The neurophysiology of tES

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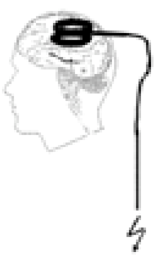
Modulation of cortical activity and excitability of the human brain

Activity

Plasticity

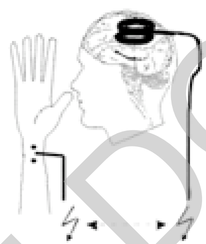
Oscillations

TMS



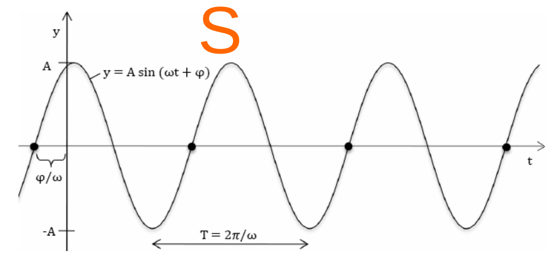
rTMS

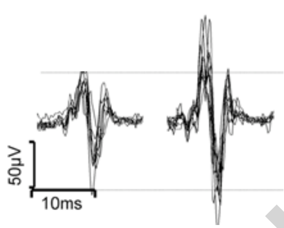
PAS

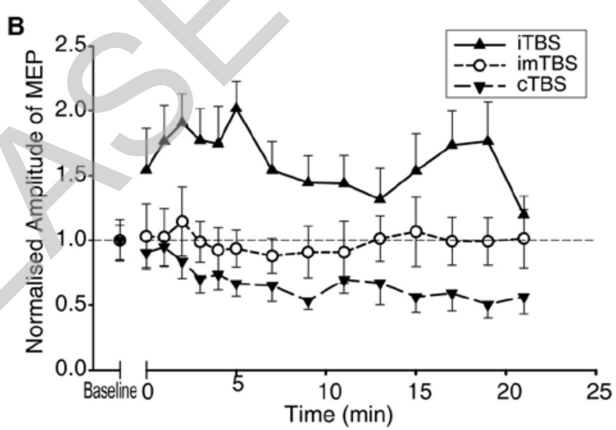


tDCS

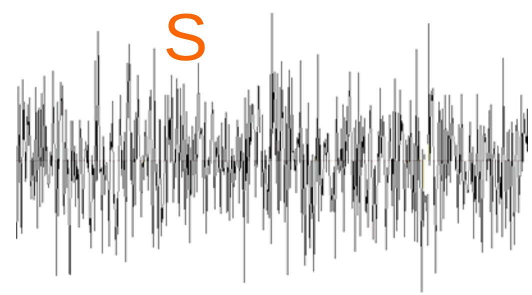
tACS







tRNS



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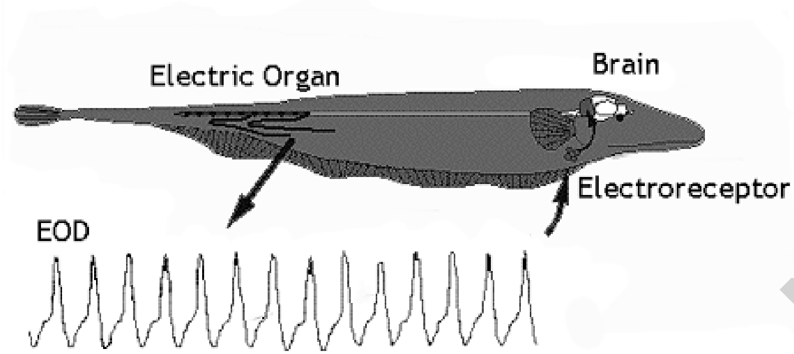
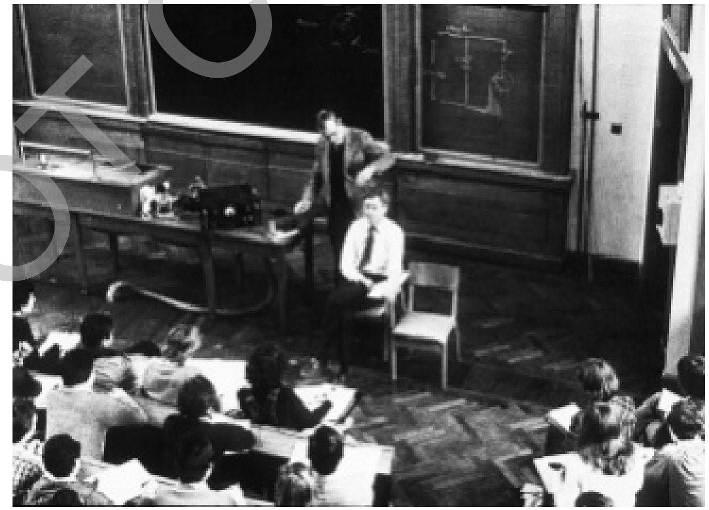
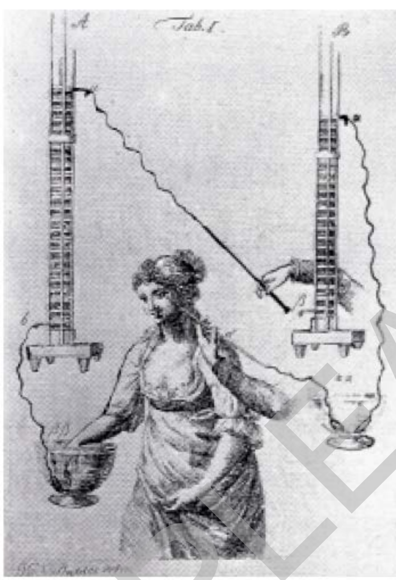
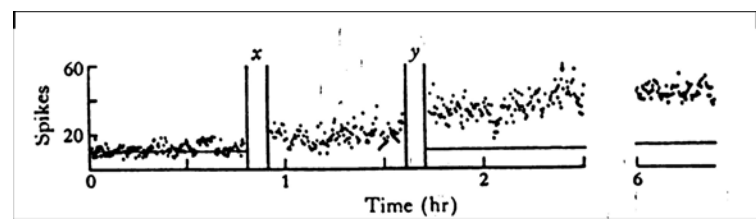
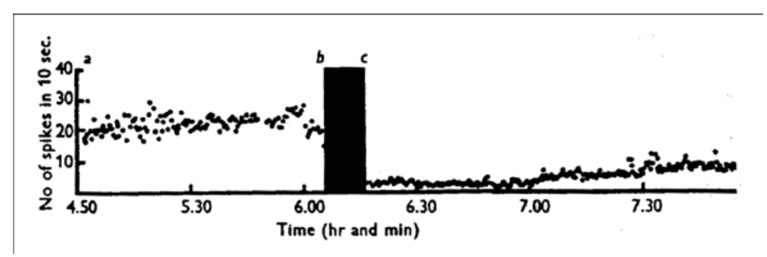
Actually, electrical brain stimulation has a long history...











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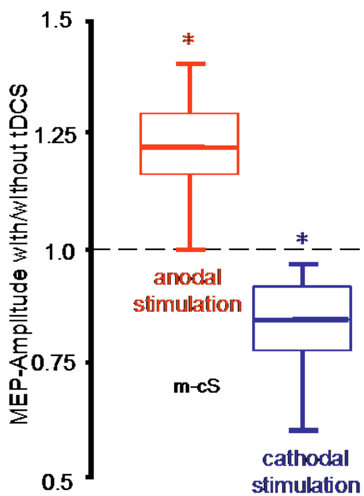
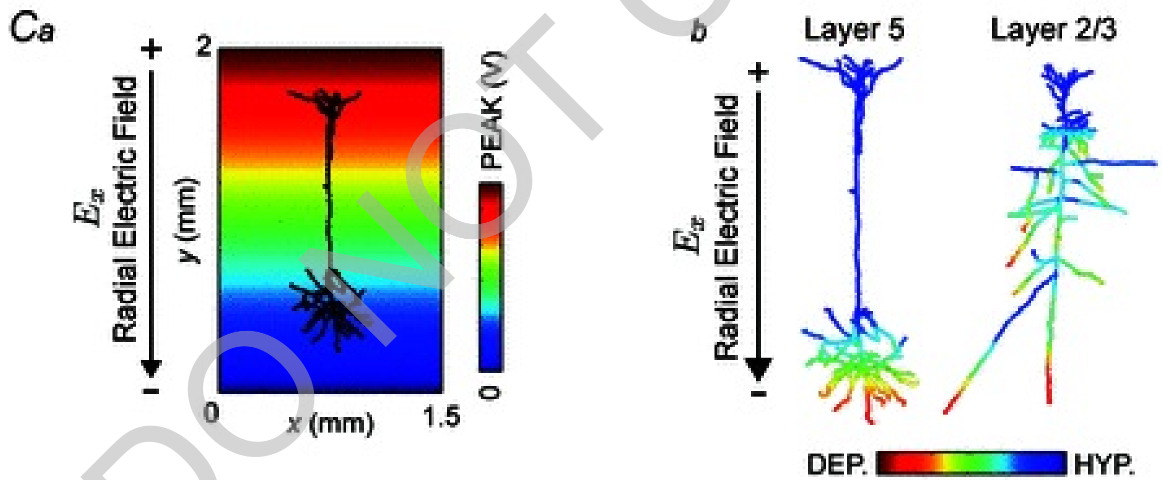
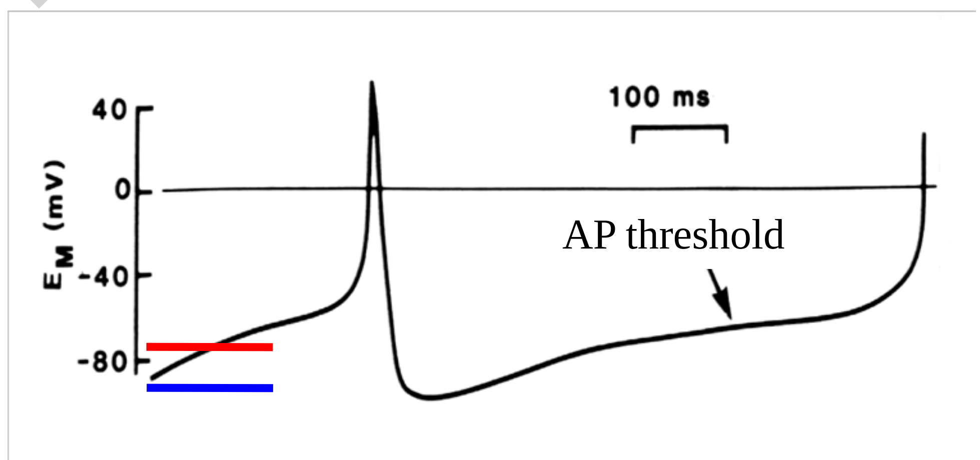
Primary action of tE-stimulation: modulation of resting membrane potential







Rahman et al. 2013

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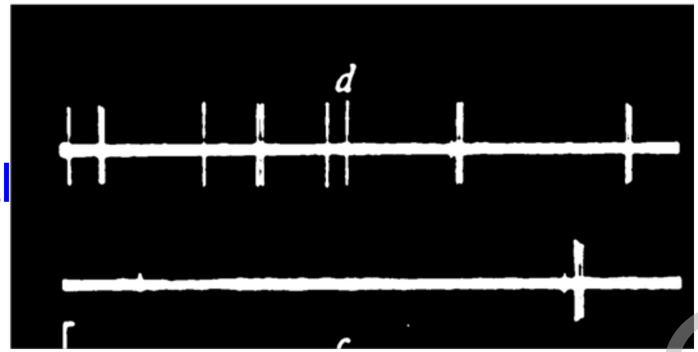
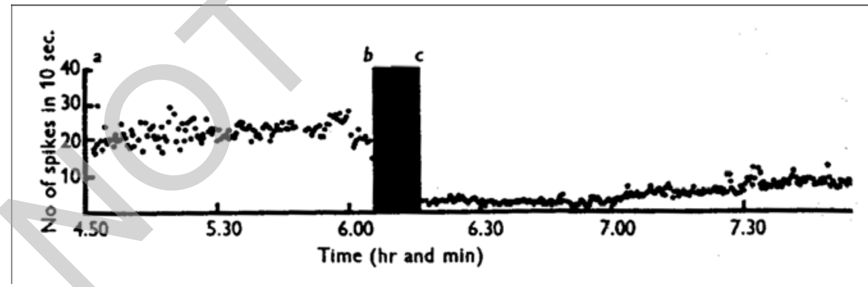
Cortical DC-stimulation of the rat

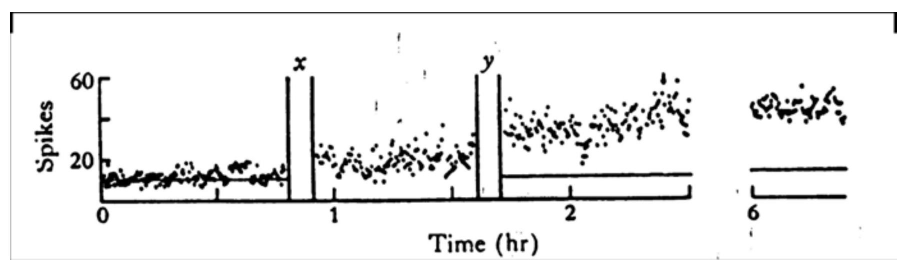
during *after*

cathodal





anodal



Bindman et al. 1964

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50% (?) of transcranially applied direct currents reach the brain

- *calculations on realistic head models, validation in animal experiments (Rush & Driscoll 1968)*
- *validation in humans (Dymond et al. 1975)*

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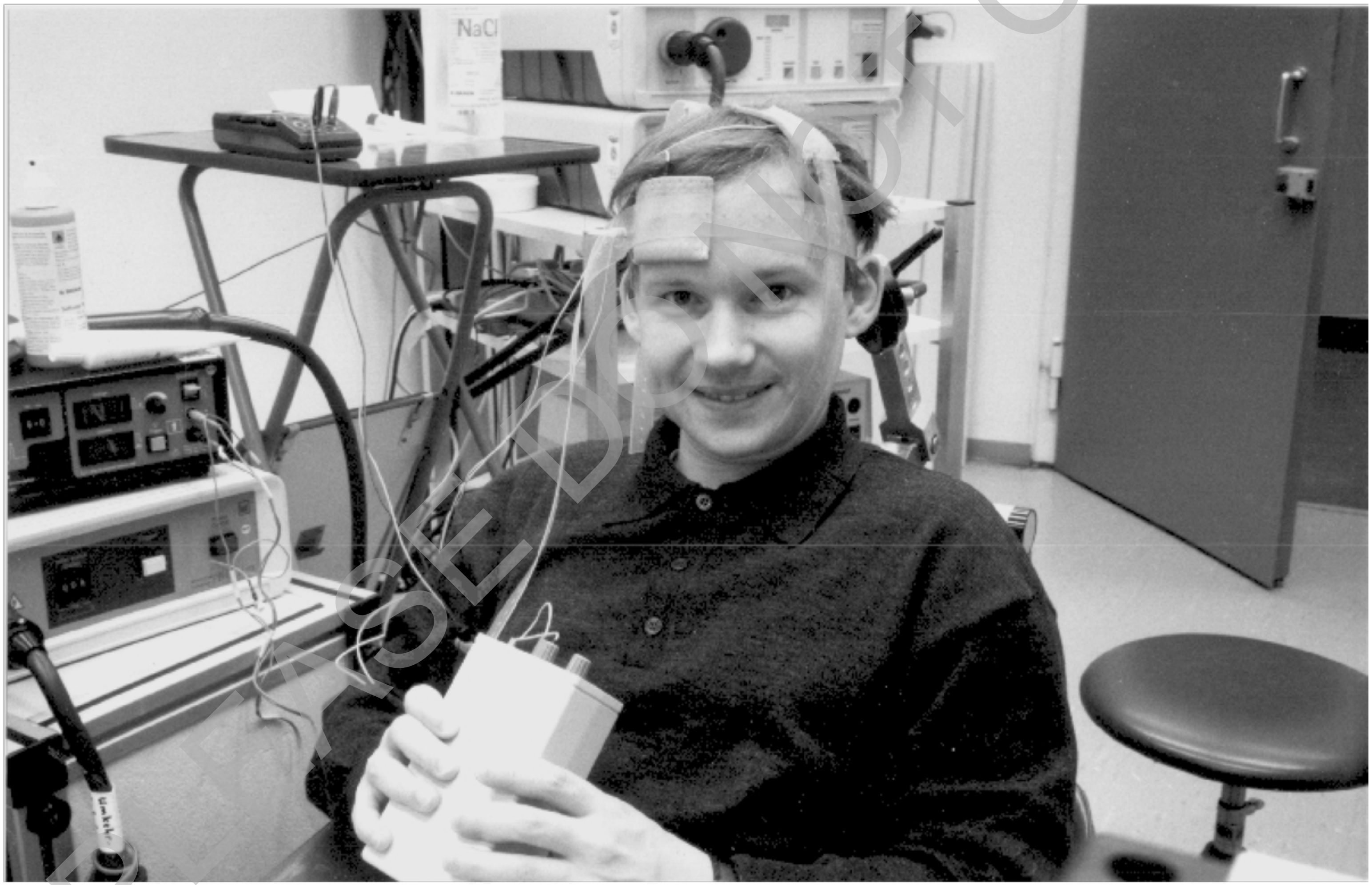
tDCS in humans



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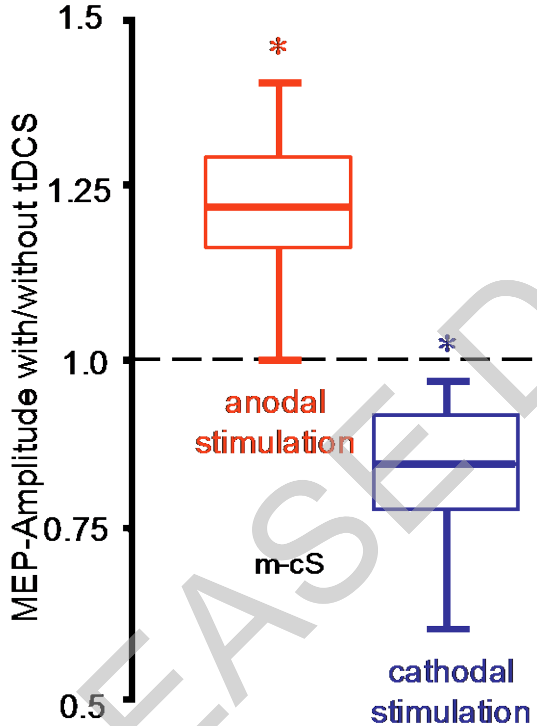
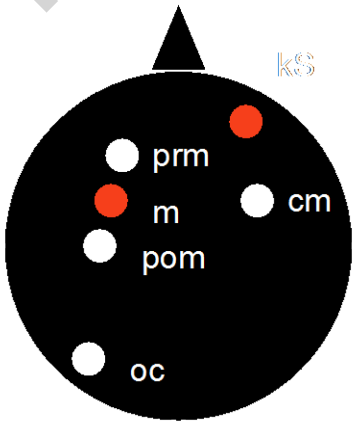
Polarity-dependent excitability-modulation *during* tDCS





Electrode positions:

m = motor cortex; prm = premotor cortex; pom = post-motor cortex; oc = occipital; cS = contralateral forehead; cm = kontralateral motor cortex

Nitsche & Paulus 2000

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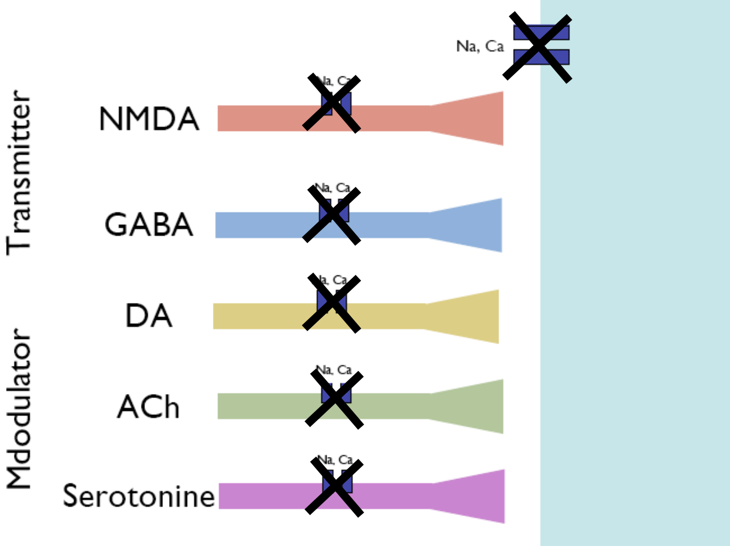
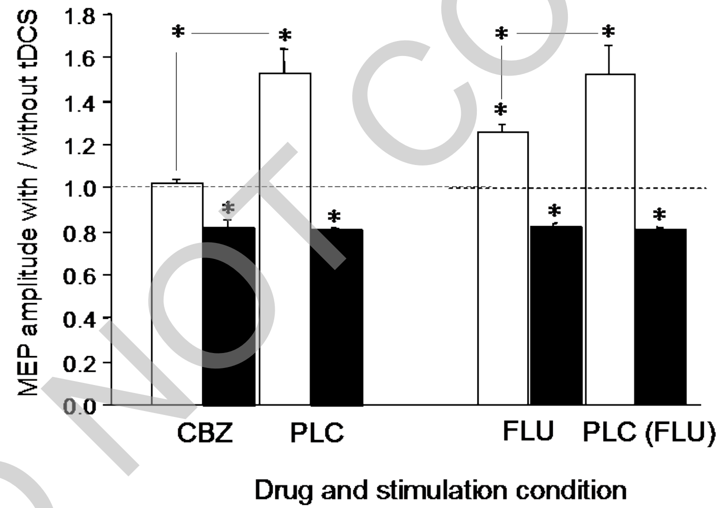
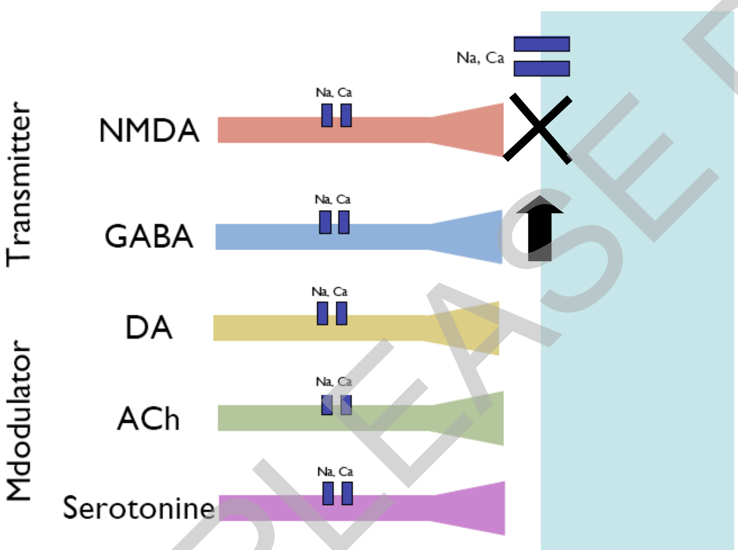
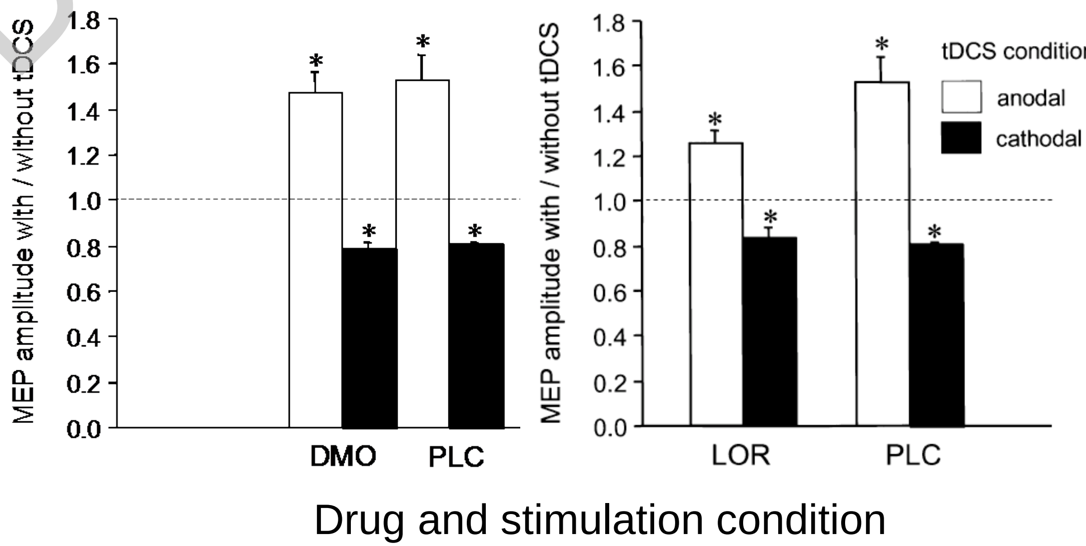
Pharmacological determinants of acute tDCS effects









Nitsche et al. 2003, 2004

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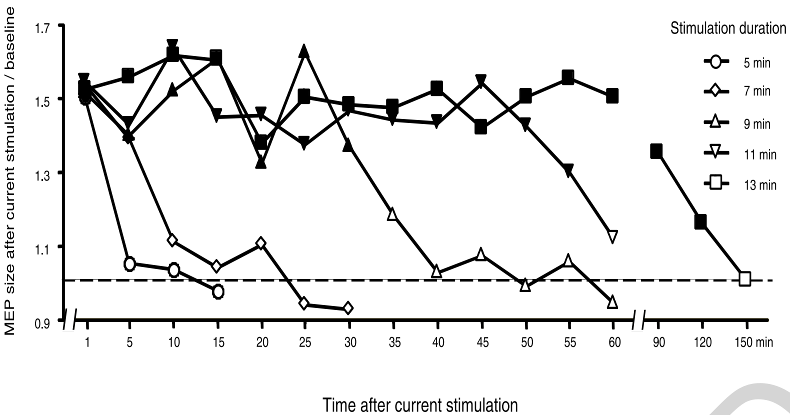
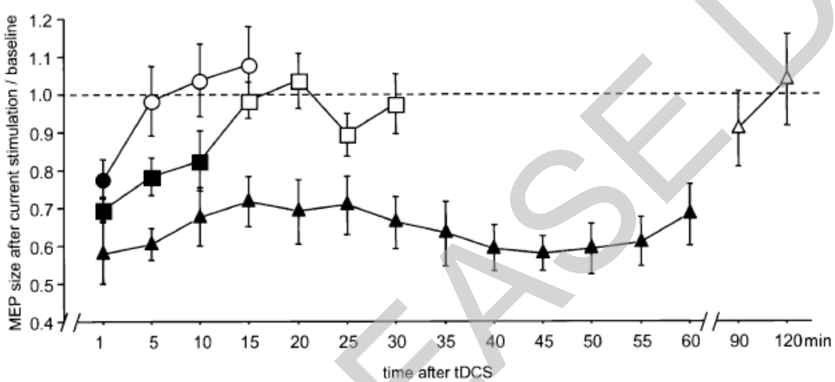
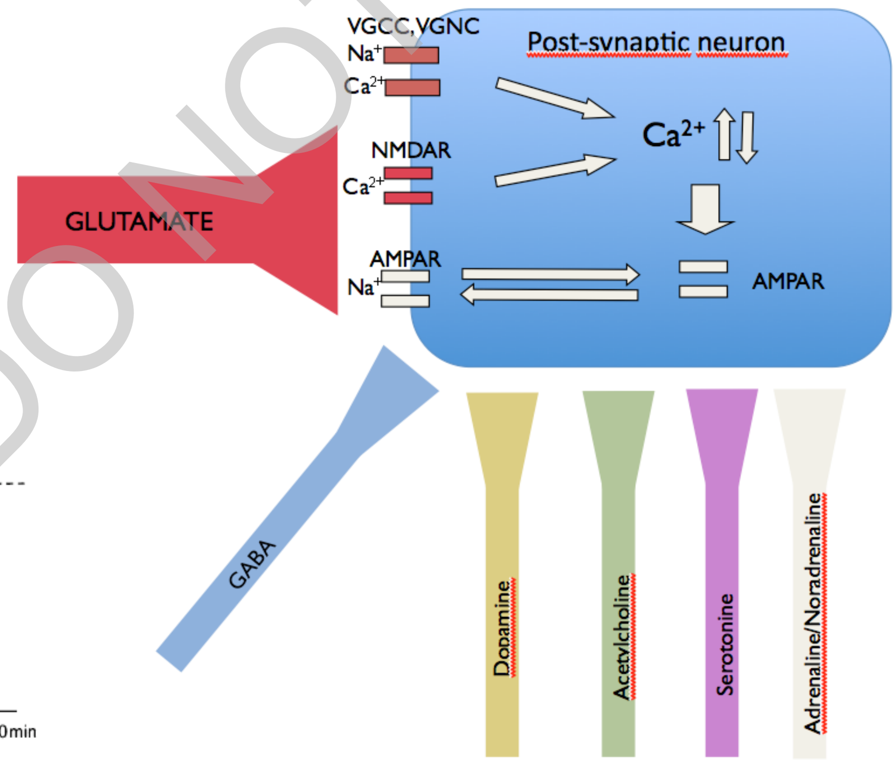
After-effects of tDCS - plasticity







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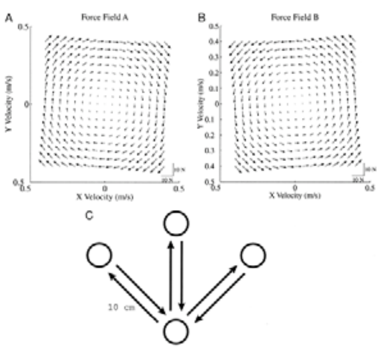
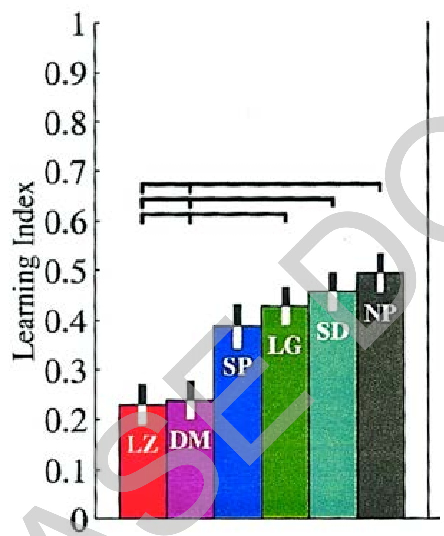
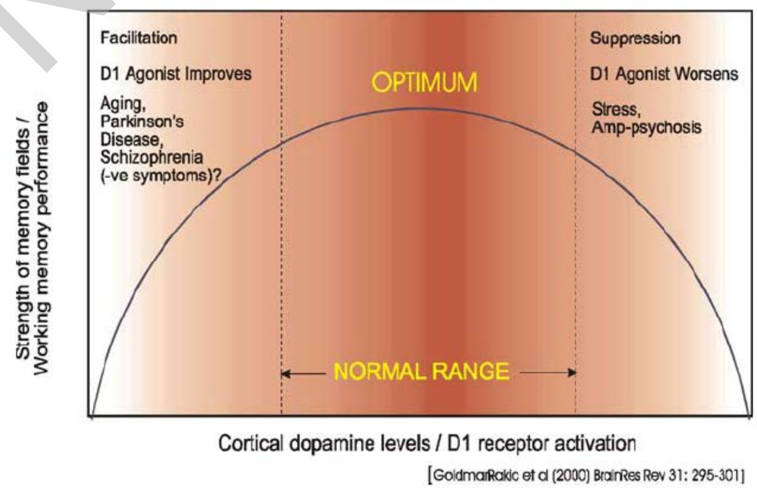
Drivers and modulators of plasticity

Glutamate





Dopamine



Donchin et al. 2010, Goldman-Racic et al. 2000

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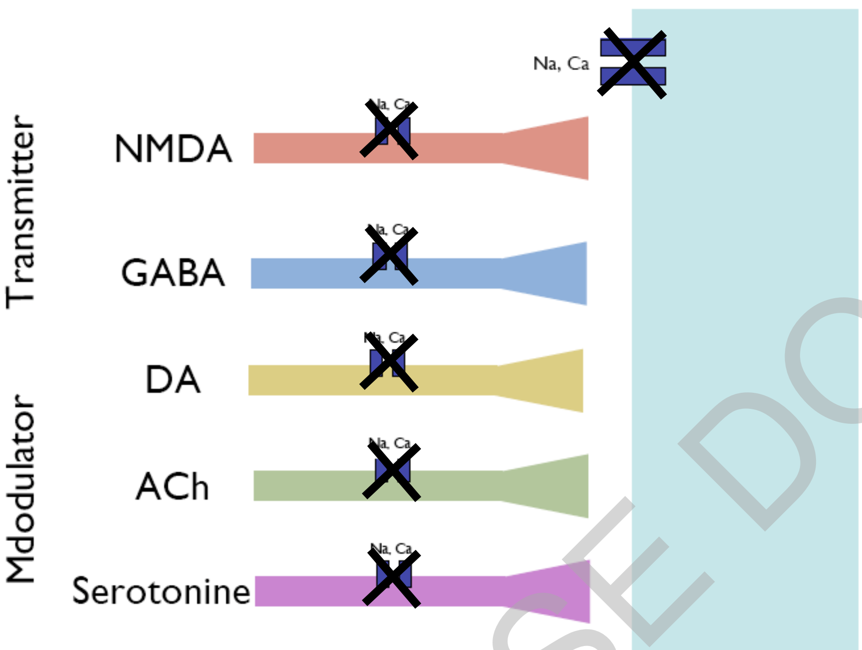
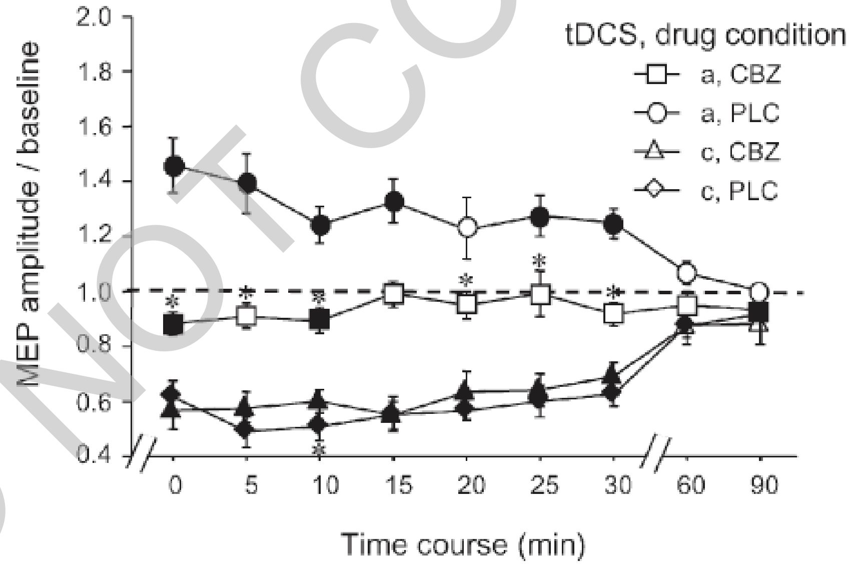
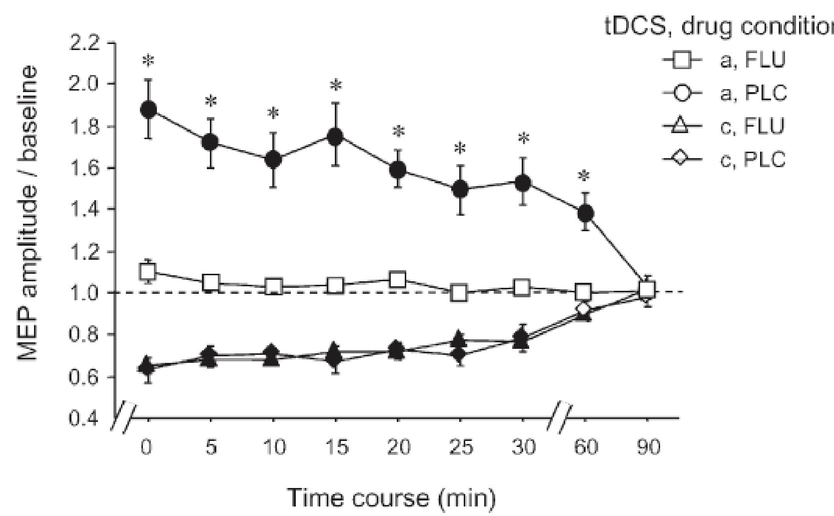
Drivers of after-effects of tDCS – ion channels







Nitsche et al. 2003

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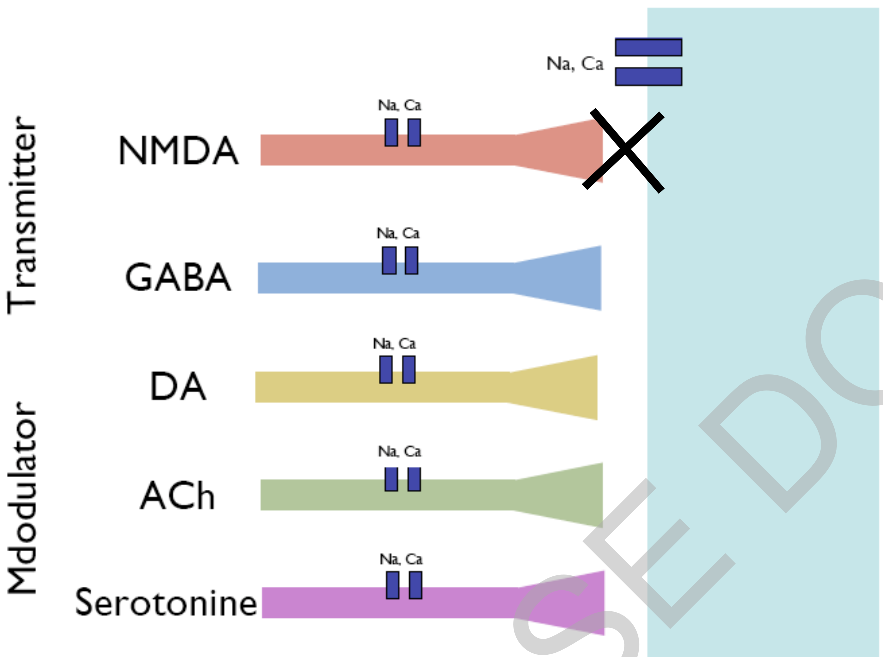
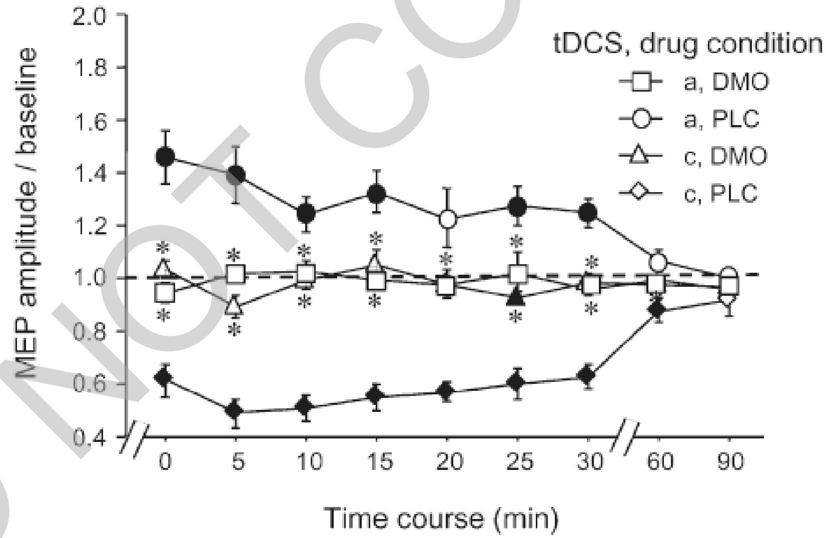
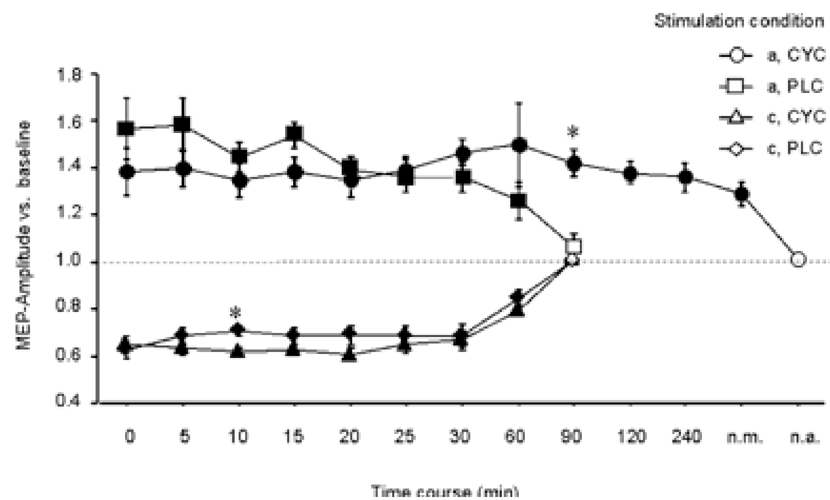
Drivers of after-effects of tDCS - glutamate







Nitsche et al. 2003, 2004

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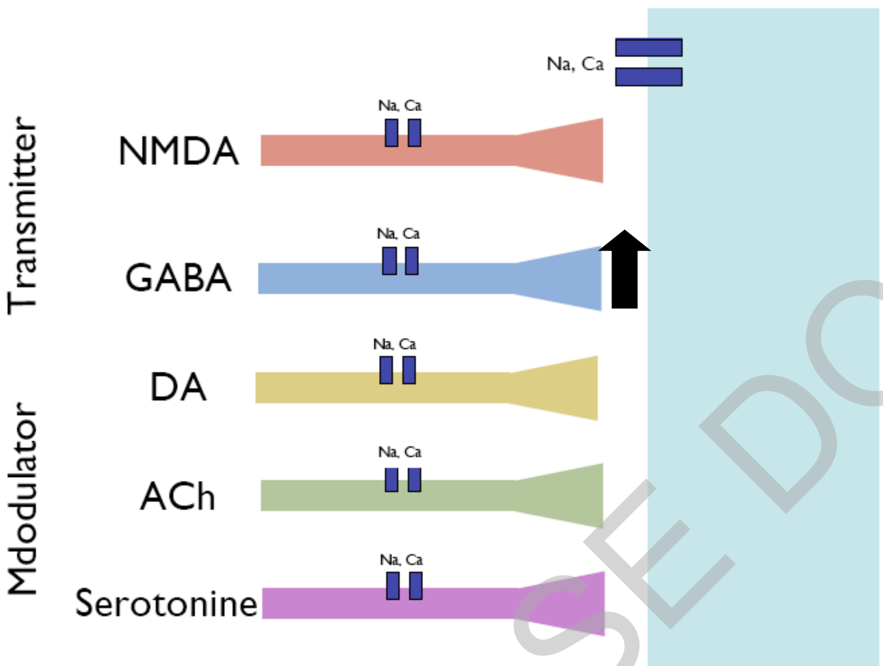
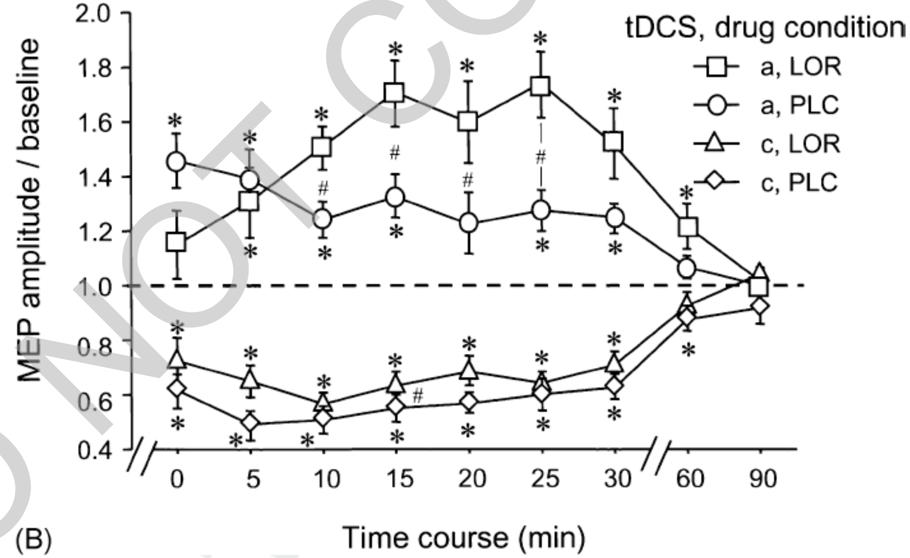
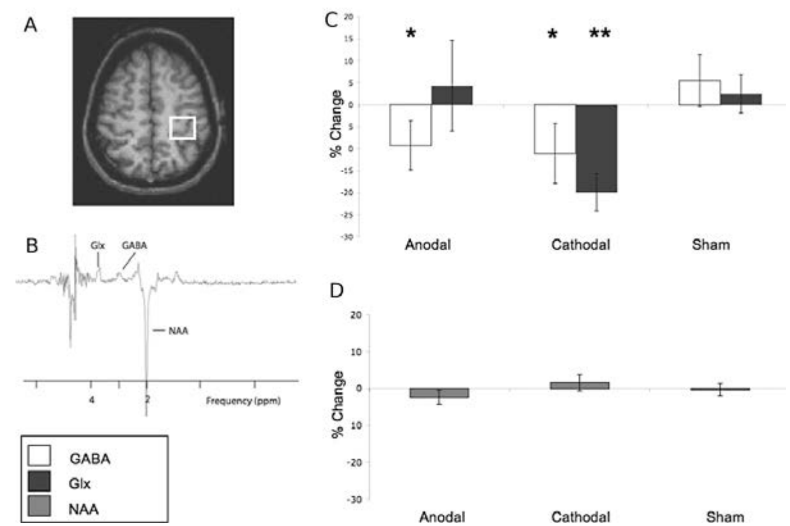
Drivers of after-effects of tDCS - GABA







Nitsche et al. 2004, Stagg et al. 2009

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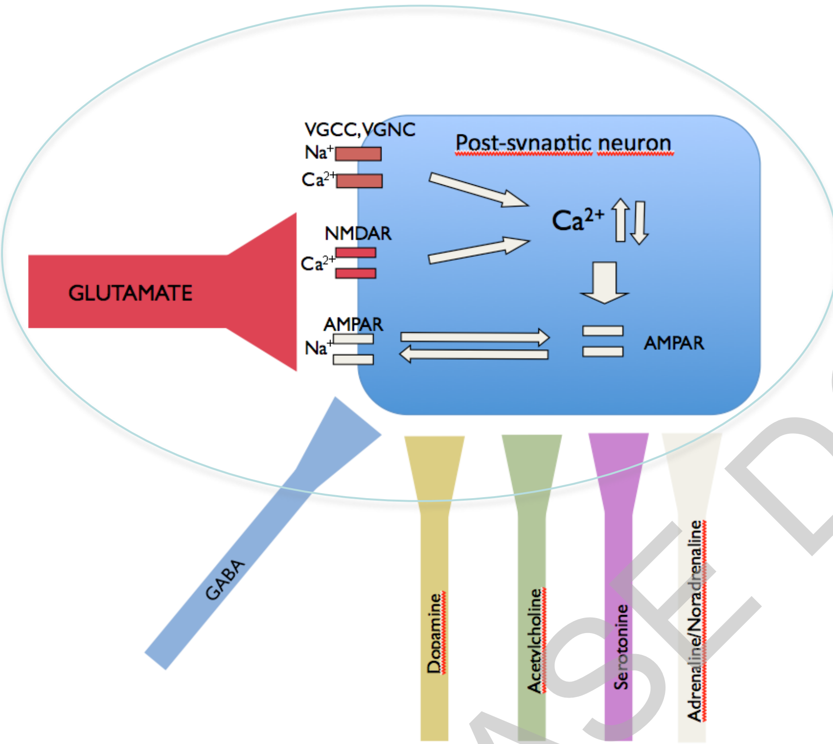
Conclusion I



-Primary effects of tDCS depend on
 ion channel activity/polarization

- After-effects of tDCS depend on glutamate

- GABA reduction might contribute

- For tDCS, calcium-dependent glutamatergic plasticity can be assumed

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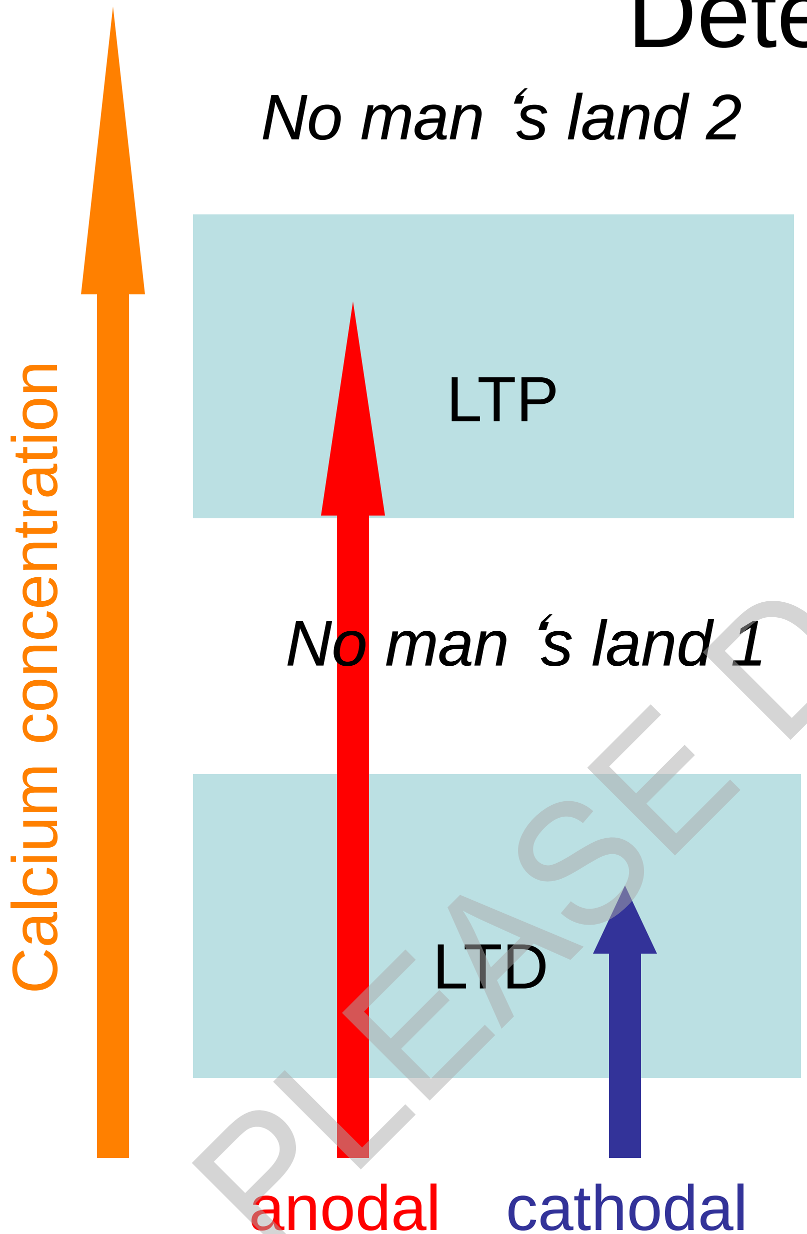
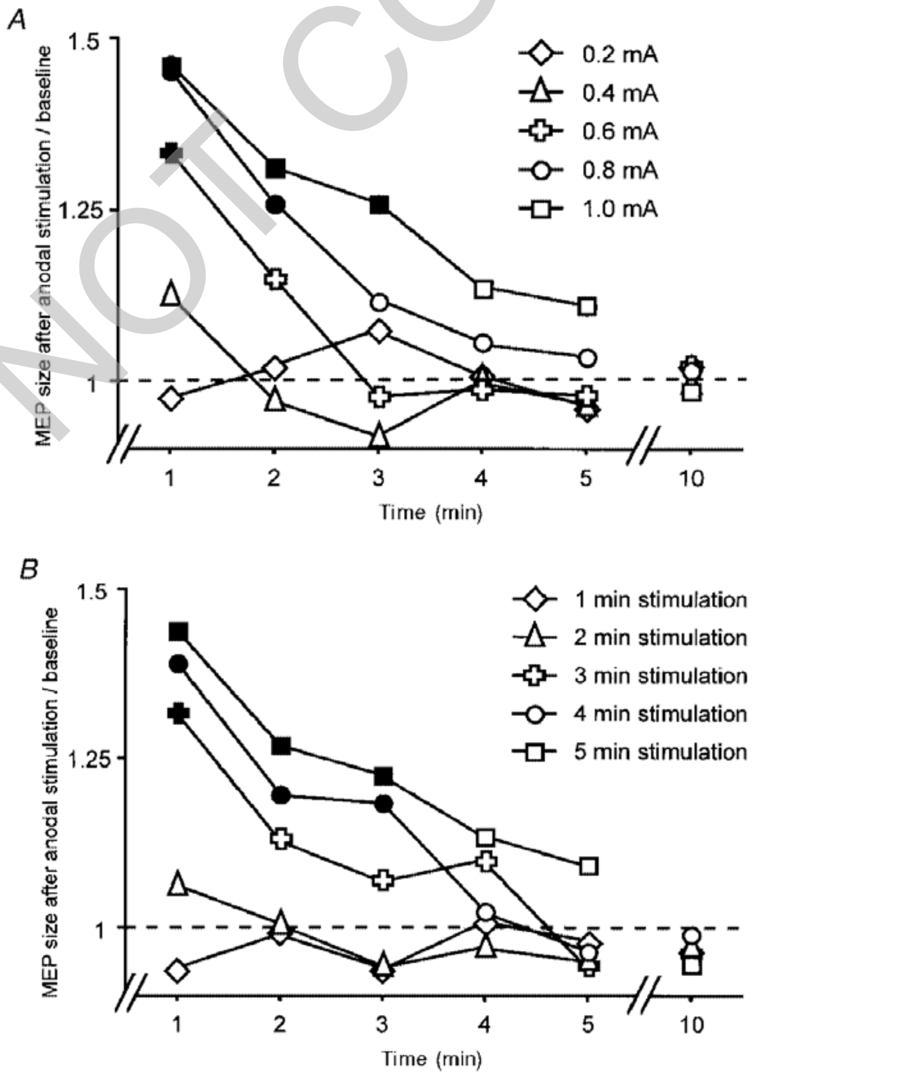
Physiology of plasticity I - Determinants





Lisman 2001, Nitsche & Paulus 2000

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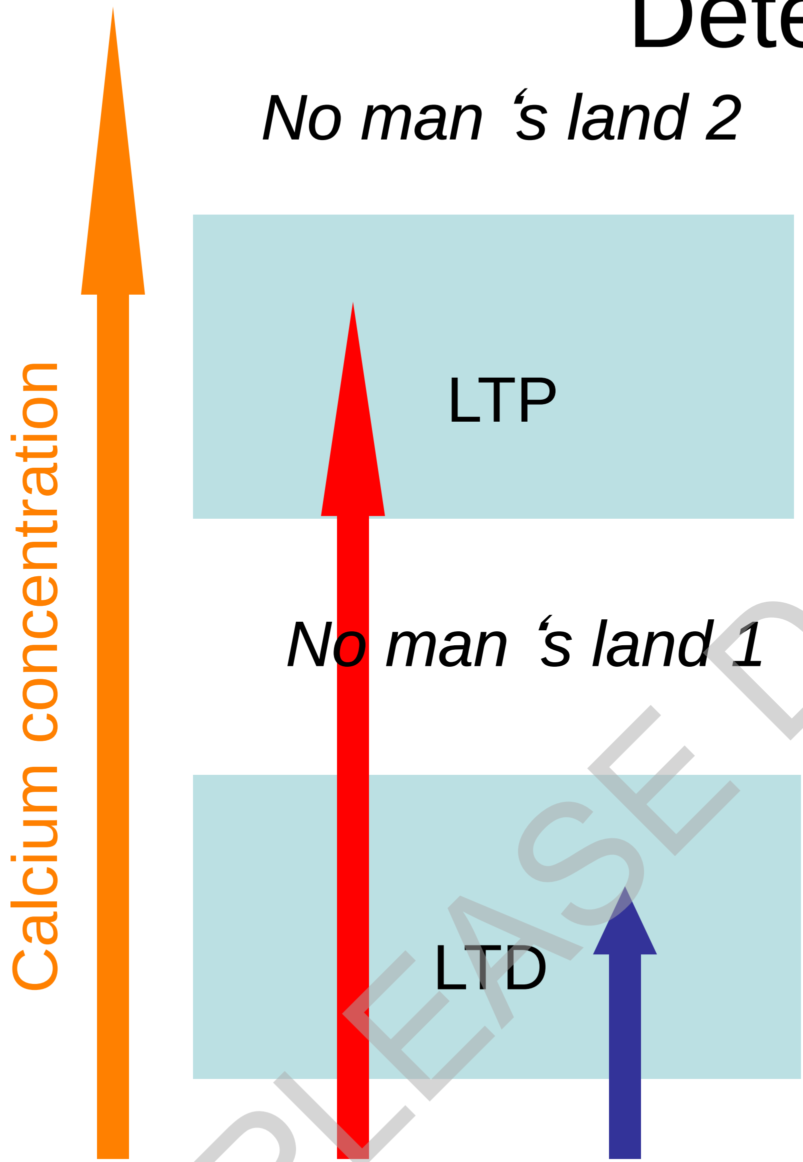
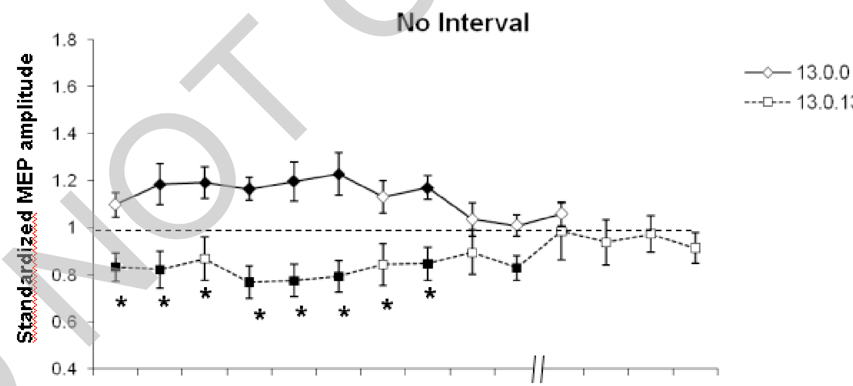
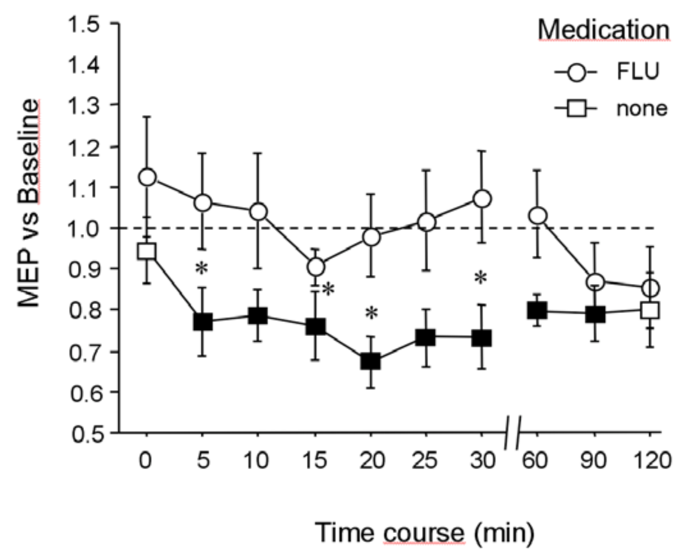
Physiology of plasticity II - Determinants







Monte-Silva et al., 2013

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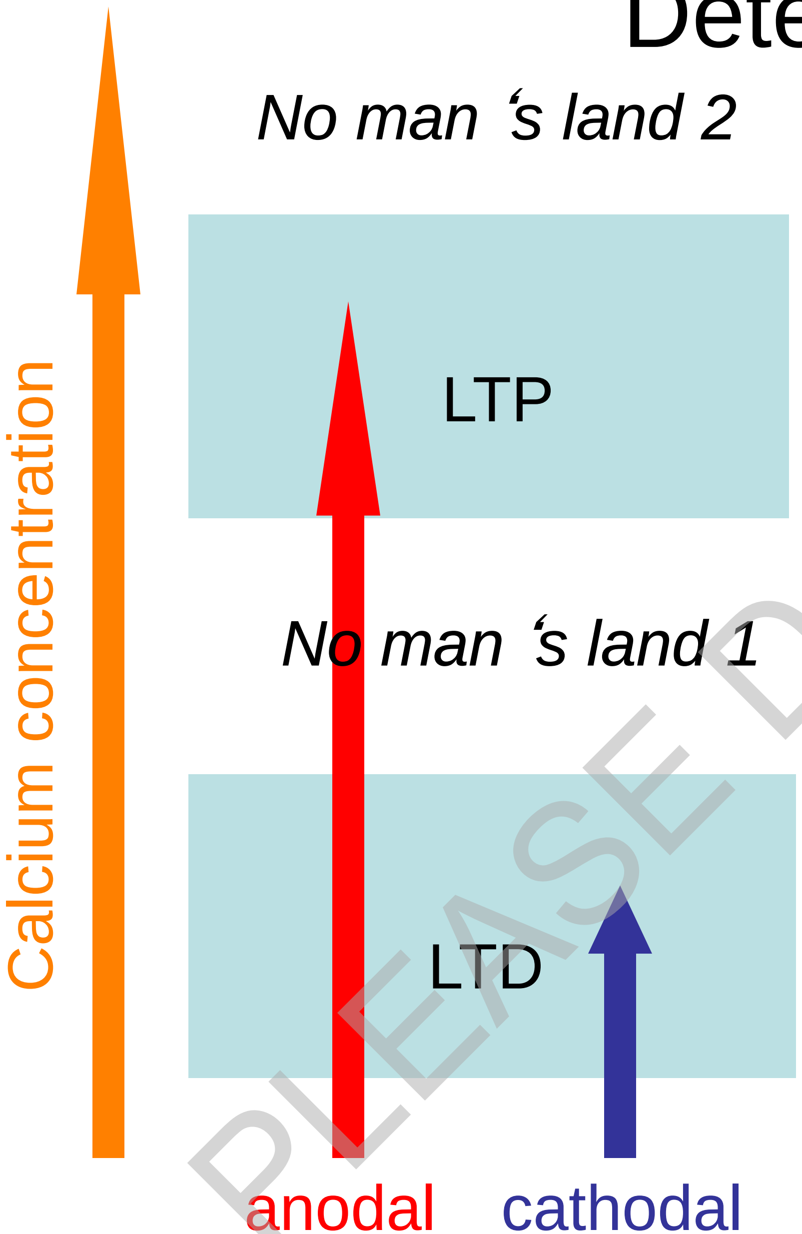
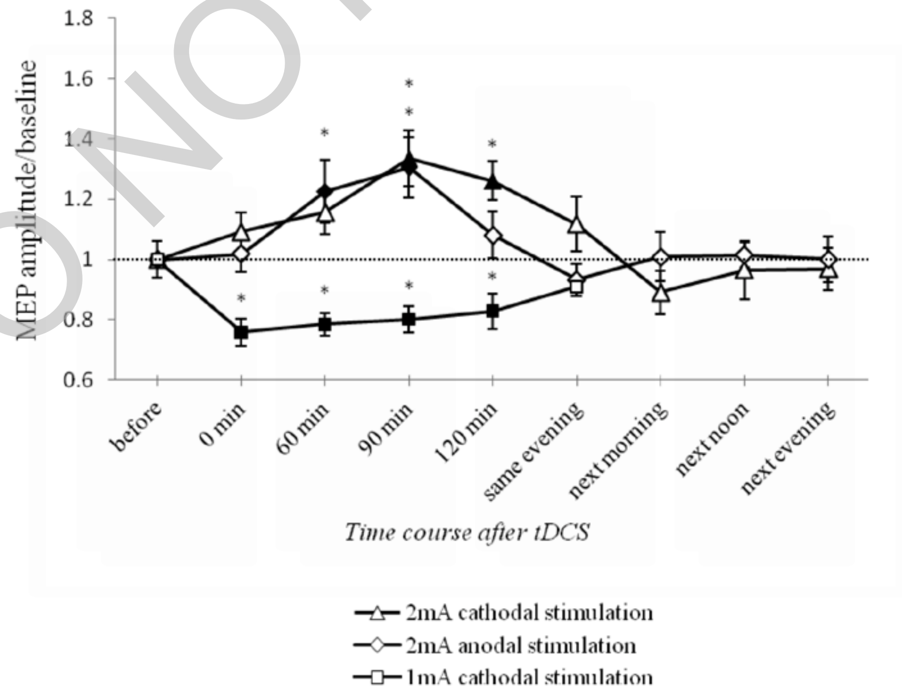
Physiology of plasticity III - Determinants





Badsikadze et al., 2013

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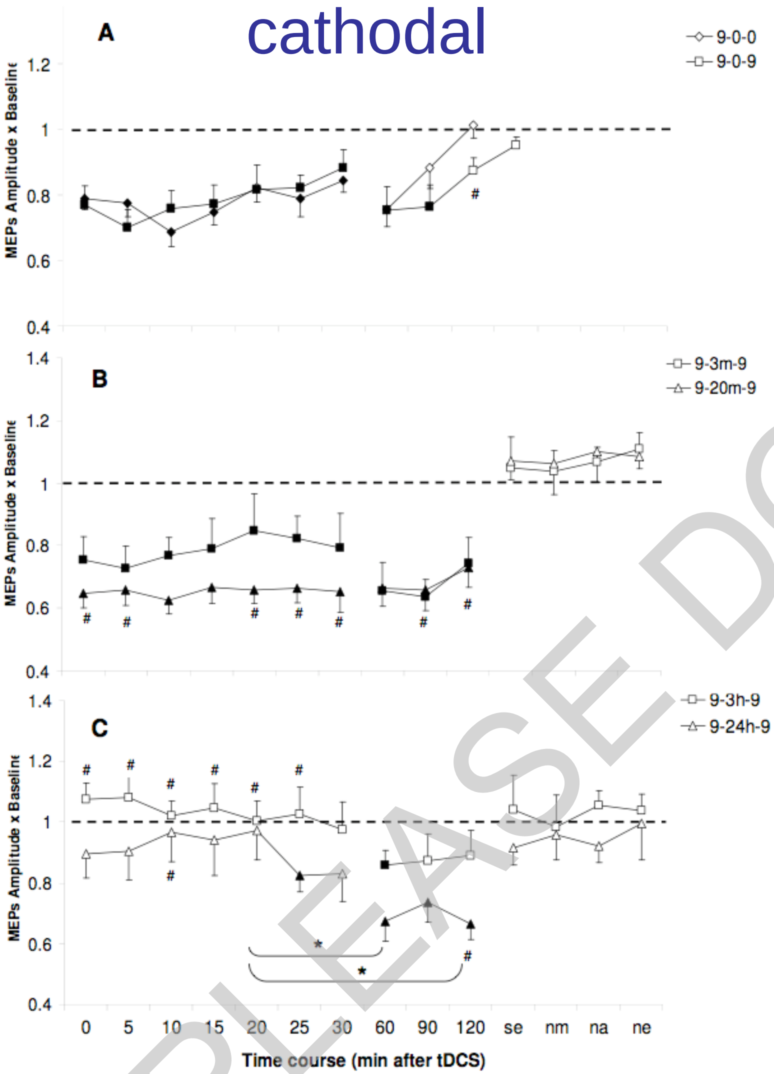
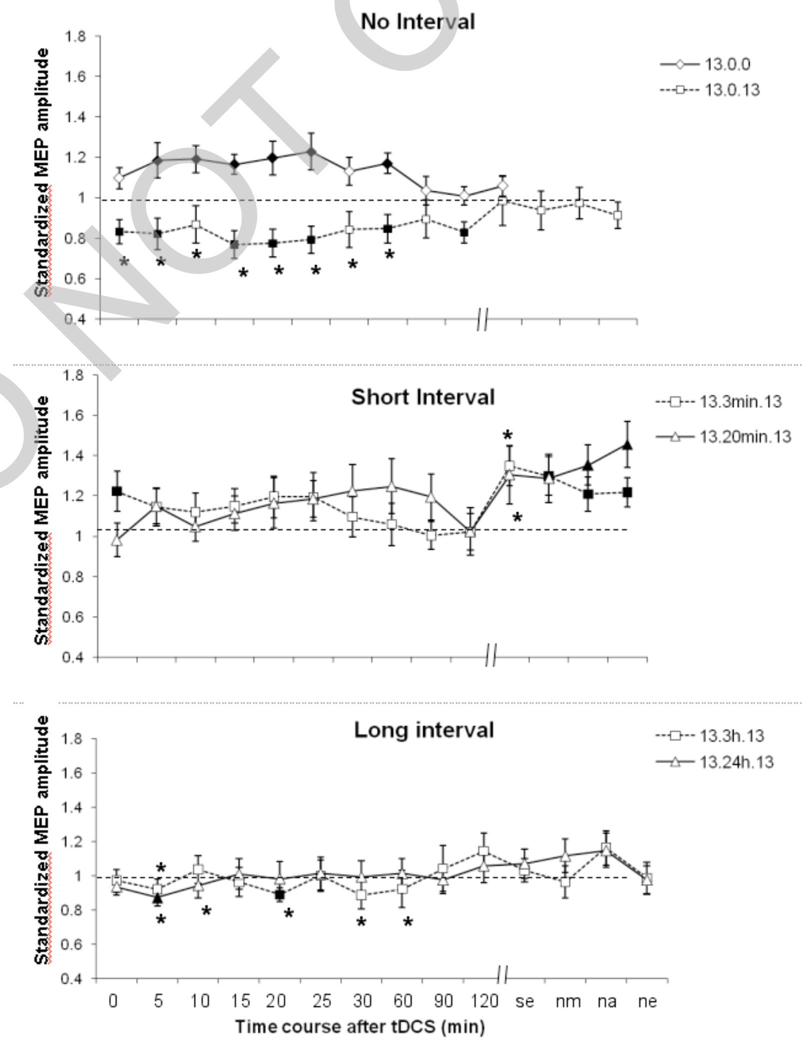
Physiology of plasticity IV – Modulation by repetition

cathodal



anodal



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Monte-Silva et al. 2010, 2013

Conclusion II

- tDCS is well suited to induce/model non-focal plasticity in the human brain
- Non-linear effects, dependent on stimulation duration, and strength
- Late-phase plasticity accomplished by specific protocols

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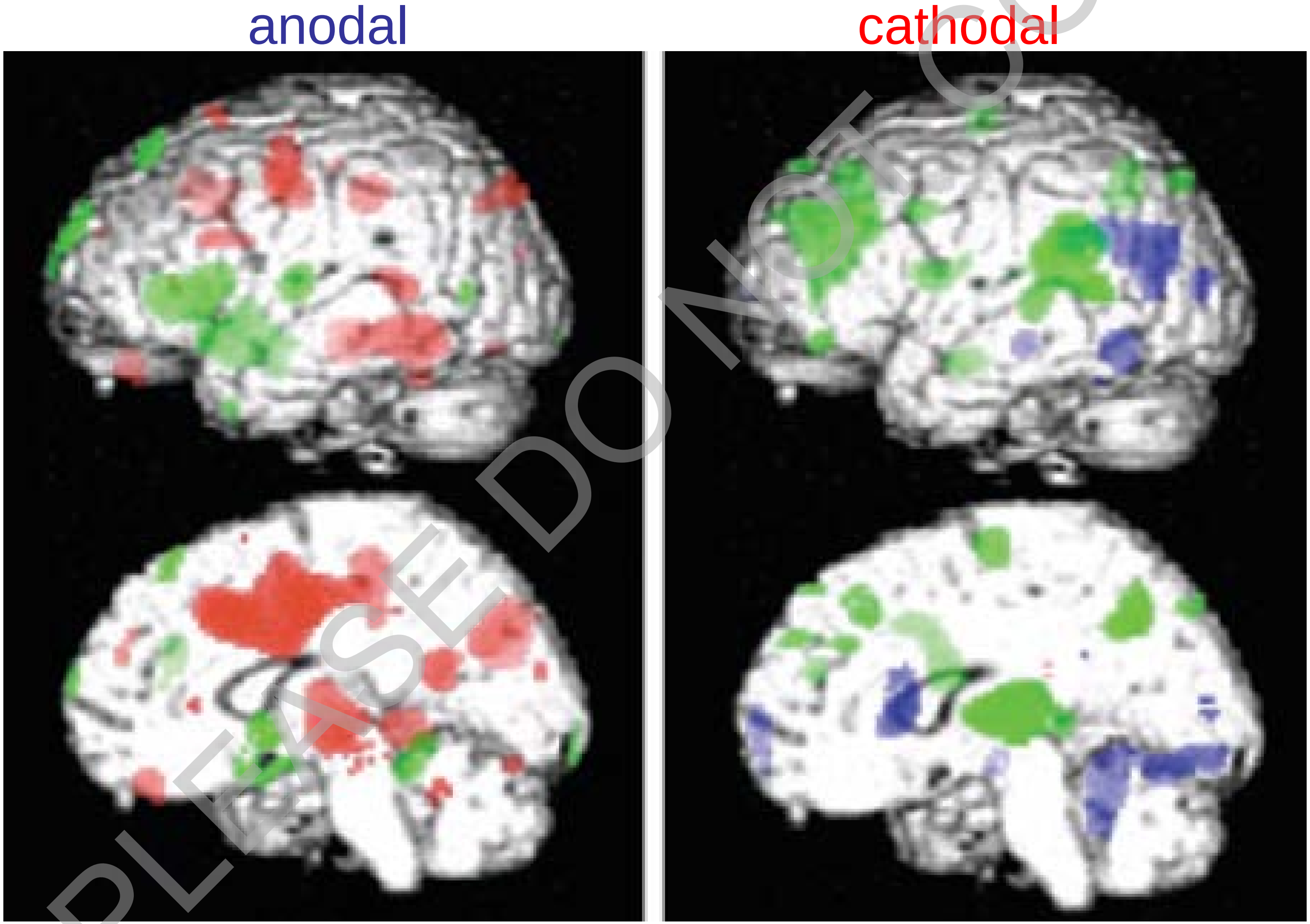
Network effects of tDCS



Lang et al. 2005

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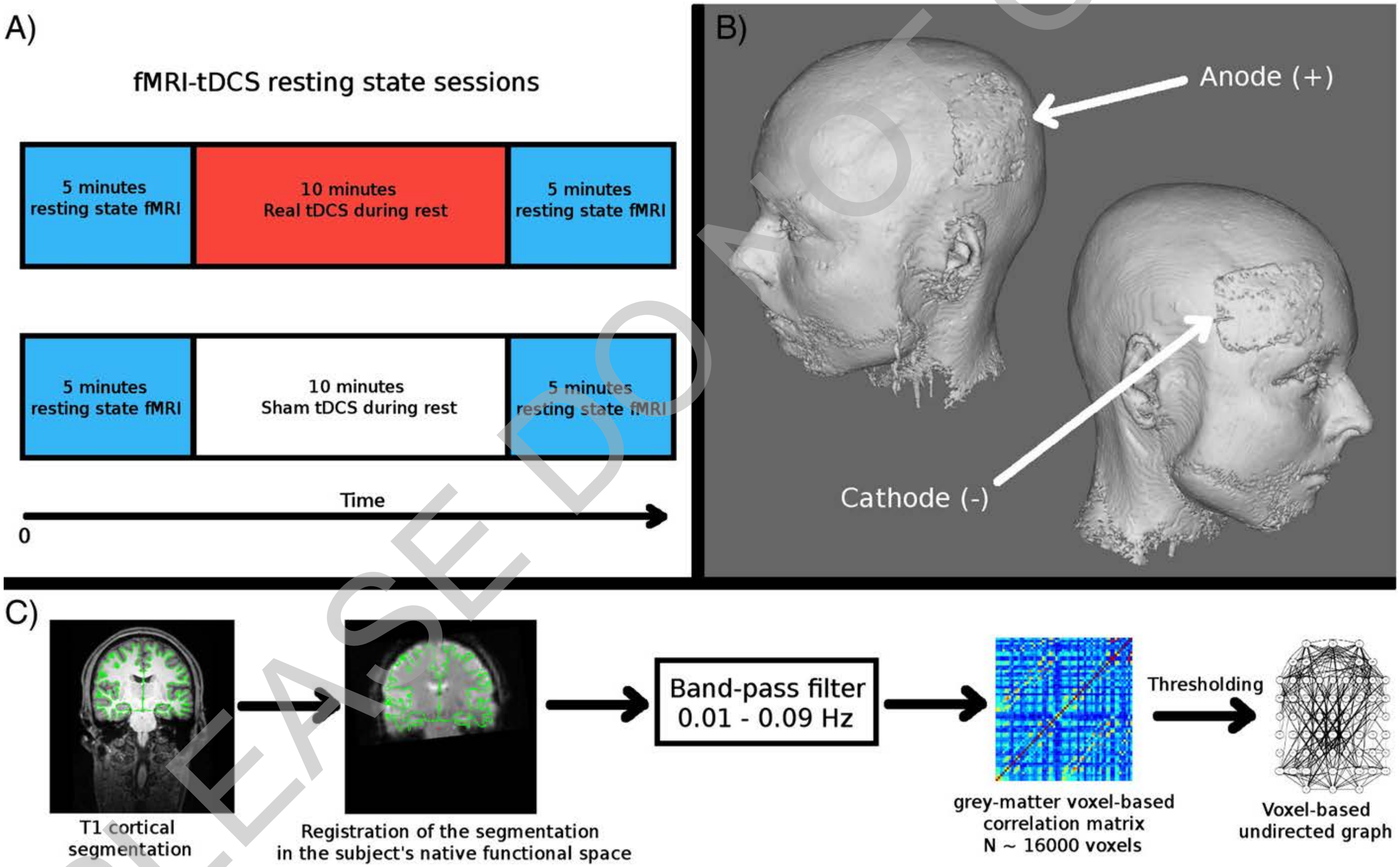
tDCS-induced functional connectivity alterations in motor-related networks - fMRI



Polania et al. 2011a

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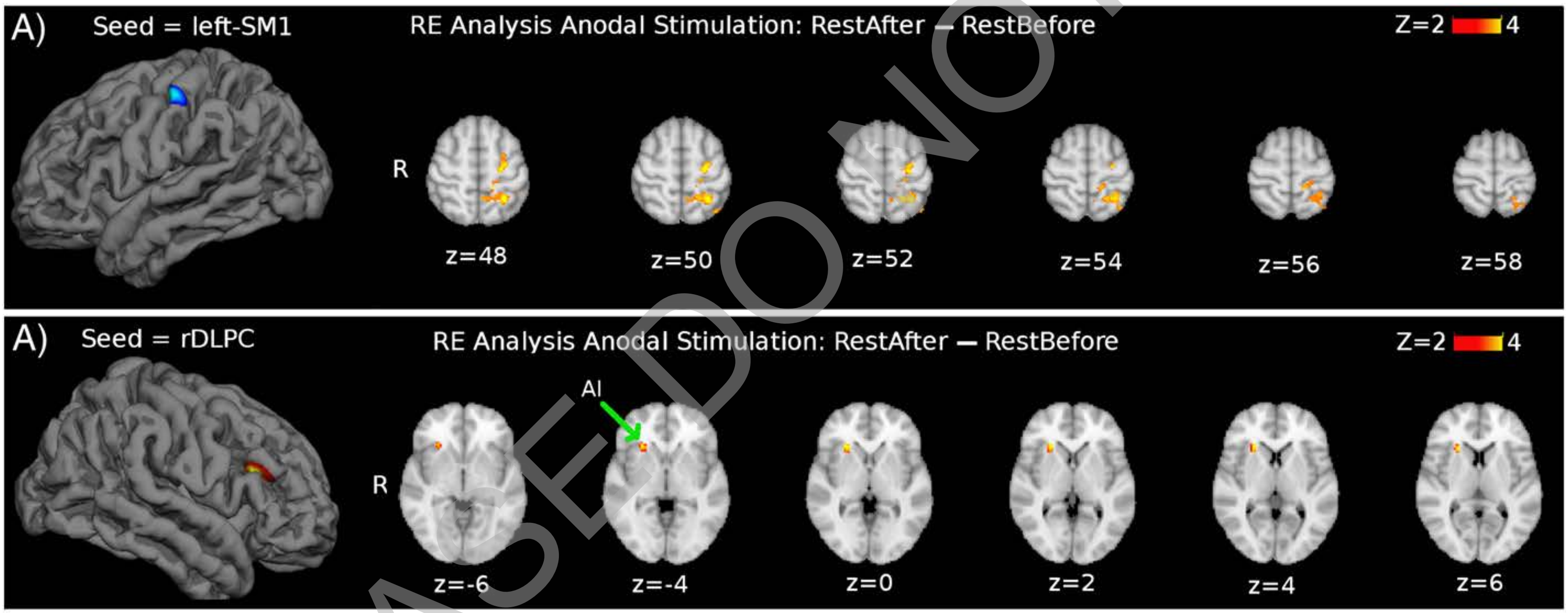
tDCS-induced functional connectivity alterations in motor-related networks - fMRI



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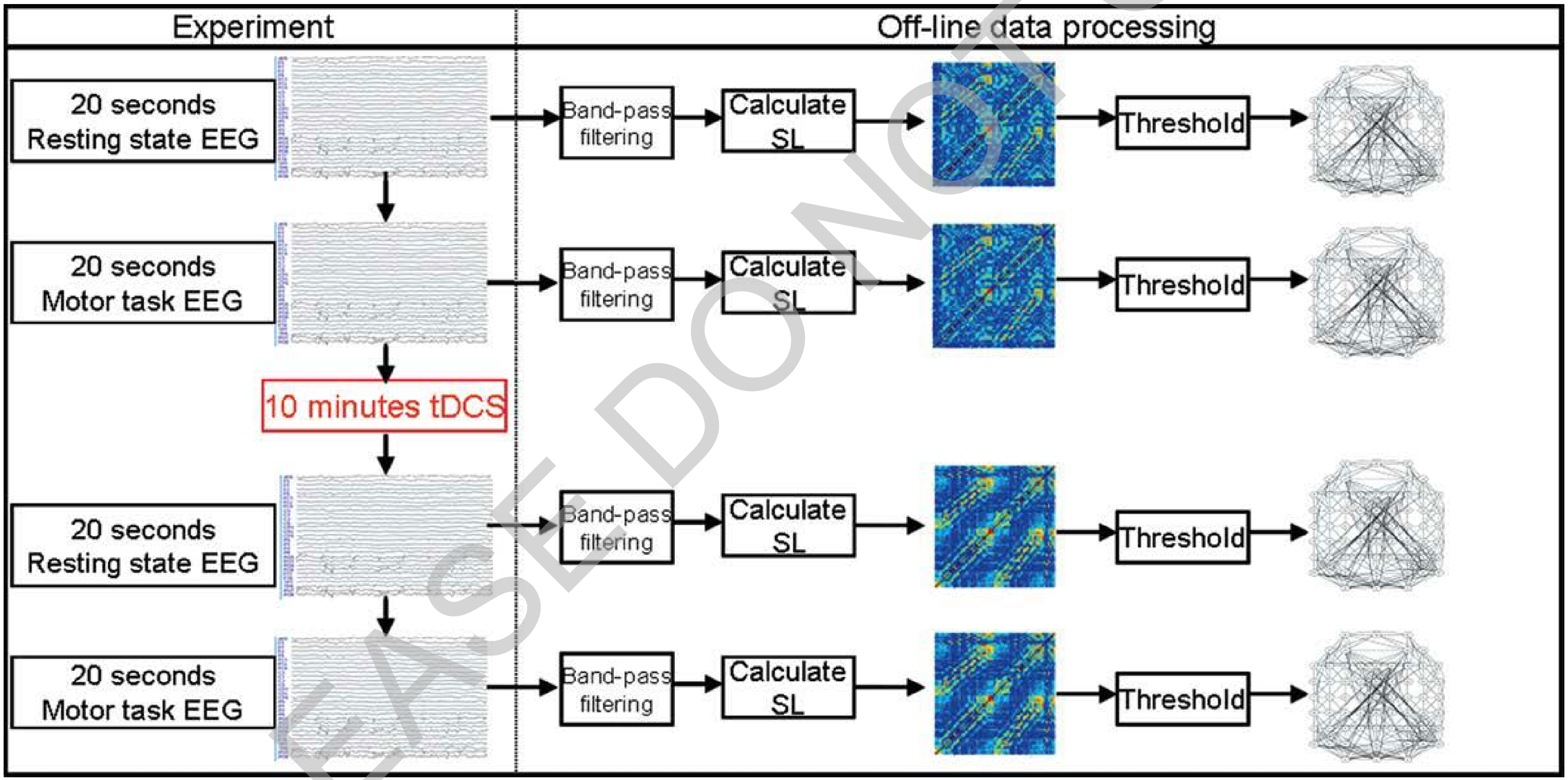
Polania et al. 2011a

tDCS-induced functional connectivity alterations of motor cortical networks - EEG



Polania et al. 2011c

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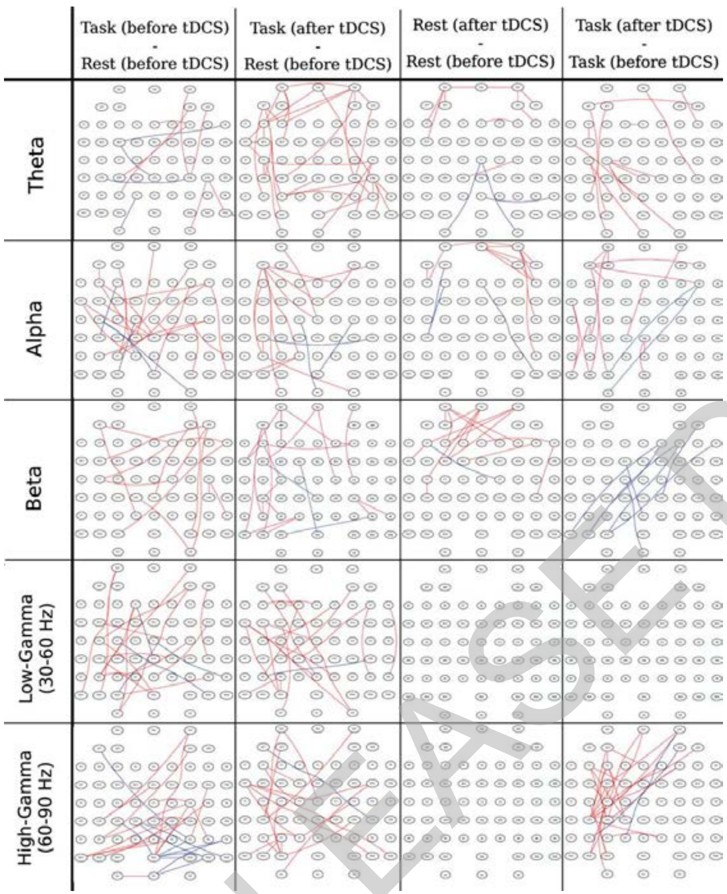
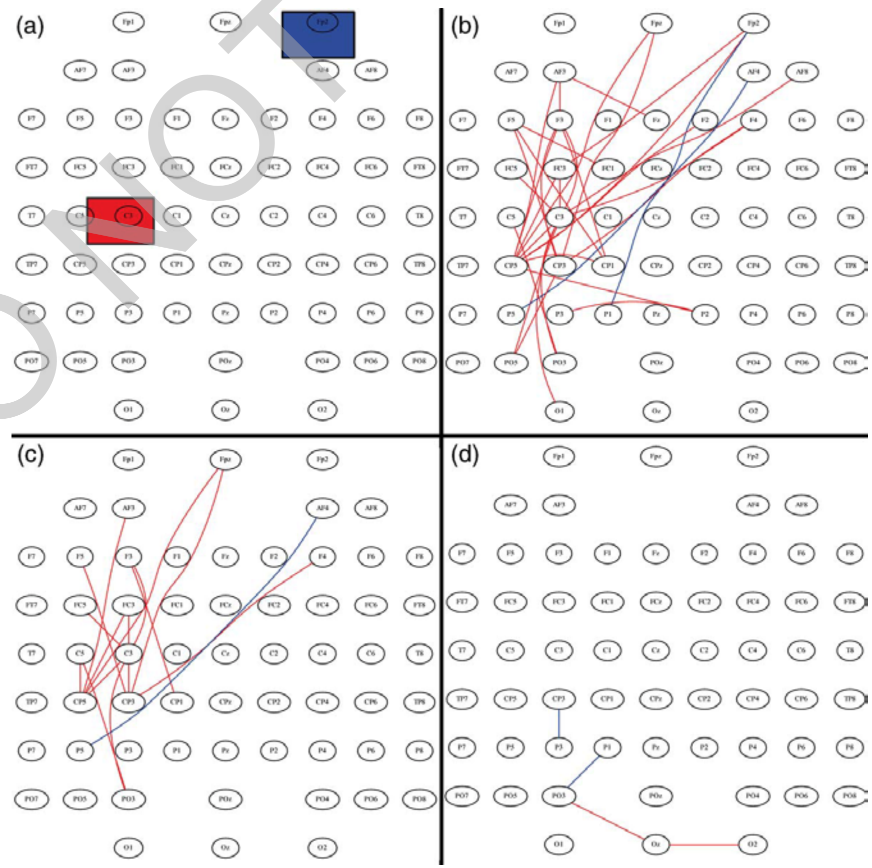
tDCS-induced functional connectivity alterations of motor cortical networks - EEG





Polania et al. 2011c

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Conclusion III

- Functional MRI, and EEG allow the identification of stimulation-induced alterations of functional connectivity of interregional cortical networks

- Remote effects of tDCS depend at least partially on activation of functionally defined networks

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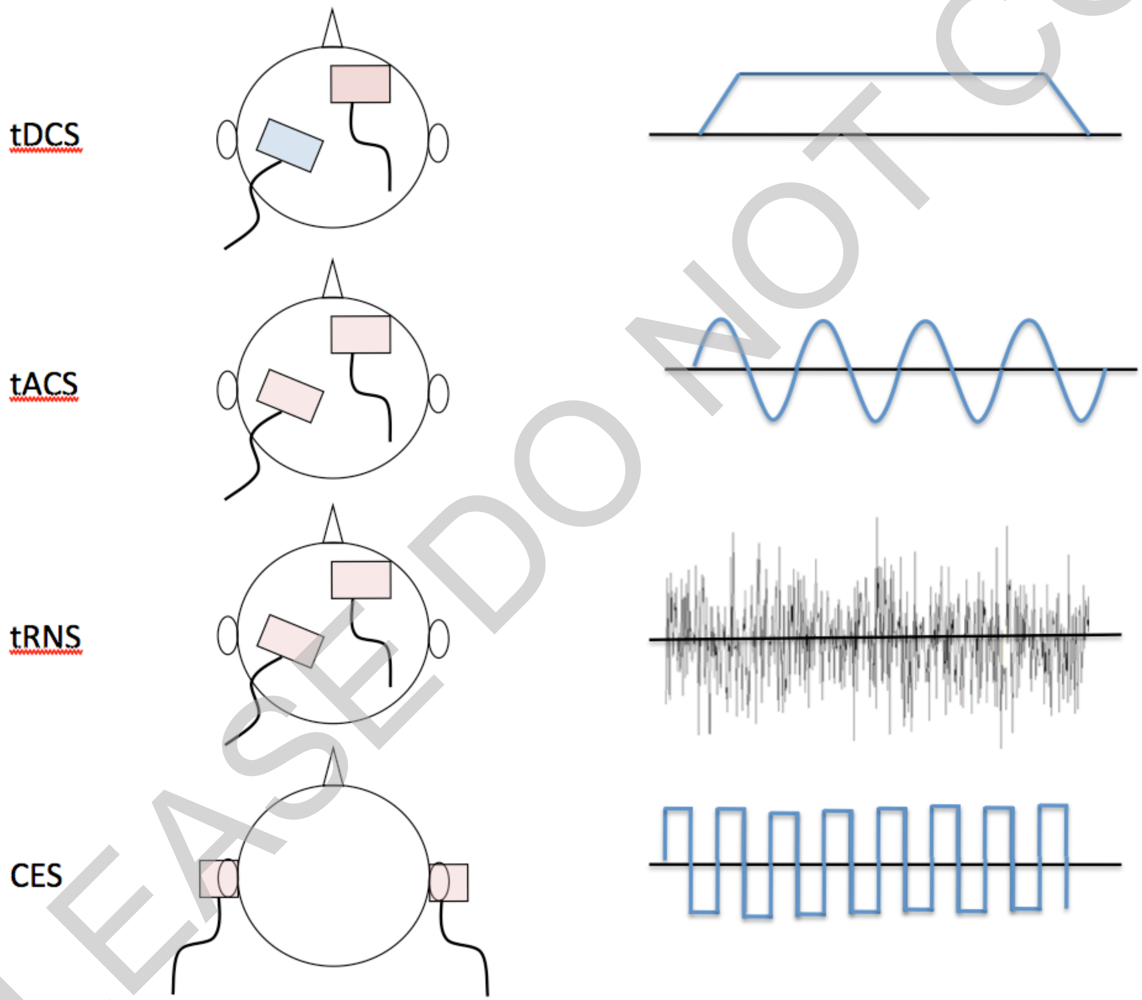
Modulation of cortical oscillations by tES



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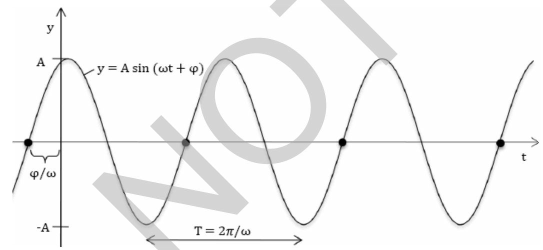
Oscillatory stimulation with alternating currents (tACS)



No neuroplastic effects (?)

Table 1 Mean MEP amplitudes (SEM) before and after tACS at 1-, 5-, 10-, 15-, and 30-Hz stimulation

	1 Hz	10 Hz	15 Hz	30 Hz	45 Hz	Sham
Before	1.02 ± 0.11	1.03 ± 0.13	1.03 ± 0.09	1.03 ± 0.08	1.04 ± 0.09	1.02 ± 0.11
0 min	1.01 ± 0.30	0.93 ± 0.31	1.15 ± 0.37	1.06 ± 0.33	1.15 ± 0.46	1.19 ± 0.42
2 min	1.04 ± 0.44	0.94 ± 0.31	1.05 ± 0.41	1.11 ± 0.38	1.11 ± 0.47	1.20 ± 0.38
4 min	1.16 ± 0.37	0.91 ± 0.37	1.17 ± 0.34	1.16 ± 0.33	1.30 ± 0.51	1.20 ± 0.31
8 min	1.14 ± 0.35	0.92 ± 0.43	0.98 ± 0.27	1.15 ± 0.29	1.19 ± 0.45	1.20 ± 0.36
10 min	1.20 ± 0.45	0.99 ± 0.36	1.13 ± 0.37	1.14 ± 0.29	1.06 ± 0.51	1.31 ± 0.46
15 min	1.32 ± 0.53	1.08 ± 0.40	1.13 ± 0.27	1.20 ± 0.20	1.09 ± 0.41	1.16 ± 0.41
20 min	1.27 ± 0.52	0.99 ± 0.27	1.21 ± 0.20	1.11 ± 0.33	1.06 ± 0.43	1.04 ± 0.22

A decrease of the MEP amplitude after 10-Hz stimulation was observed, but was not significant.

Antal et al. Brain Stimul 2008

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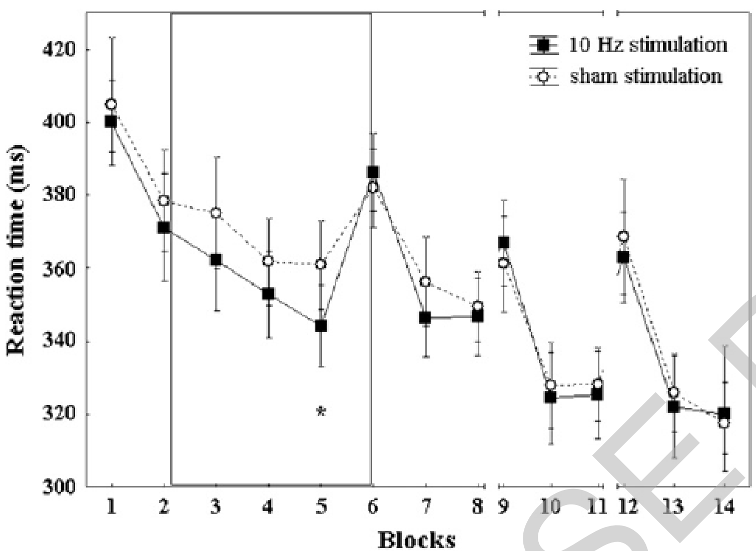
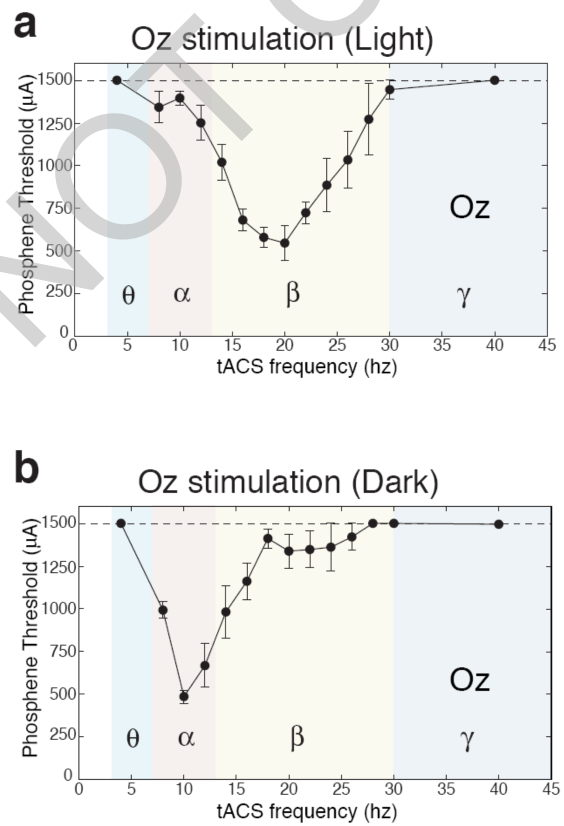
...but frequency-dependent functional effects





Antal et al. 2008, Kanai et al. 2008

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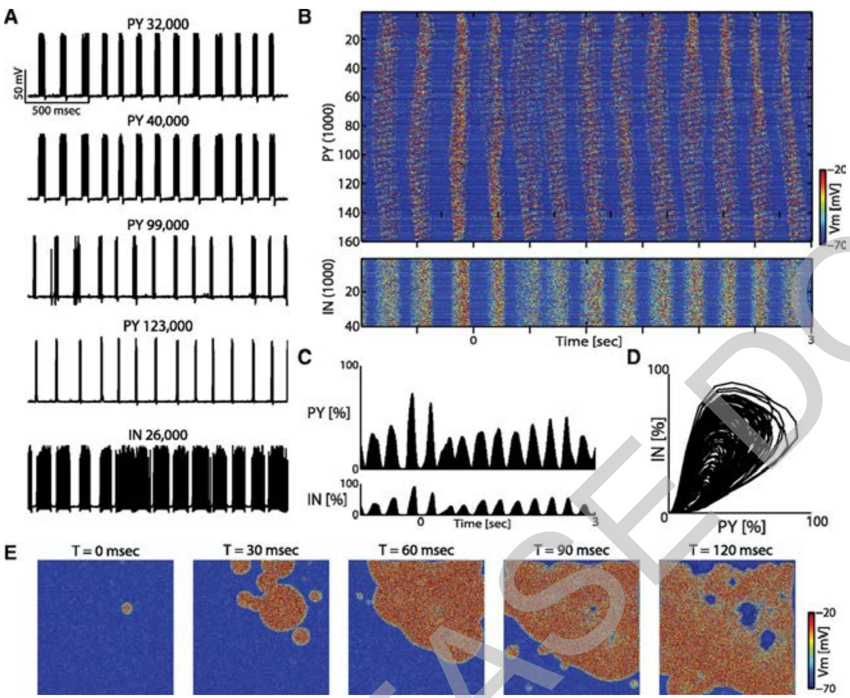
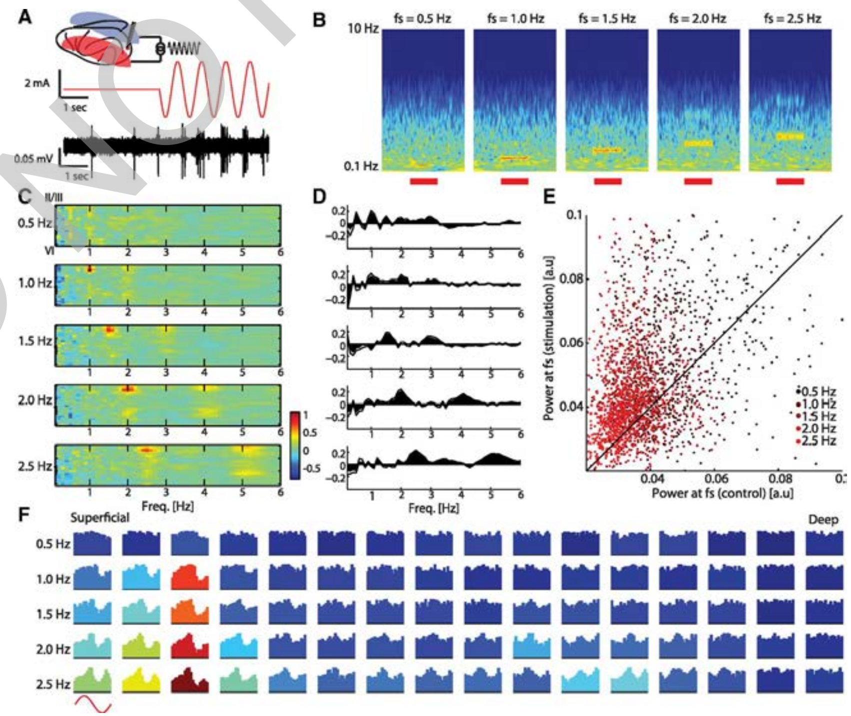
Physiology: Modulation of oscillatory activity by transcranial alternating current stimulation (tACS) I





Ali et al. 2013

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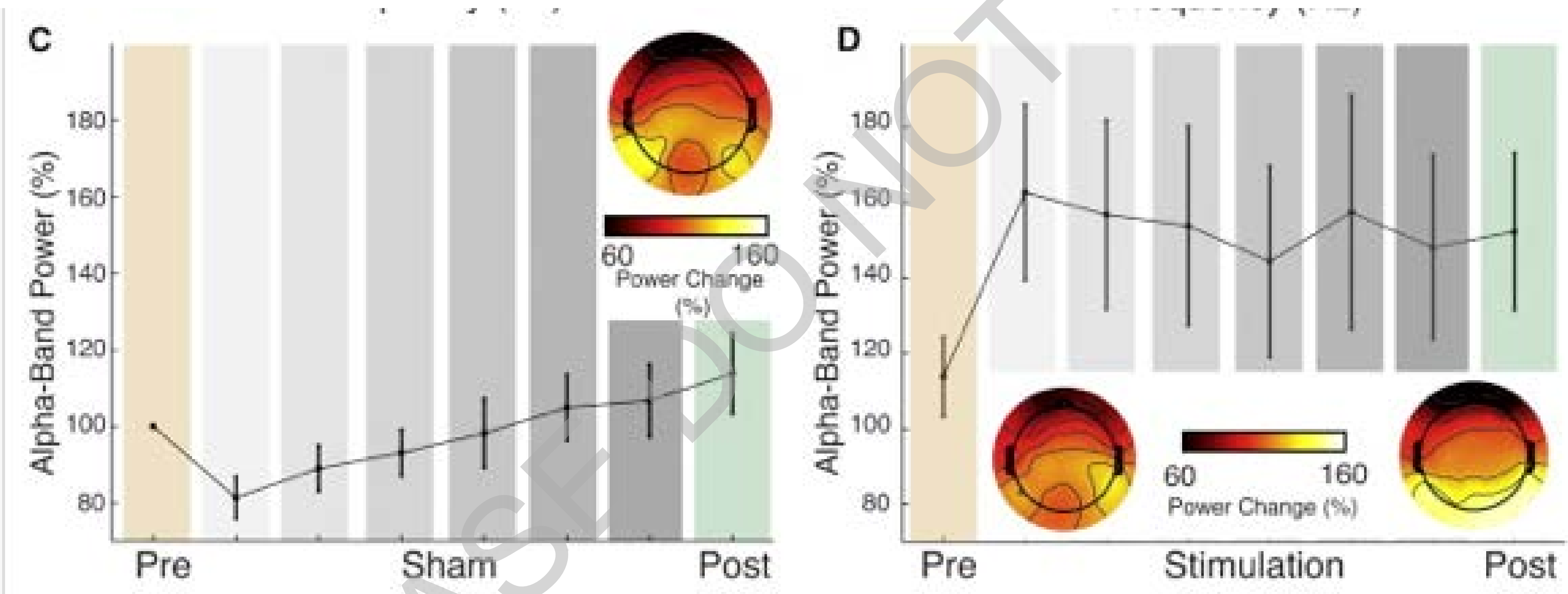
Physiology: Modulation of oscillatory activity by transcranial alternating current stimulation (tACS) II



Helfrich et al. et al. 2014

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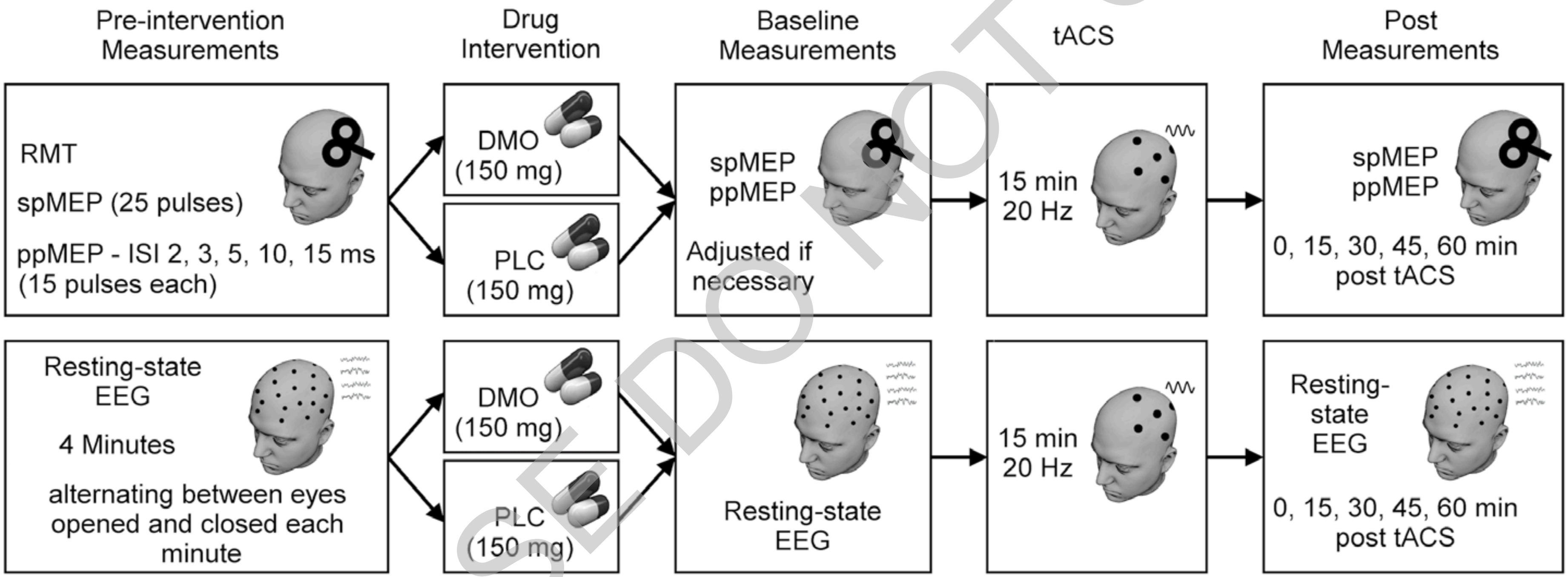
Physiology: Modulation of oscillatory activity by transcranial alternating current stimulation (tACS) III



Wischnewski et al., Cerebral Cortex, 2019

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Physiology: Modulation of oscillatory activity by transcranial alternating current stimulation (tACS) IV

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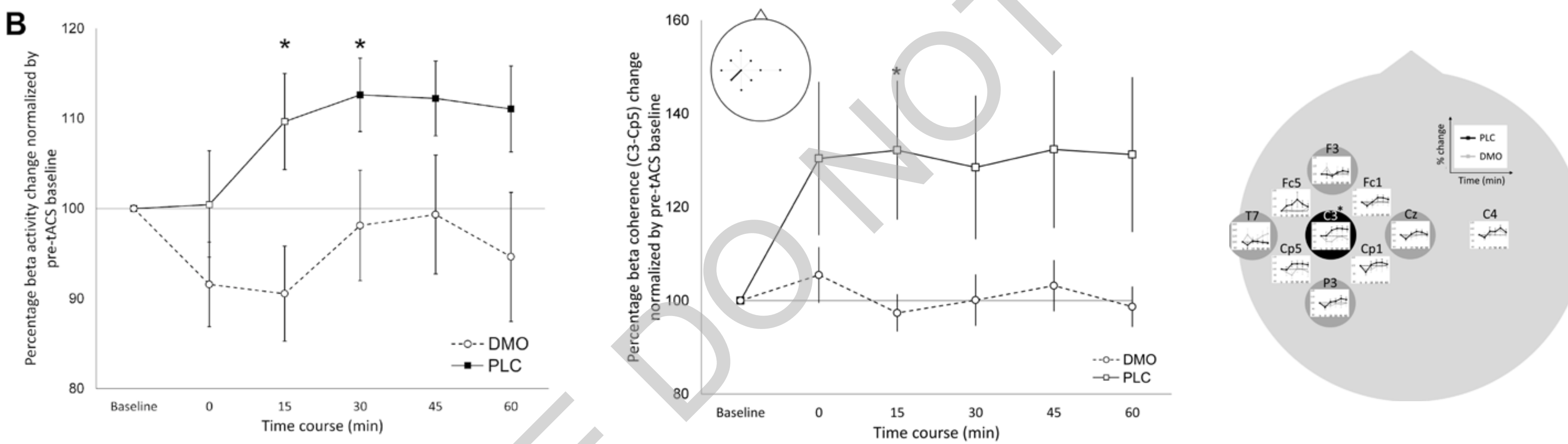
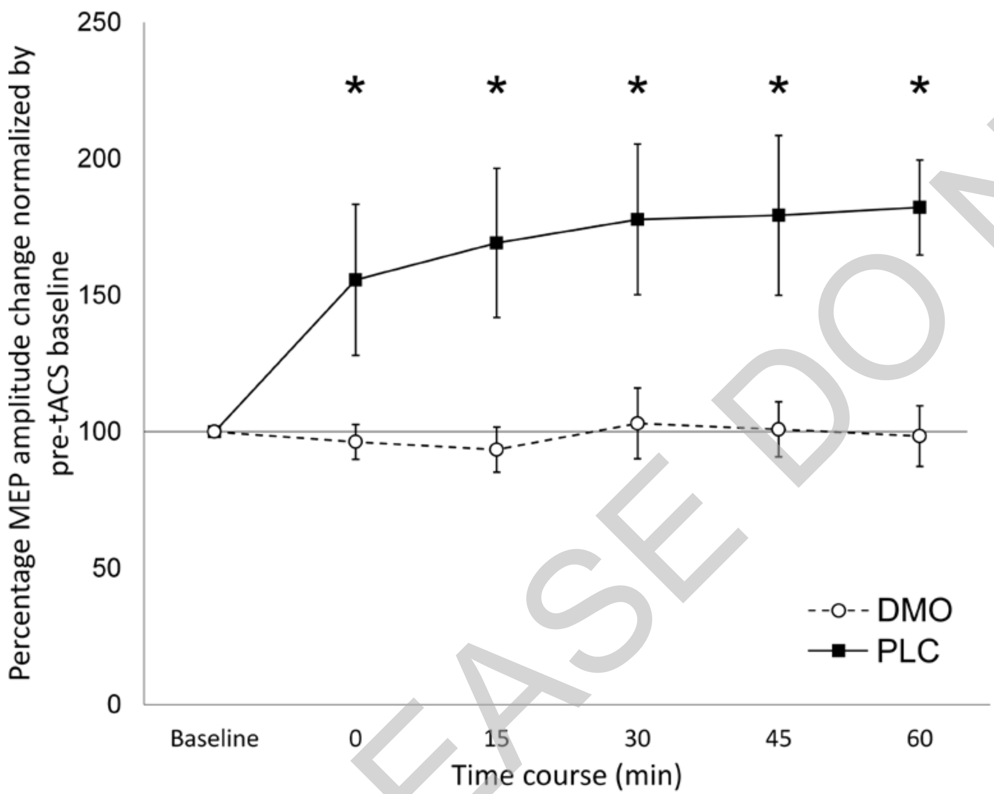


Wischnewski et al., Cerebral Cortex, 2019

Neuroplastic effects



Conclusions

- Alteration of oscillations via prolonged tACS
- Frequency-specificity of effects
- Enhancement of synchronization with neighbored areas
- Relatively regional effects
- Additional neuroplastic effects
- Both, oscillatory, and neuroplastic effects, depend on NMDA receptors

Wischnewski et al., Cerebral Cortex, 2019

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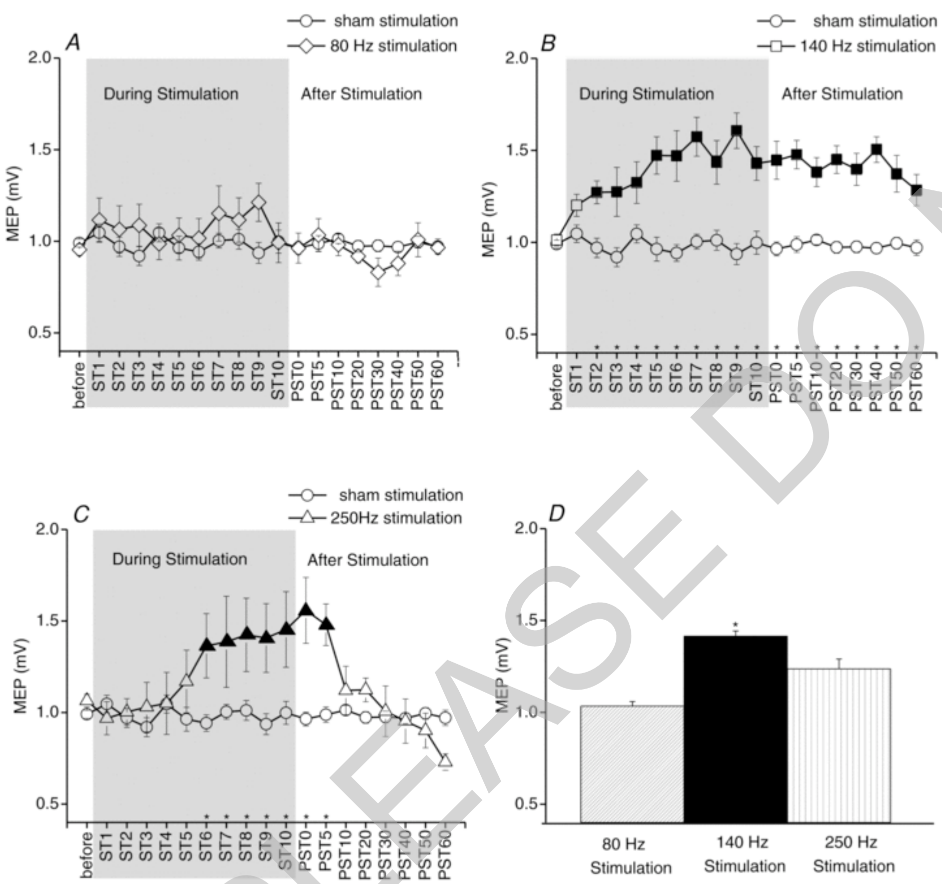
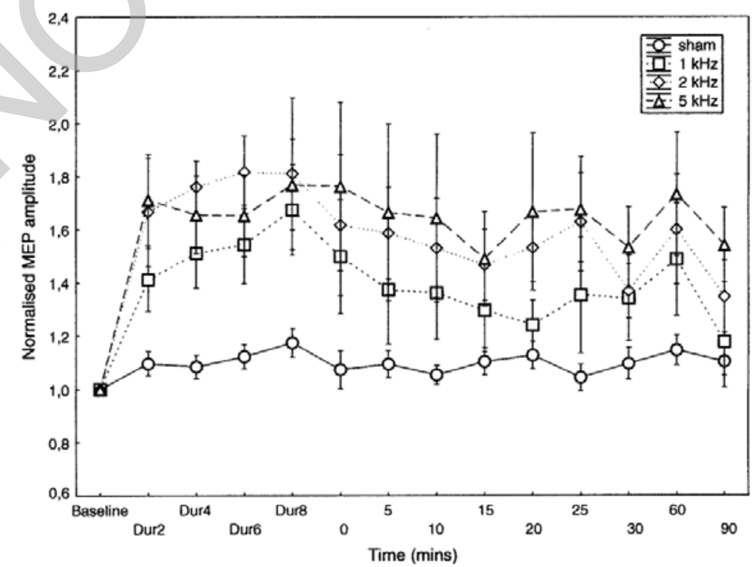
More neuroplastic effects induced by tACS

Ripple frequencies

Low kHz



tAC stimulation under complete muscle relaxation



Moliadze et al. 2010, Chaieb et al. 2011

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Conclusion IV

- tACS entrains oscillatory cortical activity
- Like tDCS, it has a modulatory, but not inducing effect
- Dependent on stimulation parameters, also neuroplastic effects are induced

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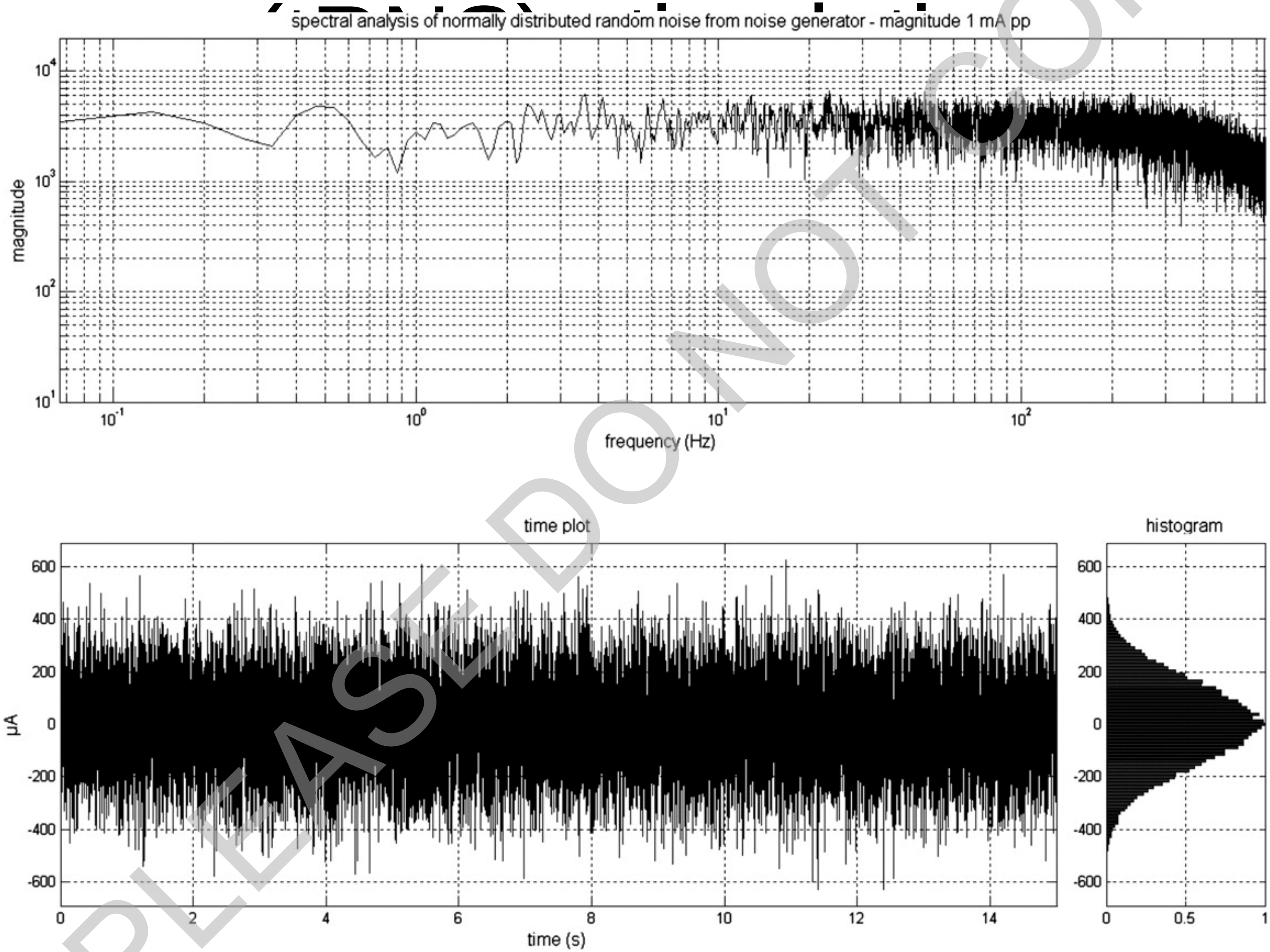
Transcranial random noise



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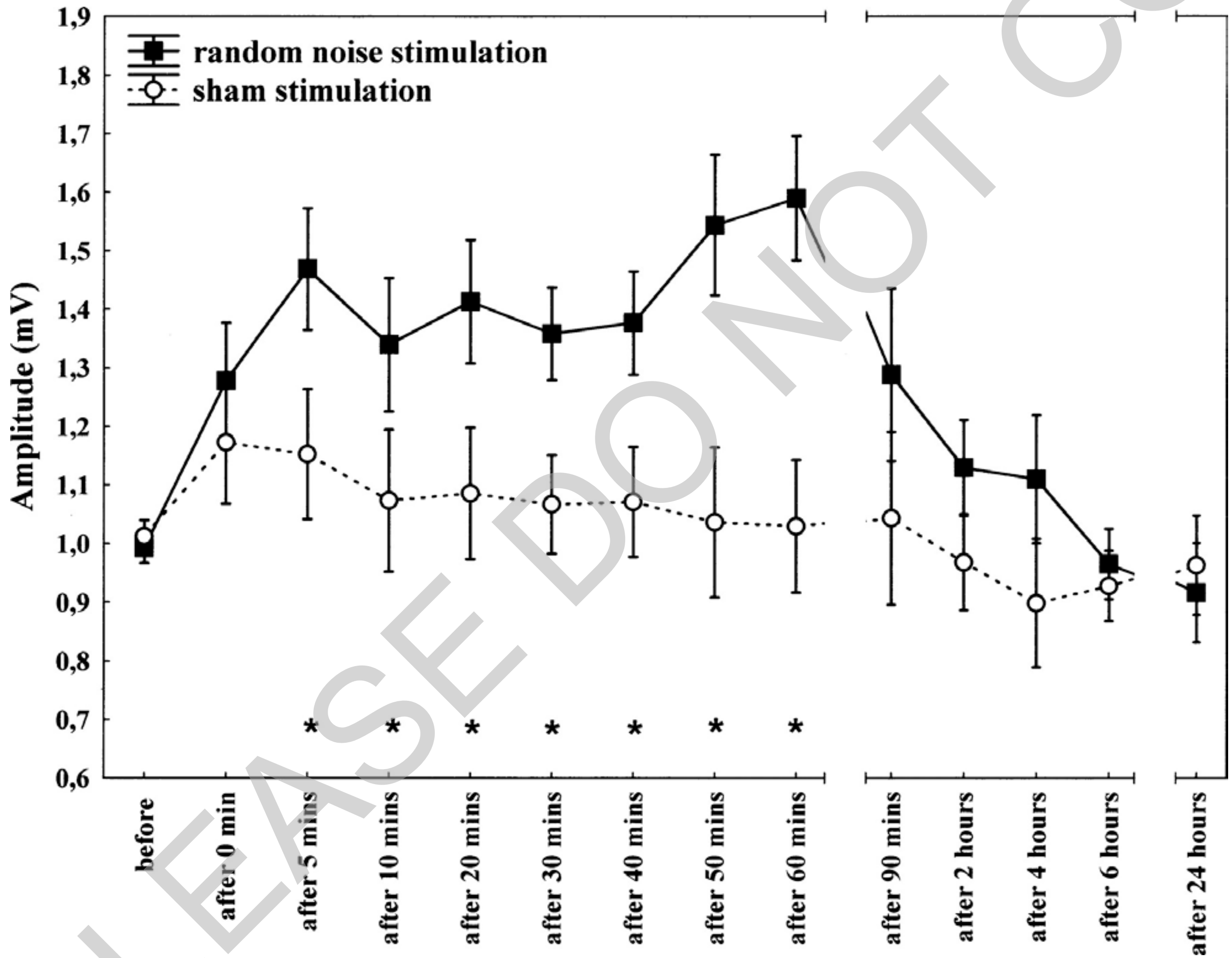
Terney et al. 2008

tRNS – physiological effects I



Terney et al. 2008

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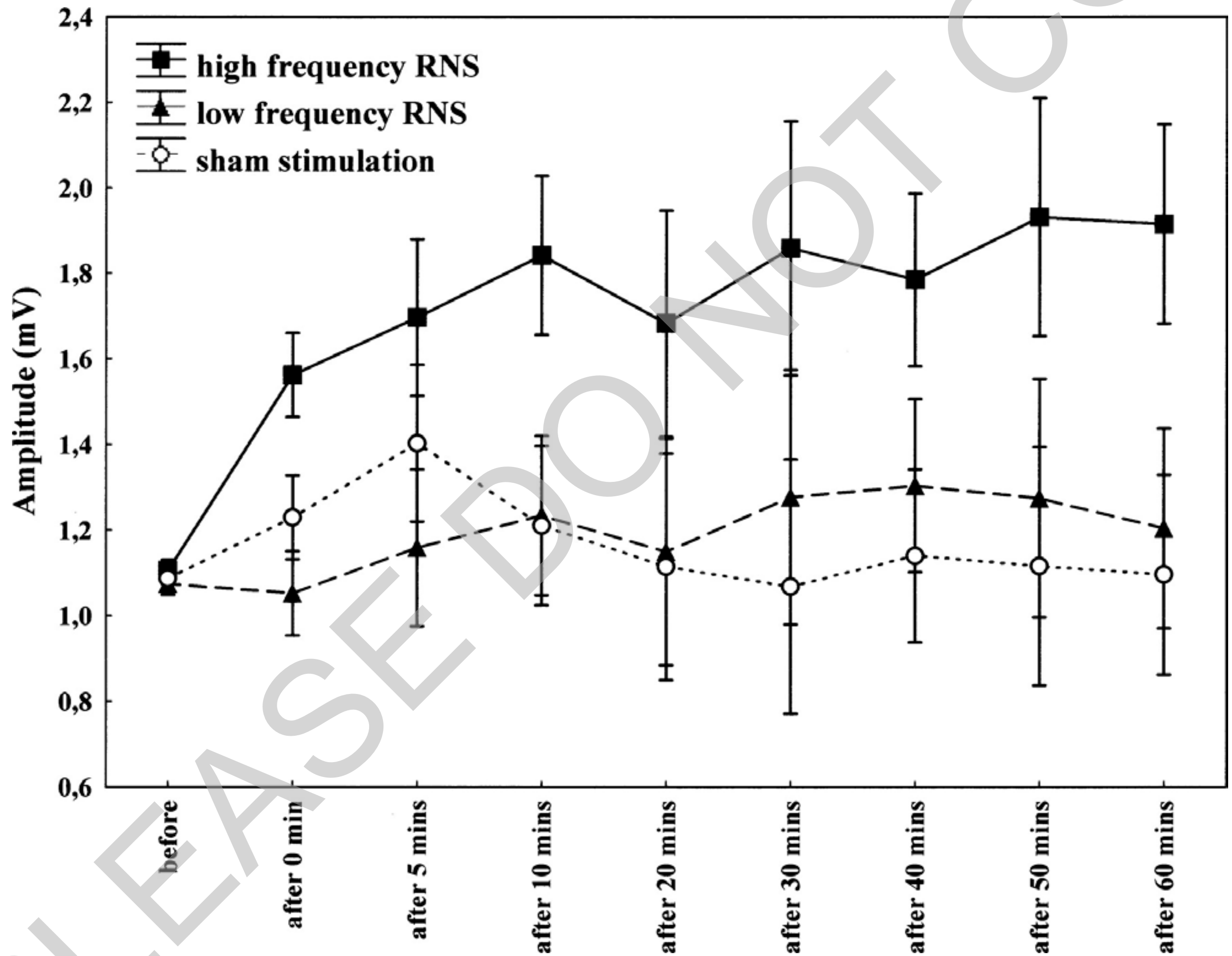
tRNS – physiological effects II



Terney et al. 2008

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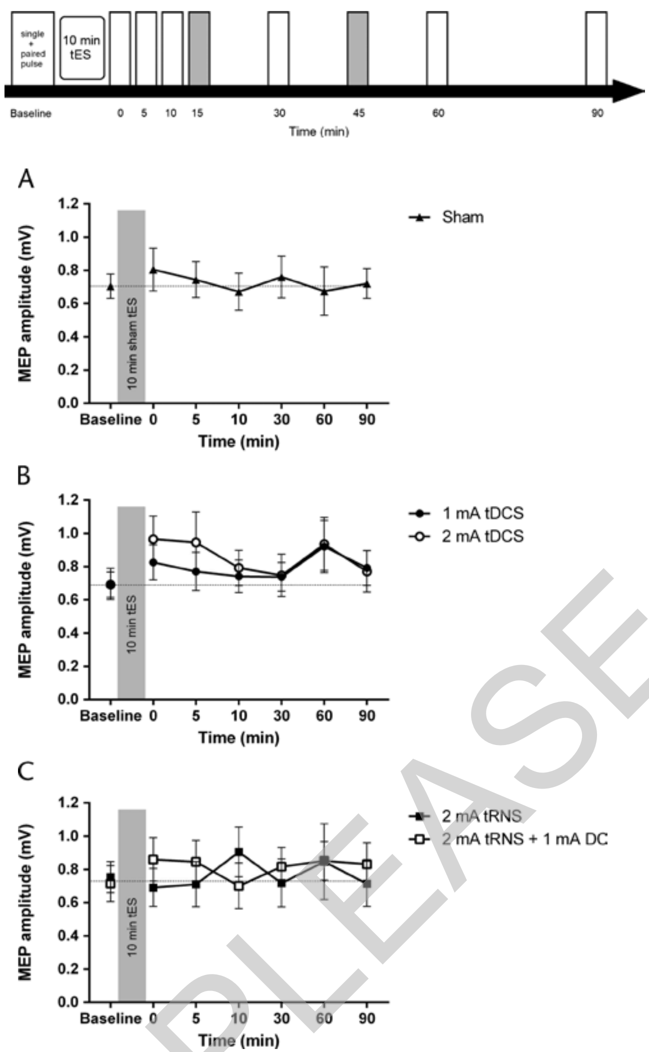
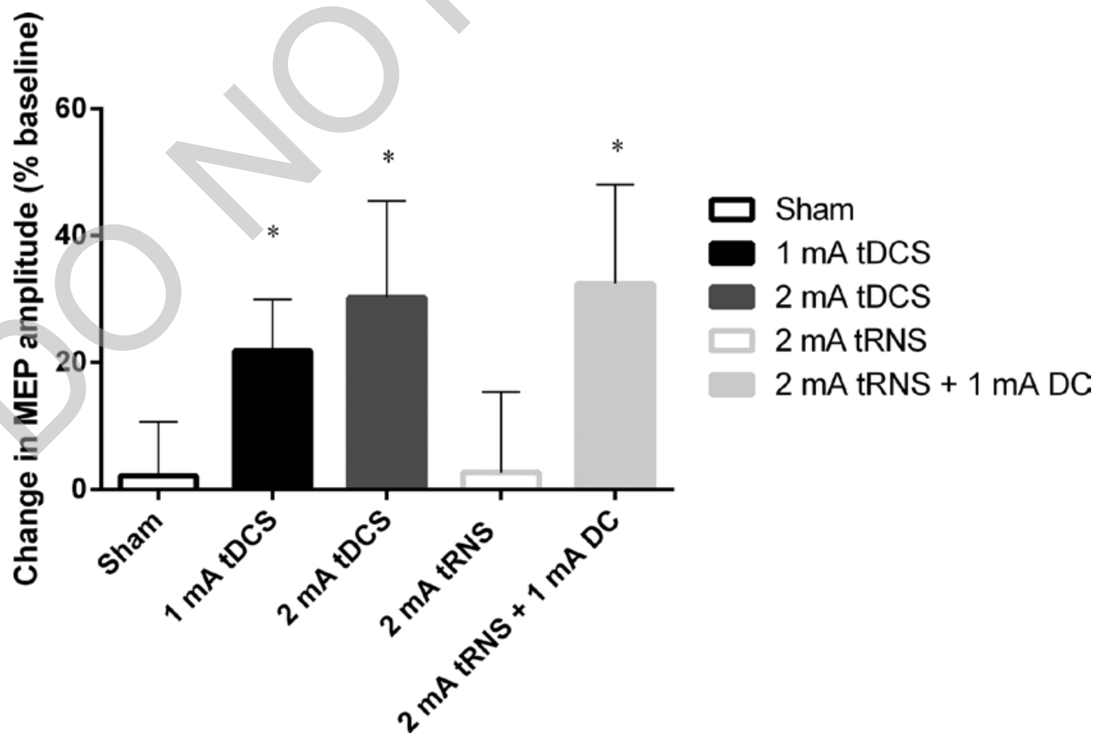
tRNS – physiological effects III





Ho et al. 2014

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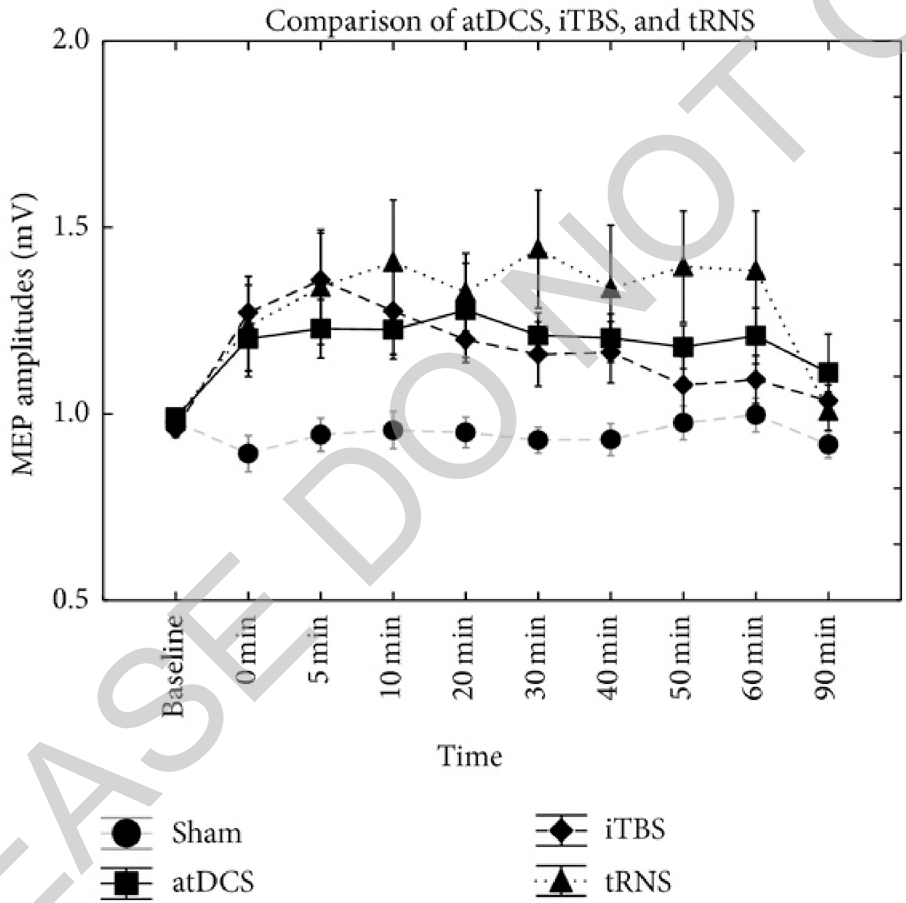
tRNS – physiological effects IV



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Moliadze et al. 2014

Conclusion V

- tRNS at high frequencies induces excitatory neuroplasticity, although mixed effects

- not clear if it induces random oscillations

- Effects look similar to anodal tDCS

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Final Remarks

- transcranial electrical stimulation induces acute alterations of cortical excitability and activity

- Prolonged tDCS induces neuroplastic after-effects

- tACS entrains cortical oscillations, some stimulation protocols also induce neuroplasticity

- tRNS induces plasticity which share similarities with anodal tDCS

- Beyond regional effects, also network effects are obtained

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Many thanks for your attention!

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The 13th CME International Conference on Complex Medical Engineering – in Dortmund, Germany on September 23-25, 2019

Venue: Westfalenhallen Dortmund
Rheinlanddamm 200
44139 Dortmund, Germany

General Chair: Prof. Michael Nitsche
Head of Department of Psychology & Neurosciences, Leibniz Research Centre for Working Environment and Human Factors (IfADo)

Important Dates:
February 28, 2019: Proposals for organized sessions
April 30, 2019: Submission of abstracts for organized sessions and posters
June 30, 2019: Submission of full papers
July 31, 2019: Notification

23.-25. September 2019

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