Improvement of consciousness after transcranial direct current stimulation - a sham-controlled double blind study

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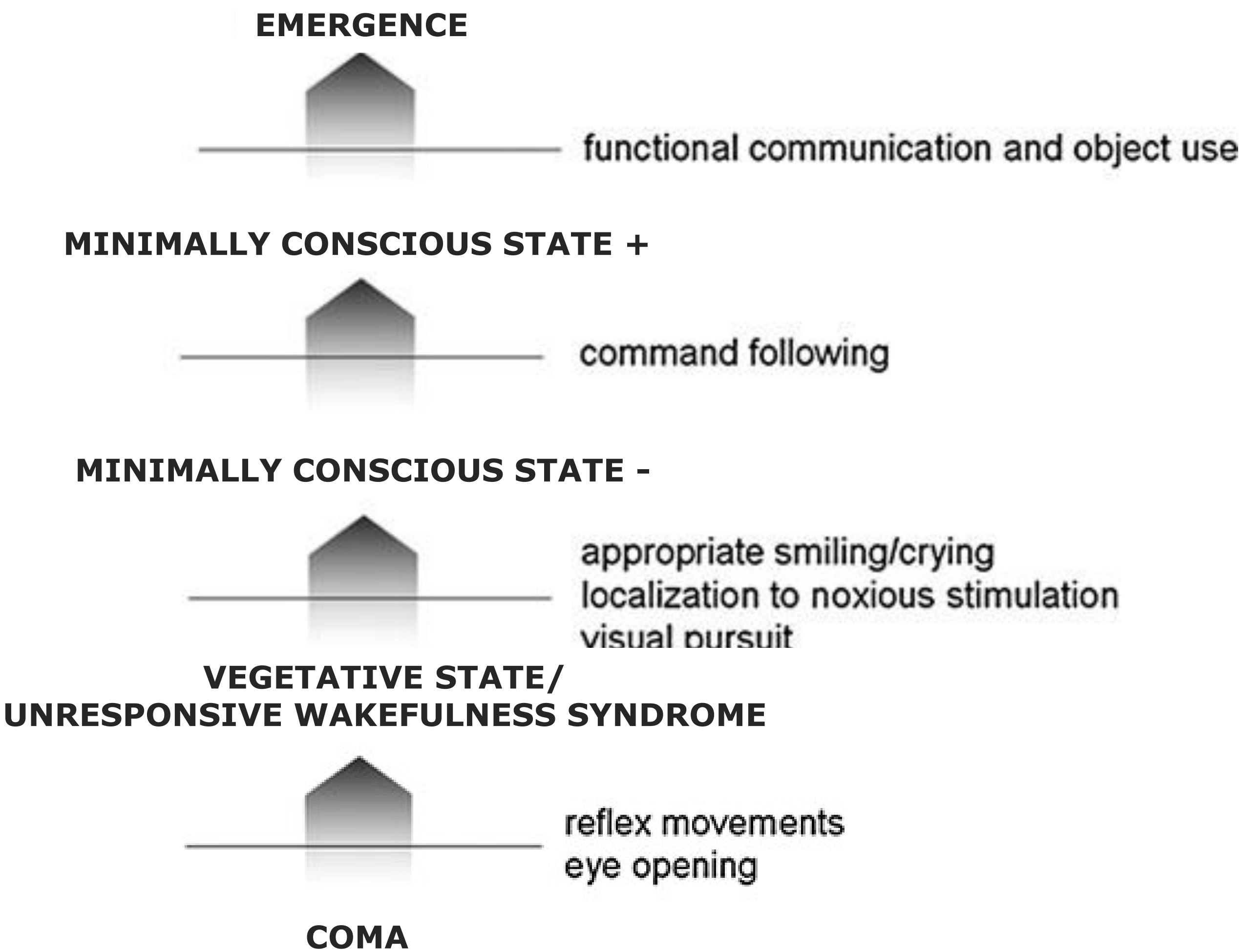
Patients



Laureys et al, *Nature Clinical Medicine, 2008*
Bruno & Vanhaudenhuyse et al, *Journal of Neurology,* 2011

Aim of the study

Assessing the effect of transcranial direct current stimulation (**tDCS)** on consciousness in VS/UWS and MCS patients

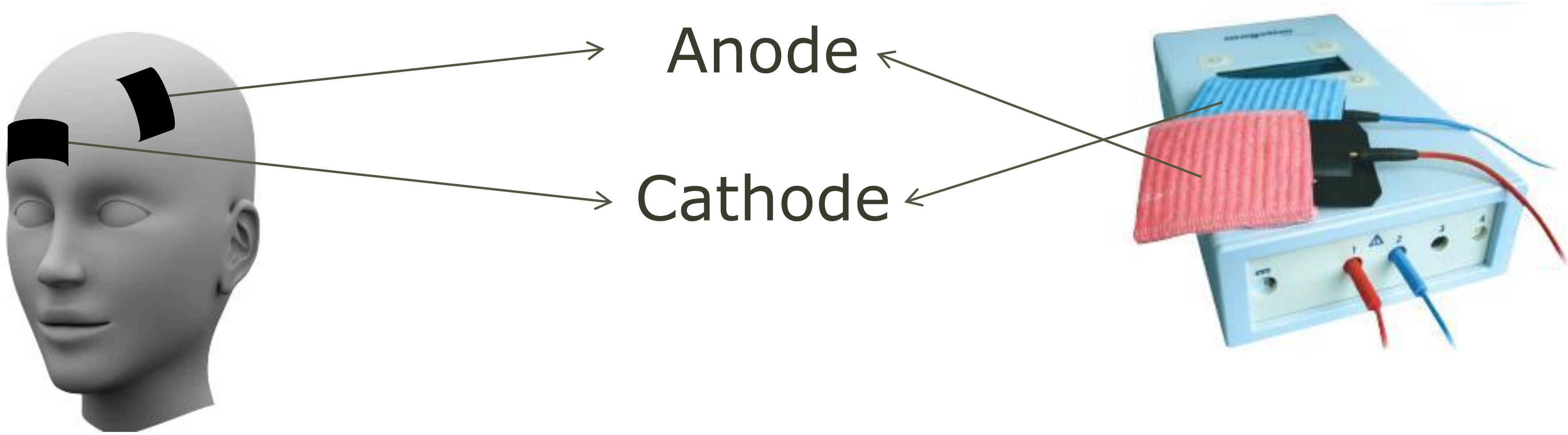
double blind sham controlled randomized study

Why direct current stimulation?

Stimulation	Population	Effects	Authors
Prefrontal cortex	Healthy subjects	Memory	Marshall et al, *J Neurosci* 2004
	Alzheimer's disease	Memory	Ferrucci et al, *Neurology* 2008
	Stroke	Attention	Jo et al, *Am J Phys Med* Rehabil 2009
	Aphasia	Language	Baker et al, *Stroke* 2010

- Non-invasive
- Easy to apply

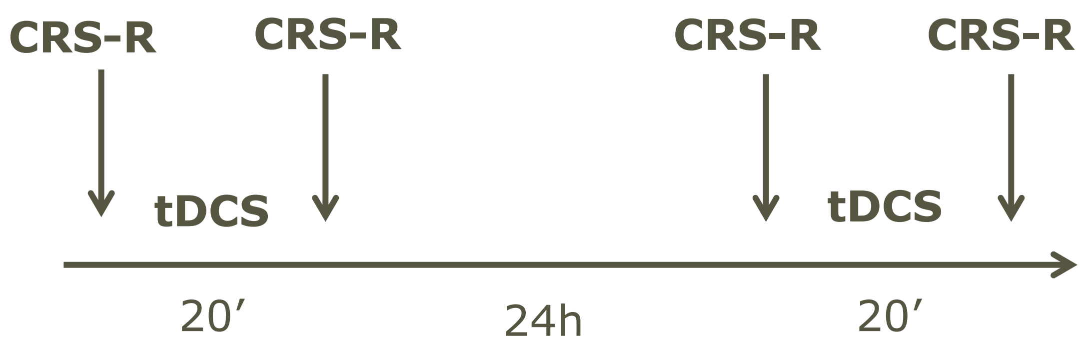
Methods



- Direct current
- 2 mA
- 20 minutes

Randomized
double blind
sham/placebo
controlled

Methods



Responders : CRS-R total score post tDCS > pre-tDCS

> sham

> pre-sham

Statistics: Stata 10.0

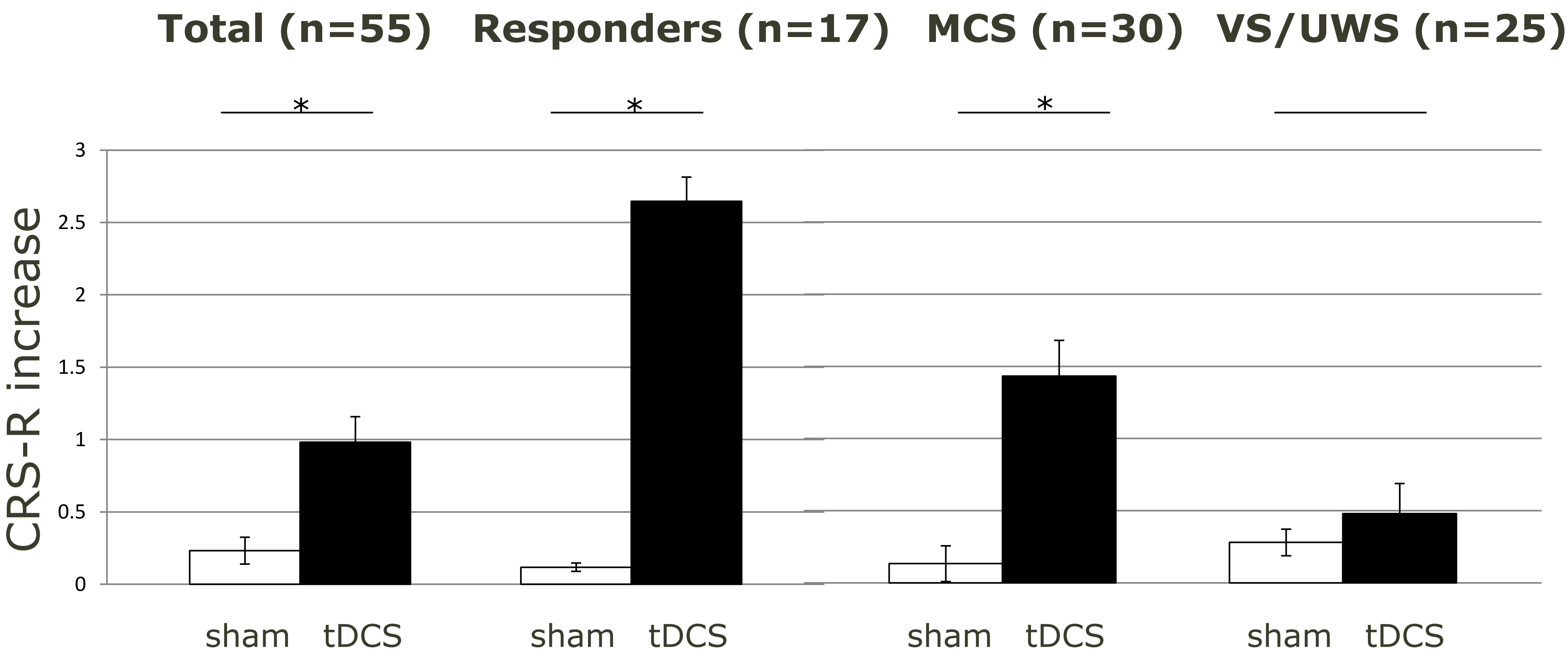
ANOVA

Wilcoxon signed-rank test

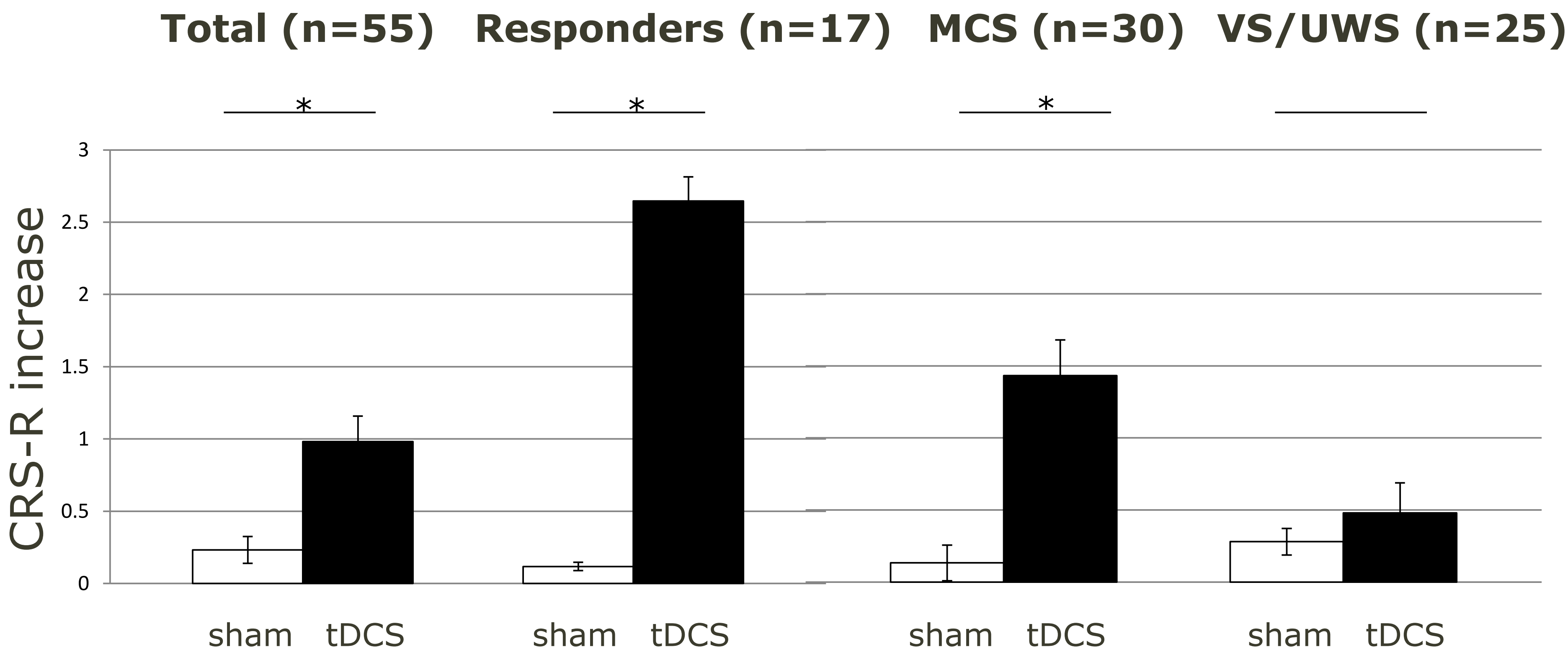
Population

- 55 patients (16 women)
- 25 VS/UWS, 30 MCS (18 MCS-/12MCS+)
- aged 43 ± 18 y
- 25 traumatic/30 non-traumatic
- 20 acute/35 chronic (>3 months post insult)

Effect of tDCS



Effect of tDCS



No effect of ethiology or chronicity

Observed improvements

17 responders

⇨ Response to command (n=7)

Visual pursuit (n=4)

Object manipulation (n=3)

Functional communication (n=3)

Conclusion

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

THANK YOU!

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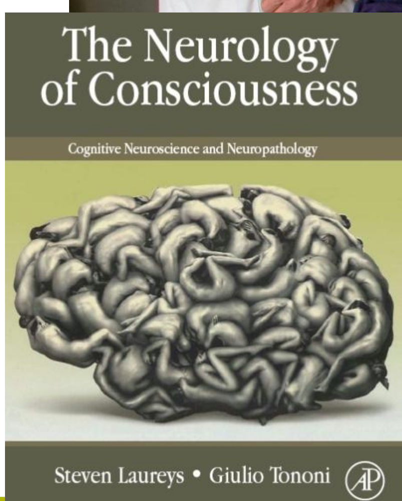

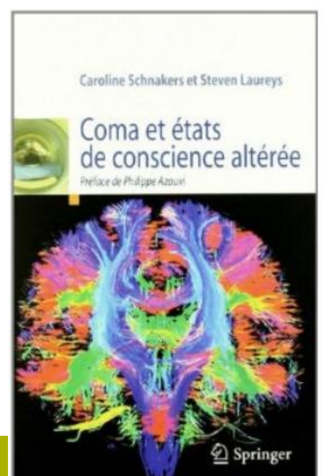

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Responders

25 VS/UWS → 2 responders

2/11 VS/UWS acute

0/14 VS/UWS chronic

30 MCS → 15 responders

7/9 acute

8/21 chronic

Neuroimagery

Prefrontal stimulation

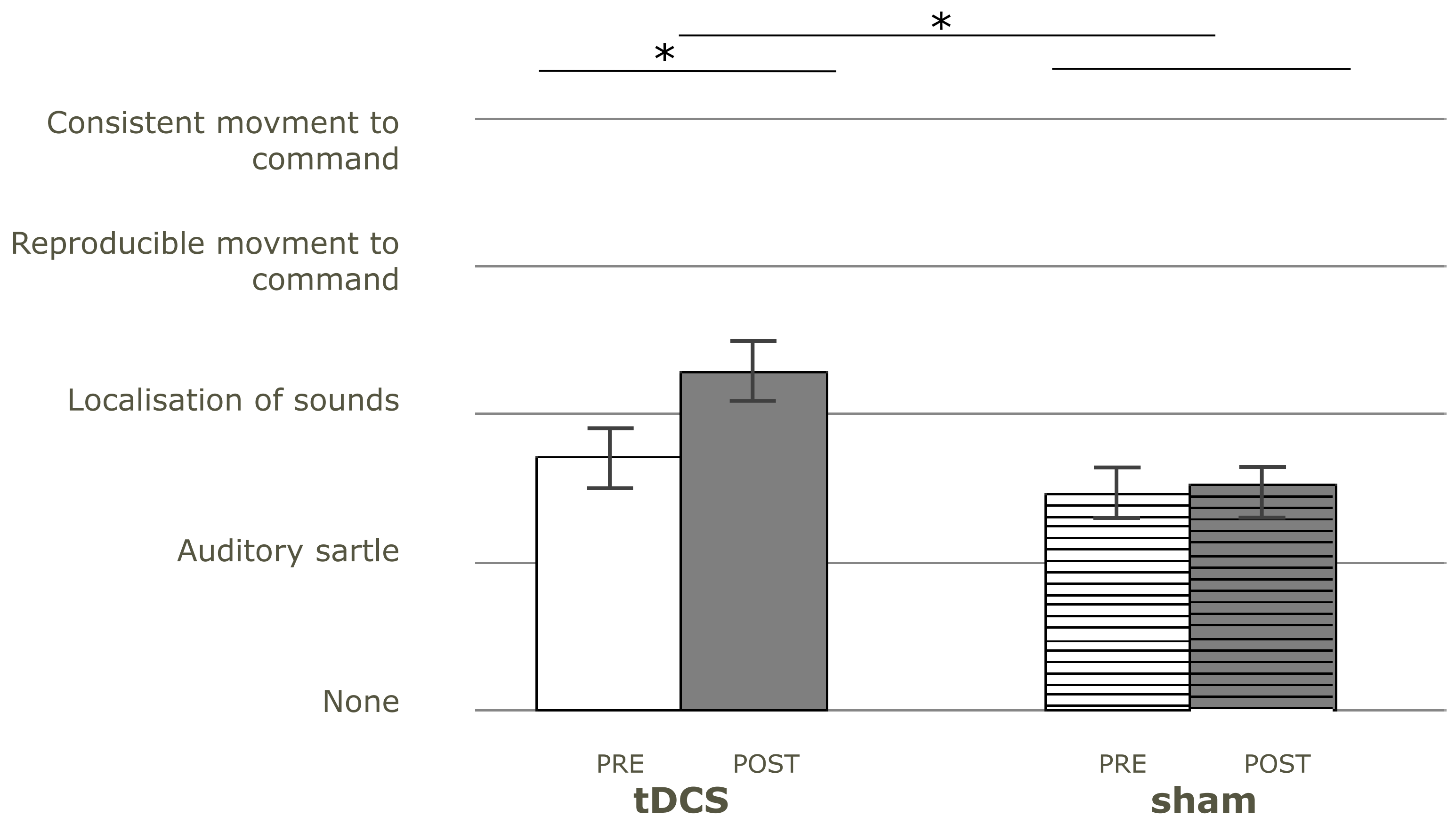
- Improvement of DMN connectivity (MRI)
- Increase of regional electrical activity in the PF and AC cortexes (EEG) (↗ ß and ↘ δ/θ)

Motor stimulation

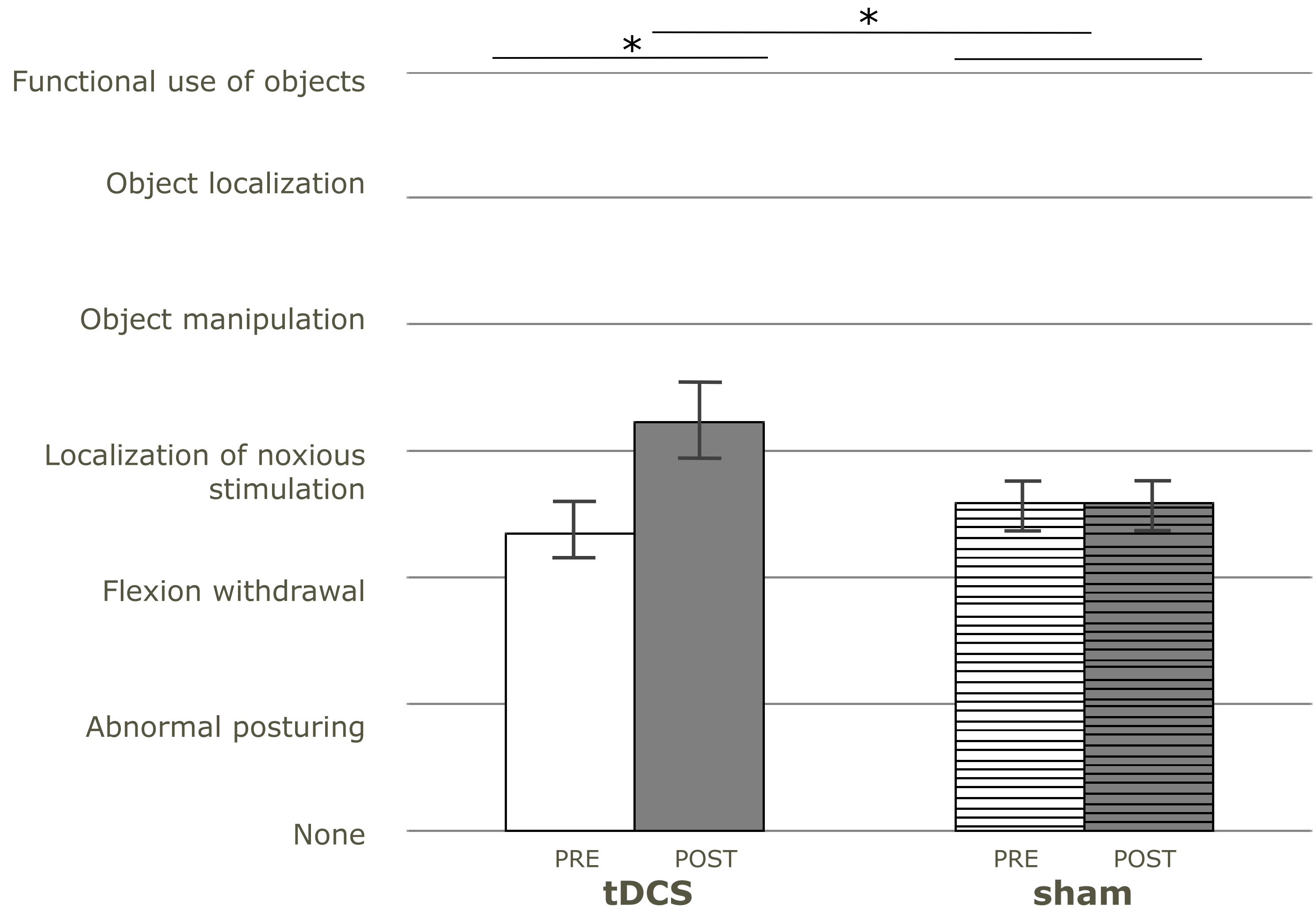
- rCBF increase in the left M1, right prefrontal cortex, right S1 (PET-scan)
- Functional connectivity increased within premotor, motor and sensorimotor areas (EEG)

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

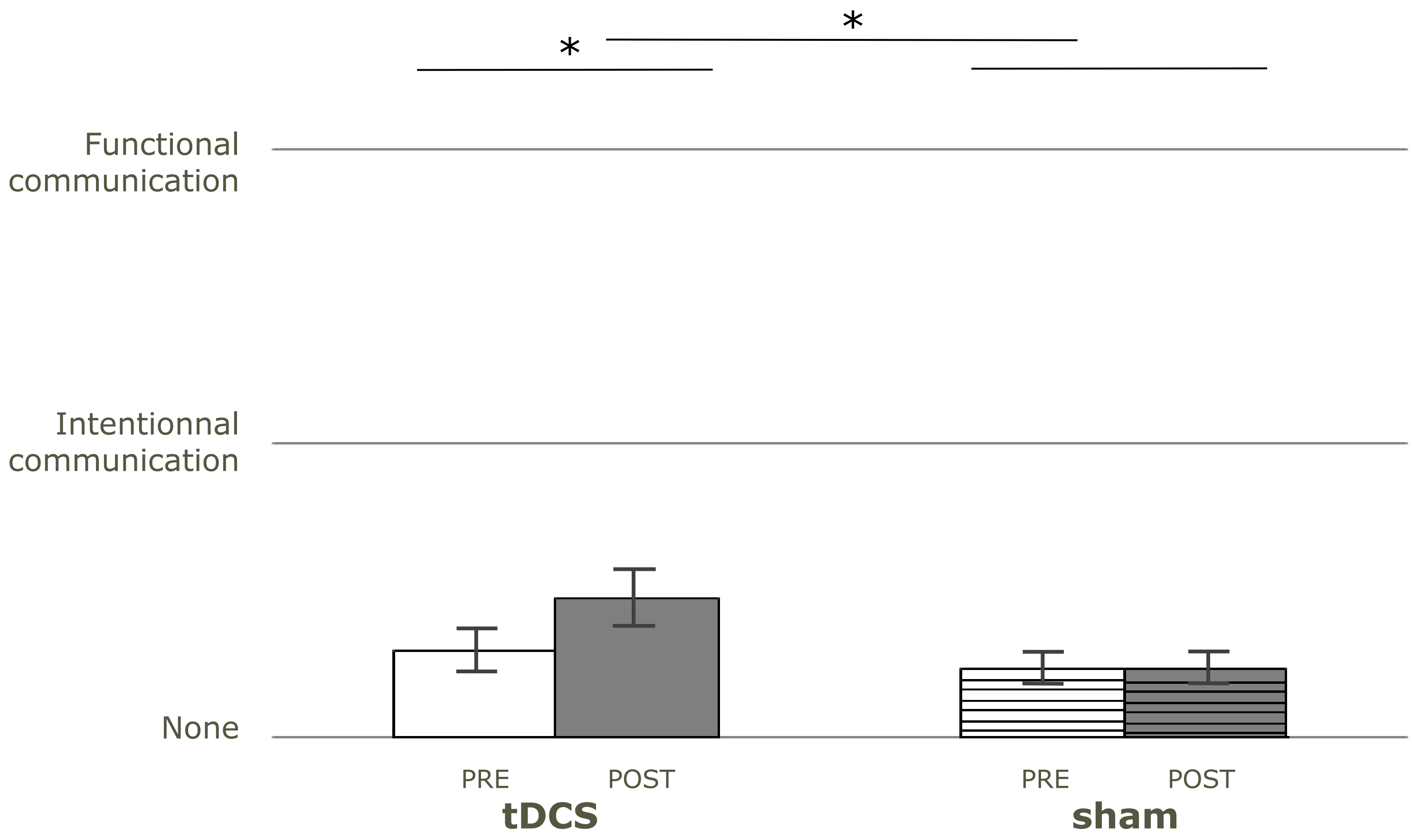
Responders: audition subscale



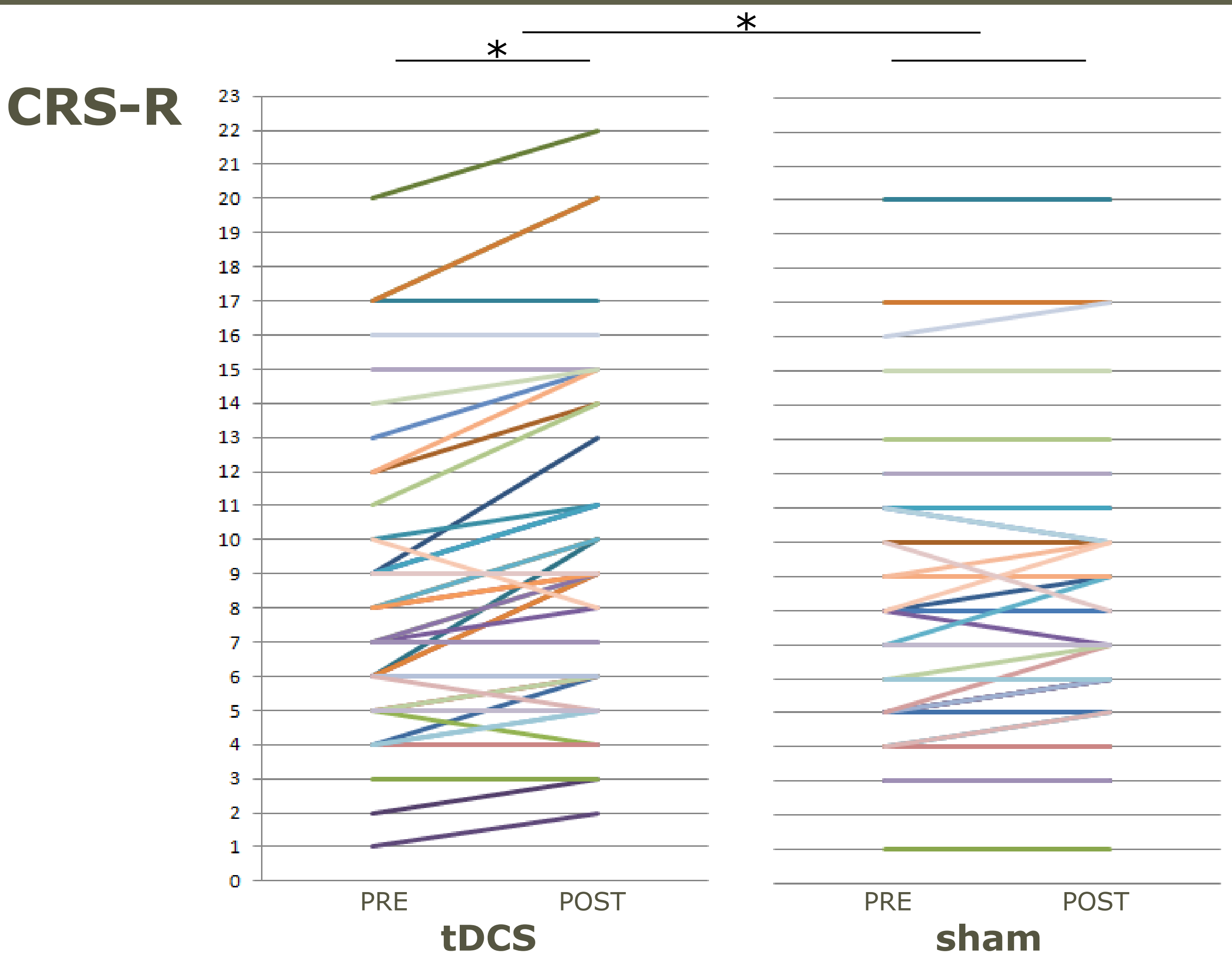
Responders: motor subscale



Responders: communication



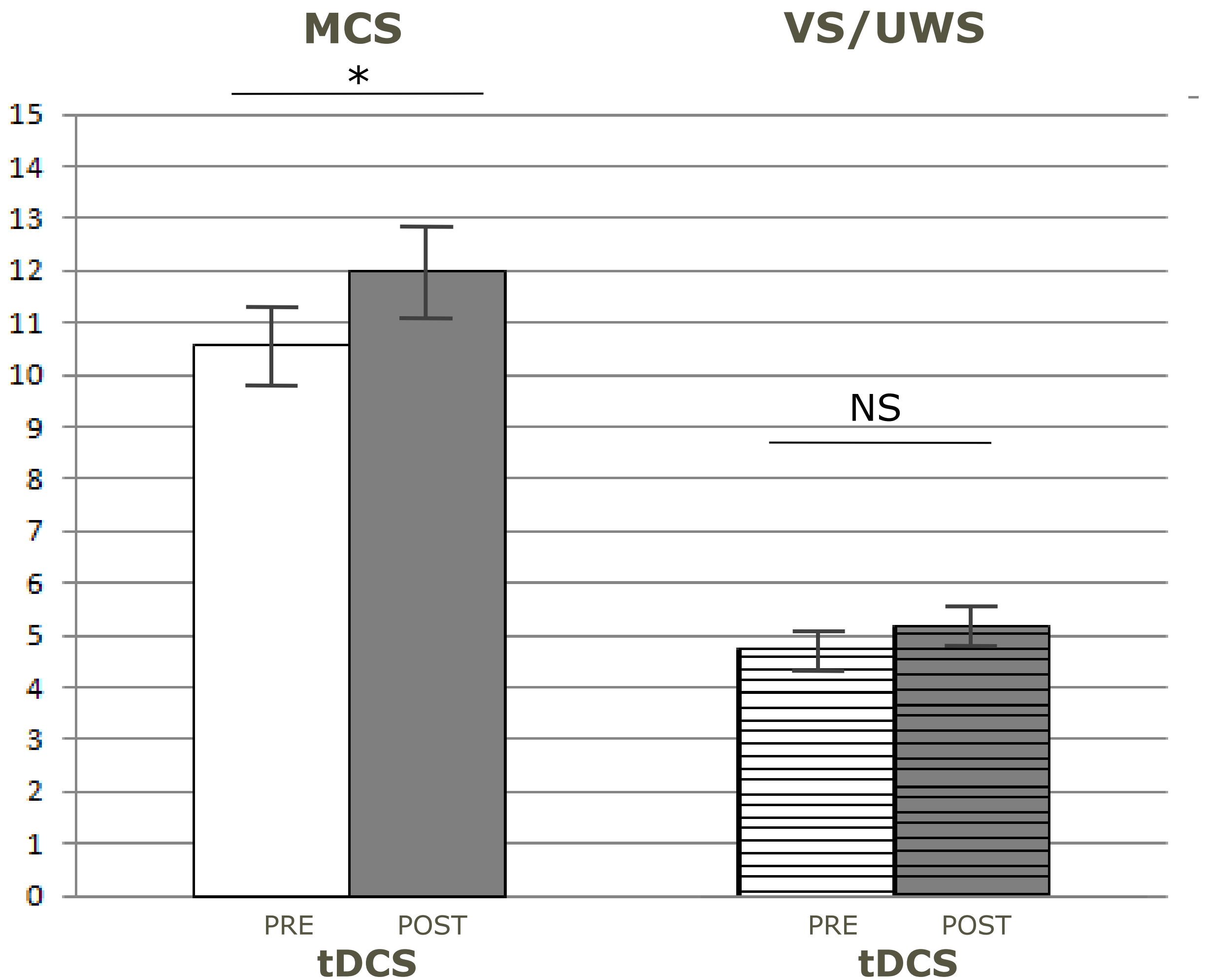
Group data (n=55)



17 responders

- 2 VS/UWS; acute
- 15 MCS; 7acute/8chronic

VS/UWS vs MCS


MCS
*
VS/UWS
NS
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
PRE
POST
tDCS
PRE
POST
tDCS

Status improvement

3 VS/UWS ⮚ MCS

- Visual pursuit (n=2)
- Response to command (n=3)

3 MCS ⮚ EXIT

- Functional communication (n=3)
- Functional use of objects (n=1)

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

tDCS – advantages

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

But side effects

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 change
- Unknown physiological effects (cathode)
- Improve electrode position?

tDCS parameters and safety

Intensity: 2mA

Time: 20 minutes

Voltage: max 26V

Electrodes: 35cm²

Max: 0.1mA/cm²

U=R*I

2mA et 10kOhm
= 20V OK

2mA and 20kOhm
= 40V STOP