New insights on how ketamine can lessen symptoms of depression but also cause dissociative side effects

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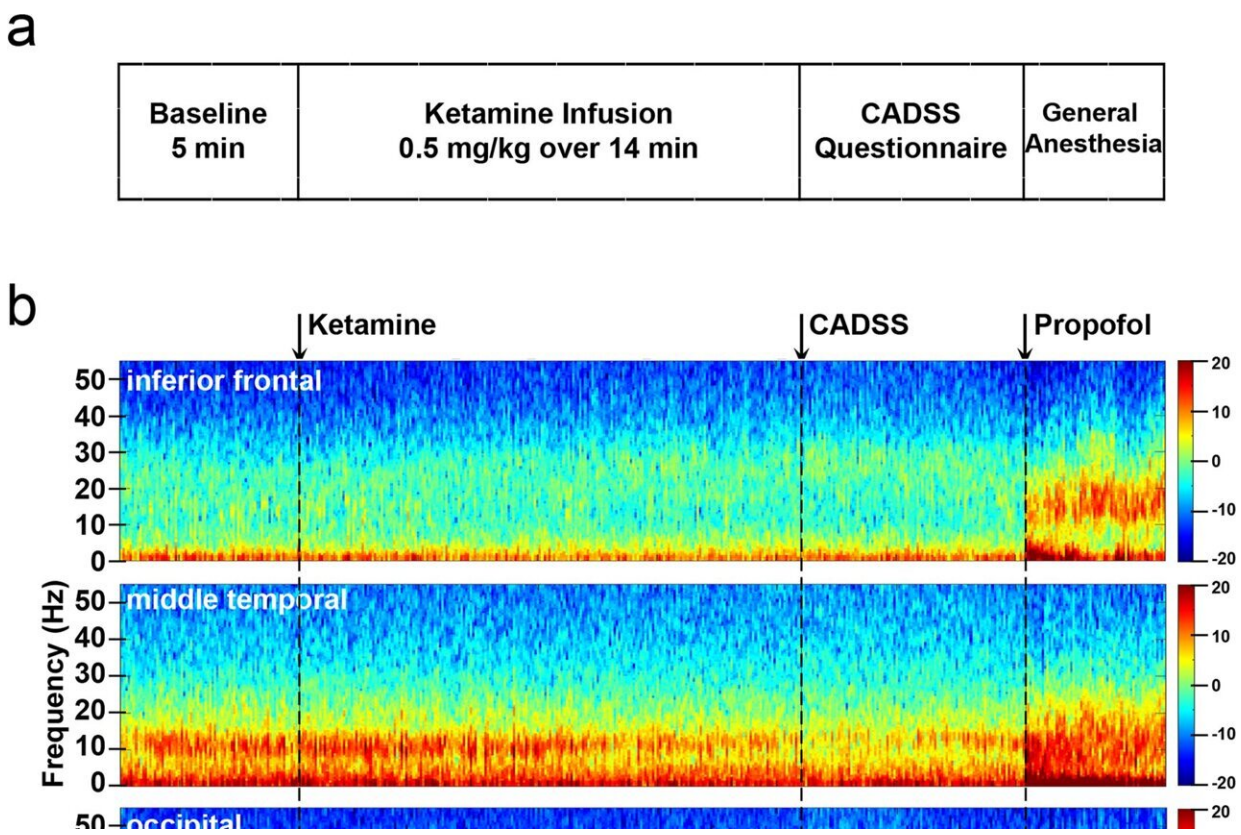

Study protocol and intracranial EEG power changes for example channels. a Study protocol. b Power spectrogram (dB) for three example channels: inferior frontal, middle temporal and occipital from Subject #9. c Power spectrum averaged across time during baseline, ketamine, and propofol conditions for the three example channels. CADSS: clinician-administered dissociative states scale. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-37463-3

Ketamine is useful for treating depression, but unfortunately, it can cause dissociative symptoms—such as having an out-of-body experience or feeling emotionally numb.

A team led by investigators at Massachusetts General Hospital (MGH) recently uncovered how ketamine influences different circuits in the brain to produce its antidepressant and dissociative effects.

The research, which is published in *Nature Communications*, could lead to novel treatments for depression with fewer side effects.

The study involved 10 patients with epilepsy who had received electrode implants in the brain to detect abnormal electrical activity that causes seizures. The patients were given ketamine before they underwent general anesthesia for electrode removal surgery.

Before the electrode implants were removed, they collected data on patients' brain activity before and after exposure to ketamine.

The electrode recordings revealed that ketamine engages different neural circuits in distinct frequency-dependent patterns of brain activity to produce its antidepressant and dissociative effects.

Ketamine produced "gamma oscillations" (25 to 55 Hz) in brain areas related to depression—specifically, the prefrontal cortex and hippocampus. It produced a 3 Hz oscillation in the posteromedial cortex, a region involved in dissociative symptoms.

"In this study, we show, for the first time to our knowledge in humans, a detailed description of the principal oscillatory changes in a variety of cortical and subcortical structures after administration of a subanesthetic

dose of ketamine," says lead author Fangyun Tian, Ph.D., an Instructor in the Department of Anesthesia, Critical Care and Pain Medicine at MGH and an Instructor in Anesthesia at Harvard Medical School.

More information: Fangyun Tian et al, Characterizing brain dynamics during ketamine-induced dissociation and subsequent interactions with propofol using human intracranial neurophysiology, *Nature Communications* (2023). DOI: 10.1038/s41467-023-37463-3

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