

Psychedelics, brain complexity, and consciousness

Presenter:

***Paolo Cardone
PhD Student
FNRS Aspirant
GIGA-Doctoral School***

GIGA-Consciousness Day
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Promoters:

***Pr. Olivia Gosseries
Dr. Charlotte Martial***

Psychedelics: what are they?



Credits: Lunae Parracho, Reuters

- “Mind-manifesting” drugs
- Millennial use for religious and shamanic purposes
- Good safety profile
- Neuroplastic effects

Nutt et al., *Lancet* 2010

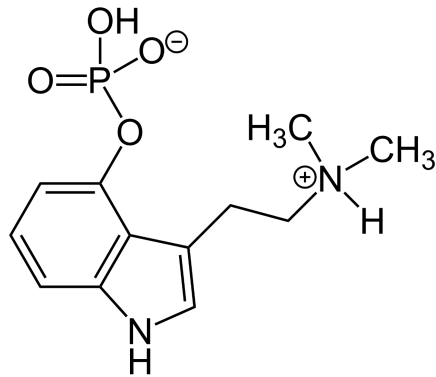
Ly et al., *Cell Rep.*, 2018



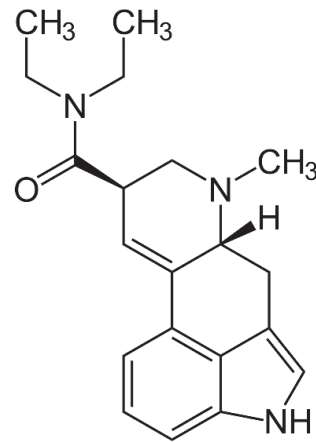
Two classes of psychedelics

Typical psychedelics → **5HT_{2A} agonists**

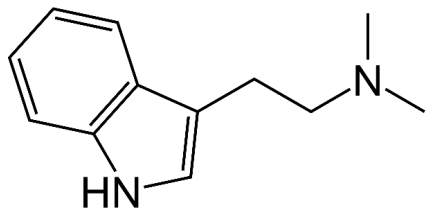
Atypical psychedelics



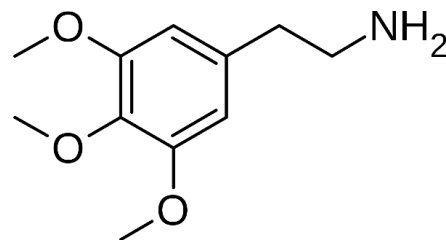
Psilocybin



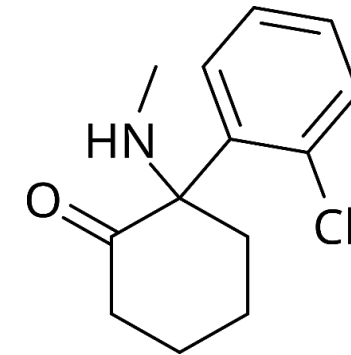
LSD



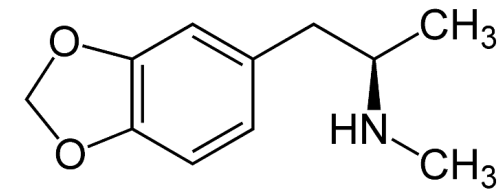
DMT



Mescaline

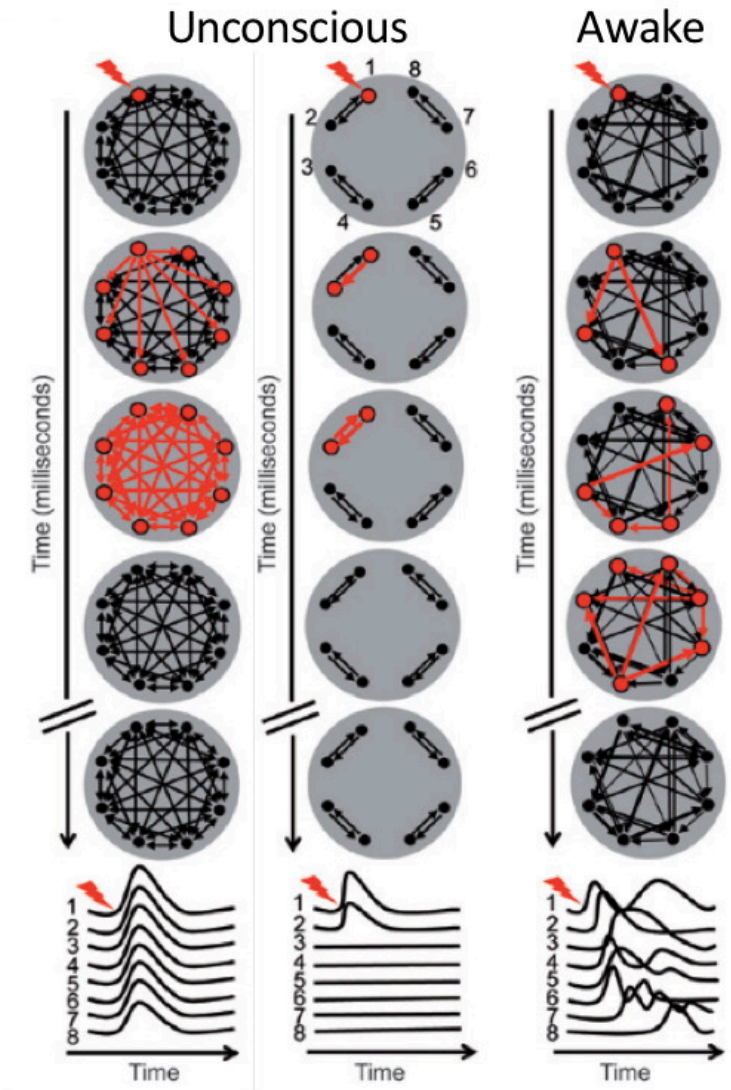


Ketamine



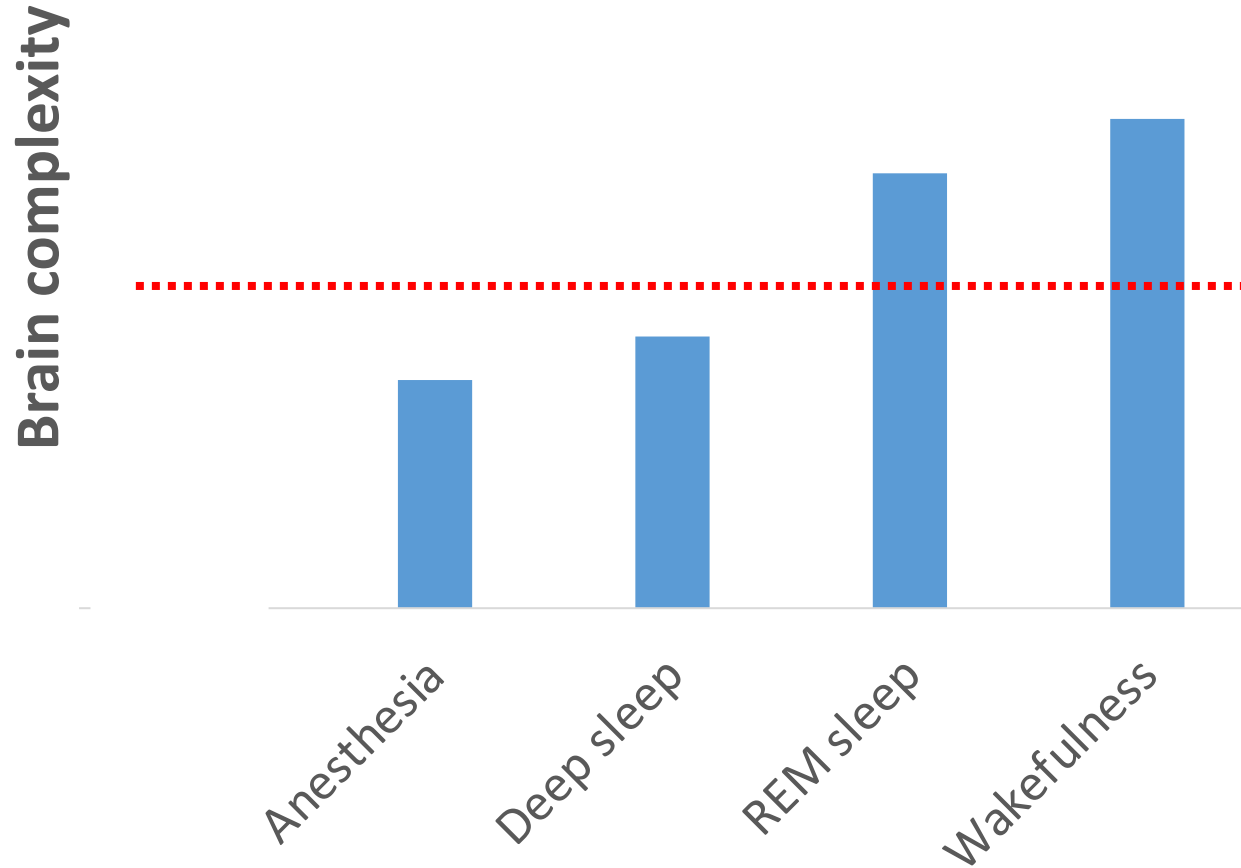
MDMA

The case of complexity



- Degree of integration and information
 - Graph theory representation
- Wakefulness is complex over **time and space**
- Various measures (e.g. LZC, PCI)

Complexity and global conscious states



- High complexity in conscious states; low in unconscious ones

Could we increase complexity?




KET

[nature](#) > [scientific reports](#) > [articles](#) > [article](#)

Article | [Open access](#) | [Published: 19 April 2017](#)

Increased spontaneous MEG signal diversity for psychoactive doses of ketamine, LSD and psilocybin

[Michael M. Schartner](#), [Robin L. Carhart-Harris](#), [Adam B. Barrett](#), [Anil K. Seth](#)  & [Suresh D. Muthukumaraswamy](#)

LL- LL- AC-

[nature](#) > [communications biology](#) > [articles](#) > [article](#)

Article | [Open access](#) | [Published: 28 January 2023](#)

Distributed harmonic patterns of structure-function dependence orchestrate human consciousness

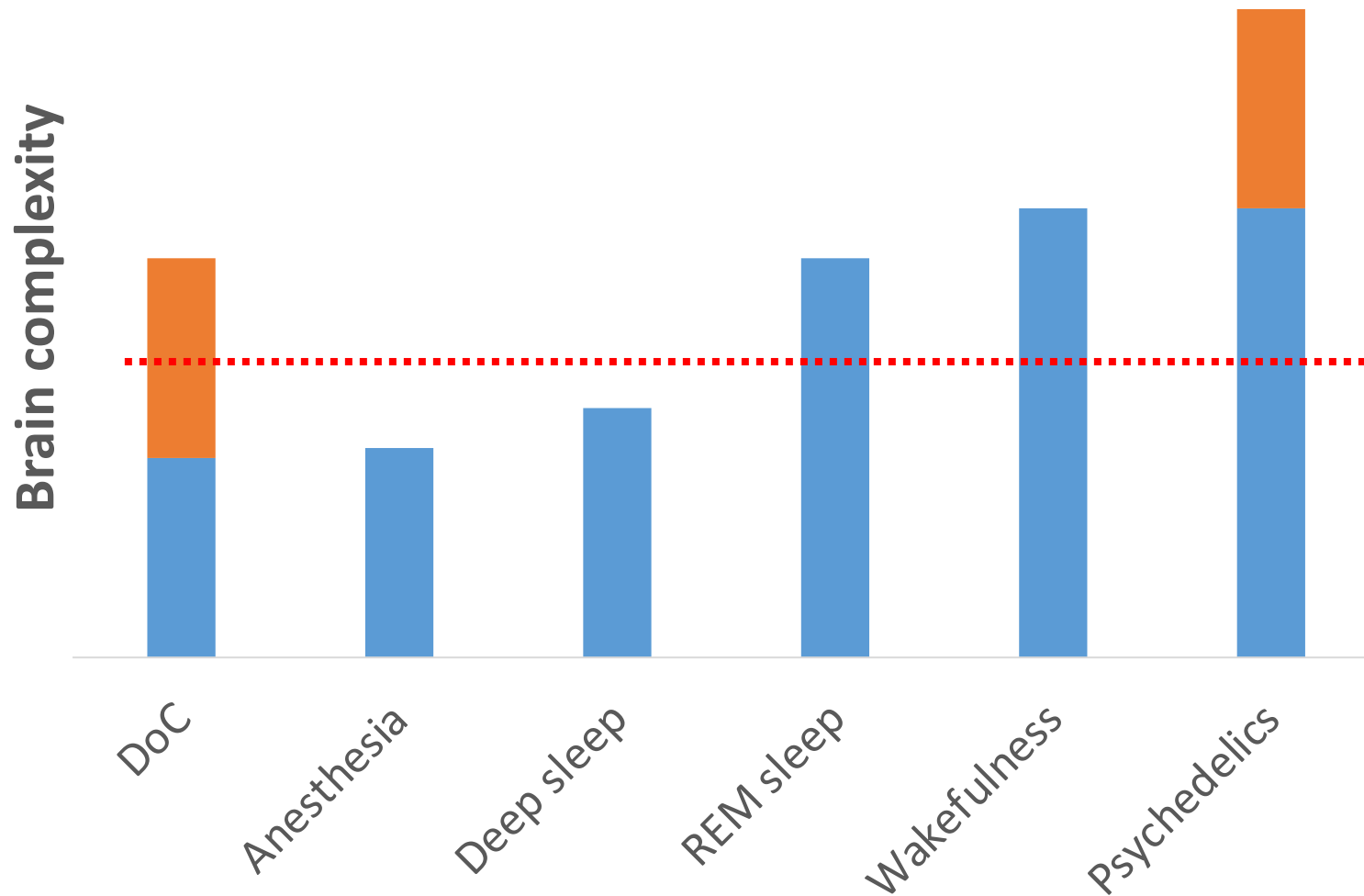
[Andrea I. Luppi](#) , [Jakub Vohryzek](#), [Morten L. Kringelbach](#), [Pedro A. M. Mediano](#), [Michael M. Craig](#), [Ram Adapa](#), [Robin L. Carhart-Harris](#), [Leor Roseman](#), [Ioannis Pappas](#), [Alexander R. D. Peattie](#), [Anne E. Manktelow](#), [Barbara J. Sahakian](#), [Paola Finoia](#), [Guy B. Williams](#), [Judith Allanson](#), [John D. Pickard](#), [David K. Menon](#), [Selen Atasoy](#) & [Emmanuel A. Stamatakis](#)

- In healthy participants psychedelics increase complexity
 - Different techniques: fMRI, EEG, MEG
 - Several studies, with some differences

Schartner et al. *Sci. Rep.*, 2017
Luppi et al.. *Comm. Biol.*, 2023
Farnes et al.. *PLoS ONE*, 2020
Ort et al.. *iScience*, 2023



The case of DoC



- High complexity in conscious states; low in unconscious ones
- Psychedelics increase brain complexity
→ Could psychedelics boost complexity in patients with DoC?



Aims of the project

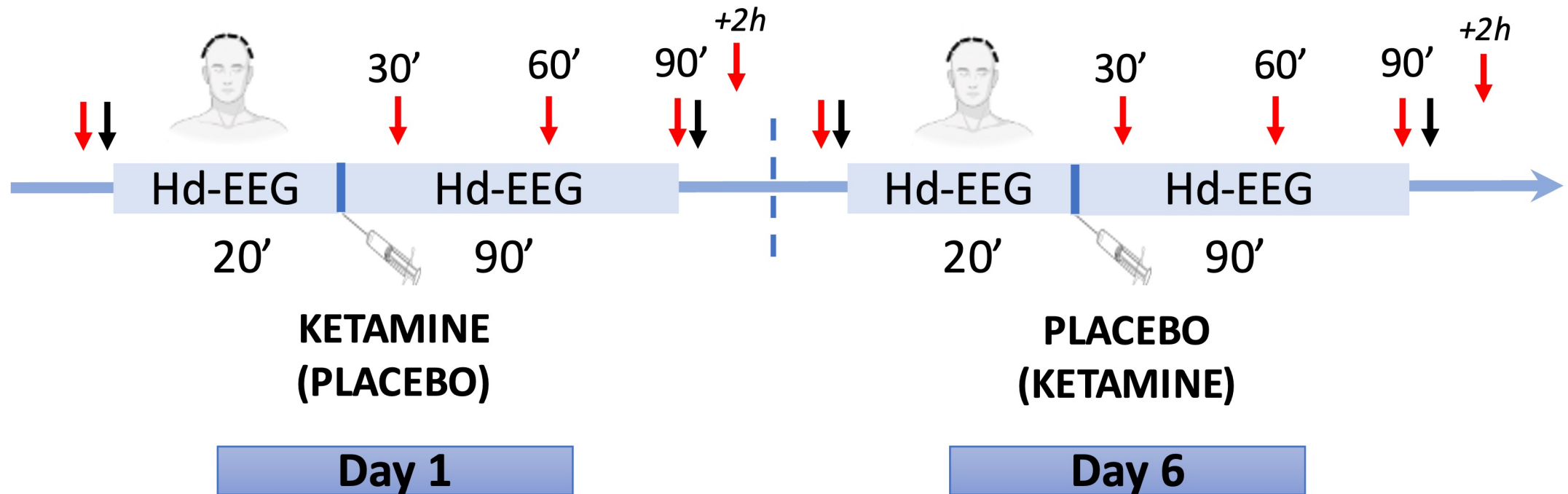
- Psychedelics as treatment
 - Can ketamine ameliorate conscious state in DoC patients?
- Look for baseline biomarkers of efficacy
 - Future predictions on responsiveness?

Feasibility study using ketamine



↓ = Clinical diagnosis (SECONDS)

↓ = Spasticity (MAS)

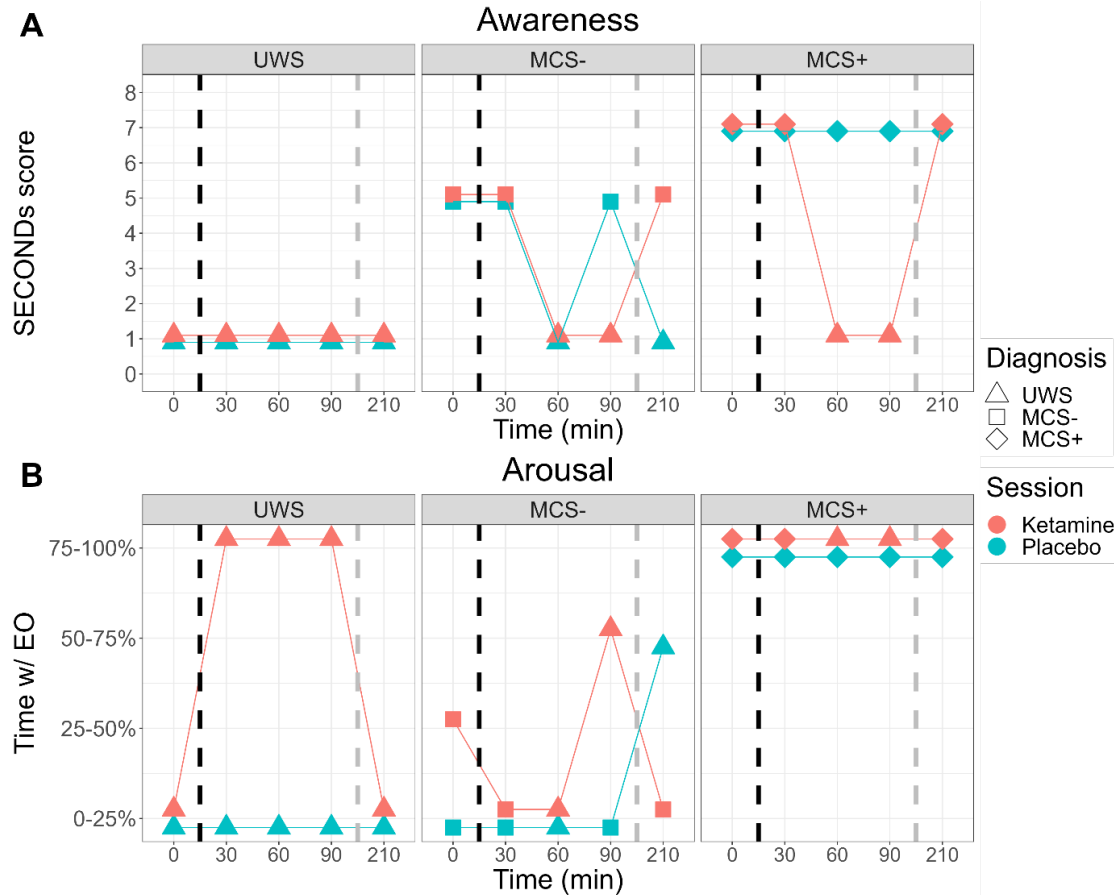
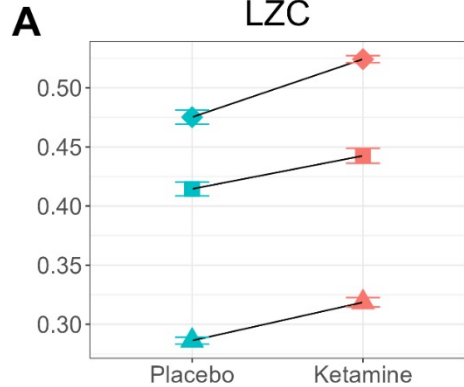


- 3 patients with DoC: 1 UWS, 1 MCS-, 1 MCS+
- IV subanesthetic concentration of ketamine (max: 0.75 ng/ml)

- Psychedelic guides and anesthesiologist present



Results from feasibility study



- Increased brain complexity measured as LZC
- More time awake, but no new overt behaviour



Take-home messages

- Psychedelics drugs change transiently consciousness
- Brain complexity seems tightly linked with consciousness
- Proved effects for psychiatric disorders, not yet for neurological ones



Acknowledgments



Pr. Olivia
Gosseries



Dr. Charlotte
Martial

Patients & families!

For more information:
p.cardone@uliege.be

