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EDITORIAL

New Standards for Negative Symptom Assessment

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Introduction

The need to deconstruct schizophrenia into domains of psychopathology was clear with Kraepelin's presentation of dissociative pathology and "weakening of the well-springs of volition" as the 2 critical clinical features. Strauss et al[1] advocated syndrome deconstruction when introducing the positive and negative symptom terminology in 1974. For much of our history, the field of schizophrenia has focused on positive psychotic symptoms, especially the reality distortion aspect influenced by Schneider's concept of first rank symptoms and the preeminence given in DSM-III and DSM-IV to bizarre delusions and Schneiderian forms of auditory hallucinations. Negative symptoms were not even included in criterion A in DSM-III. A growing awareness of the need to focus on domains of pathology has emerged, energized by the National Institute of Mental Health (NIMH) MATRICS initiative, which defined impaired cognition and negative symptoms as unmet therapeutic needs,[2,3] and further strengthened by the NIMH Research Domain Criteria initiative[4] and the 8 pathology dimensions relevant to psychotic disorders presented in DSM-5, Section 3.

Negative symptoms have been used in an effort to define a meaningful subgroup of schizophrenia, but study of negative symptoms as a dimension of schizophrenia, rather than as the basis for subgrouping, has been the more common approach. Several instruments are widely used to quantify negative symptoms, notably the Scale for the Assessment of Negative Symptoms, the negative symptom factor of the Brief Psychiatric Rating Scale, the Positive and Negative Symptom Scale, and the Negative Symptom Assessment. These instruments have been important in many aspects of schizophrenia research, including defining brain pathophysiology and revealing the lack of efficacy of antipsychotic drugs for this aspect of illness.

In 2005, NIMH convened a Consensus Development Conference on Negative Symptoms, which included academic and industry experts in schizophrenia phenomenology, psychology, cognition, and treatment research, as well as representatives from NIMH and the Food and Drug Administration. The purpose of the Conference was to address evidence regarding separable factors within negative symptoms, negative symptoms as an indication for regulatory approval, appropriate designs for testing efficacy in clinical trials, what symptoms are within the negative symptom construct, and the relationship of negative symptoms to cognition and function. The Conference participants agreed that there are at least 5 domains of negative symptoms: anhedonia, avolition, asociality, blunted affect, and alogia.[3] Another point of consensus was the need for a new assessment instrument that included the 5 symptom domains judged to be components of this psychopathology. Conference materials were published in the April, 2006 issue of Schizophrenia Bulletin.

After the Conference, a workgroup was formed to develop new assessment approaches. Initial work involved extensive literature reviews, feedback from participants in the original Conference and clinical trial researchers, presentations at conferences, and feedback on material posted on a public Website. A beta version of a negative symptom scale resulted from this process. Subsequently, 2 groups formed with different plans for developing final instruments. One group shortened the beta version (resulting in the Brief Negative Symptom Scale, BNSS) and collected data to encourage early adoption. The other group obtained funding from NIMH to conduct large-scale multisite studies to refine their measure (the Clinical Assessment Interview for Negative Symptoms, CAINS) within a more extensive iterative scale development process. Both scales include the 5 domains with extensive overlap in items (table 1) and the BNSS includes an item assessing the lack of normal distress—a construct not included in the CAINS. Here we briefly describe the CAINS and BNSS, provide citations and a guide for

Table 1. Items in the Brief Negative Symptom Scale (BNSS) and the Clinical Assessment Interview for Negative Symptoms (CAINS)

BNSS		CAINS	
Subscale	Items	Subscale	Items
Anhedonia	Intensity of pleasure during activities	Motivation and Pleasure	Motivation for close family/spouse/ partner relationships
	Frequency of pleasurable activities		Motivation for close friendships and romantic relationships
	Intensity of expected pleasure from future activities		Frequency of pleasurable social activities
Asociality	Asociality: behavior		Frequency of expected pleasurable social activities
	Asociality: internal experience		Motivation for work and school activities
Avolition	Avolition: behavior		Frequency of expected pleasurable work and school activities
	Avolition: internal experience		Motivation for recreational activities
Blunted affect	Facial expression		Frequency of pleasurable recreational activities
	Vocal expression		Frequency of expected pleasurable recreational activities
	Expressive gestures	Expression	Facial expression
Alogia	Quantity of speech		Vocal expression
	Spontaneous elaboration		Expressive gestures
Lack of normal distress	Lack of normal distress		Quantity of speech

access to the scales and training in hopes of increasing the use of these scales in relevant research designs.

Clinical Assessment Interview for Negative Symptoms

The CAINS was designed to address limitations of existing negative symptom instruments[5] and to assess the 5 consensus negative symptom subdomains.[3] Scale development was funded by NIMH and based on 3 principles: the ratings of negative symptoms integrate information from behavior, environmental context, and patient's descriptions of their internal states; item selection relied on a data-driven iterative process that guided psychometric refinement; and application in various settings would be supported by training materials.

The CAINS has been evaluated and refined across 2 large-scale multisite studies. Horan et al[6] examined the structure and psychometric properties of the original 23-item version of the CAINS in 281 outpatients across 4 sites. Structural analyses indicate 2 factors reflecting deficits in motivation and pleasure, and in expressive impairments. Inter-rater agreement and preliminary validity data guided subsequent item modification and deletion. A revised 16-item CAINS was subsequently evaluated in 162 outpatients.[7] Data-informed item trimming resulted in the final 13-item CAINS with a motivation/pleasure factor defined by 9 items and a 4-tem expression factor. The final CAINS has good internal consistency, inter-rater agreement, test–retest stability, discriminant validity, and strong convergent validity including relations to real-world functioning.

The CAINS was subsequently evaluated in over 500 participants across 15 geographically dispersed centers (J. J. Blanchard, K. R. Bradshaw, C. P. Garcia, et al., unpublished data, 2015). Factor structure was confirmed with high internal consistency and temporal stability across a 3-month period. There was a strong relationship with clinician-rated functioning and patient self-reported quality of life. These results indicate that the CAINS can be successfully utilized in nonacademic clinical settings and administered by bachelor and master-educated raters. Time required for administration is approximately 25 minutes. The CAINS has been translated into Czech, French, Spanish, Mandarin, Cantonese, Korean, Polish, Greek, Swedish, Lithuanian, and German. A detailed interview guide and user's manual are freely available from the developers and online training videos can be accessed for clinical and research purposes free of charge (http://www.med.upenn.edu/bbl/downloads/CAINSVideos.shtml).

The Brief Negative Symptom Scale

The BNSS was designed with several principles in mind: ease of use, feasibility for multicenter trials, brevity, simple language, and relatively culture-free anchors. It has 13 items and administration of the scale typically takes 12–15 minutes. It includes the 5 domains recognized by the Consensus Development Conference, as well as an additional item, Lack of Normal Distress. Items in the anhedonia, avolition, and asociality subscales separate objective behavior from subjective experience and consummatory from appetitive anhedonia. Its basic

psychometric properties—inter-rater and test–test reliability, and discriminant and convergent validity—are excellent.[8,9] Published studies demonstrating strong psychometric properties in Spanish and Italian versions show that the BNSS can also perform well in translation, and the BNSS has been successfully applied in a large, multicenter Italian study.[10] It has been translated into several languages other than Spanish and Italian, but at the time of writing its psychometric performance in those translations has not been published. It can be administered by bachelors through doctoral raters if they have experience with people with schizophrenia and receive appropriate training.

In addition to the CAINS, 2 other negative symptom instruments, the SANS and SDS, found similar factor structures for negative symptoms, with expressivity (blunted affect and alogia) and avolition/anhedonia/asociality (AAA) factors. The BNSS has a similar factor structure, with 1 factor consisting of pleasure and motivation items, and the other including blunted affect and alogia items.[11] Of the scales that find these 2 factors, the BNSS has a particularly crisp separation. The AAA factor had a fairly robust relationship with level of function in the multicenter Italian study,[10] and appears to have a weak correlation with cognitive function. The AAA factor does not correlate with depressive or positive psychotic symptoms.[9,10] The loading of the Lack of Normal Distress item on the 2 BNSS factors is weak and inconsistent although other psychometric measures such as Cronbach's alpha support, its inclusion in the concept of negative symptoms.

The BNSS is available without charge for academic and nonprofit groups and can be accessed at http://bingweb.binghamton.edu/~gstrauss/Resources.htm. Training videos with gold standard ratings are available. Commercial entities can access materials through ProPhase.

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