Effects of sham-controlled double blind transcranial direct current stimulation in patients with disorders of consciousness

THIBAUT Aurore
PhD Student
Physiotherapist
Coma Science Group
Cyclotron Research Centre &
University & University Hospital of Liège
Belgium

Cyclotron research centre

CHU de Liège

Université de Liège ULg

COMA SCIENCE GROUP

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AIM of the study

Assessing the effect of **transcranial direct current stimulation (tDCS)** on cognition in patients with disorder of consciousness

In a double blind sham controlled randomized study

Why direct current stimulation?

Stimulation	Population	Effects	Authors
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

- Non-invasive
- Easy to apply
- Cheap equipment

Methods

- Anode
- Cathode

- Direct current
- 2 mA
- 20 minutes

Randomised
double blind
sham controlled

Methods

CRS-R CRS-R CRS-R CRS-R

tDCS tDCS

20' 24h 20'

Responder : CRS-R post tDCS

> pre-tDCS
> sham
> pre-sham

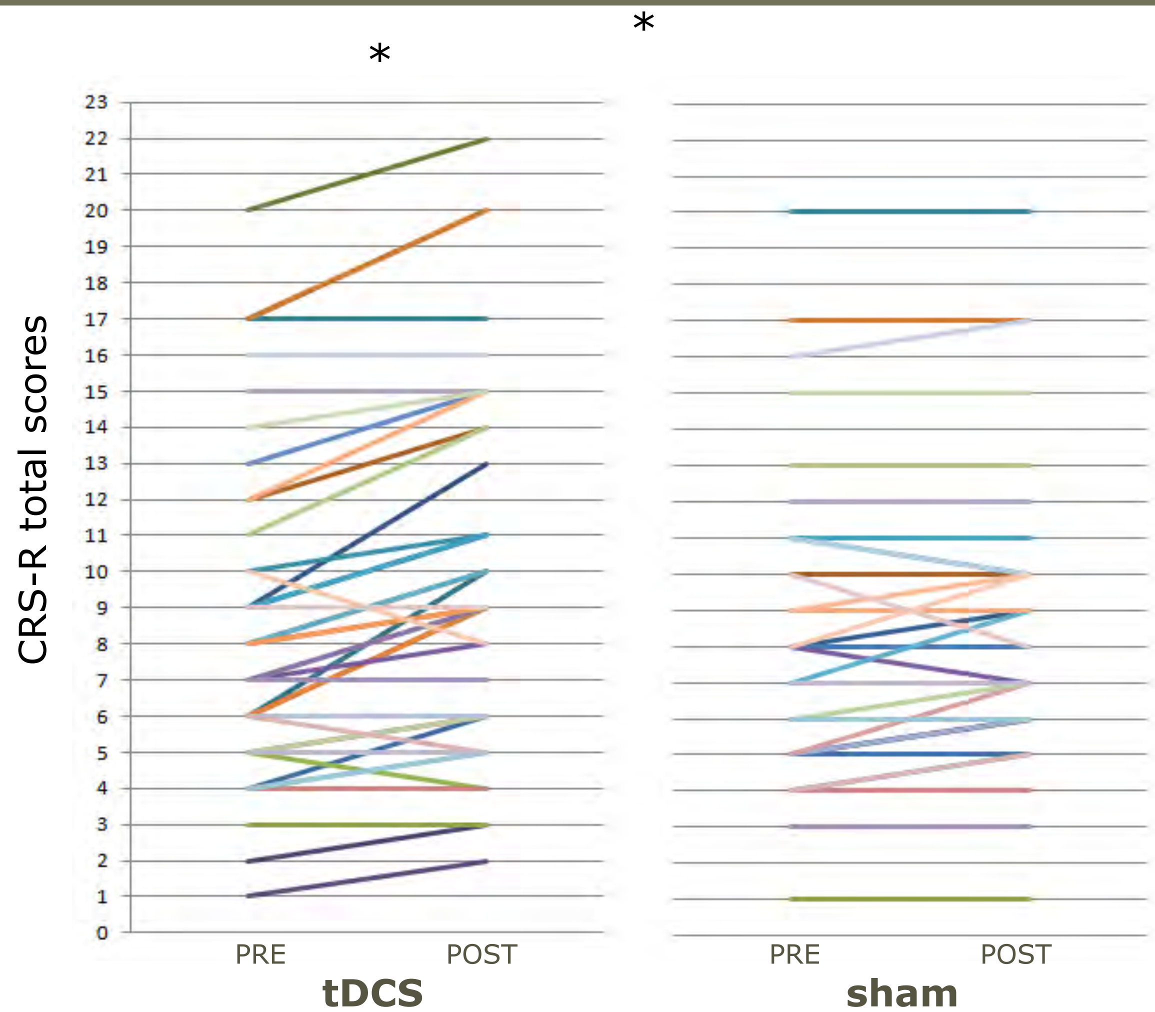
Statistics: Stata 10.0
ANOVA
Wilcoxon signed-rank test

Giacino, Arch Phys Med Rehabil 2004
Stata 10.0 (StataCorp. 2007. Stata Statistical Software: Release 10. College Station, TX: StataCorp LP)

Population

- 55 patients (16 women)
- 25 VS/UWS, 30 MCS
- aged 43 ± 18 y
- 25 traumatic / 30 non-traumatic
- 20 acute / 35 chronic (>3 months post insult)

Group data (n=55)



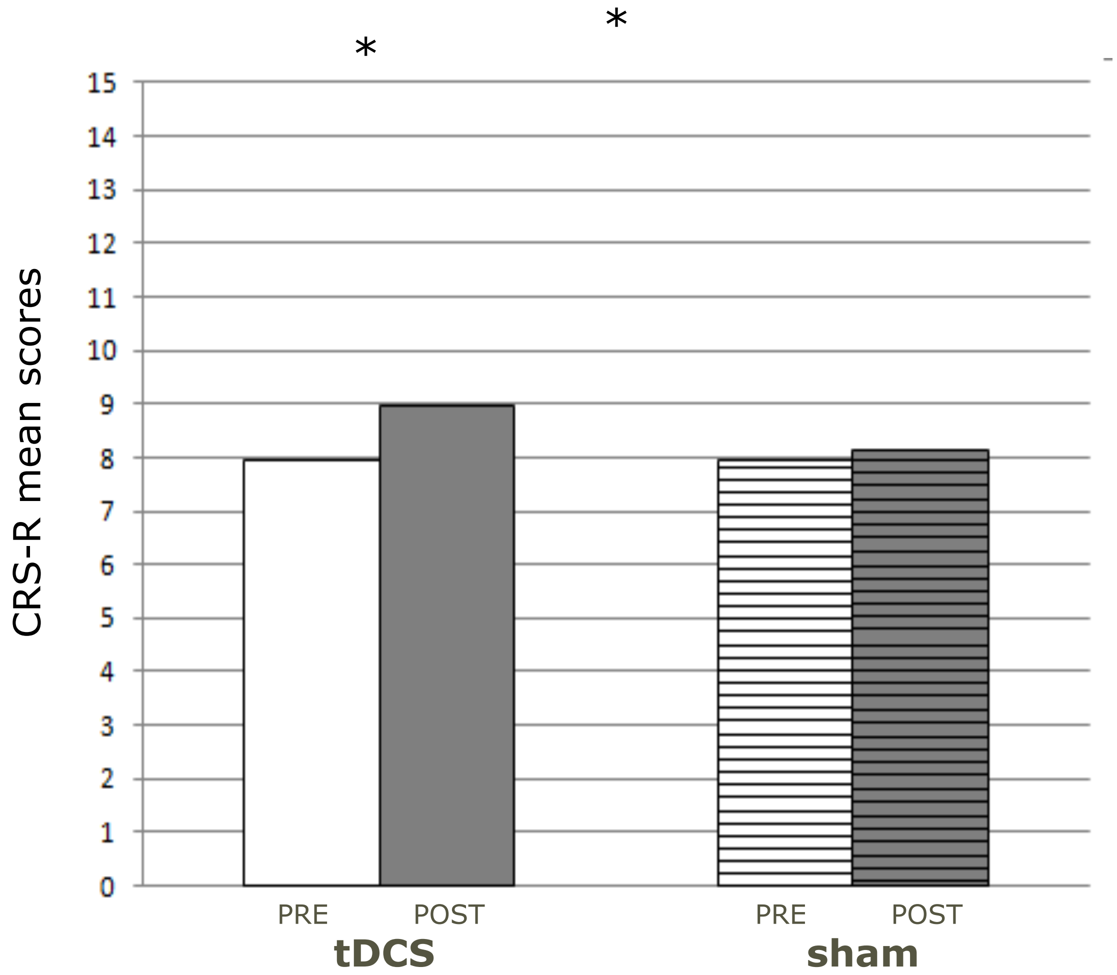
N=55

17 responders

- 2 UWS; acute
- 15 MCS;

7acute/8chronic

Group data (n=55)

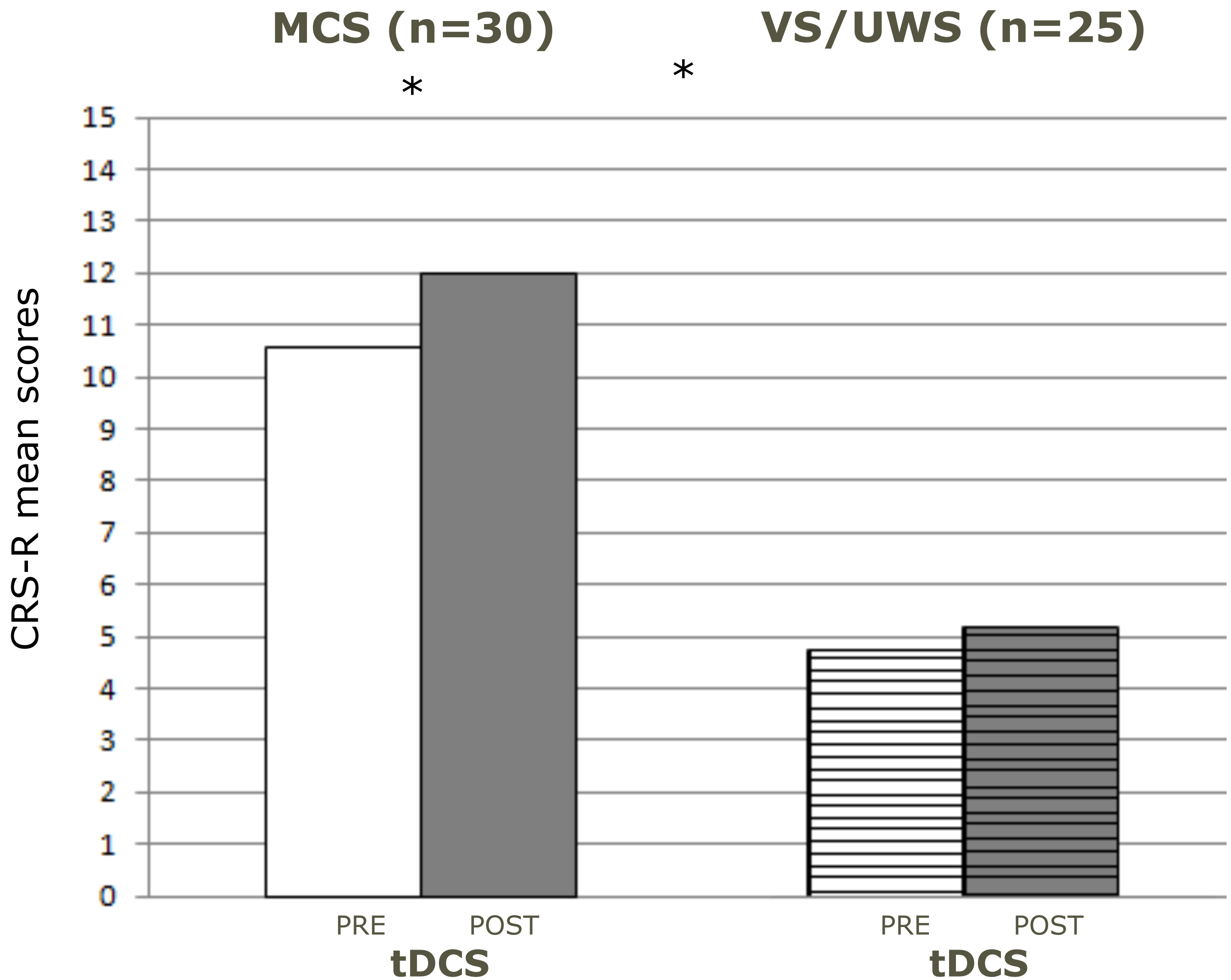


17 responders

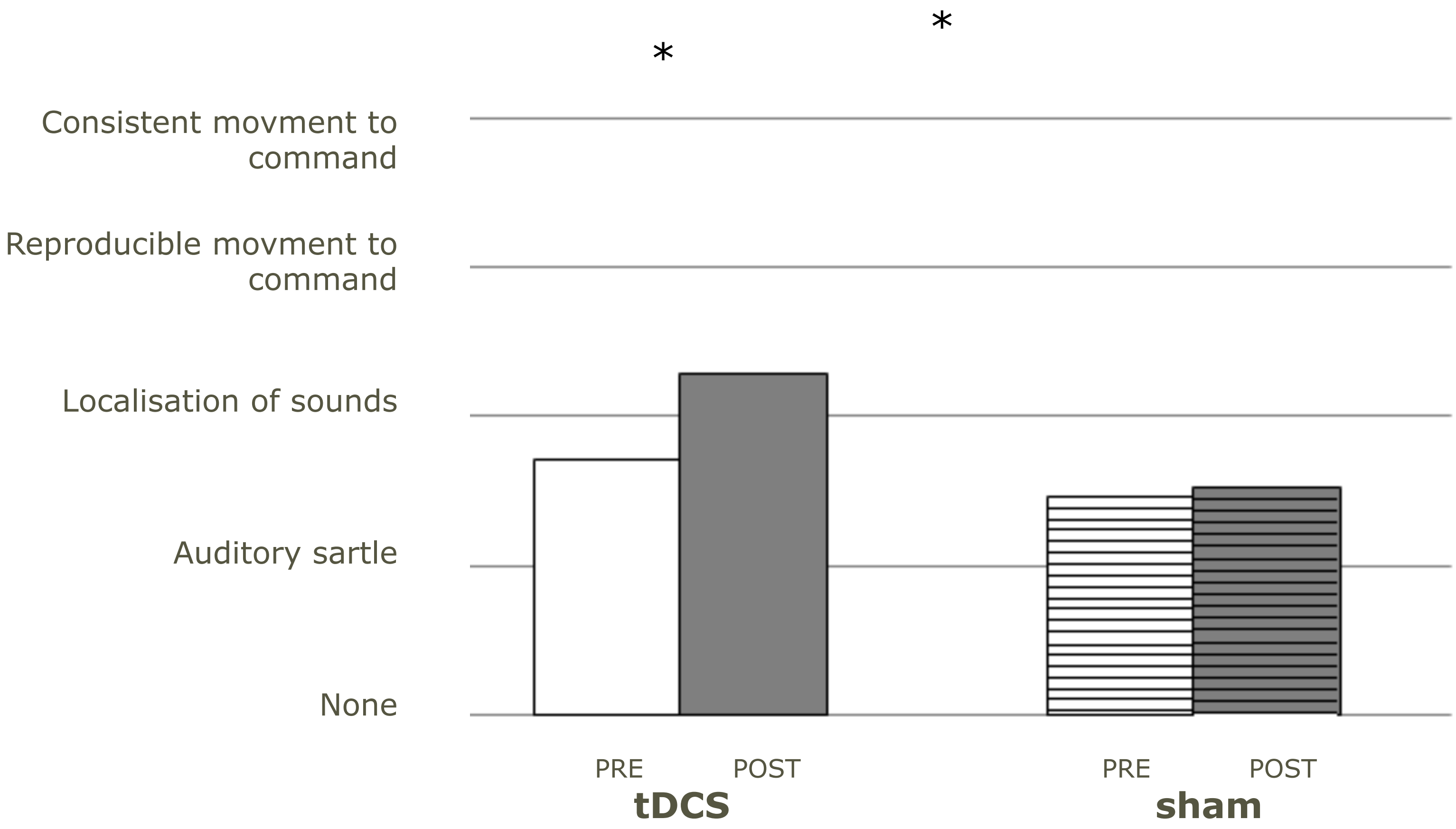
- 2 UWS; acute
- 15 MCS;

7acute/8chronic

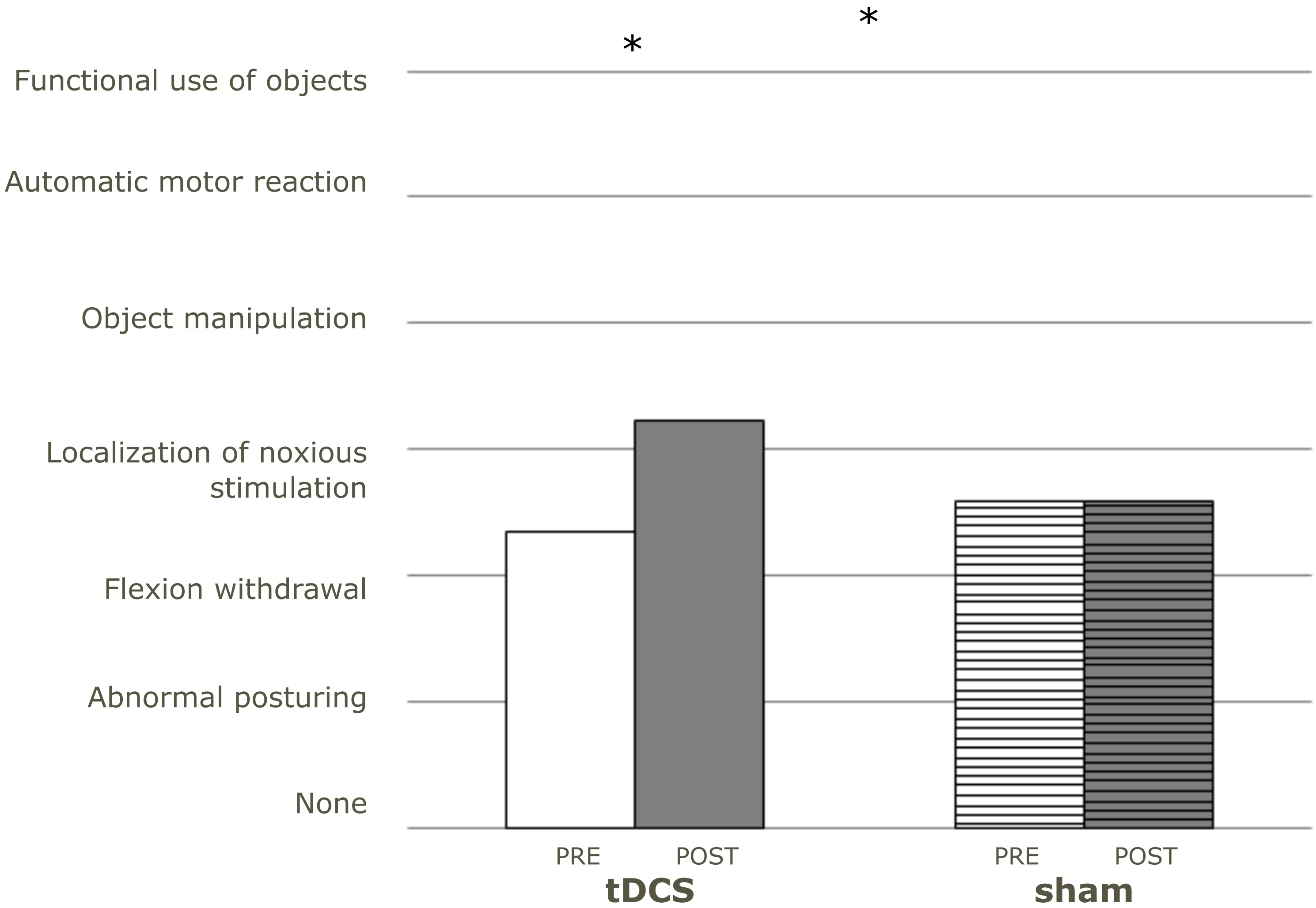
UWS/UV vs MCS


MCS (n=30)
VS/UWS (n=25)
*
*
CRS-R mean scores
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
PRE
POST
tDCS
PRE
POST
tDCS

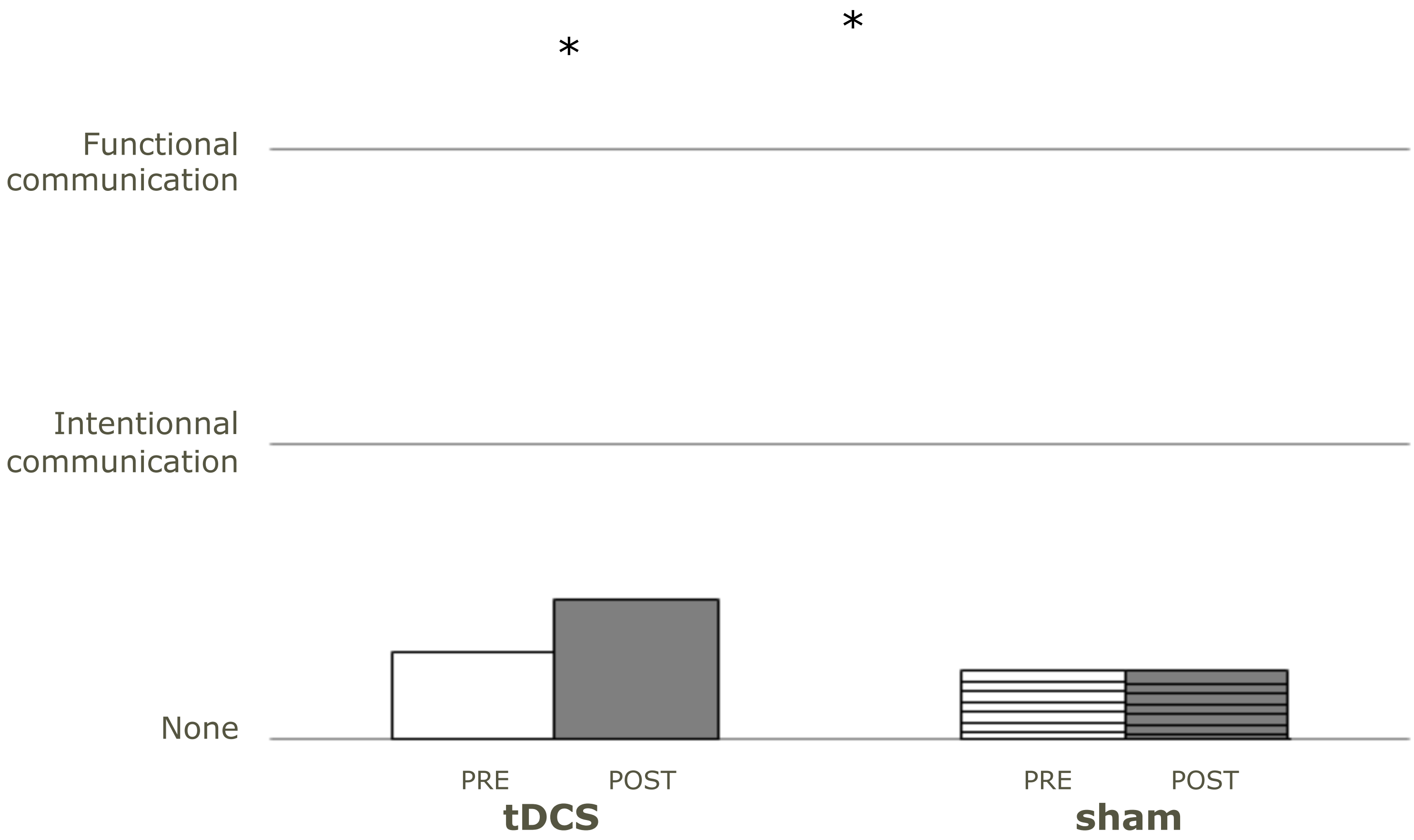
Responders: audition subscale



Responders: motor subscale



Responders: communication



tDCS presumed mode of action

Short term effects

Modification of neuronal excitability (action potential)

Long term effects

Action on opening of ion channels (Na^{+}, Ca^{2+})

Increase NMDA receptors excitability

improve neuron excitability

Nitsche et al., J Physiol 2000
Nitsche et al., Neuroscientist 2010

Neuroimagery

Prefrontal stimulation

- Improvement of DMN connectivity (MRI)
- Increase of regional electrical activity in the PF and AC cortexes (EEG) (ß and δ/θ)

Motor stimulation

- rCBF increase in the left M1, right prefrontal cortex, right S1 (PET-scan)
- Functional connectivity increased within premotor, motor and sensorimotor areas (EEG)

Keeser et al., J Neurosci, 2011
Keeser et al., Neuroimage, 2011
Lang et al., Eur J Neurosci, 2005
Polania, Nitsche and Paulus, HBM, 2010

tDCS – advantages

DBS and **Amantadine** improve cognitive functions of patients with disorder of consciousess

But invasive and pharmacological

tDCS improve cognition of patients in minimally conscious state without risk of brain damage or seizure

Schiff et al., Nature 2008
Giacino et al., New Eng J Med, 2012
Thibaut et al., in prep

tDCS critisisms

Limitations:

- Short term effect
- Moderate clinical changes
- Superficial effect
- Improve electrode position

tDCS – long term

Effects last ± 90 minutes

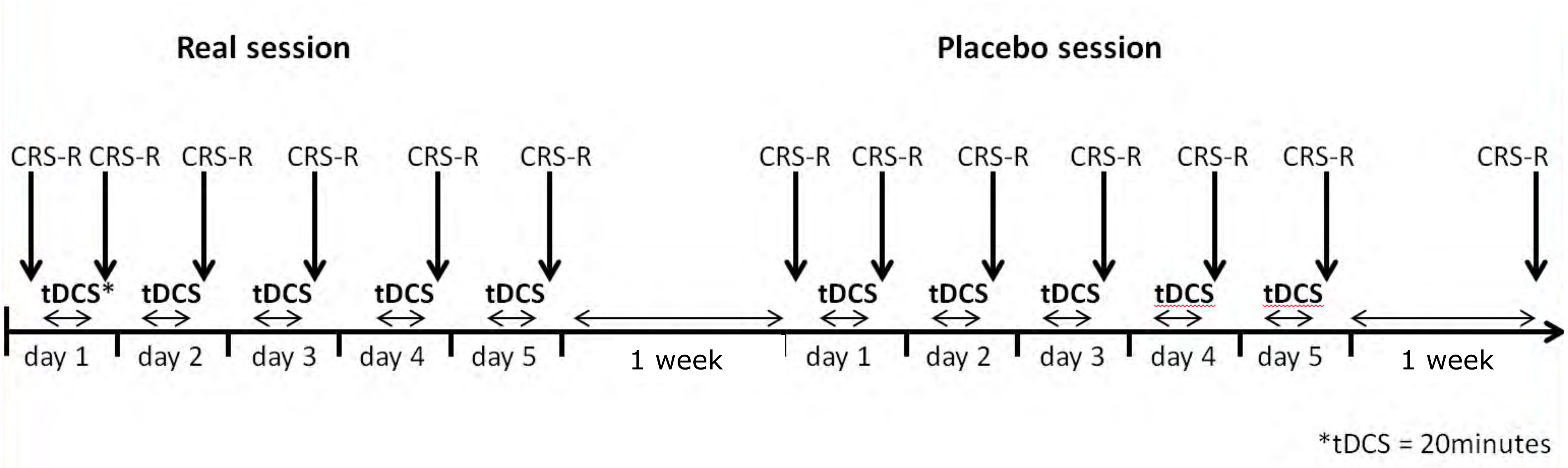
- Short improvement
- Back to initial state

Daily stimulations (5days)

improvement and extension of benefits

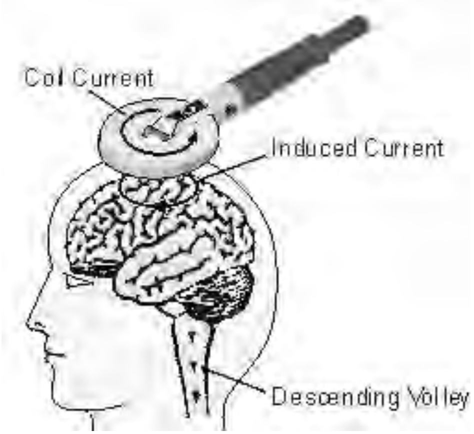
Hummel et al., Lancet 2006
Antal et al., J Pain Symptom Manage 2010

tDCS – long term



Prospective, randomized, controlled and double-blind study

tDCS - M1



Cognitive effects +

Motor effects ?

Parameters:

2 mA – 20 min

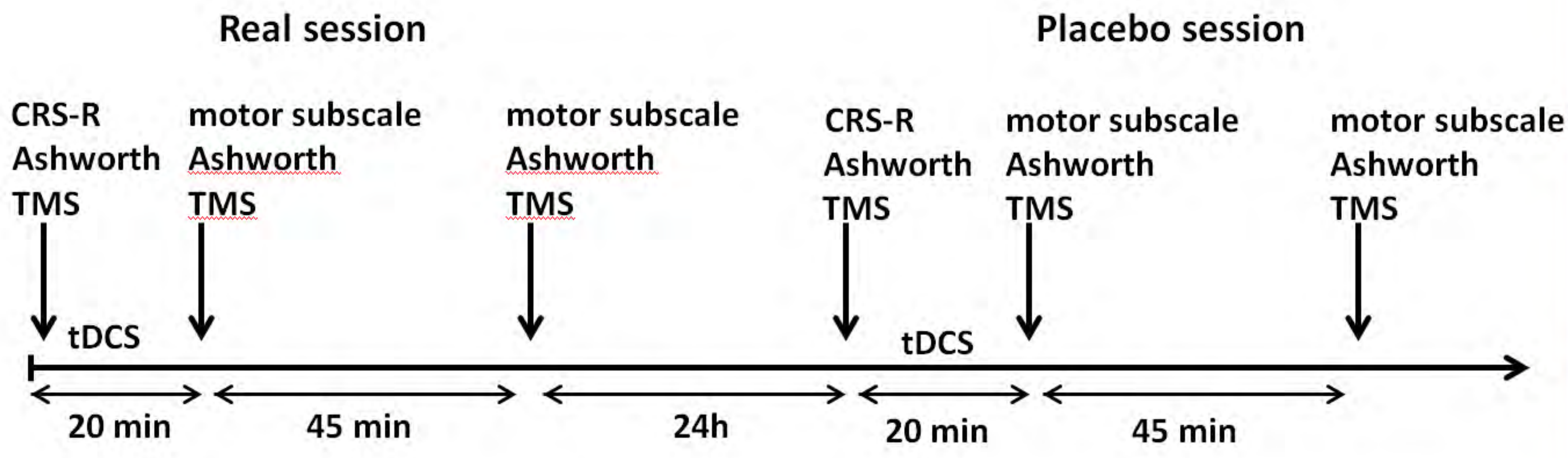
Anode: M1

Cathode: supraorbicular controlateral cortex

- 1. Behavioral assessments: **CRS-R** & **Ashworth**
- 2. **TMS**: MEP & motor threshold

Lang et al., 2004
Bohannon and Smith, 1987

tDCS – M1


Real session
Placebo session
CRS-R
Ashworth
TMS
motor subscale
Ashworth
TMS
motor subscale
Ashworth
TMS
CRS-R
Ashworth
TMS
motor subscale
Ashworth
TMS
motor subscale
Ashworth
TMS
tDCS
tDCS
20 min
45 min
24h
20 min
45 min

tDCS – neurophysiology

1. Comparison of the results with:

- cortical lesions (MRI)
- cerebral metabolism (PET-scan)

Stimulation of preserved or damaged cortex?

2. EEG brefore and after tDCS

Better understanding of neurophysiological effect of tDCS

Conclusion

tDCS improves **cognition** in minimally conscious state patients both acute and chronic; traumatic and non traumatic

Future studies:

1. long term tDCS
2. tDCS on M1
3. neurophysiological effects