

Apomorphine treatment in a patient with chronic disorders of consciousness following brain hemorrhage

Leandro R. D. Sanz¹, Nicolas Lejeune^{1,2}, Séverine Blandiaux¹, Estelle Bonin¹, Federico Raimondo^{1,3}, Rajanikant Panda¹, Helena Cassol¹, Neal Farber⁴, Steven Laureys¹, Olivia Gosseries¹

¹ GIGA Consciousness, Coma Science Group, University and University Hospital of Liège, Belgium

³ Institut du Cerveau et de la Moelle épinière, Sorbonne Université, Paris, France

² CHN William Lennox, Groupe Hospitalier Saint-Luc, Ottignies, Belgium & Institute of Neurosciences, UCLouvain, Brussels, Belgium ⁴ NeuroHealing Pharmaceuticals Inc., Waban, MA, USA

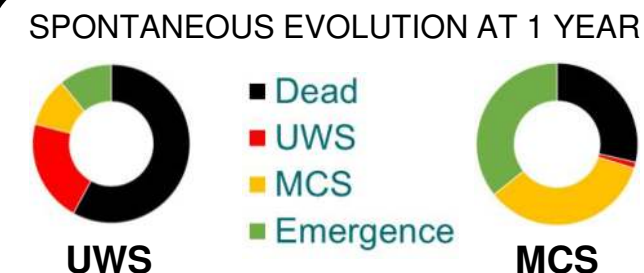
Background

DIAGNOSIS

- UNRESPONSIVE WAKEFULNESS (UWS)**
- eye opening
 - reflexive behaviors
- MINIMALLY CONSCIOUS (MCS)**
- reproducible signs of consciousness
 - no functional communication

[1,2]

PROGNOSIS



COST

HEALTHCARE FOR 1 TYPICAL UWS
121,000\$
per year

[3]

DISORDERS OF CONSCIOUSNESS

TREATMENT

NO APPROVED TREATMENT FOR CHRONIC DISORDERS OF CONSCIOUSNESS

NEUROSTIMULATION

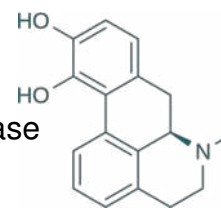
- Transcranial direct current stimulation
- Deep brain stimulation

PHARMACOLOGICAL

- Zolpidem
- Amantadine

APOMORPHINE

- Dopamine agonist
 - Approved for Parkinson's Disease
 - Subcutaneous infusion
 - Well-documented safety
 - Preliminary behavioral results in UWS & MCS
- promising therapeutic candidate



[5]

[6]

Methods

CASE Woman, 47 years old, left carotid aneurysm rupture (132 days since onset), best diagnosis: MCS-

TREATMENT 30 days of subcutaneous apomorphine (12h/d, max. rate 6 mg/h)

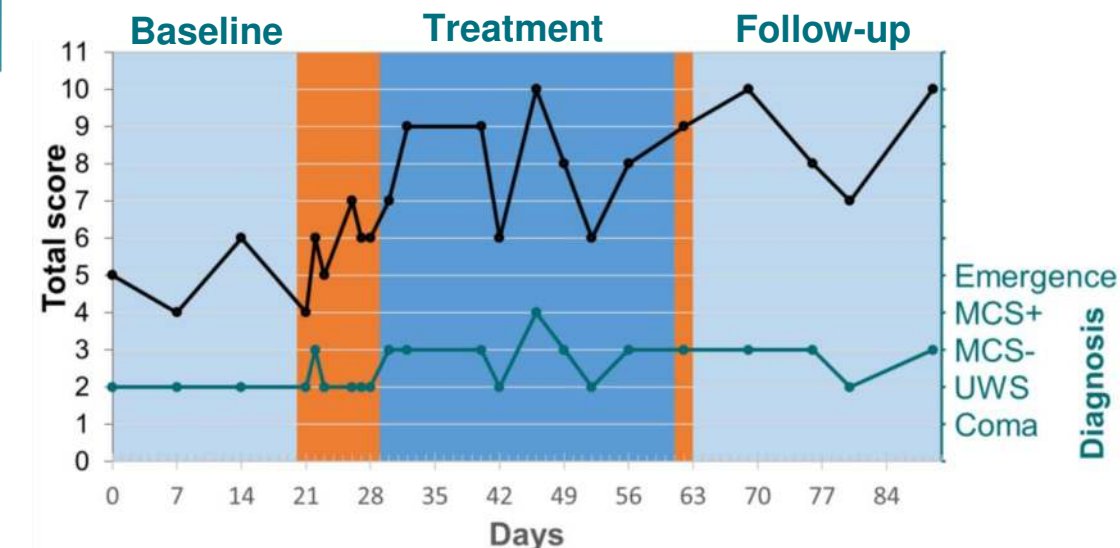
OUTCOMES Behavioral standardized scales (CRS-R) | Brain metabolism (FDG-PET) | Brain functional connectivity (high-density EEG)

[7]

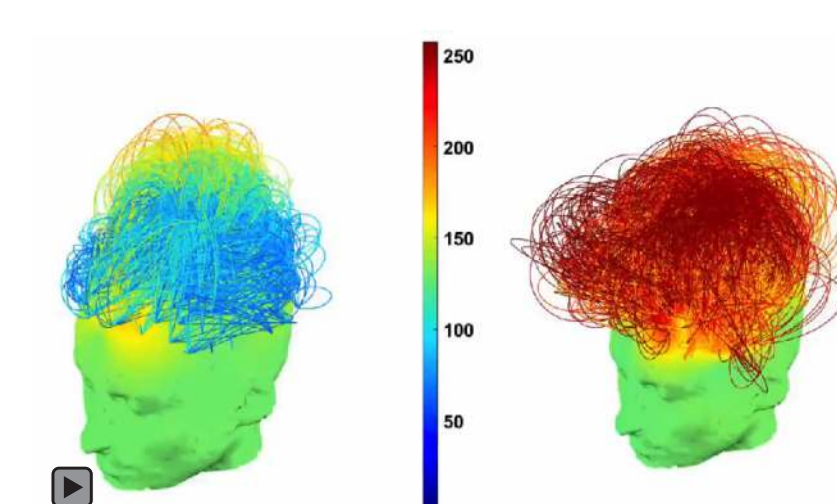
	1 - Baseline			2 - Treatment				3 - Follow-up				
				D30	D60	D90	6m	12m	24m			
Coma Recovery Scale-R	x	x	x	xxxxxx	x	x	x	x	x	x	x	x
Resting-state EEG	x	x	x	x	x	x	x	x	x	x	x	x
Auditory & Sleep EEG				x								
FDG-PET				x								
Adverse Events Questionnaire				x	x	x	x	x	x	x	x	x
Outcome Questionnaires										x	x	x

Results

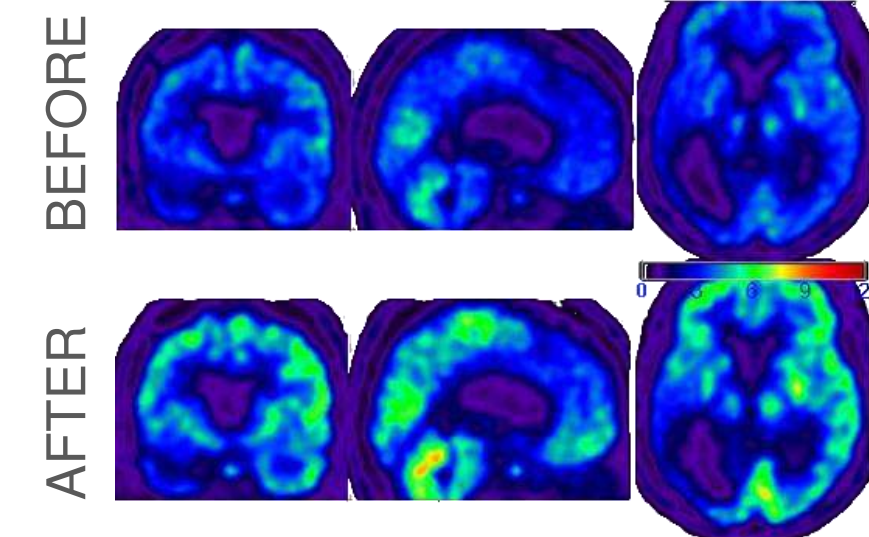
COMA RECOVERY SCALE - REVISED [8]



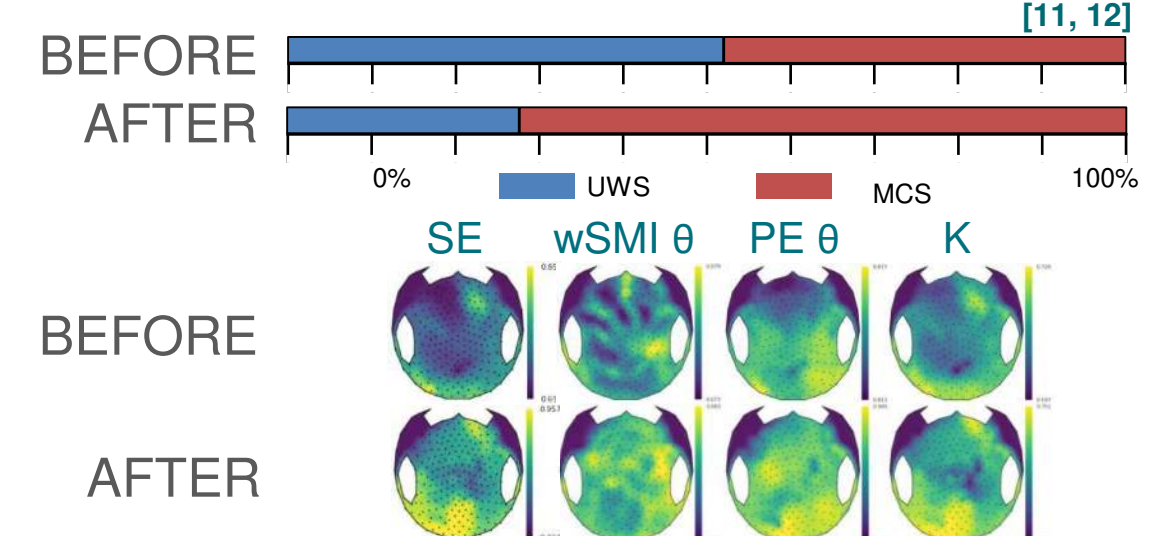
EEG FUNCTIONAL CONNECTIVITY [10]



FDG-PET [9]



EEG MULTIVARIATE CLASSIFIER [11, 12]



Discussion

- Behavioral and neuroimaging **improvements** after 30 days of treatment
- Change of diagnosis **persisted** after treatment withdrawal (MCS+)
- First results of apomorphine for **non-traumatic** disorders of consciousness
- All measures of **brain function** improved
- A larger placebo-controlled double-blind clinical trial will confirm **efficacy**

REFERENCES

- [1] Laureys et al, *BMC Med*, 2010
 [2] Giacino et al, *Neurology*, 2002
 [3] Bruno et al, *Coma and Disorders of Consciousness*, 2012
 [4] Formby et al, *CHE Research Paper 208*, 2015
 [5] Schnakers & Monti, *Curr Opin Neurol*, 2017
 [6] Fridman et al, *Brain Injury*, 2010
 [7] Sanz et al, *Front Neurol*, 2019
 [8] Giacino et al, *Arch Phys Med Rehabil*, 2004
 [9] Stender et al, *Lancet*, 2014
 [10] Chennu et al, *Brain*, 2017
 [11] Sitt et al, *Brain*, 2014
 [12] Engemann et al, *Brain*, 2018

leandro.sanz@uliege.be