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A Positive Take on Schizophrenia Negative Symptom Scales: Converting Scores Between the SANS, NSA and SDS

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Abstract

Aims—To provide quantitative conversions between commonly used scales for the assessment of negative symptoms in schizophrenia.

Method—Linear regression analyses generated conversion equations between symptom scores from the Scale for the Assessment of Negative Symptoms (SANS), the Schedule for the Deficit Syndrome (SDS), the Positive and Negative Syndrome Scale (PANSS), or the Negative Symptoms Assessment (NSA) based on a cross sectional sample of 176 individuals with schizophrenia.

Intraclass correlations assessed the rating conversion accuracy based on a separate sub-sample of 29 patients who took part in the initial study as well as an independent sample of 28 additional subjects with schizophrenia.

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Conflict of Interest

Dr. Preda consulted for Boehringer-Ingelheim. Dr. Bustillo consulted with Otsuka Pharmaceuticals. Dr. Van Erp consulted for Roche pharmaceuticals and has a contract with Otsuka Pharmaceutical, Ltd. (OPCJ). Dr. Mathalon is a consultant for Bristol-Myers Squibb and Roche pharmaceuticals. Dr. Potkin has financial interests in Bristol-Myers Squibb, Eisai, Inc., Eli Lilly, Forest Laboratories, Genentech, Janssen Pharmaceutical, Lundbeck, Merck, Novartis, Organon, Pfizer, Roche, Sunovion, Takeda Pharmaceutical, Vanda Pharmaceutical, Novartis, Lundbeck, Merck, Sunovion and has received grant funding from Amgen, Baxter, Bristol-Myers Squibb, Cephalon, Inc., Eli Lilly, Forest Laboratories, Genentech, Janssen Pharmaceutical, Merck, Otsuka, Pfizer, Roche, Sunovion, Takeda Pharmaceutical, Vanda Pharmaceutical, NIAAA, NIBIB, NIH/NCRR, University of Southern California, UCSF, UCSD, Baylor College of Medicine. The remaining authors declare no potential conflict of interest.

Results—Between-scale negative symptom ratings were moderately to highly correlated ($r=0.73 - 0.91$). Intraclass correlations between the original negative symptom rating scores and those obtained via using the conversion equations were in the range of $0.61 - 0.79$.

Conclusions—While there is a degree of non-overlap, several negative symptoms scores reflect measures of similar constructs and may be reliably converted between some scales. The conversion equations are provided at <http://www.converteasy.org> and may be used for meta- and mega-analyses that examine negative symptoms.

Keywords

schizophrenia; negative symptoms; PANSS; SANS; NSA; SDA; conversion; meta-; multi-site; multi-center

1. Introduction

Defining and measuring negative symptoms in schizophrenia (SZ) is important, as negative symptoms have been linked to functional impairment, prognosis and response to medications (Rabinowitz et al., 2013; Ventura et al., 2009). Negative symptoms have been commonly assessed via the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982, 1984a), Schedule for the Deficit Syndrome (SDS; Kirkpatrick et al., 1989), the Negative Symptoms Scale (NSA; Alphs et al., 2010), and the Negative Subscale of the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). A number of studies confirm the existence of the negative symptoms constructs for the SANS (Arndt et al., 1991) and the PANSS (Marder et al., 1997). However while an NIMH consensus statement indicates that both the SANS and PANSS may be used for the measurement of negative symptoms in schizophrenia (Kirkpatrick et al., 2006), and while some of the important differences between some of these scales are known (Daniel, 2013), there have surprisingly been no studies examining whether negative symptom scores can be converted between scales. To date there are no between-scale score conversion equations that allow for the interpretation of results from studies that use different negative symptom scales.

This challenges efforts to reliably estimate the prevalence of negative symptoms (Buchanan, 2007), compare treatment effects across studies using different negative symptoms scales, and combine different study results in meta- and mega-analyses. Finally, in this age of open-access data, the lack of a conversion “translator” or common denominator for all the different negative symptoms scales undermines efforts to share data across studies where different instruments were used.

To address this gap we analyzed data from a large multi-center schizophrenia imaging project (Phase 3 of the Function Bioinformatics Research Network; FBIRN) where symptom assessment, including negative symptoms, was systematically scored by experienced raters on the SANS, SDS, NSA as well as PANSS.

In a previous publication (van Erp et al., 2013) we presented regression equations for converting negative symptom rating as well as the score conversion reliabilities between

SANS and PANSS negative. This paper is an extension of our prior work with a focus on additional negative symptom rating scales, including the SANS, SDS, and NSA.

Methods

Participants

The Function Biomedical Informatics Research Network (FBIRN) Phase 3 study collected negative symptoms severity data in a sample of individuals with schizophrenia (n=205; mean age \pm SD = 39.5 \pm 11.6; 156 males) recruited from 7 sites (Table 1). An independent study collected additional data from 28 subjects with schizophrenia to confirm rating conversion accuracy. All patients, including those from the independent sample, met DSM-IV criteria for schizophrenia based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I/P; First et al., 2002) administered by experienced clinical raters. At each site, all subjects' ratings were performed by a single rater. All clinical data was collected in a single session with breaks where needed. Items with similar face validity on different scales were clustered and rated together. The administration of the individual items was preserved across subjects. Patients with comorbid major psychiatric disorders, including depression, were excluded. All subjects were clinically stable on antipsychotic medication for at least 2 months, and had an illness duration of at least 1 year. Subjects with schizoaffective disorder were excluded. Other exclusion criteria included a history of major medical illness that could affect brain function, contraindications for magnetic resonance imaging (MRI), insufficient eyesight to see with normal acuity with MRI compatible corrective lenses, a history of drug dependence in the last 5 years or a current substance abuse disorder (except for nicotine), an IQ less than 75, and current clinically significant extrapyramidal symptoms or tardive dyskinesia. In addition to the SCID-I/P, patient symptom severity was evaluated on a number of standard clinical assessments, including the following negative symptom scales: the SANS (Andreasen, 1984), the SDS (Kirkpatrick et al., 1989), the NSA (Alphs et al., 2010), and the PANSS (Kay et al., 1987) (Table 2). Symptoms were rated based on their severity over the last month. Ratings were standardized across sites through cross-site group training sessions with experienced clinical raters (psychiatrist or clinical psychologist at Ph.D. level) and by comparing ratings of videotaped interviews of several patients with the ratings provided by "gold standard" expert clinical assessors. The same rater administered all the scales for a given patient.

The study was approved by the University of California Irvine, the University of California Los Angeles, the University of California San Francisco, Duke University, University of North Carolina, University of New Mexico, University of Iowa, University of Minnesota Institutional Review Boards. Written informed consent, including permission to share de-identified data between the centers, was obtained from all study participants.

Symptom Scales

SANS (Scale for the Assessment of Negative Symptoms).—The SANS (Andreasen, 1984) includes 19 negative symptom item ratings, and 5 global factor ratings. Each item is scored on a six point scale from 0–5. The SANS composite total is the sum of the nineteen item ratings. The SANS global total is the sum of the five global ratings. The

two attention items and the attention global score are considered cognitive scores and are often not included as part of the SANS composite and global totals, respectively.

PANSS (Positive and Negative Syndrome Scale).—The PANSS (Kay et al., 1987) includes 30 item ratings on a seven point scale (1–7). The sum of the first seven items creates the PANSS Positive score, the sum of the next 7 items (8–15) creates the PANSS Negative score, and the sum of the final 16 items created the PANSS General psychopathology score. It must be noted that some have suggested that the items scores should be recoded to 0–6 (Leucht et al., 2010; Thompson et al., 1994).

SDS (Schedule for the Deficit Syndrome).—The SDS (Kirkpatrick et al., 1989) includes 6 negative symptom item ratings and one global severity item rating on a 5 point scale from 0 (normal) to 4 (severely impaired). In addition, it includes 4 Yes/No deficit syndrome criteria and a global deficit/non-deficit categorization based on having a score that higher or equal to 2 on 2 of the 6 negative symptom items.

NSA-4 (Negative Syndrome Scale - 4 Item Version).—The NSA-4 (Alphs et al., 2010) is derived from the NSA-16 (Alphs et al., 1989), and includes 4 negative symptom items that are rated on a 6 point scale (1–6; or rated as 9=not ratable) and a global negative symptom rating (GNSR) that is rated on a 7-point scale (1–7) from least to most severe.

Symptom Rating Scores

Negative symptom scores were calculated using the following formulas: PANSS Negative = sum(PANSS items N1–7), (4) Marder Negative Symptom Factor Score (Marder Negative) = sum(PANSS items N1–4, G7 and G16). Of note, PANSS ratings were based on the 1–7 rating system with a score of 1 indicating that the symptom was not present and a score of 7 indicating extreme severity of the symptom. The PANSS ratings that make up the Marder Factor scores are weighted as in the original publication (Marder et al., 1997).

SANS Total (Composite) score was calculated as the sum of SANS items 1–7, 9–12, 14–16, 18–21, and 23–24, while SANS (Global) Summary score was calculated as the sum of SANS items 8, 13, 17, 22, and 25, representing affective flattening, alogia, avolition, anhedonia, and attention global rating scores, respectively; scores without the attention subscales were also calculated.

SDS Severity was calculated as the sum of the 6 negative symptoms. Of note, our SDS analysis used SDS severity scores instead of the global deficit/non-deficit categorization (Kirkpatrick et al., 1989).

The NSA Global Negative Symptom Rating (GNSR) is the rating on the “Global Negative Symptom” item of the NSA-4.

Statistical Analyses

Pearson’s correlations assessed the relationships between the negative symptom scores based on the overall sample (SAS PROC CORR, Statistical Analysis Software, Version 9.2, SAS Institute Inc., Cary, NC, USA). Regression analyses, predicting the negative symptom

scores with alternative negative symptom scores, were performed on data from 176 patients randomly selected from the overall sample (SAS PROC MIXED, Statistical Analysis Software, Version 9.2, SAS Institute Inc., Cary, NC, USA).

Intraclass correlations (ICCs; and their confidence intervals) between actual symptom rating scores and the same symptom scores predicted by alternative symptom rating scales based on the regression equations were computed in two cross-validation samples: 1. a sample of 29 patients whose data did not contribute to the analyses from which the regression equations were derived; and 2. an independent validation sample (n=28 DSM-IV schizophrenia) collected from a separately funded NIMH R21 study. The cross validation sample sizes were based on sample size estimates in the R ICC package for ICCs larger than 0.54 (i.e., fair ICCs, excluding 0 from their confidence intervals), while maintaining the largest possible derivation sample to robustly estimate the regression equations. We computed one-way random, absolute agreement ICCs using the R (Version 2.7.0) irr package. ICCs can be interpreted as excellent (> 0.8), good (0.7 – 0.8), fair (0.5 – 0.7) or poor (< 0.5) (American Psychiatric Association, 2007).

Results

Correlations

Negative symptom ratings from the various negative symptom scales were moderately to highly correlated with each other (range 0.73 – 0.91, see Table 3).

Symptom Ratings Conversion Equations

The following sections present the equations to convert between the negative symptom scores provided by the SANS, PANSS, SDS, and NSA based on the linear regression analyses (see Figure 1). The equations presented in this manuscript, as well as those between the PANSS and SAPS/SANS presented previously (van Erp et al., 2013), are available at <http://converteasy.org> for use by the scientific community.

<i>Between PANSS Negative, SDS, and NSA</i>
PANSS Negative = 9.3694 + (0.8183 * SDS Severity)
SDS Severity = -5.5988 + (0.8224 * PANSS Negative)
PANSS Negative = 6.315 + (2.8477 * NSA GNSR)
NSA GNSR = 0.1021 + (0.193 * PANSS Negative)
<i>Between SANS [Composite] Total, SDS, and NSA</i>
SANS [Composite] Total score = 9.0644 + (2.0658 * SDS Severity)
SDS Severity = -0.9933 + (0.3324 * SANS [Composite] Total score)
SANS [Composite] Total score = 1.6164 + (7.0938 * NSA GNSR)
NSA GNSR = 1.209 + (0.07685 * SANS [Composite] Total score)
<i>Between SANS [Composite] Total without Attention, SDS, and NSA</i>
SANS [Composite] Total without Attention score = 7.3985 + (1.9038 * SDS Severity)

$SDS\ Severity = -0.6769 + (0.3621 * SANS\ [Composite]\ Total\ without\ Attention\ score)$
$SANS\ [Composite]\ Total\ without\ Attention\ score = 0.3573 + (6.5935 * NSA\ GNSR)$
$NSA\ GNSR = 1.2702 + (0.08439 * SANS\ [Composite]\ Total\ without\ Attention\ score)$
<i>Between SANS [Global] Summary, SDS, and NSA</i>
$SANS\ [Global]\ Summary\ score = 3.6201 + (0.6286 * SDS\ Severity)$
$SDS\ Severity = -1.0526 + (0.9772 * SANS\ [Global]\ Summary\ score)$
$SANS\ [Global]\ Summary\ score = 1.0588 + (2.2548 * NSA\ GNSR)$
$NSA\ GNSR = 1.1233 + (0.2358 * SANS\ [Global]\ Summary\ score)$
<i>Between SANS [Global] Summary without Attention, SDS, and NSA</i>
$SANS\ [Global]\ Summary\ without\ Attention\ score = 2.7349 + (0.5438 * SDS\ Severity)$
$SDS\ Severity = -0.8477 + (1.1687 * SANS\ [Global]\ Summary\ without\ Attention\ score)$
$SANS\ [Global]\ Summary\ without\ Attention\ score = 0.4032 + (1.9911 * NSA\ GNSR)$
$NSA\ GNSR = 1.1353 + (0.2878 * SANS\ [Global]\ Summary\ without\ Attention\ score)$
<i>Between NSA and SDS</i>
$NSA\ GNSR = 1.6226 + (0.2023 * SDS\ Severity)$
$SDS\ Severity = -2.3189 + (2.9977 * NSA\ GNSR)$
<i>Between Marder Negative, SDS, and NSA</i>
$Marder\ Negative = 8.4861 + (0.9149 * SDS\ Severity)$
$SDS\ Severity = -4.4378 + (0.7566 * Marder\ Negative)$
$Marder\ Negative = 4.8843 + (3.2461 * NSA\ GNSR)$
$NSA\ GNSR = 0.3267 + (0.1809 * Marder\ Negative)$

Reliability of Predicted Ratings

Within the two cross-validation samples, ICCs (\pm 95% CI) between actual symptom ratings and those predicted by the conversion formulas ranged from moderate (ICC FBIRN/Independent = 0.61/0.63) to good (ICC FBIRN/Independent = 0.79/0.82) (see Table 4).

Discussion

The principal findings of this study include conversion formulas between several negative symptom scores based on the FBIRN Phase 3 sample as well as assessments of conversion score reliability on an FBIRN Phase3 subsample and an independent sample. While the relationships of the SAPS (Scale for the Assessment of Positive Symptoms; Andreasen, 1984b; Andreasen and Olsen, 1982) and SANS-with the PANSS positive and negative symptom scores have been examined (Lyne et al., 2012; Norman et al., 1996; Rabany et al., 2011; van Erp et al., 2013) and between-score conversion formulas for these measures have been published (van Erp et al., 2013), to our knowledge this is the first report on translating negative symptoms scores between the SANS/PANSS, NSA and SDS.

In our large schizophrenia sample the NSA, SDS, SANS and PANSS negative symptom ratings were moderately to highly correlated ($r_{205} = 0.73 - 0.91$). Further, in our linear regression-based conversion formulas converted most symptom dimension scores between

these widely-used negative symptoms scales reasonably well: ICCs indicated mostly moderate to good reliabilities ranging from 0.61 to 0.79.

Comparisons of r and ICC coefficients showed high correlations between several of the negative symptom scales, suggesting that they measure similar constructs, as well as good ICCs, suggesting reliable between-scale score conversions. These include the SDS Total Severity and Marder Negative scores ($r = 0.81$; ICC = 0.77), SDS Total Severity and PANSS Negative scores ($r = 0.78$; ICC = 0.71), NSA and Marder Negative scores ($r = 0.74$; ICC = 0.72), NSA and PANSS Negative scores ($r = 0.71$; ICC = 0.68). It is reasonable to expect that these paired measurements are in fact measuring highly overlapping constructs. For several other conversions, the ICCs were moderate, in particular those between the SANS and PANSS scores and NSA GNSR.

Our findings can be interpreted as indicating that not all negative assessments are “equal”: while some scores are highly correlated and reliable predictors of other scores, suggesting an overlap between the measured constructs, *e.g.*, the SDS Severity and the PANSS Negative and the SANS [global] Total without Attention and SDS Severity, other scores are only moderately correlated and poor predictors of each other, suggesting only partial overlap between the measured constructs, *e.g.*, the PANSS Negative predicted and NSA GNSR.

The observed moderate to good correlations indicate that the four negative symptoms scales used in the present study are likely measuring largely similar constructs. Of interest, the relatively high correlations between a scale purported to measure deficit symptoms (*e.g.*, SDS; Kirkpatrick et al., 1989) and scales designed to measure the somewhat broader set of persistent negative symptoms [*e.g.*, SANS (Andreasen, 1984a) and NSA (Alphs et al., 2010)] indicate that, at least for our population, deficit *vs.* persistent negative symptoms might not be as divergent as previously reported (Buchanan, 2007). While this is a way of understanding our findings, it is important to note that we have not assessed or controlled for secondary influences on the SDS ratings, or collected longitudinal data to confirm the persistence of symptoms over time.

An important benefit of our formula-based method for conversion of scores between scales is the conservation of the quantitative nature of the symptom ratings. As a first attempt to calculate such formulas, our regression-based formulas to convert negative symptom severity ratings represent an important step forward in standardizing schizophrenia negative symptoms studies. For the benefit of schizophrenia researchers and clinicians we have implemented these conversion formulas on an open-access website (<http://www.converteasy.org>; van Erp et al., 2014).

Our study has several limitations. First, many of the conversions have reliabilities (ICCs) that are in the good range (0.60–0.74) and not in the excellent range (0.75–1) and must therefore be used with caution. Our study provides empirical evidence that there is a range of quality of conversions across multiple negative symptom and high quality conversion of scores appears to not be possible between all the scores. Second, the 2006 NIMH-MATRICES consensus meeting highlighted that the existing negative symptoms scales have a number of conceptual and psychometric limitations. For example, the SANS includes items that assess

attention (Kirkpatrick et al., 2006) which is not considered part of negative symptoms. To determine its influence on our conversion equations, we calculated the correlation between total SANS scores and total scores without the attention items. We found a correlation of 0.99 indicating that attention had little influence on the total SANS score and therefore did not appreciably affect the conversion results. However the inclusion of attentional items may be a concern on conceptual grounds and we therefore provide conversion equations with and without attention included.

The range of ICC and r coefficients we report is consistent with previous studies suggesting that different negative symptoms scales may address different aspects of negative symptoms (Marder et al., 2013). Five domains-- blunted affect, alogia, asociality, anhedonia, and avolition-- have been identified in the 2006 workshop (Kirkpatrick et al., 2006). Our conversion equations are limited to conversions between total negative symptoms rating scores. Moreover, the included scales are not entirely conceptually equivalent. For example, the SDS assesses stable, primary, negative symptoms over a 12-month period, whereas the other scales do not consider the primary/secondary distinction or the stability of symptoms. The SDS is primarily designed to qualitatively differentiate deficit from non-deficit schizophrenia, a dichotomous approach, as opposed to SANS, PANSS negative, and NSA, which measure continuous intervals by quantitatively rating negative symptoms.

Our findings are based on a sample size of $n=205$ spread across multiple sites ($n=7$) covering the east and west coasts as well as the middle of the United States, which provides a measure of reassurance with regards to having a representative community-based patient sample. Nevertheless our subjects are medically and psychiatrically stable with mild to moderate symptoms of chronic schizophrenia and no substance abuse. Thus, it is not clear whether our formulas can be reliably used for first episode patients, patients with acute decompensation, patients with symptoms at the extremes of severity, or patients with illicit substance misuse comorbidity. Further, the inclusion of clinically stable subjects and exclusion of subjects with schizoaffective disorder, comorbid depressive symptoms, or significant extrapyramidal symptoms might decrease the potential for secondary negative symptoms. To the extent to which the different scales may vary in their inclusion of secondary negative symptoms, our sample selection requirements might change the correlation strength for summary scores from the different negative symptom measures. Finally, our ICCs have relatively large confidence intervals indicating a degree of underlying heterogeneity in patients and possibly reflecting variation in items sampling the five domains in the negative symptoms construct.

Alternatively, validity can be estimated via convergent validity. Specifically, for negative symptoms convergent validity can be assessed against functional measures or measures of cognitive deficits (Harvey, 2013; Ventura et al., 2009). Estimating convergent validity of the negative symptoms construct against cognitive measures will be the focus of a follow up study; while equally important, the current study did not consider assessment of functioning.

The study did not include a formal assessment of interrater reliability training. Finally, to maximize reliability, the study design required that patients were rated by the same rater for all symptom severity clinical scales during the same assessment visit. These provisions,

while necessary for consistent clinical rating, might also increase the correlation of scores between different scales, as raters may cross-check the scales for consistency. For minimizing inter-rater variance on conversion formulas, ideal inter-rater consistency is desirable. At the same time, due to our single rater scenario, the consistency of the ratings may be larger than if ratings were to be completed by independent raters and represent the upper limit of what is possible when converting scores between raters. It is not clear if ratings by less experienced raters or scores from different scales administered by different raters (*i.e.*, rater for SANS is different than rater for SDS and NSA) would have the same degree of correlation as ours. The question of the best way to assess of negative symptoms is yet to be settled. Two new instruments, the Brief Negative Symptom Scale (Kirkpatrick et al., 2011) and the Clinical Assessment Interview for Negative Symptoms (CAINS; Kring, et al., 2013), have been developed in the wake of the 2006 NIMH negative symptoms consensus meeting (Kirkpatrick et al., 2006). Our results can serve as a bridge fostering cross validation of the older and newer instruments for meta- and mega-analyses. While such conversions are limited because the items are not identical they provide a method to optimally use the wealth of legacy and longitudinal data that may be difficult to interpret otherwise.

Our methodology of clustering and rating together items with similar face validity on different scales improved test efficiency to an extent that allowed for same session completion of extensive clinical testing, decreased testing redundancy, minimized subject and test fatigue and thus the risk for false negative ratings, but also presents a risk for cross-contamination of the ratings. At the same time, clustering provides the advantage of using many questions about the same study domain for each negative symptom item, thus improving the chance that each item is rated on its own merit and closer to an ideal standard rating for that specific item.

In conclusion, we report regression-based formulas for the conversion between schizophrenia negative symptom severity scores as measured by the PANSS, SANS, SDS and NSA. Such formulas can be used for the comparison of epidemiological data, rates of negative symptom response across treatments, as well as in allowing pooling of data from different studies or multi-site data repositories for meta-, mega- or combined analyses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

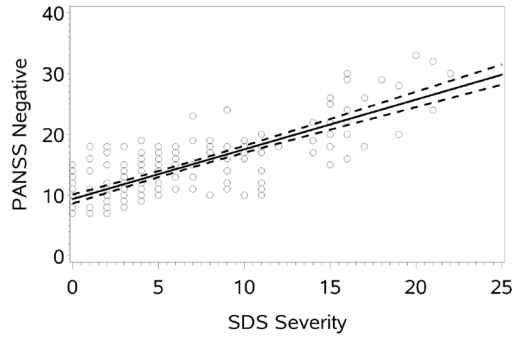
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References

- Alphs L, Morlock R, Coon C, van Willigenburg A, Panagides J, 2010 The 4-item negative symptom assessment (NSA-4) instrument: A simple tool for evaluating negative symptoms in schizophrenia following brief training. *Psychiatry (Edgmont)* 7 (7), 26–32. [PubMed: 20805916]
- American Psychiatric Association, 2007 *Handbook of Psychiatric Measures*, Second Edition American Psychiatric Association, Washington, DC
- Andreasen NC, 1982 Negative symptoms in schizophrenia: Definition and reliability. *Arch. Gen. Psychiatry* 39 (7), 784–788. [PubMed: 7165477]
- Andreasen NC, 1984a The scale for the assessment of negative symptoms (SANS). University of Iowa.
- Andreasen NC, 1984b The scale for the assessment of positive symptoms (SAPS). University of Iowa.
- Andreasen NC, Olsen S, 1982 Negative v positive schizophrenia: Definition and validation. *Arch. Gen. Psychiatry* 39 (7), 789–794. [PubMed: 7165478]
- Arndt S, Alliger RJ, Andreasen NC, 1991 The distinction of positive and negative symptoms: The failure of a two-dimensional model. *Br. J. Psychiatry* 158, 317–322. [PubMed: 2036528]
- Buchanan RW, 2007 Persistent negative symptoms in schizophrenia: An overview. *Schizophr Bull.* 33 (4), 1013–1022. [PubMed: 17099070]
- Daniel DG, 2013 Issues in Selection of Instruments to Measure Negative Symptoms. *Schizophr. Res* 150 (2–3), 343–345. [PubMed: 23899996]
- First MB, Spitzer RL, Gibbon MG, Williams JBW, 2002 *Structured Clinical Interview for DSM-IV-TR Axis I Disorders – Patient Edition (SCID-I/P, 11/2002 revision)* (New York).
- Harvey PD, 2013 Assessment of everyday functioning in schizophrenia: Implications for treatments aimed at negative symptoms. *Schizophr. Res* 150 (2–3), 353–355. [PubMed: 23668973]
- Hollingshead AB, 1975 *Four Factor Index of Social Status*. Yale University, New Haven, CT.
- Kay SR, Fiszbein A, Opler LA, 1987 The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull* 13 (2), 261–276. [PubMed: 3616518]
- Kirkpatrick B, Buchanan RW, McKenny PD, Alphs LD, Carpenter WT Jr., 1989 The schedule for the deficit syndrome: An instrument for research in schizophrenia. *Psychiatry Res.* 30 (2), 119–123. [PubMed: 2616682]
- Kirkpatrick B, Fenton WS, Carpenter WT Jr., Marder SR, 2006 The NIMH-MATRICES consensus statement on negative symptoms. *Schizophr. Bull* 32 (2), 214–219. [PubMed: 16481659]
- Kirkpatrick B, Strauss GP, Nguyen L, Fischer BA, Daniel DG, Cienfuegos A, Marder SR, 2011 The brief negative symptom scale: Psychometric properties. *Schizophr. Bull* 37 (2), 300–305. [PubMed: 20558531]
- Kring AM, Gur RE, Blanchard JJ, Horan WP, Reise SP, 2013 The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. *Am. J. Psychiatry* 170 (2), 165–172. [PubMed: 23377637]
- Lyne JP, Kinsella A, O'Donoghue B, 2012 Can we combine symptom scales for collaborative research projects? *J Psychiatr Res* 46 (2), 233–238. [PubMed: 22056401]
- Marder SR, Davis JM, Chouinard G, 1997 The effects of risperidone on the five dimensions of schizophrenia derived by factor analysis: Combined results of the North American trials. *J Clin Psychiatry* 58 (12), 538–546. [PubMed: 9448657]
- Marder SR, Rabinowitz J, Kapur S, 2013 Clinical trials for negative symptoms--emerging directions and unresolved issues. *Schizophr. Res* 150 (2–3), 327. [PubMed: 24209763]
- Norman RM, Malla AK, Cortese L, Diaz F, 1996 A study of the interrelationship between and comparative interrater reliability of the SAPS, SANS and PANSS. *Schizophr. Res* 19 (1), 73–85. [PubMed: 9147498]
- Oldfield RC, 1971 The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 9 (1), 97–113. [PubMed: 5146491]
- Rabany L, Weiser M, Werbeloff N, Levkovitz Y, 2011 Assessment of negative symptoms and depression in schizophrenia: revision of the SANS and how it relates to the PANSS and CDSS. *Schizophr. Res* 126 (1–3), 226–230. [PubMed: 21115328]

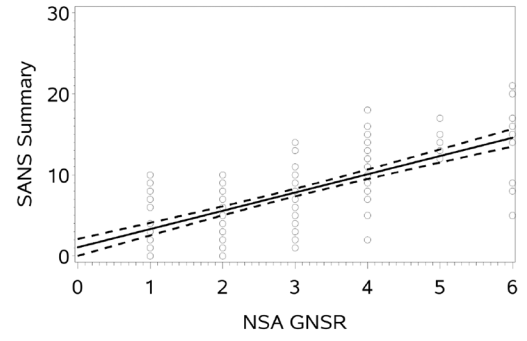
- Rabinowitz J, Werbeloff N, Caers I, Mandel FS, Stauffer V, Menard F, Kinon BJ, Kapur S, 2013 Negative symptoms in schizophrenia--the remarkable impact of inclusion definitions in clinical trials and their consequences. *Schizophr. Res* 150 (2–3), 334–338. [PubMed: 23815975]
- van Erp TGM, Preda A, Nguyen D, Faziola L, Turner J, Bustillo J, Belger A, Lim KO, McEwen S, Voyvodic J, Mathalon DH, Ford J, Potkin SG, FBIRN, 2014 Converting positive and negative symptom scores between PANSS and SAPS/SANS. *Schizophr. Res* 152 (1), 289–294. [PubMed: 24332632]
- Ventura J, Helleman GS, Thames AD, Koellner V, Nuechterlein KH, 2009 Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: A meta-analysis. *Schizophr. Res* 113 (2–3), 189–99. [PubMed: 19628375]

Simple Linear Regression with 95% Confidence Limits for Mean Predicted Values



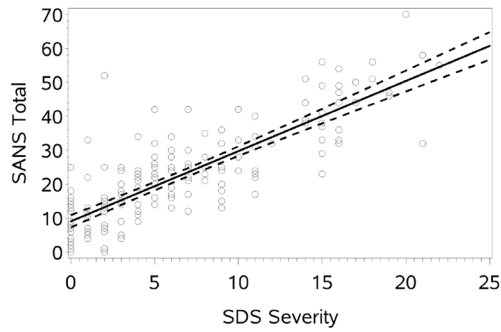
A.

Simple Linear Regression with 95% Confidence Limits for Mean Predicted Values



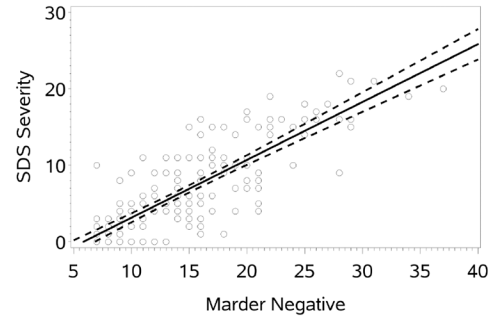
B.

Simple Linear Regression with 95% Confidence Limits for Mean Predicted Values



C.

Simple Linear Regression with 95% Confidence Limits for Mean Predicted Values



D.

Figure 1:

Simple linear regressions with 95% confidence intervals between scales:

- A. PANSS Negative and SDS Severity
- B. SANS Global and NSA Global
- C. SANS Total and SDS Severity
- D. SDS Severity and Marder Negative

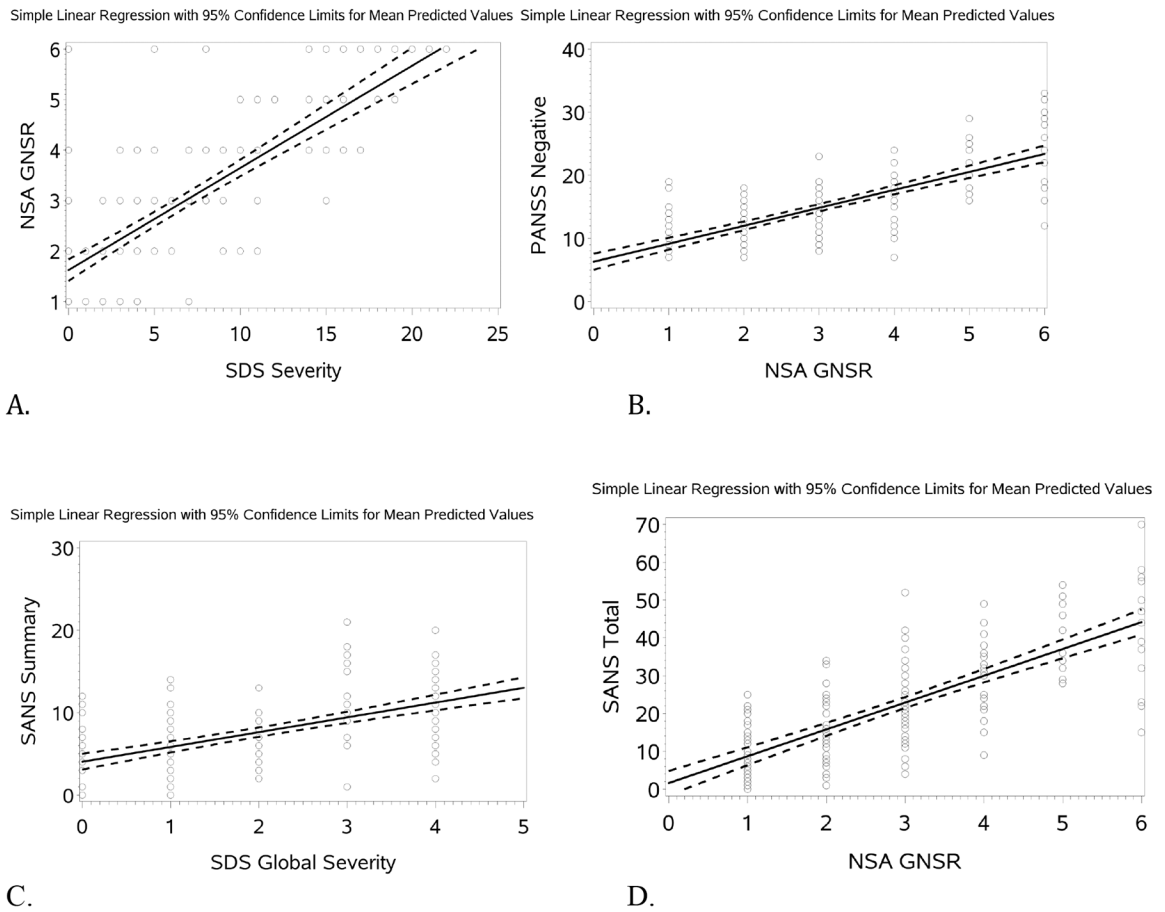


Figure 2:
 Simple linear regressions with 95% confidence intervals between scales:
 A. NSA Global and SDS Severity
 B. PANSS Negative and NSA Global
 C. SANS Summary and SDS Global
 D. SANS Total and NSA Global

Table 1.

Sample Demographics

Demographics	Schizophrenia Patients (N=205)
Mean Age (SD)	39.5 (11.6)
Gender (M / F)	156 / 49
Handedness ^a (bilateral / left / right)	4 / 13 / 188
Race	
American Indian or Alaskan Native	4
Asian	22
Black or African American	43
Native Hawaiian or Pacific Islander	3
White	133
NAART FSIQ (SD)	103 (9.5)
Subject Education ^b (SD)	3.7(0.9)
Highest Parental Education ^b (SD)	4.6(1.9)
Age at Onset (SD)	21.8 (7.5)
Duration of Illness (SD)	17.7 (11.5)
Diagnosis Subtype	
Paranoid	146
Disorganized	7
Undifferentiated	36
Residual	16
Antipsychotic Medications	
Chlorpromazine Equivalent (SD) ^c	398 (400)
Number Typical / Atypical / Both / No ^d	18 / 130 / 10 / 0

^aBased on the Edinburgh Handedness Questionnaire (Oldfield, 1971).

^bBased on the Hollingstead Socioeconomic Status Scale (Hollingstead, 1975).

^cBased on data from 142 participants.

^dBased on data from 158 participants.

Table 2.

Absolute Means (SD) of Negative Symptom Measures

Schizophrenia Patients (N=205)	
PANSS Positive (SD)	15.7 (5.3)
PANSS Negative (SD)	14.9 (5.9)
PANSS General (SD)	28.6 (7.5)
PANSS Composite (SD)	0.77 (6.5)
PANSS Total (SD)	59.1 (15.4)
Marder Positive (SD)	17.8 (6.3)
Marder Negative (SD)	14.6 (6.4)
SANS	
Flat Affect (SD)	6.2 (6.8)
Alogia (SD)	2.4 (3.2)
Apathy (SD)	4.6 (3.3)
Anhedonia (SD)	7.0 (5.1)
Attention (SD)	2.7 (2.4)
SANS (composite) Total (SD)	23.0 (14.6)
SANS (composite) Total without Attention (SD)	20.2 (13.4)
SANS (global) Summary (SD)	7.8 (4.7)
SANS (global) Summary without Attention (SD)	6.4 (3.9)
SAPS	
Hallucinations (SD)	6.0 (6.1)
Delusions (SD)	8.2 (7.8)
Bizarre Behavior (SD)	1.3 (1.7)
Thought Disorder (SD)	1.3 (1.7)
SAPS (composite) Total (SD)	16.8 (14.2)
SAPS (global) Summary (SD)	5.7 (3.7)
SDS_Severity (SD)	6.5 (5.7)
NSA (GNSR) (SD)	3.0 (1.5)

Table 3.

Pearson's Correlations between Symptom Ratings (N=205)

	PANSS Negative	SANS (composite) Total	SANS (composite) Total without Attention	SANS (global) Summary	SANS (global) Summary without Attention	Marder Negative	NSA GNSR	SDS Severity
PANSS Negative	1	0.84	0.82	0.82	0.80	0.93	0.74	0.81
SANS (composite) Total		1	0.99	0.92	0.91	0.85	0.73	0.83
SANS (composite) Total without Attention			1	0.89	0.92	0.85	0.73	0.82
SANS (global) Summary				1	0.97	0.81	0.73	0.79
SANS (global) Summary without Attention					1	0.82	0.75	0.81
Marder Negative						1	0.77	0.83
NSA GNSR							1	0.79
SDS Severity								1

Note: NSA data was available on 204 patients. All p-values < 0.0001.

Table 4. Intra-class Correlations (95% CI) Between Measured and Predicted Symptom Ratings Obtained with Regression-Based Conversion Equations

Predicted Symptom Rating	ICC (95% CI) FBIRN Sample N=29	ICC (95% CI) Validation Sample ** N=28
PANSS Negative predicted by SDS Severity *	0.71 (0.48 – 0.85)	0.80 (0.61 – 0.90)
PANSS Negative predicted by NSA GNSR	0.68 (0.42 – 0.83)	0.63 (0.35 – 0.81)
SANS [composite] Total by SDS Severity	0.76 (0.56 – 0.88)	0.76 (0.55 – 0.88)
SANS [composite] Total by NSA GNSR	0.62 (0.34 – 0.80)	0.74 (0.52 – 0.87)
SANS [composite] Total without Attention by SDS Severity	0.74 (0.52 – 0.87)	0.77 (0.56 – 0.89)
SANS [composite] Total without Attention by NSA GNSR	0.61 (0.33 – 0.80)	0.74 (0.52 – 0.87)
SANS [global] Total by SDS Severity	0.79 (0.60 – 0.90)	0.82 (0.66 – 0.91)
SANS [global] Total by NSA GNSR	0.66 (0.39 – 0.82)	0.79 (0.60 – 0.90)
SANS [global] Total without Attention by SDS Severity	0.81 (0.64 – 0.91)	0.82 (0.66 – 0.91)
SANS [global] Total without Attention by NSA GNSR	0.69 (0.44 – 0.84)	0.80 (0.61 – 0.90)
NSA GNSR by SDS Severity	0.79 (0.60 – 0.89)	0.73 (0.50 – 0.86)
SDS Severity by Marder Negative	0.77 (0.57 – 0.88)	0.81 (0.64 – 0.91)
NSA GNSR by Marder Negative	0.72 (0.48 – 0.86)	0.68 (0.43 – 0.84)

* Note that the ICCs for the vice versa predictions (e.g., SDS Severity predicted by PANSS Negative are equivalent).

** The validation (second) sample was collected independently from the FBIRN sample and included individuals that met DSM-IV criteria for schizophrenia based on SCID-I/P with similar inclusion and exclusion criteria as those used in the FBIRN study.