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Toward the Next Generation of Negative Symptom Assessments: The Collaboration to Advance Negative Symptom Assessment in Schizophrenia

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Negative symptoms in schizophrenia are related to poor functional outcome, persistent over time, a source of burden for caregivers, and only minimally responsive to currently available medications. A major challenge to developing efficacious interventions concerns the valid and reliable assessment of negative symptoms. In a recent consensus statement on negative symptoms, a central recommendation was the need to develop new assessment approaches that address the limitations of existing instruments. In the current report, we summarize the background and rationale for the Collaboration to Advance Negative Symptom Assessment in Schizophrenia (CANSAS). The CANSAS project is an National Institute of Mental Health-funded multisite study that is constructing a next-generation negative symptom scale, the Clinical Assessment Interview for Negative Symptoms (CAINS). The CAINS is being developed within a data-driven iterative process that seeks to ensure the measure's reliability, validity, and utility for both basic psychopathology and treatment development research.

Key words: schizophrenia/negative symptoms/assessment

In 2006, an National Institute of Mental Health (NIMH) consensus statement on negative symptoms summarized the results of an expert consensus development conference.[1] This consensus statement observed that despite years of research, negative symptoms remained an unmet therapeutic need. Importantly, among the key recommendations to facilitate future developments for the treatment of negative symptoms were (1) the creation of a new negative symptom instrument to address noted limitations in existing assessment scales and (2) that a workgroup should be formed to develop this next-generation approach to assessing negative symptoms as well as obtain funding to assess the reliability and validity of this instrument. As members of the workgroup that was tasked to develop new assessment approaches to negative symptoms, the authors summarize the background, rationale, and development of one new instrument that grew out of the 2006 consensus statement and highlight the ongoing research effort to move the next generation of research on negative symptoms forward.

Background

At a broad level, definitions of negative symptoms all involve the significant diminution or lack of a normal function.[2–5] The specific domains of "normal functioning" that are considered can vary across assessment measures but typically include: (*a*) affective experience, either focused on reduced pleasure (ie, anhedonia[3]) or on a broader reduction in the range and intensity of both positive and negative emotions[2,5]; (*b*) interest in and motivation for productive activities or sense of purpose (relating to avolition or apathy); (*c*) social drive or interest and desire for affiliation (relating to asociality); and (*d*) expressive or communicative behaviors, including diminished facial expression, decreased gestures, and decreased vocal intonation (all aspects of flat or blunted affect), as well as diminished verbal production or reduced spontaneous speech (alogia). Although the above would indicate that aspects of the negative symptom construct clearly relate to experiential deficits (emotional experience, interest, motivation, sense of purpose, desire for social affiliation), existing clinical measures of negative symptoms differ markedly in what information is considered (patient reports of internal states, patient reports of behavior outside of the interview, and interviewer observations of behavior during the interview), and how these different forms of information are considered in rating symptom severity—these assessment issues will be considered in more detail below.

Aided by the development of the first generation of clinical instruments to assess negative symptoms in the

1980's,[2–5] an accumulation of research has clearly indicated the clinical importance of this symptom domain. For example, studies have repeatedly demonstrated that negative symptoms are cross-sectionally associated with current poor social functioning [6–11] and that these symptoms longitudinally predict social and occupational impairment.[12–14] Negative symptoms also contribute to caregiver burden and, more broadly, to the family conflict that also portends poor prognostic outcomes for people with schizophrenia.[15,16] Critically, negative symptoms have been shown to be factorally distinct from other symptom domains and not merely secondary to psychotic symptoms, depression, and anxiety. For review, see Blanchard and Cohen.[17]

Despite the clinical importance of negative symptoms, this illness domain remains inadequately addressed by current pharmacotherapy with only limited evidence for minor symptom improvement.[18–21] The lack of treatment options is reflected in the fact that the Food and Drug Administration has yet to approve any medication with an indication for negative symptoms.[22] In short, negative symptoms remain a critical unmet therapeutic need. In considering how best to move the field forward, one impediment to treatment development may be serious limitations with how negative symptoms are currently measured.[1]

Measurement Limitations in Current Instruments

Recent work has pointed to significant limitations associated with the current instruments used to assess negative symptoms, including some of the most widely employed instruments: the Scale for the Assessment of Negative Symptoms (SANS),[23] the Positive and Negative Syndrome Scale (PANSS),[4] and the Negative Symptom Assessment (NSA).[2] One problem with these instruments concerns their item content, which in some cases appear outdated and do not reflect our current understanding of the negative symptoms construct and in others do not incorporate highly relevant contemporary research findings. For example, 2 measures include items that assess cognitive functioning; the SANS includes ratings of "attention" while the PANSS rates "abstract thinking" and "stereotyped thinking." However, factor analytic studies indicate that these items do not cohere well with the other negative symptom ratings [24–26] and cognitive impairment appears to be conceptually distinct from negative symptoms.[27]

As another example, existing measures of anhedonia do not make a distinction between the anticipation of pleasure, "anticipatory pleasure," and pleasure experienced while engaging in an activity, "consummatory pleasure." Contemporary neurobehavioral models of hedonic experience differentiate these 2 forms of pleasure and evidence from animal and human research indicates that they have distinct neural circuits.[28–31] Kring and colleagues[32,33] have noted that evidence from laboratory and clinical studies across different cultures and countries is consistent with schizophrenia involving intact consummatory or "in the moment" pleasure but impaired anticipatory pleasure.[34–37] Given this preliminary evidence, assessment of deficits in hedonic capacity may benefit from a differentiation between these 2 forms of pleasure. This approach may be useful regardless of whether a differential deficit is ultimately found to exist (as assessed within a clinical interview) in that it may ensure a broad hedonic assessment across current and expected pleasure. It should be noted that evaluation of the consummatory aspect of pleasure is complicated within an interview assessment in that reports are not of in the moment pleasure but rather reflect the recall of such experiences. The precise role of memory deficits, if any, in such reports will require empirical scrutiny—one short-term study did not find a reduced recall of affective experience in schizophrenia compared with controls. For a broader discussion of affective memory in schizophrenia, see Horan et al.[38] and also see Herbener.[39] Of course, the role of memory deficits is relevant for any item on a clinical rating scale that relies upon a patient to report on past experience.

Existing negative symptom measures also have a number of key conceptual limitations. One issue is that individual item ratings on the SANS and PANSS can actually reflect several, conceptually distinct processes or domains that are not necessarily part of the negative symptom domain.[40] For example, in rating "anhedonia–asociality" on the SANS, item ratings can reflect frequency of social contact and social activity, decreased interest, decreased pleasure, or even hostility. This is problematic as it is not possible to determine precisely what psychological process is reflected in the ratings given that anhedonia–asociality may reflect impoverished pleasure, lack of motivation, or problematic social relations unrelated to either of these more experiential deficits. Along these lines, the NSA includes a rating of reduced emotional range that reflects both anhedonia and the lack of negative emotional experiences, such as anxiety, sadness, or anger. This introduces a potentially problematic situation of providing a higher negative symptom rating to individuals who may have generally healthy emotional functioning but experienced no negative emotional events during the rating period (it also creates the peculiar scenario where a treatment that results in greater anxiety or depression would actually be seen as "improving" this particular symptom).

A further problem with existing measures is that items often include largely behavioral referents of what are essentially experiential deficits (e.g., lack of pleasure, lack of interest, and lack of motivation) or they explicitly instruct raters to only consider behavior and not any other factors that may contribute to the symptom ratings (e.g., the NSA). With the PANSS, items such as "emotional withdrawal," "poor report," and "passive/apathetic social withdrawal" are conceptually defined in terms of internal

states, including interest, affect, empathy, and closeness, yet none of these items includes probes tapping these experiential states. Instead, the negative symptoms ratings in the PANSS rely solely on observation of behavior during the interview and reports of social behavior and functioning from care workers or family. Thus, ratings that presumably reflect deficits in the experience of emotion, interest, and feelings of empathy and closeness in fact do not consider patient reports but instead derive from observer ratings of social success and functioning. This is potentially problematic because performance deficits can be determined by multiple factors other than experiential deficits, including lack of opportunity related to social and economic privation associated with this disorder, lack of social skill,[6,41] constraints on social and occupational activities imposed by housing requirements or disability payments, or social rejection related to family conflict[42] or stigma.[43] All of these factors can contribute to observations of impoverished social networks or occupational impairment, yet these factors are distinct from social or occupational failures that derive from emotional (anhedonia) or motivational (avolition) deficits that are core to the conceptualization of negative symptoms. Thus, reliance on behavioral observations or self-reports of performance deficits alone can lead to elevated ratings on existing scales for reasons that do not reflect core negative symptoms.

A related difficulty in relying on purely behavioral observations and deficits for assessing negative symptoms is that the relationship between these negative symptom ratings and presumably independent measures of functional outcome risks tautology. That is, negative symptom ratings that are based on behavioral deficits, such as few friendships, lack of romantic partners, or lack of employment are then used to predict "functional" outcomes, such as lack of relationships and unemployment. Other investigators studying functional correlates of negative symptoms have also pointed to the problem of content overlap in current measures.[13] When correlations between functional measures and negative symptoms can exceed 0.80,[44] it is clear that there is little unique variance in negative symptom assessments (NSAs). This circular observation provides limited information concerning the psychological processes that may actually underlie the functional deficits (processes that would appear to be at the core of conceptualizations of negative symptoms and targets for therapeutic intervention). Attempting to control for shared variance across measures by excluding shared content items and scales from negative symptom measures[13] to focus only on alogia or blunted affect ensures that broad domains of conceptual and clinical importance are not included in model testing.

Implications

The above limitations have important theoretical and clinical implications. From a theoretical perspective, current measurement approaches drive available data that then inform conceptualizations of negative symptoms. This is clearly seen in structural models of symptoms that rely on instruments such as the SANS.[17,45] As we have previously reviewed,[17] factor analytic studies have demonstrated that negative symptoms (as measured by the SANS) are multifactorial and that the most replicable findings suggest 2 factors involving diminished expression and anhedonia–asociality (ie, experience). We have noted[17] that such a factor solution may be used to propose that this structure reflects the underlying pathological mechanisms associated with deficits in emotional expression and deficits in emotional experience. This factorial structure, and other evidence, has been recently elaborated upon further[46] to suggest that amotivation or avolition is the core deficit in schizophrenia. Although such conjecture is highly informative in developing testable theoretical models of symptoms, it is critical to acknowledge the basic measurement data from which all of these are models derived. Factor solutions are only as good as the variables used in the analyses. Thus, given the limitations noted in existing instruments, a serious concern arises as to the adequacy and validity of structural solutions based on these symptom ratings. In other words, factor solutions that have previously been identified and theoretical models deriving from such solutions will need to be empirically tested utilizing more extensive assessment instruments that avoid the measurement flaws identified with current clinical measures. Ideally, such future assessment measures will provide information beyond behavioral or performance deficits and allow for an assessment of the core psychological processes that are presumed to be central to negative symptoms.

Clinically, existing negative symptom measures may hamper accurate symptom assessment and undermine advances to treatment. As reviewed above, when using existing instruments, elevated negative symptoms may reflect a range of possible factors that are not directly related to the presumed underlying deficits. If negative symptom assessments essentially reflect performance deficits similar to functional outcome measures, then these ratings provide little insight into underlying mechanisms and may do little to direct future interventions. Critically, if interventions are intended to influence processes, such as hedonic capacity or motivational drive, it will be essential to utilize clinical assessment tools that can actually measure changes in these processes rather than distant functional outcomes that may have a different timeline for manifesting improvement and reflect the impact of other nontreatment-related factors.

Toward the Next Generation of Negative Symptom Assessments

Following from the second recommendation of the NIMH Negative Symptom consensus development

conference (January, 2005), a workgroup was established to develop new assessment approaches to negative symptoms (in addition to the authors, members of the initial working group included: Larry Alphs, George Gharabawi, Philip Harvey, Brian Kirkpatrick, Dolores Malaspina, and Stephen Marder). The workgroup adopted a transparent, multistage process modeled on the MATRICS consensus development process,[47,48] which has been highly successful in establishing an assessment approach to neurocognitive deficits that is now being applied to treatment development. Indeed, this broad collaborative approach is unique with respect to schizophrenia symptom scale development, and it was adopted to avoid a narrow perspective on the conceptualization or measurement of negative symptoms and to permit an objective and critical assessment of existing instruments and benefit from a diverse array of basic and applied research.

The initial workgroup conducted extensive literature reviews on negative symptoms and collaboratively developed initial items for a clinical rating scale across biweekly conference calls and a follow-up conference with workgroup participants to further address conceptual and measurement issues. A draft version of a new instrument was crafted and circulated among participants in the original Consensus Development Conference as well as clinical trial researchers. Following additional revisions within the workgroup, a preliminary measure was presented at national conferences and was posted to a public Web site with requests for input from clinical researchers and industry representatives. From this feedback, a beta measure was constructed.

With a beta measure in hand, the workgroup then developed 2 smaller groups to pursue 2 different plans for moving forward. One group shortened the beta measure (now called the Brief Negative Symptom Scale[49]) and administered it to a 20 patients with schizophrenia in order to gather preliminary data that might encourage early adoption of the brief measure.

The second group comprised of the current authors and subsequently named the Collaboration to Advance Negative Symptom Assessment in Schizophrenia (CANSAS), obtained funding from the NIMH in 2009 to pursue scale development and validation in a larger representative sample. This research program involves 4 research sites including the University of Maryland (Blanchard), University of Pennsylvania (Gur), UCLA (Horan), and UC Berkeley (Kring). From this effort, we have developed the Clinical Assessment Interview for Negative Symptoms (CAINS). In the development process for CAINS, our efforts have been guided by several principles:

1. When assessing core processes related to negative symptoms, including pleasure, affiliation, interest, and motivation, ratings must integratively consider behavior, contextual environmental factors, and patient descriptions of their internal states. The goal of this strategy was to ensure a thorough evaluation of the constructs underlying the symptom domain targeted and avoid an overreliance on purely behavioral performance (as well as avoiding errors in the other direction with overreliance on exclusively self-reported internal states). This interview strategy requires raters to consider multiple perspectives and pursue inconsistencies to enhance the accuracy of the clinical ratings. By addressing these multiple considerations, a more valid assessment of the constructs considered core to negative symptoms ought to be achieved.
2. In developing items and accompanying interview probes, we adopted a strategy of ensuring breadth and inclusiveness. This was expected to yield a longer initial scale that would include items which may be of theoretical or clinical significance but whose empirical status was uncertain. Given the iterative data-driven scale development process (described below), it was expected that items and scales may ultimately be abbreviated or trimmed but it was preferred that such editing would be based on empirical results.
3. Decisions concerning item revision and retention would be based on a data-driven iterative process. Although the CAINS is the result of an extensive collaborative effort, we emphasize that the measure requires empirical scrutiny. Despite what are seen as important advancements to the assessment of negative symptoms, it is necessary to ensure that the CAINS avoids limitations of other instruments—this can only be achieved by requiring that further refinement is based on empirical data gleaned from large and representative clinical samples. This data-driven approach will permit the CAINS to be psychometrically refined based on data rather than clinical fiat. Furthermore, by conducting an evaluation of the CAINS across multiple studies and sites, we seek to ensure the development of an instrument that will have convincing generalizability and will be ready for adoption in therapeutic trials and other research on negative symptoms.
4. In addition to the above issues, the final CAINS instrument is intended to be in a format that will aid in its adoption across a variety of applications from basic psychopathology research to clinical intervention trials. Thus, the interview is expected to compare with existing instruments in time to administer and can be used by clinical assessors with masters-level training or clinical experience. To aid in dissemination, the scale will include training materials including a detailed user's manual.

As reviewed above, we view the exclusive consideration of behavior in rating negative symptoms as problematic because the central defining features of these symptoms involve experiential deficits. We acknowledge that an assessment approach that considers experiential deficits when rating negative symptoms raises the issue of

whether "patient self-reports" of internal states are valid in schizophrenia. Findings from a variety of paradigms document the ability of individuals with schizophrenia to provide reliable and valid reports of anhedonia and other constructs related to negative symptoms. Individuals with schizophrenia provide self-report data (e.g., anhedonia, trait affect, and emotion experience) that yield high internal consistency.[38,50] Additionally, self-report questionnaire responses of individual differences in anhedonia and trait affect have been shown to have high test-retest reliability over 90 days and 1 year,[50,51] even when assessments occur during changes in symptoms and hospitalization status.[51] Using multidimensional scaling techniques, Kring[52] has demonstrated that schizophrenia patients' representations of emotion are reflected in the same 2-dimensional structure (valence and arousal) as are nonpatients' representations, thus bolstering confidence in patients' self-reports. Self-report affect traits are significantly associated with clinician ratings of functioning[50] and clinical ratings of deficit symptoms.[53]

Validity data are provided by laboratory research demonstrating that patients' reports of emotional states covary with laboratory emotion induction methods in the same manner as found in healthy controls and that these self-reports obtained from patients are consistent with psychophysiological responding.[54] Horan and colleagues[38] have found patients can reliably report on approach and avoidance motivation system sensitivities and that motivation was related to reports of emotion in a predictable manner. Self-reported individual difference traits in schizophrenia are predictive of stress reactivity above and beyond clinical ratings of symptoms or independent assessments of cognitive deficits.[55] In sum, when properly assessed, there is considerable evidence that self-reports of emotion and other domains can be reliable and valid in individuals with schizophrenia. It is also worth noting that assessments of other symptom domains (e.g., psychosis, depression, and anxiety) typically rely on patients' self-reports of their perceptions, thoughts, beliefs, and affective states (and evidence suggests that self-report questionnaire responses for symptom severity including psychosis show relatively good agreement with clinician-based ratings[56]).

Importantly, our position is not that negative symptom assessment should rely solely on self-reported internal experience or that behavior should not be considered – the CAINS is not a self-report questionnaire but a clinician-rated interview. Rather, from a measurement perspective, we view patient reports of behavior, internal states, environmental context, and interviewer observations as all fallible indicators of the latent constructs that are of interest (e.g., avolition and anhedonia). Given the core conceptual definitions of negative symptoms reviewed above, it is critical to consider behavior "along with" environmental context and self-reports of relevant internal states (such as motivation, interest, or pleasure) to best understand behavioral deficits and to obtain the most informed clinical assessment. By integrating across these domains, our intent is to yield a more comprehensive clinical rating of the intended negative symptom constructs rather than an approach that relies on any single domain (whether that is behavior or self-reported internal states).

The content covered in the CAINS reflects the 2006 consensus statement that the domains of negative symptoms to be assessed should include anhedonia, asociality, avolition, blunted affect, and alogia. Although there is some evidence that the structure of negative symptoms may simplify to fewer domains (e.g., 2 rather than 5[17]), our data-driven approach mandated that we include all 5 domains and empirically evaluate whether further simplification is warranted. While the basic domains assessed mirror somewhat the content of other instruments, the CAINS departs from these measures in a number of critical domains. As reviewed above, the major theme of the CAINS that sets it apart from existing measures is its focus on the experiential aspects of negative symptoms that are considered to be at the conceptual core of the emotional, social, and motivational deficits that define negative symptoms. The CAINS also avoids confounding experiential deficits in hedonic capacity or drive with behavioral success or functional outcomes. Additionally, across its items, the CAINS departs from other instruments in its use of detailed interview probes. This feature is intended to allow for a thorough assessment of experiential deficits while at the same time minimizing reliance on collateral informants who are typically unavailable in clinical trials. Furthermore, such detailed interview probes ensures interviewer consistency and facilitates training and dissemination. Key characteristics of the 5 CAINS domains are summarized below.

Asociality

In order to avoid the pitfalls associated with other symptom measures of asociality, we sought to constrain the definition of asociality based on an informed review of personality and social psychological research on social affiliation,[57] social approach,[58] and relationships.[59,60] Thus, our approach to asociality emphasizes feelings and attitudes of affection and a desire for close relationships rather than relying exclusively on quantitative behavioral indicators of frequency of social activites.[57] To address this problem of conflating behavioral success with interest in social activity, the CAINS rates asociality based on both reports of interests or values (ie, the degree to which an individual values and desires close social bonds) and observable behaviors (ie, the extent to which the subject actually engages in interactions with others and the nature of those interactions). Consideration of both internal experiences and behavior is critical as decreased social activity may result from sources other than a true asociality, such as housing arrangements,

social anxiety, or paranoid beliefs. The interview includes probes tapping relationships in multiple domains, including family, romantic relationships, and friendships. Ratings of asociality do not reflect pleasure derived from social activities (which is rated under anhedonia) or the extent to which the subject initiates or is motivated to seek out social activity (which is rated under avolition).

Avolition

Our development of avolition was informed by basic science literatures in psychology and neuroscience on motivated behavior.[61] Importantly, both overt behavior and internal motivation are considered in making the ratings of Avolition, and interviewer prompts are designed to tap into both of these across 4 areas: social activity, work/vocation/school, recreation, and self-care. The assessment of both behavior and motivation is critical as a failure to initiate and persist in activity may be due to several sources that do not reflect avolition, including decreased opportunity or paranoid beliefs. A patient may have a decrease in goal-directed behavior but still receive a relatively low rating on avolition if he/she has a strong desire to engage in such behavior. From another perspective, patients who report participating in many activities because they are required to (as in, eg, a day treatment program) but are not motivated to do so or do not initiate the activities themselves may receive a higher score on avolition than those who are less active but initiate activities on their own. As described above, the goal is to conduct a full assessment considering both patient report of internal drive and motivation while also considering behavior and environmental context. To minimize overlap with anhedonia, avolition ratings focus on interest or motivation in initiating and participating in activities not the pleasure experienced during the activities or looking forward to them. To minimize overlap with asociality, avolition ratings of social activity reflect the motivation to seek out social activities along with the extent to which a person initiates and persists in social activity, independent of the quality of the social relationship, the desire for affiliation, or the value placed on relationships.

Anhedonia

Three major innovations have been implemented in the assessment of anhedonia. First, given that other instruments fail to differentiate experiential (or "hedonic capacity") deficits from achievement (or "performance") deficits, the CAINS anhedonia ratings focus specifically on pleasurable experience, including both the frequency and intensity of these experiences. Second, as reviewed above, research suggests the importance of differentiating anticipatory pleasure from consummatory pleasure. Thus, the CAINS anhedonia ratings differentiate between these 2 forms of pleasure. Third, pleasure experience is assessed in a range of activities including social, physical, and recreational/vocational.

Blunted Affect

Blunted affect refers to a decrease in the outward expression of emotion. A challenge in rating this symptom is that it is based exclusively on observations of expressivity within the clinical interview. A concern with prior instruments is that they rarely provide an opportunity to formally elicit "emotional" expression to ensure that observations accurately reflect individual differences. Thus, the CAINS provides interview prompts that are designed to elicit emotion (tapping both positive and negative emotional experiences). Such probing is expected to yield more valid and reliable ratings of individual differences in blunted affect.

Alogia

Alogia ratings tap diminished speech based on quantity of speech and spontaneous elaboration. Quantity ratings are restricted to the amount of words produced in responding to the CAINS interview. Other speech abnormalities, such as disorganization, neologisms, or psychotic content are not rated here. For instance, a disorganized patient may produce a large quantity of speech and have a low (normal) score on this item. Spontaneous elaboration rates the amount of information given beyond what is strictly necessary in order to respond to the interviewer's questions. Whether or not the responses are appropriate is not considered, so elaboration in this sense can include appropriate background information given to clarify an answer, irrelevant or unnecessary material, delusional or thought-disordered responses.

We are in the midst of a 3-year study to empirically refine item and scale content and validate the CAINS across 4 sites. As part of our data-driven approach, we conducted a 2-day training workshop with investigators from all 4 sites to ensure that administration and scoring of the CAINS were consistent across the sites. The initial version of CAINS was administered to a pilot group of 37 patients, and analyses of this sample led to a further refinement and ordering of the items with respect to item content, anchors, and interview probes.[62] We have also developed an extensive training manual for the measure that guides the investigators at the 4 sites and is in turn revised as we devise clearer methods for describing the procedures for administration and scoring of the CAINS. To date, we have collected data on over 200 patients with schizophrenia and schizoaffective disorder, and the sample is richly diverse with respect to gender (over a third are women), ethnicity (a quarter are Hispanic), race (half are nonwhite), clinical status (early in the course of illness to more chronic), and age (ranging from 18 to 60).

Current Status and Future Directions

As noted above, a key feature of the CAINS is its development process that included a broad and integrative assessment of the literature with feedback for diverse scientific perspectives including clinical trial investigators. Critically, subsequent scale refinement will continue in an iterative data-driven process. Our initial test of the instrument's psychometric characteristics indicates good reliability and excellent convergent validity with other negative symptom measures as well as discriminant validity in that the CAINS ratings were unrelated to positive symptoms or depression.[62] Furthermore, data from this pilot project led to other important refinements of the measure. For example, due to difficulty in obtaining representative ratings across a 7-point scale, we altered the scale to be a 5-point scale. Additionally, because raters had difficulty assigning values for patients' reported pleasure, an inherently subjective experience, we altered the measure so that patients could report this more clearly. These and other changes were implemented to further improve the reliability and validity of the CAINS.

Refinements made from this preliminary examination of the CAINS set the stage for our current ongoing work. In Study 1 of the NIMH-funded CANSAS (currently nearing completion, with over two-thirds of the data collected), the CAINS is administered to 300 outpatients with diagnoses of schizophrenia and schizoaffective disorder. Participants are assessed for general symptoms as well as for depression to allow for an assessment of the discriminant validity of the scale, specifically its hypothesized independence from positive symptoms and depression. Scale psychometrics will be assessed with Item Response Theory analyses to fully examine item and scale performance. Interrater agreement will be evaluated both within- and across sites. Results of Study 1 will again be utilized to revise and improve the CAINS. Study 2 will then deploy the revised CAINS in 160 outpatients to examine convergent validity as well as discriminant validity. Relations with social functioning will also be assessed and short-term temporal stability will also be evaluated. Final revisions will be made to the CAINS following Study 2, and this completed instrument will be made available for dissemination with a users manual and interview guide.

Negative symptoms remain an unmet therapeutic need in schizophrenia that contribute to profound impairment within this disorder. Importantly, existing negative symptom measures have remained largely unaltered over the last 2 decades and retain a number of limitations. We have reviewed the development of a next generation negative symptom scale that is currently undergoing empirical assessment and revision. By employing a data-driven iterative process to scale development, the CAINS is expected to provide an enhanced assessment approach to negative symptoms that will be appropriate for use in future treatment studies, both pharmacological and psychosocial as well as in clinical treatment trials. Moreover, the CAINS will be useful in devising the next generation of treatments. For example, psychosocial treatments aimed at particular emotion deficits, such as anhedonia will be informed by the careful assessment approach provided by the CAINS.

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