Treatments for patients with disorders of consciousness

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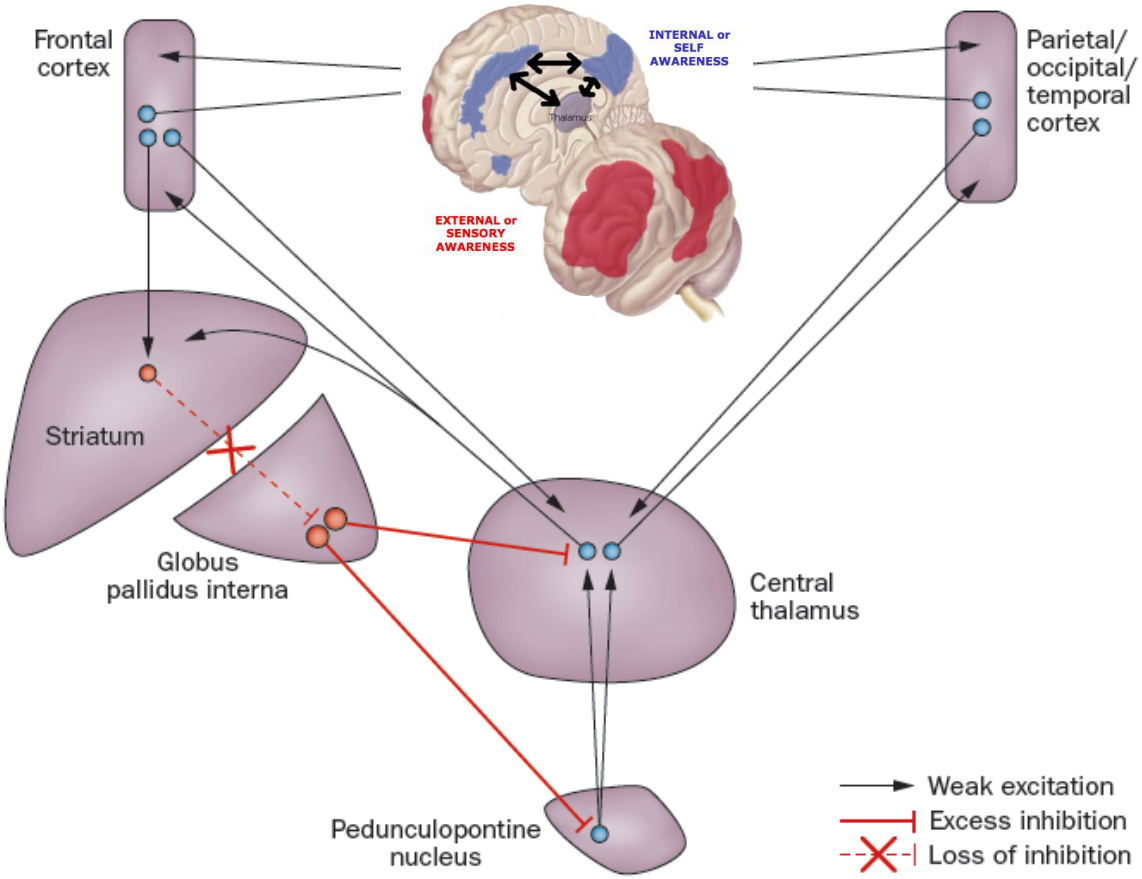
Introduction

Mesocircuit fronto-parietal model

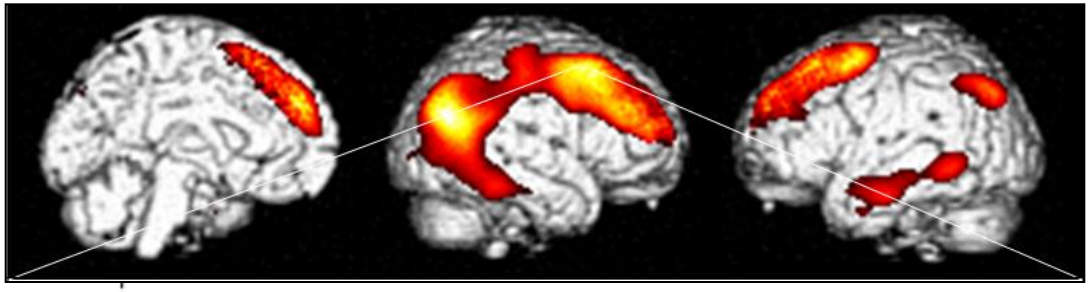


nature REVIEWS NEUROLOGY

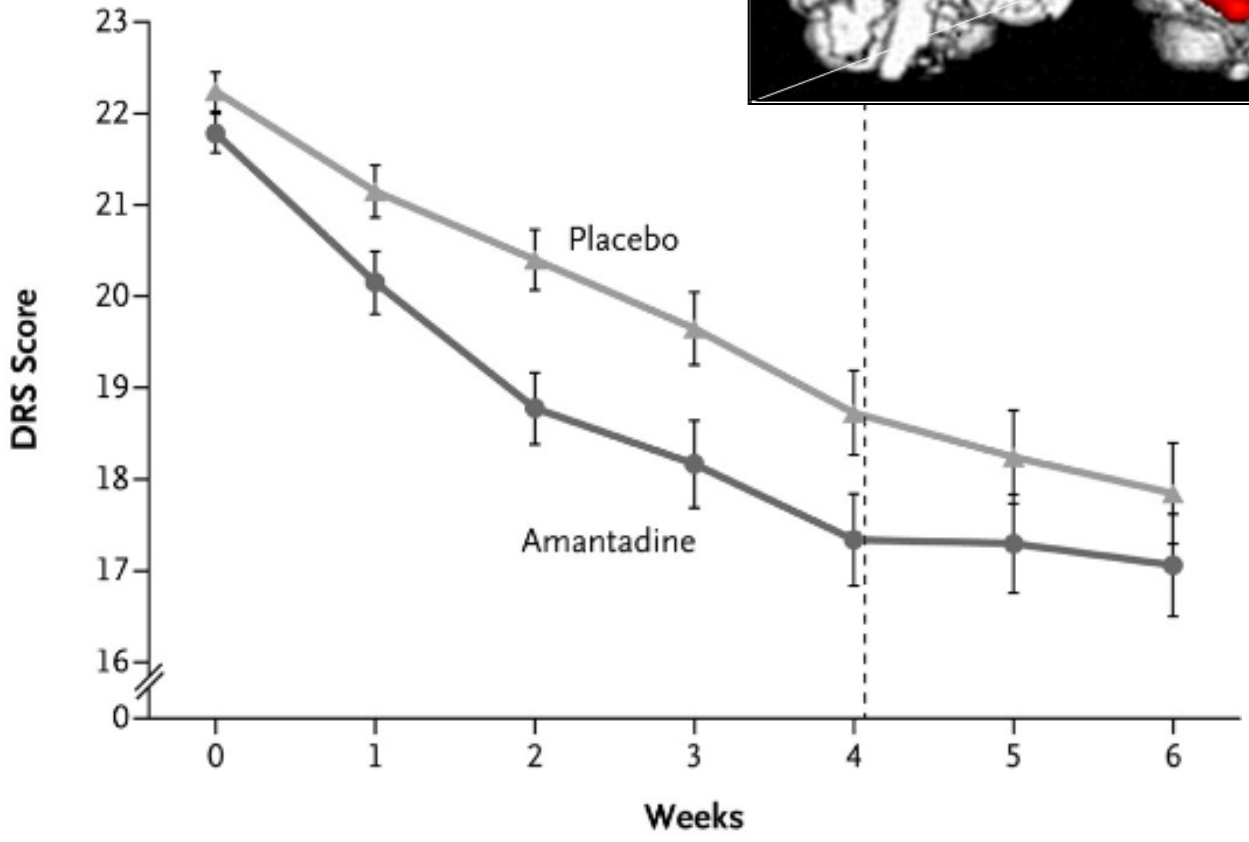
Giacino, Fins, Laureys, Schiff, *Nature Rev Neurol* 2014

Amantadine

Dopaminergic agent
(Parkinson)



Schnakers et al, *JNNP,* 2008



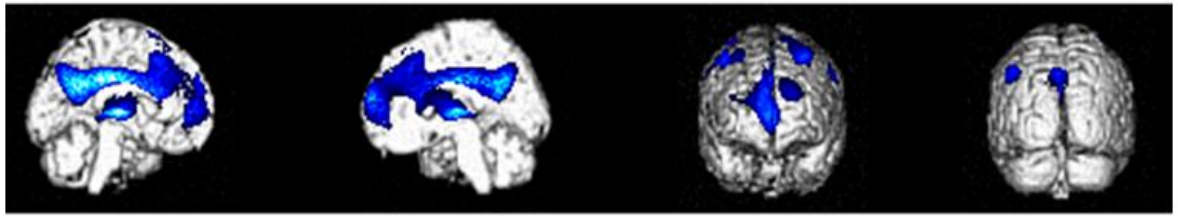
n=184

Giacino et al, N Engl J Med, 2012

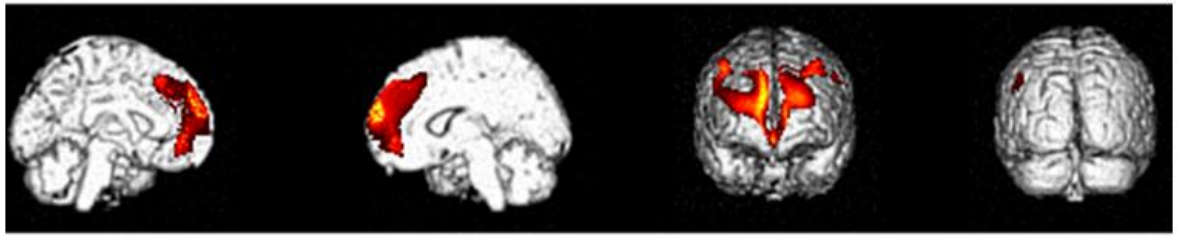
Zolpidem

Short-acting nonbenzodiazepine GABA-A agonist hypnotic

1/15 responders
= 6.7%
Whyte & Meyers, 2009



4/84 responders
=5%
Whyte et al, 2014

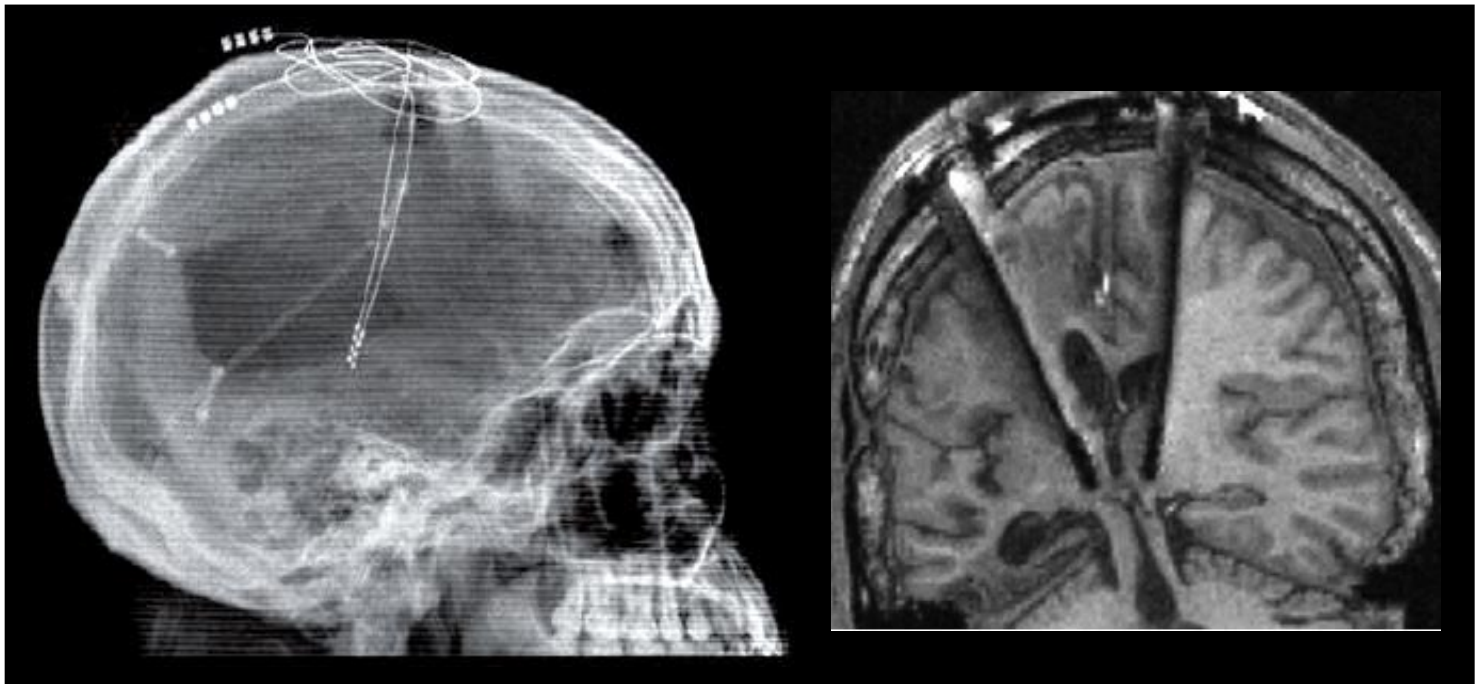


4/60 responders
= 6.7% no change of diagnosis
Thonnard & Gosseries et al, 2014

N=3

Deep brain stimulation

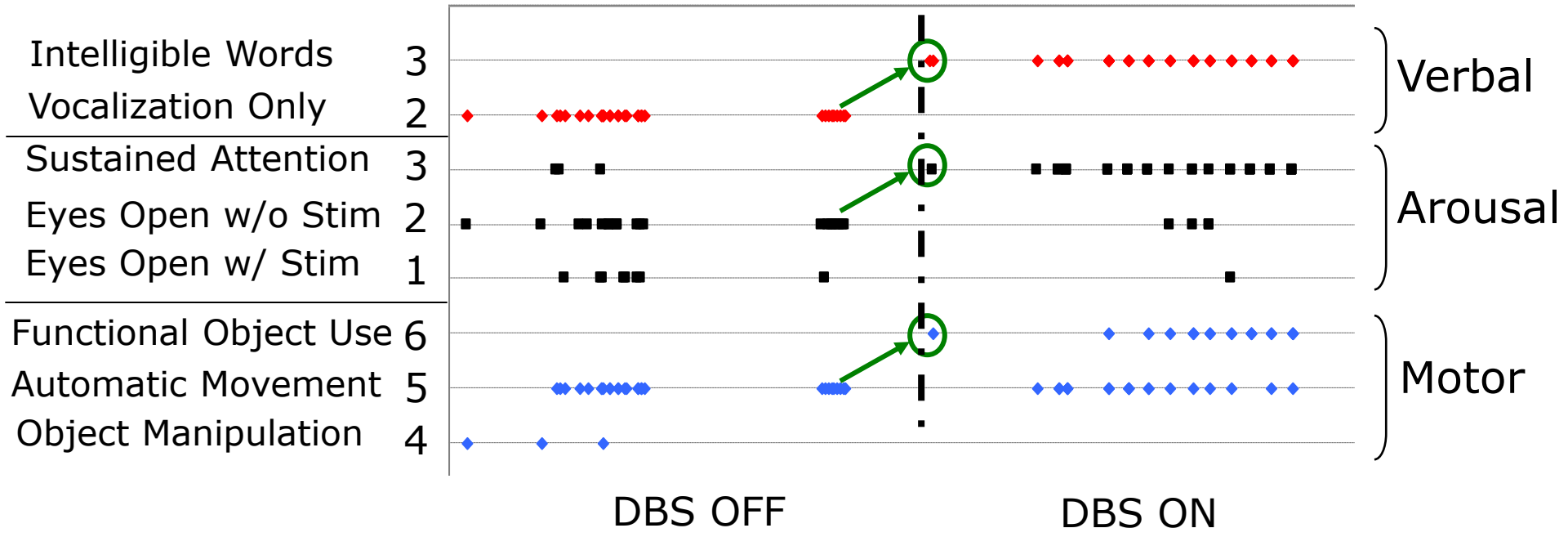
Intralaminar nuclei stimulation
induces “recovery” from
minimally responsive state



Schiff et al*, Nature,* 2007
Giacino et al, *Neurmodulation*, 2012

Deep brain stimulation

Clinical improvement



Schiff et al, *Nature*, 2007

Why tDCS?

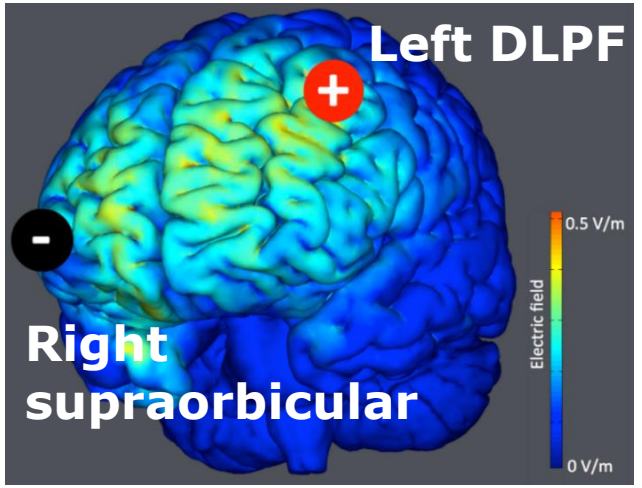
Stimulation	Population	Effects	Authors
Motor cortex	Healthy subjects	Dexterity	Boggio et al. Neurosci Lett, 2006
	Hemiplegic patients	Dexterity and strength	Hummel et al. Lancet, 2006
	Spastic patients	Spasticity & ADL (activity of daily life)	Wu et al., Arch Phys Med Rehabil 2012
Prefrontal cortex	Healthy subjects	Memory	Marshall et al. J Neurosci, 2004
	Alzheimer's patients	Memory	Ferrucci et al. Neurology, 2008
	Stroke patients	Attention	Jo et al. Am J Phys Med Rehabil, 2009
	Aphasic patients	Language	Baker et al. Stroke, 2010

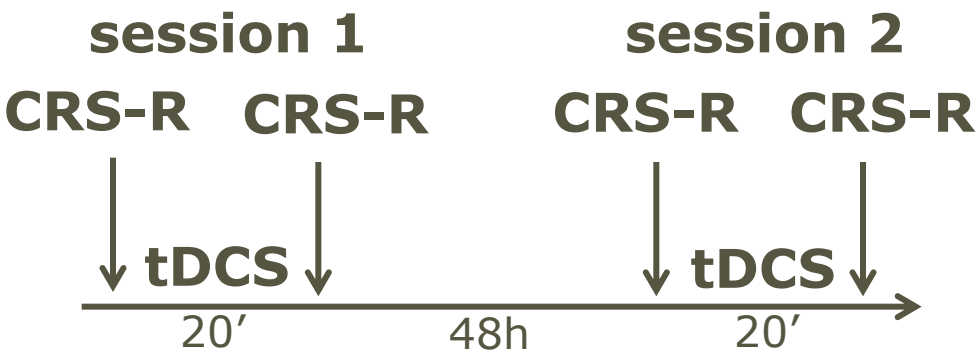
➔ Cheap, easy to use & no severe side-effects

Thibaut et al, Rev Neurol, 2013

tDCS single session

- Randomized, double blind, sham controlled, cross-over study
- Direct current; 2 mA; 20 min
- 55 patients included
  (25 VS/UWS; 30 MCS;
  35 chronic; 25 TBI; 43±18y)

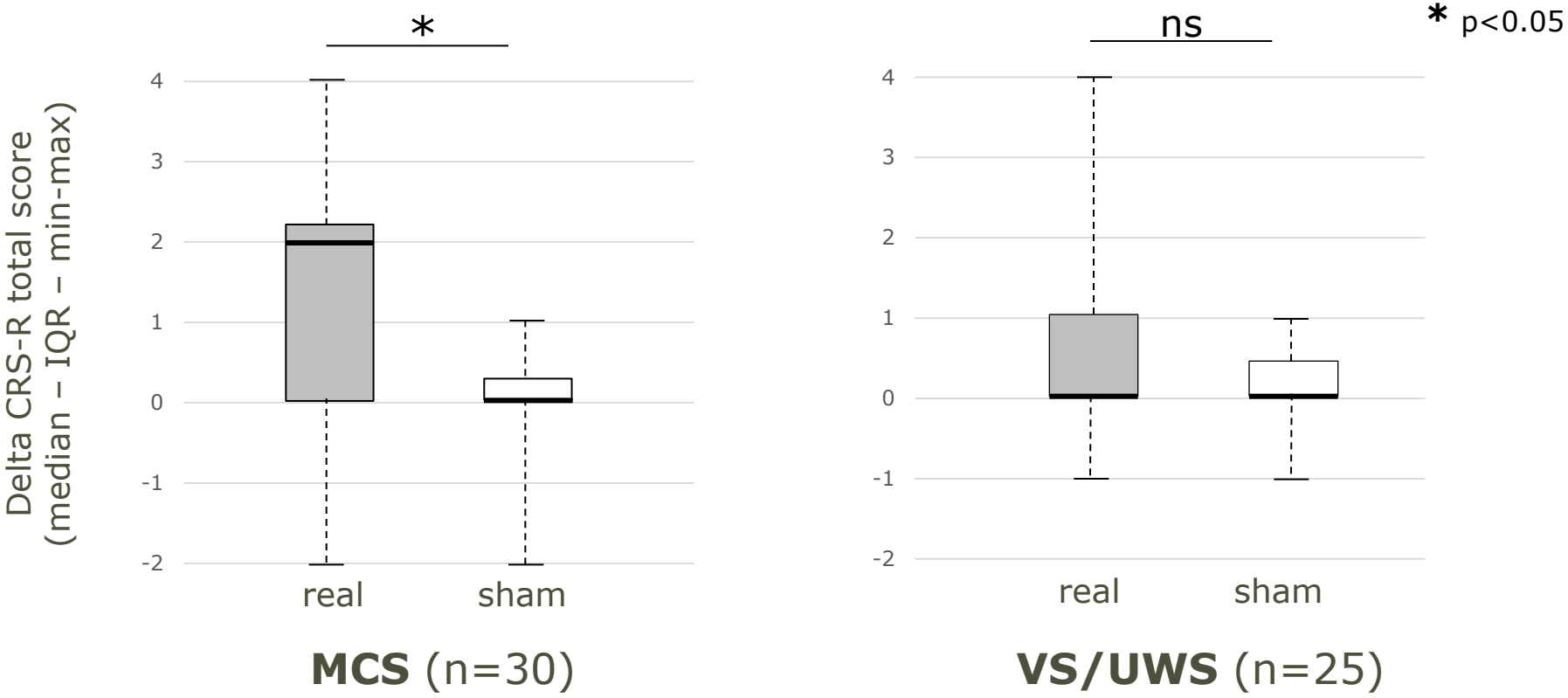




Thibaut *et al.*, Neurology, 2014

tDCS single session

Treatment effect: delta CRS-R total scores



tDCS single session

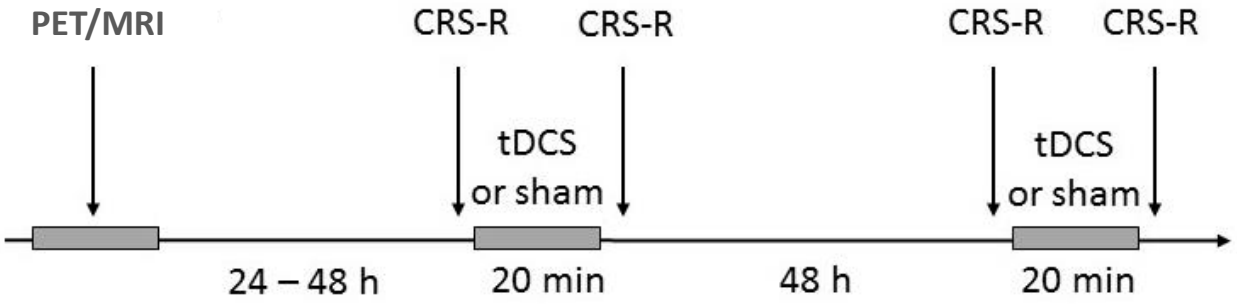
- **15/55 responders** : sign of consciousness after tDCS and not before tDCS or before and after sham
  - 2 VS/UWS; acute
  - 13 MCS (5 patients >1y post insult)
- Change of diagnosis
  - 3 MCS ➔ EMCS (acute)
  - 2 VS/UWS ➔ MCS (acute)
- No effect of time since injury or etiology
- No side effects

Thibaut *et al.*, Neurology, 2014

Neural correlates

➔ Can functional brain activity & grey matter atrophy predict tDCS clinical response?

- Data from study 1 – chronic MCS (n=24)
- FDG-PET – MRI (VBM)
- 8 tDCS responders (4 TBI, mean age: 38±19y)
  13 tDCS non-responders (8 TBI, mean age:36±14y)

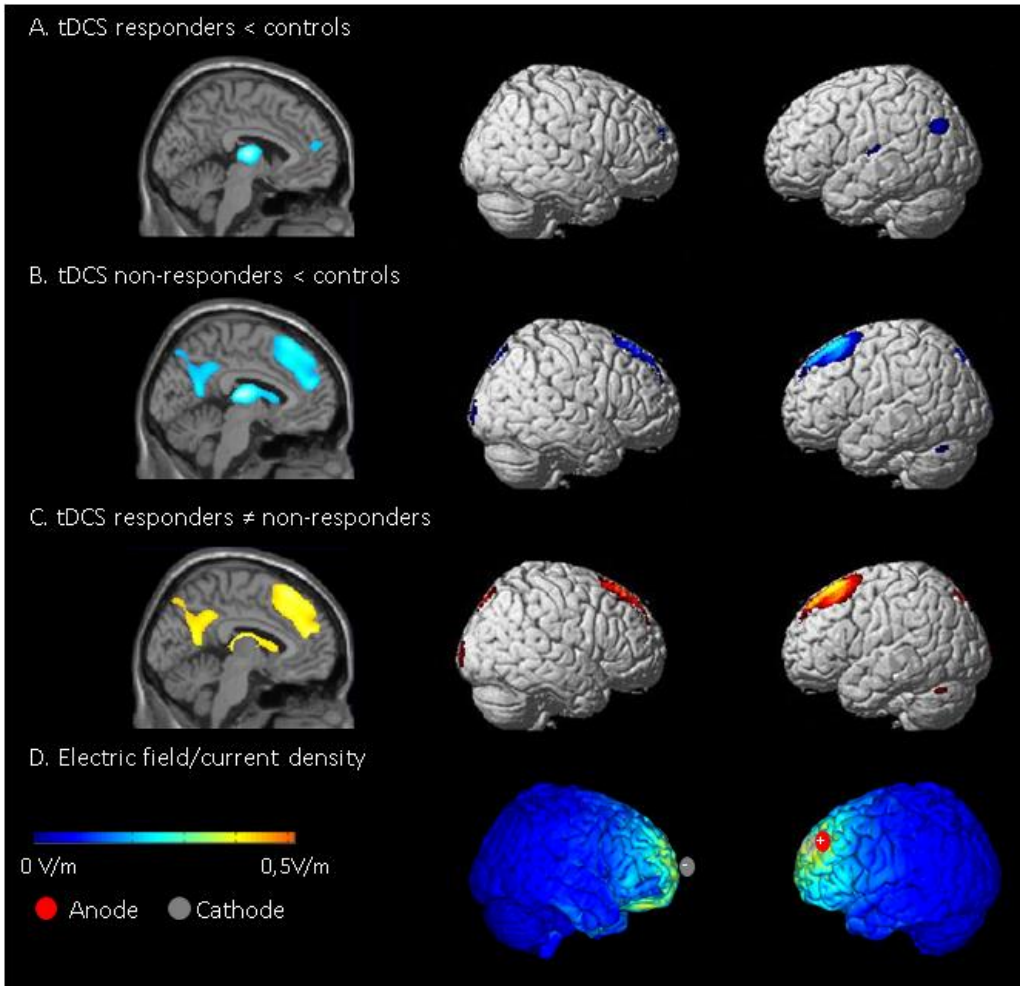


Thibaut & Di Perri *et al.*, under review

Neural correlates

- hypometabolic
- preservred

p<0.05



PFDL cortex, precuneus, thalamus also more atrophic in non-resp.

Thibaut & Di Perri *et al.*, under review

Repeated stimulations

Single stimulation: effects ± 60 min[1]

➔ short-lasting improvements, back to initial state

1. Increase the duration of the effects
2. Increase the number of responders

Randomized sham controlled double blind cross-over

16 patients included in chronic MCS (12TBI; mean age 47±16y)

S1: real or sham

S2: sham or real

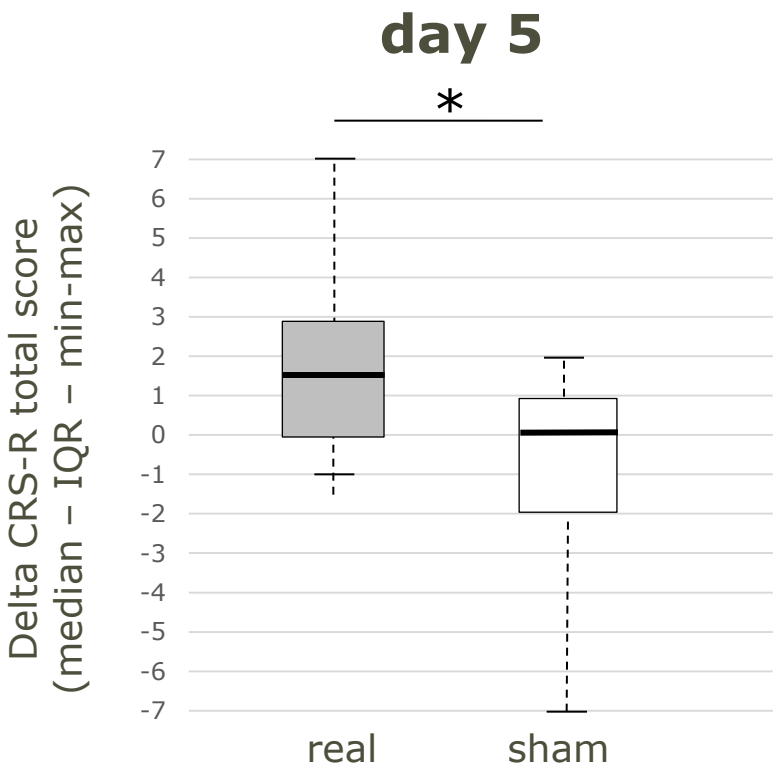
CRS-R

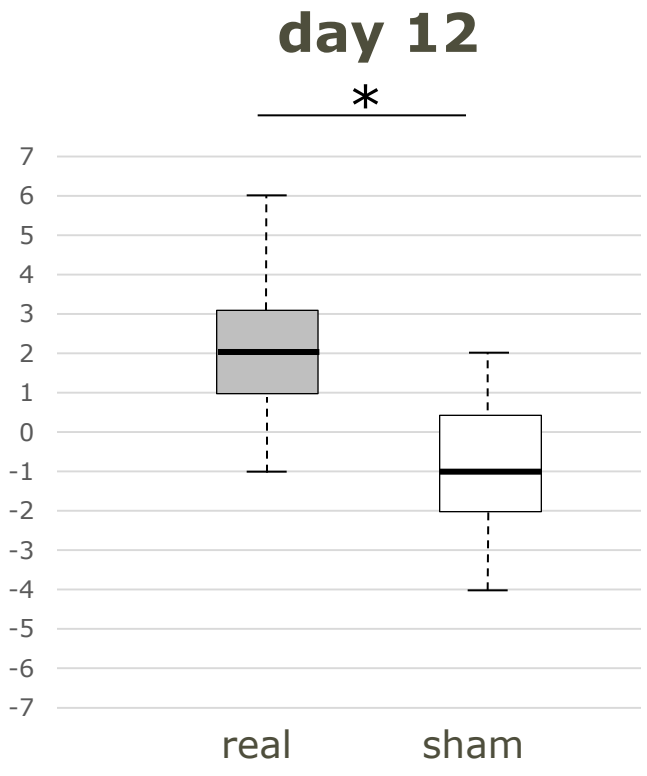
20 min tDCS

[1]Nitsche et *al.*, 2001
Thibaut *et al.*, submitted

Repeated stimulations

Treatment effect: day5 & day 12 – 53% of responders



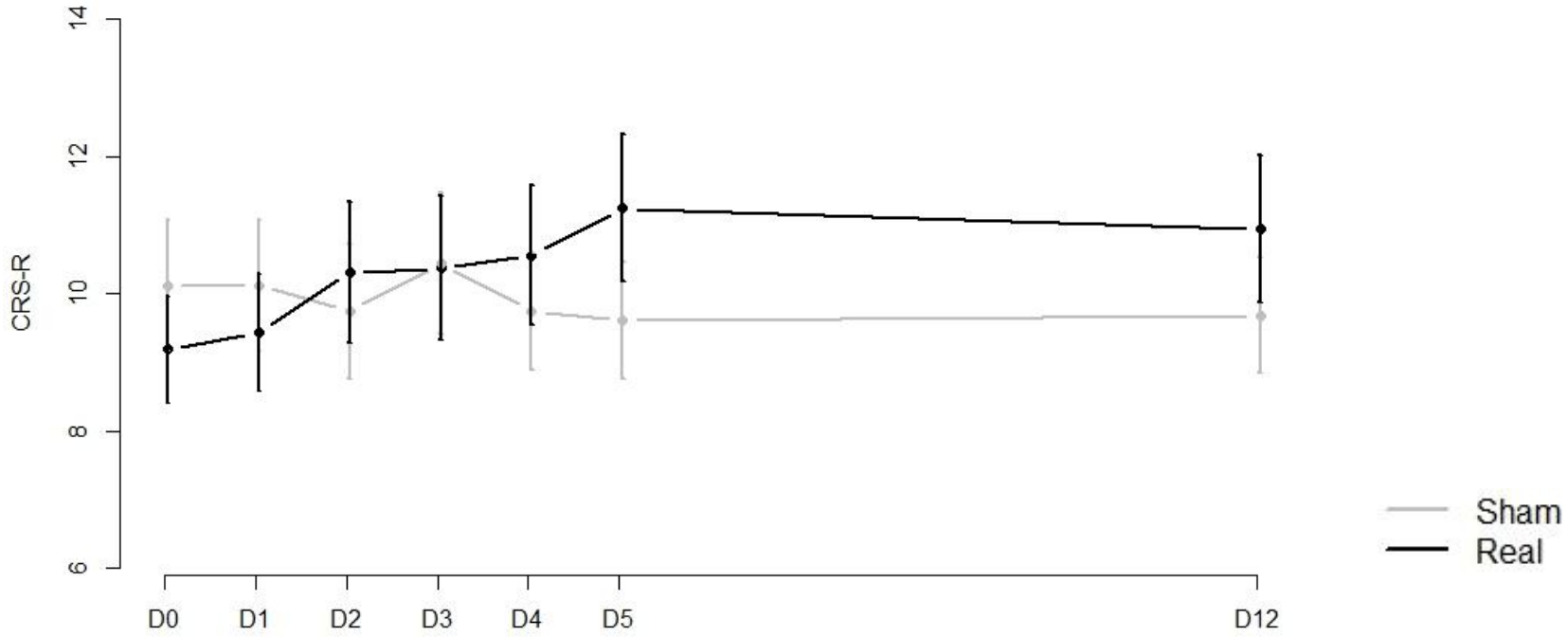


* p<0.05

Thibaut *et al.*, submitted

Repeated stimulations

- Longitudinal analysis:
  - Real session: significant + time evolution (p<0.001)
  - Sham session: no evolution across time (p=0.64)



Thibaut *et al.*, submitted

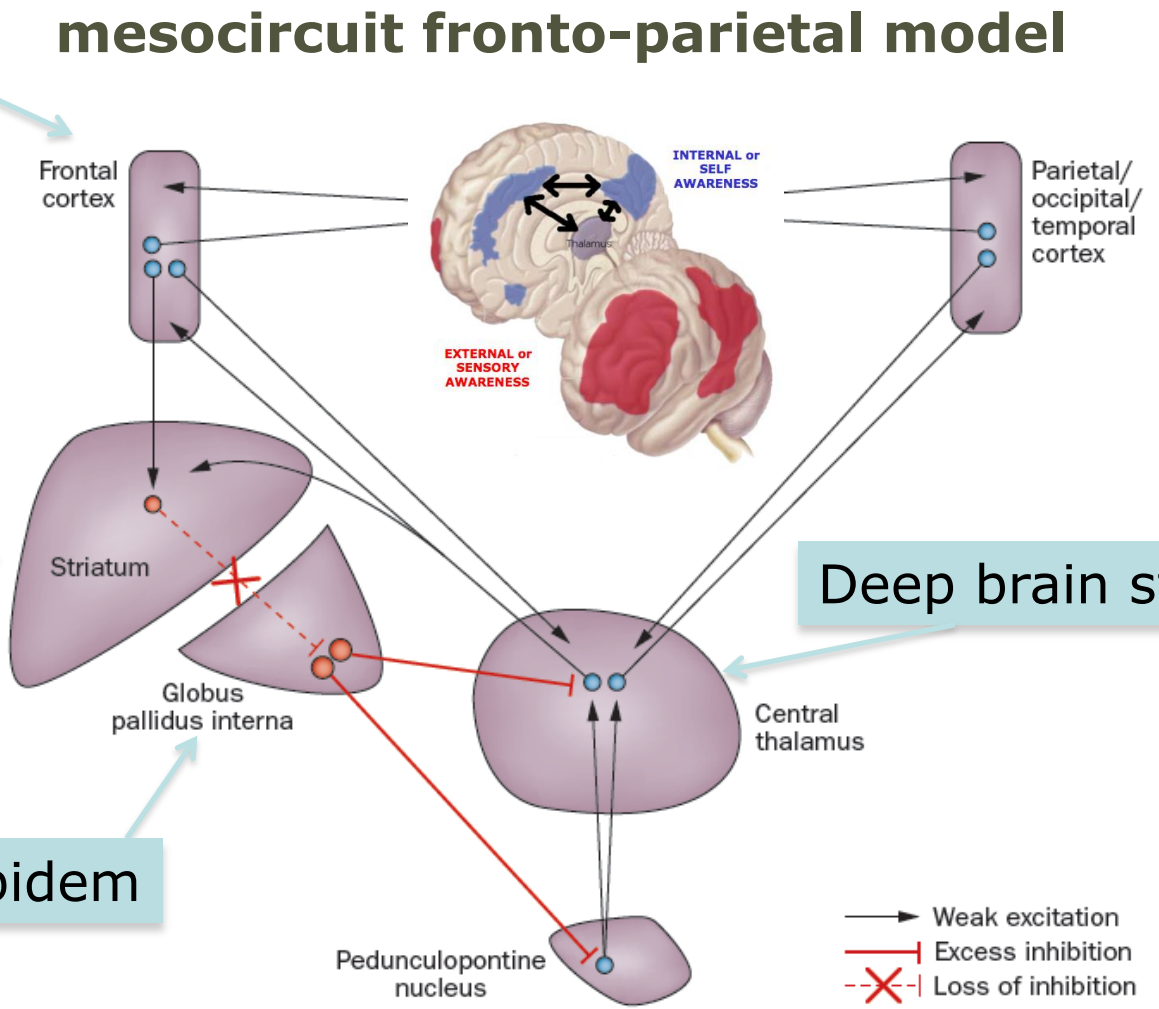
Conclusion

transcranial Direct Current Stimulation

amantadine

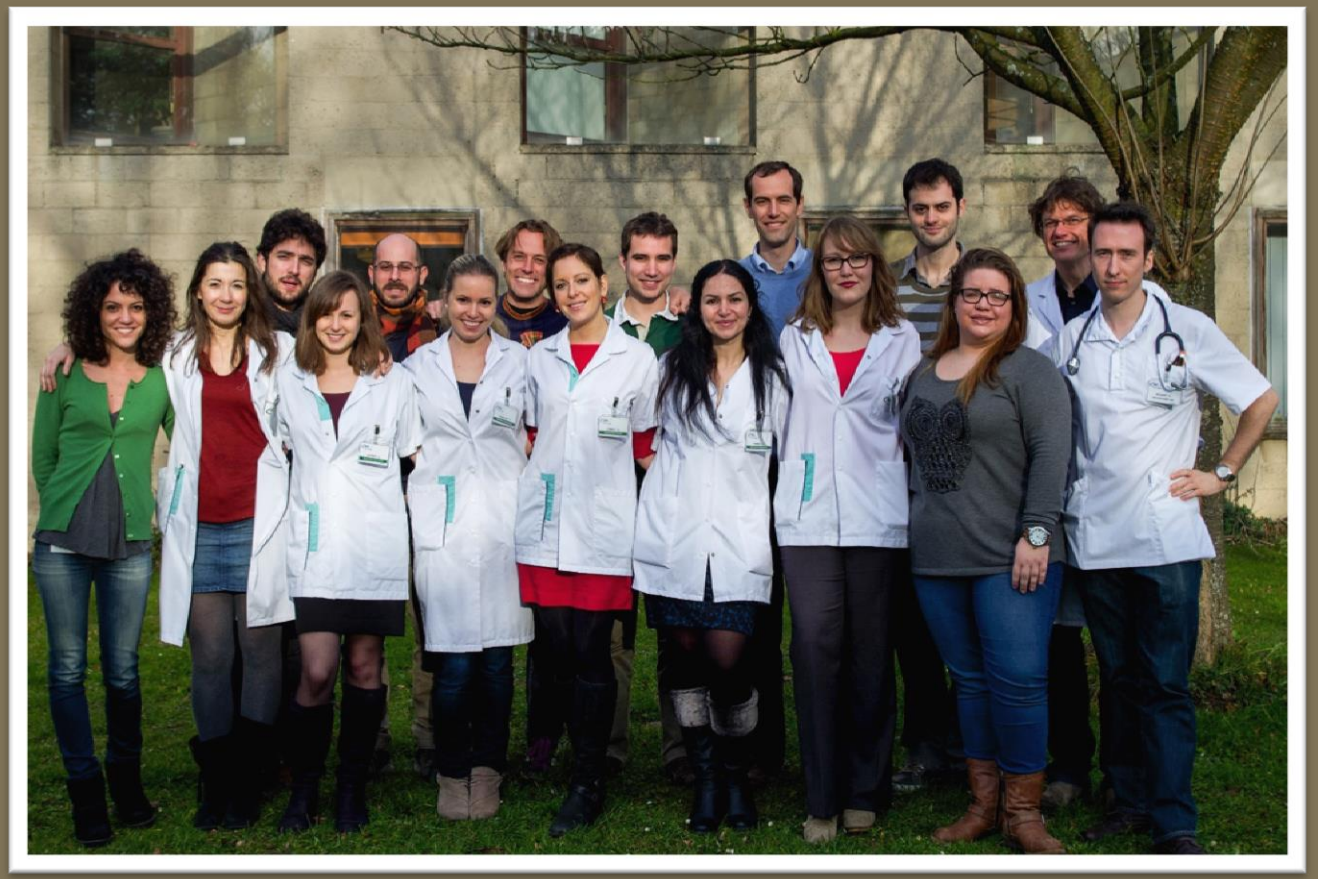
zolpidem

Deep brain stimulation



Giacino, Fins, Laureys, Schiff, *Nature Rev Neurol* 2014

THANK YOU



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