Reliability and Validity of the PANSS Negative Symptom Factor Score in Outpatients with Schizophrenia Prescribed Select Antipsychotics and with Prominent Negative or Disorganized Thought Symptoms

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INTRODUCTION

• Negative symptoms of schizophrenia lead to poorer functional outcomes and greater reductions in quality of life than positive symptoms, and targeting negative symptoms may have significant functional benefits. 1,2
• No consensus exists regarding the best instrument for measuring negative symptoms in clinical trials.
• A 5-factor model of the Positive and Negative Syndrome Scale (PANSS) has been developed which groups the 30 items into negative symptom (NSFS), positive symptom (PSFS), disorganized thought, hostility/eclamency, and anxiety/depression factor scores.1
• The NSFS (items N1, N2, N3, N4, N8, G7, and G16) has improved content validity compared with the original prior negative subscale and covers symptom domains as defined in the National Institute of Mental Health Measurement and Treatment Research to Improve Cognition in Schizophrenia (NIMH-MATRICS) consensus statement (Table 1). 3

Table 1. Negative Symptom Mapping – NIMH-Agreed Term vs NSFS Items

<table>
<thead>
<tr>
<th>Criterion</th>
<th>NIMH Term*</th>
<th>NSFS Term</th>
<th>Negative Symptoms Factor Score</th>
<th>PANSS Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysfunction of communication</td>
<td>Alogia</td>
<td>Lack of spontaneity and flow of conversation</td>
<td>Reduction in normal flow of communication associated with apathy, apathy, disinterest, or cognitive deficit.</td>
<td>Dimensional fluidity and productivity of the global interaction process</td>
</tr>
<tr>
<td>Dysfunction of affect</td>
<td>Blunted effect</td>
<td>Reduced range of emotions</td>
<td>Diminished emotional responsiveness as characterized by a reduction in facial expression, modulation of affect, and emotional communication.</td>
<td></td>
</tr>
<tr>
<td>Dysfunction of socialization</td>
<td>Avolition</td>
<td>Diminished motivation</td>
<td>Diminished motivation and initiative in social interactions due to poverty of speech, apathy, or avolition. This leads to reduced interpersonal involvement and neglect of activities of daily living.</td>
<td></td>
</tr>
<tr>
<td>Dysfunction of capacity for pleasure</td>
<td>Anhedonia</td>
<td>Emotional withdrawal</td>
<td>Lack of interest in, involvement with, or affective commitment to life’s events.</td>
<td></td>
</tr>
</tbody>
</table>

• The NSFS appears robust and has been replicated in at least 6 subsequent factor analyses. 1,2 Internal consistency reported in 3 of these analyses was high for the NSFS item grouping (Cronbach’s α, 0.85 to 0.88).
• Despite wide use of the NSFS, some aspects of validation remain to be established in patients with predominant negative symptoms.
• The present analyses are from a phase 2 proof-of-concept study in outpatients with schizophrenia treated with select antipsychotics and with prominent negative or disorganized thought symptoms; these analyses evaluate the reliability, validity, and ability to detect change of the NSFS.

METHODS

• All analyses were based on the intent-to-treat (ITT) population, which included all patients who received at least 1 dose of study medication and had at least 1 postbaseline primary efficacy assessment (n = 312).
• Analyses were conducted to assess:
  - Test-retest reliability (between all postbaseline visits for the subset of patients with no change in Clinical Global Impression-Severity (CGI-S) score – Negative Symptoms [CGI-S-N] score)
  - Internal consistency (Cronbach’s α)
  - Construct validity (correlation between the scales [Spearmen correlation with Fischer transformation]) and 1-way analysis of variance (ANOVA) using CSNI-S-N scores of 4 [moderate], 5 [marked], and 6 [severe] as groups)
• Ability to detect change/responder criteria (level of change on the Personal and Social Performance scale [PSP] from baseline to week 8 associated with either a 20% improvement in NSFS, a Clinical Global Impression-Improvement [CGI-I]-N score of 1 or 2, or both criteria combined).

RESULTS

• The majority of patients were male (64%) and white (66%). The age ranged from 18 to 60 years, with a median age of 40 years. All patients had a diagnosis of schizophrenia, mostly of the paranoid type (70% to 80%), with a mean age at first diagnosis of ~28 years and mean duration of disease of ~15 years (range, 0 to 51 years).
• The population had a high level of negative symptoms (NSFS mean, 19.2; standard deviation [SD], 14.6; range, 4 to 86). The majority of patients were male (64%) and white (66%). The age ranged from 18 to 60 years, with a median age of 40 years. All patients had a diagnosis of schizophrenia, mostly of the paranoid type (70% to 80%), with a mean age at first diagnosis of ~28 years and mean duration of disease of ~15 years (range, 0 to 51 years). The majority of patients were male (64%) and white (66%). The age ranged from 18 to 60 years, with a median age of 40 years. All patients had a diagnosis of schizophrenia, mostly of the paranoid type (70% to 80%), with a mean age at first diagnosis of ~28 years and mean duration of disease of ~15 years (range, 0 to 51 years).

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CONCLUSIONS

• The NSFS demonstrated good test-retest reliability and validity as a negative symptom assessment in patients with prominent negative or disorganized thought symptoms.
• The NSFS has a good relationship to global (CGI) ratings of negative symptom severity and improvement and also change in functional (PSP), in these patients.
• A 20% improvement was associated with the minimally important difference/responder threshold established for the PSP, in stable patients with schizophrenia, and thus would be a meaningful responder criterion for assessing improvement in negative symptoms.

REFERENCES


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