

# Evaluation of Relationship between Negative Symptoms Scales in an IRT Framework



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## METHODOLOGICAL QUESTION

The assessment of negative symptoms continues to be an important area of research in schizophrenia. Studies examining the psychometric properties of negative symptom scales have focused on estimates of reliability, validity, and factor analysis using classical test theory (CTT). These methods rely primarily on statistics that average across levels of individual variation and may obscure the fact that scale reliability is likely to vary across different levels of performance on the construct being measured. Examining the properties of individual scale items can lead to improvements in both the efficiency and reliability in mapping the full continuum of negative symptoms. Item Response Theory (IRT) methodology can help identify scales that work best across varying levels of severity and identify which items are most informative based on the severity of the study population. Identifying the correct clinical endpoint for a study population, including assessment of severity of impairment, can improve measurement precision and endpoint selection in clinical trials.

## AIMS

We evaluated four negative symptom scales (CAINS, BNSS, Marder PANSS negative symptom factor (NSF), and the NSA-16) by:

- examining the performance of items at both the response (severity) and item (symptom) levels,
- examining the ability to discriminate individual differences in severity, and
- addressing which scale provides the most information at different severity levels for each item.

## METHODS

### Data Source

Data from screening or baseline evaluations were assessed for:

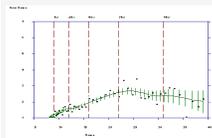
- Negative Symptom Assessment – 16 items (NSA-16): R04917838 (Bitopertin) in patients with persistent, predominant negative symptoms of Schizophrenia. **n = 841**
- Positive and Negative Symptom Scale – Marder Negative Symptom Factors (PANSS): Janssen Risperidone programs (1999-2005). **n = 7,186**
- Clinical Assessment Interview for Negative Symptoms (CAINS): clinical trials conducted at Maryland Psychiatric Research Center (MPRC), University of California, San Diego and CANSAS validation study (Kring et al., 2013) in patients with negative symptoms of schizophrenia. **n = 528**
- Brief Negative Symptom Scale (BNSS): clinical trials conducted at Maryland Psychiatric Research Center (MPRC), University of Nevada, Las Vegas (UNLV), Italian national sample (Mucci et al., 2013), Clinical Affective Neuroscience Laboratory – University of Georgia in patients with negative symptoms of schizophrenia. **n = 1,293**

### IRT Procedure

jMetrik™ was used to fit the Item Response Model. Each Option Characteristic Curve (OCC) relates the probability of endorsing a particular option of an item given the overall level of psychopathology. Individuals were ranked according to the total score on each of the scales used (PANSS Negative Symptom factor score, NSA-16 total score (does not include the Negative symptom global score), CAINS Motivation and Pleasure Subscale and Emotional Expressivity Subscale, BNSS Total Score). These rank values were converted to standard normal scores (ranks within fixed values are assigned randomly), at which the values of the OCCs are estimated.

## Operational Definition for Item Selection

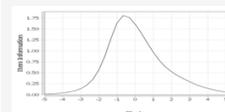
**Criterion 1. There is a range of severity in which the majority of items is expected to be more likely scored (<1.00% of the time, the specific option is selected). This is represented by the number of options (item score) for which the item was more likely to be endorsed than all other options.**



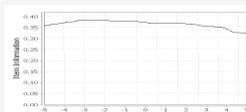
The y axis shows options from 1 to 7 on the PANSS, and the ICC curve shows only options 1 to 3 are selected for this item (Slope = 0.100)

**Criterion 2. The steeper a slope of the ICC, the more discriminant the item is. The slope or steepness of the curves indicate the item's ability to discriminate individuals along the latent continuum (i.e., negative symptom severity level). If the slope was higher than 0.40 and it was noted as either, "Yes," ( $\geq 0.40$ ) or "No" ( $\leq 0.40$ ). The steeper a slope, the more discriminant the item is.**

**Criterion 3. Item information function which shows at what point in the level of severity is the item more informative.**

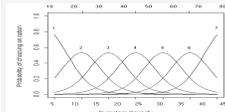


The item is providing more information for the individuals with moderate severity as the curve shows a Leptokurtic curve.



The item is providing a similar amount of information for all severity levels as the curve shows a Platykurtic curve.

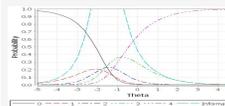
**Criterion 4. The extent to which OCCs increase rapidly with changes in overall severity.**



OCC for an "ideal" item. The OCC shows the probability (y-axis) of endorsing a particular option for the item at different levels of the trait (y-axis)

**Criterion 5. The region in which each option is more likely to be selected is ordered, left to right, in accordance with their option scores on the OCC graphs.**

**Criterion 6. Options for an item span the full continuum of severity.**



OCCs do not span the full x-axis and appear to be primarily on the left side of the figure which shows endorsement for individuals with overall lower severity levels.

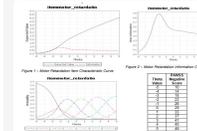
## RESULTS

	Very Good Items	Good Items	Poor Items
	≥ 5 IRT Criteria Met	4 IRT Criteria Met	≤ 3 Criteria Met
<b>PANSS Marder Negative Symptom Factor</b>	Passive Apathetic Social Withdrawal, Lack of Spontaneity and Flow of Conversation	Blunted Affect, Poor Rapport, Active Social Avoidance, Emotional Withdrawal	Motor Retardation
<b>NSA-16</b>	Impoverished Speech, Poor Grooming and Hygiene, Prolonged Time to Respond, Reduced Expressive Gestures, Reduced Interoception, Reduced Sense of Purpose,	Reduced Affect Display on Demand, Reduced Modulation of Intensity, Reduced Emotional Range, Poor Rapport, Slowed Movements	Reduced Speech, Inarticulate Speech, Reduced Daily Activity, Reduced Social Interest in Intimacy
<b>BNSS</b>	Intensity of Expected Pleasure, Distress, Anxiously Inner Experience, Avoidant behavior, Facial Expression, Expressive Gestures, Quantity of Speech, Spontaneous Elaboration	Intensity of Pleasure during Activities, Frequency of Pleasure During Activities, Anxiously Inner Experience, Vocal Expression	
<b>CAINS</b>	Motivation for Close Friendships/Romantic Relationships, Motivation for Recreational Activities, Frequency of Pleasure for Recreational Activities, Facial Expression, Vocal Expression, Expressive gestures, Quantity of Speech	Motivation for Close Family/Spouse/Partner Relationships, Frequency of Pleasurable Social Activities – Past Week, Frequency of Expected Pleasurable Social Activities – Next Week, Frequency of Expected Pleasure from Recreational Activities	Motivation for Work and School Activities, Expected Pleasure for Work and School

### Items that performed poorly in IRT Framework

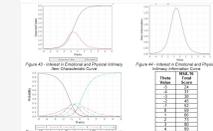
#### PANSS Motor Retardation

IRT Criteria	Criteria Met
Criterion 1 (Fig 1, Table 1)	No
Criterion 2 (Fig 1)	0.312
Criterion 3 (Fig 2) - Skewed	No
Criterion 4 (Fig 3) – see option 4	Yes
Criterion 5 (Fig 3)	Yes
Criterion 6 (Fig 3)	Yes



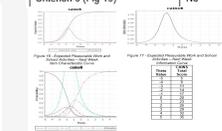
#### NSA-16 Interest in Intimacy

IRT Criteria	Criteria Met
Criterion 1 (Fig 43, Table 29)	Yes
Criterion 2 (Fig 43)	0.536
Criterion 3 (Fig 44) - skewed	No
Criterion 4 (Fig 45)	No
Criterion 5 (Fig 45)	No
Criterion 6 (Fig 45)	No



#### CAINS Expected Pleasure for Work or School

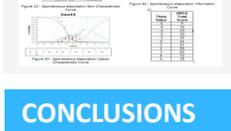
IRT Criteria	Criteria Met
Criterion 1 (Fig 16, Table 11)	Yes
Criterion 2 (Fig 16)	0.553
Criterion 3 (Fig 17) - skewed	No
Criterion 4 (Fig 18)	No
Criterion 5 (Fig 18)	Yes
Criterion 6 (Fig 18)	No



### Items that performed the best in IRT Framework

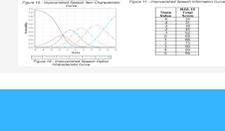
#### BNSS Spontaneous Elaboration

IRT Criteria	Criteria Met
Criterion 1 (Fig 43, Table 29)	Yes
Criterion 2 (Fig 43)	0.530
Criterion 3 (Fig 44)	No
Criterion 4 (Fig 45)	Yes
Criterion 5 (Fig 45)	Yes
Criterion 6 (Fig 45)	Yes



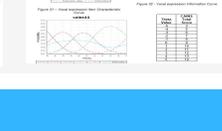
#### NSA-16 Impoverished Speech

IRT Criteria	Criteria Met
Criterion 1 (Fig 10, Table 7)	Yes
Criterion 2 (Fig 10)	0.653
Criterion 3 (Fig 11) - skewed	No
Criterion 4 (Fig 12)	Yes
Criterion 5 (Fig 12)	Yes
Criterion 6 (Fig 12)	Yes



#### CAINS Vocal Expression

IRT Criteria	Criteria Met
Criterion 1 (Fig 31, Table 21)	Yes
Criterion 2 (Fig 31)	0.686
Criterion 3 (Fig 32)	Yes
Criterion 4 (Fig 33)	Yes
Criterion 5 (Fig 33)	Yes
Criterion 6 (Fig 33)	Yes



## CONCLUSIONS

The BNSS, CAINS and NSA-16 were more informative for subjects with moderate severity, compared to those with low or severe severity levels. In contrast, the PANSS NSF was equally informative for all levels of severity, although the BNSS and CAINS have distinct conceptual advantages over the PANSS NSF and NSA-16 and captures a broader spectrum of negative symptoms.

## DISCLOSURES AND CONTACT INFORMATION

A Khan is a full-time employee of VeraSci, Durham, NC, USA, and has received support from National Institute of Mental Health, Janssen, Celgene, and Tria Pharmaceuticals, C.P.S. is an original developer of the Brief Negative Symptom Scale (BNSS) and receives royalties and consultation fees from ProPhase LLC in connection with commercial use of the BNSS and other professional activities; these fees are donated to the Brain and Behavior Research Foundation. G.P. receives consulting fees and travel support from InVivo Neurosciences. Due to the large number of authors with disclosures only disclosed for 2 authors are presented and additional disclosures can be provided upon request. Dr. Anzalee Khan can be reached by email at [anzalee.khan@vera-sci.com](mailto:anzalee.khan@vera-sci.com) or by phone at (919) 401-4842.