Development of the Assessment of Rapid Affect Change (ARAC): A Novel Measure for Psychoplastogen Response

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Methodological Issue Being Addressed Rapid-acting psychoplastogens present unique psychometric challenges. Traditional psychiatric scales lack validation for capturing simultaneous improvement in depression and anxiety symptoms alongside temporary increases in arousal within hours of administration. This measurement gap limits clinicians' ability to optimize treatment timing and dosing, particularly when tracking concurrent positive and negative affect changes characteristic of these compounds.

Introduction We aimed to develop the Assessment of Rapid Affect Change (ARAC) through a randomized, double-blind, placebo-controlled trial of ketamine across multiple VA and military sites. The scale development prioritized measurement at 120 minutes post-infusion - selected a priori based on pharmacokinetic/dynamic modeling to follow resolution of acute psychoactive effects while capturing therapeutic affect changes. This timing enables repeated measurement data collection necessary for comprehensive psychometric evaluation. Participants received high-dose ketamine, low-dose ketamine, or placebo.

Methods Initial exploratory factor analysis employed principal axis factoring with promax rotation using Session 1 data (N=161) from U.S. Veterans and active-duty personnel. The ARAC uses a 5-point Likert scale (0="Not at all" to 4="Extremely") to rate current affect states. After filtering for 2% missingness threshold and applying iterative imputation, analyses revealed severe violations of normality across items (skewness 0.17-3.83, kurtosis 1.88-24.54), necessitating use of polychoric correlations for the ordinal data. Factor analysis appropriateness was confirmed by KMO=0.923 and Bartlett's test ($p<0.001$). High factor loadings and strong communalities (>0.70 for 48/49 items) necessitated moving beyond elastic net regularization to hierarchical clustering (threshold=0.6). Cluster pairs were evaluated using factor loadings, distance metrics, and theoretical distinctiveness to identify redundant items while maintaining construct coverage. Confirmatory factor analyses (CFA) using WLSMV estimation (selected for robust handling of ordinal, non-normal data) were performed using data from two subsequent treatment sessions (N=130 each) in the same participants.

Results EFA identified four distinct factors that align with both the circumplex model of affect (valence × arousal) and clinical phenomenology: Valence Drop (negative affect), Valence Surge (positive affect), Arousal Surge (activation/alertness), and Arousal Drop (fatigue/sedation). These factors span multiple clinically relevant domains including mood, anxiety, and arousal. Factor correlations demonstrated good discriminant validity between positive and negative dimensions

(r=-0.27 to -0.35), with expected associations between Valence Drop and Arousal Surge (r=0.60). The initial 49-item pool was refined to 26 items maintaining excellent communalities and strong factor loadings (0.51-0.98). CFAs demonstrated excellent fit (robust RMSEA=0.037-0.038, robust CFI=0.98, robust TLI=0.98) and factor stability. The final scale comprises 12 Valence Drop, 6 Valence Surge, 4 Arousal Surge, and 4 Arousal Drop items.

Conclusion The ARAC represents one of the first measures developed specifically for measuring rapid affect changes following psychoplastogen administration. Its robust factor structure, demonstrated across multiple sessions, careful timing selection, and strong psychometric properties provide initial evidence supporting its potential utility. The theoretically-grounded four-factor structure enables simultaneous tracking of positive and negative affect shifts. Future studies will examine convergent and predictive validity, investigate response profiles across different populations and compounds, and evaluate potential utility for treatment optimization.

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Keywords

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Guidelines I have read and understand the Poster Guidelines

Disclosures Dr. Abdallah has served as a consultant, speaker and/or on advisory boards for Genentech, Janssen, Lundbeck, FSV7 and Aptinyx, and editor of Chronic Stress for Sage Publications, Inc.; Filed a patent for using mTORC1 inhibitors to augment the effects of antidepressants (filed on Aug 20, 2018). Dr. L. Averill has served as a consultant, speaker and/or on advisory boards for Transcend Therapeutics, Beond, Reason for Hope, Source Research Foundation, Guidepoint, Techspert, and owns NPSYT, PLLC. All other co-authors declare no conflict of interest.

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