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The Latent Structure of Negative Symptoms in Schizophrenia

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IMPORTANCE Negative symptoms are associated with a range of poor clinical outcomes, and currently available treatments generally do not produce a clinically meaningful response. Limited treatment progress may be owing in part to poor clarity regarding latent structure. Prior studies have inferred latent structure using exploratory factor analysis, which has led to the conclusion that there are 2 dimensions reflecting motivation and pleasure (MAP) and diminished expressivity (EXP) factors. However, whether these conclusions are statistically justified remains unclear because exploratory factor analysis does not test latent structure. Confirmatory factor analysis (CFA) is needed to test competing models regarding the latent structure of a construct.

OBJECTIVE To evaluate the fit of 4 models of the latent structure of negative symptoms in schizophrenia using CFA.

DESIGN, SETTING, AND PARTICIPANTS Three cross-sectional studies were conducted on outpatients with schizophrenia who were rated on the 3 most conceptually contemporary measures: Scale for the Assessment of Negative Symptoms (SANS), Brief Negative Symptom Scale (BNSS), and Clinical Assessment Interview for Negative Symptoms (CAINS). Confirmatory factor analysis evaluated the following 4 models: (1) a 1-factor model; (2) a 2-factor model with EXP and MAP factors; (3) a 5-factor model with separate factors for the 5 domains of the National Institute of Mental Health consensus development conference (blunted affect, alogia, anhedonia, avolition, and asociality); and (4) a hierarchical model with 2 second-order factors reflecting EXP and MAP and 5 first-order factors reflecting the 5 consensus domains.

MAIN OUTCOMES AND MEASURES Outcomes included CFA model fit statistics derived from symptom severity scores on the SANS, BNSS, and CAINS.

RESULTS The study population included 860 outpatients with schizophrenia (68.0% male; mean [SD] age, 43.0 [11.4] years). Confirmatory factor analysis was conducted on each scale, including 268 patients for the SANS, 192 for the BNSS, and 400 for the CAINS. The 1- and 2-factor models provided poor fit for the SANS, BNSS, and CAINS as indicated by comparative fit indexes (CFIs) and Tucker Lewis indexes (TLIs) less than 0.950, RMSEAs that exceeded the 0.080 threshold, and WRMRs greater than 1.00. The 5-factor and hierarchical models provided excellent fit, with the 5-factor model being more parsimonious. The CFIs and TLIs met the 0.95 threshold and the 1.00 threshold for both factor models with all 3 measures. Interestingly, the RMSEAs for the 5-factor model and the hierarchical model fell under the 0.08 threshold for the BNSS and the CAINS but not the SANS.

CONCLUSIONS AND RELEVANCE These findings suggest that the recent trend toward conceptualizing the latent structure of negative symptoms as 2 distinct dimensions does not adequately capture the complexity of the construct. The latent structure of negative symptoms is best conceptualized in relation to the 5 consensus domains. Implications for identifying pathophysiological mechanisms and targeted treatments are discussed.

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Supplemental content

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Negative symptoms have long been considered a core symptom of schizophrenia.[1,2] Factor analytic studies support these early clinical impressions, indicating that negative symptoms are distinct from positive and disorganized symptoms.[3-5] However, studies examining the factor structure of items within negative symptom scales alone suggest that the construct may not be unidimensional.[6] Consistent evidence suggests that there are 2 distinct factors reflecting diminished motivation and pleasure (MAP, including anhedonia, avolition, and asociality) and diminished expressivity (EXP, including blunted affect and alogia) across a variety of scales.[7-13] These findings have led the field to shift away from a unidimensional conceptualization of negative symptoms in favor of a 2-dimensional conceptualization consisting of MAP and EXP.[14]

However, whether current views on the latent structure of negative symptoms are theoretically or statistically justified remains unclear. Evidence supporting the 2-dimensional structure comes primarily from studies using exploratory factor analysis (EFA). Exploratory factor analysis is a data reduction technique that infers the presence of latent factors responsible for shared variance among a set of items. It does not specify an underlying structure, but rather assumes that each item could be related to each latent factor. Exploratory factor analysis is an important first step in generating hypotheses regarding the latent structure of a construct, but it does not actually test competing models regarding the number of dimensions that exist or that evaluate which items are part of those dimensions. Confirmatory factor analysis (CFA) is needed to achieve these aims and make definitive conclusions regarding the latent structure of a construct, because CFA allows for direct comparison of competing theoretical models. Prior CFA studies[15,16] have been restricted to the Scale for the Assessment of Negative Symptoms (SANS) and have included items that are no longer considered part of the negative symptom construct (eg, inappropriate affect, inattention), limiting conclusions regarding the latent structure of negative symptoms.

The present study used CFA to evaluate competing hypotheses regarding the latent structure of negative symptoms. Four models were examined across 3 studies using data on outpatients with schizophrenia who underwent rating using the SANS,[17] the Brief Negative Symptom Scale (BNSS),[18] or the Clinical Assessment Interview for Negative Symptoms (CAINS).[12] The first model was unidimensional, which considered whether all items best reflect a single latent construct. A unidimensional model is important to test because original conceptualizations of the construct posited a single dimension.[19] In addition, most negative symptom scales are still evaluated using a single total score, which may or may not be justified. The second model evaluated the 2 dimensions identified in prior EFA studies,[7,11-13] which indicate separate EXP and MAP factors. The EFA studies supporting the 2 factors have been influential, informing how researchers search for pathophysiological mechanisms of negative symptoms[20-22] and how pharmaceutical companies have recently been approaching targeted treatment development.[23] However, these decisions may not be empirically supported, and a more fine-grained approach may be warranted. The most contemporary conceptualization resulted from the 2005 National Institute of Mental Health (NIMH) consensus development conference, which proposed the existence of the following 5 core domains: blunted affect, alogia, avolition, anhedonia, and asociality.[24] Although EFAs indicate that these 5 domains load onto EXP and MAP factors, examination of more complex theoretical models is required to understand the underlying structure of negative symptoms. Confirmatory factor analysis can be used for this purpose. If more complex models are superior, the current focus on the 2 factors may preclude identification of pathophysiological mechanisms or treatment effects that are specific to the 5 domains. As such, more complex models were also examined. The third model was a 5-factor model that specified 1 factor for each of the 5 consensus domains. The fourth model was a hierarchical model with 2 second-order factors reflecting EXP and MAP and 5 first-order factors reflecting the 5 consensus domains. In the hierarchical model, first-order factors representing anhedonia, avolition, and asociality were specified to load on the MAP second-order factor, whereas the first-order factors blunted affect and alogia were specified to load on the EXP second-order factor. Collectively, evaluating the fits of 1-, 2-, 5-, and hierarchical-model solutions provides a comprehensive test of the latent structure of negative symptoms that is informed by theory.

Key Points

Question What is the latent structure of negative symptoms in schizophrenia?

Findings Three cross-sectional studies were conducted on 860 outpatients with schizophrenia who underwent rating with the 3 most conceptually contemporary measures. Confirmatory factor analysis indicated that the 1- and 2-factor models provided a poor fit for the data; however, 5-factor and hierarchical models provided an excellent fit.

Meaning These findings suggest that a change is warranted regarding diagnostic criteria for schizophrenia, how pathophysiological mechanisms are explored, and how to search for targeted treatments for negative symptoms.

Methods

Participants

Data were examined for 3 studies that used different negative symptom scales to evaluate samples of predominantly outpatients with chronic schizophrenia. This study was approved by the local institutional review boards, and all participants provided written informed consent.

Study 1 included data from 268 outpatients with schizophrenia who underwent rating using the SANS.[25] Participants were recruited from the outpatient research clinics at the Maryland Psychiatric Research Center, Catonsville, and community mental health clinics in the Baltimore, Maryland, metropolitan area. Study 2 included 192 outpatients with schizophrenia who underwent rating using the BNSS.[18] Participants

Table 1. Demographic Characteristics

Variable	Substudy		
	SANS (n = 268)	BNSS (n = 192)	CAINS (n = 400)
Age, mean (SD), y	40.6 (11.9)	40.3 (11.7)	45.8 (10.6)
Male, No. (%)	188 (70.1)	124 (64.6)	273 (68.3)
Race/ethnicity, No. (%)			
Non-Hispanic white	143 (53.4)	114 (59.4)	169 (42.3)
African American	102 (38.1)	48 (25.0)	139 (34.8)
Hispanic	0	9 (4.7)	52 (13.0)
Asian	8 (3.0)	6 (3.1)	14 (3.5)
Native American or Alaskan	2 (0.7)	3 (1.6)	14 (3.5)
Biracial	10 (3.7)	9 (4.7)	6 (1.5)
Other	3 (1.1)	3 (1.6)	6 (1.5)

Abbreviations: BNSS, Brief Negative Symptom Scale; CAINS, Clinical Assessment Interview for Negative Symptoms; SANS, Scale for the Assessment of Negative Symptoms.

were recruited from the following 3 sites: (1) the outpatient research clinics at the Maryland Psychiatric Research Center and community mental health clinics in the Baltimore metropolitan area (n = 65); (2) the State University of New York at Binghamton, including community outpatient mental health clinics in upstate New York (n = 60); and (3) the University of Nevada, Las Vegas, including community outpatient mental health clinics in Las Vegas (n = 67). Study 3 included data from 400 outpatients with schizophrenia who underwent rating using the CAINS.[12] These patients were recruited from the Maryland Psychiatric Research Center and community mental health clinics in the Baltimore metropolitan area (n = 117) and the University of California, San Diego, Department of Psychiatry via Assertive Community Treatment teams in the San Diego metropolitan area (n = 283).

All participants met *DSM-IV-TR*[26] criteria for schizophrenia or schizoaffective disorder as determined by the Structured Clinical Interview for *DSM-IV* interview[27] (see **Table 1** for demographic characteristics). Most participants were prescribed a second-generation antipsychotic, and all were clinically stable as indicated by no change in the type or the dose of antipsychotic for 4 weeks before evaluation. Data from each study had not been used in prior EFAs.

Procedures

At each site, the SANS, the BNSS, or the CAINS was administered as part of larger protocols examining cognition, reward, or the efficacy of cognitive behavioral social skills training (baseline data are reported from that study). Raters at each site were trained to minimum reliability standards (interrater agreement >0.80 with criterion-standard training tapes) before performing study procedures. Rater training consisted of an in-depth review of the manual of and procedures for rating each instrument. Raters watched and rated a series of initial videos that were developed by the BNSS and CAINS authors or internally by the research team for the SANS. Ratings were then discussed as a group using criterion standard rationales, and interviewers were instructed in interview technique. Interviewers subsequently received ongoing supervision and participated in regular (approximately monthly) criterion-standard reliability meetings to maintain quality assurance. All raters had earned a bachelor's degree or higher and had 1 or more years of clinical experience.

Data Analysis

Mplus software (version 5.0; Muthén and Muthén)[28] was used to conduct the CFAs. The CFAs compared 4 models that differed in their number of factors and item-loading patterns (models are described in eTables 1-3 in the Supplement). Owing to violation of multivariate normality for the BNSS and SANS as indicated by a Mardia coefficient greater than 3,[29] robust estimation procedures were used. These procedures included the weighted least-squares estimator with SEs and mean- and variance-adjusted χ^2 test that used a full-weight matrix and the maximum likelihood with robust SEs. A numerical integration algorithm was used in maximum likelihood robust SE model estimation. Numerical integration becomes computationally demanding in the estimation of models as the number of factors increases. Therefore, a Monte Carlo method of designating integration points was used. The number of selected integration points ranged from 5000 to 10 000 in the estimation of tested models.

For the BNSS, the lack of a normal distress item was not included in the CFA models because the distress item was not part of the agreed NIMH consensus conference domains, and prior EFA studies reported low communalities for this item.[13] For the SANS, the anhedonia item was specified to load by itself on the anhedonia factor, because no other items on the SANS assessed anhedonia. Similarly, for the CAINS, the quantity of speech item was specified to load by itself on the alogia factor because it is the only CAINS item that assesses alogia (eTables 1-3 in the Supplement).[30]

Model fit was evaluated using indices of absolute fit, including the model χ^2 test, the comparative fit index (CFI), the Tucker Lewis index (TLI), the root mean square error of approximation (RMSEA), the standardized root mean square residual (SRMR), and the weighted root mean square residual (WRMR). Information criteria including the Akaike information criterion, Bayesian information criteria, and the sample size–adjusted Bayesian information criteria evaluated the relative fit of alternate models. The model χ^2 reflects the degree to which the data agree with the hypothesized model.[31] The CFI and TLI are incremental fit indices that compare the independence model with the hypothesized model.[32] The SRMR and the WRMR are residual-based indices of the difference between sample and hypothesized variance-covariance matrices. Whereas the SRMR is obtained in EFA estimation, WRMR

Table 2. Model Fit Results From CFA of Negative Symptom Measures

Model by Substudy[a]	Log likelihood	Free Parameters, No.	Confirmatory Factor Analysis[b] AIC	BIC	aBIC	χ^2 Value (*df*)	CFI	TLI	RMSEA	WRMR
SANS[c]										
1-Factor	−5729.04	99	11 656.08	12 010.48	11 696.59	539.97 (45)[d]	0.782	0.879	0.204	1.98
2-Factor	−5607.89	100	11 415.79	11 773.76	11 456.71	237.75 (47)[d]	0.916	0.955	0.124	1.30
5-Factor	−5556.59	109	11 331.08	11 721.27	11 375.68	161.51 (46)[d]	0.949	0.972	0.097	1.00
Hierarchical	−5564.74	101	11 331.48	11 693.03	11 372.81	154.92 (46)[d]	0.952	0.974	0.095	0.99
BNSS[e]										
1-Factor	−2939.06	84	6046.13	6319.76	6053.67	225.95 (11)[d]	0.934	0.952	0.319	2.13
2-Factor	−2748.99	85	5668.00	544.88	5675.63	104.17 (16)[d]	0.973	0.986	0.169	1.08
5-Factor	−2606.95	94	5401.90	5708.10	5410.34	39.87 (19)[f]	0.994	0.997	0.076	0.43
Hierarchical	−2630.18	84	5428.36	5701.99	5435.90	21.77 (16)[g]	0.998	0.999	0.043	0.47
CAINS[h]										
1-Factor	−6769.83	65	13 669.66	13 929.11	13 722.86	982.64 (19)[d]	0.770	0.794	0.356	4.25
2-Factor	−6433.37	66	12 998.74	13 262.18	13 052.75	481.65 (20)[d]	0.890	0.906	0.240	2.80
5-Factor	−6418.02	75	12 986.03	13 285.39	13 047.41	76.52 (19)[d]	0.986	0.988	0.077	0.89
Hierarchical	−6436.61	66	13 005.21	13 268.65	13 059.23	56.44 (21)[d]	0.992	0.993	0.065	0.79

Abbreviations: AIC, Akaike information criterion; aBIC, sample size–adjusted Bayesian information criterion (BIC); BNSS, Brief Negative Symptom Scale; CAINS, Clinical Assessment Interview for Negative Symptoms; CFA, confirmatory factor analysis; CFI, confirmatory fit index; RMSEA, root mean square error of approximation; SANS, Scale for the Assessment of Negative Symptoms; TLI, Tucker Lewis index; WRMR, weighted root mean square residual.

[a] Models included the unidimensional 1-factor model; the motivation and pleasure (MAP) and diminished expression (EXP) 2-factor model; the 5-factor (anhedonia, asociality, avolition, blunted affect, and alogia) consensus model; and the hierarchical model with the 5 first-order consensus factors and 2 second-order MAP and EXP factors.

[b] Weighted least squares and maximum likelihood with robust SE (MLR) estimators were used in the analyses. Monte Carlo–based numerical integration was used in the MLR estimation of models to ease computation time. The number of Monte Carlo–generated integration points ranged from 5000 to 6000.

[c] $\chi^2_{25} = 2293.82$ ($P < .001$) on the baseline model.

[d] $P < .001$.

[e] $\chi^2_8 = 3247.08$ ($P < .001$) on the baseline model.

[f] $P < .01$.

[g] $P = .15$

[h] $\chi^2_{17} = 4199.74$ ($P < .001$) on the baseline model.

is obtained in the estimation of CFA models. The RMSEA is a parsimony index that evaluates the fit between the hypothesized model and the population covariance matrix.[33] The information criteria are relative fit indices of model parsimony that take into account model complexity based on degrees of freedom.[34] Evidence of model fit was determined according to standard interpretations of the fit indices, including a χ^2 value that is not statistically significant,[35] CFI and TLI values of at least 0.950, and an RMSEA no greater than 0.080.[31] The SRMR values range from 0 to 1, with values of 0.080 or lower indicative of good-fitting models. The WRMR values of 1.00 and lower are considered strong fits. The information criteria allow for comparisons between nonnested models, with lower values indicating better model fit,[34] so the lowest value was used to determine optimal model fit. Of note, the χ^2 test tends to falsely reject adequate statistical model fit with large sample sizes,[36] and, thus, the descriptive fit indices are preferred for interpretation of model fit.[1]

Results

A total of 860 outpatients were included in the study (585 men [68.0%] and 275 women [32.0%]; mean [SD] age, 43.0 [11.4] years). Results of the CFAs of evaluated models are presented in **Table 2**. The 1- and 2-factor models provided poor fit for the SANS, BNSS, and CAINS as indicated by CFIs and TLIs less than 0.950, RMSEAs that exceeded the 0.080 threshold, and WRMRs greater than 1.00.

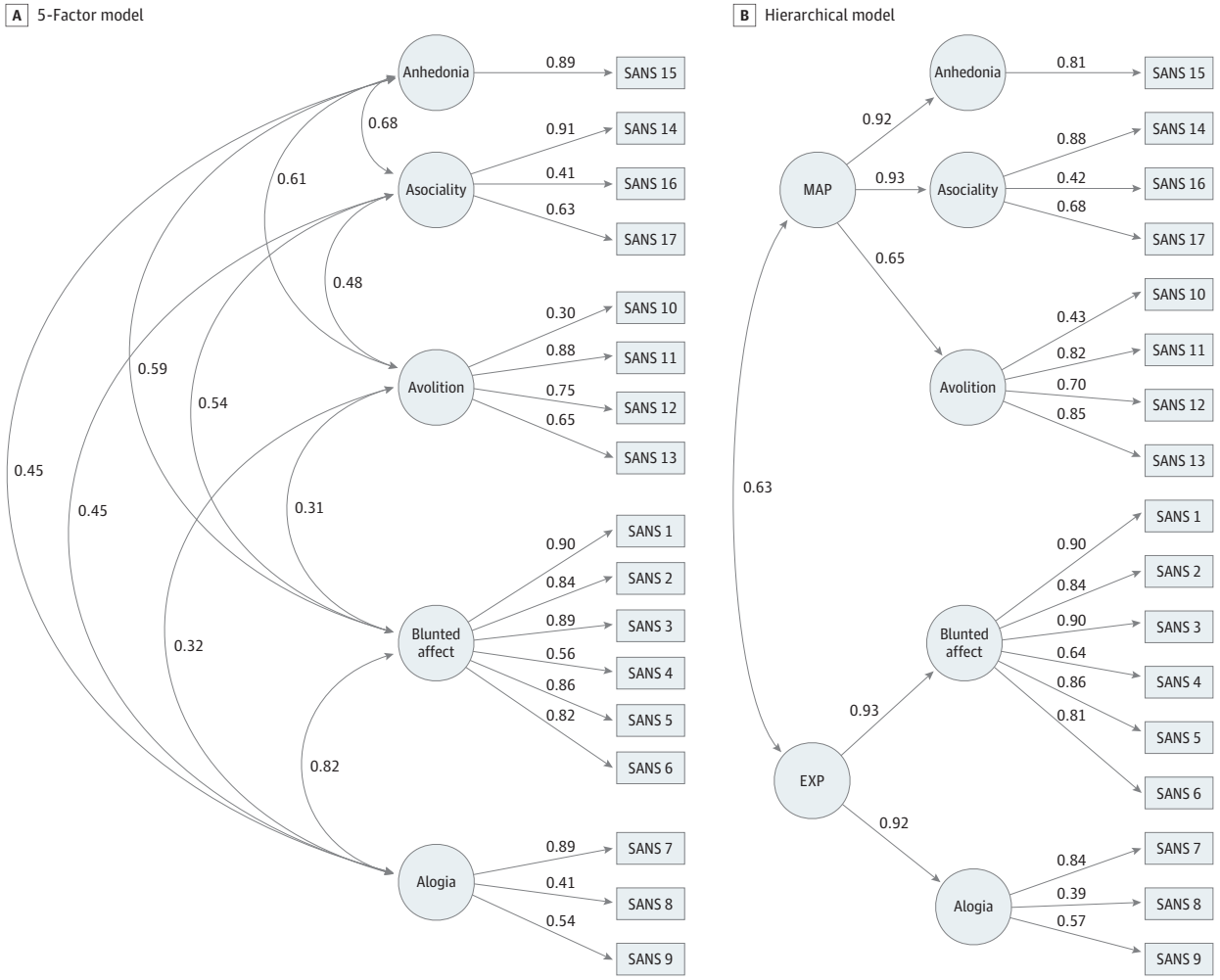
In contrast, the 5-factor model and the hierarchical model provided strong fit for the SANS, BNSS, and CAINS (Table 2, **Figure 1**, **Figure 2**, and **Figure 3**). The CFIs and TLIs met the 0.95 threshold and the 1.00 threshold for both factor models with all 3 measures. Interestingly, the RMSEAs for the 5-factor model and the hierarchical model fell under the 0.08 threshold for the BNSS and the CAINS but not the SANS.

The information criteria indices favored the 5-factor model and the hierarchical model compared with the 1- and the 2-factor models for all 3 measures. Although the 5-factor and hierarchical models are supported, the information criteria by majority demonstrated a preference for the 5-factor model compared with the hierarchical model on the BNSS and the CAINS. In contrast, information criteria slightly favored the hierarchical model on the SANS.

Discussion

We used CFA to evaluate the latent structure of negative symptoms using data from 3 contemporary negative symptom scales (SANS, BNSS, and CAINS). Results were highly consistent across all 3 studies, indicating that the 1- and 2-factor models

Figure 1. Five-Factor and Hierarchical Models of the Scale for the Assessment of Negative Symptoms (SANS)

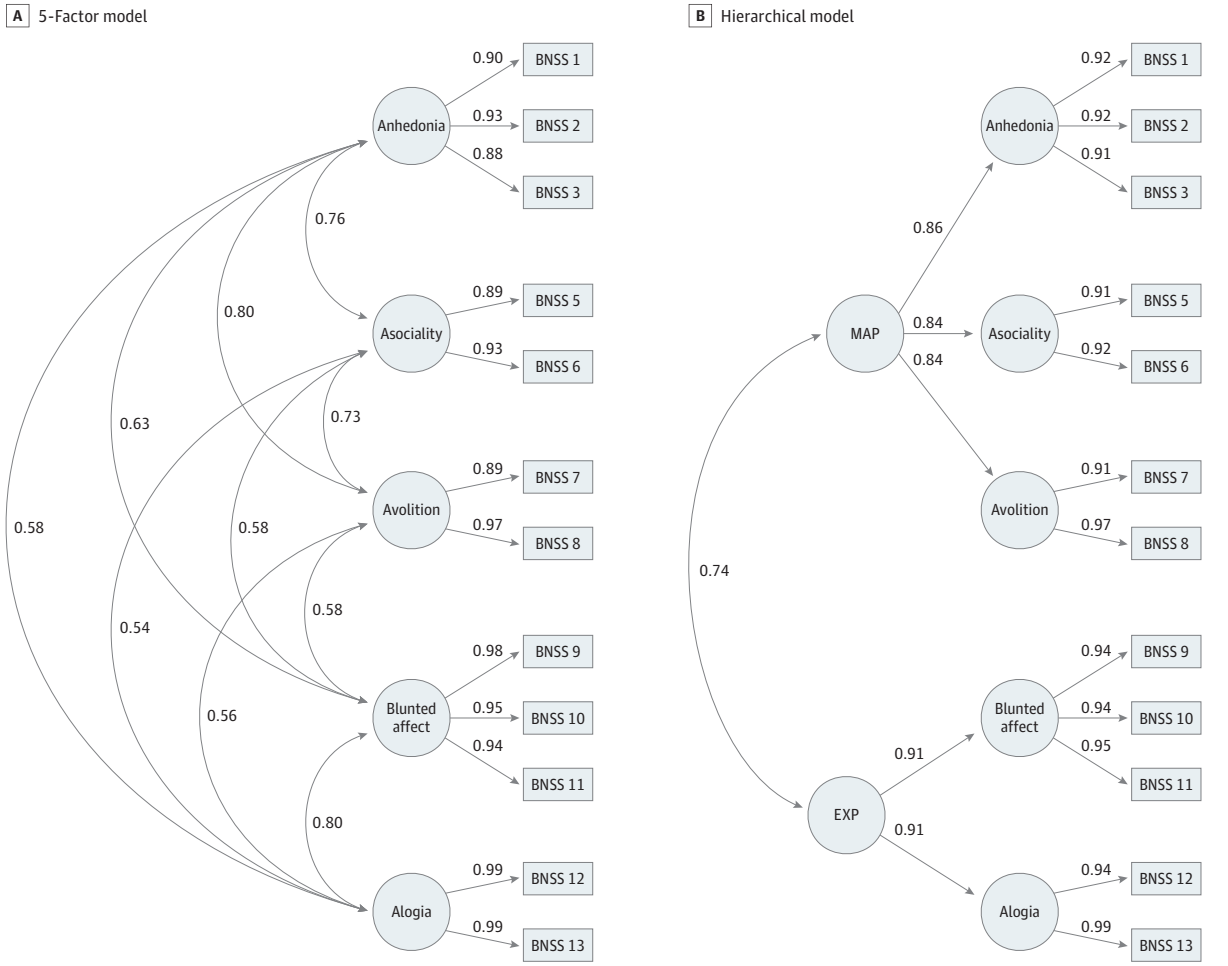


The 5 factors of anhedonia, asociality, avolition, blunted affect, and alogia were included in the consensus model. The hierarchical model consists of the 5 factors and the second-order factors of motivation and pleasure (MAP) and diminished expressivity (EXP). Solid lines represent factor loadings and curved lines represent the correlation among factors (A) and second-order factors (B). Numbers indicate item numbers on each scale.

provided relatively poor fit for the data. The 2 more complex models provided excellent fit for the data. Indices of relative fit favored the 5-factor model over the hierarchical model in the BNSS and CAINS data, and the hierarchical model had a slight edge in the SANS data. When interpreting these results, we should clarify that good fit for the hierarchical model is not simply further support for the 2-dimensional conceptualization, nor does it negate the importance of the 5 domains, because MAP and EXP are secondary dimensions in these hierarchical models and the 5 factors are primary. Because primary dimensions are the ones directly influencing ratings of all negative symptoms in these hierarchical models, this factor suggests that the 5 domains, not the MAP and EXP dimensions, are the most fundamental aspect of negative symptoms that best account for latent structure. The consistency of findings across the 3 scales suggests that nothing about the organization of the scale, manual, or worksheet, for example, arbitrarily produces the 5-domain structure, because these elements are very different across measures.

These findings have several important clinical implications. First, the *DSM-5* describes negative symptoms in association with the 2 factors (MAP and EXP). This decision was driven by published EFA studies. Our results suggest that a revision to *DSM-5* descriptions of negative symptoms is in order. Specifically, the 5 consensus domains should be defined and considered individually. Second, several important implications apply for clinical trials. Should studies of neurocognitive function, animal models, and biological correlates demonstrate differential relationships to the 5 domains, industry and the US Food and Drug Administration would have a compelling reason to develop targeted treatments for individual domains rather than the broader negative symptom construct. Most studies have explored neurobiological correlates of negative symptoms in association with a total score or the broader MAP and EXP dimensions,[21,37] precluding observa-

Figure 2. Five-Factor and Hierarchical Models of the Brief Negative Symptom Scale (BNSS)

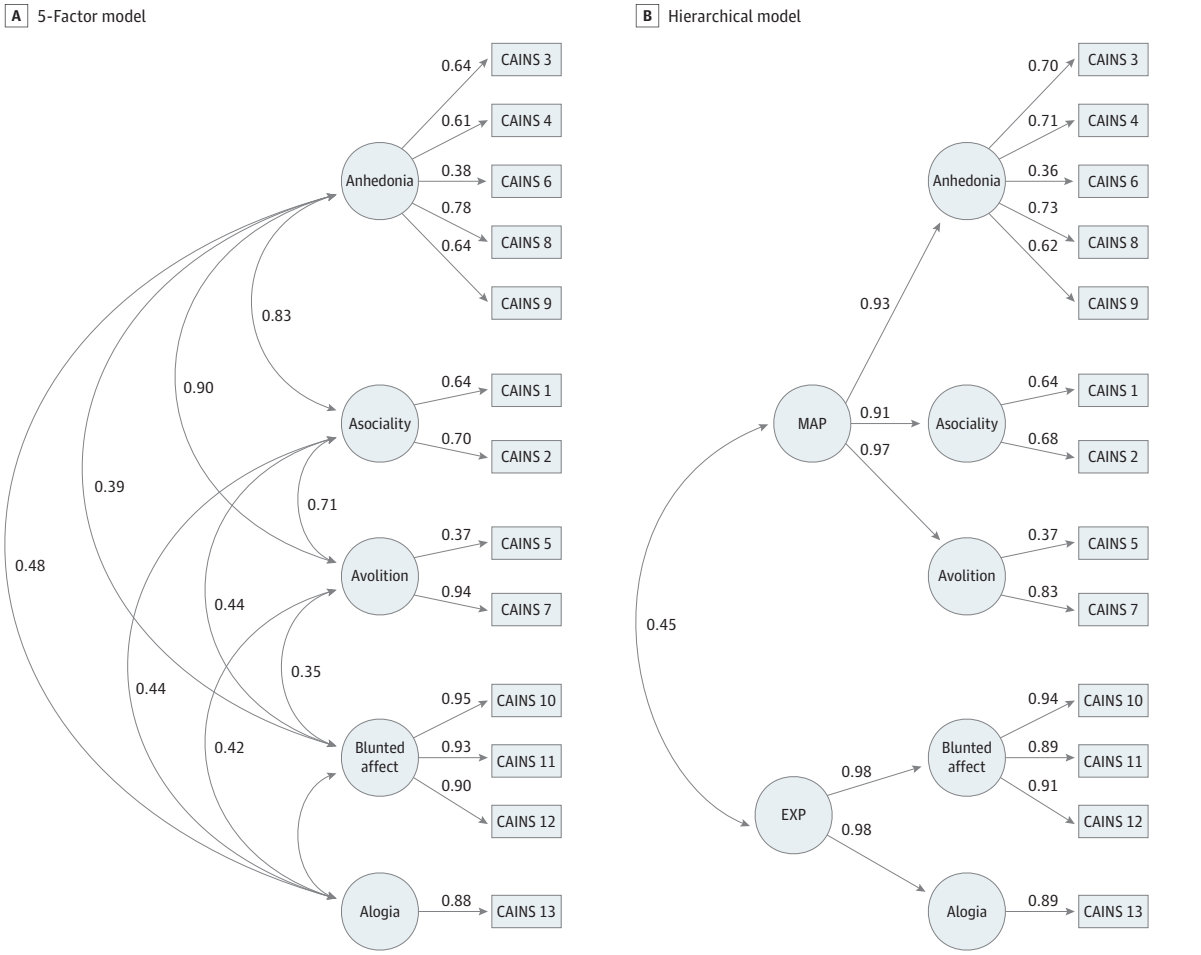


The 5 factors of anhedonia, asociality, avolition, blunted affect, and alogia were included in the consensus model. The hierarchical model consists of the 5 factors and the second-order factors of motivation and pleasure (MAP) and diminished expressivity (EXP). Solid lines represent factor loadings and curved lines represent the correlation among factors (A) and second-order factors (B). Numbers indicate item numbers on each scale.

tion of domain-specific neural correlates. However, among the few studies that separate out the domains, some evidence suggests distinct neural correlates among domains[38] and the need for further investigation. The NIMH Research Domain Criteria initiative offers a promising framework for exploring mechanisms related to each domain. In particular, the Research Domain Criteria positive valence systems and social processes contain constructs that are conceptually associated with the 5 negative symptom domains. Tasks have been developed in the field of basic neuroscience to assess these constructs, which have distinct cellular and circuit-level mechanisms.[39] Some of these tasks have already been translated to human populations[40-42] and are ideal for exploring neurobiology specific to the 5 domains. Psychosocial intervention trials also demonstrate that taking a targeted approach to treating specific psychological mechanisms (eg, defeatist performance beliefs) underlying individual domains of negative symptoms (eg, avolition)[43] is a fruitful approach, which could indeed be adopted by pharmacologic trials once relevant biological mechanisms are identified. In addition, clinical trials should consider adjusting procedures for how they determine primary outcome measures. In pharmaceutical trials, total scores are the most common primary outcome measures. This approach has distinct statistical advantages (eg, sample size, power, or reducing type I error); however, it does not adequately capture the complexity of the construct. Once specific mechanistic targets are identified for individual domains, industry should shift toward using single domains as primary outcome measures in trials. Until that time, the 5 domains should be considered for secondary analyses, and the *DSM-5* should retain the 2 dimensions. eTables 1 through 3 in the Supplement list which items should be considered within each of the 5 domains for the SANS, BNSS, and CAINS, which will facilitate exploration of these domains.

We also have several scoring recommendations. When calculating domain scores, we recommend calculating the mean of the items within these domains rather than summing because the different domains have differing numbers

Figure 3. Five-Factor and Hierarchical Models of the Clinical Assessment Interview for Negative Symptoms (CAINS)



The 5 factors of anhedonia, asociality, avolition, blunted affect, and alogia were included in the consensus model. The hierarchical model consists of the 5 factors and the second-order factors of motivation and pleasure (MAP) and diminished expressivity (EXP). Solid lines represent factor loadings and curved lines represent the correlation among factors (A) and second-order factors (B). Numbers indicate item numbers on each scale.

of items, complicating comparisons across domains. We also generally do not recommend calculating factor scores using factor loadings because these scores are driven by sample-specific differences, and such calculations prevent comparisons across studies. When using the SANS, we recommend omitting global items when calculating domain scores to prevent redundancy, conflation across domains, and undue influence of halo effects. First-generation negative symptom scales[17,44] or subscales[45,46] do not adequately cover the 5 domains and conflate constructs. Newer scales, such as the CAINS and BNSS, may be more ideal for measuring negative symptoms, and each of these scales has unique advantages for use in experimental psychopathology and clinical trial studies that make them optimal for specific purposes.[47]

Limitations

Limitations of our study should be considered. First, only patients in the chronic illness phase were studied, and results may not generalize to earlier phases of illness with higher symptom severity; whether the factor structure would differ between patients whose negative symptoms are primary vs secondary (or deficit vs nondeficit) is also unclear. Second, we were unable to evaluate whether the 5 domains have distinct correlates. Future studies should validate the significance of the 5 domains by exploring a range of external correlates (ie, clinical, cognitive, molecular, cellular, structural, functional, and genetic). Third, the mean severity ratings in our samples were relatively low. However, this finding is not expected to have had an effect on results, because prior studies[48] indicate little factorial invariance across samples that differ in negative symptom severity. Fourth, debate as to whether use of single-item indicators is problematic or ideal for testing latent structure is ongoing[30,49-53]; given that structure was comparable across scales with and without single-item indicators, we doubt that this factor greatly influenced results. Fourth, longitudinal data were not available on these scales to determine whether these factors change along independent trajectories. Finally, results are limited by how well the scales used assess the construct; as measures become more objective and precise, the domains may become even more granular. Furthermore, as

acknowledged in the NIMH consensus statement, other aspects of negative symptoms may not have been recognized.

Conclusions

Collectively, these findings suggest that negative symptoms should no longer be considered a single unitary construct, as was assumed when negative symptom scales were originally developed. They should not be considered a simple 2-dimensional construct, as has recently been concluded based on EFA results.[11-13] Rather, the latent structure of negative symptoms is best conceptualized in relation to the 5 domains identified in the 2005 NIMH consensus development conference: anhedonia, avolition, asociality, alogia, and blunted affect. If distinct clinical and pathophysiological correlates of these 5 domains are identified in future research, this approach will warrant a change in how negative symptoms are conceptualized and how targeted treatment development is approached.

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Concept and design: Strauss, Ahmed, Kirkpatrick, Allen.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Strauss, Nuñez, Ahmed, Barchard, Allen.
Critical revision of the manuscript for important intellectual content: Strauss, Nuñez, Ahmed, Barchard, Granholm, Kirkpatrick, Gold.
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