

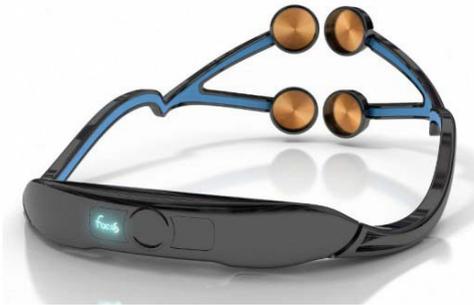
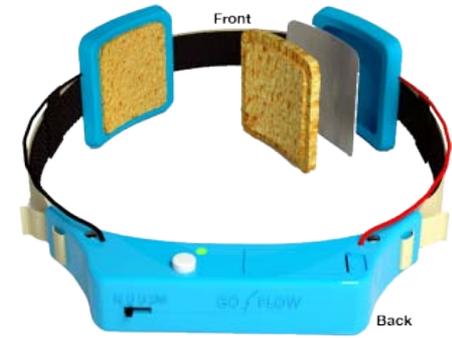
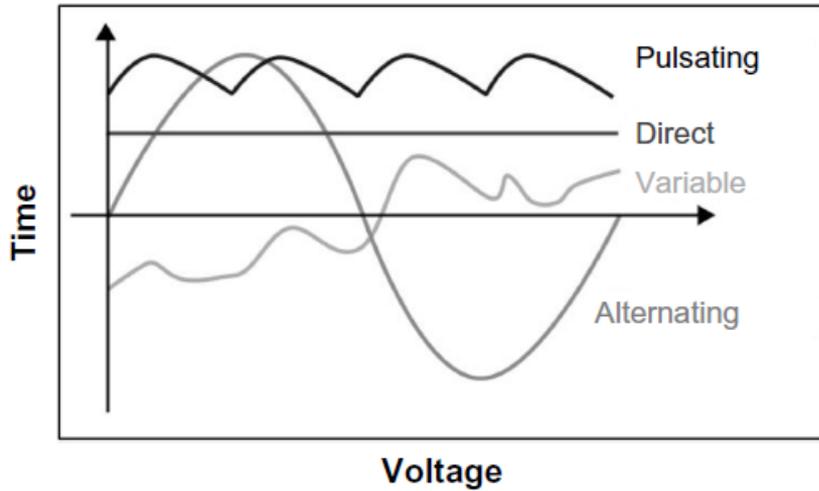


Trans-spinal direct current stimulation: a novel tool to promote plasticity in humans

Jean-Charles Lamy, PhD

Brain and Spine Institute, Paris

Background



the guardian
Warning: transcranial direct current stimulation can do your head in

People have been doing it for more than 100 years, but it turns out that zapping your brain with an electric current might not be too good for your IQ

Background: tDCS applied at the spinal cord level



Spinal DC stimulation / polarization
Trans-spinal DC stimulation
Transcutaneous spinal DC stimulation
tsDCS...

Transcutaneous Spinal Direct Current Stimulation (tsDCS)

J. Physiol. (1954) 126, 494-506

DIRECT CURRENT STIMULATION OF MOTONEURONES

By M. G. F. FUORTES

*From the Army Medical Service Graduate School,
Walter Reed Army Medical Center, Washington 12, D.C.*

1. The resting activity present in ventral roots of non-anaesthetized (spinal or decerebrate) cats is increased by constant currents flowing from root to cord and decreased by currents of opposite direction. These actions are limited to the fibres subjected to direct current stimulation, no effect being observed in neighbouring fibres.

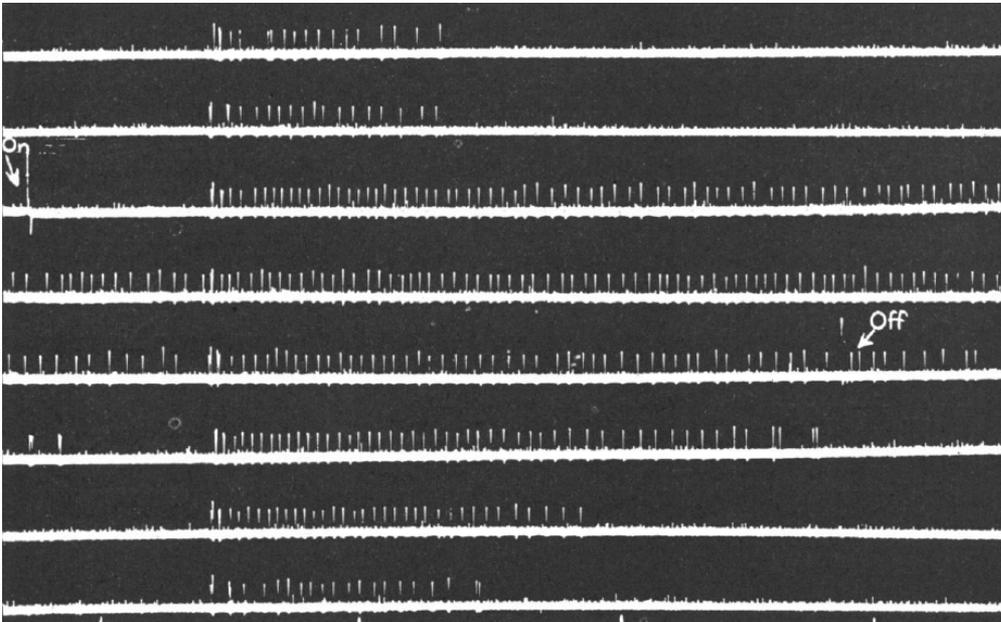
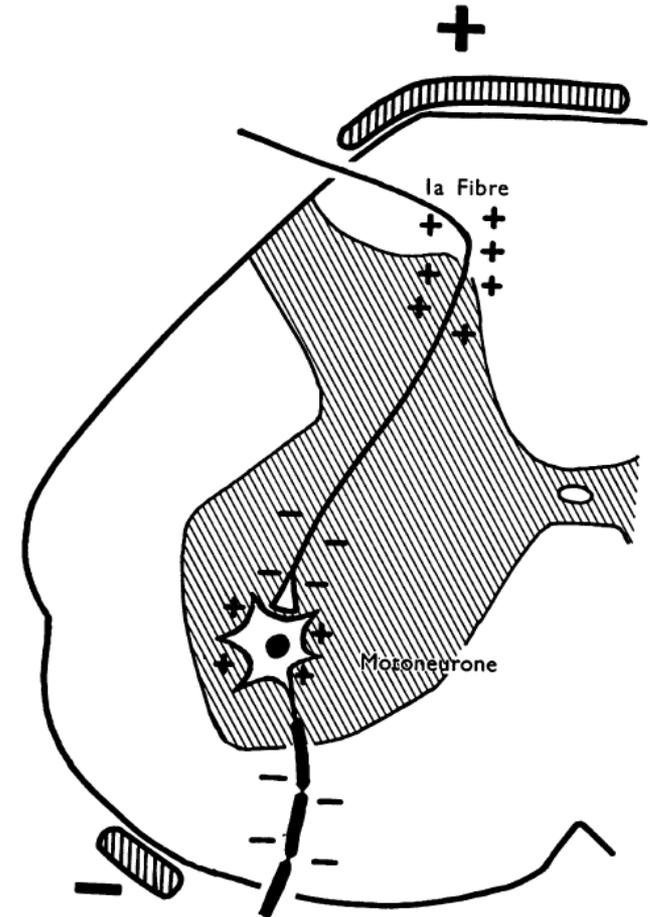
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*J. Physiol. (1962), 162, pp. 138-150
With 6 text-figures
Printed in Great Britain*

THE EFFECT OF ELECTRIC POLARIZATION OF THE SPINAL CORD ON CENTRAL AFFERENT FIBRES AND ON THEIR EXCITATORY SYNAPTIC ACTION

By J. C. ECCLES, P. G. KOSTYUK* AND R. F. SCHMIDT†

*From the Department of Physiology, The Australian National University,
Canberra, Australia*



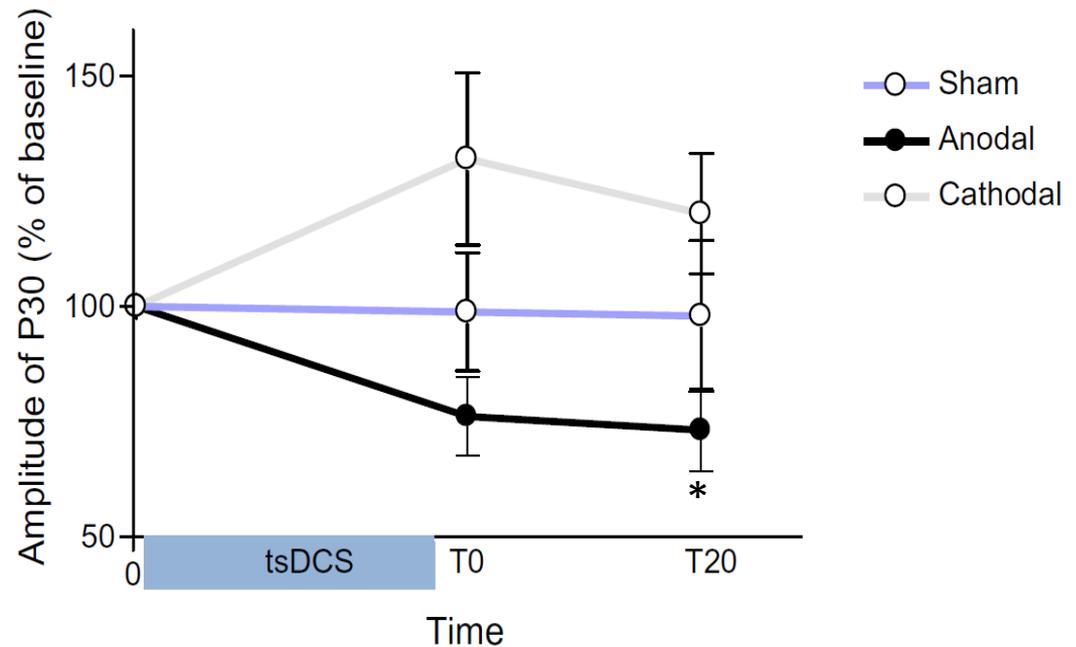
tsDCS and modulation of ascending pathways

Effect of spinal transcutaneous direct current stimulation on somatosensory evoked potentials in humans

Filippo Cogiamanian, Maurizio Vergari, Francesca Pulecchi, Sara Marceglia, Alberto Priori*

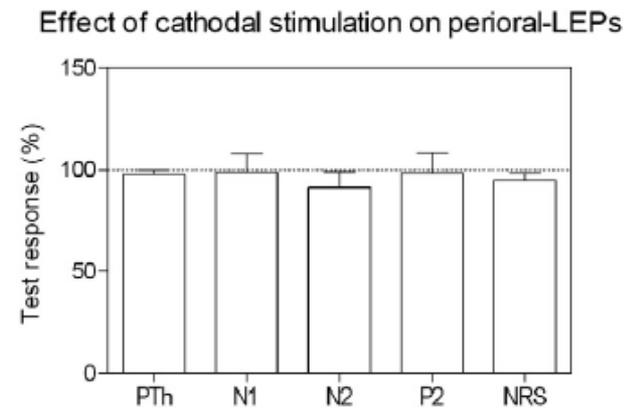
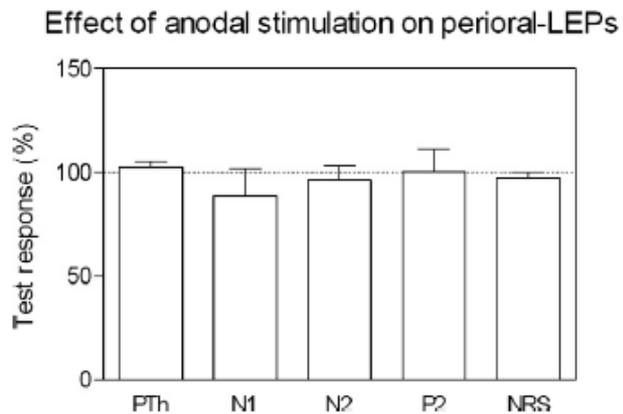
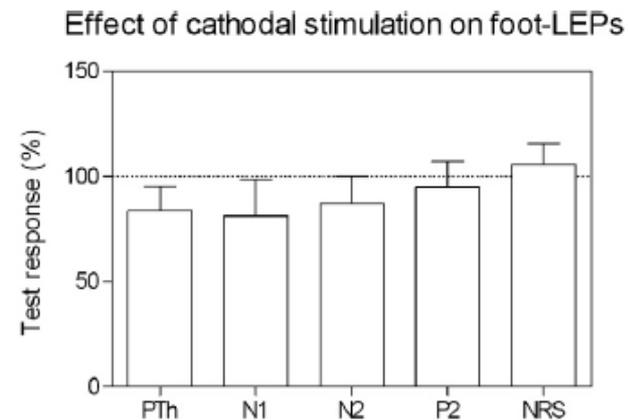
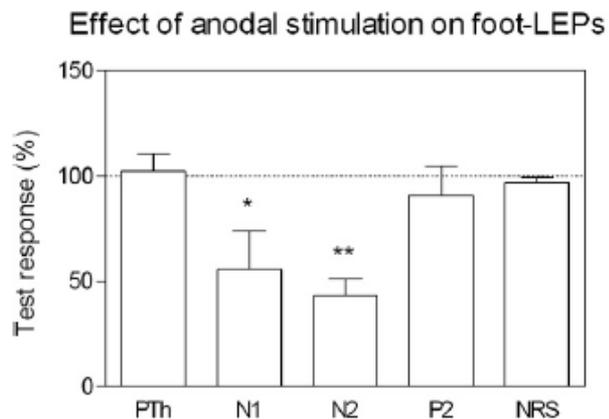
Dipartimento di Scienze Neurologiche, Università di Milano, Fondazione IRCCS, Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Padiglione Ponti, Via F. Sforza 35, Milano 20122, Italy

- **Lemniscal pathway:**
 - A-tsDCS decreases the amplitude of the posterior tibial nerve SEPs (P30)
 - C-tsDCS tends to increase it
 - Median nerve SEPs unchanged



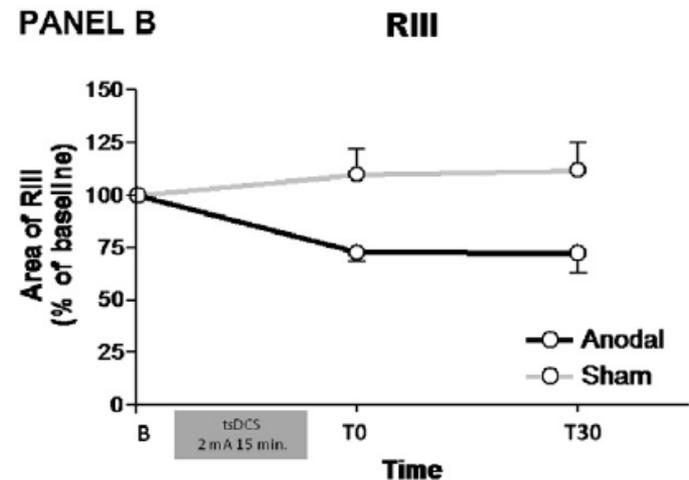
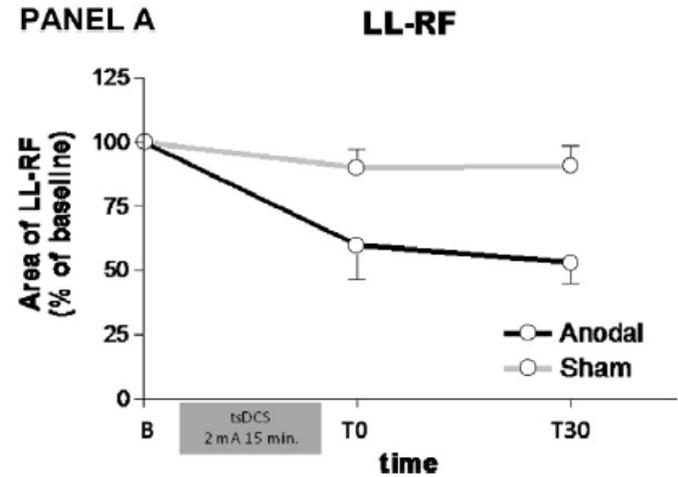
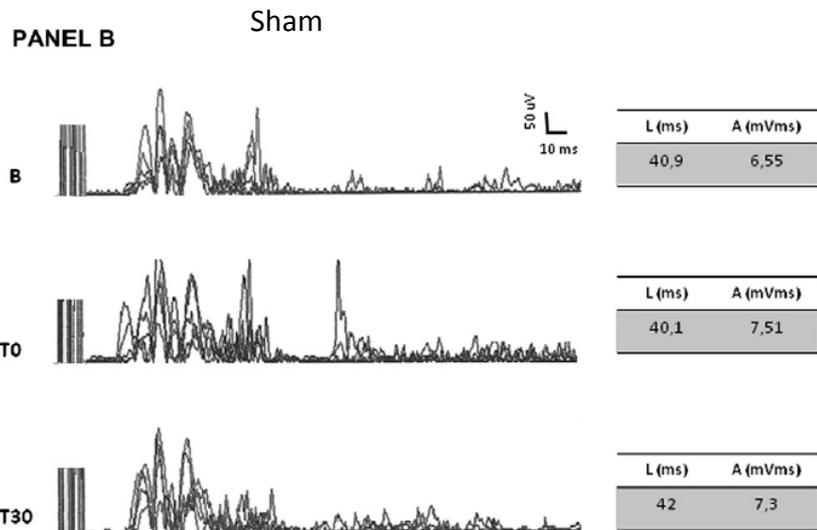
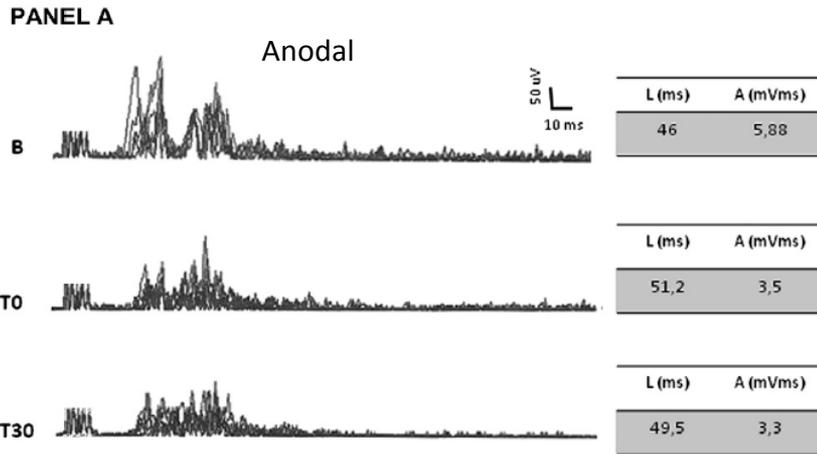
tsDCS and modulation of ascending pathways

- **Nociceptive pathway:**
 - A-tsDCS decreases the amplitude of the N1 and N2 components of foot LEPs but not of the face LEPs
 - A-tsDCS improves the pain tolerance
 - No effects of cathodal tsDCS



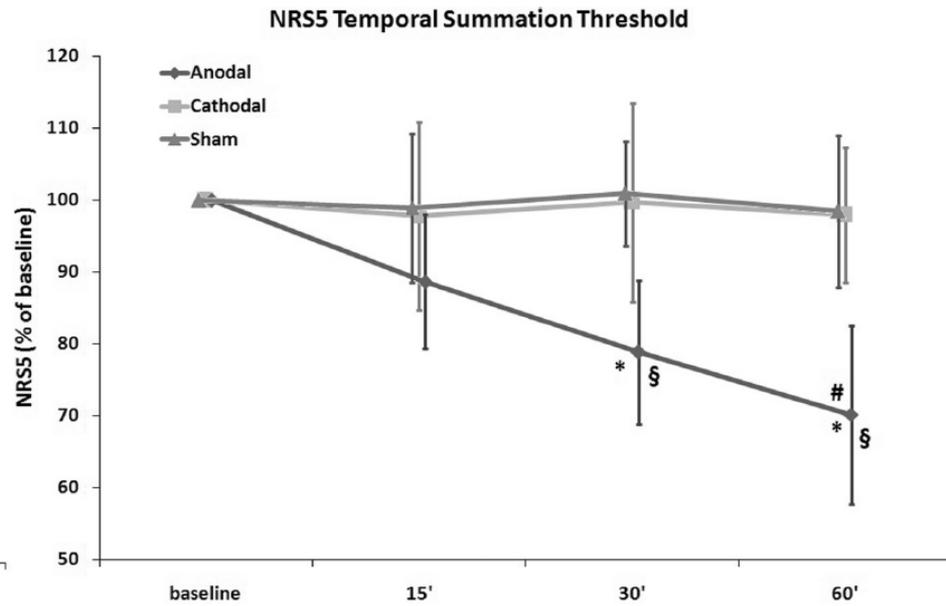
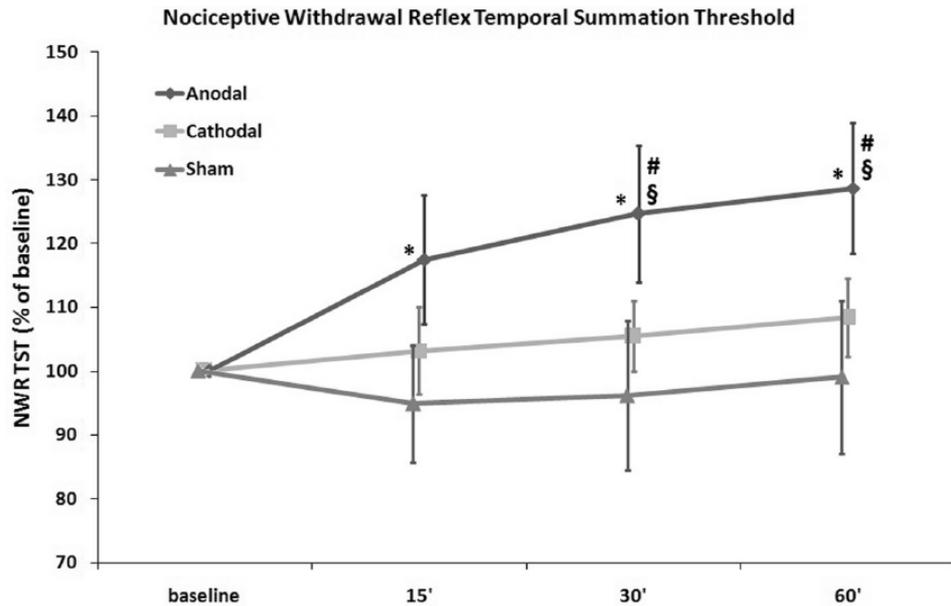
tsDCS and spinal reflexes

- Lower limb nociceptive flexion reflex:
 - A-tsDCS decreases the lower-limb flexion reflex area
 - The RIII component (nociception) tends to be more affected



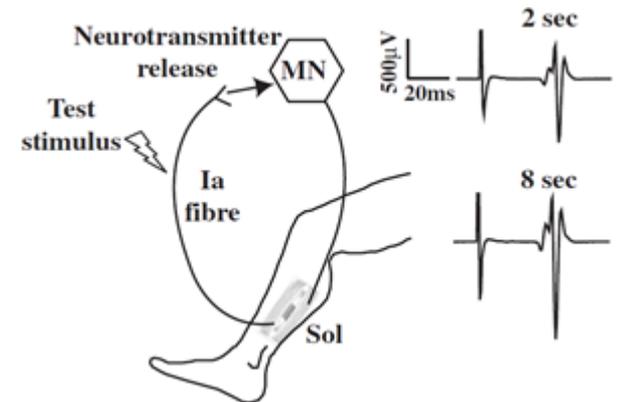
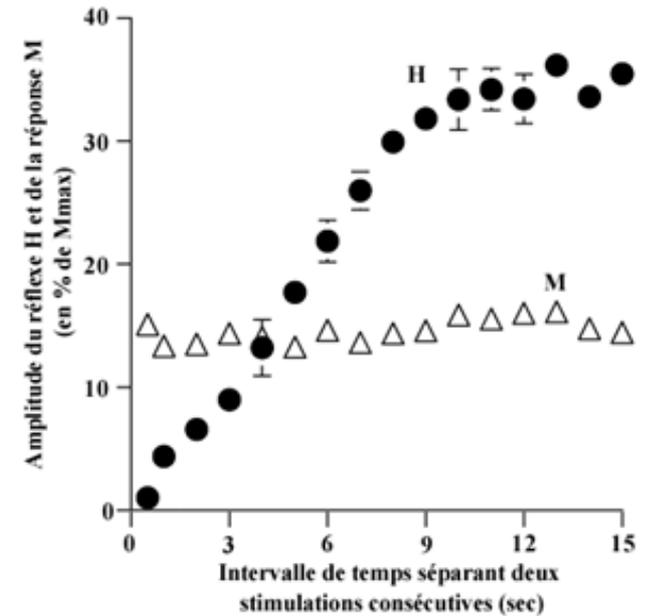
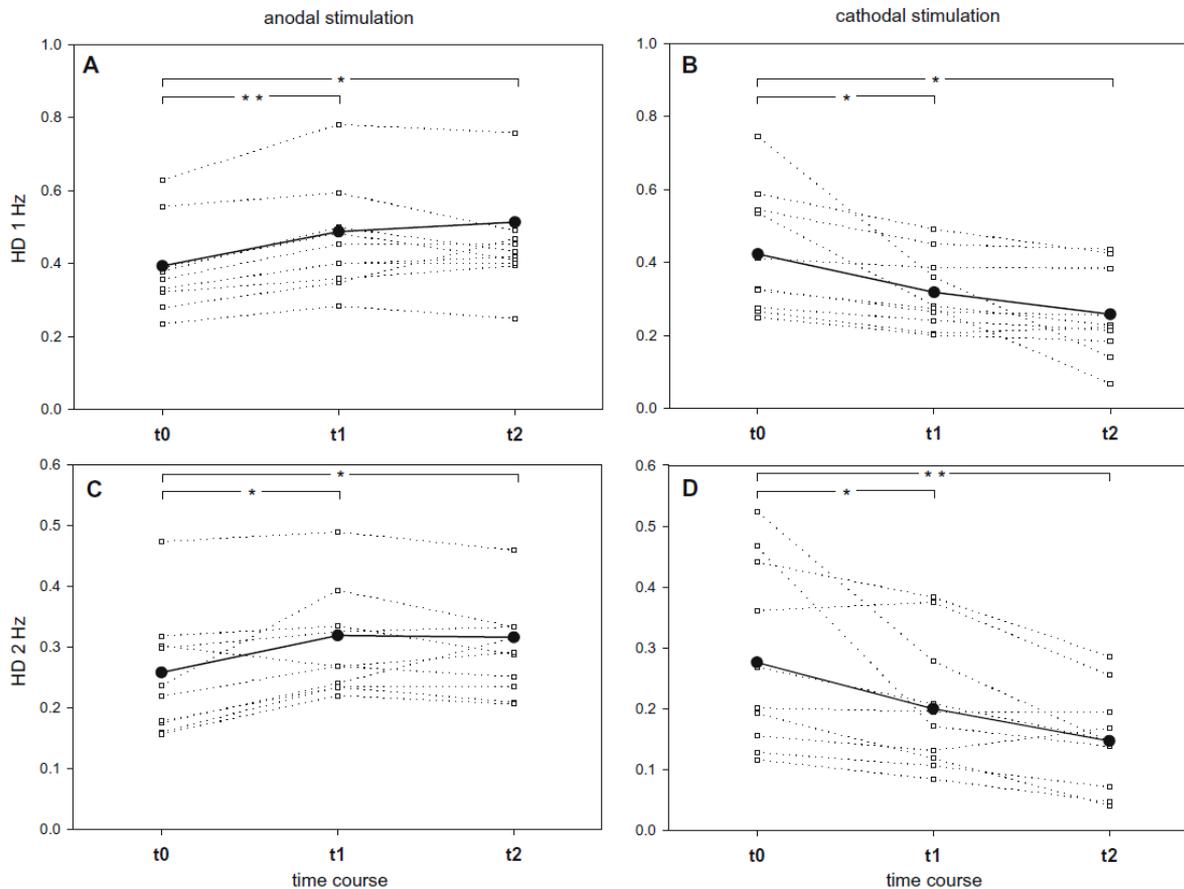
tsDCS and spinal reflexes

- **Nociceptive spinal pathway:**
 - A-tsDCS induces long lasting increase (>1h) in threshold of the nociceptive withdrawal reflex
 - A-tsDCS also improves psychophysical temporal summation of pain
 - No effects of S-TsDCS or C-tsDCS



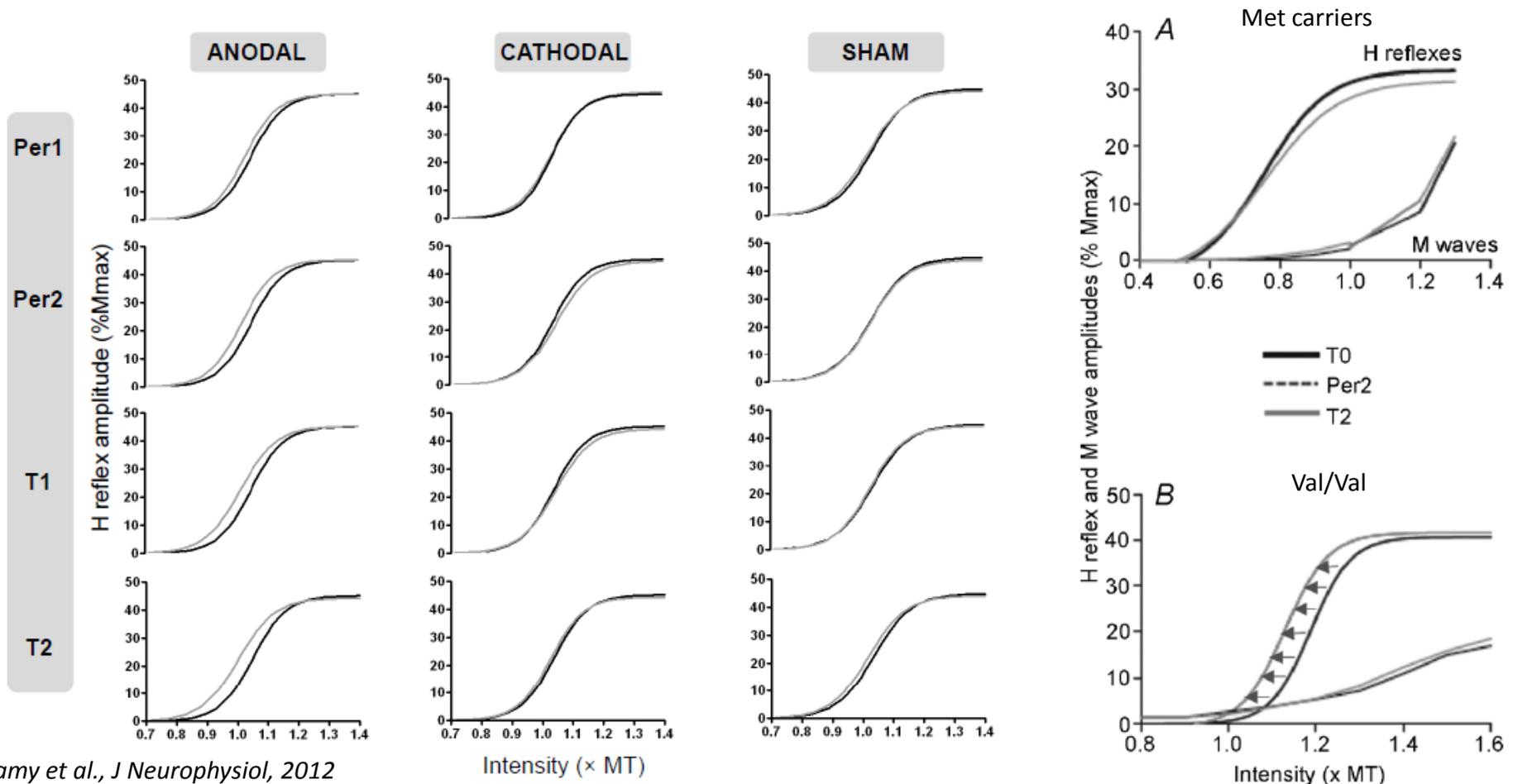
tsDCS and spinal reflexes

- Post-activation depression of the H reflex:
 - A-tsDCS decreases post-activation depression
 - C-tsDCS increases post-activation depression
 - Hmax/Mmax ratio remains unchanged



tsDCS and spinal reflexes

- I/O curve of the H reflex:
 - A-tsDCS induces a leftward shift of the I/O curve of the Sol H reflex
 - No effect of C-tsDCS and S-tsDCS
 - This shift is impacted by the BDNF Val66Met polymorphism



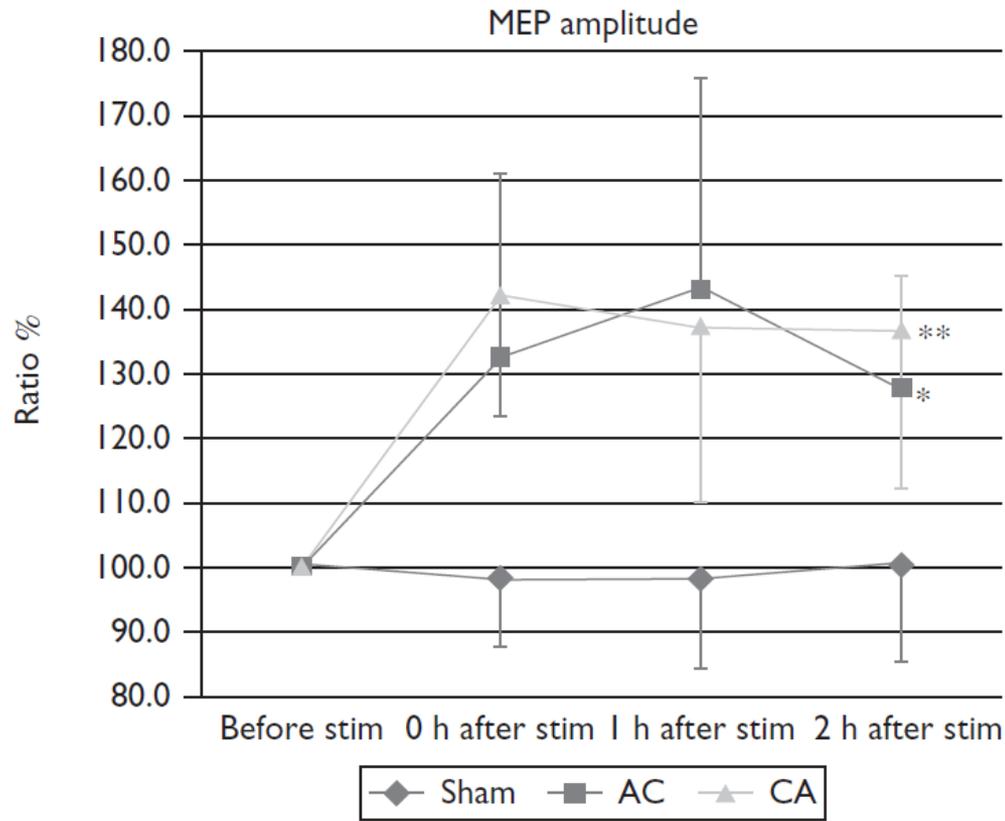
Lamy et al., *J Neurophysiol*, 2012

Lamy and Boakye, *J Neurophysiol*, 2013

tsDCS and motor pathways

- Corticospinal pathway:

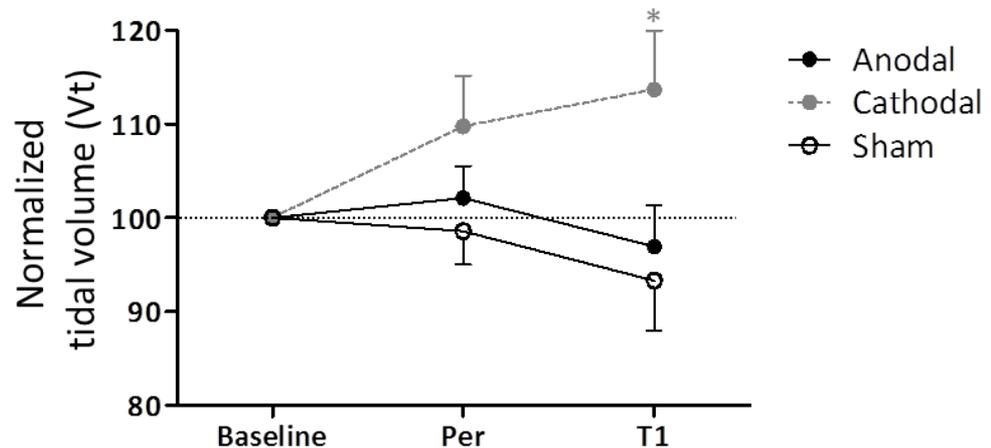
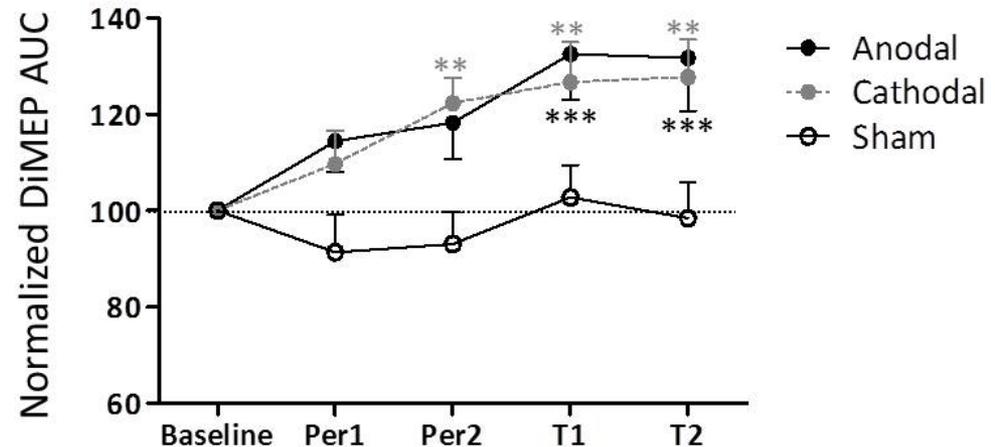
- Both A-tsDCS and C-tsDCS increases the amplitude of MEP in the FCR muscle
- No change in the FCR H reflex



tsDCS and motor pathways

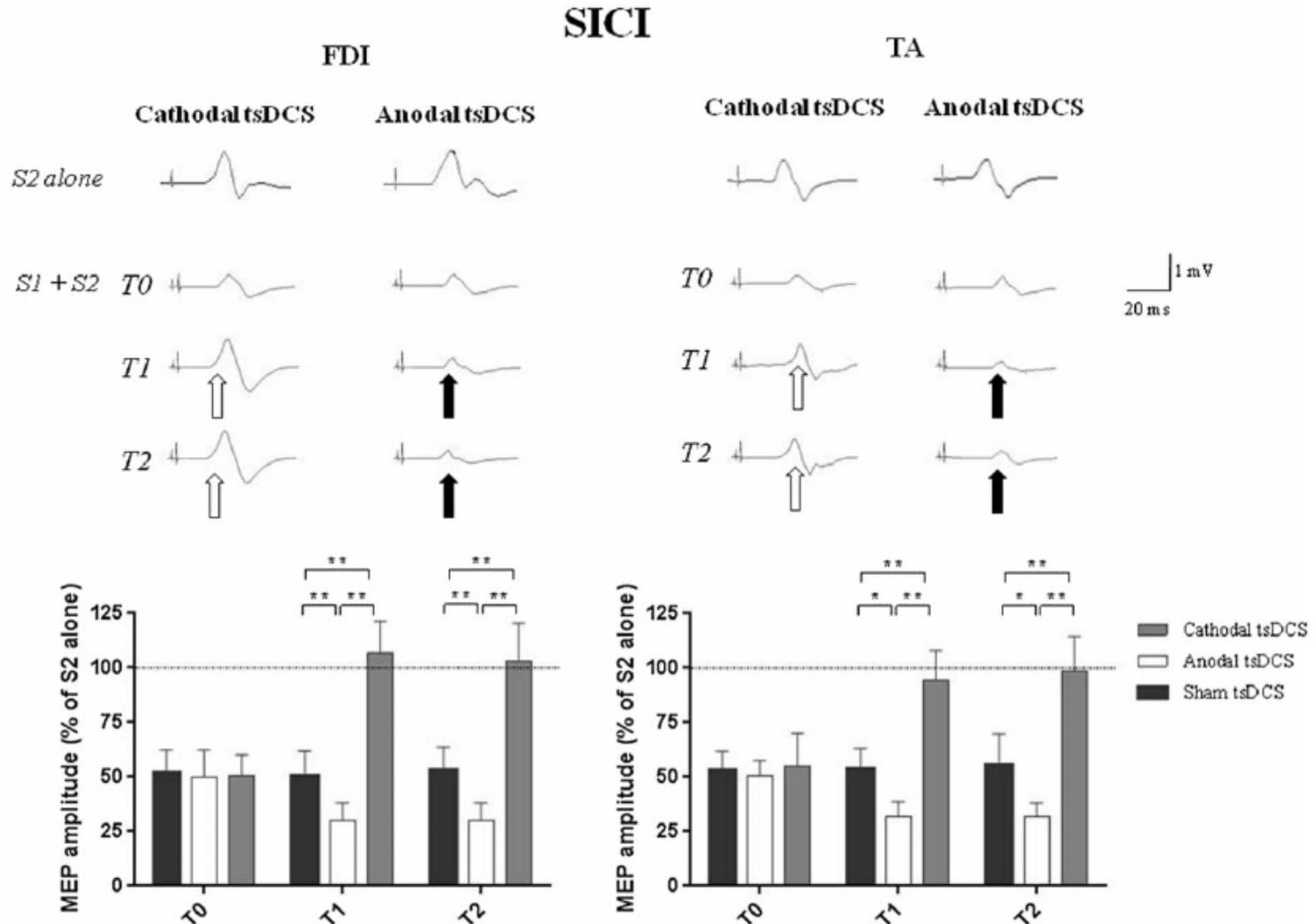
■ Cortico-diaphragmatic pathway:

- Both A-tsDCS and C-tsDCS increase the amplitude of Dia MEP (return electrode just below the cervicomental angle)
- C-tsDCS only increase the tidal volume (respiratory inductance plethysmography)
- No effect on sICI, ventral roots or autonomic functions...

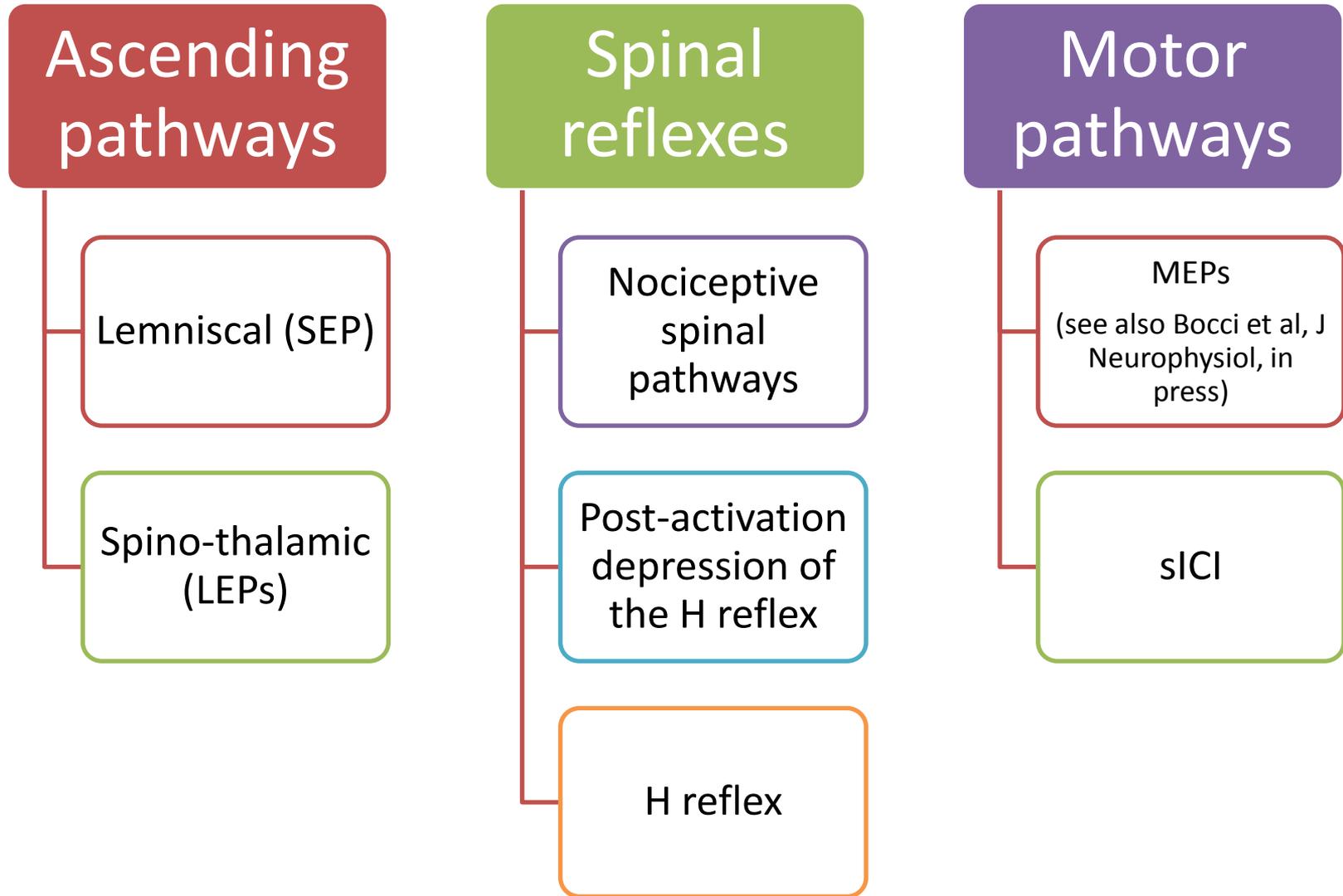


tsDCS and motor pathways

- **Intracortical excitability:**
 - A-tsDCS enhances sICI whereas C-tsDCS decreases it in both TA and FDI
 - No effect on ICF or cSP



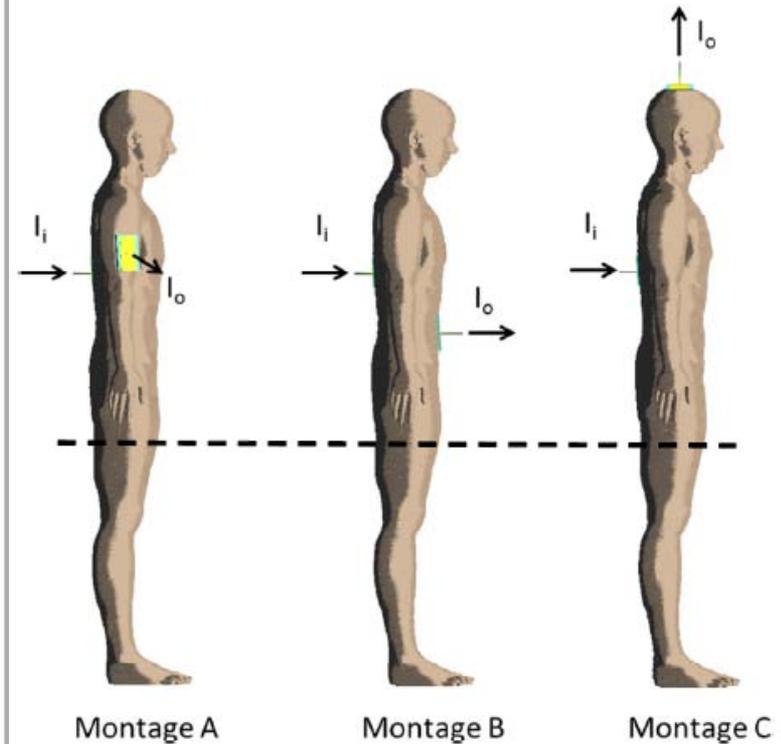
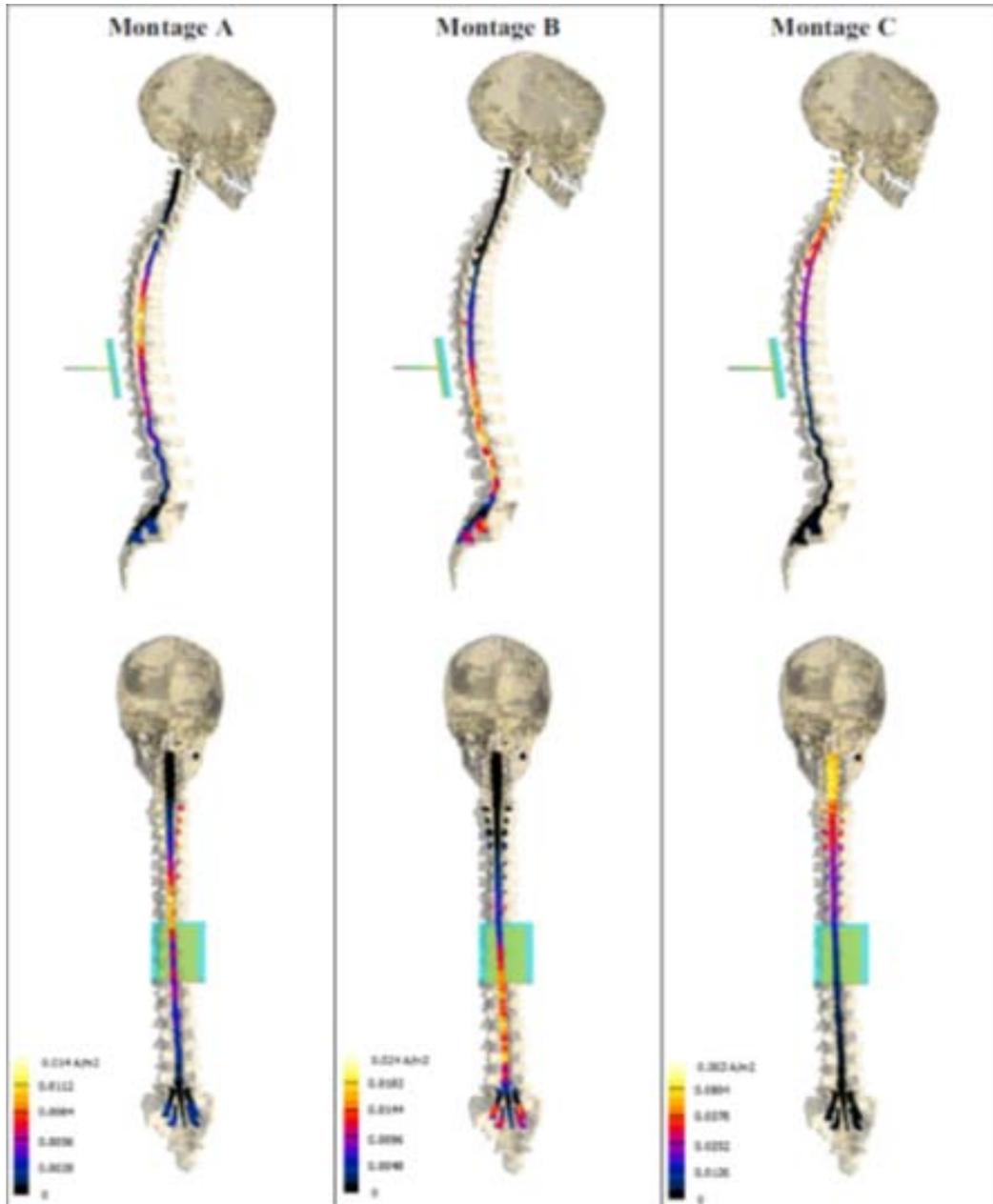
tsDCS in humans: summary



tsDCS: safety limits

- Not established yet
- No AE reported
- Serum «Neuron Specific Enolase», a marker a neuronal damage, is unchanged by tsDCS (*Cogiamanian et al., Clin Neurophysiol, 2008*)
- No exclusion criteria (except pacemaker, surgical clips, metal in the body...)
- Parameters used in tsDCS are closed to those of tDCS but what about current density?

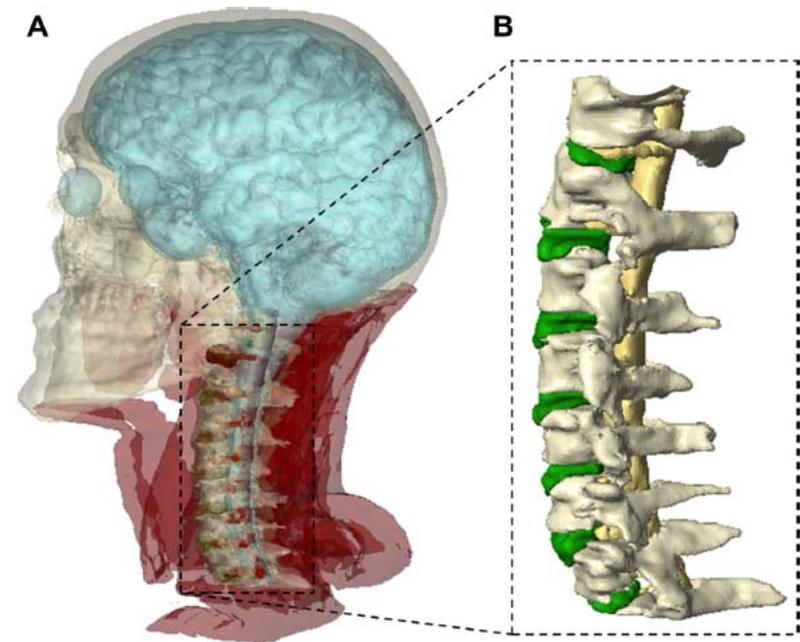
tsDCS: modeling of the current density using the FEM method



For cervical tsDCS see
Grecco et al., J Neurorestor, 2015

tsDCS: modeling of the current density using the FEM method

- Main conclusions made by the authors:
 - The current reaches the spinal cord in all montages
 - The current density is higher when the return electrode is placed over Cz.
 - The current spreads to trunk muscles but also to spinal nerves
- Limitations of the model: (Toshev and Bikson, Clin Neurophysiol 2014) :
 - Uniform model
 - Anisotropy of the white matter of the spinal cord is not considered
 - Likely more complex (anatomy, etc...)



tDCS ≠ tsDCS

■ Current density:

- The volume of the conductor surrounding the target tissue is much larger in the spinal cord than in the brain ==> dispersion of the current or reduction of its density (thoracic tsDCS)? The opposite for cervical tsDCS?
- On the opposite, it cannot be rule out that electric current could densified through the intervertebral foramina (*Winkler et al., Clin Neurophysiol, 2010*)

■ Electrodes:

- The distance between electrodes strongly differs between tDCS (few cms) and thoracic tsDCS (~ 50cms).
- This is likely critical since the distance between two electrodes correlated negatively with the duration and the magnitude of tDCS-induced aftereffects (*Moliatze et al., Clin Neurophysiol, 2010*).
- Location of the return electrode

■ Target neurons:

- Target neurons are ≠ ==> properties of neurons ≠

tDCS ≠ tsDCS

- Biophysical properties of membranes:

- DC stimulation modifies biophysical properties of neuronal membranes depending on the fiber orientation (*Creutzfeldt et al. , Exp Neurol, 1962*)
- It is likely that the different orientation of cortical and spinal fibers would result in a different polarization of neurons.

- Mecanisms:

- There are direct evidence from both animal and human studies that tDCS influences the spontaneous corticospinal cells firing rate by tonic de- or hyperpolarization of resting membrane potential, resulting in changed corticospinal drive onto motoneurons (*Lang et al., J Neurophysiol, 2011*).
- Data not available for tsDCS

==> tsDCS strongly differs from tDCS

How it works?

■ Hypotheses :

- Development of LTP/LTD-like plasticity?
- Change in the efficacy of NMDA receptors?
- Change in neurotransmission (GABA, Glu) ?
- Involve synaptic and non-synaptic mechanisms?
- Change in the intrinsic properties of motoneurons (a shift in motoneuron firing threshold, change in the afterhyperpolarization amplitudes, change in synaptic contacts on motoneurons or change in firing threshold of the axon... (*see Carp et al., Exp Brain Res, 2001; Wolpaw et Carp, Prog Neurobiol, 2006*)
- Change in the excitability of spinal networks acting at pre- or post-synaptic level (presynaptic Ia inhibition, reciprocal inhibition, recurrent inhibition...)

To summarize, same mechanisms than tDCS

■ The facts:

- tsdCS-induced plastic changes have a gradual development over the course of the intervention
- These changes outlast the stimulation period by at least 30min

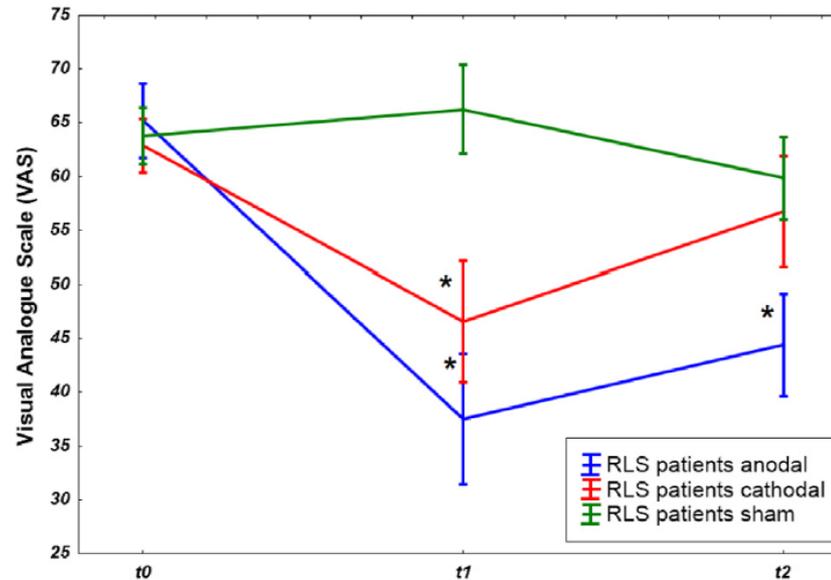
==> important need for further studies in animals

tsDCS: animal studies

Authors	Year	Sample/Animals	Lesioned	Polarity	Configuration	Parameters	Technique	Effects
Ascending pathway								
Aguilar <i>et al.</i>	2011	44	—	Anodal\cathodal	Active electrode on thoracic spinal cord Reference on anterior abdominal area	1 mA; 15 min; AEA = 0.79 cm ²	Somatosensory-evoked potentials	A-spinal tDCS increased spontaneous activity in the gracile nucleus while decreasing its local field potential responses to somatosensory stimuli; C-spinal tDCS did the opposite
Descending pathways and spinal reflexes								
Ahmed	2011	33	—	Anodal\cathodal	Active electrode at T10–L1 Reference on lateral abdominal muscles	From 0.5 mA to 3 mA for 3 min; AEA = 0.79 cm ²	Spontaneous activity recording and repetitive cortical electrical stimulation (rCES)	A-spinal tDCS increased the spike frequency and the amplitude of spontaneous discharges; C-spinal tDCS + rCES increased cortical-elicited muscle twitches
Ahmed & Wieraszko	2012	87	Contusive and hemisectioned mice	Anodal\cathodal	Active electrode at T10–L1 Reference on lateral abdominal muscles	2 mA; 5 s; AEA = 0.79 cm ²	Cortically elicited muscle actions and low-frequency repetitive cortical stimulation (rCS) Repetitive spinal stimulation (rSS) for in vitro glutamate analog release evaluation	Combination of C-spinal tDCS/rCS enhanced spinal cord responses in control and SCI animals; C-spinal tDCS/rSS released the maximum amount of glutamate
Ahmed	2013B	116	Unilateral SCI	Cathodal	Active electrode at T13–L4 (spinal level L3–L6) Reference on abdominal skin flap	0.8 mA; different durations; AEA = 3.5 cm ²	Spino-Sciatic (SSA) and Cortico-Sciatic (CSA) associative plasticity	C-spinal tDCS + SSA or CSA is able to increase associative plasticity in healthy animals and to improve recovery from unilateral SCI
Ahmed	2013A	30	—	Cathodal	Active electrode on lumbar enlargement area Reference on abdominal skin flap	0.8 mA; 8 s; AEA = 3.5 cm ²	Spinal network and complex multijoint movements	C-spinal tDCS modulates the kinematics of elicited movements and bursting activity in spinal circuitries

tsDCS and clinical implications

- Few data are currently available:
 - Both A-tDCS et C-tsDCS improve restless legs syndrome (visual analog scale) (*Heide et al., Brain Stimulation, 2014*)



- Improvement of pain in spinal cord injury (VAS) (*Hubli et al., Clin Neurophysiol, 2013*)
- Possibility to modulate muscle tone in healthy animals but also in animals with spinal cord injury (*Ahmed, J Neurosci, 2014*)
- Improvement of motor recovery, when paired with cortical stimulation, in a model of animals with unilateral SCI (*Ahmed, J Neurosci, 2013*)

Conclusion

- New tool to promote spinal and supraspinal plasticity
- Inexpensive, few exclusion criteria, no AE
- Easy to use
- This technique shows good promise (strong increase in the number of publications the past months, several patents...)

BUT

- Safety limits not established
- Mechanisms are still poorly understood: more studies are needed in animals
- Few studies in humans (especially in patients): need for double-blind, randomized, cross-over, and sham-controlled studies
- Effects of repetitive sessions not tested