

Ketamine to Treat Disorders of Consciousness: a Feasibility Study

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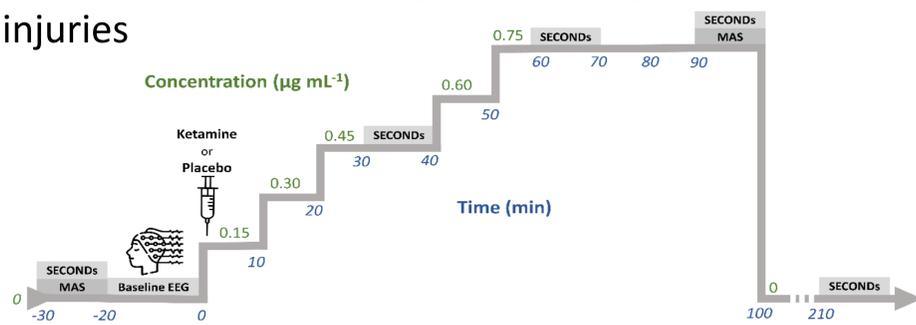
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Introduction

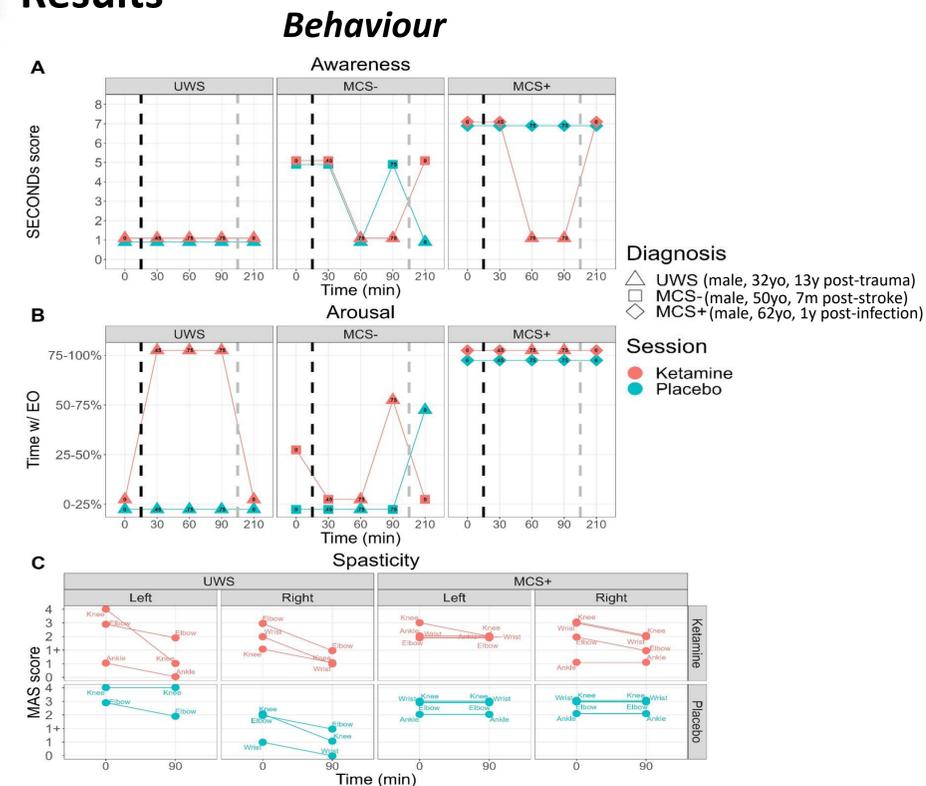
- **Brain complexity**, the degree of integration and differentiation of brain activity, covariates with state of consciousness¹⁻³
- Patients with post-comatose disorders of consciousness (**DoC**) have low complexity. Conscious level may be increased by increasing complexity⁴
- Sub-anesthetic doses of ketamine increase complexity in healthy participants⁴.
→ **Possible treatment** for DoC^{5,6}
- Here, first human trial on DoC

Methods

- Double-blind, randomized, placebo-controlled pilot study (N=3). Patients stratified per etiology and diagnosis. Incremental IV ketalar with TCI* (0.15 µg/ml steps every 10', max 0.75 µg/ml).
- Measures: behavior (SECONDS*)⁷, spasticity (MAS*)⁸, high-density EEG* (BrainVision 128Ch) complexity (LZC*), ECG* and blood pressure
- Excl. criteria: psychiatric disorders, cardiac insufficiency, active epilepsy, less than 18yo, drugs interacting with ketamine, previous brain injuries

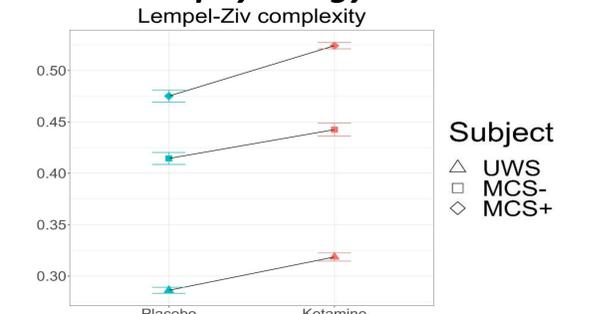


Results



Behavioral results. **A:** SECONDS scores following infusion of ketamine and placebo. The given concentration is displayed inside every point. **B:** Time spent with eyes open as considered in the SECONDS. **C:** MAS scores, divided by different joints, before and after infusion. For representational purposes a jitter was added to avoid overlaps. Legend: UWS: unresponsive wakefulness syndrome, MCS: minimally conscious state

Neurophysiology



Brain Complexity: Distribution of brain complexity measured via whole-brain LZC shown for placebo and ketamine for each patient.

- No adverse effects and no relevant changes in blood pressure or heart rate
- MCS patients were unresponsive after ketamine; UWS patient showed 1 response (/3) to command
- More time spent with eyes open during ketamine compared to placebo
- Serendipitous observation of decrease in spasticity
- Increased whole-brain complexity as indexed with LZC in ketamine session compared to placebo

Conclusions

1. Ketamine administration is feasible and safe in DoC patients
2. Ketamine might increase arousal and have effects on spasticity
3. No better diagnostic; unresponsiveness after ketamine → Disconnected consciousness?
4. Higher brain complexity after ketamine

EudraCT



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*Abbreviations

- TCI: target controlled infusion
EEG: electroencephalogram
ECG: electrocardiogram
SECONDS: Simplified Evaluation of Consciousness Disorders
MAS: modified Ashworth scale
LZC: Lempel-Ziv complexity

Cardone, Alnagger et al.,
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