Gamma Oscillations as a Prognostic Marker for Ketamine Therapy in Treatment Resistant Depression

Julia Engelhardt[1], Haley Cox[1], Krisha Shah[1], Brittany O'Brien[1], Charles Green[2], Jesse Wells[3], Allison Wells[3], Alan Swann[1], Sanjay Mathew[1], Nicholas Murphy[1]

[1] Baylor College of Medicine; [2] UT Health; [3] Wells Medicine

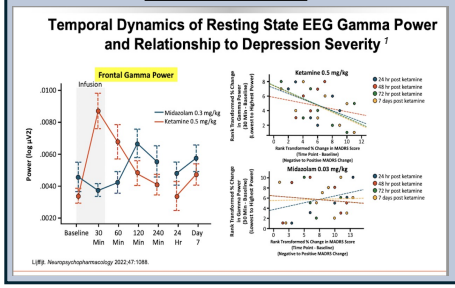
Baylor College of Medicine

Mood and Anxiety Disorders Program

wells medicine

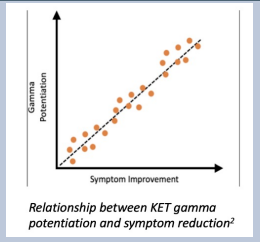
Background

Ketamine and TRD

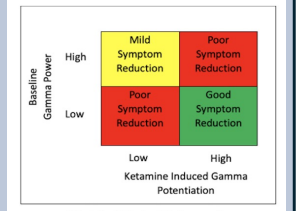


Gamma and TRD

- Predicting individual responses to ketamine remains challenging.
- KET modulates excitatory-inhibitory (E/I) balance in cortical circuits, increasing synaptic formation and strength.
- Gamma band power (GBP), a neurophysiological measure of cortical excitability, has shown potential as a biomarker for ketamine response.
- Potentiation of the amplitude of gamma band activity during a KET post-infusion time-window



Relationship between KET gamma potentiation and symptom reduction[2]



Model of Clinical Outcomes[3]

- KET treatment of TRD could be individualized by the degree of gamma dysregulation and reinforces the potential for gamma potentiation to be used as a biomarker of KET outcomes.

Study Aims

Primary Aim: Examine potentiation of gamma band power (GBP) by ketamine in TRD patients relative to MDD patients and healthy controls.

Hypothesis 1: Baseline GBP is reduced in TRD and MDD compared to healthy controls, serving as a disease-specific marker.

Hypothesis 2: TRD patients exhibit greater GBP in response to ketamine compared to other groups.

Secondary Aim: Investigate the relationship between GBP and the antidepressant effects of ketamine in TRD patients who are receiving ketamine in the real world.

Hypothesis: Greater reductions in depressive symptoms correlate with higher GBP during initial ketamine infusions.

Exploratory Aim: Assess the stability of GBP at the midpoint of the ketamine induction course and its relationship to treatment outcomes.

Methods

Participants

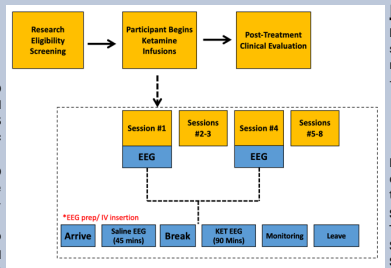
Age: 18-55

All subject will receive 0.5mg/kg KET

-TRD Group (n=60): MDD diagnosis, ≥2 failed antidepressant trials, MADRS ≥27, stable psychotropic regimen for 4+ weeks.

-MDD Controls (n=20): MDD diagnosis, MADRS ≤12, stable psychotropic regimen for 4+ weeks.

-Healthy Controls (n=20): No psychiatric diagnoses, matched by age and sex to TRD and MDD groups.



Study Schematic

Measures

Primary Biological Measure: Resting state and auditory steady-state response (ASSR) gamma activity.

- EEG: 20-channel recordings performed at 30 minutes pre-infusion, post-saline, and post-ketamine to isolate GBP changes 512 hz.

Primary Clinical Measure: Percent change in MADRS scores from baseline to post-treatment (infusion #8).

Secondary Measures: QIDS-SR, Thematic Apperception Test, Emotional Stroop Test

Safety and tolerability

CSSRS, Adverse Events, Clinical Evaluation

Analysis

- Bayesian multi-level modeling to evaluate GBP as a predictor of clinical response.
- Correlation analyses to explore relationships between baseline gamma, GBP changes, and antidepressant outcomes.
- Covariate adjustments for age, sex, and menstrual cycle effects in female participants.

Future Direction

- Investigate how GBP can be integrated into routine clinical practice to guide treatment decisions.
- By establishing GBP as a reliable biomarker, this research paves the way for more effective, personalized treatments for depression and related disorders.

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References

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