



Are Shorter Versions of the Positive and Negative Syndrome Scale (PANSS) Doable?

A Critical Review

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ABSTRACT

ABSTRACT: The Positive and Negative Syndrome Scale (PANSS) is a well-established assessment tool for measuring symptom severity in schizophrenia. Researchers and clinicians have been interested in the development of a short version of the PANSS that could reduce the burden of its administration for patients and raters. The author presents a comprehensive overview of existing brief PANSS measures, including their strengths and limitations, and discusses some possible next steps. There are two available scales that offer a reduced number of original PANSS items: PANSS-14 and PANSS-19; and two shorter versions that include six items: Brief PANSS and PANSS-6. The PANSS-6 has been tested quite extensively in established trials and appears to demonstrate high sensitivity to change and an established cut off definition for remission. Prospective testing in new antipsychotic treatment trials is still required for these shorter versions of PANSS. In addition, they need to be supplemented with interview guides, as well as provide conversion formulas to translate total scores from the short PANSS versions to the PANSS-30. Both short versions of the PANSS are essentially designed to evaluate response to antipsychotic treatment. Future PANSS scale development needs to address specific measurement of treatment-responsive positive symptoms by including treatment-sensitive items, as well as illness-phase specific PANSS tools.

KEYWORDS: Positive and Negative Syndrome Scale, PANSS, Brief PANSS, PANSS-6, schizophrenia, patient assessment

The Positive and Negative Syndrome Scale (PANSS), a well-established scale for measuring symptom severity in schizophrenia,¹ evaluates 30 separate items grouped in positive, negative, and general psychopathology subscales. The PANSS has been translated and validated in numerous languages^{2,3} and is considered the world-wide “gold standard” for the measurement of symptoms of schizophrenia. The PANSS is predominantly used as an outcome measure for the evaluation of psychopharmacological and nonpsychopharmacological treatment interventions in schizophrenia. The scale was created by merging the 18-item Brief Psychiatric Rating Scale⁴ with 12 items from the Psychopathology Rating Schedule.⁵ These items were essentially added in order to capture negative symptoms and general psychopathology symptoms.

Advantages of a shorter PANSS.

Generally, the administration and scoring of the PANSS, which includes the use of a semi-structured clinical interview (SCI-PANSS⁶), can take up to 50 minutes, placing a burden on both patient and rater/clinician. Thus, researchers and clinicians have long been interested in the development of a shorter version of the PANSS that can measure the severity of symptoms in schizophrenia and take less time to administer. In addition, a shorter version of the PANSS offers the

possibility of using the same tool in clinical care as is used in research.

Another, more fundamental reason for developing a brief version of the PANSS is based on the failure to replicate a common factor structure underlying the current 30 PANSS items across different patient samples. Since the original five-factor model was published,⁹ many more factor analyses have been published with varying numbers of factors, varying numbers of items assigned to factors, and varying levels of goodness-of-fit data. Even the widely used Marder model,¹⁰ which contains all 30 PANSS items, performed poorly as measured by the goodness-of-fit statistics (root mean square error of approximation [RMSEA] and the confirmatory fit index [CFI]). In contrast, the pentagonal model¹¹ performed well using only 25 PANSS items in the confirmatory factor analysis (CFA). However, more recently, a study examined 25 published five-factor models on a new dataset containing nearly 6,000 patients from clinical trials, finding unsatisfactory fit indices.¹² Wallwork et al¹³ examined 29 published models with a new patient sample; again, none fit the data well.

Interestingly, Hayashi et al¹⁴ reported that using fewer than half of the PANSS items produced the most resilient models. These findings suggest that a shorter PANSS containing fewer items (but not necessarily

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fewer factors) could be more robust than models using all 30 items.

Further, a shorter PANSS version also offers the possibility to retain only those PANSS items that are psychometrically very robust. We have shown using item response analysis (IRT) that not all PANSS items demonstrate optimal option characteristic curves (OCCs) and item characteristic curves (ICCs), while most items performed very well.^{15, 16} A shorter PANSS could potentially allow for retention of the items that perform well psychometrically.

Finally, Bech¹⁷ has pointed out that in order to obtain valid measures of illness severity, it is essential that rating scales are both scalable and transferable. By “scalability,” Bech means that each item in a rating scale “provides unique information regarding syndrome severity and is a statistical prerequisite for using the total score as a measure of overall severity.” Further, a “severity rating scale has to have an additive structure, implying that each manifest item scores in the scale can be added to a simple sum, which is a psychometrically valid measure of overall illness severity.”¹⁷

Ostergaard et al¹⁸ found that neither the full PANSS-30 nor any other, shorter versions of the PANSS have been evaluated for their scalability by means of the Rasch rating scale model. These authors proposed a six-item PANSS, whereby each item was chosen based on its scalability, meaning that all items provide unique information regarding syndrome severity.

Disadvantages of a shorter PANSS.

Whatever the scientific and practical rationale is for the development of a shorter version of the PANSS, there are a number of potential disadvantages to be kept in mind. One of the most important is the issue of successful comparability and translation of results between studies using the full PANSS and those studies using a shorter version. While there might be statistical models capable of translating PANSS total scores from a short version to the full version,¹⁶ this will always introduce a complicating factor in comparing results between studies. Notably, this issue was fairly easy to mitigate when the results obtained with PANSS ratings had to be compared with results measured with BPRS ratings, given that the PANSS contains all BPRS items.

Another issue potential problem is that the *a priori* chosen focus in a short PANSS version, given the restricted number of items, might include predominantly treatment-responsive items. This would help to discriminate between active treatments and placebos in controlled clinical trials. However, this would, at the same time, limit explorations of newer treatments or interventions that are not dopamine blockers, the main model of all antipsychotic pharmacological treatments until now. Another potential limitation related to this issue is that a short PANSS might focus on a single psychopathological domain and not measure other common schizophrenia domains. On the research side, a brief PANSS version with significantly fewer items could potentially present psychometric challenges in terms of construct validity, discriminant validity, and sensitivity to change to statistically evaluate significant changes to a treatment intervention. Short scales extracted from a longer scale can compromise the reliability of an instrument.⁷ As items of the scale are removed, the Cronbach's alpha tends to decrease. Scales with many items tend to be more reliable, with higher alpha values.⁸ Finally, a short version of the PANSS might have to be phase-specific and not be applicable to all illness phases over time.

With these multiple issues in mind, this article presents a comprehensive overview of existing brief PANSS measures, including their strengths and limitations, and discusses some possible next steps in more detail.

BRIEF PANSS MEASURES

The Mini-PANSS. Using the new statistical technique of item response analysis on all 30 PANSS items, Santor et al¹⁵ found that most items forming the positive and negative subscales of the PANSS performed very well, but several areas for improvement in items of the general psychopathology subscale were identified. The positive and the negative subscales were more discriminating of individual differences in symptom severity than the general psychopathology subscale score and were shown to be more efficient on average than the 30-item total score. These authors suggested that the retained 14 items could form a shorter version of the PANSS—the 14-item PANSS. Building further on these

data and using the same IRT technique, Kahn et al¹⁶ examined baseline PANSS scores from 7,187 patients with schizophrenia or schizoaffective disorder who were enrolled in psychopharmacology trials in the years 1995 to 2005.¹⁶ OCCs and ICCs were constructed to examine the probability of rating each of seven options (equaling levels of severity) within each of the 30 PANSS items as a function of subscale severity, and summed-score linking was applied to items selected for the Mini-PANSS. This statistical process resulted in six of the seven positive symptom items, six of the seven negative symptom items, and seven of the 16 general psychopathology items, all of which were retained as items that performed well and as closely linked to overall severity. The authors retained these 19 items for inclusion in the Mini-PANSS. They also produced, via using summed score-linking and linear interpolation, a translation table for comparing total subscale scores of the Mini-PANSS with total subscale scores of the original PANSS.¹⁶ Results showed scores on the subscales of the Mini-PANSS could be linked with scores on the original PANSS subscales, with very little bias. The authors also examined similarities and differences between the 30-item PANSS and the Mini-PANSS using a series of descriptive analyses, including high correlations between subscale and total scores. Results of the principal component analysis of the Mini-PANSS assumed dimensionality for all three of the subscales. The elimination of the under-performing PANSS items resulted in high correlation between PANSS 30-item subscales and Mini-PANSS subscales, indicating that omission of these items in future clinical trials is not likely to significantly alter the PANSS subscales. Such a 19-item Mini-PANSS might be more reliable given the psychometric soundness of the retained items, might require shorter administration and training time, and might possibly reduce the sample size needed for future research studies. However, the 19-item Mini-PANSS still needs to be tested for its construct validity, reliability, and sensitivity to change. Specificity and cutoff scores for the Mini-PANSS also need to be determined for improvement and remission. Another consideration to investigate is the Mini-PANSS's ability to better separate placebo response from antipsychotic response.

The Brief PANSS. Yamamoto et al¹⁹

extracted six items from the full PANSS with the aim of developing a brief scale that could be administered within 10 minutes and be sensitive to changes resulting from antipsychotic treatment.¹⁹ The authors aimed at selecting at least two specific items from each of the three PANSS subscales (i.e., the positive symptoms, negative symptoms, and general psychopathology scales) to sufficiently reflect the profiles of schizophrenia. All selected items had to have high levels of correlation with changes in the Clinical Global Impression (CGI-I) scale that reflected their sensitivity to change, as well as high levels of correlation with the CGI-S scale that reflected the severity of illness. Data was derived from 714 patients with schizophrenia involved in antipsychotic trials. The six items were Delusion, Suspiciousness, Emotional Withdrawal, Passive/Apathetic Social Withdrawal, Tension, and Unusual Thought Content. The Brief PANSS showed a high correlation of 0.86 with the full PANSS at study entry and 0.92 at the end of antipsychotic treatment. The correlation between the change as measured with the Brief PANSS and with the total PANSS was 0.93 ($p < 0.001$), while the correlation of change measured with the Brief PANSS and the change in the CGI scale score was 0.73 ($p < 0.001$). Similar to the Mini-PANSS, the Brief PANSS has not yet undergone psychometric testing regarding its construct validity and reliability with respect to its use in patient samples other than the original study population used in the development of the Brief PANSS.

The six-item PANSS. Ostergaard et al¹⁸ have presented a six-item PANSS (PANSS-6) based on the Rasch rating scale model that comprises the scalable items Delusions, Conceptual Disorganization, Hallucinations, Blunted Affect, Social Withdrawal, and Lack of Spontaneity and Flow of Conversation.¹⁸ The Rasch rating model indicated that the three scalable items (all items provide unique information regarding syndrome severity) covering positive symptom items (Delusions, Conceptual Disorganization, and Hallucinations) had the highest prevalence, whereas the three scalable negative items (Blunted Affect, Social Withdrawal, and Lack of Spontaneity and Flow of Conversation) had the lowest prevalence. Furthermore, the PANSS-6 was shown by the authors to be sensitive to change in patients in two antipsychotic trials

(haloperidol and sertindole versus placebo¹⁸) and to differentiate the active treatment symptom reduction from the placebo symptom reduction. The remission rate as measured by the PANSS-6 was defined at less than 14, when using a CGI scale score of 3 or less as an index of validity for remission. Using this cutoff point, the PANSS-6 also measured higher remission rates during treatment with haloperidol and sertindole versus placebo. The authors support the construct validity of the PANSS-6 by the observation that it covers four of the five symptoms included as criteria for schizophrenia (except for "Grossly Disorganized or Catatonic Behavior") according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*^{19a} (DSM-5). In a more recent study that tested the validity and sensitivity of the PANSS-6 in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study,^{19b} Ostergaard et al²⁰ reanalyzed the 1,432 subjects (intention-to-treat [ITT] sample) and found that the PANSS-6 and PANSS-30 total scores were highly correlated (Spearman correlation coefficient=0.86). However, these investigators did not remove from the PANSS-30 the items from the PANSS-6, resulting in error variance of these six correlated items and inflation of the reported correlations. The same limitation affects the reported high correlations between PANSS-6 and PANSS-30 for the relative changes in total scores (Spearman correlation coefficient=0.77), between the total score ratios (Spearman correlation coefficient=0.77), and between the total score log-ratios (Spearman correlation coefficient=0.77). The PANSS-6 identified symptom remission with an accuracy of 0.99 (95% confidence interval [CI]=0.99–0.99). In ITT analyses, PANSS-6 and PANSS-30 identified the same statistically significant differences in antipsychotic efficacy (i.e., that olanzapine was superior to risperidone [p -value for PANSS-6 was 0.0003 and for PANSS-30 was 0.0003] and ziprasidone [p -value for PANSS-6 was 0.0018 and for PANSS-30 was 0.0046]). Psychometric testing of the PANSS-6 needs to be expanded to prospective testing of its sensitivity to change and its use in longitudinal remission studies.

CONCLUSION

Reducing the burden of administration would be a key advantage the shorter PANSS would have over the PANSS-30, for clinicians,

researchers, and patients. There are newer scales available that have a reduced number of original PANSS items. The PANSS-14 and PANSS-19 are scales based on IRT application with inclusion of psychometrically highly reliable items, which closely reflect overall severity. However, both of these scales have not yet been evaluated in prospective trials. Two shorter versions, the Brief PANSS and the PANSS-6, both include six items, which represent in a balanced fashion the positive and negative domains of schizophrenia. Two of their respective items overlap (Delusions and Social Withdrawal), while other items are quite different between the two scales. The PANSS-6 has been tested quite extensively in established trials and appears to demonstrate high sensitivity to change and an established cutoff definition for remission. Prospective use of PANSS-6 and Brief PANSS in antipsychotic treatment trials is still required for these scales, however. In addition, these scales need to be supplemented with interview guides, as well as provide conversion formulas to translate total scores from the short PANSS versions to the PANSS-30.

PANSS-6 and Brief PANSS are essentially designed to evaluate patient response to antipsychotic treatment. Most, if not all, antipsychotic treatments aim at decreasing positive symptoms and have no or significantly lesser effects on negative symptoms. Improvement or score reduction in any rating scale measuring current antipsychotic treatment effects will therefore measure predominantly positive symptoms and, to a much lesser degree, negative symptoms. It might therefore be possible to develop a short PANSS version that focuses predominantly on uniquely treatment-sensitive positive symptoms.

On the other hand, explorations of drug effects with novel mechanisms of action might require a fuller PANSS instrument in order to find new and/or additional treatment effects in domains other than positive symptoms. Additionally, investigations of symptom structure and biological correlates of schizophrenia might continue to need the full PANSS in order to investigate the full spectrum of schizophrenia symptoms. The development of a phase-specific version of PANSS should also be

considered. Research has suggested that the PANSS factor structure and item relationships differ by illness phase.²⁰ Hence, there might be a need for the development in future research of a specific PANSS capable of measuring treatment effects in first-episode patients and established, multi-episode patients, and for use in treatment-resistant patients.

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