Assessing Neuroplasticity and Cognition with a Portable Platform Throughout Esketamine Treatment for Therapy-Resistant Depression

S. Vestring[1,$], B. Murphy[2,$], V. Galuba[1], H. Kiiski[3], R. Rea[3], M. N. Islam, E. McWilliams[3], A. Watrous[4], E. Tunbridge[4,$] & C. Normann[1,$]

[1] Department of Psychiatry and Psychotherapy, University Medical Center Freiburg, Germany; [2] Cumulus Neuroscience, Dublin, Ireland; [3] Cumulus Neuroscience, Belfast, United Kingdom; [4] Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riß, Germany;
[$] these authors contributed equally to the work

Introduction & Aims

The ongoing PlastiCogMDD study aims to evaluate the feasibility, adherence, and data quality of a multimodal platform (NeuLogiq® [1]) for repeated cognitive and neurophysiological assessment in patients with therapy-resistant MDD. The study aims to capture the effects of esketamine on neuroplasticity and cognitive performance across both home-based and in-clinic settings. As esketamine is known to enhance synaptic plasticity, an effect robustly demonstrated in preclinical models, this study additionally provides an opportunity to investigate whether neurophysiological plasticity markers relate to functional cognitive improvement in this patient cohort. The change in visually evoked potential (VEP)-measured plasticity (see [2,3,4] for details of methodological validation and grounding in preclinical studies) before and after esketamine treatment compared to a treatment-as-usual (TAU) control group serves as the primary clinical outcome, measured using portable dry electroencephalography (EEG).

Methods

PlastiCogMDD is a single-centre, unblinded, parallel-group study conducted at the University Medical Center Freiburg (N=54). Patients with therapy-resistant MDD are randomised with respect to the observation timeframe, not to treatment itself. Group 1 (MDD TAU + esketamine, n=27) is observed during esketamine initiation; Group 2 (MDD TAU, n=27) is assessed during the clinically indicated waiting period prior to esketamine. All patients continue standard antidepressant treatment throughout. The 22-day observation window combines four structured in-clinic visits, including EEG-based assessments (VEP modulation, auditory steady-state response (ASSR), resting-state EEG), a visual associative memory task and clinical ratings (Montgomery-Åsberg Depression Rating Scale, Beck Depression Inventory) with continuous at-home assessments via a dedicated tablet twice daily. At-home tasks include cognitive tests (Digit Symbol Substitution Test, N-Back Task) and mood ratings (Visual Analogue Scale). Patient-reported platform usability is assessed at end-of-study via System Usability Scale (SUS). This design allows longitudinal tracking of cognitive and neurophysiological parameters across both settings simultaneously. As the study is ongoing, interim blinded analyses are presented from 17 study completers (4F 13M, mean age 48.9 years, mean MADRS score at baseline 31.3). A further participant withdrew following baseline session completion.

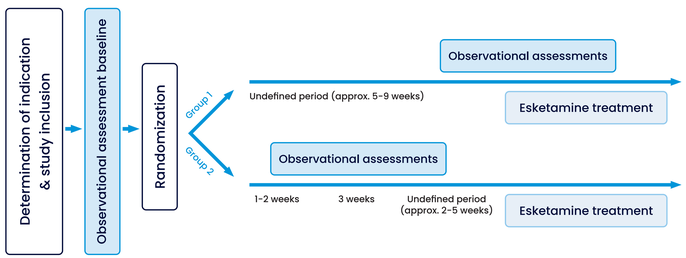


Figure 1: Study scheme

Results

Data Quality (in clinic)

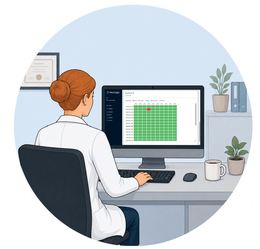
Over 90% of all EEG recordings collected using the NeuLogiq dry 16 sensor EEG headset fulfilled the a priori defined signal quality criteria.

Task Performance (at-home)

Frequent sampling to capture learning effects and daily fluctuations in performance.

Feasibility & Adherence

Adherence and session quality remotely monitored during data collection. Participants gave a mean SUS rating of 87.5 following at-home use, indicating very good usability.



Single session example of VEP-LTP recording

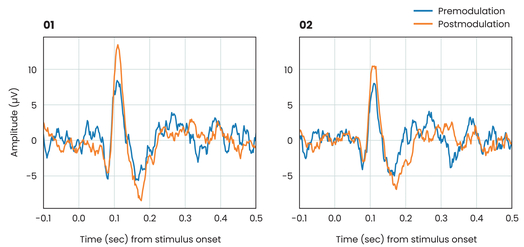


Figure 2: Example VEP-LTP recording (median ERP).

Tablet-based app

Figure 3: Example of app touch screen showing presentation of Symbol Swap digit symbol substitution task.

At home session adherence

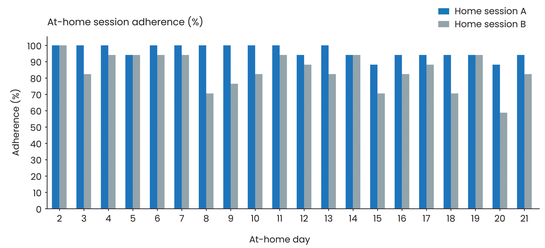


Figure 4: Adherence of two at home sessions per day, indicating high adherence.

Baseline measures

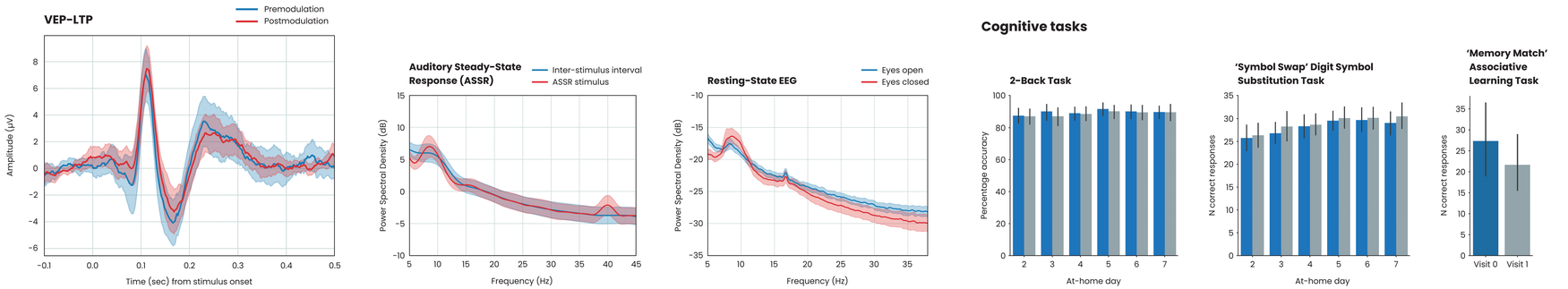


Figure 5: Mean EEG and cognitive task outcomes. Includes sessions collected prior to beginning of treatment only. Interim sample (n = 17). Shading shows 95% confidence intervals.

Conclusions

These interim results demonstrate that repeated clinic and home cognitive and neurophysiological assessment using a multimodal platform is highly feasible and well tolerated in patients with treatment-resistant MDD. The randomisation approach, assigning patients to different observation timeframes rather than to treatment, enables the effects of esketamine on neuroplasticity and cognitive markers to be captured within a naturalistic clinical context. These findings support the broader utility of wearable EEG technology for longitudinal monitoring in depression research and clinical practice.

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