Preliminary Results of the First Pilot of Ketamine to Treat Disorders of Consciousness

14th Biennial World Congress on Brain Injury

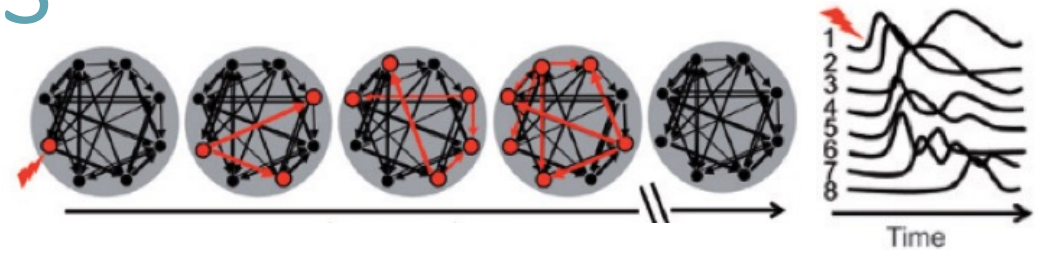
31st March 2023

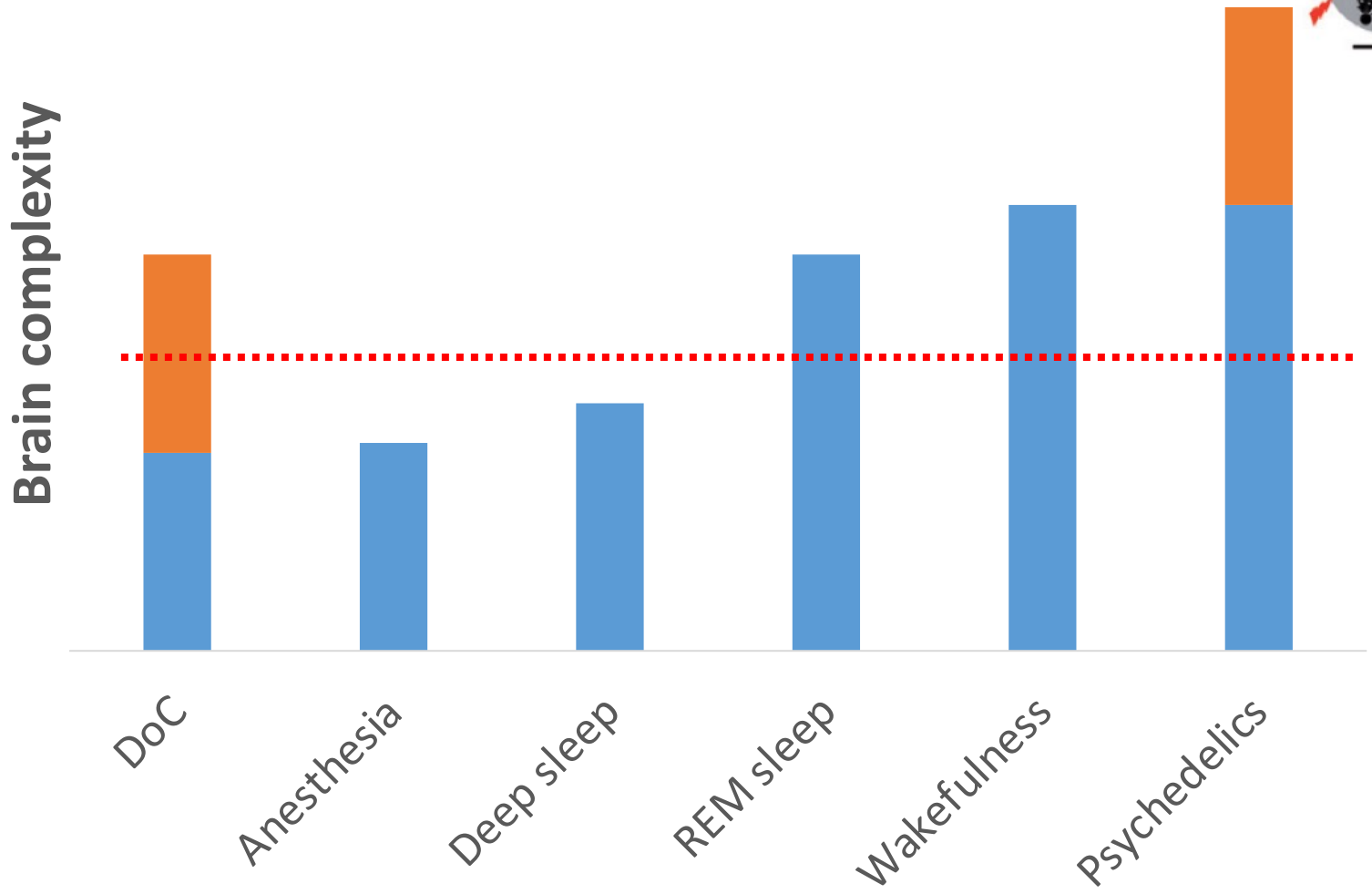
Presenter: Paolo Cardone

Authorlist:

Cardone P, Bonhomme A, Bonhomme V, Staquet C, Lejeune N, Van Goethem S, Ezan P, Alnagger N, Defresne A, Montupil J, Laureys S, Thibaut A, Martial C*, Gosseries O*

Consciousness, complexity, and psychedelics



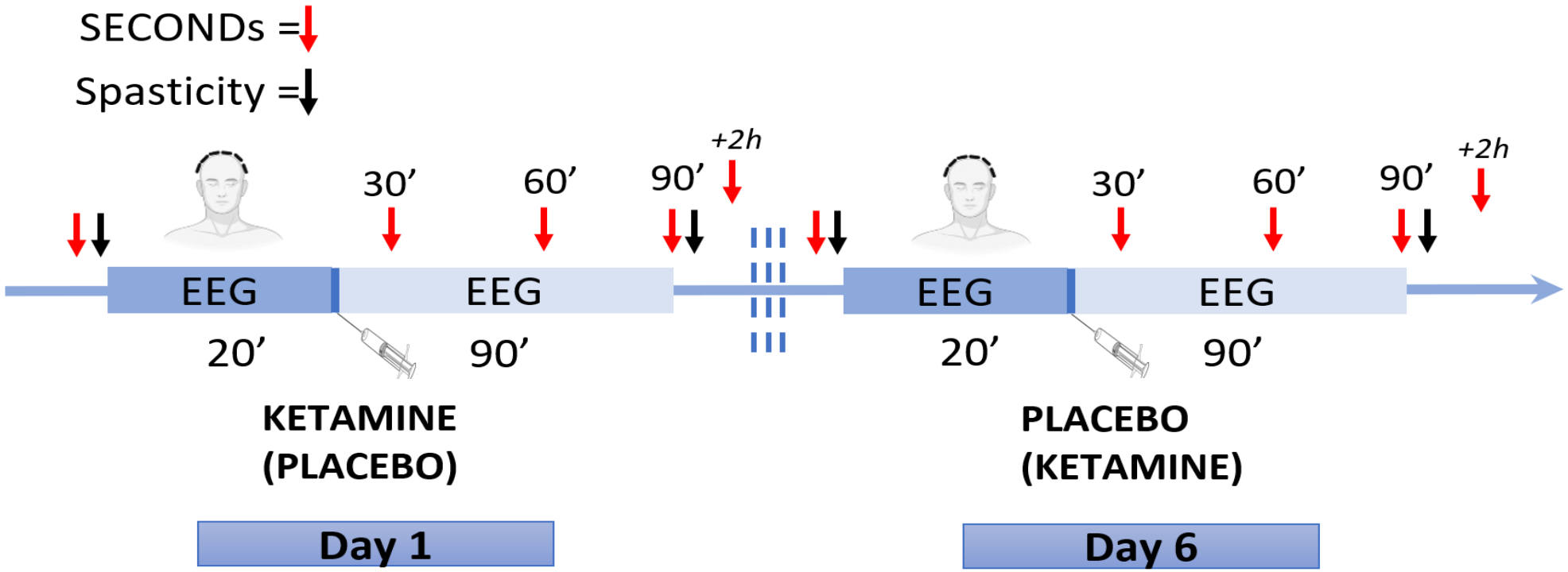


- High complexity in conscious states; low in unconscious ones
- Psychedelics increase brain complexity

  →Could psychedelics boost complexity in patients with DoC?

Sarasso et al., *Clin EEG Neurosci.* 2014
Scott & Carhart-Harris, *Neurosci Conscious.* 2019

Protocol



Additional information:

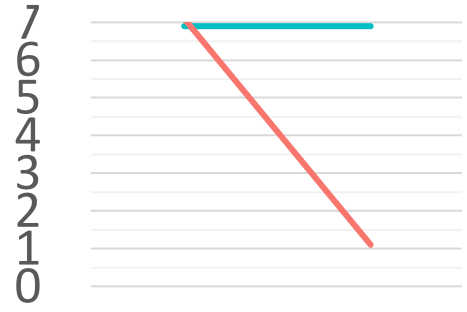
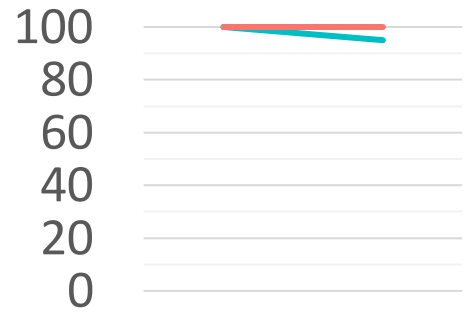
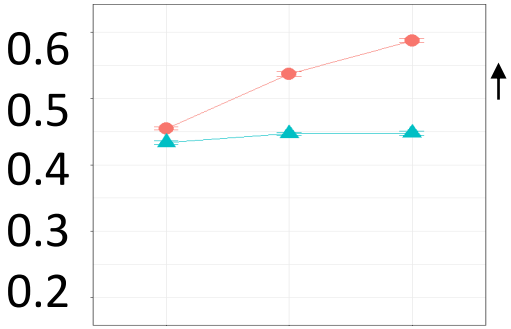
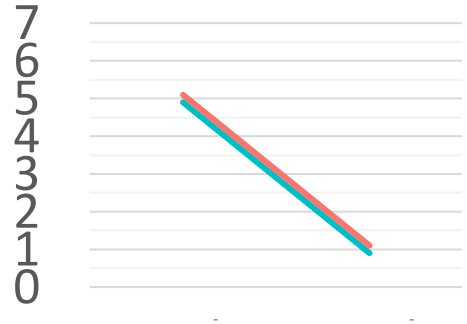
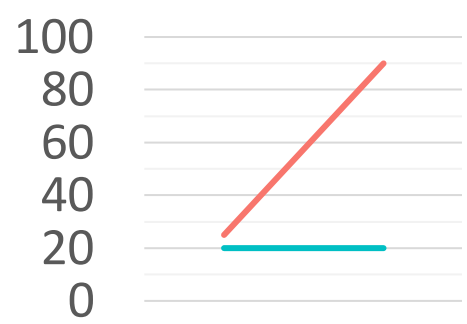
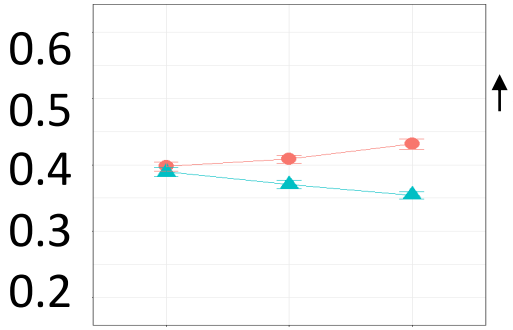
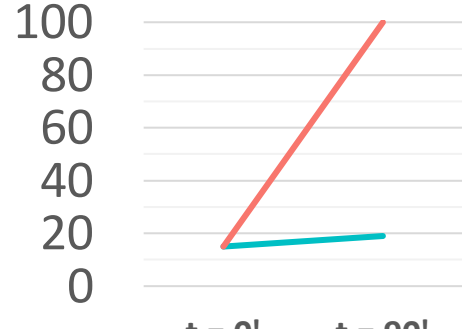
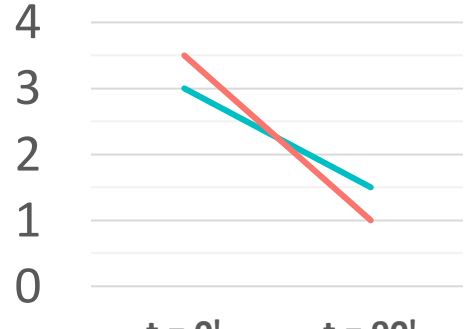
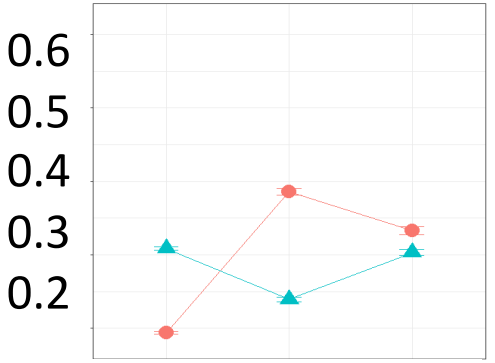
1. TCI: maximal concentration of 0.75 µg/ml, steps of 0.15 µg/ml
2. ECG and oxygenation monitored
3. Presence of an anesthesiologist and a psychedelic sitter
4. EEG: BrainVision, 128Ch
5. Assessments: SECONDs and MAS

Future RCT:

- N=30
- All aetiologies
- Time since injury >28days
- Medically stable
- No contraindication to ketamine infusion

Pilot results

Ketamine Placebo

	SECONDs	Arousal	MAS (median)	Lempel-Ziv Complexity	
EMCS 62yo, M, 1y post leukoencephalop					↑Arousal and LZC ↓Spasticity
MCS- 50yo, M, 7m, post-aneurysm rupture			Spontaneous decrease in spasticity		↑Arousal and LZC No positive change in diagnosis
UWS 32yo, M, 13y post-TBI					↑Arousal No positive change in diagnosis; one response to command

Dose (µg/ml): .15-.30 .45-.60 .75

Take-home messages

1. Ketamine safe to be administered in DoC patients
2. Ketamine increases arousal (eyes opening) in 2/3 patients; ceiling in the EMCS patient
3. Ketamine decreases spasticity in 2/3 patients
   - Systematically investigated in the RCT (MAS + EMG)
4. Ketamine increases brain complexity in conscious patients (MCS & EMCS); not clear in UWS
   - Disconnected consciousness? Need for outcomes and other complexity measures