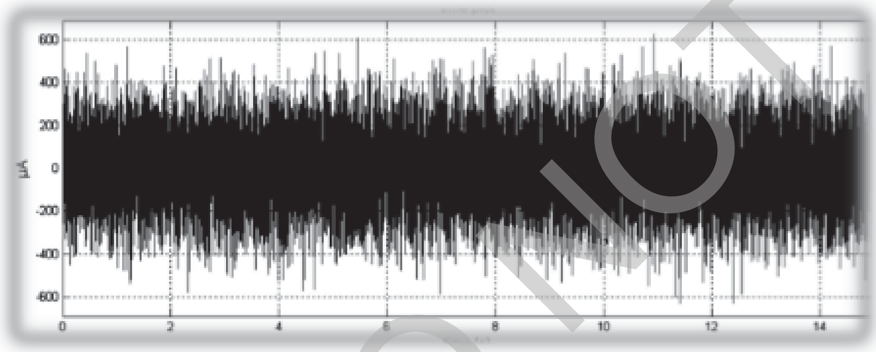
Transcranial Random Noise Stimulation- tRNS



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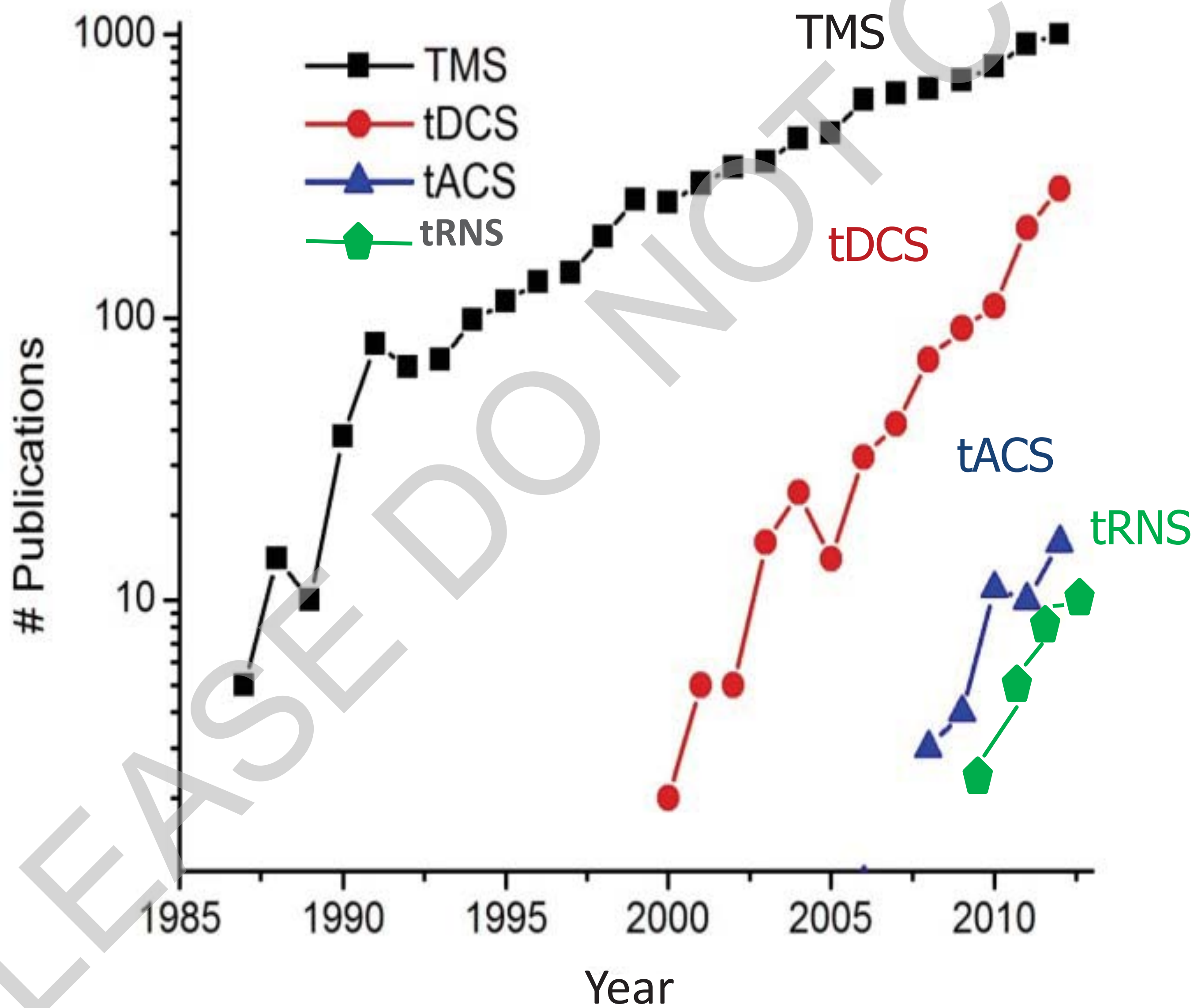
Boston, June 24th 2019

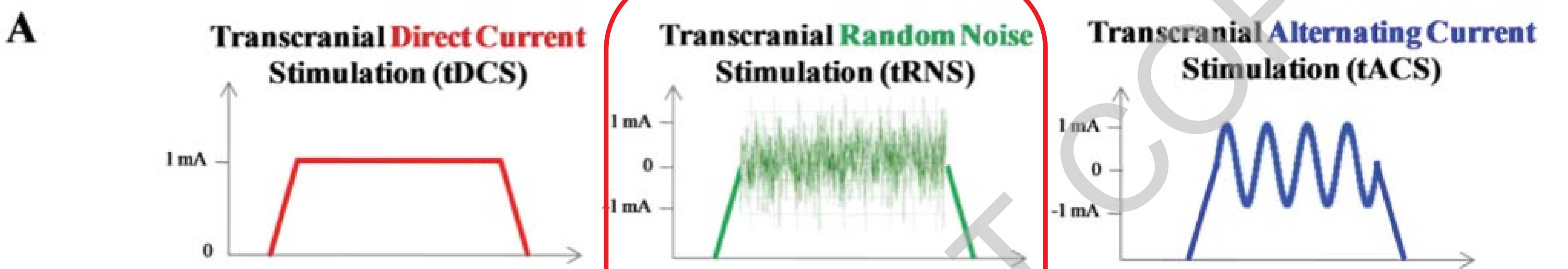
BA CNBS Berenson-Allen Center For Noninvasive Brain Stimulation

VE RI TAS HARVARD

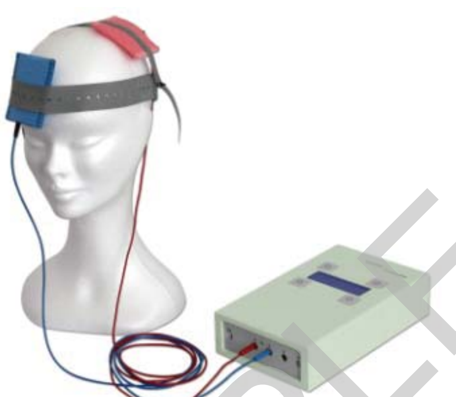
Transcranial Random Noise Stimulation (tRNS)



tCS family



	tDCS	tRNS	tACS
Current	Constant/Direct	Oscillatory/Alternating	Oscillatory/Alternating
Stimulation parameters	Anode: excitatory Cathode: inhibitory	1-640 Hz (random) 100-640 Hz: excitatory	Frequency (Hz) Phase (Degrees)
Mechanism	Membrane polarization	Stochastic resonance	Entrainment
Effect on	Cortical excitability	Cortical excitability	- Brain oscillations (power, phase) - Cortical excitability (>100Hz)
Neuronal effect	During and After	During and after	During and After

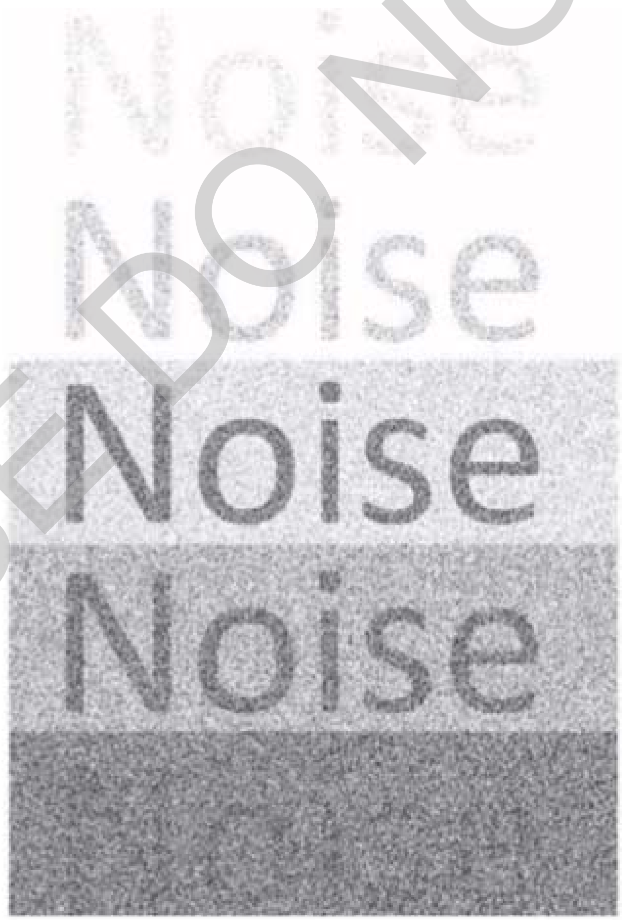


Santarnecchi et al. 2015

Noise in a complex system

If everything else is ideal, then noise is the enemy.

However, in the presence of a *weak* signal <u>noise is beneficial for signal detection</u>



Beneficial Effect of Noise

Benefits have been reported in diverse systems, including:

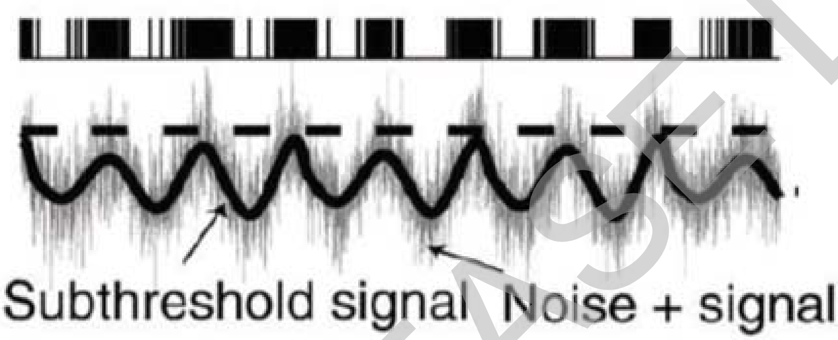
- Climate models
- Electronic circuits
- Differential equations
- Lasers
- Neural models
- Physiological neural populations and networks
- Chemical reactions
- Ion channels
- SQUIDs (superconducting quantum interference devices)
- Ecological models
- Cell biology
- Financial models
- Psychophysics
- Nanomechanical oscillators
- Organic semiconductor chemistry
- Social systems

McDonnell & Abbott, 2009, PLoS Comp Biol

Noise in Nonlinear Systems: Stochastic Resonance

Nonlinearity: presence of noise in a nonlinear system is better for output signal quality than its absence. Noise cannot be beneficial in a linear system

Performance (noise + nonlinearity) > Performance (nonlinearity)



Stochastic facilitation: Random noise enhances the detection of weak stimuli and/or the information content of a signal (Moss et al., 2004, Clin Neurophysiol; McDonnell & Ward, 2011, Nat Rev Neurosci)

Noise in Nonlinear Systems: Stochastic Resonance

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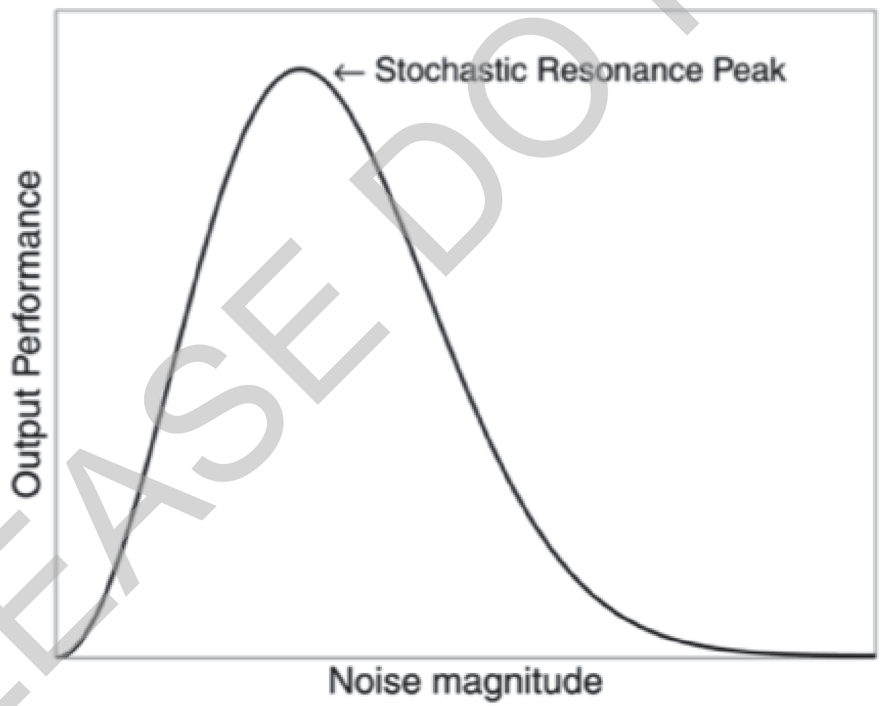
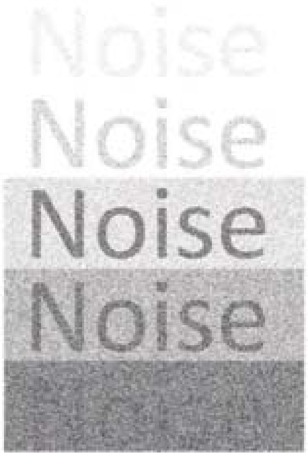
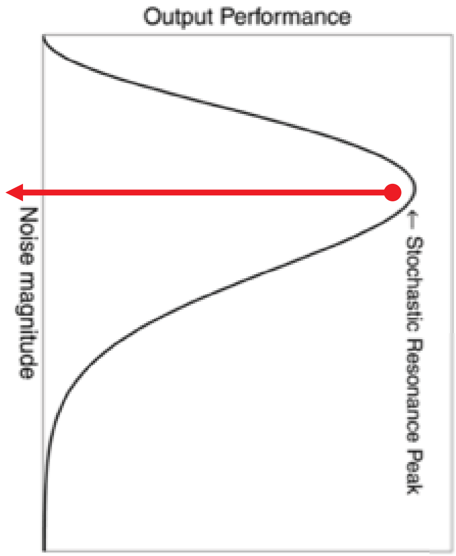
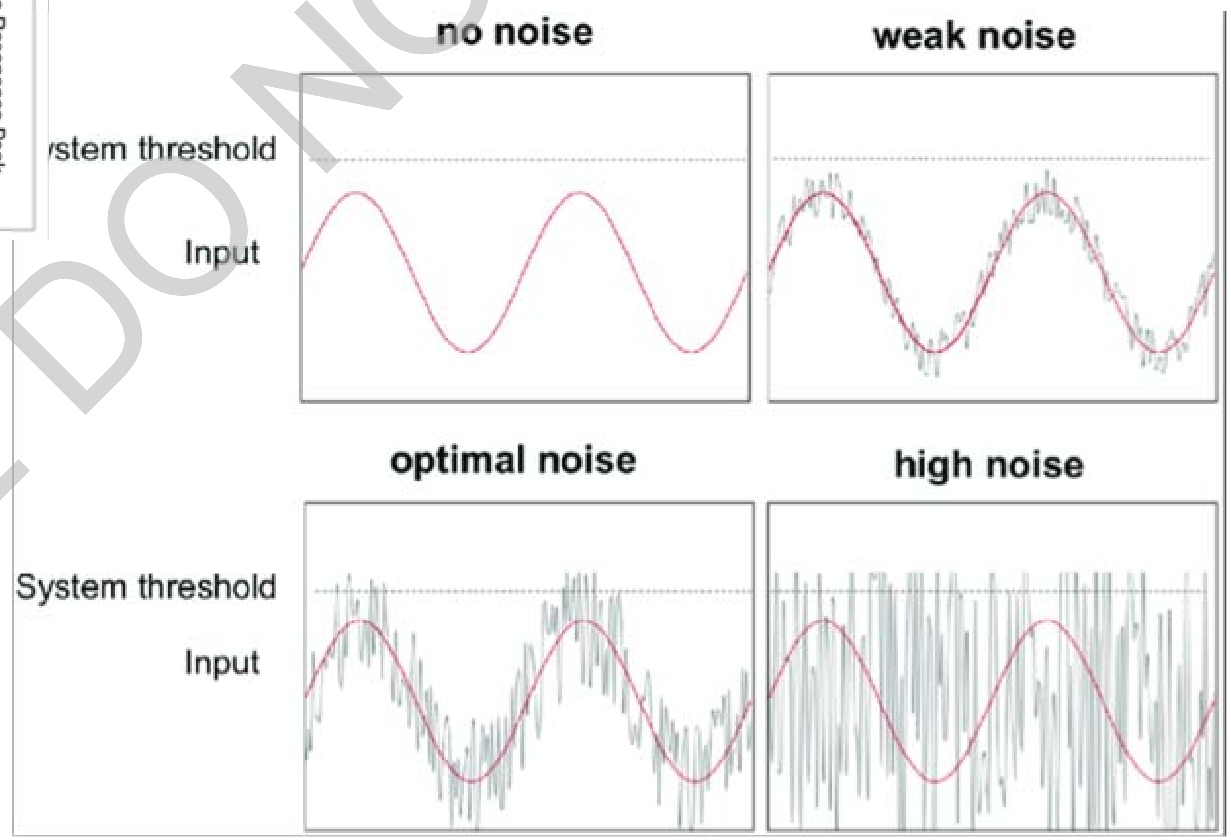


McDonnell & Abbott, 2009, PLoS Comp Biol

Optimal Amount of Noise

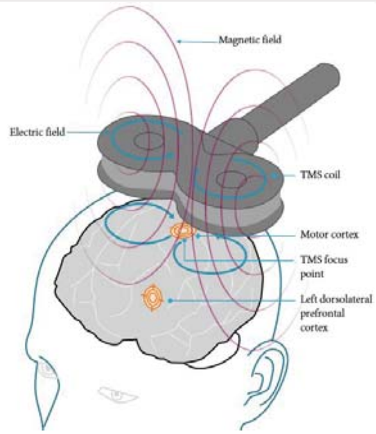






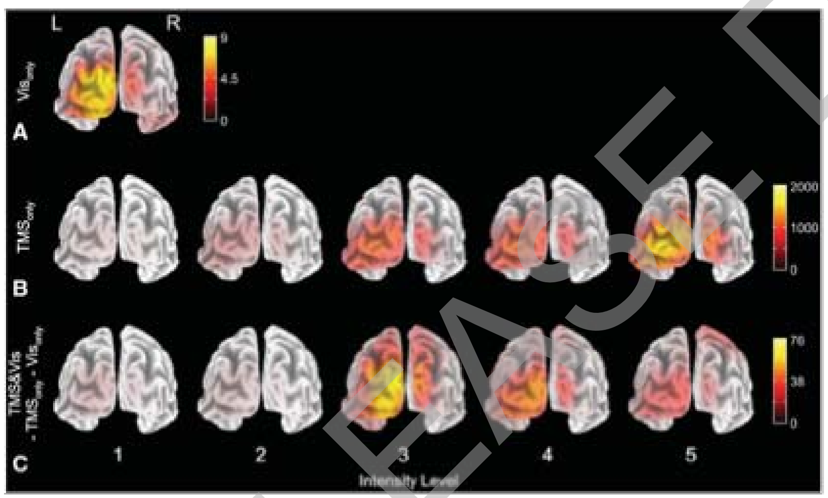
Impact of Noise in the Human Brain..?

Stochastic resonance theory and TMS



TMS: Transcranial Magnetic Stimulation

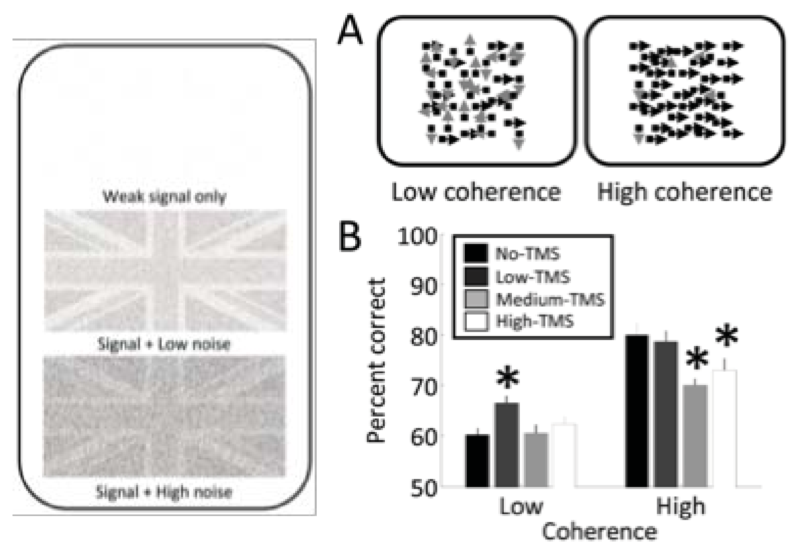
Lower intensity of TMS enhances processing of visual stimuli; higher intensity impairs it



Effects of transcranial magnetic stimulation on visual evoked potentials in a visual suppression task

A. Reichenbach [a,1], K. Whittingstall [b,1], A. Thielscher [a,*]

Lower intensity of TMS facilitates visual motion detection; higher intensity of TMS disrupts it



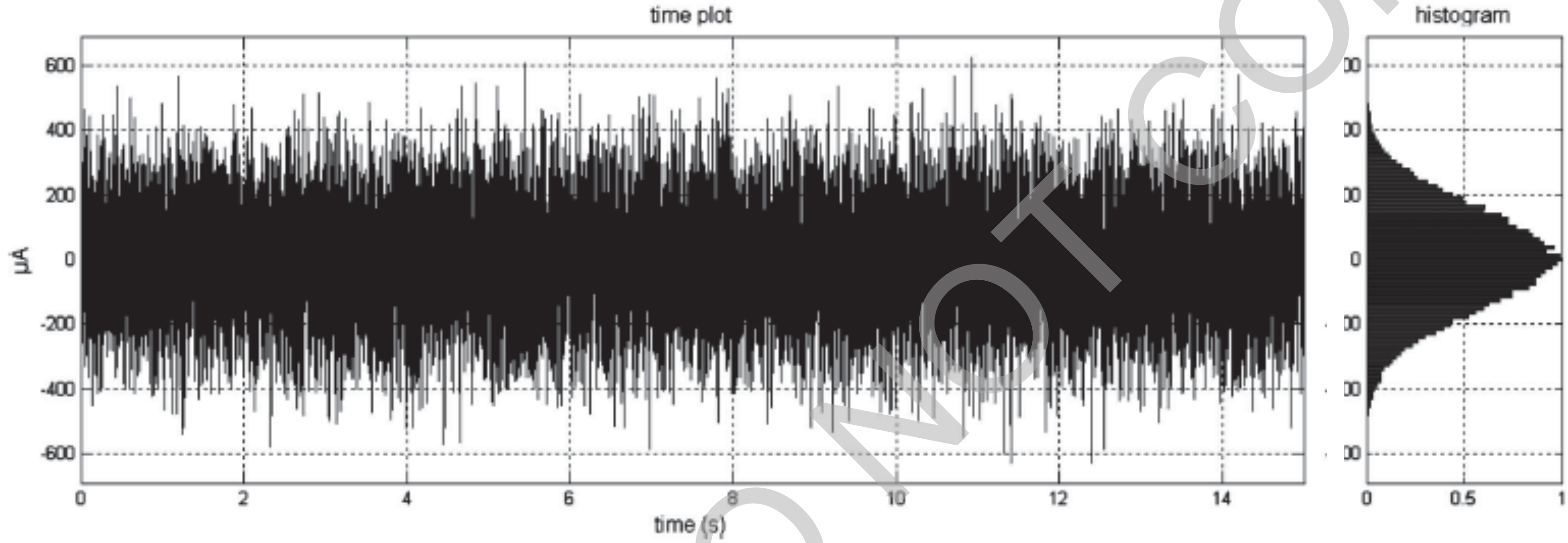
Stochastic resonance effects reveal the neural mechanisms of transcranial magnetic stimulation

Dietrich Samuel Schwarzkopf [1,2,*], Juha Silvanto [3], and Geraint Rees [1,2]

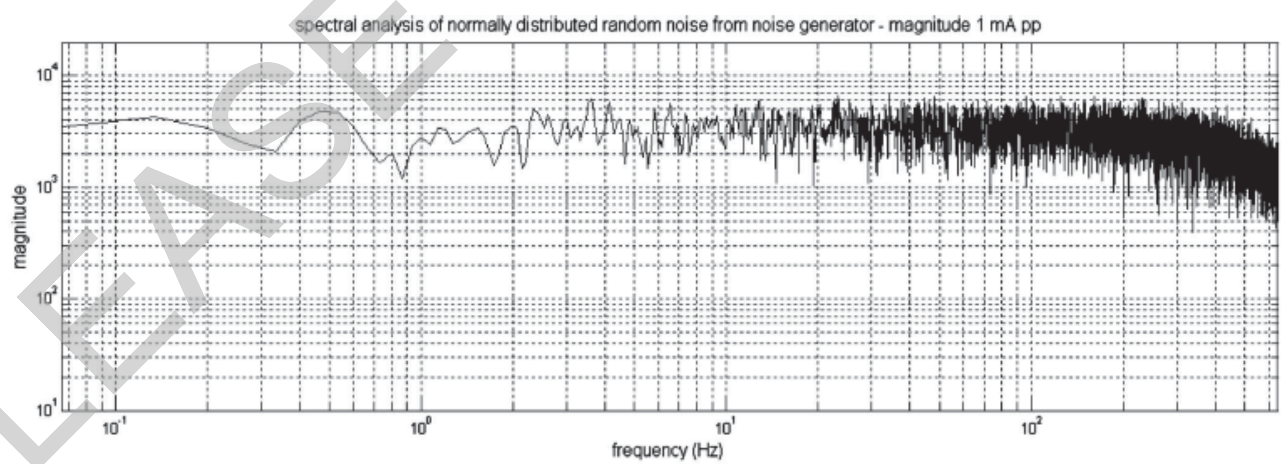
tRNS: First evidence in humans

tRNS - Method

Terney et al., 2008



Random level of current generated for every sample (frequency 1-640Hz). The signal is normally distributed, with the current intensity constantly fluctuating around 0uA. For a 1mA amplitude, 99% of the Current is between -500/500uA (Peak to Peak amplitude)



Stimulation frequency constantly change within a predefined spectrum

tRNS – Neurophysiological evidence

Terney et al., 2008

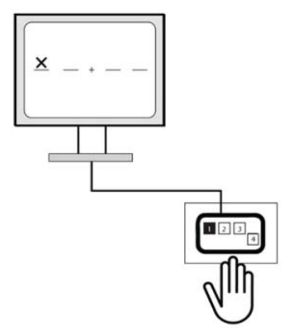
Experiment 1
10'
tRNS (1-640Hz)

Experiment 2
10'
tRNS (1-100Hz) *vs* (101-640Hz)

Stimulation site: Primary Motor Cortex, Premotor cortex

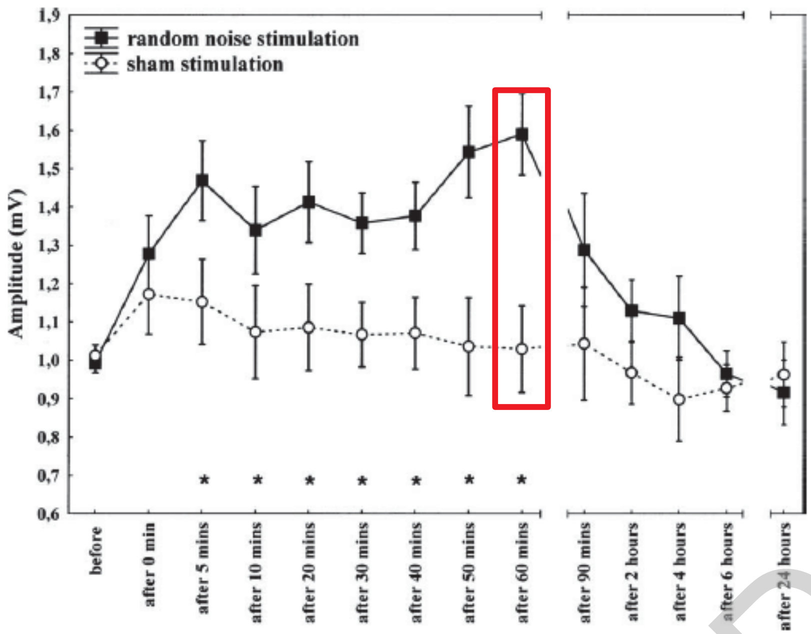
Electrophysiological evaluation: Motor Evoked Potential (MEP), Rectruitment Curve, Short-Interval Intracortical Inhibition (SICI), Intracortical Facilitation (ICF), Long-Interval Intracortical Faciliation (LICI), Cortical Silent Period (CSP).

Behavioural evaluation: Serial Reaction Time Task (SRTT)



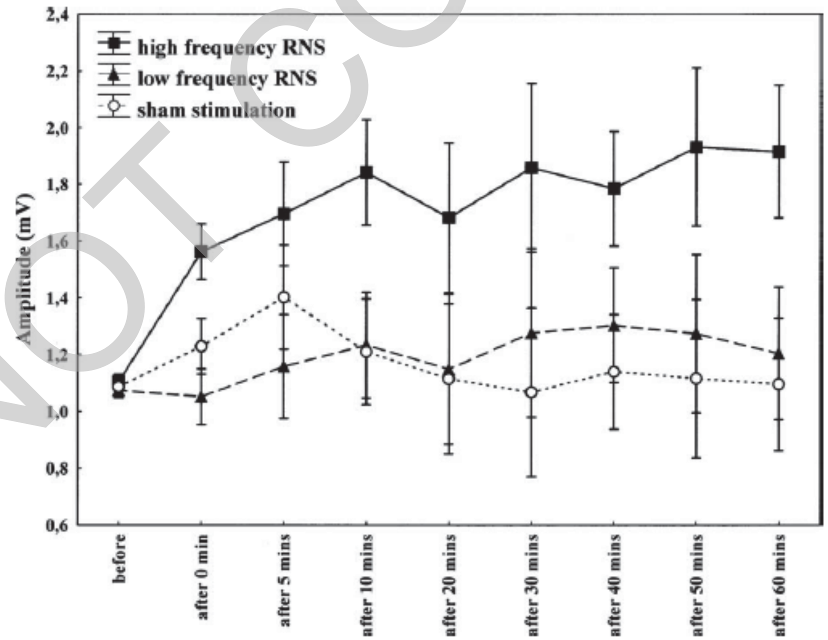
tRNS - Results

Experiment 1
tRNS (1-640Hz)

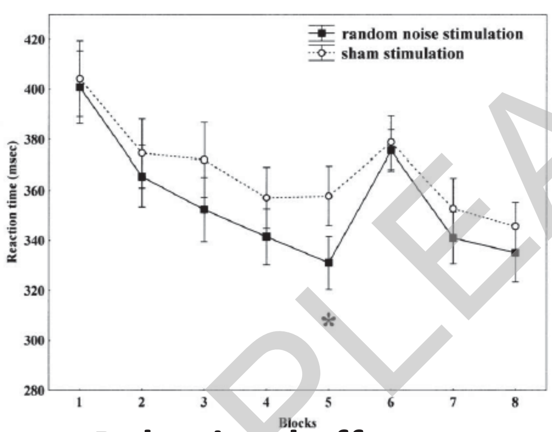


Increase in cortical excitability lasting for 60' after stimulation.

Experiment 2
tRNS (1-100Hz) *vs* (101-640Hz)



Effect is selective for **High-Frequency tRNS** (101-640Hz)



Behavioral effect

tRNS improves **implicit motor learning** in its early phase (<RT).

Significant effect on ICF (12, 15ms)
No changes in Recruitment Curve, SICI, LICI, CSP.
No effect for premotor cortex stimulation.

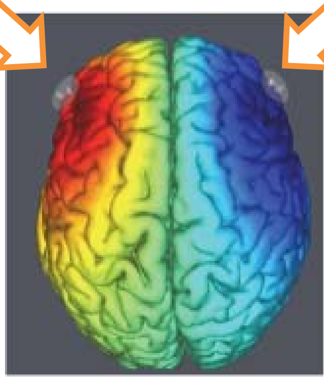
tRNS vs other tCS techniques

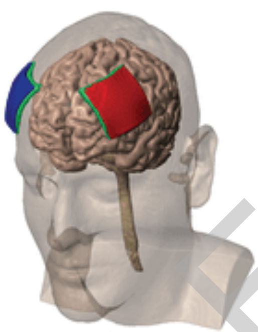
tRNS vs tDCS vs tACS: Induced Electrical field and Polarity

tDCS

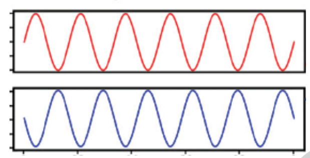
Anodal stimulation

Cathodal stimulation



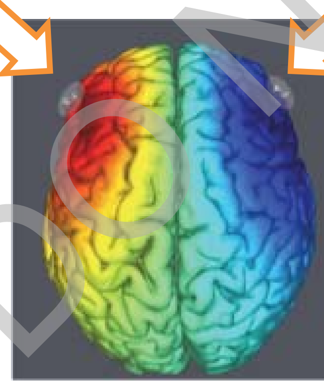


tACS



tACS @ 0 Degrees Phase

tACS @ 180 Degrees Phase

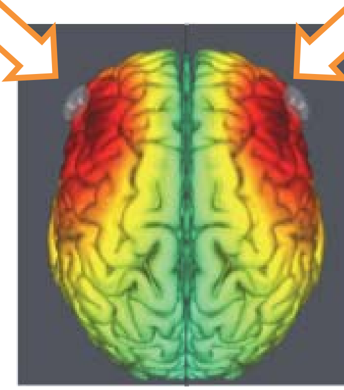


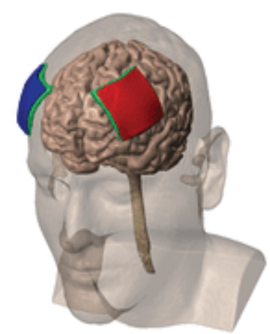
tRNS

No anode and cathode..

Excitatory Effect

Excitatory Effect





tRNS vs tDCS: effect on on cortical excitability

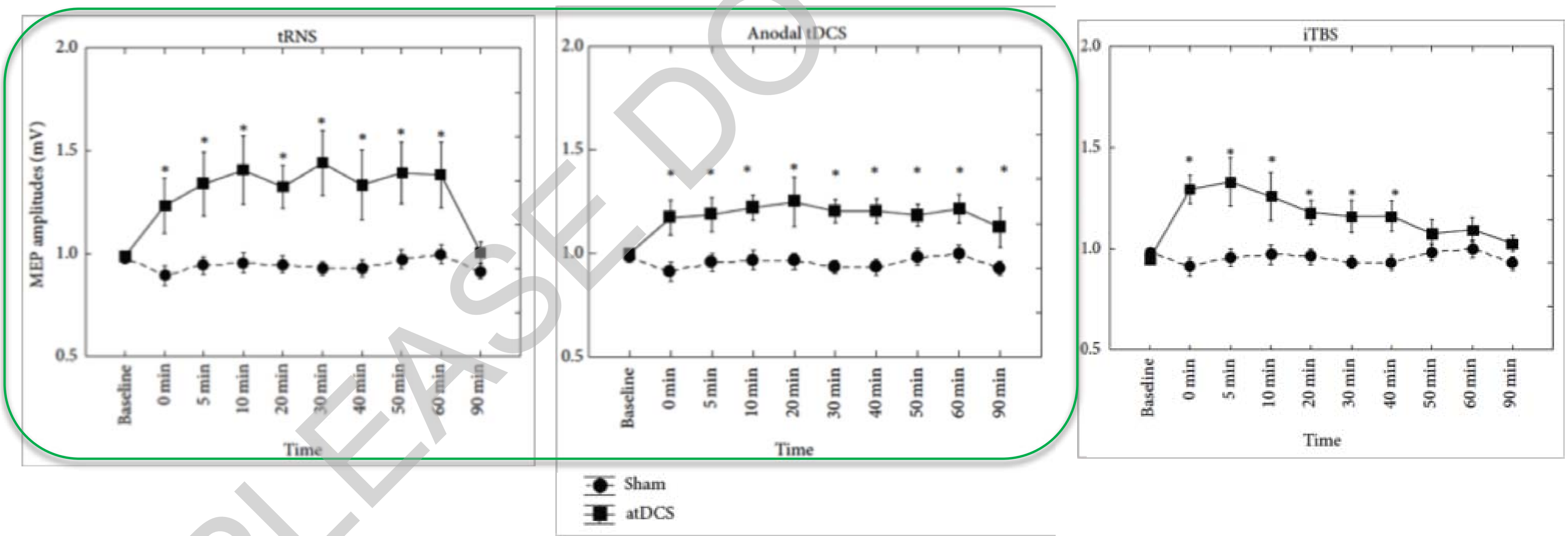
Moliadze et al. 2014 *Neural Plast*

tRNS vs. anodal tDCS vs. iTBS (intermittent Theta Burst TMS)

- tRNS, tDCS: 1mA over Left M1 (4x4cm sponges) and Right orbit (6x14cm) for 10 min.

- iTBS: 3 pulses at 50 Hz repeated at 5 Hz, 80% of the active motor threshold (600 pulses) over the L M1.

- 12 healthy subjects

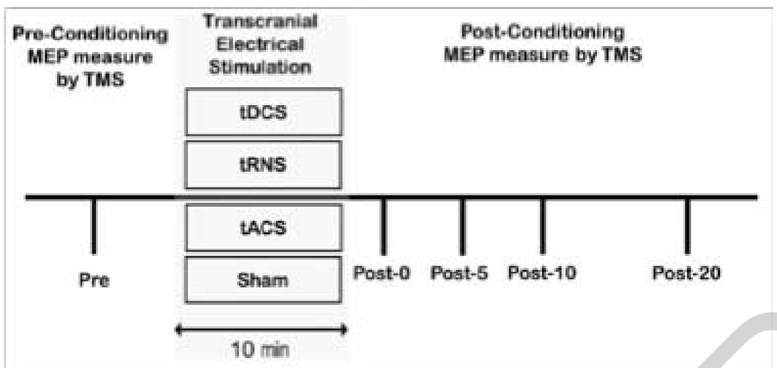


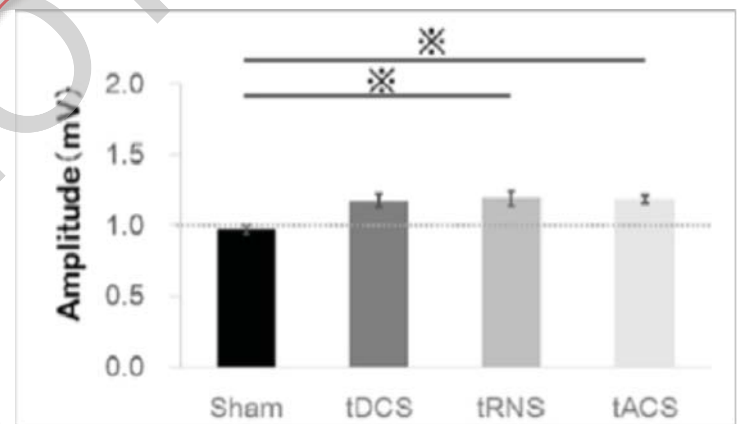
tRNS vs tDCS vs tACS: effect on on cortical excitability

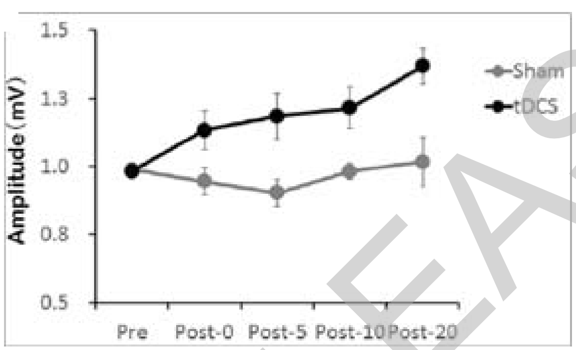
Inukai et al. 2016 *Front Hum Neurosci*

tRNS vs. tDCS vs. 140Hz tACS

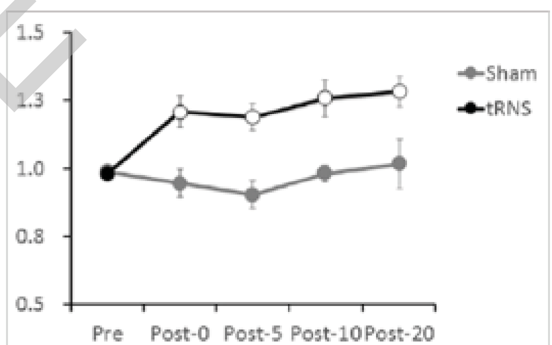
1mA over Left M1 and Right orbit (5x7cm) for 10 min in 15 healthy subjects



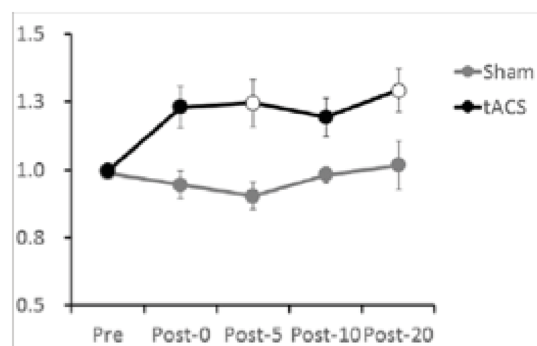




↑ MEP size



↑ MEP size



↑ MEP size

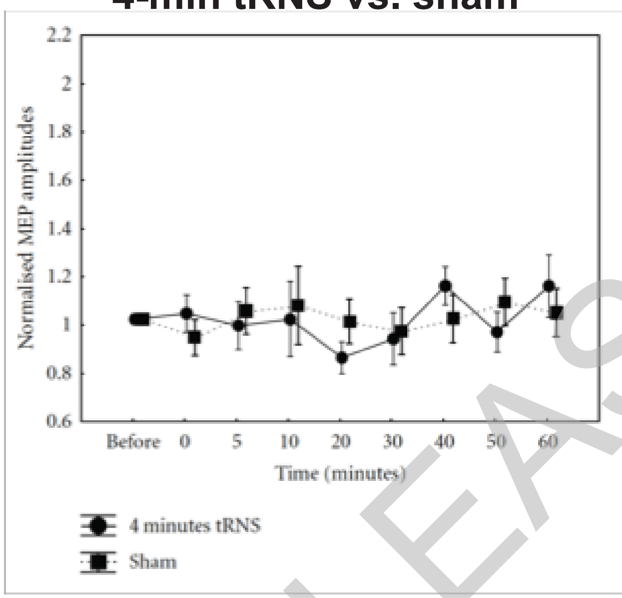
tRNS vs tDCS vs tACS: effect of stimulation duration

Chaieb et al. 2011 *Neural Plast*

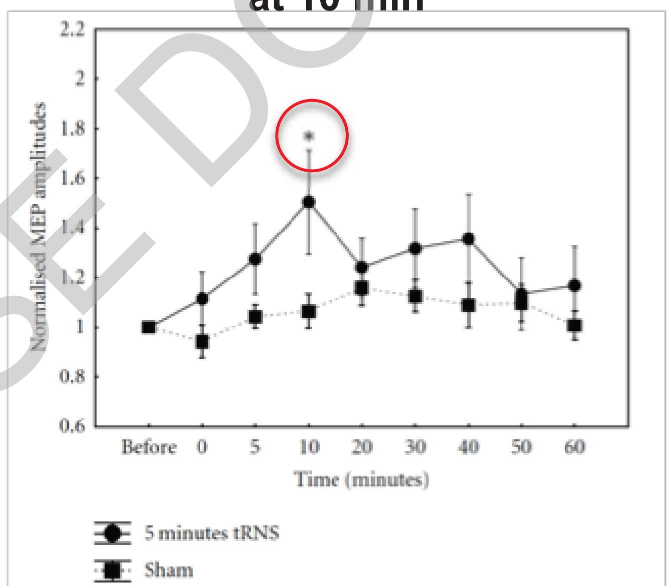
tRNS vs. sham

1mA over Left M1 (4x4cm) and Right orbit (6x14cm) during 4 min (N=10 subjects), 5 min, and 6 min (N=12 subjects).

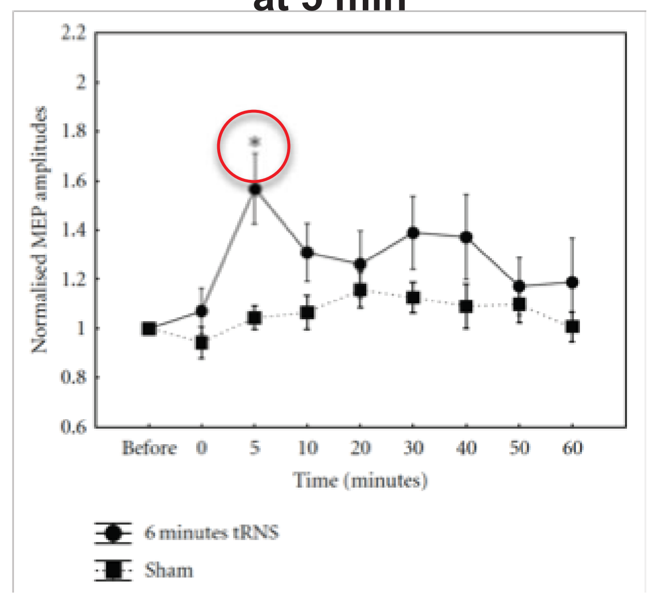
No difference between 4-min tRNS vs. sham



Difference between 5-min tRNS vs. sham at 10 min



Difference between 6-min tRNS vs. sham at 5 min



Duration

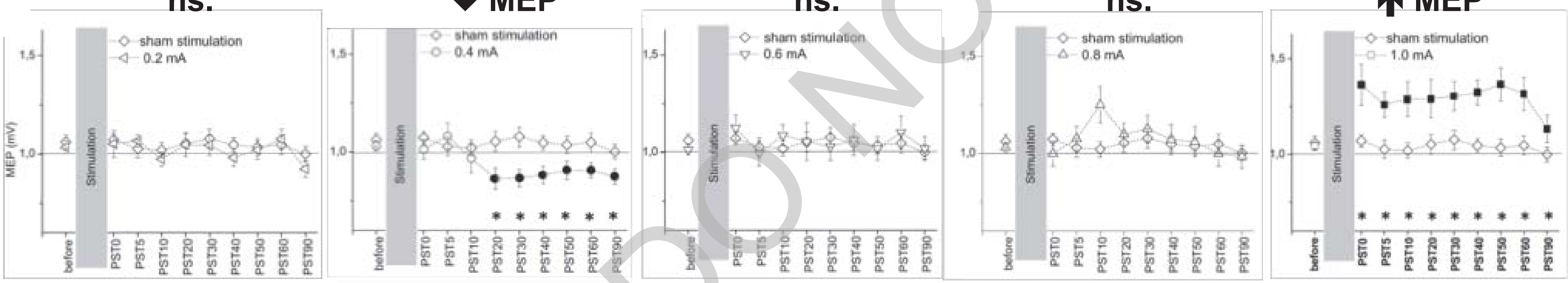
tRNS vs. 140Hz tACS on cortical excitability: effects of stimulation intensity

Moliadze et al. 2012 *Brain Stimul*

0.2, 0.4, 0.6, 0.8, 1mA over Left M1 (4x4cm) and Right orbit (6x14cm) for 10 min in 14 healthy subjects (tRNS) and 11 healthy subjects (tACS).

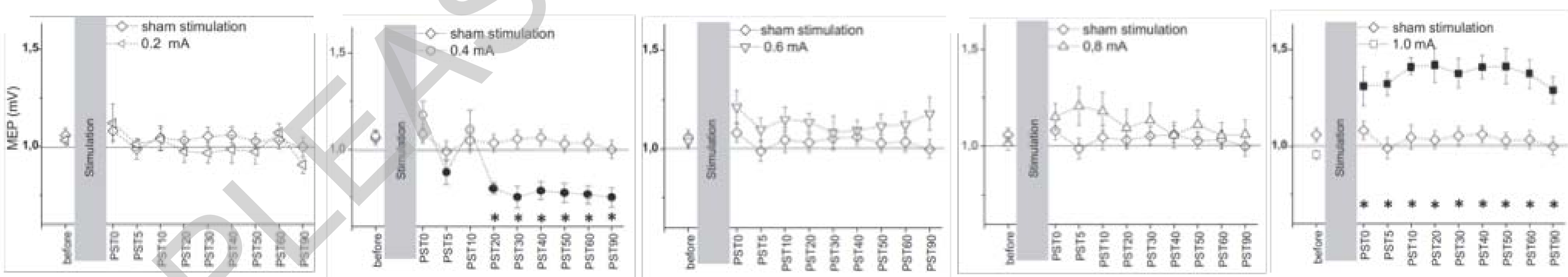
tRNS:

0.2 mA vs. sham: ns. | 0.4 mA vs. sham: ↓ MEP | 0.6 mA vs. sham: ns. | 0.8 mA vs. sham: ns. | 1mA vs. sham: ↑ MEP



tACS:

0.2 mA vs. sham: ns. | 0.4 mA vs. sham: ↓ MEP | 0.6 mA vs. sham: ns. | 0.8 mA vs. sham: ns. | 1mA vs. sham: ↑ MEP

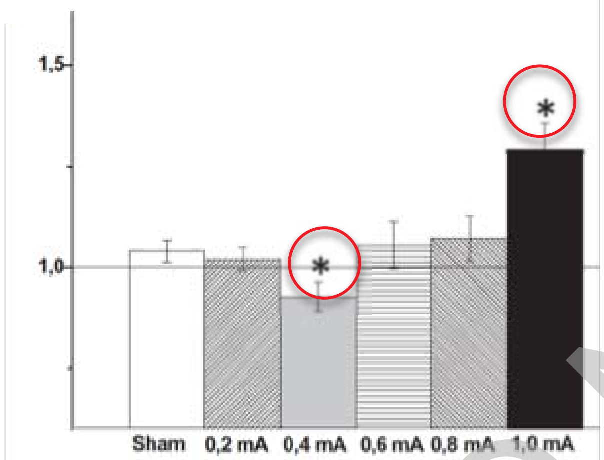


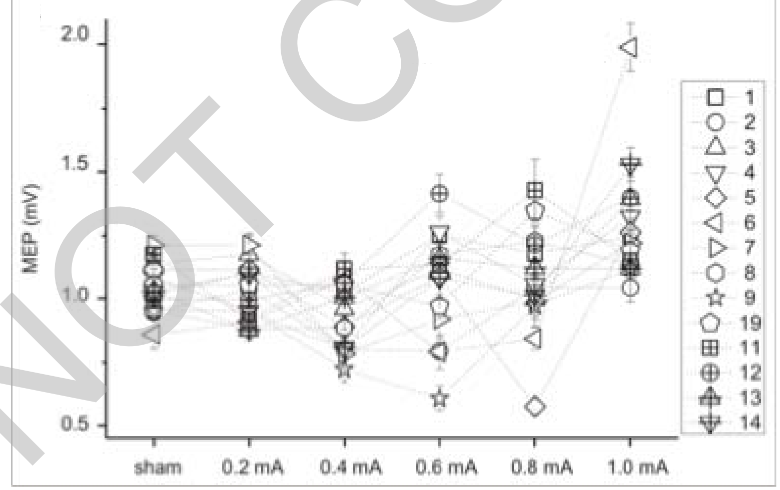
tRNS vs. 140Hz tACS on cortical excitability: effects of stimulation intensity

Moliadze et al. 2012 *Brain Stimul*

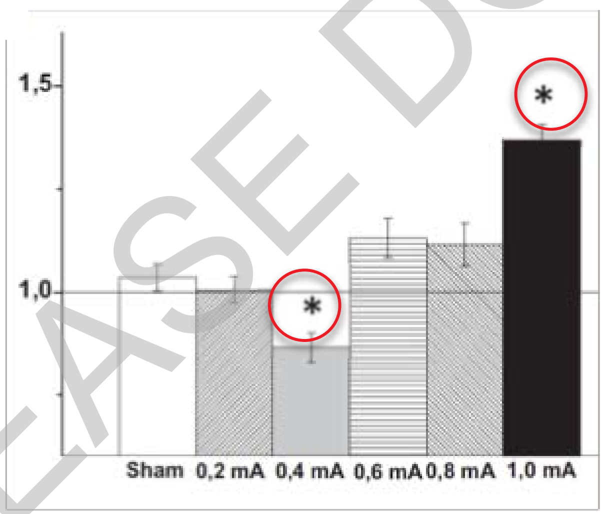
Group data | **Individual data**

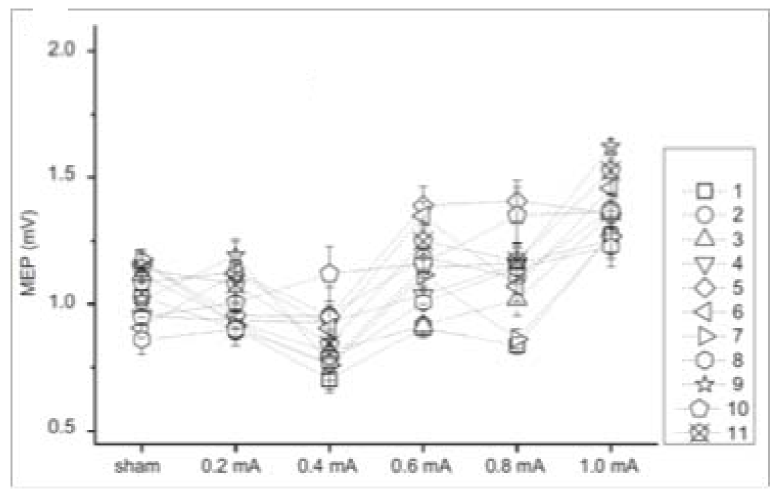
tRNS:





tACS:



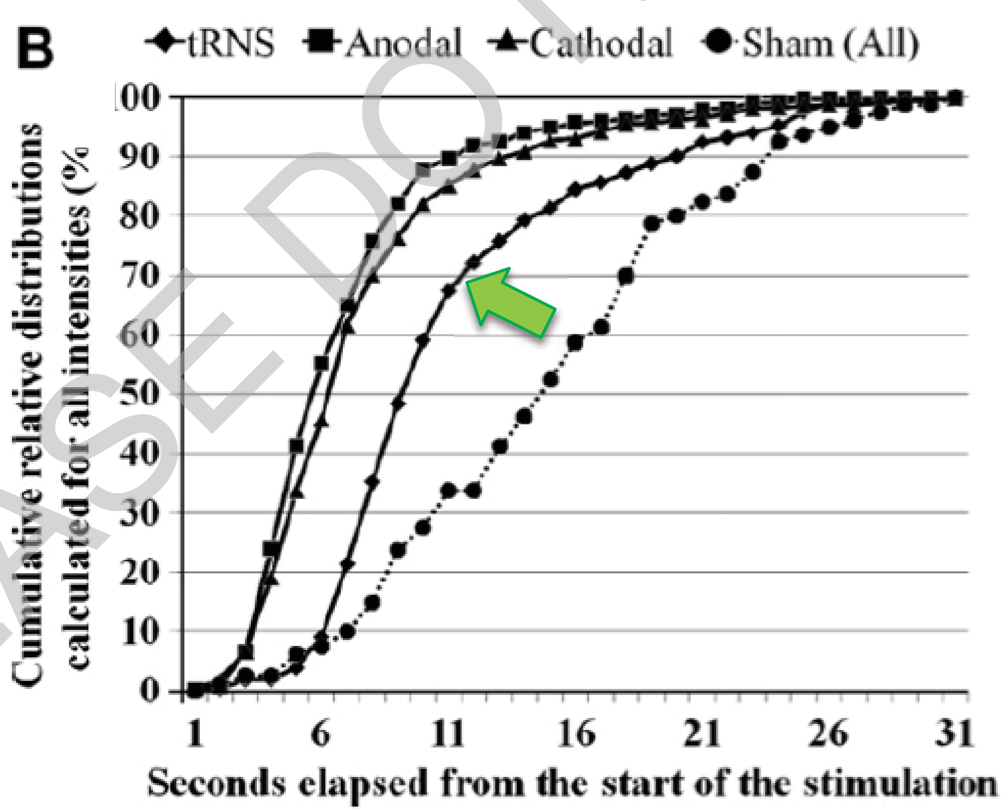


tRNS: a better SHAM than tDCS/tACS?

Ambrus et al. 2010 *Clin Neurophysiol*

Cutaneous perception of tRNS vs. anodal tDCS vs. cathodal tDCS

Three groups of 10 healthy subjects (naive, experienced, investigators) received tCS at 200-2000µA over the right primary motor cortex (M1) and left supraorbital area (SOA) (5x7cm sponges).



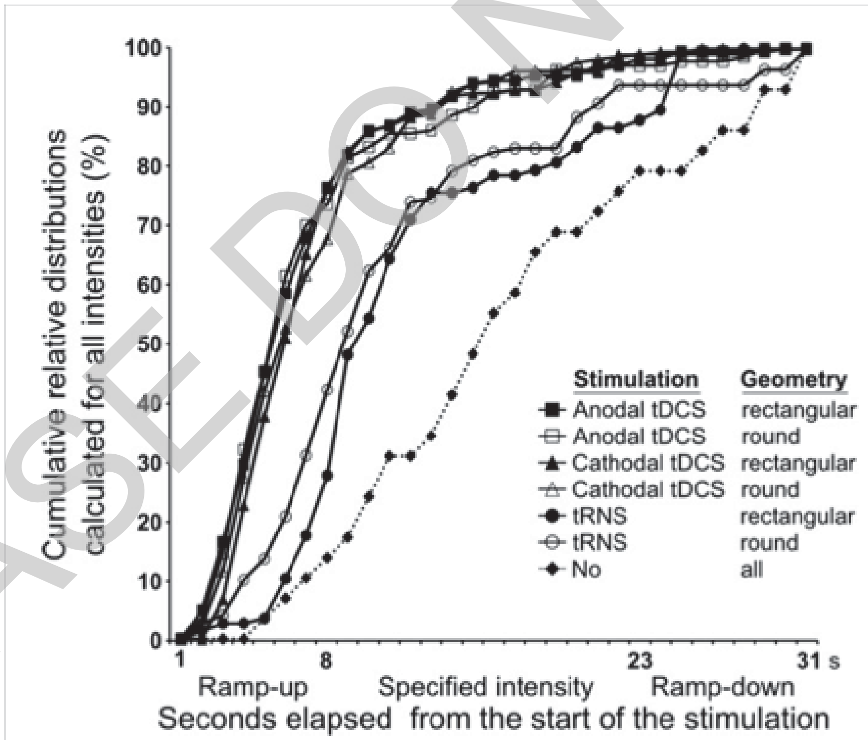
tRNS: a better SHAM than tDCS/tACS?

Ambrus et al. 2011 *Clin Neurophysiol*

Cutaneous perception of rectangular vs. round electrodes during anodal tDCS, cathodal tDCS and tRNS.

19 trials of active tCS at 200-2000µA and 7 trials of sham tCS over the right M1 and left SOA in 12 healthy subjects.

- Rectangle electrode: 5x7cm
- Round electrode: d = 6.6755cm



Blinding properties appear similar across electrode conditions

tRNS: effects on Cognition

Overview

Categorization learning

Ambrus et al. 2011 *Neuropsychologia*

Working memory

Mulquiney et al. 2011 *Clin Neurophysiol*

but see Holmes et al. 2016 *J Cogn Neurosci*

Numerosity and arithmetic

Cappellitti et al. 2013, 2015 *J Neurosci*

Sakar & Kadosh, 2016 *Can J Exp Psychol*

Dormal et al. 2016 *Neuropsychologia*

Popescu et al. 2016 *Neuropsychologia*

review from Looi & Kadosh, 2016 *Prog Brain Res*

Perceptual learning

Pirulli et al. 2013 *Brain Stimul*

Auditory processing

Van Doren et al. 2014 *Brain Stimul*

Face and emotion perception

Romanska et al. 2015 *Cereb Cortex*

Prete et al. 2017 *Brain Stimul*

Penton et al. 2017 *Sci Rep*

Political belief

Chawke & Kanai, 2016 *Front Hum Neurosci*

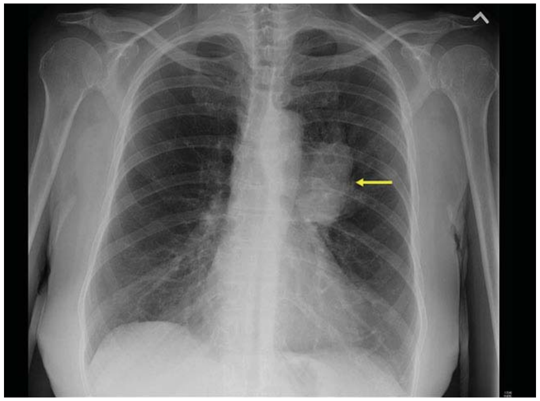
Visual motion adaptation

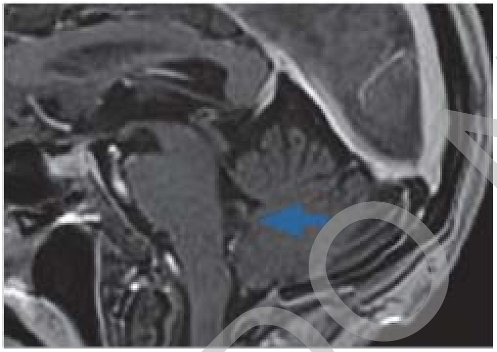
Campana et al. 2016 *Sci Rep*

Reward learning

van Koningsbruggen et al. 2016 *Soc Cogn Affect Neurosci*

Process by which training leads to *improvement* in abilities to detect, discriminate and identify sensory stimuli

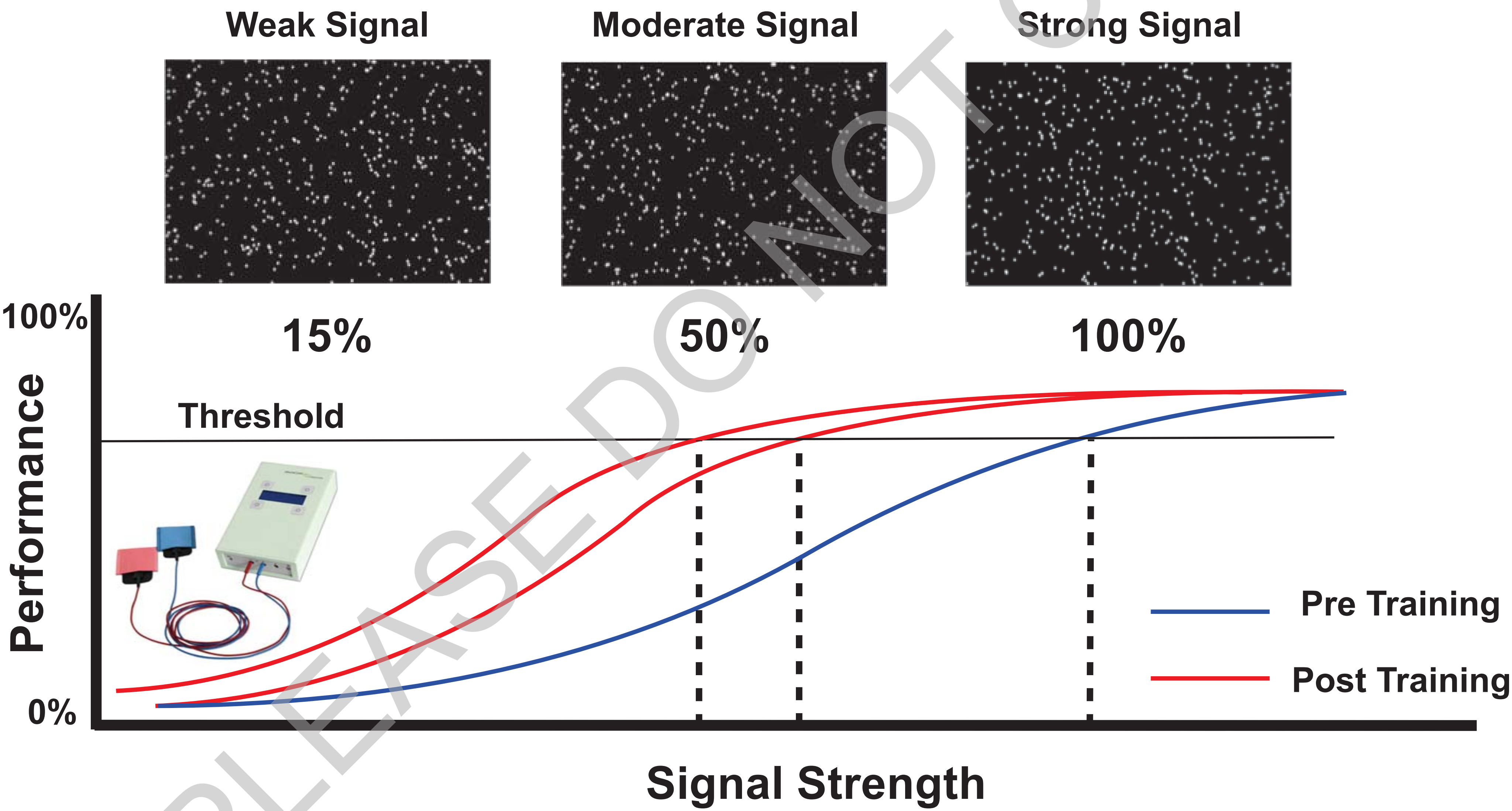




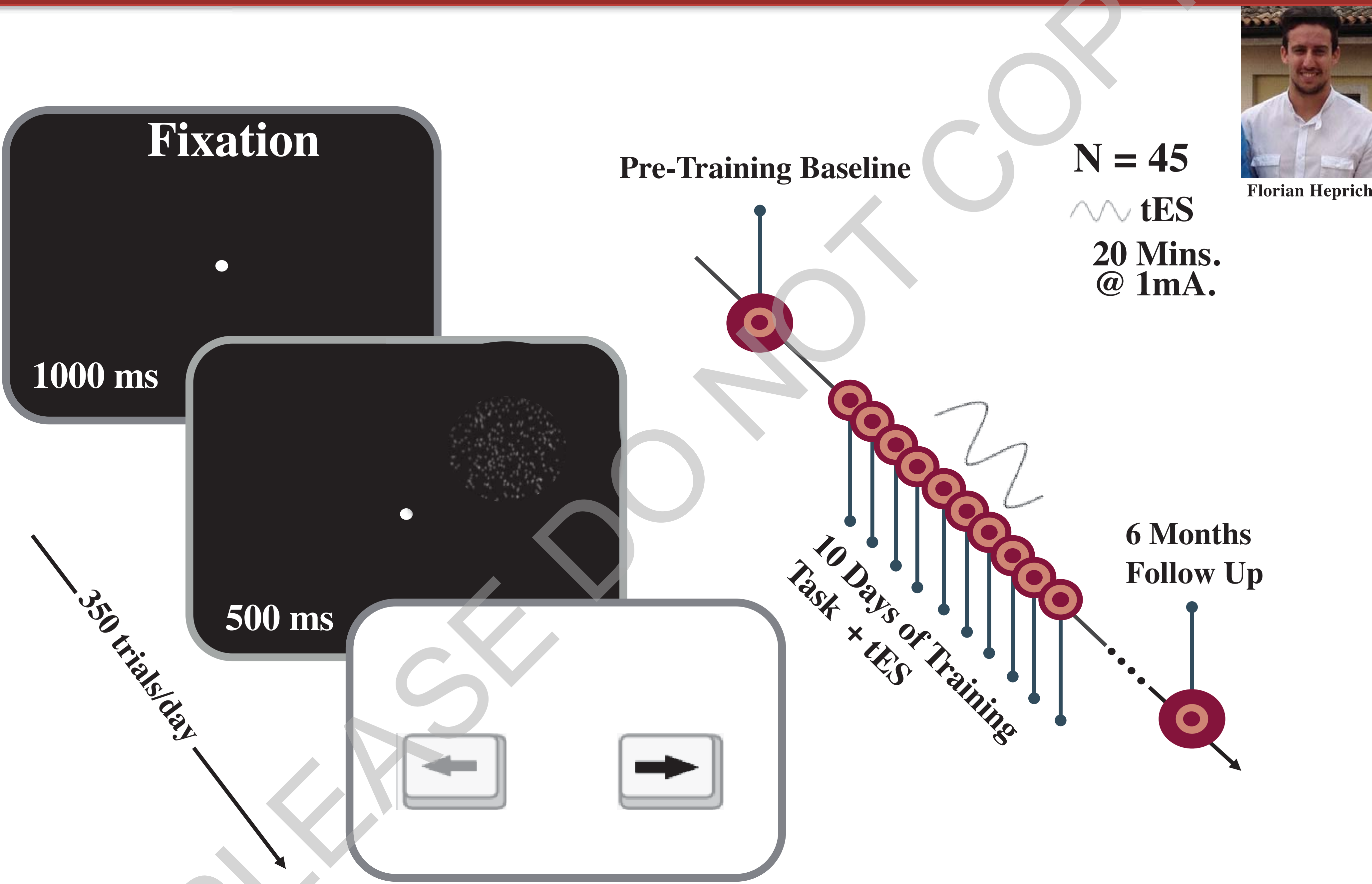
Radiologist can spot a tumor more efficiently

PL to help recover functions in amplyopia

Coherent Motion Detection in Noise

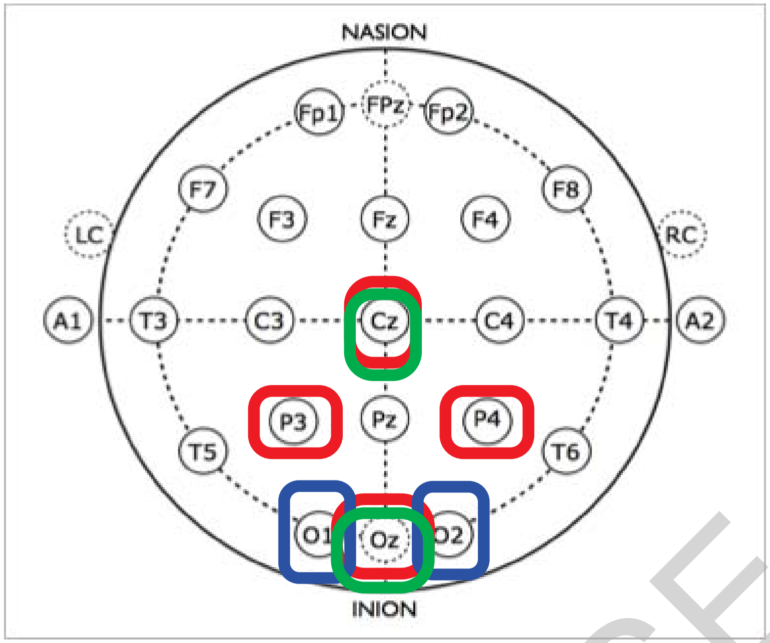


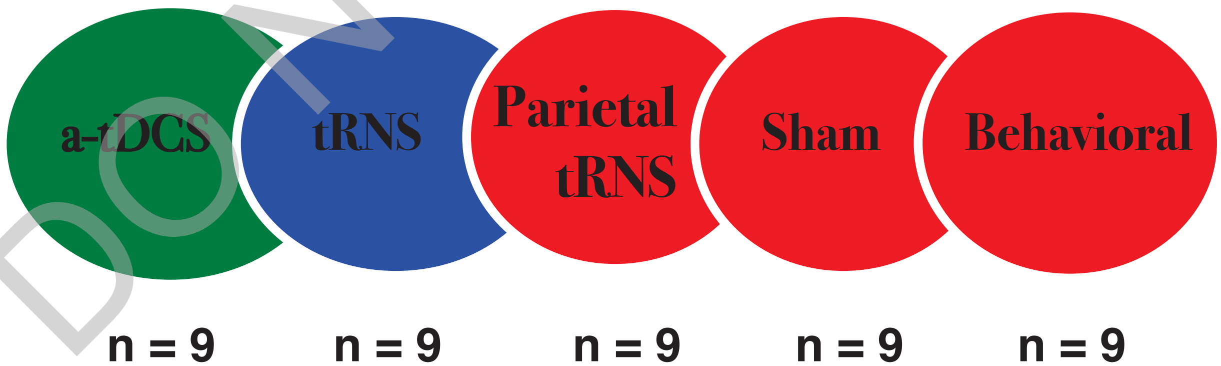
tRNS to boost PL in healthy subjects



Stimulation Protocol

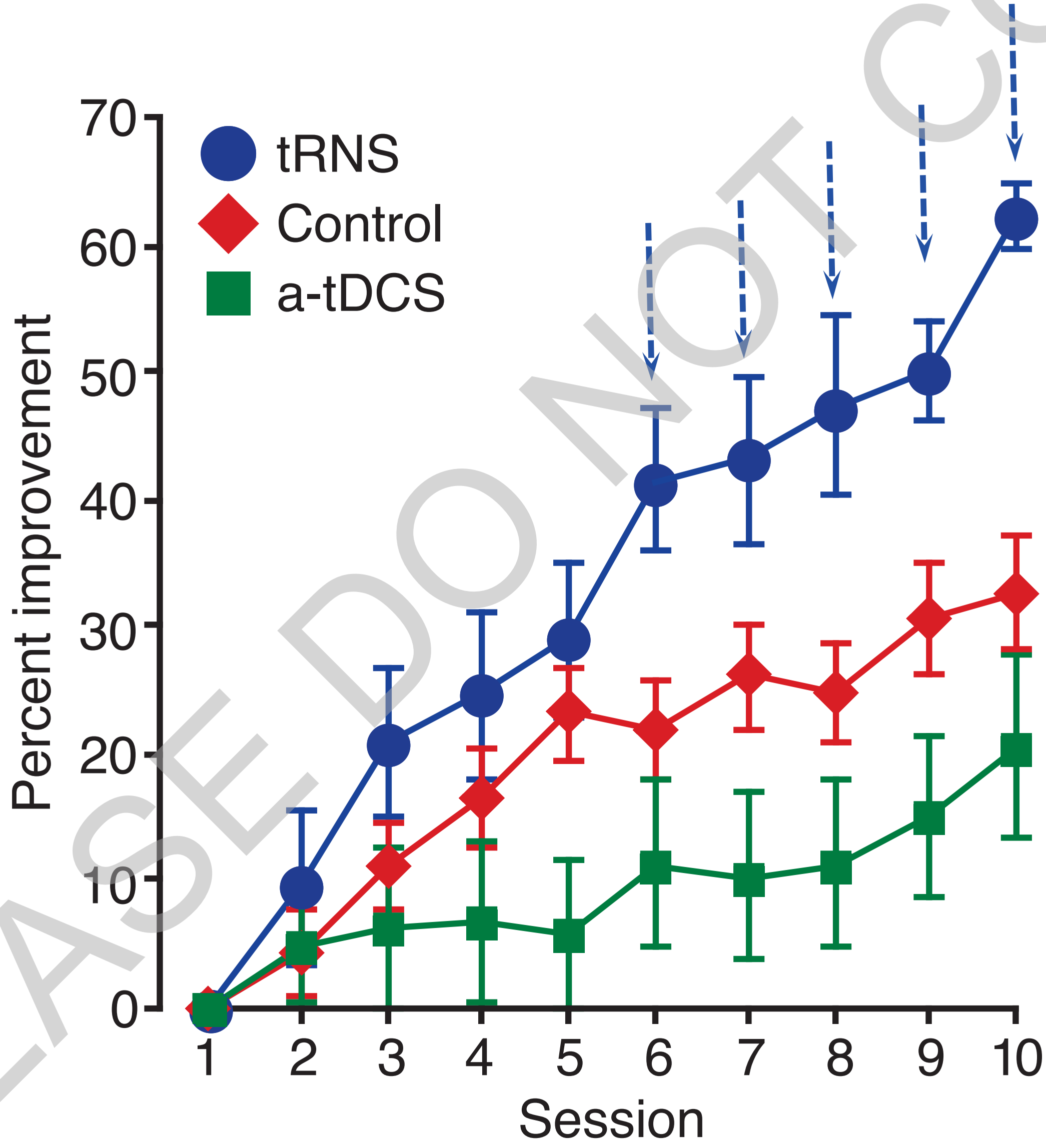
Herpich et al., Journal of Neuroscience *2019*





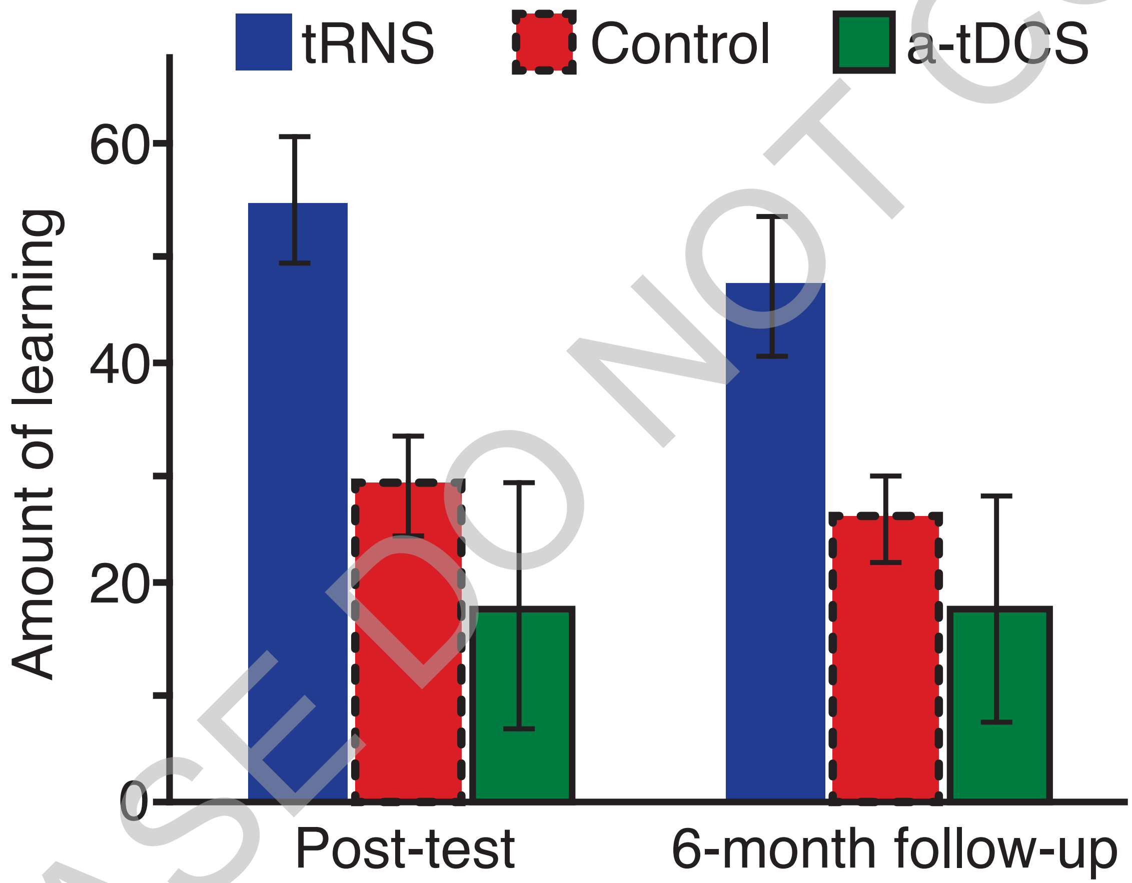
Results

Herpich et al., Journal of Neuroscience *2019*



Long-lasting effects

Herpich et al., Journal of Neuroscience *2019*



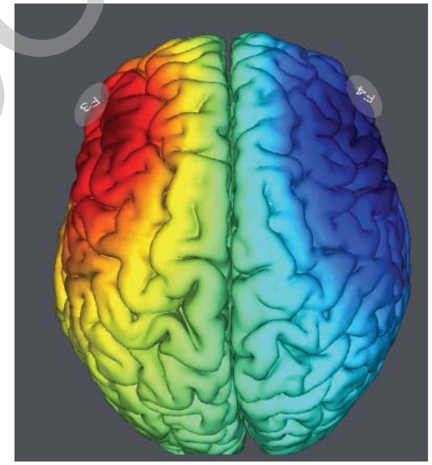
tRNS and Arithmetic training

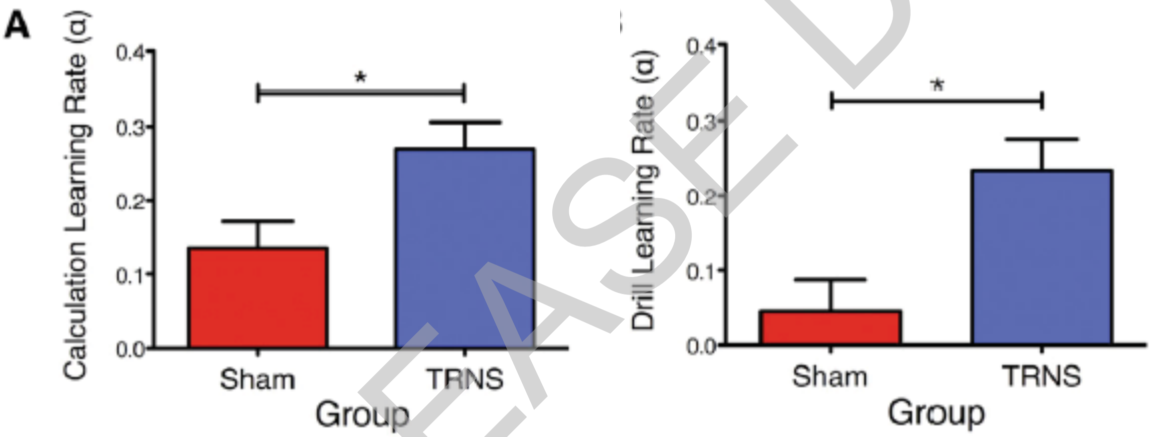
Snowball et al., 2013

• tRNS on **Bilateral Dorsolateral Prefrontal Cortex** (DLPFC), a key region in **Arithmetic.**

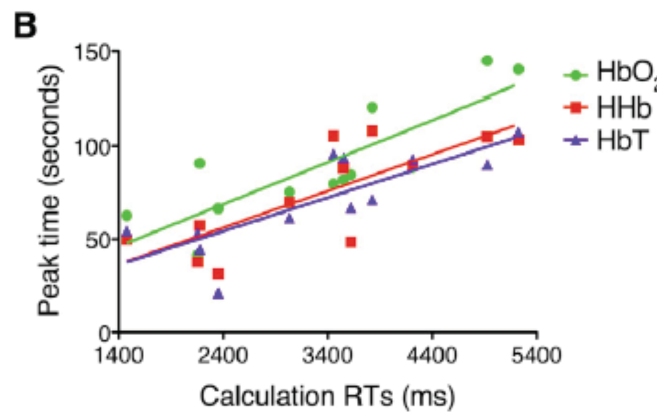
• **5 Days of training** (Calculation and Memory-recall-based arithmetic training) + **tRNS/Sham**

• Near Infrared Spectroscopy (NIRS) recording during training





Calculation learning rates increase during tRNS

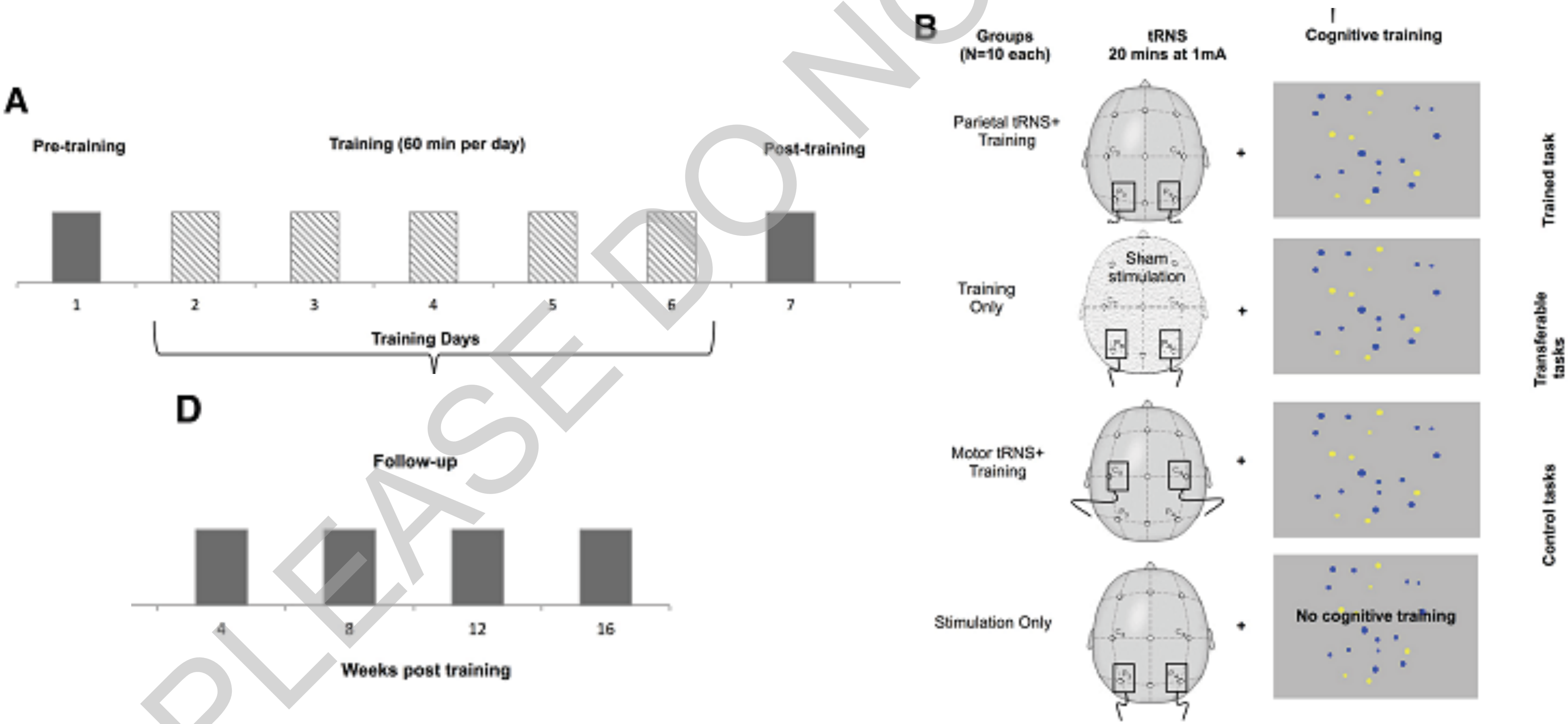


tRNS effect correlates with changes in the hemodynamic response

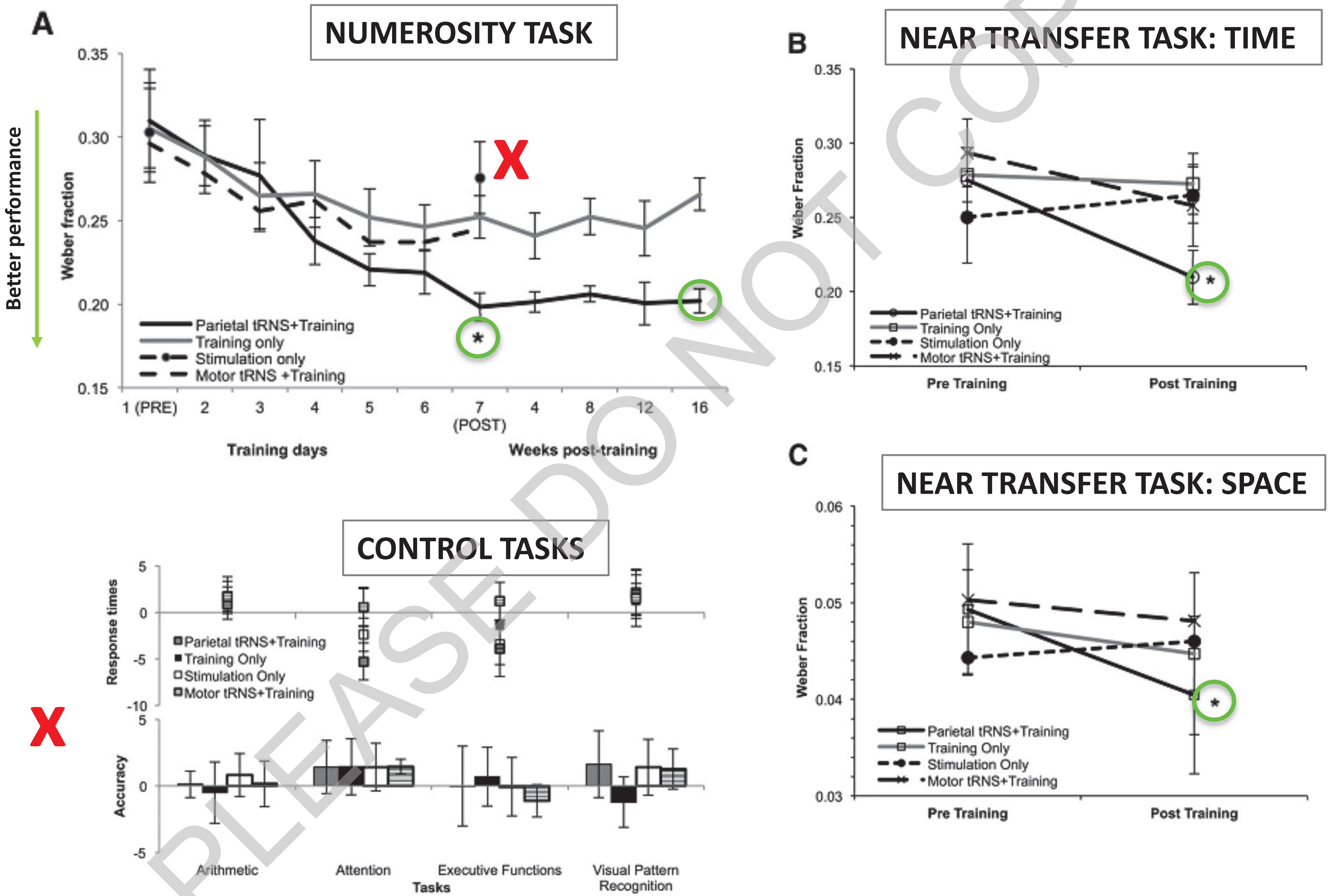
tRNS and Perceptual Learning

Cappelletti et al. 2013

- Training of “ability to discriminate numerosity” (6 days)
- Key region → **Parietal lobe**
- Tested for other Parietal lobe functions linked to ***quantity judgement*** (time and space discrimination) as well as other quantity judgment unrelated functions.
- Stimulation= **High frequency tRNS**



tRNS contributes to Cognitive/Skill Transfer

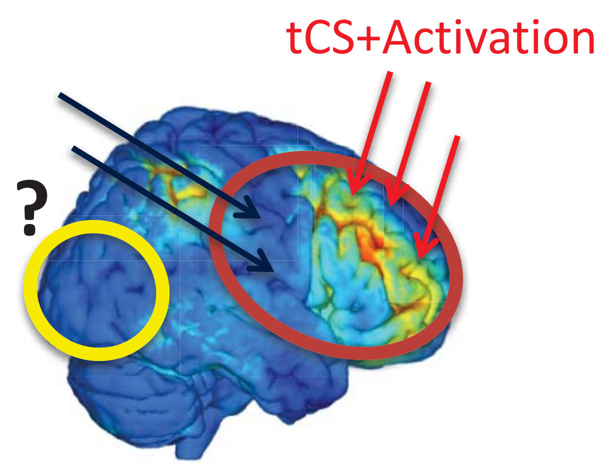


Is tCS alone not enough..?

• Better and longer lasting improvement (up to 16 weeks post-training) for tRNS+training compared to (1) ***cognitive training without stimulation***, (2) **cognitive training coupled to stimulation of a control site** (motor areas), (3) ***stimulation in absence of cognitive training.***

• Task improvement induced by parietal tRNS + Training **transferred to proficiency in other parietal lobe-based quantity judgment**, i.e., time and space discrimination, but not to quantity-unrelated tasks measuring attention, executive functions, and visual pattern recognition.

Can be a matter of ***Dose*** (tCS alone may require longer stimulation time?) and **precision** in terms of targeting.



tRNS: clinical applications

Overview

Auditory related disorders, tinnitus
Vanneste et al. 2013 *Front Psychiatry*
Joos et al. 2015 *Exp Brain Res*
To et al. 2017 *J Neural Transm*
Case report: Kreuzer et al. 2017 Pain Physician
* review from Heimrath et al. 2016 *Front Cell Neurosci*

Parkinson's disease
trend in MEP size for 8 patients: Stephani et al. 2011 *Parkinsonism Relat Disord*

Major depressive disorders
case report: Chan et al. 2012 *Brain Stimul*

Schizophrenia
two case studies: Palm et al. 2013 *Schizophr Res*

Pain
trend in multiple sclerosis: Palm et al. 2016 *Restor Neurol Neurosci*
Fibromylagia Curatolo et al. 2017 *Clin Exp Rheumatol*

Stroke
case series: Hayward et al. 2017 *J Neuroeng Rehabil*

Children with mathematical learning disabilities
Looi et al. 2017 *Sci Rep*

tRNS on tinnitus

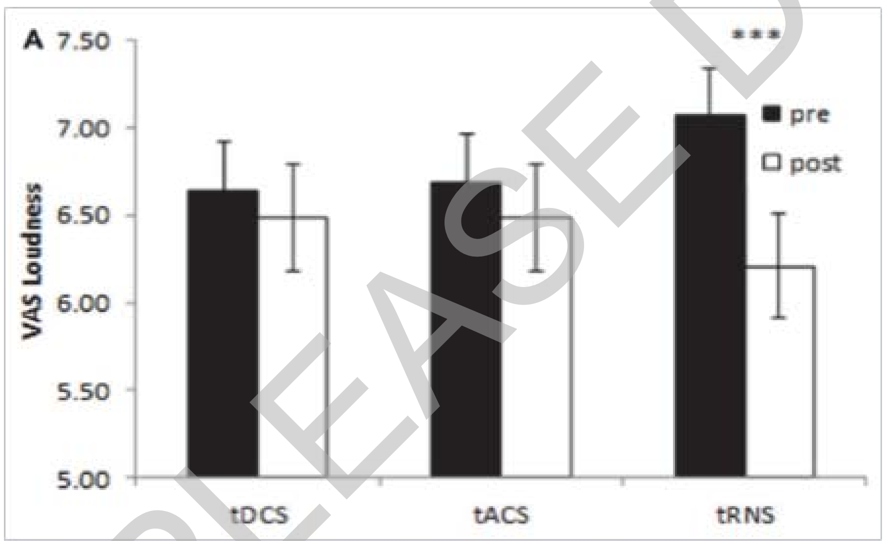
Vanneste et al. 2013

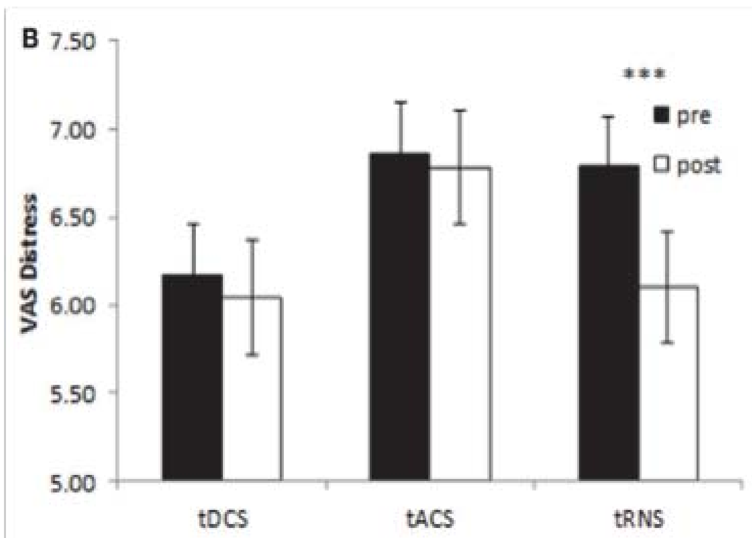
Single session over Temporal lobe bilaterally (electrodes T3 and T4), at 1.5mA (35cm²) for 20 min.

111 patients with tinnitus divided in 3 groups:

1. **tDCS (N=36; → T4: N=16; → T3: N=20)**
2. **6-13Hz tACS (N=37)**
3. **tRNS (N=38)**

↓ tinnitus loudness and distress with tRNS





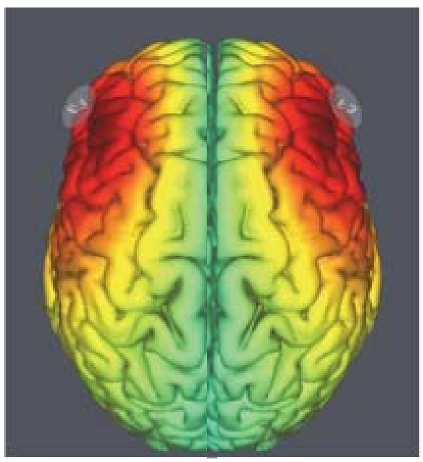
tRNS in the Atypical brain

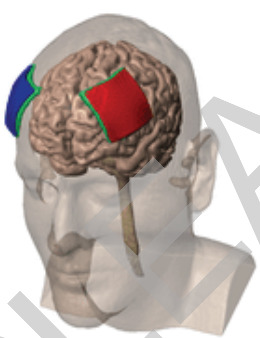
Looi et al. 2017

Article | OPEN | Published: 05 July 2017

Transcranial random noise stimulation and cognitive training to improve learning and cognition of the atypically developing brain: A pilot study

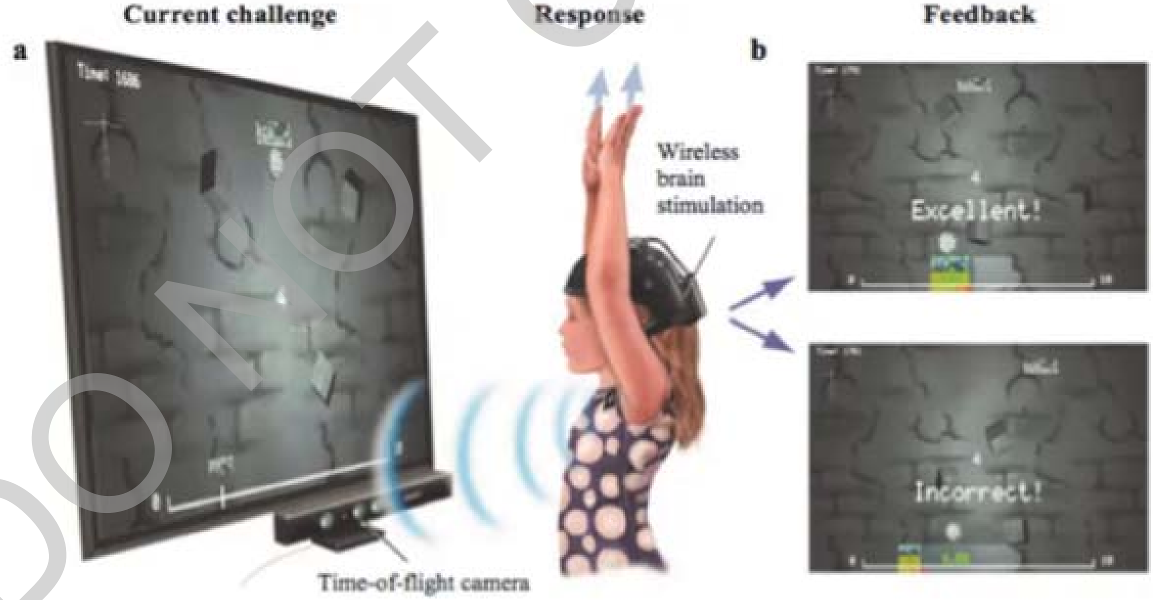
Chung Yen Looi, Jenny Lim, Francesco Sella, Simon Lolliot, Mihaela Duta, Alexander Alexandrovich Avramenko & Roi Cohen Kadosh





tRNS over bilateral DLPFC

Figure 1

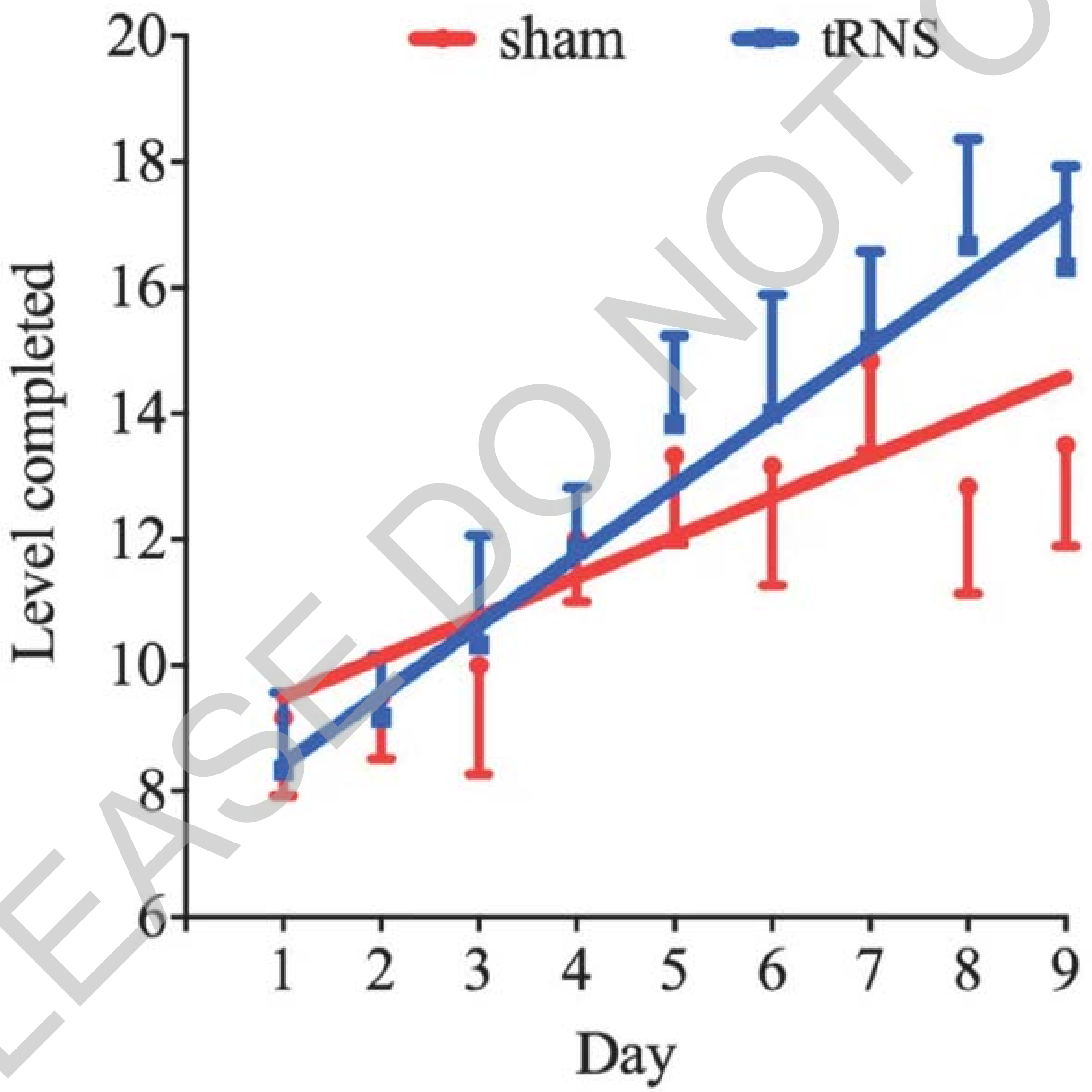


Transcranial random noise stimulation coupled with cognitive training to improve learning of children with mathematical learning disabilities at school (**a**) Illustration of a child moving from side-to-side to map a number on a number line while receiving transcranial random noise stimulation from a wireless brain stimulator. Response was registered for each trial when both hands were raised. Body movements were detected by a time-of-flight camera, Kinect^{TM}. (**b**) Examples of feedback on correct and incorrect responses. The game was adaptive to children's performance; every 3 consecutive correct answers promoted the following trial to a more difficult level and vice versa.

tRNS in the Atypical brain

Looi et al. 2017

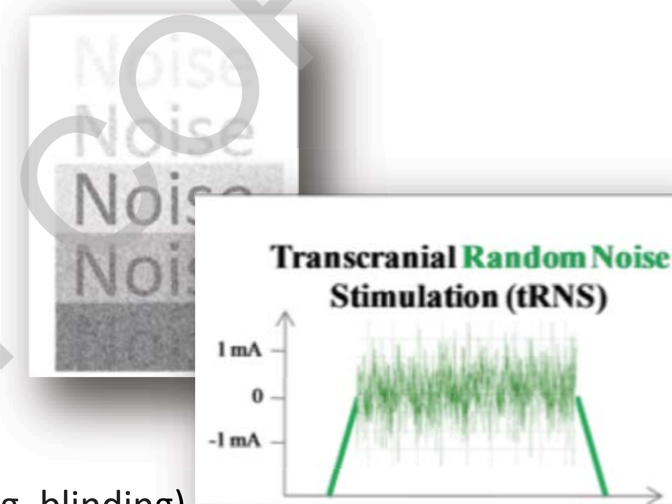
Figure 3



Summary

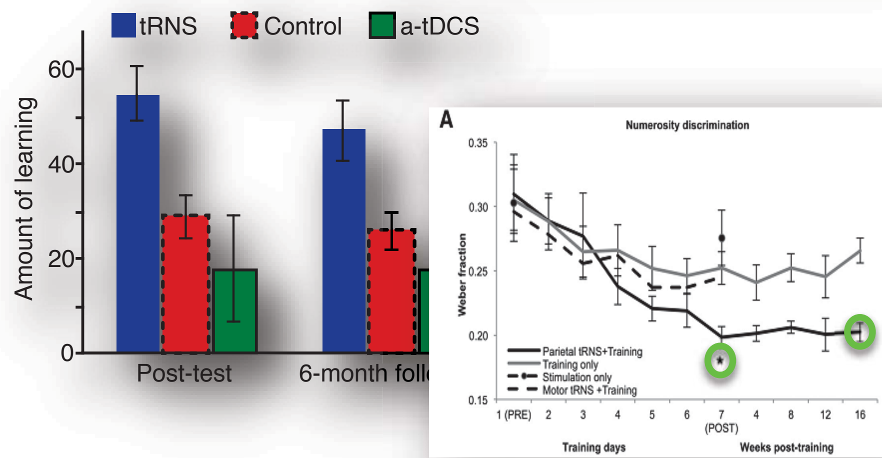
1. Principles of tRNS

- Stochastic Resonance phenomenon
  - Noise can be beneficial in nonlinear systems
  - Applying noise to the brain improves performance
  - The effect can be long-lasting
  - tRNS has some advantages over tDCS and tACS (e.g. blinding)

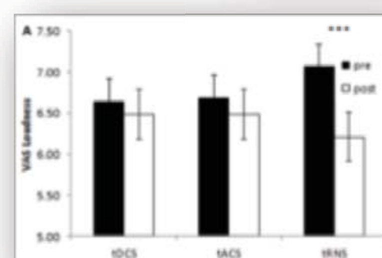


2. tRNS Effects

- Cortico-Spinal Excitability
- Perception
- Cognition



3. Promising Therapeutic Opportunities



Berenson-Allen Center
For Noninvasive Brain Stimulation

Thank you for your attention!

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