symptoms and everyday functioning in schizophrenia: a cross-sectional study in a real world-setting. *Psychiatry Res.* 2014;218:284–9.
- Harvey PD, Koren D, Reichenberg A, Bowie CR. Negative symptoms and cognitive deficits: what is the nature of their relationship? *Schizophr Bull.* 2006;32:250–8.
- Möller HJ. Clinical evaluation of negative symptoms in schizophrenia. *Eur Psychiatry.* 2007;22:380–6.
- Evensen J, Røssberg JI, Barder H, Haahr U, Hegelstad WtV, Joa I, et al. Flat affect and social functioning: a 10 year follow-up study of first episode psychosis patients. *Schizophr Res.* 2012;139:99–104.
- Chang W, Hui CL, Tang JY, Wong GH, Lam MM, Chan SK, et al. Persistent negative symptoms in first-episode schizophrenia: a prospective three year follow-up study. *Schizophr Res.* 2011;133:22–8.
- Rabinowitz J, Werbeloff N, Caers I, Mandel FS, Stauffer V, Menard F, et al. Negative symptoms in schizophrenia – the remarkable impact of inclusion definitions in clinical trials and their consequences. *Schizophr Res.* 2013;150:334–8.
- Möller HJ, Czobor P. Pharmacological treatment of negative symptoms in schizophrenia. *Eur Arch Psychiatry Clin Neurosci.* 2015;265:567–78.
- Stahl SM, Buckley PF. Negative symptoms of schizophrenia: a problem that will not go away. *Acta Psychiatr Scand.* 2007;115:4–11.
- Overall JE, Gorham DR. The brief psychiatric rating scale. *Psychol Rep.* 1962;10:790–812.
- Andreasen NC. Scale for the assessment of negative symptoms. Iowa City, IA: University of Iowa; 1983.
- Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987;13:261–76.
- Alphs LD, Summerfelt A, Lann H, Muller RJ. The negative symptom assessment: a new instrument to assess negative symptoms of schizophrenia. *Psychopharmacol Bull.* 1989;25:159–63.
- Axelrod BN, Goldman RS, Alphs LD. Validation of the 16-item negative symptom assessment. *J Psychiatr Res.* 1993;27:253–8.
- Axelrod BN, Alphs LD. Training novice raters on the Negative Symptom Assessment Scale. *Schizophr Res.* 1993;9:25–8.

20. Axelrod BN, Goldman RS, Woodard JL, Alphas LD. Factor structure of the negative symptom assessment. *Psychiatry Res.* 1994;52:173-9.
21. One World Nations Online. Available from: http://www.nationsonline.org/oneworld/most_spoken_languages.htm [accessed 28.09.17].
22. Haro JM, Kamath SA, Ochoa S, Novick D, Rele K, Fargas A, et al. The Clinical Global Impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. *Acta Psychiatr Scand Suppl.* 2003;416:16-23.
23. Peralta V, Cuesta MJ. Validación de la Escala de los Síndromes Positivo y Negativo (PANSS) en una muestra de esquizofrénicos españoles. *Actas Luso-Esp Neurol Psiquiatr.* 1994;22:171-7.
24. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry.* 1960;23:56-62.
25. Ramos-Brieva JA, Cordero Villafáfila A. Validación de la versión castellana de la Escala de Hamilton para la Depresión. *Actas Luso Esp Neurol Psiquiatr Cienc Afines.* 1986;14:324-34.
26. Bobes J, Bulbena A, Luque A, Dal-Ré R, Ballesteros J, Ibarra N, et al. Evaluación psicométrica comparativa de las versiones en español de 6, 17 y 21 ítems de la Escala de valoración de Hamilton para la evaluación de la depresión. *Med Clin (Barc).* 2003;120:693-700.
27. American Psychiatric Association. Global Assessment of Functioning (GAF). In: *Diagnostic and statistical manual on mental disorders.* 3rd ed., text rev. Washington, DC: American Psychiatric Association; 1987.
28. Garcia-Portilla MP, Saiz PA, Bousono M, Bascaran MT, Guzmán-Quilo C, Bobes J. Validation of the Spanish Personal and Social Performance scale (PSP) in outpatients with stable and unstable schizophrenia. *Rev Psiquiatr Salud Ment (Barc).* 2011;4:9-18.
29. Marder SR, Davis JM, Chouinard G. The effects of risperidone on the five dimensions of schizophrenia derived by factor analysis: combined results of the North American trials. *J Clin Psychiatry.* 1997;58:538-46.
30. Alphas L, Morlock R, Coon C, Cazorla P, Szegedi A, Panagides J. Validation of a 4-item Negative Symptom Assessment (NSA-4): a short, practical clinical tool for the assessment of negative symptoms in schizophrenia. *Int J Methods Psychiatr Res.* 2011;20:e31-7.
31. Daniel DG, Alphas L, Cazorla P, Bartko JJ, Panagides J. Training for assessment of negative symptoms of schizophrenia across languages and cultures: comparison of the NSA-16 with the PANSS Negative Subscale and Negative Symptom factor. *Clin Schizophr Relat Psychoses.* 2011;5:87-94.
32. Harvey PD. Disability in schizophrenia: contributing factors and validated assessments. *J Clin Psychiatry.* 2014;75:15-20.
33. Velligan DI, Alphas L, Lancaster S, Morlock R, Mintz J. Association between changes on the Negative Symptom Assessment scale (NSA-16) and measures of functional outcome in schizophrenia. *Psychiatry Res.* 2009;169:97-100.
34. Garcia-Portilla MP, Garcia L, Saiz PA, Al-Halabi S, Bobes-Bascaran T, Bascaran MT, et al. Psychometric evaluation of the negative syndrome of schizophrenia. *Eur Arch Psychiatry Clin Neurosci.* 2015;265:559-66.
35. Mucci A, Galderisi S, Merlotti E, Rossi A, Rocca P, Bucci P, et al. The Brief Negative Symptom Scale (BNSS): Independent validation in a large sample of Italian patients with schizophrenia. *Eur Psychiatry.* 2015;30:641-7.
36. Kring AM, Gur RE, Blanchard JJ, Horan WP, Reise SP. The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. *Am J Psychiatry.* 2013;170:165-72.
37. Kirkpatrick B, Strauss GP, Nguyen L, Fischer BA, Daniel DG, Cienfuegos A, et al. The brief negative symptom scale: psychometric properties. *Schizophr Bull.* 2011;37:300-5.