

Effects of Esketamine on EEG temporal dynamics in individuals with major depressive disorder

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Introduction. Esketamine is an effective rapid-acting pharmacological intervention for treatment-resistant depression. However, the temporal dynamics of underlying brain networks associated with the improvement of depressive symptoms remain elusive. This observational study seeks to delineate alteration in network activity within 90 minutes of nasal Esketamine administration, with a focus on exploring its associations with subjective drug effect and mood fluctuations.

Methods. At this point, we enrolled five participants diagnosed with MDD undergoing Esketamine treatment at the UNC Chapel Hill Interventional Neuropsychiatry Unit. High-density resting-state EEG was recorded before and subsequently repeated for seven times up to 90 min post Esketamine administration. Prior to each recording, participants completed Visual Analogue Scales (VAS) assessing mood changes. The primary outcomes are the change in oscillatory power in canonical frequency bands and their relationship with VAS measures.

Results. In line with expected plasma peak Esketamine concentration, we observed a peak of subjective "Highness" (+31.73%) and "Happiness" (+22.75%) 15 min post administration. Linear mixed models revealed elevated "Highness" up to 75 min (all $p < .035$), whereas "Happiness" exhibited significant improvement up to 35 min post administration ($p = .025$). This temporal pattern was paralleled by a reduction of alpha power (8-12 Hz), peaking 35 min post administration (-46.36%), which was maintained up to 50 min (all $p < .05$). Importantly, alpha power had a significant effect on "Highness" ($\beta = -2.760$, $SE = 1.20$, $p = .034$). This study offers preliminary findings regarding the acute, temporal patterns in oscillatory power and mood during Esketamine treatment, which may lend insight to clinically relevant, network-level effects of the drug.