

Rapid and Longitudinally Sustained Antidepressant Effects of Ketamine-Assisted MBCT for Treatment-Resistant Depression

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Background

- Treatment-resistant depression affects about 44% of patients who have tried at least two consecutive antidepressant therapies.
- Ketamine is a NMDA receptor antagonist that offers rapid antidepressant effects; however, its benefits are often short-lived.
- Mindfulness-Based Cognitive Therapy (MBCT) prevents relapse in depression by redirecting focus from negative thoughts and reducing distress.

Methods

- Study Design:** an 8-week Mindfulness-Based Cognitive Therapy (MBCT) program, with participants attending weekly 2-hour virtual group sessions and completing daily home mindfulness practices.
- An IV ketamine infusion (0.5 mg/kg) was administered between weeks 2 and 3, and completed Mystical Experiences Questionnaire (MEQ), followed by three “booster” mindfulness sessions.
- Participants completed weekly self-report measures (PHQ-9), clinician-administered interviews (MADRS), EEG, Blood Draw, and Ecological Momentary Assessments (EMA).

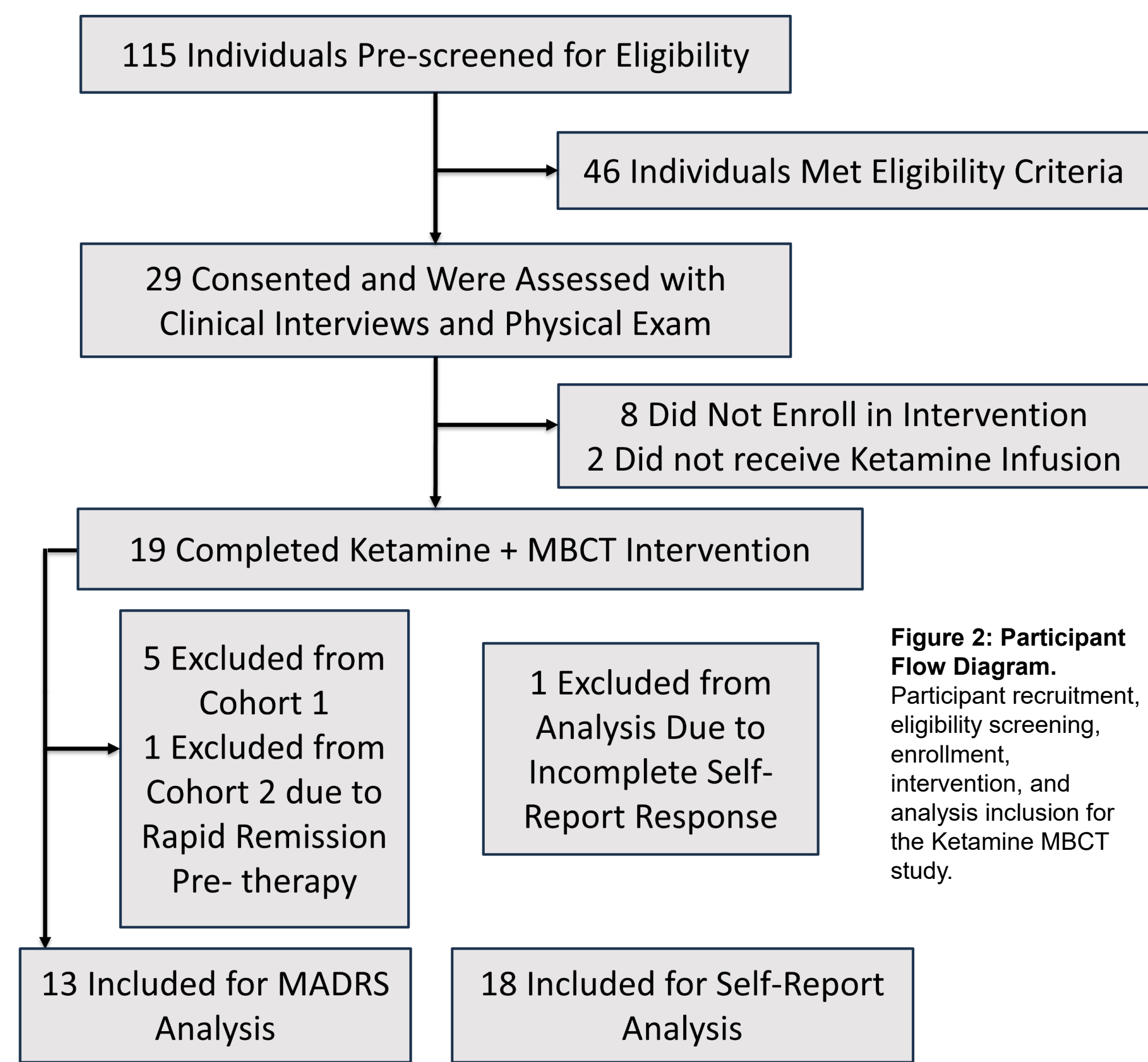


Figure 2: Participant Flow Diagram. Participant recruitment, eligibility screening, enrollment, and analysis inclusion for the Ketamine MBCT study.

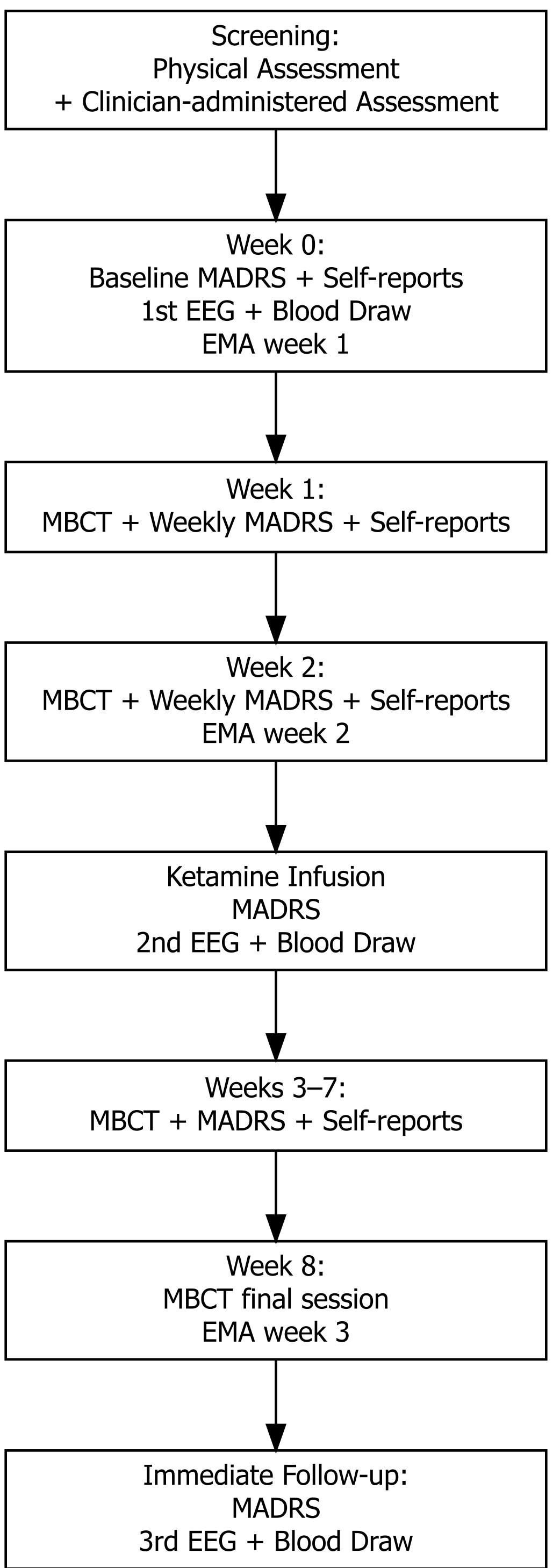


Figure 1: Study Procedure Timeline. Overview of Ketamine MBCT intervention schedule

Discussion

- MBCT extended antidepressant effect of a single ketamine infusion in most participants to 6 weeks or longer, rather than typical time course of depression relapse in 1-2 weeks
- Combining Ketamine and MBCT may produce a fast-acting and sustained antidepressant response for TRD.
- In future studies, we aim to replicate these findings across multiple groups and investigate enhanced metacognitive regulation in the PCC and dIPFC regions using fMRI.

Results

- 29 participants enrolled, 19 completed MBCT group therapy. Only 18 participants were included in analysis due to dropouts and incomplete assessment collection.
- MADRS scores reflect experiences in the past one week, PHQ-9 scores reflect experiences in the past two weeks, FFMQ-15 scores reflect mindfulness in daily life, these 3 scales are used as primary outcome measures.
- Cohort 2 & 3 participants are grouped based on change in MADRS score after ketamine infusion, cohort 1 participants are grouped based on change in PHQ-9 scores.
 - Sustained Responders / Remission (N=12)
 - Transient Responders (N=3)
 - Non-Responder (N=3)
- N=10 reached criteria of remission (MADRS ≤ 10, PHQ-9 < 5) at the end of therapy, N=8 remained in remission at follow-ups.
- MEQ scores predicted acute Ketamine effects post infusion and combined K+MBCT effects post therapy.

Baseline Characteristics	N	%
Gender		
Female	14	77.8
Male	4	22.2
Race		
White	15	88.3
Black / African American	2	11.1
Asian / Asian American	1	5.6
	Mean	SD
Age	38.9	10.1
MADRS	27.6	4.3
PHQ-9	14.8	3.9

Table 1: Participants Demographics
This table represents the participants demographics information, including Age, Gender, Race, and intake scores for MADRS and PHQ-9.

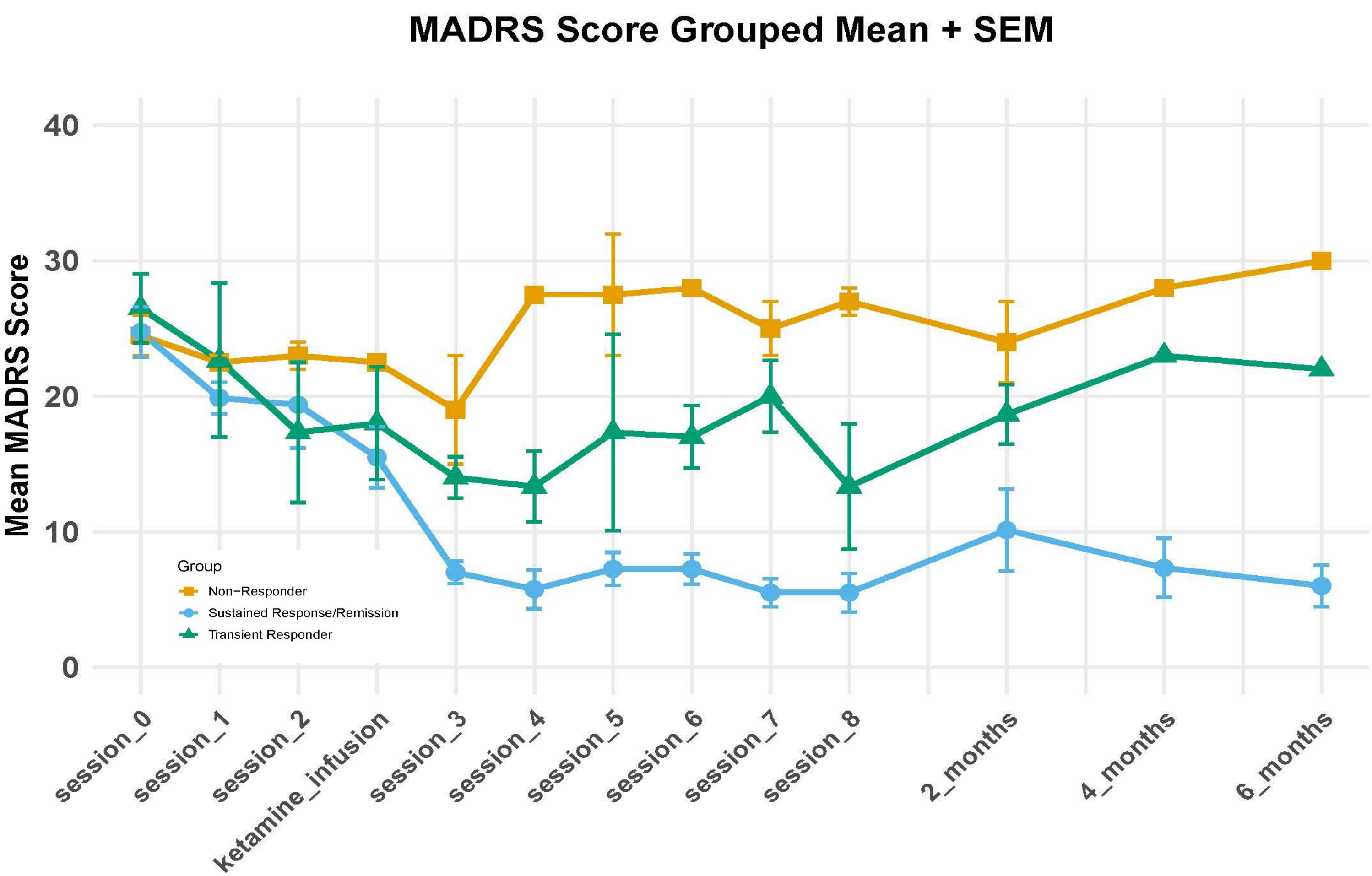


Figure 3: Trends in MADRS Scores by Response Type (Cohort 2 + 3)
This figure illustrates the mean ± standard deviation of MADRS scores over time for participants in Cohort 2 and Cohort 3, categorized by clinical response type: Sustained Responders/Remission, Transient Responders, and Non-Responders.

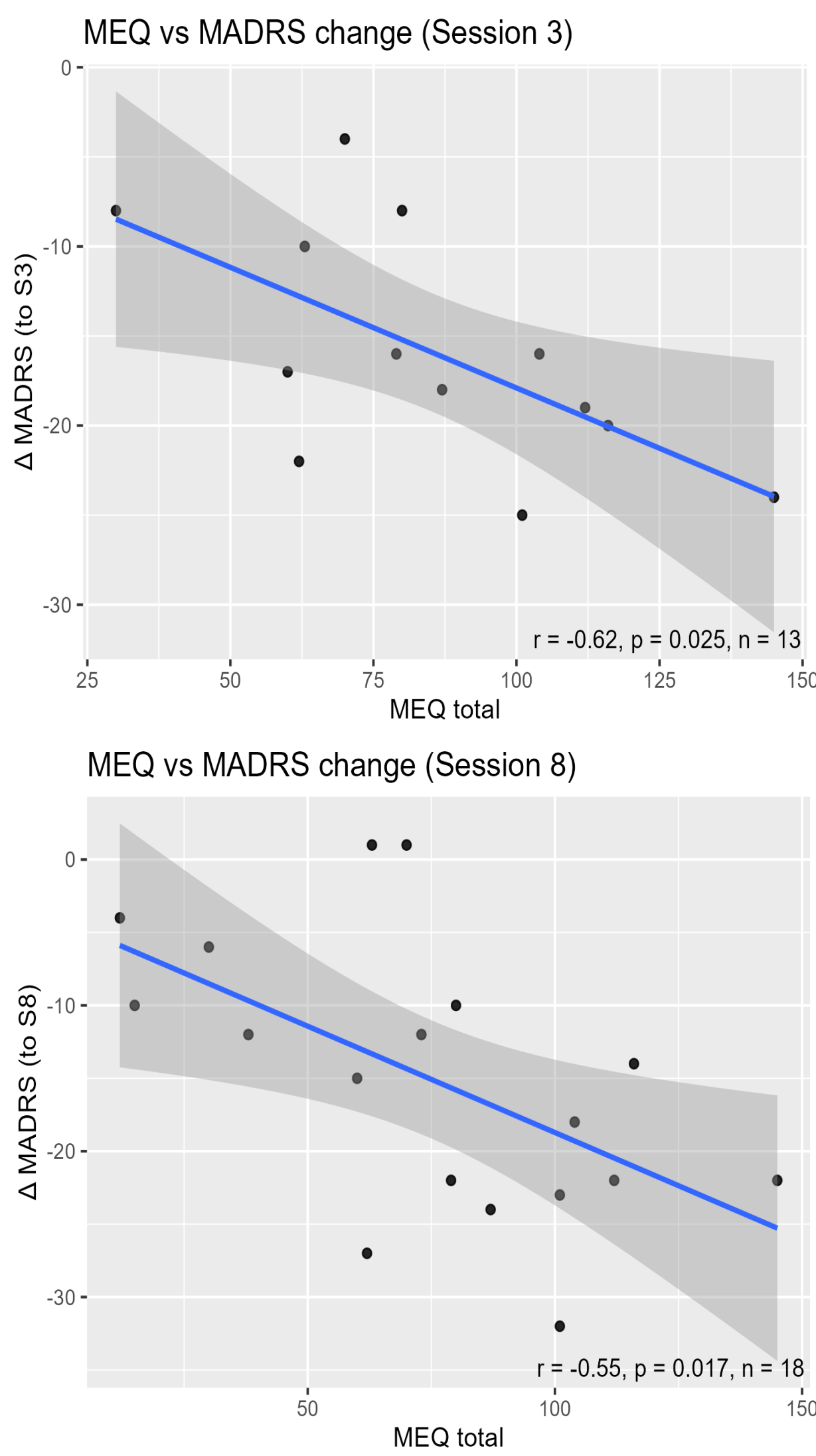


Figure 3: Correlations between MEQ scores and changes in MADRS scores
These figures presents and significant negative correlation between Mystical Experiences Questionnaire (MEQ) score measured during ketamine-infusion and change in MADRS scores post-infusion (session 3) and post-therapy (session 8).

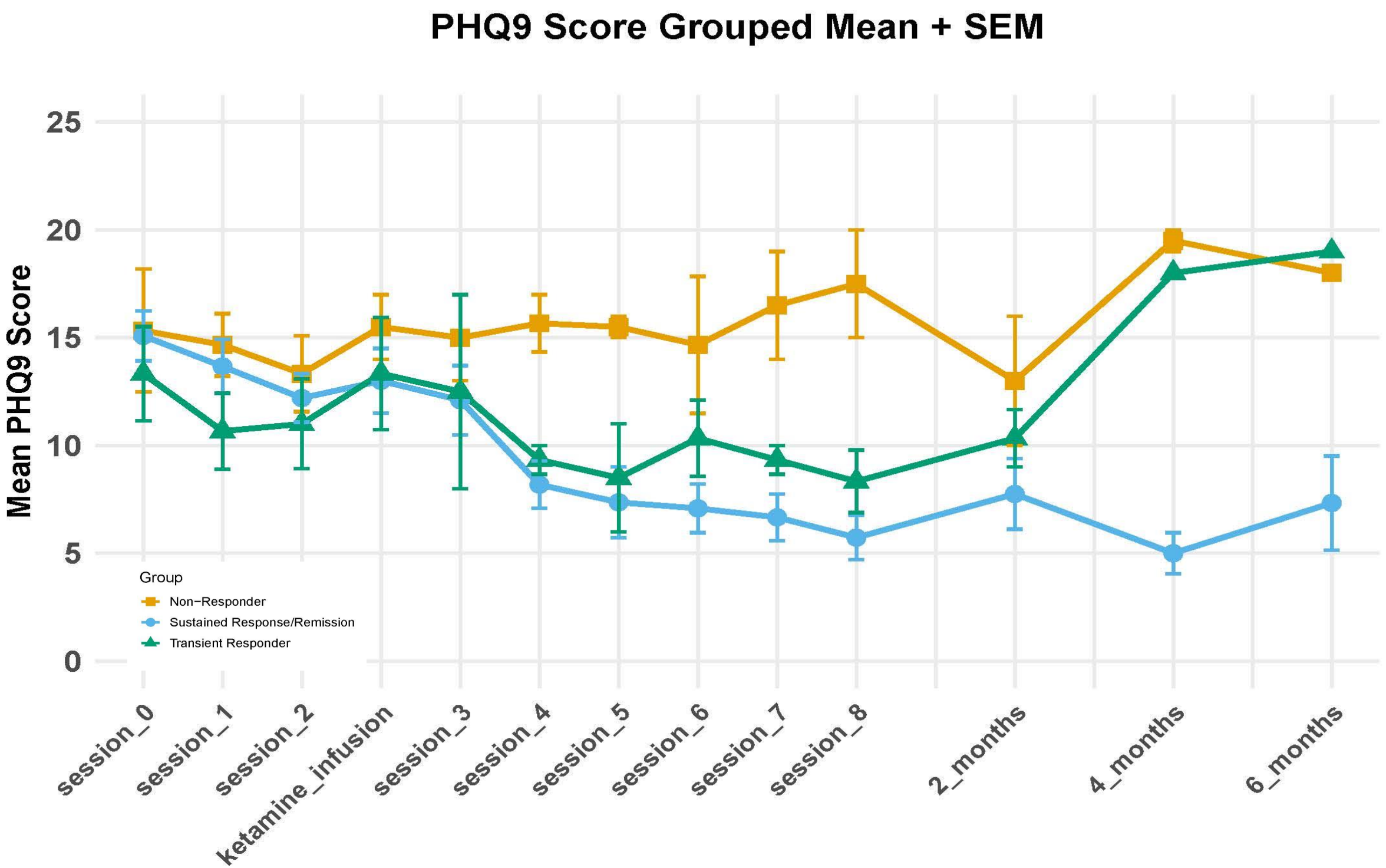


Figure 4: Trends in PHQ-9 Scores by Response Type (Cohort 1 + 2 + 3)
This figure illustrates the mean ± standard deviation of PHQ-9 scores over time for participants in Cohort 1, 2, and 3, categorized by clinical response type: Sustained Responders/Remission, Transient Responders, and Non-Responders.

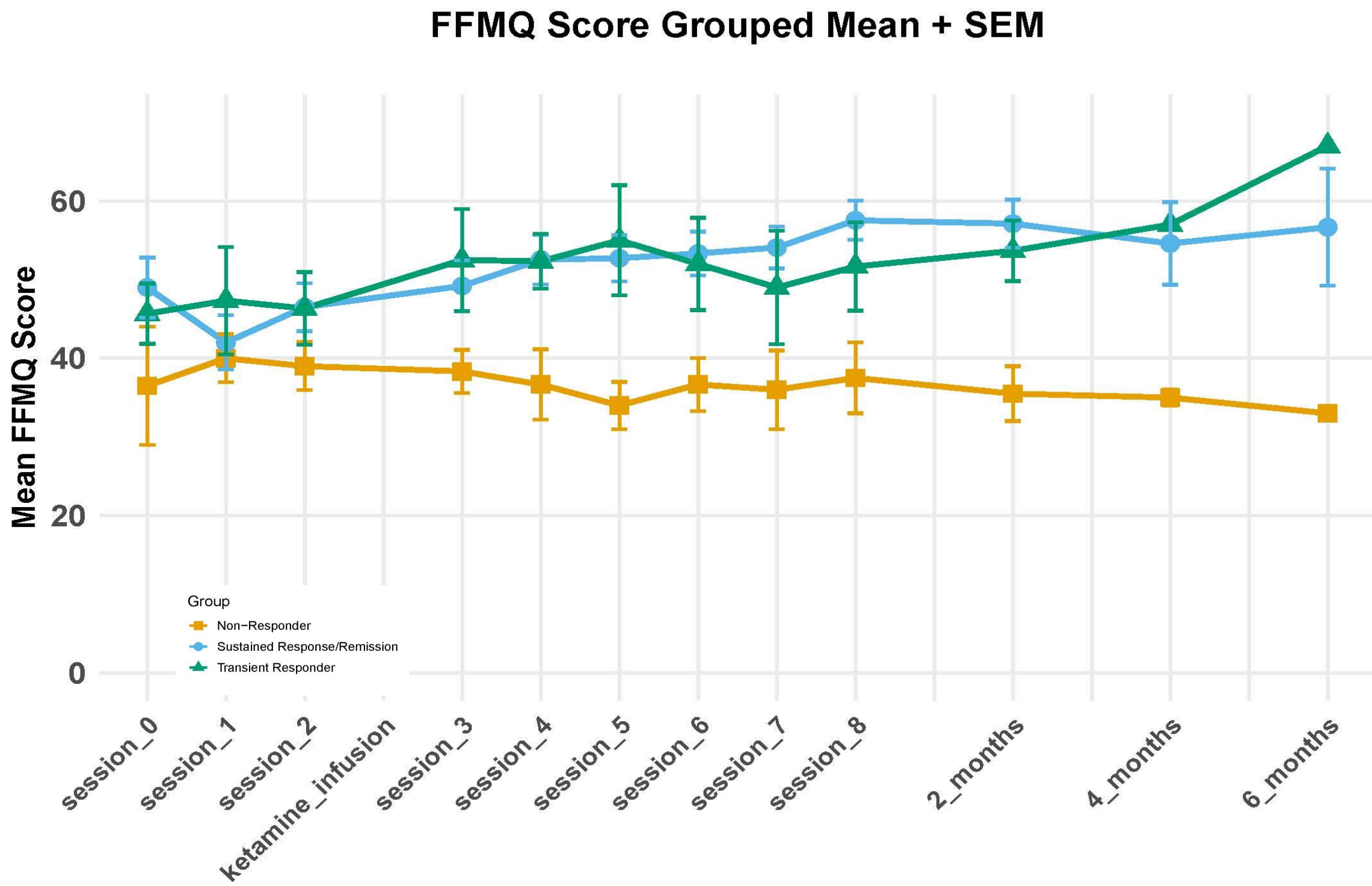


Figure 5: Trends in FFMQ Scores by Response Type (Cohort 1 + 2 + 3)
This figure illustrates the mean ± standard deviation of FFMQ scores over time for participants in Cohort 1, 2, and 3, categorized by clinical response type: Sustained Responders/Remission, Transient Responders, and Non-Responders.

1. Bergfeld JO, Martione M, Figue M, Schuurman PR, Lok A, Denys D. Treatment-resistant depression and suicidality. J Affect Disord. 2018;235:362-367. doi:10.1016/j.jad.2018.04.016

2. Wan LB, Levitch CF, Perez AM, et al. Ketamine Safety and Tolerability in Clinical Trials for Treatment-Resistant Depression. J Clin Psychiatry. 2015;76(03):247-252. doi:10.4088/JCP.13m08852

3. Kuyken W, Warren FC, Taylor RS, et al. Efficacy of Mindfulness-Based Cognitive Therapy in Prevention of Depressive Relapse: An Individual Patient Data Meta-analysis From Randomized Trials. JAMA Psychiatry. 2016;73(6):565. doi:10.1001/jamapsychiatry.2016.0076

4. Kral TRA, Imhoff-Smith T, Dean DG, et al. Mindfulness-Based Stress Reduction-related changes in posterior cingulate resting brain connectivity. Soc Cogn Affect Neurosci. 2019;14(7):777-787. doi:10.1093/scan/nsz050

5. Kuyken W, Hayes R, Barrett B, et al. The effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse/recurrence: results of a randomised controlled trial (the PREVENT study). Health Technol Assess. 2015;19(73):1-124. doi:10.3310/hta19730