Comparison of CAINS and PANSS as Assessments of Negative Symptoms in Outpatients with Schizophrenia in a Clinical Trial Setting

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What is the Methodological Issue Being Addressed? The Positive and Negative Syndrome Scale (PANSS) - the established outcome for clinical trials of schizophrenia - emphasizes observable behaviors, has incomplete coverage of negative symptoms, and may be less sensitive as compared to more contemporary measures, particularly in populations with stable positive symptoms.

Introduction Negative symptoms represent a profound unmet need as the primary source of functional impairment in schizophrenia; therefore, detecting meaningful therapeutic signal is exceptionally important. The PANSS has long served as the gold standard instrument in clinical trials on the basis of decades of historical validation data. The PANSS Marder Negative Factor Score (NSFS) provides a more refined measurement of core negative symptoms, but it heavily emphasizes observable behavioral deficits (e.g., motor retardation, blunted affect) and the expressive domain. The Clinical Assessment Interview for Negative Symptoms (CAINS) was developed to better capture the full range of contemporary models of negative symptoms with greater sensitivity, while minimizing confounding variance from depression, medication side effects, and cognitive impairment. CAINS operationalizes the NIMH consensus two-factor model, differentiating the experiential and expressive domains via the Motivation and Pleasure (MAP) from Expression (EXP) scores, respectively. This study provides a descriptive comparison of the convergent validity and longitudinal sensitivity of both scales.

Methods We conducted an exploratory, post hoc analysis of PANSS and CAINS assessments using data from the CONVOKE randomized controlled trial evaluating CT-155, a 16-week novel digital therapeutic intended to treat negative symptoms, compared to a digital control in individuals with schizophrenia (n=457). For PANSS, we calculated the 7-item NSFS, a 2-item proxy MAP, and a 2-item proxy EXP (Wolpe et al., 2025) at Baseline, Week 16 and change from Baseline. For CAINS, we calculated MAP, EXP and Total scores at Baseline, Week 16 and change from Baseline. CAINS and PANSS negative symptom scores were compared using Spearman correlations; forthcoming results will include 95% confidence intervals. Additionally, we propose to explore longitudinal performance of CAINS MAP and PANSS NSFS with Mixed Models for Repeated Measures on a subset of participants (n=73) who completed two courses of CT-155.

Results Cross-sectional correlations with PANSS NSFS were stronger for CAINS-EXP (ρBL=0.19; ρw16=0.29) than CAINS-MAP (ρBL=0.01; ρw16=0.12) or Total (ρBL=0.1; ρw16=0.2) scores at Baseline and Week 16 , consistent with the known overemphasis of expressive negative symptoms

in PANSS. However, NSFS and CAINS-EXP change scores showed lower convergence (ρ=0.04) than cross-sectional correlations at each time point. Within the subset of participants who completed two cycles of treatment, we expect that CAINS-MAP will show earlier and sustained negative symptom reduction as compared to NSFS.

Conclusion Newer endpoints like the CAINS may offer distinct advantages in accurately detecting therapeutic effects of interventions targeting negative symptoms. These findings provide further evidence of the partial coverage of PANSS, as well as differences in cross-sectional and longitudinal convergence between CAINS and PANSS. These analyses offer methodological considerations for future psychosis trials, suggesting that leveraging contemporary instruments may optimize signal detection.

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Guidelines I have read and understand the Poster Guidelines

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