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The brief negative symptom scale (BNSS): Sensitivity to treatment effects

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ABSTRACT

The Brief Negative Symptom Scale (BNSS) grew out of a recommendation by the NIMH-sponsored Consensus Development Conference on Negative Symptoms that a scale based on contemporary concepts be developed. We assessed sensitivity to change of the BNSS in a trial of MIN-101, which showed efficacy for negative symptoms (PANSS pentagonal model) at daily doses of 32 and 64 mg/day. Using mixed-effects model for repeated measures, we examined change in BNSS total score and in the BNSS factors of anhedonia/avolition/asociality (AAA), and expressivity (EXP). Compared to placebo, the 64 mg group (N = 83) showed a significant decrease in BNSS total score (effect size *d* [ES] 0.56, $p < 0.01$) and both factor scores (AAA ES = 0.48, EXP ES = 0.46, $p < 0.02$ for both). Patients in the trial had minimal depression and positive symptom scores; covarying for disorganization, positive symptoms, or anxiety/depression did not cause a meaningful change in the significance of the BNSS total or factor scores in this group. The 32 mg group (N = 78) did not differ significantly from placebo (N = 83) on BNSS total score (ES = 0.33, $p < 0.09$), AAA (ES = 0.25, $p < 0.20$) or EXP (ES = 0.30, $p < 0.12$) scores. These results demonstrate the BNSS is sensitive to change.

1. Introduction

The NIMH Consensus Development Conference on Negative Symptoms recommended that a negative symptom scale be developed that would embody recent changes in the concept of negative symptoms (Kirkpatrick et al. 2006). In response to that recommendation, the Brief Negative Symptom Scale (BNSS), which was designed for ease of us in clinical trials, was developed and tested. Psychometric studies of the BNSS have shown excellent reliability, discriminant validity, and convergent validity in English and in translation (Kirkpatrick et al. 2011; Strauss et al. 2012b; Mané et al. 2014; Mucci et al. 2015; Polat Nazli et al., 2016; Bischof et al. 2016; Yao et al. 2014' Strauss and Gold 2016; Strauss et al. 2016a). Translations and back translations exist in Spanish, Italian, Turkish, Chinese (simplified and traditional script), German, Russian, Dutch, Danish, Polish, Norwegian, Japanese, Korean, and Portuguese versions (Bischof et al. 2016; Choi et al. 2016; Mucci et al. 2015; Polat Nazli et al., 2016; Yao et al. 2014; and personal communications).

The BNSS consists of 13 items organized into six subscales (Table 1). Five of these subscales reflect the domains recognized as part of the construct of negative symptoms: anhedonia, avolition, asociality, blunted affect, and alogia. The Consensus Conference participants left open the possibility that other domains belong in this construct, and the BNSS contains an additional item, Lack of Normal Distress. A conceptually similar item, Diminished Emotional Range, is part of the Schedule for the Deficit Syndrome (SDS; Kirkpatrick et al. 1989). Psychometric studies of the BNSS and the SDS (Bischof et al. 2016; Kimhy et al. 2006; Kirkpatrick et al. 2011; Mané et al. 2014; Mucci et al. 2015; Nakaya and Ohmori 2008; Polat Nazli et al., 2016; Strauss et al. 2012b) have suggested that this item's content also belongs in the construct of negative symptoms.

The BNSS has a two-factor structure in English and in translation (Kirkpatrick et al. 2011; Strauss et al. 2012a; Mucci et al. 2015; Yao et al., 2014; Polat Nazli et al., 2016; Bischof et al. 2016) that is very similar to the factor structure of the Scale for the Assessment of Negative Symptoms (Blanchard and Cohen 2006) and the Clinical Assessment Interview for Negative Symptoms (Blanchard et al. 2017). The two BNSS factors consist of items from 1) the anhedonia, avolition, and asociality (AAA) subscales, and 2) the blunted affect and alogia subscales (expressivity; EXP). Although measures such as Cronbach's alpha suggest the

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Table 1
Items and subscales in the brief negative symptom scale.

Subscale	Item	AAA factor	EXP Factor
Anhedonia	Intensity of pleasure	√	
	Frequency of pleasurable activities	√	
	Intensity of expected pleasure	√	
Lack of normal distress	Lack of normal distress[a]		
Asociality	Asociality: behavior	√	
	Asociality: Internal experience	√	
Avolition	Avolition: behavior	√	
	Avolition: internal experience	√	
Blunted affect	Facial expression		√
	Vocal expression		√
	Expressive gestures		√
Alogia	Quantity of speech		√
	Spontaneous elaboration		√

AAA: Anhedonia/avolition/asociality; EXP: Expressivity.
[a] Lack of normal distress usually does not load strongly onto either factor. See text for references.

BNSS Lack of Normal Distress item belongs in the construct of negative symptoms (Strauss et al. 2012a), it does not load as strongly on either factor as do the other BNSS items.

The BNSS has shown sensitivity to change in a psychosocial treatment trial (Choi et al. 2016), variation in multi-locus genetic profile scores reflecting elevated subcortical dopaminergic signaling capacity (Eisenstein et al. 2017), and factor-specific correlations with regional brain activation (Kirschner et al. 2016) and real-world function (Galderisi et al. 2014). The study of real world function demonstrated the practicality of use of the BNSS in large multicenter studies. The BNSS has also shown sensitivity to groups differences in reward processing, which is currently the most influential theoretical model for negative symptoms, with the AAA factor having a specific relationship to reward (Barch et al. 2014; Culbreth et al. 2016; Strauss et al. 2016b).

MIN-101 (a proprietary drug of Minerva Neurosciences, Inc.) is an antagonist of 5HT2A and sigma2 receptors (Mestre et al. 2013; Köster et al. 2014; Davidson et al., in press). In a 12-week, double blind phase 2b trial, two doses of MIN-101 were found to be superior to placebo as monotherapy for negative symptoms (Davidson et al., 2017) as measured by the negative factor score of the pentagonal structure model of the PANSS (White et al. 1997). The results of the trial suggest the change in negative symptoms were not "pseudospecific," i.e. secondary to changes in positive psychotic symptoms or depression, as there was no significant change in positive symptoms, and the negative symptom effect remained significant after covarying for change in depression scores (and see below).

The BNSS was a secondary outcome measure in the MI-101 phase 2b trial. As the BNSS has not previously been assessed in a pharmaceutical trial, we examined in detail its performance in that trial.

2. Materials and methods

In brief, this was an international, multicenter, double-blind study with three parallel arms: MIN-101 at a daily oral dose of either 32 mg (N = 78) or 64 mg (N = 83), and placebo (N = 83; study registered as EudraCT Number: 2014-004878-42). Both MIN-101 and placebo were given as monotherapy, and patients were withdrawn from any antipsychotic medication prior to receiving study treatment. For details of the protocol and detailed results, see Davidson et al. (in press).

2.1. Inclusion/exclusion criteria

Two hundred forty-four patients between the ages of 18 and 60 entered the trial. Entry criteria included 1) a DSM-5 diagnosis of schizophrenia, 2) clinically stable and exhibiting negative symptoms for 3 months prior to entering the study, as determined by their treating psychiatrist, and 3) on the Positive and Negative Syndrome Scale, a total score ≥ 20 on the PANSS negative syndrome subscale (items N1-N7), and scores <4 on the PANSS excitement, hyperactivity, hostility, suspiciousness, uncooperativeness, and poor impulse control items. Exclusions were a diagnosis of another mental disorder, a significant risk of suicide, a positive urine test for illicit drugs, a history of substance abuse, or an unstable medical disorder. There were also exclusion criteria related to QT values, and for poor and intermediate metabolizers for P450 CYP2D6 (Davidson et al., in press).

2.2. Study design

Eligible patients were withdrawn from depot antipsychotics, if any, for ≥1 month. All patients were then hospitalized and withdrawn from all psychotropic drugs for ≥5 days prior to randomization to oral MIN-101 32 mg/day, 64 mg/day, or placebo, in a 1:1:1 ratio. They remained hospitalized for at least 36 h after randomization, longer at the discretion of the investigator if clinically indicated.

Study treatment lasted for 12 weeks. No psychotropic medications were allowed during the trial, other than 1) oral lorazepam, oral zolpidem, or injectable sodium amytal for insomnia or agitation, or 2) anticholinergic medications for any extrapyramidal symptoms that emerged during the study. After the 12 weeks of double blind treatment, there was a 24-week open continuation phase. Data shown here are from the double-blind phase only. The primary outcome measure was the negative factor score of the PANSS from the pentagonal structure model (N1-N4,G5-G8 G13,14; White et al. 1997).

2.3. BNSS factors

As the BNSS item 4, Lack of Normal Distress, has not loaded as strongly on either the AAA or EXP factor as do other items, it was not included in either of the factor scores in the current analyses. The AAA score was therefore defined for the present analyses as the sum of the scores for items 1–3 and 5–8 (range: 0–42), and the EXP score was defined as the sum of the scores for items 9–13 (range 0–30).

2.4. Analyses

We present data related to the BNSS or its performance; details on other measures can be found in Davidson et al. (2017).

Using Mixed-Effect Model Repeated Measure (MMRM) analysis, we examined changes in BNSS total score and the AAA and EXP factors in the three treatment arms. We also examined whether the effect of MIN-101 was specific to negative symptoms or could be attributed to changes in positive symptoms and/or depression anxiety, using MMRM covarying for the positive, disorganization, and depression factors.

Using data from the endpoint ratings, confirmatory factor analysis was used to determine whether the raters separated the two factors found in previous studies. We examined the relative fits of two-factor and one-factor models of the BNSS, omitting the lack of normal distress item, using weighted least squares and maximum likelihood as methods of estimation. The comparative fit index (CFI), the Tucker Lewis Index (TLI), the root-mean-square-error-of-approximation (RMSEA), and information criteria (Akaike [AIC], Bayesian [BIC], and sample size adjusted BIC) were used to evaluate the relative fit of the two models, and of a `m,v null model, in which items are assumed to have zero covariance.

3. Results

Consistent with the recommendation of the Consensus Development Conference on Negative Symptoms on appropriate selection criteria for inclusion in negative symptom treatment trials (Kirkpatrick et al. 2006), patients entering the study had substantial negative symptoms but minimal positive and depressive symptoms.

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Table 2
Demographic and clinical characteristics of the sample.

		MIN-101	
	Placebo (N = 83)	32 mg/day (N = 78)	64 mg/day (N = 83)
Age (SD)	40.0 (10.2)	39.8 (10.2)	40.6 (10.6)
% male	57.8	52.6	57.8
PANSS total score	80.2 (10.7)	81.2 (9.8)	79.7 (11.1)
PANSS pentagonal model negative symptom score (SD)	31.5 (4.7)	31.7 (4.2)	31.4 (4.3)
PANSS pentagonal model positive symptom score (SD)	10.4 (2.9)	10.5 (3.0)	10.2 (2.9)
Calgary depression scale for schizophrenia score (SD)	2.2 (3.2)	2.2 (3.0)	2.0 (2.5)

The three treatment groups were also similar on demographic factors (Table 2, and see Davidson et al., in press for further details).

At 12 weeks, the 64 mg treatment dose (N = 83) differed significantly from placebo on BNSS total score ($p < 0.01$) and on the AAA and EXP factors ($p > 0.02$ on both factors; Table 3, Figs. 1 & 2). The 32 mg group (N = 78) had greater change in these three measures than did the placebo group (Table 2, Figs. 3 & 4), but these differences were not significant (total score, $p < 0.09$; AAA, $p < 0.20$; EXP, $p < 0.12$; Table 3, Figs. 3 & 4, Supplementary Table 1).

In the 64 mg group, the BNSS had effect sizes (Cohen's d) of 0.56, 0.48, and 0.46 for the total, AAA, and EXP scores. Among patients receiving the effective 64 mg group, the effect size for the two BNSS factors did not differ significantly, that is, the drug was not significantly more effective for one factor than for the other (data not shown). Covarying for the disorganization, anxiety/depression, and positive symptom factors from the PANSS produced no meaningful change in *p*-values for either the BNSS AAA or EXP factors (Table 4). In addition, removing a small number of patients with the highest scores on depression at baseline left a significant drug/placebo difference in negative symptoms, but no significant change in depression (data not shown).

Differences from placebo in the (smaller) 32 mg group were not significant, with respective effect sizes for BNSS total score, AAA, and EXP of 0.33, 0.25, and 0.30 (Table 3).

Confirmatory factor analysis showed that raters in this study separated the AAA and EXP factors. The two-factor model, which was essentially the structure found in previous studies (Supplementary Table 2), provided a fit to the data ($\chi^2 = 1199.80$, $p < 0.0001$, CFI = 0.743, TLI = 0.854, RMSEA = 0.571) superior to the fit for a one-factor model ($\chi^2 = 1161.50$, $p < 0.0001$, CFI = 0.732, TLI = 0.831, RMSEA = 0.603) or the null model (Supplementary Table 3).

4. Discussion

In this twelve week study of the efficacy of MIN-101 for negative symptoms in schizophrenia, the BNSS showed sensitivity to change

Table 3
Effect size and *p* value of BNSS total and factor scores at 12 weeks.

	Group	Adjusted score change	Effect size	p value
Total score	placebo	−3.23		
	32 mg	−5.44	0.33	<0.09
	64 mg	−6.94	0.56	<0.01
Factor scores				
AAA	placebo	−1.63		
	32 mg	−2.66	0.25	<0.20
	64 mg	−3.61	0.48	<0.02
EXP	placebo	−1.45		
	32 mg	−2.36	0.30	<0.12
	64 mg	−2.80	0.46	<0.02

Placebo: N = 83.
32 mg: N = 78.
64 mg: N = 83.

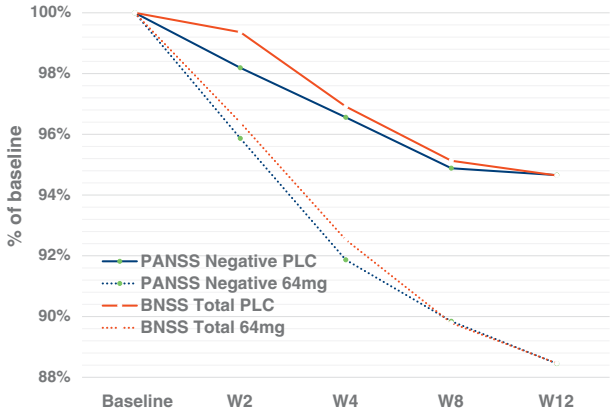

Fig. 1. BNSS total score for drug (64 mg) vs. placebo: $p < 0.01$. W2, W4, etc. refer to weeks of the study. PLC: placebo arm.

similar in effect size to that of the negative factor score of the pentagonal structure model of the PANSS (Davidson et al., 2017). Covarying for disorganization, positive symptom, anxiety/depression measures did not cause a meaningful change in the significance in either of the BNSS factor scores. These finding suggest that the effect of MIN-101 may not have been "pseudospecific," that is, due to an effect on these causes of secondary negative symptoms (Kirkpatrick et al. 2006). Depression improved in the MIN-101 trial, but the drug/placebo differences remained significant after covarying for change in depression scores (Davidson et al. 2017), and removing a small number of patients with the highest scores on depression at baseline left a significant drug/placebo difference in negative symptoms, but no significant change in depression.

Both BNSS factor scores (AAA and EXP) had a significant decrease compared to placebo in the 64 mg treatment group. The confirmatory factor analysis suggests this was not due to a halo effect, that is, the raters did not tend to give high ratings on the AAA items because of high EXP ratings, or vice versa, as the raters did preserve the factor structure. This lack of a specific relationship to one of the factors contrasts with the factor-specific correlations with regional brain activation (Kirschner et al. 2016) and real-world function (Galderisi et al. 2014) in studies that used the BNSS. However, in a psychosocial treatment trial (Choi et al. 2016), both factors improved. The significance of this lack of specificity in the MIN-101 trial is not clear; future treatment studies with MIN-101 may help clarify this issue.

While results with the BNSS parallel those of the primary negative symptom measure in the MIN-101 phase 2b trial, there are limitations to this study of the BNSS. The most important limitation of this

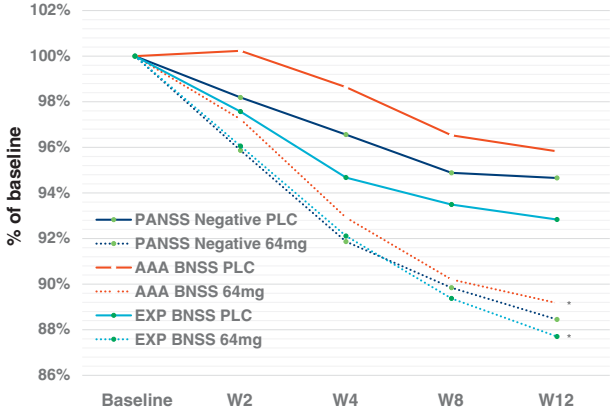

Fig. 2. BNSS factor scores for drug (64 mg) vs. placebo: $p < 0.02$ for AAA, $p < 0.02$ for EXP. W2, W4, etc. refer to weeks of the study. PLC: placebo arm. AAA: anhedonia/avolition/asociality factor. EXP: expressivity factor.

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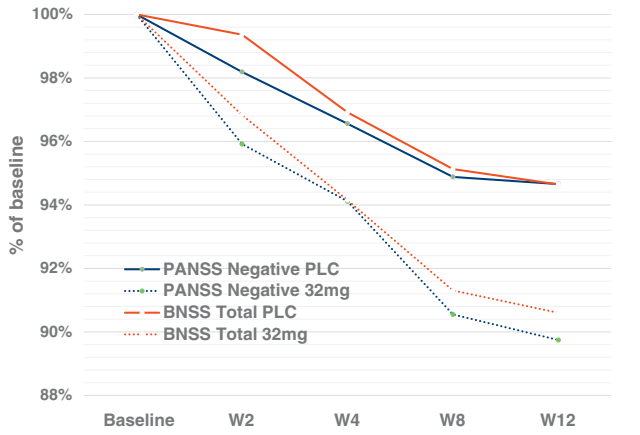

Fig. 3. BNSS total score for drug (32 mg) vs. placebo: $p < 0.09$. W2, W4, etc. refer to weeks of the study. PLC: placebo arm.

examination of the BNSS is that it is the first pharmacological study in which the BNSS was used that had an effect on another negative symptom measure that did not appear to be pseudospecific. The BNSS also showed sensitivity to change in one psychosocial treatment trial (Choi et al. 2016), but not in another study of a psychosocial intervention (Velligan et al. 2015), while two other scales did show a treatment effect. This discrepancy may be due to the relatively small sample (N = 51) in the study of Velligan and coworkers. Another limitation is that the MIN-101 phase 2b trial included patients with low depression and positive symptom scores, rather than a sample with more variation in symptoms.

Overall, the results of these studies suggest that the BNSS is successful in its primary intended purpose, which is to serve as a sensitive outcome measure in clinical trials. The BNSS has advantages over existing scales for use in clinical trials, including its brief interview time, a comprehensive manual, suitability for multicenter trials, crisp separation of the AAA and EXP factors, ease of training, successful translation and validation in multiple languages, standardized training materials, and implementation of recommendations of the Consensus Conference.

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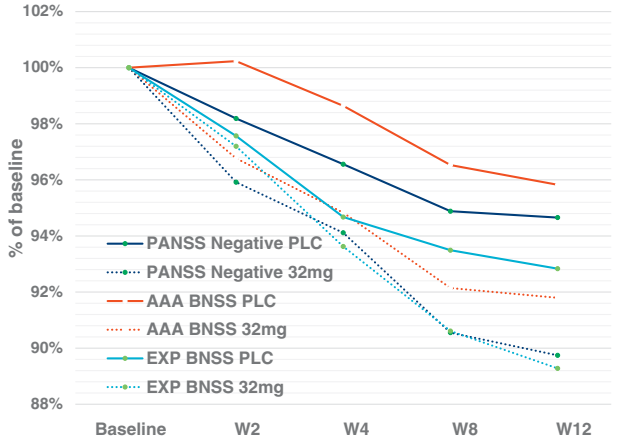

Fig. 4. BNSS factor scores for drug (32 mg) vs. placebo: $p < 0.20$ for AAA, $p < 0.12$ for EXP. W2, W4, etc. refer to weeks of the study. PLC: placebo arm. AAA: anhedonia/avolition/asociality factor. EXP: expressivity factor.

Table 4
Change in *p* values in the BNSS AAA and EXP factors covarying for other factor scores: combined 32 mg & 64 mg groups.

	AAA		EXP	
	Not covarying for the factor	Covarying for the factor	Not covarying for the factor	Covarying for the factor
Factor				
Disorganization	0.0278	0.0240	0.0224	0.0210
Anxiety/depression	0.0278	0.0268	0.0224	0.0221
Positive symptoms	0.0278	0.0283	0.0224	0.0222

AAA: Anhedonia/avolition/asociality factor; EXP: Expressed emotion factor.

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Contributors

***All authors had final approval.*

Brian Kirkpatrick designed the analyses and wrote the first draft.

Jay Saoud did most of the analyses and helped in interpretation of the data.

Gregory P. Strauss consulted on analyses and helped develop the concept of the paper.

Anthony O. Ahmed conducted some of the statistical analyses and helped with data interpretation.

Kaunori Tatsumi assisted in data analysis.

Mark Opler helped developed the concept of the paper.

Remy Luthringer helped design and oversee the clinical trial from which the data came.

Michael Davidson helped design and oversee the clinical trial from which the data came.

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References

Barch, D.M., Treadway, M.T., Schoen, N., 2014. Effort, anhedonia, and function in schizophrenia: reduced effort allocation predicts amotivation and functional impairment. J. Abnorm. Psychol. 123, 387–397.

Bischof, M., Obermann, C., Hartmann, M.N., Hager, O.M., Kirschner, M., Kluge, A., et al., 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.

Blanchard, J.J., Cohen, A.S., 2006. The structure of negative symptoms within schizophrenia: implications for assessment. Schizophr. Bull. 32, 238–245.

Blanchard, J.J., Bradshaw, K.R., Garcia, C.P., Nasrallah, H.A., Harvey, P.D., Casey, D., et al., 2017. Examining the reliability and validity of the Clinical Assessment Interview for Negative Symptoms within the Management of Schizophrenia in Clinical Practice (MOSAIC) multisite national study. Schizophr. Res. 185, 137–143.

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. 7.

Culbreth, A., Westbrook, A., Barch, D., 2016. Negative symptoms are associated with an increased subjective cost of cognitive effort. J. Abnorm. Psychol. 125, 528–536.

Davidson, M., Saoud, J., Staner, C., Noel, N., Luthringer, E., Werner, S., et al., 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 (12), 1195–1202.

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

Galderisi, S., Rossi, A., Rocca, P., Bertolino, A., Mucci, A., Bucci, P., et al., 2014. The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. World Psychiatry 13, 275–287.

Kimhy, D., Yale, S., Goetz, R.R., McFarr, L.M., Malaspina, D., 2006. The factorial structure of the schedule for the deficit syndrome in schizophrenia. Schizophr. Bull. 32, 274–278.

Kirkpatrick, B., Buchanan, R.W., McKenney, P.D., Alphs, L.D., Carpenter Jr., W.T., 1989. The schedule for the deficit syndrome: an instrument for research in schizophrenia. Psychiatry Res. 30, 119–123.

Kirkpatrick, B., Fenton, W.S., Carpenter, W.T., Marder, S.R., 2006. The NIMH-MATRICS consensus statement on negative symptoms. Schizophr. Bull. 32, 214–219.

Kirkpatrick, B., Strauss, G.P., Nguyen, L., Fischer, B.A., Daniel, D.G., Cienfuegos, A., et al., 2011. The brief negative symptom scale: psychometric properties. Schizophr. Bull. 37 (2), 300–305.

Kirschner, M., Hager, O.M., Bischof, M., Hartmann, M.N., Kluge, A., Seifritz, E., et al., 2016. Ventral striatal hypoactivation is associated with apathy but not diminished expression in patients with schizophrenia. J. Psychiatry Neurosci. 41, 152–161.

Köster, L.S., Carbon, M., Correll, C.U., 2014. Emerging drugs for schizophrenia: an update. Expert Opin. Emerg. Drugs 19, 511–531.

Mané, A., García-Rizo, C., Garcia-Portilla, M.P., Bergé, D., Sugranyes, G., Garcia-Alvarez, L., et al., 2014. Spanish adaptation and validation of the brief negative symptoms scale. Compr. Psychiatry 55, 1726–1729.

Mestre, T.A., Zurowski, M., Fox, S.H., 2013. 5-Hydroxytryptamine 2A receptor antagonists as potential treatment for psychiatric disorders. Expert Opin. Investig. Drugs 22, 411–421.

Mucci, A., Galderisi, S., Merlotti, E., Rossi, A., Rocca, P., Bucci, P., et al., 2015. The brief negative symptom scale (BNSS): independent validation in a large sample of Italian patients with schizophrenia. Eur. Psychiatry 30, 641–647.

Nakaya, M., Ohmori, K., 2008. A two-factor structure for the schedule for the deficit syndrome in schizophrenia. Psychiatry Res. 158, 256–259.

Polat Nazlı, I., 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, 265–271.

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

Strauss, G.P., Hong, L.E., Gold, J.M., Buchanan, R.W., McMahon, R.P., Keller, W.R., et al., 2012a. Factor structure of the brief negative symptom scale. Schizophr. Res. 142, 96–98.

Strauss, G.P., Keller, W.R., Buchanan, R.W., Gold, J.M., Fischer, B.A., McMahon, R.P., et al., 2012b. Next-generation negative symptom assessment for clinical trials: validation of the brief negative symptom scale. Schizophr. Res. 142, 88–92.

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., Whearty, K.M., Morra, L.F., Sullivan, S.K., Ossenfort, K.L., Frost, K.H., 2016b. Avolition in schizophrenia is associated with reduced willingness to expend effort for reward on a progressive ratio task. Schizophr. Res. 170, 198–204.

Velligan, D.I., Roberts, D., Mintz, J., Maples, N., Li, X., Medellin, E., Brown, M., 2015. A randomized pilot study of MOtiVation and Enhancement (MOVE) Training for negative symptoms in schizophrenia. Schizophr. Res. 165, 175–180.

White, L., Harvey, P.D., Opler, L., Lindenmayer, J., 1997. Empirical assessment of the factorial structure of clinical symptoms in schizophrenia. Psychopathology 30, 263–274.

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

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