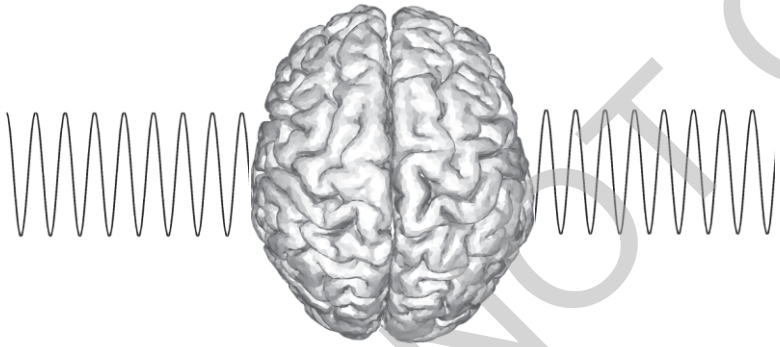
Transcranial Alternating Current Stimulation - tACS



Emiliano Santarnecchi

- Berenson-Allen Center for Non-invasive Brain Stimulation, Department of Cognitive Neurology | Beth Israel Deaconess Medical Center | Harvard Medical School | Boston, MA, USA

esantarn@bidmc.harvard.edu

Boston, June 24th 2019

A rapidly growing field

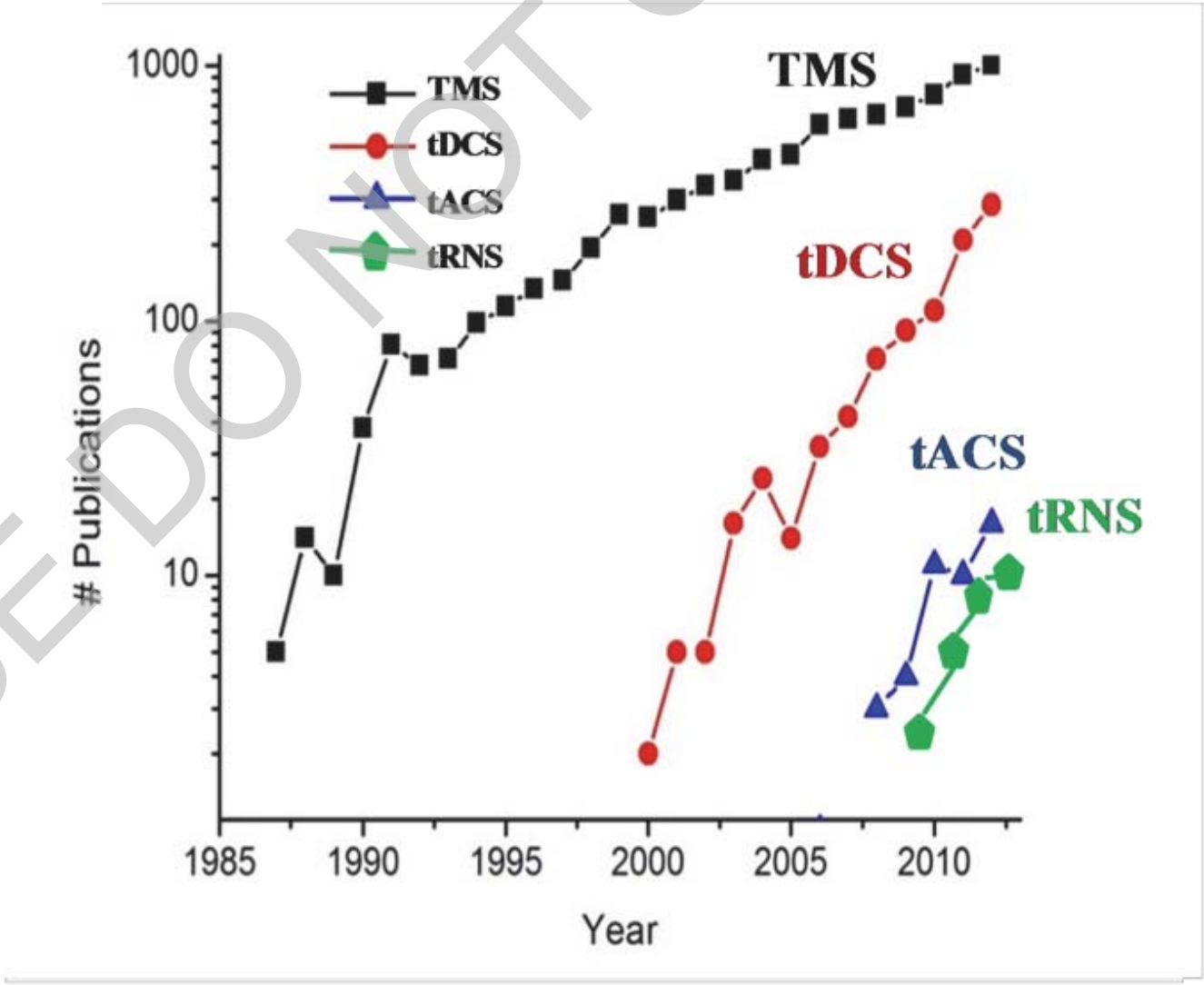
“tACS allows to modulate brain oscillations in a frequency specific manner”

TMS: Transcranial Magnetic Stimulation

tDCS: transcranial Direct Current Stimulation

tACS: transcranial Alternate Current Stimulation

tRNS: transcranial Random Noise Stimulation



Santarnecchi et al. 2015 Curr Opin Behav Sci

Outline

- **Oscillatory pattern and synchronicity in the brain**
  - ✓ tACS - Mechanism of action
- **tACS evidence**
  - ✓ Perception (Hands-On session tomorrow)
  - ✓ *Cortico-spinal excitability and effects on the motor system*
  - ✓ *Cognition*
  - ✓ *Phase-Related activity*
  - ✓ *State & Trait – Dependency*
  - ✓ *Therapeutic potential*

2’ about me

Boston

Berenson-Allen Center For Non-Invasive Brain Stimulation
BIDMC, Harvard Medical School

- Assistant professor of Neurology, **Harvard Medical School**
- Director, Network Control Laboratory, **BIDMC**
- Affiliated Associate Professor, **Center for Complex Network Research, Department of Physics, Northeastern University**
- Affiliated Faculty Member, **Center for Cancer Research, BIDMC**

Siena (Piazza del campo), Italy

Co-Director (Prof. Simone Rossi), Brain Investigation and Neuromodulation Laboratory (SiBIN lab, **University of Siena School of Medicine, Italy**)

Interests:

- **Translational/Clinical applications:** Aging, Dementia (MCI, AD), Brain Tumors, Stroke, Disorders of Consciousness, Traumatic Brain Injury
- **Brain Physiology**: Placebo Effect, Plasticity, Brain connectivity and Network Mapping, Brain oscillations, Sleep
- **Cognitive Enhancement:** Attention, Abstract Reasoning, Memory, Motor learning, videogames/cognitive training

Questions? Comments? Ideas? Feedback?

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Berenson-Allen Center for Non-invasive Brain Stimulation

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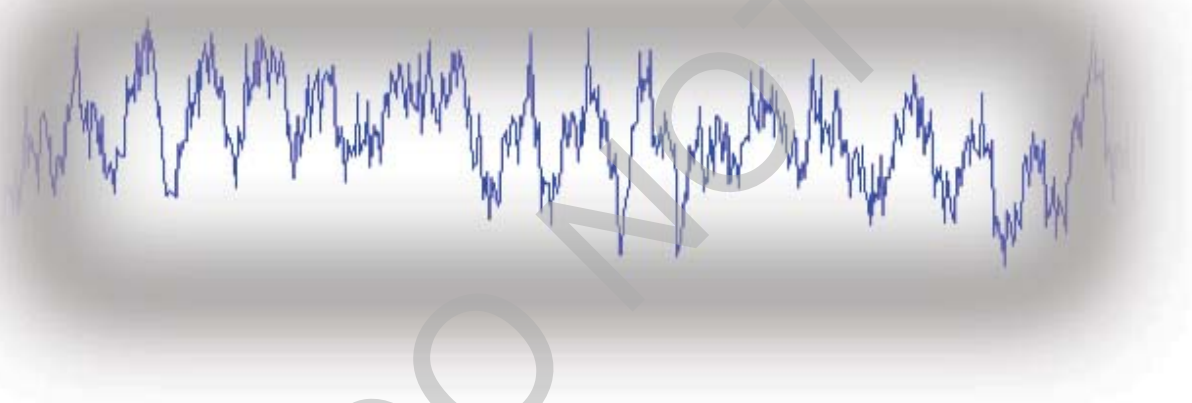
Disclosure

Emiliano Santarnecchi serves as Scientific Advisor for EBNeuro, a company developing biomedical devices for neurostimulation, neuromodulation and electroencephalography. ES serves as Scientific Advisor for Neuroelectrics, a manufacturer of transcranial electrical stimulation and EEG devices.

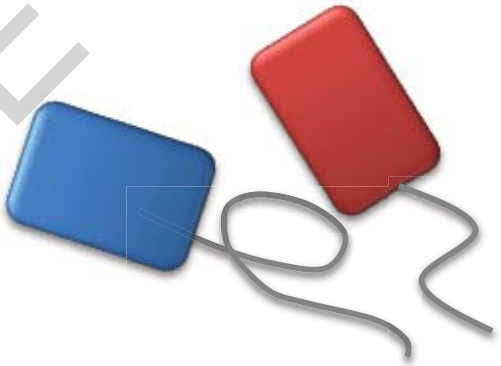
The research shown in this presentation is supported by BIDMC, NIH, DARPA, IARPA, the Harvard-MIT BROAD institute.

ES holds patents about technology for eye-tracking and for the application of noninvasive brain stimulation to modulate brain activity in patients with neurological and psychiatric conditions, enhance protein clearance in Dementia and modulate perfusion in brain tumors.

- Experience with EEG/Brain Oscillations?

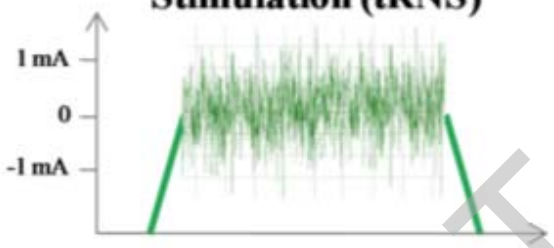


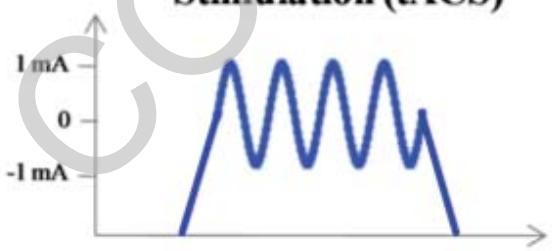
- Experience with tACS?



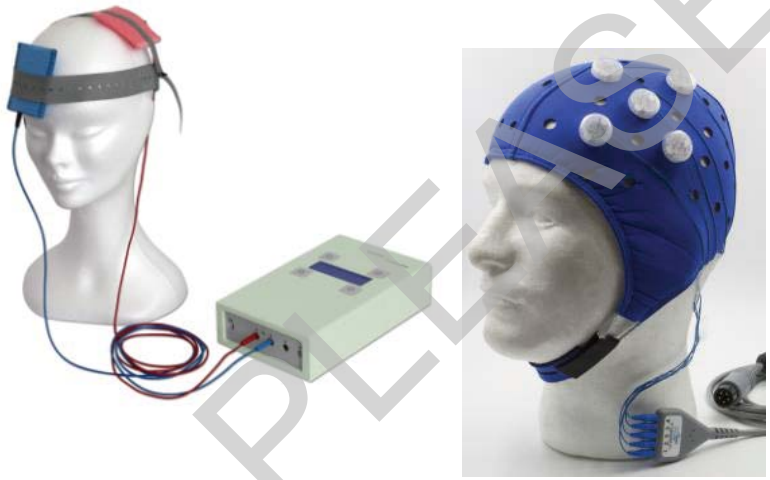
tES methods and devices

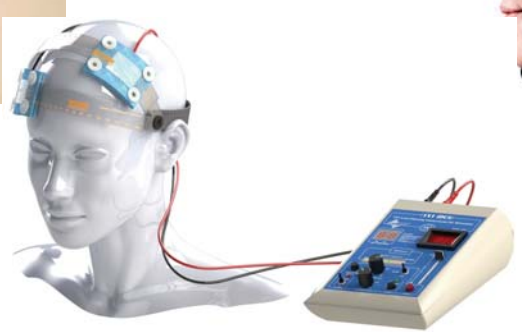
A





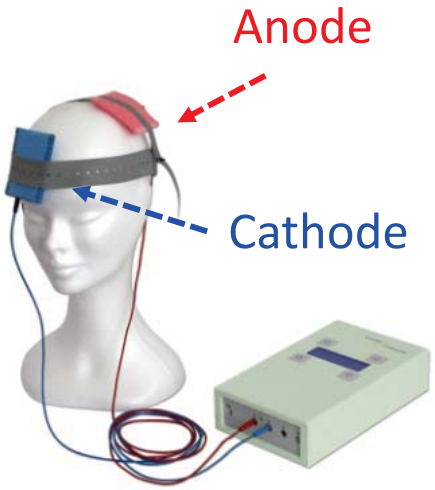
Current	Constant/Direct	Oscillatory/Alternating	Oscillatory/Alternating
Stimulation parameters	Anode: excitatory Cathode: inhibitory	1-640 Hz (random) 100-640 Hz: excitatory	Frequency (Hz) Phase (Degrees)
Mechanism	Membrane polarization	Stochastic resonance	Entrainment
Effect on	Cortical excitability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

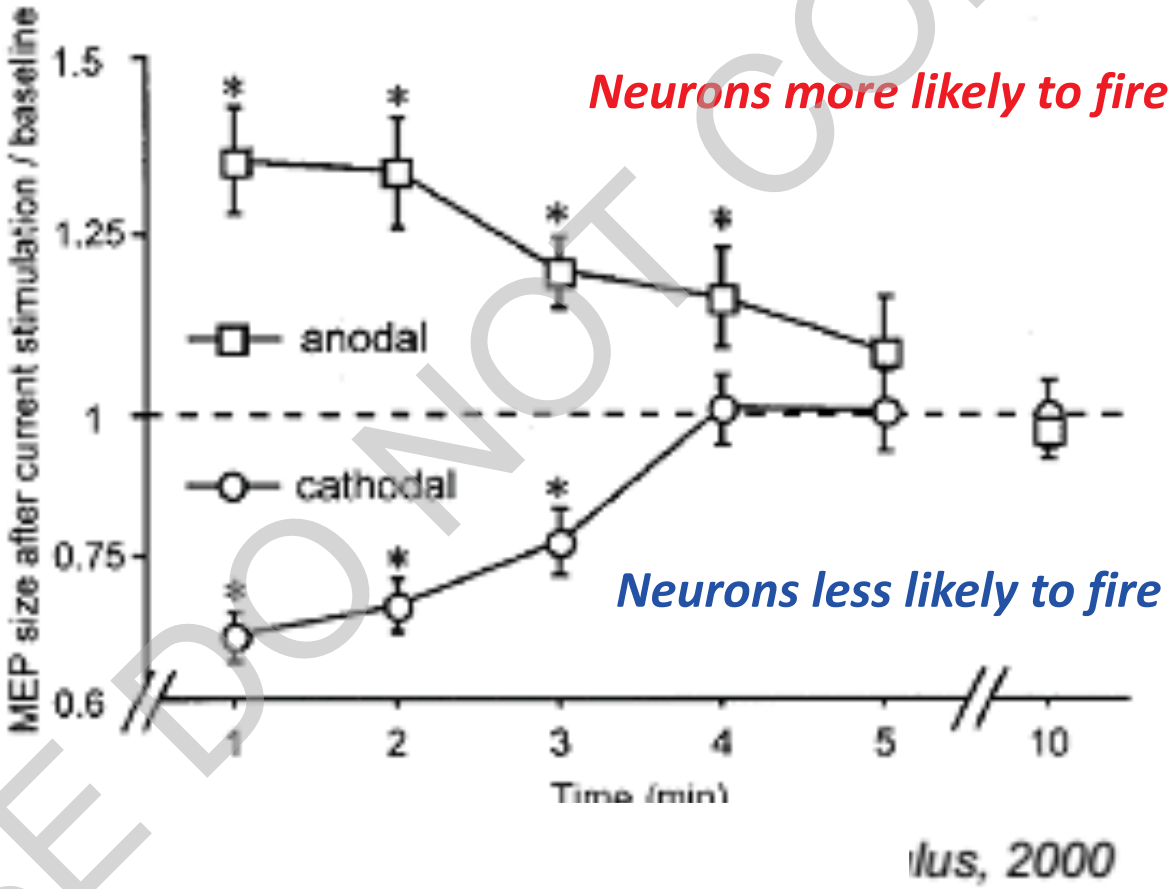




Santarnecchi et al. 2015

tDCS





First evidence of tDCS after effect from **Nitsche and Paulus, 2000**

Changes in cortical excitability assessed using TMS-EMG

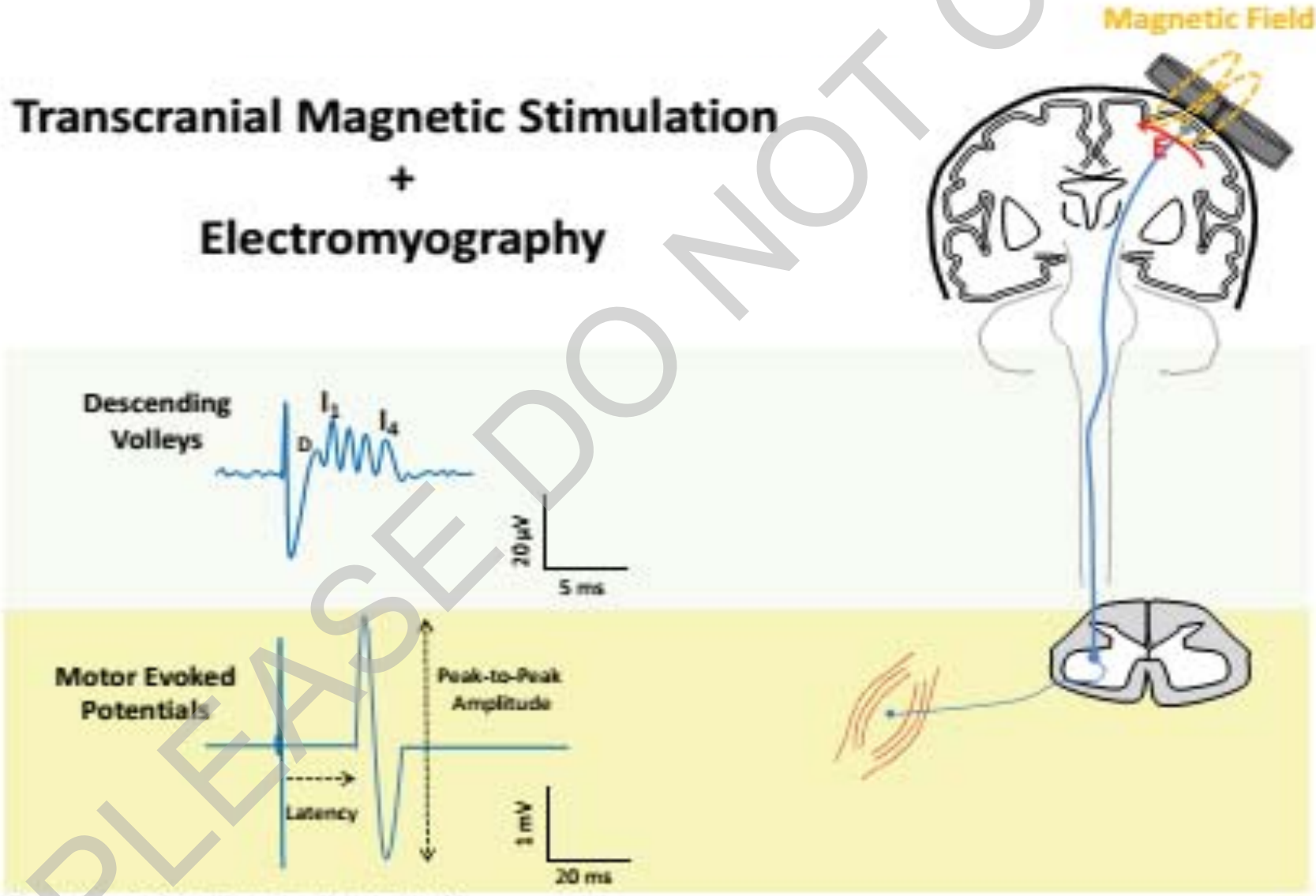
Measuring tES effects on Corticospinal excitability

Recording Motor Evoked Potentials (MEPs)

Transcranial Magnetic Stimulation

+

Electromyography



Mechanism of action

DC Stimulation

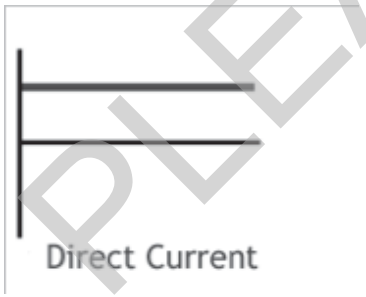
Constant Fields

↓

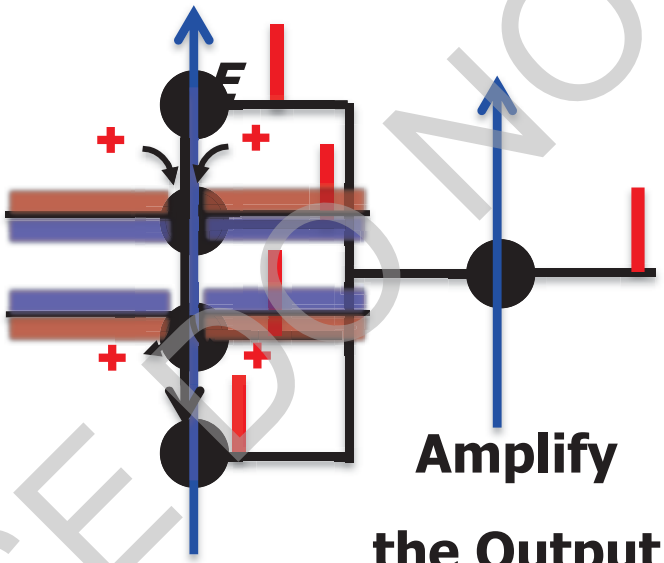
Membrane Polarization

↓

Spike Rate Change



Synchrony Effect



Synchronize the Input

Amplify the Output

AC Stimulation

Oscillating Fields

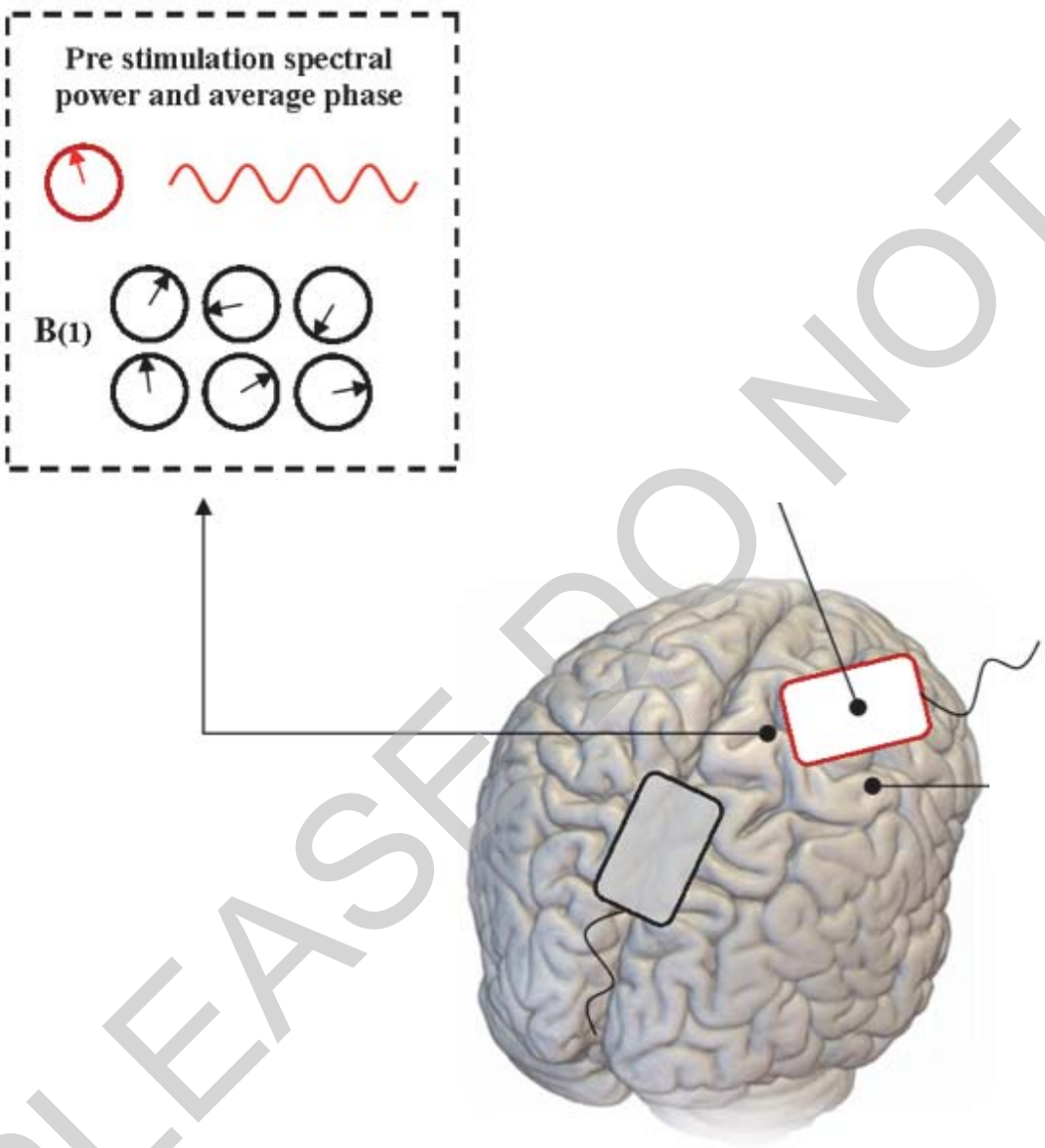
↓

Network Synchrony

↓

Spike Phase Change

tACS effect

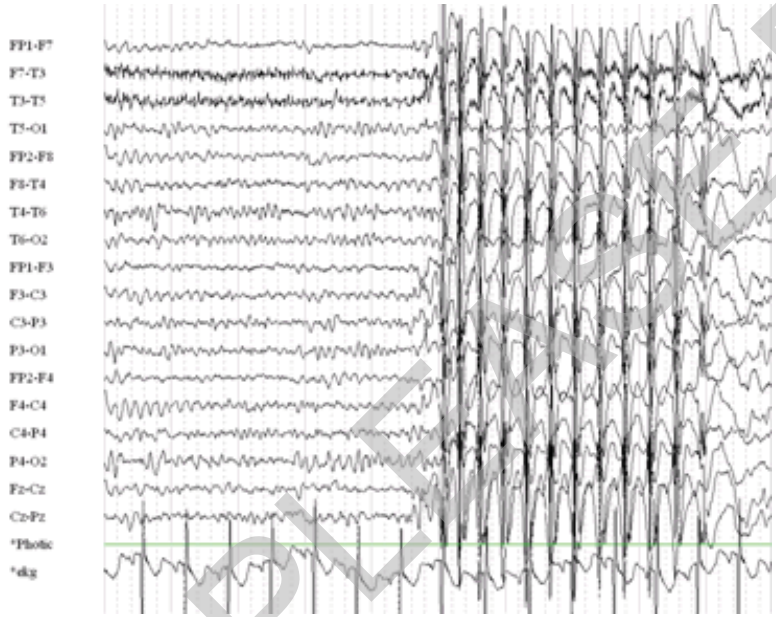


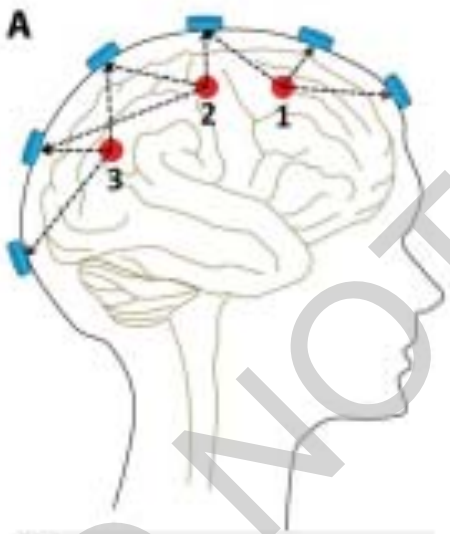
Santarnecchi and Rossi (2017)

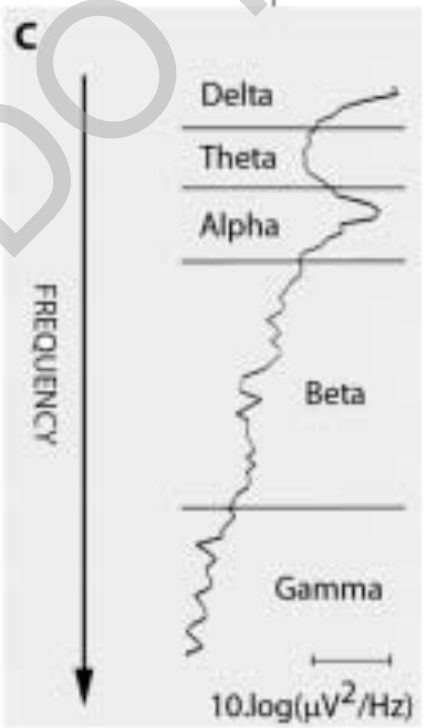
Why tACS?

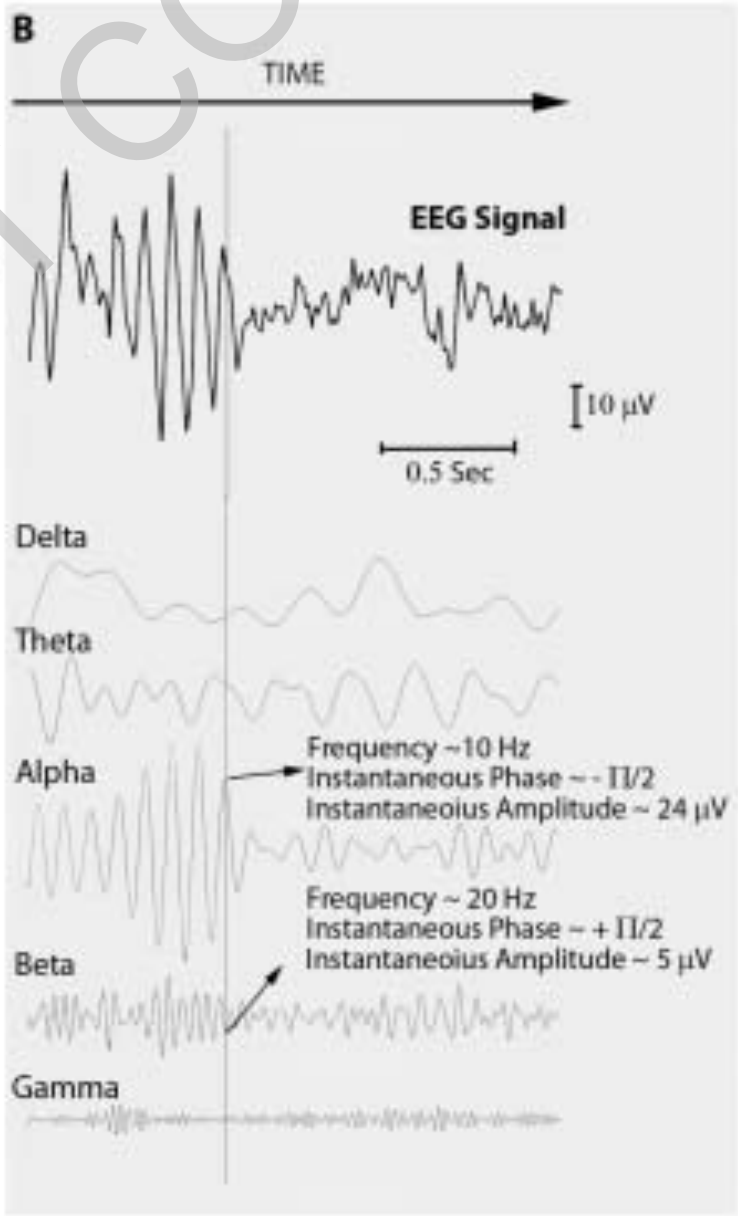
Brain Oscillatory Activity recording: Electroencephalography (EEG)

Hans Berger (1921)







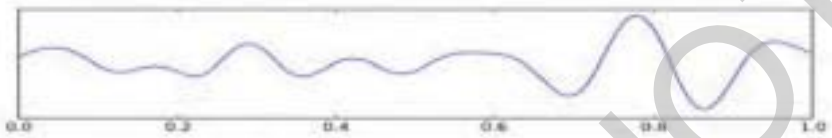


EEG Oscillations and Cognition

Delta (1 – 4 Hz)

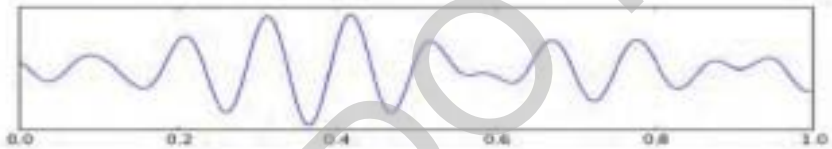
Sleep, learning, motivational processing

Theta (4 – 8 Hz)



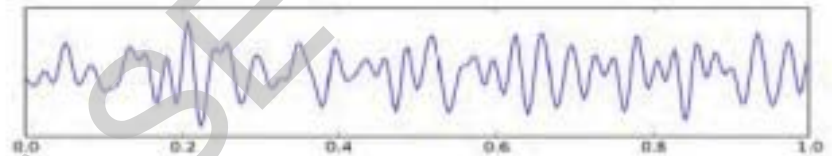
Memory, emotional regulation, creativity

Alpha (8 – 13 Hz)



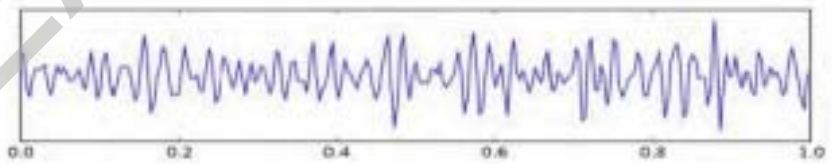
Active inhibition of task-irrelevant areas

Beta (13 – 30 Hz)



Mainly Motor activity

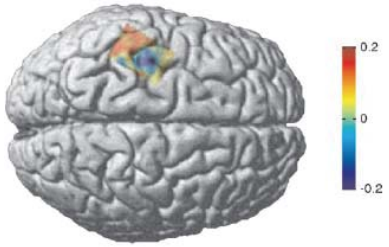
Gamma (30 – 80 Hz)



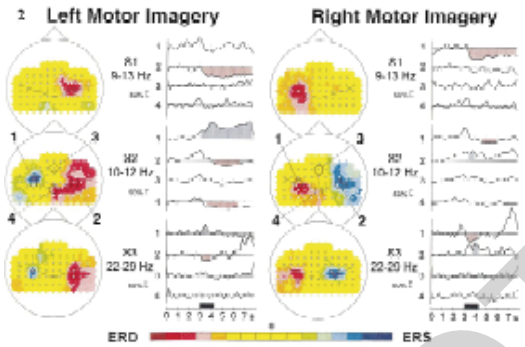
Abstract mental activity, cognitive control, perceptual binding

“Natural Frequencies”

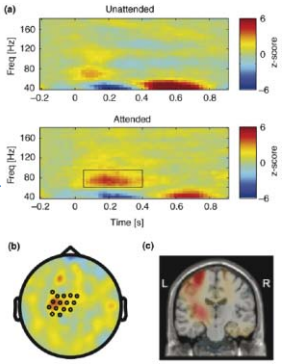
Alpha: motor planning



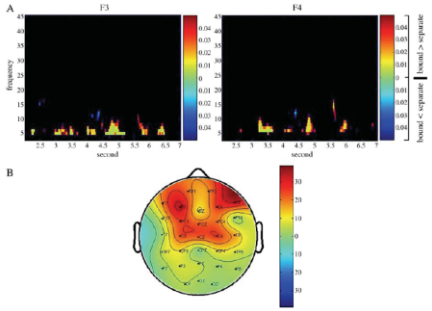
Beta: motor system

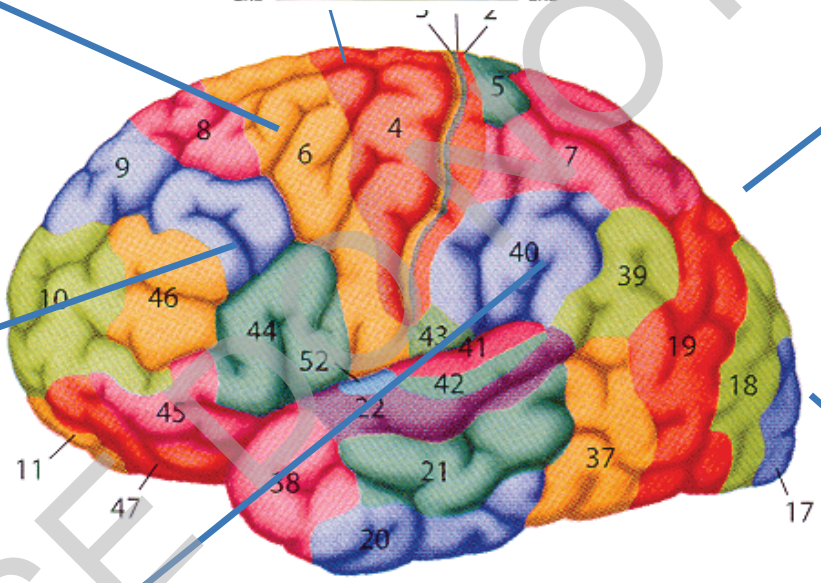


Gamma: selective attention, coding,

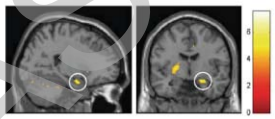


Θ: working /long-term memory

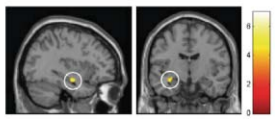




A

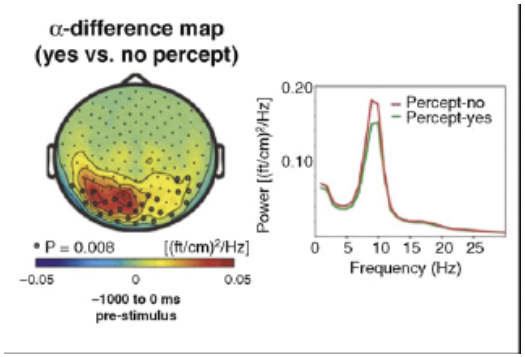


B



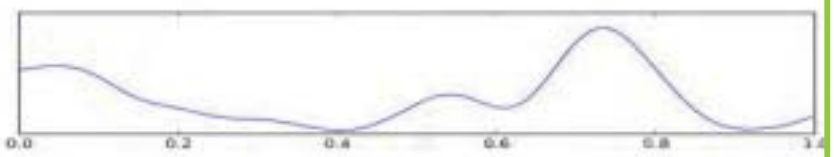
Θ: spatial orienting

Alpha: visual perception



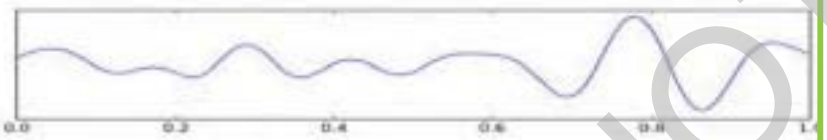
EEG Oscillations and PATHOLOGY

Delta (1 – 4 Hz)



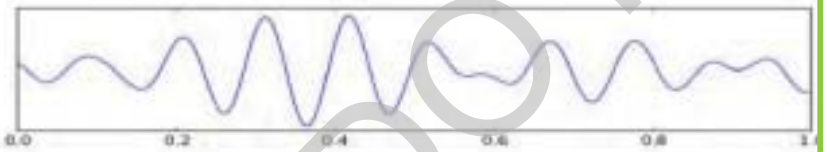
- Reduced synchrony in Schizophrenia
- Reduced amplitude in Alzheimer
- Increased Amplitude in Bipolar dis.

Theta (4 – 8 Hz)



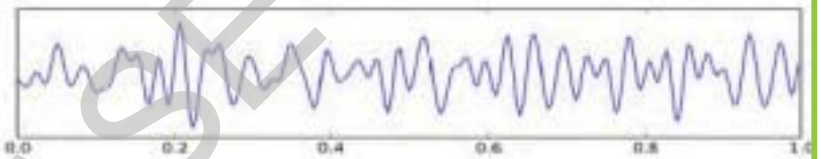
- Reduced synchrony in Schizophrenia
- Reduced synchrony in Alzheimer

Alpha (8 – 13 Hz)



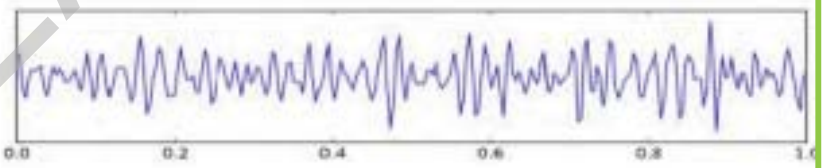
- Reduced coherence in Alzheimer
- Increased phase-locking at Frontal and Central electrodes in Schizophrenia

Beta (13 – 30 Hz)



- Reduced Coherence in Alzheimer and Schizophrenia
- Increased amplitude in Parkinson
- Increased Coherence in Bipolar dis.

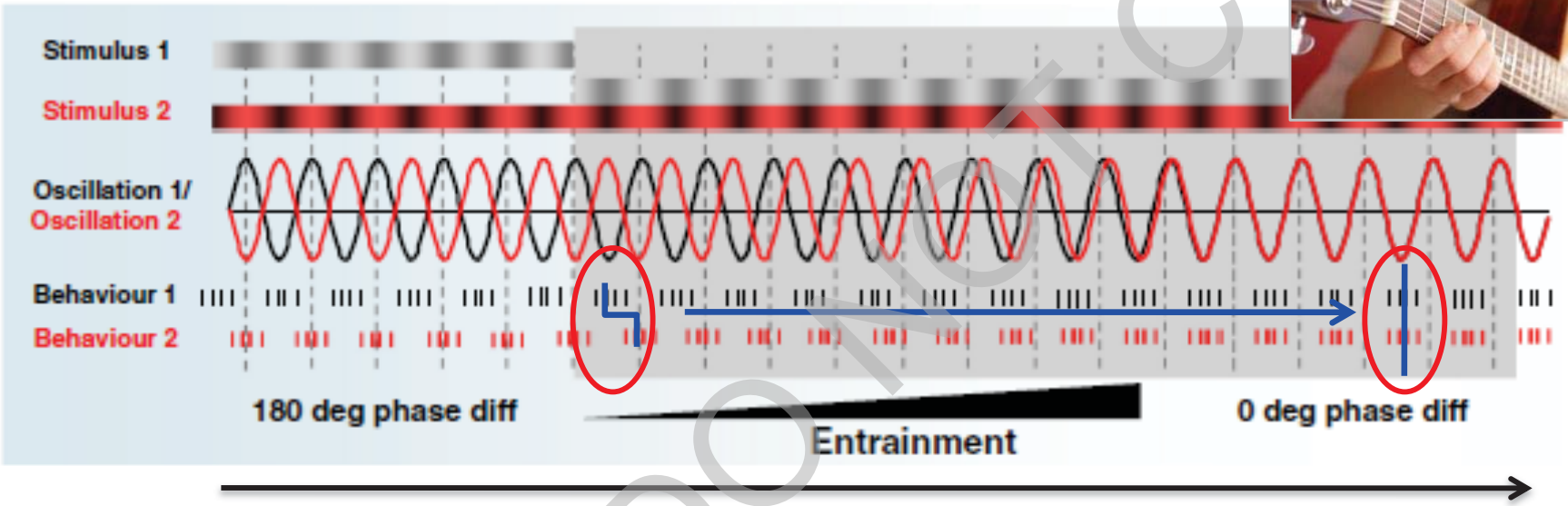
Gamma (30 – 80 Hz)



- Decreased/increased amplitude in Schizophrenia (?)
- Increased Phase-locked response in ADHD

Inducing "Entrainment"

- **Are these oscillatory patterns immutable?**



Entrainment of endogenous oscillatory pattern → Changes in behaviour

- Oscillatory cycle establishes a recurrent temporal reference frame that allows for the coding of temporal relations between groups of neural elements

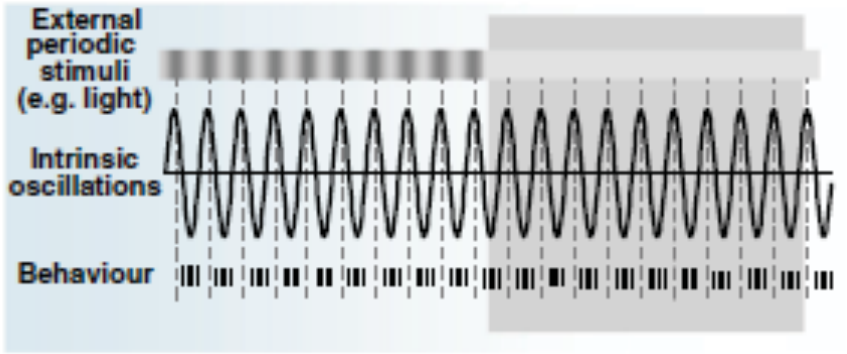
- This reference frame is not fixed but is **subject to dynamic changes** (phase resetting), especially in **pathological states**.

tACS induces entrainment of brain oscillations following the same principle (theta, alpha, beta, gamma, ..)

***Tuth* et al. 2012, Current Biology**

tACS: Parameters

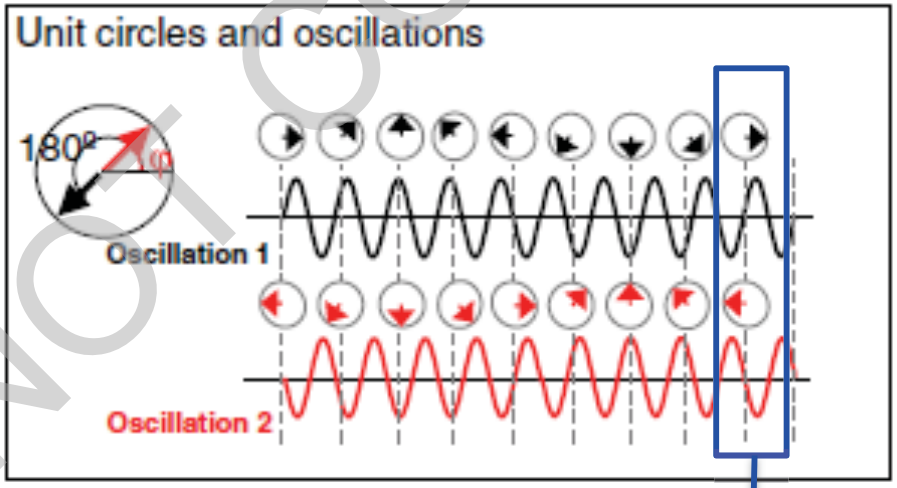
Cyclic patterns in behaviour



Sleep–wake cycles are evident even if external light conditions are held constant (grey shade)

Intrinsic oscillators (circadian clocks) which cause periodicity in bodily function

Phase?

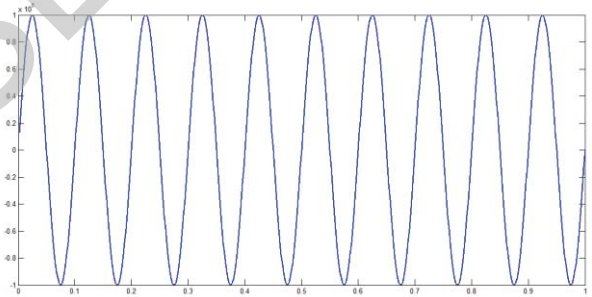


Phase, angles, degrees…..

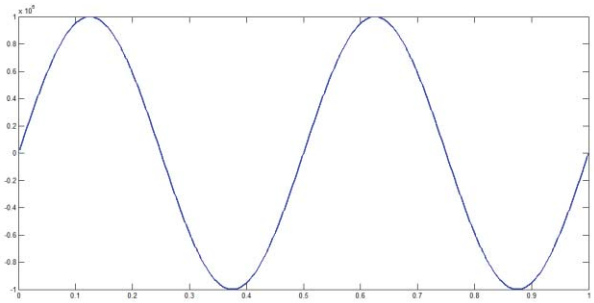
Oscillators are in opposite phase (anti-phase)

Frequency?

Number of cycles x second
(1 cycle * second=1Hz)



10Hz



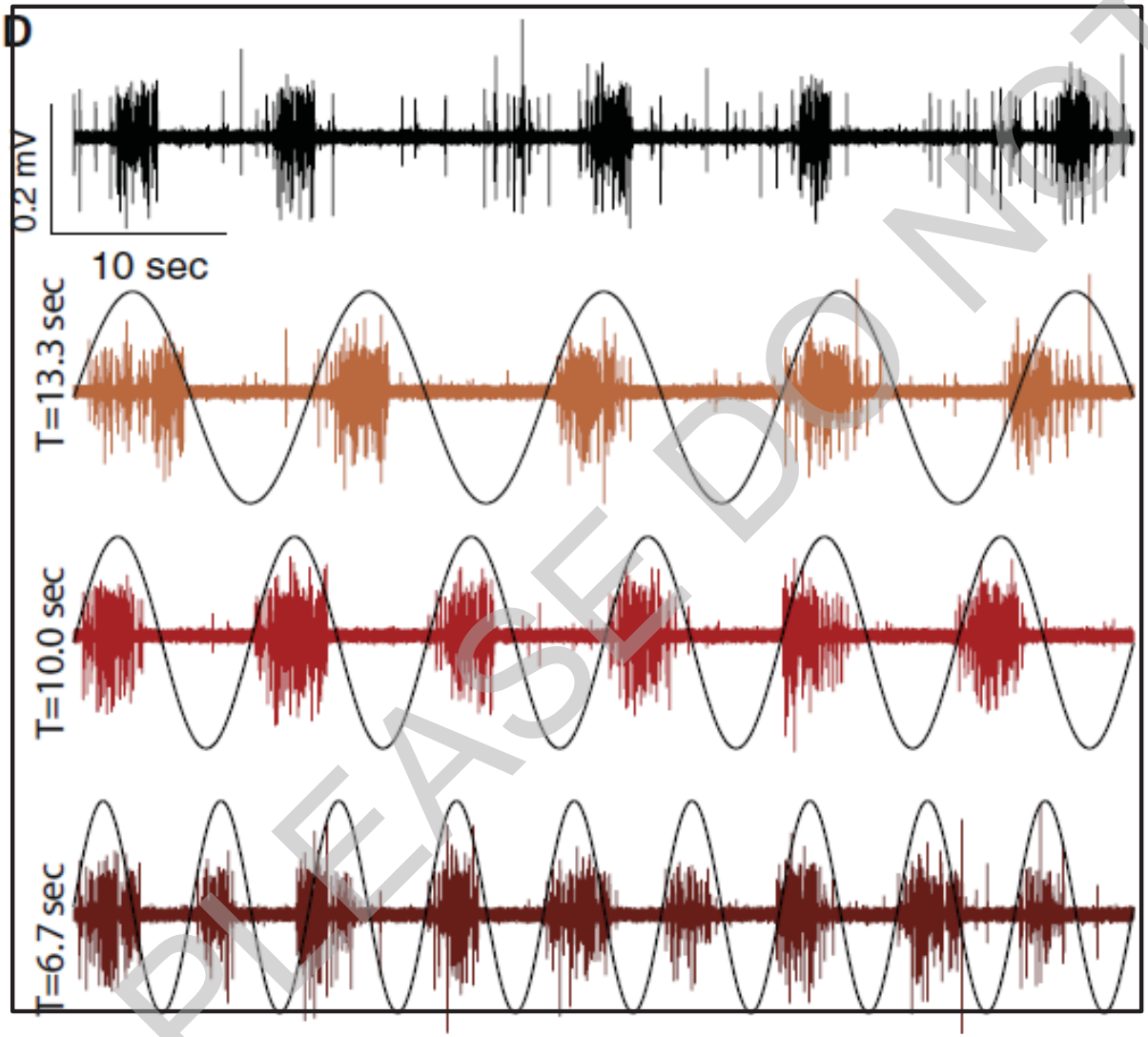
2Hz

tACS: experimental evidence

tACS effect on brain oscillations: in vitro evidence

Endogenous Electric Fields May Guide Neocortical Network Activity

Flavio Fröhlich[1] and David A. McCormick[1,*]
[1]Department of Neurobiology, Kavli Institute of Neuroscience, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA
*Correspondence: david.mccormick@yale.edu
DOI 10.1016/j.neuron.2010.06.005



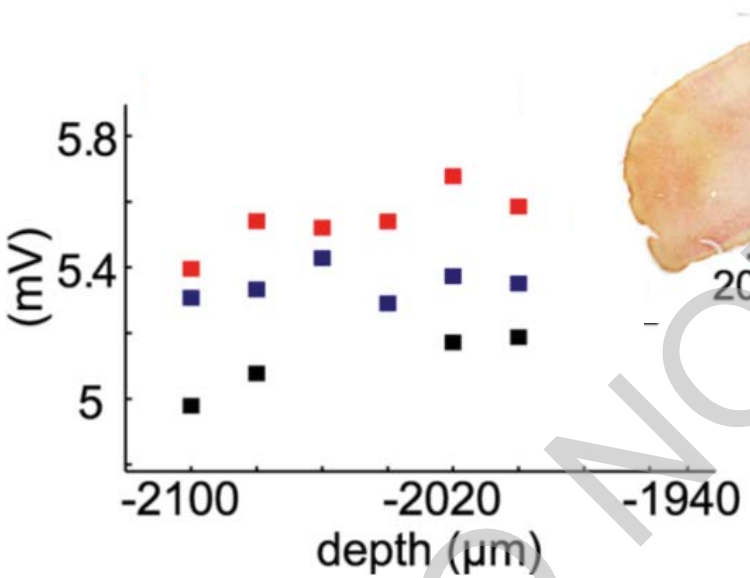
tACS might shift intrinsic dominant oscillations and "tune the system"

Higher stimulation frequency

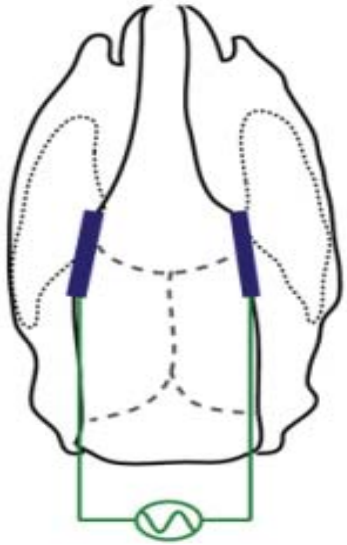
First animal evidence

- tACS at 1.5Hz (delta) induce AC Fields in the Brain

***Ozen* et al., 2010**

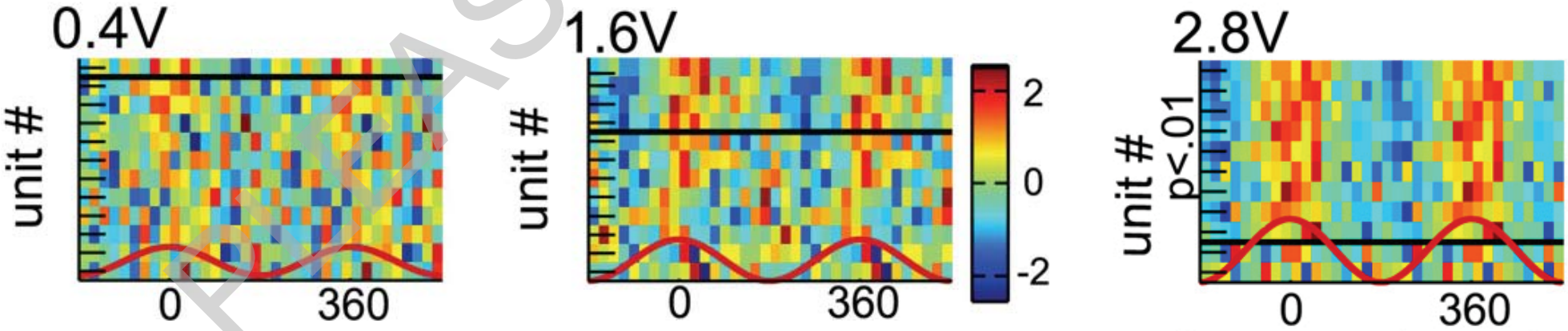


Rat (in-vivo)



- Effect of Stimulation Amplitude

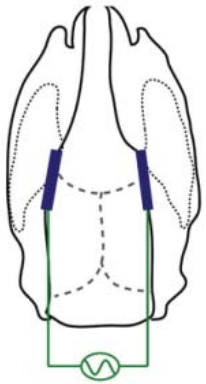
Larger Amplitude → **Homogenous Phase**
More Neurons

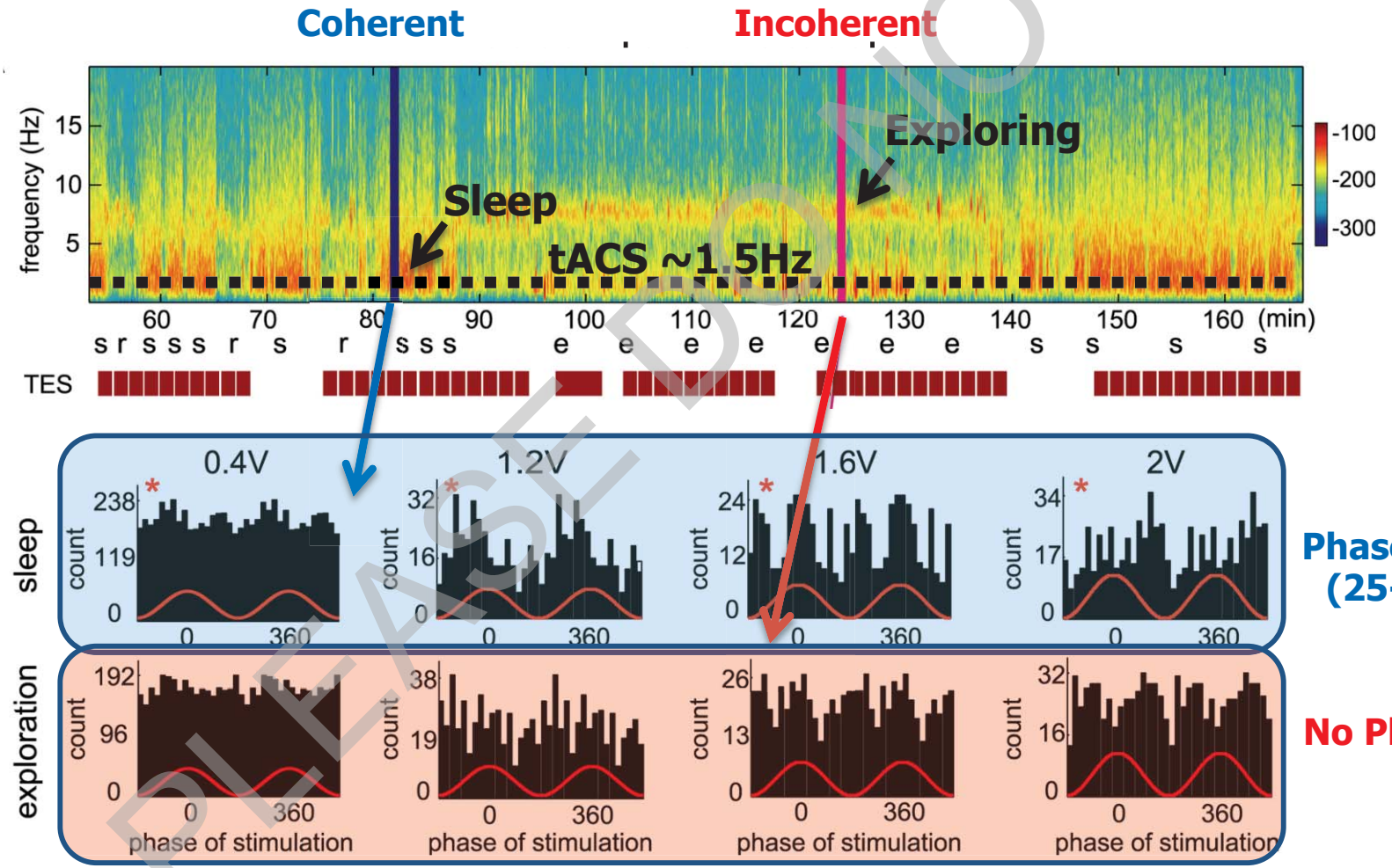


Endogenous Resonance Principle

Ozen et al., 2010

tACS induced Oscillations ⟷ Push & pull **Synaptic mediated Oscillations**





S=sleep
R=rest
E=exploration

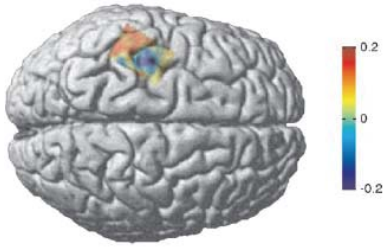
Phase-locked (25-50%)

No Phase-locked

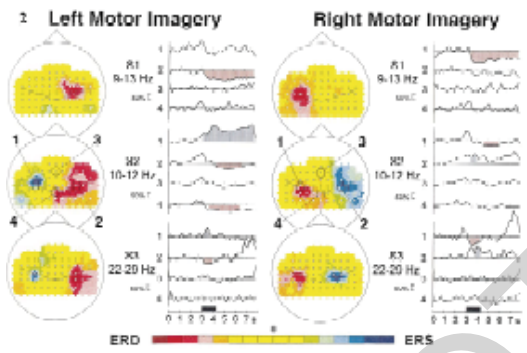
tACS in humans: effects on cortico-spinal Excitability

“Natural Frequencies”

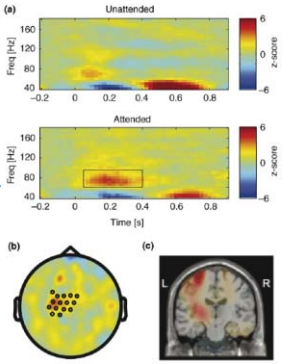
Alpha: motor planning



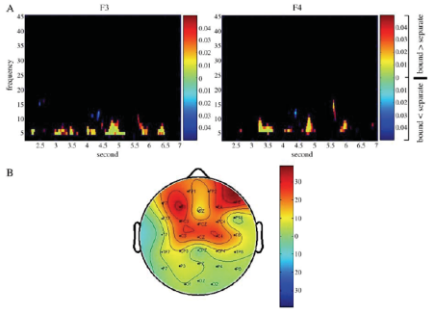
Beta: motor system

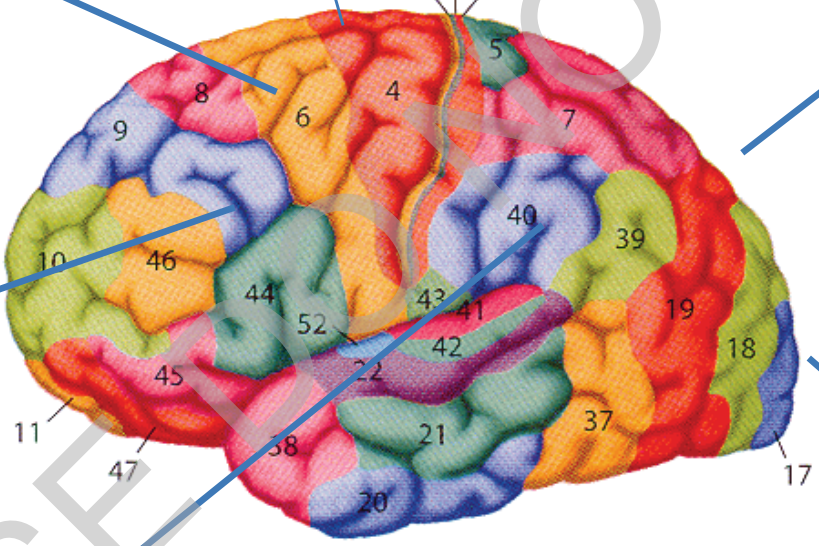


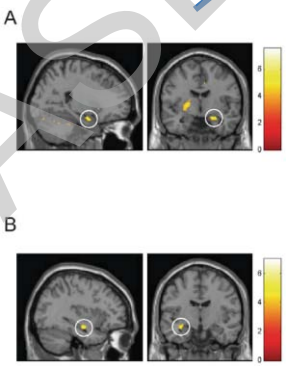
Gamma: selective attention, coding,



Θ: working /long-term memory

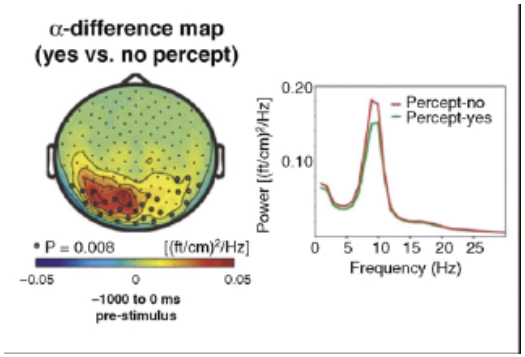






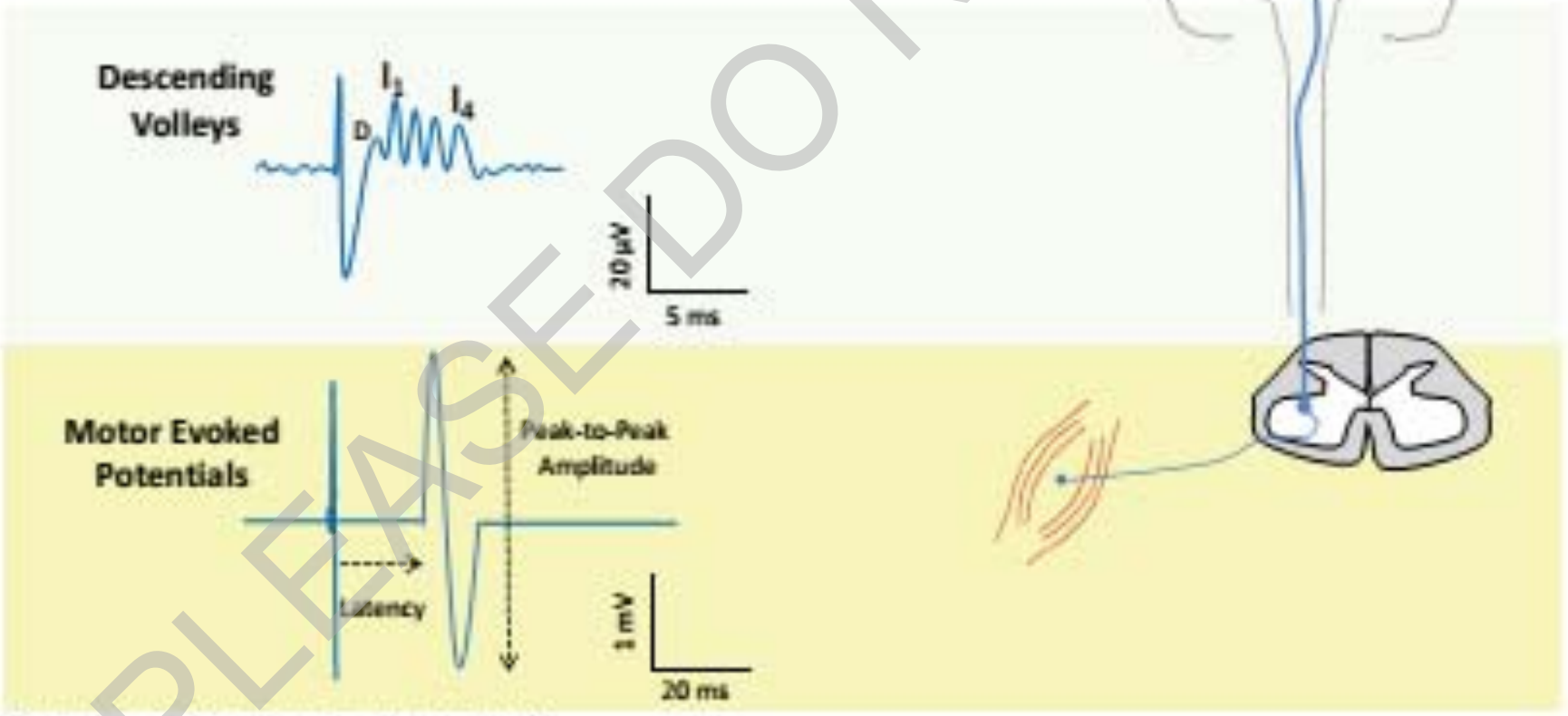
Θ: spatial orienting

Alpha: visual perception



tDCS effects on the motor cortex

Transcranial Magnetic Stimulation
+
Electromyography



tACS and Corticospinal Excitability

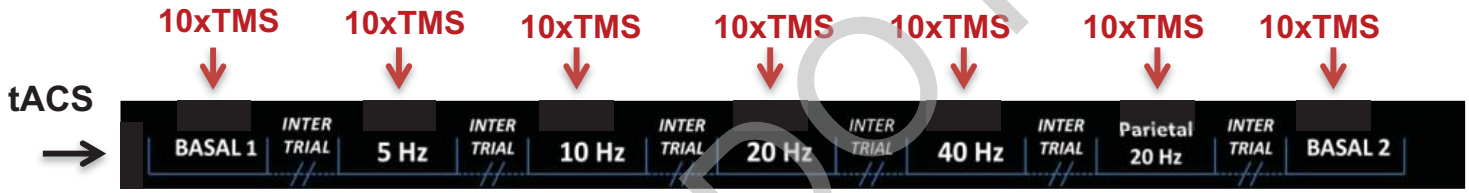
Feurra et al., 2011 *Journal of Neuroscience*

Question

- Are beta (20Hz) oscillations in motor cortex functional or epiphenomenon?

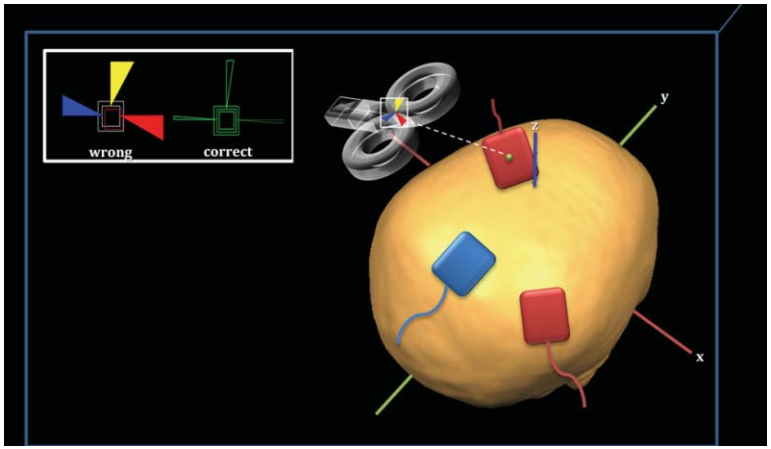
tACS over M1 → Amplitude of TMS induced MEP*

Design



Electrodes	C4 (TMS hot-spot) + P4 (control) – Pz
Current	5, 10, 20, 40Hz, 0.5mA* , 90s
Subjects	15 Healthy

* Kept below phosphene or skin sensation threshold.

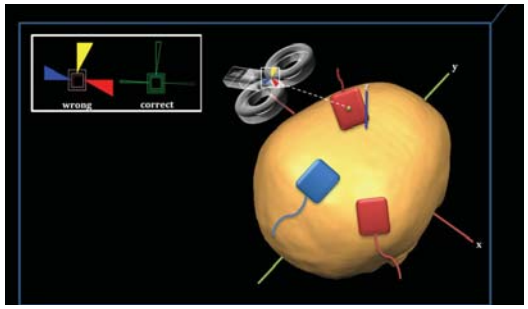


* MEP- Motor Evoked Potential ,indicating the strength of the corticospinal response

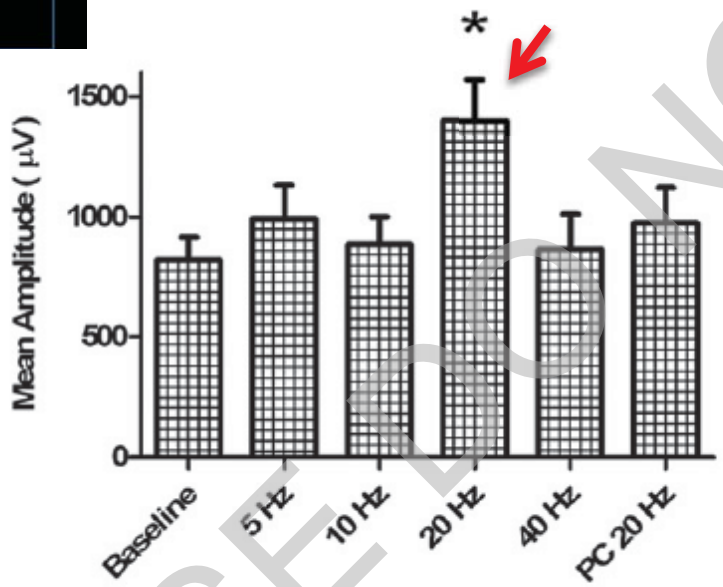
tACS and Corticospinal Excitability

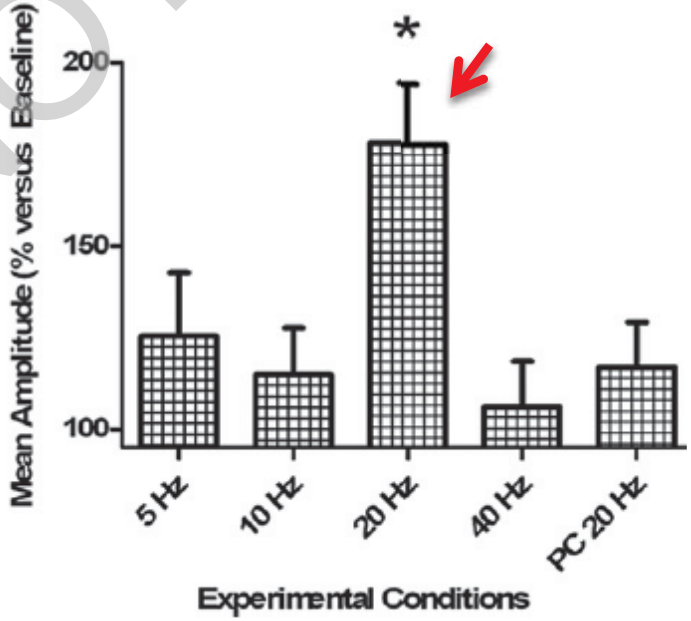
Results

Feurra et al., 2011 *Journal of Neuroscience*



MEP Amplitude (μV)





- **Parietal tACS @ 20HZ specifically increases MEP amplitude**

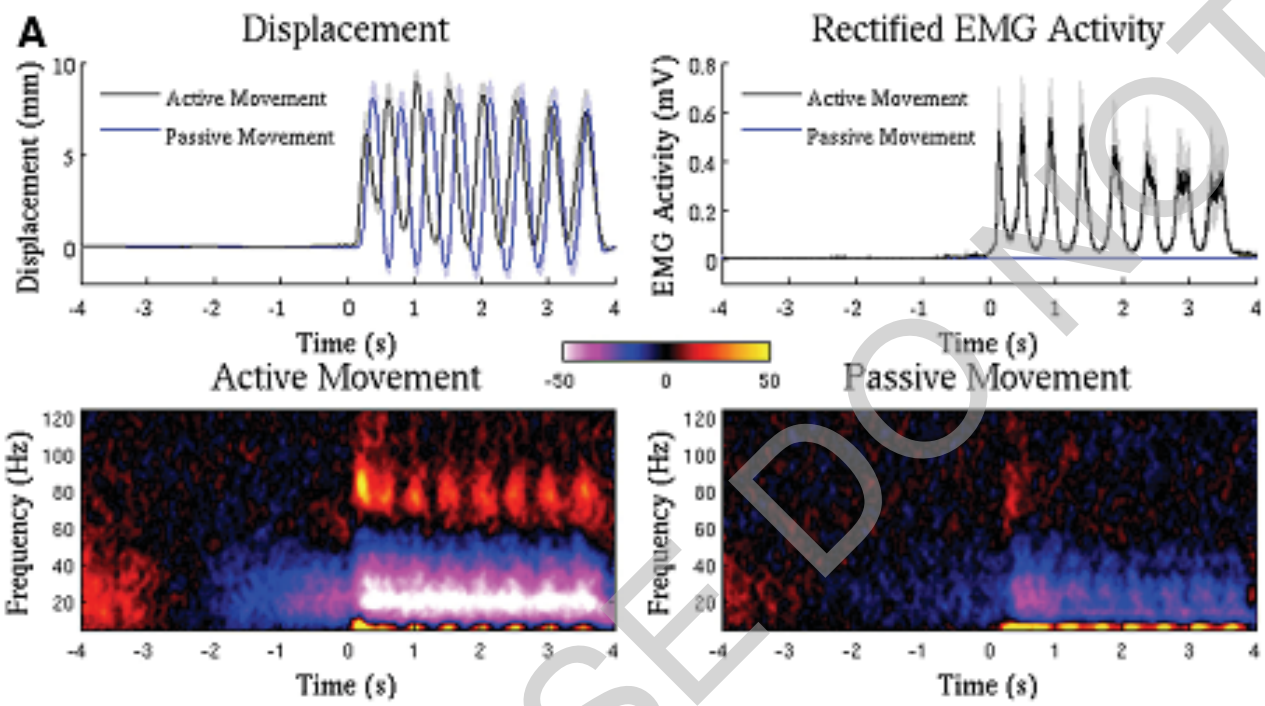
tACS and Motor Performance

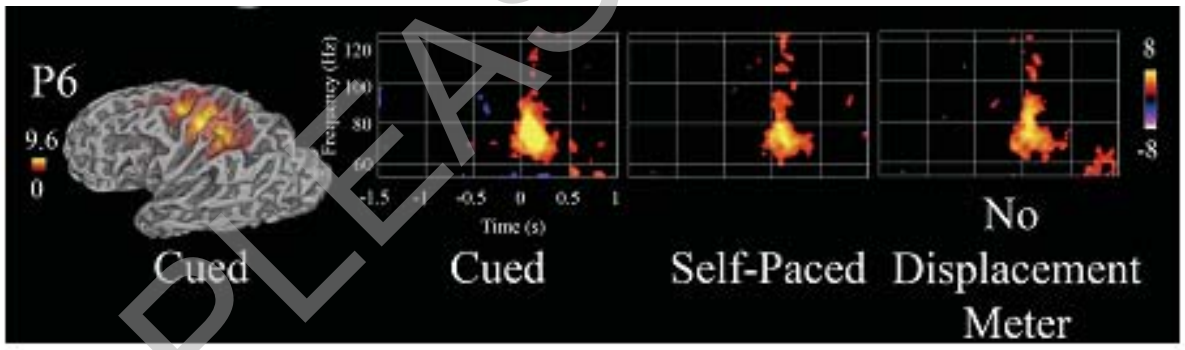
tACS and Motor performance

Santarnecchi et al. 2017, Brain Res.Bull.

Question

- Are Gamma oscillations in motor cortex functional or epiphenomenon?





Muthukumaraswamy 2010

- Tracking task using MEG
- Observed an Increase in **Gamma activity (~90HZ)** in the motor cortex during movement.

• What does Gamma oscillations in the motor cortex represent..?

tACS and Motor performance - II

Santarnecchi et al. 2017, Brain Res.Bull.

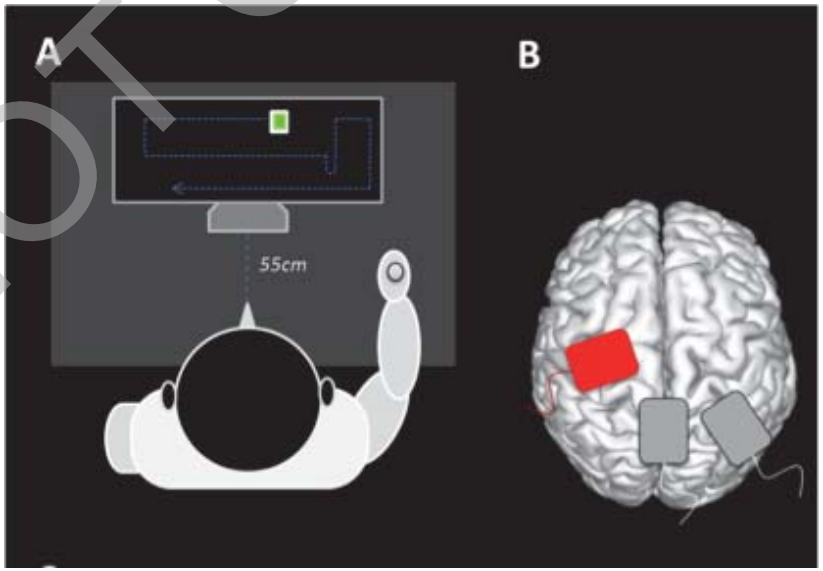
Question

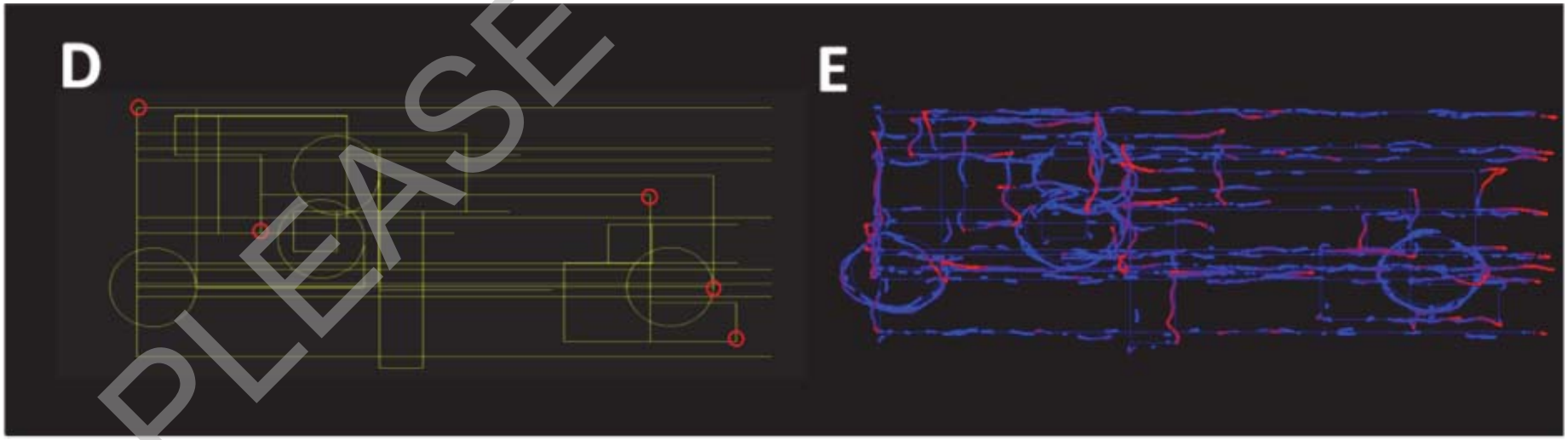
- Are Gamma oscillations in motor cortex functional or epiphenomenon?

Visuomotor task + 10, 20, 60, 80Hz and Sham tACS on the motor cortex.

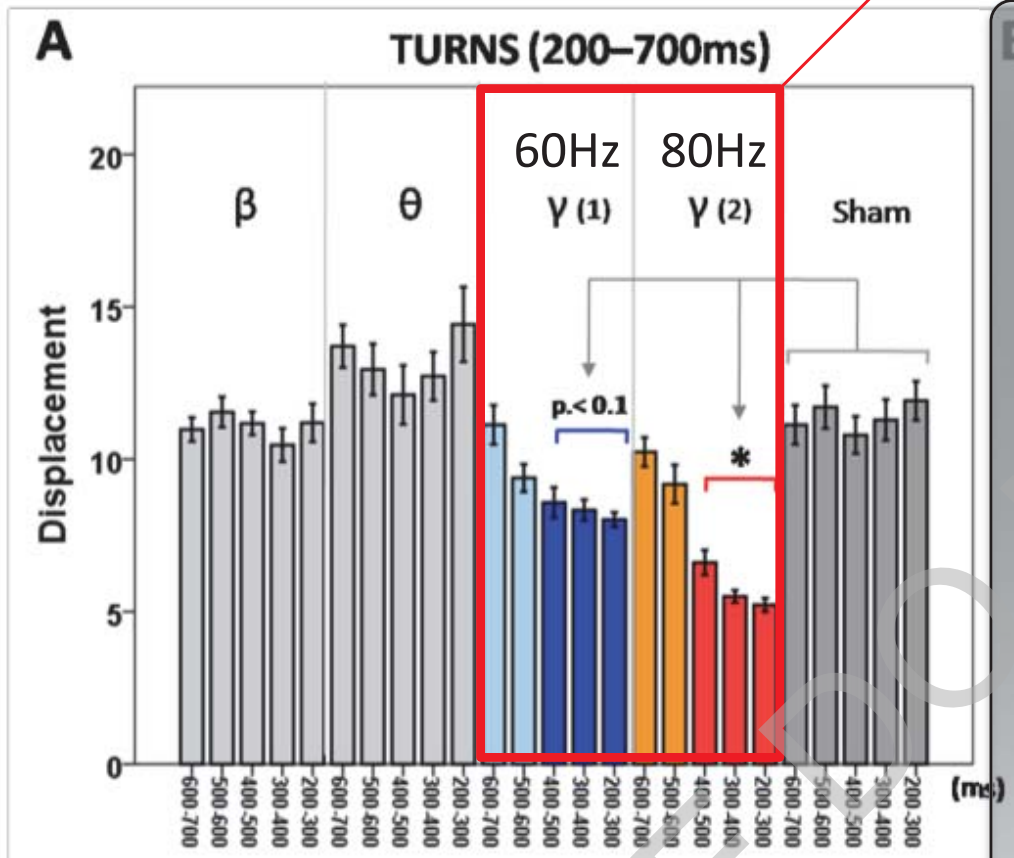
Effects on several components of the motor program: Acceleration, Pursuit, Loops, Turns, etc..
(o)

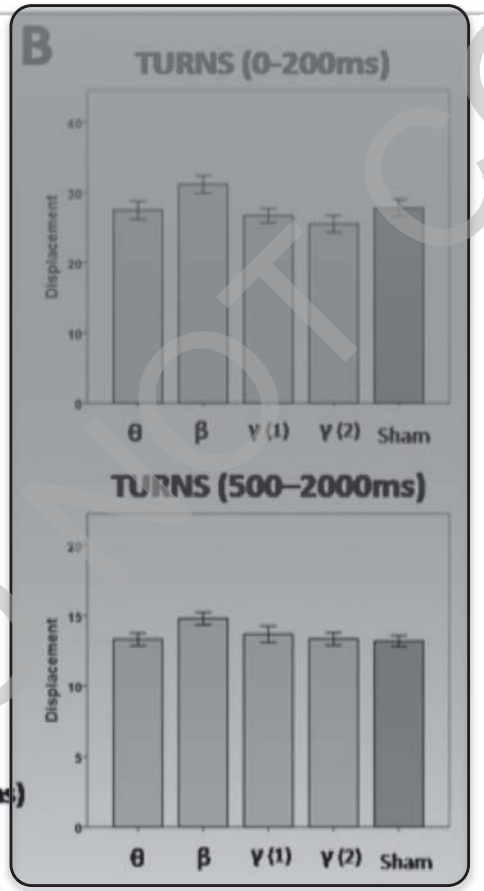
High spatial and temporal resolution analyses.

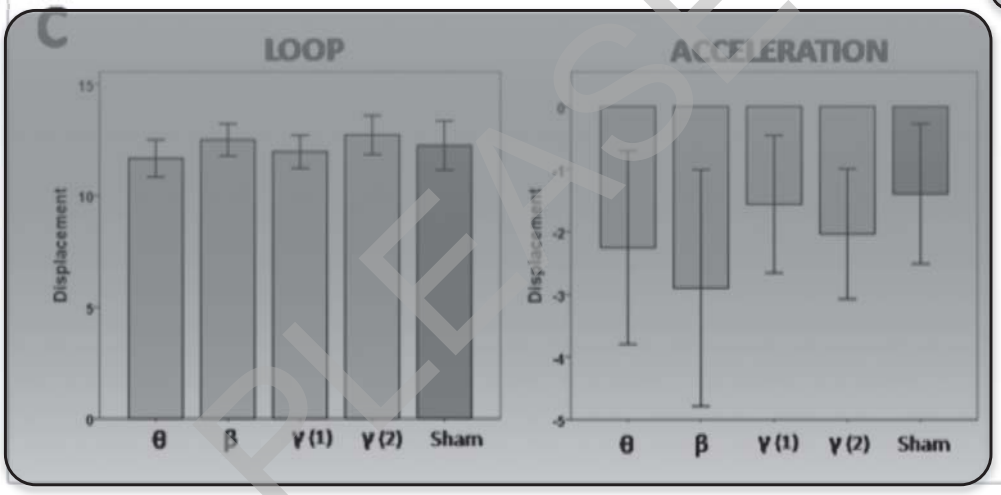


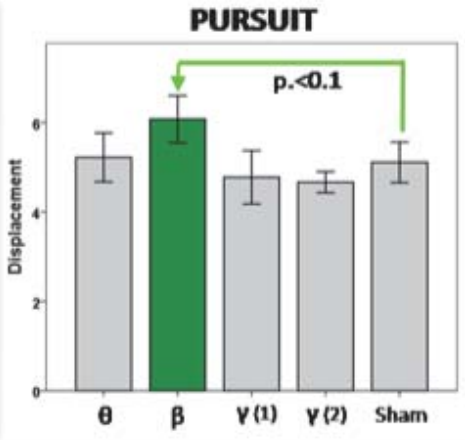


tACS and Motor performance - III









- Significant **enhancement of performance during TURNS during Gamma tACS (80Hz)**, with a trending result for 60Hz tACS.

- Effect is present in a **specific time window (200-700ms after each TURN)**, coherently with MEG studies showing increase in EEG power at 90HZ during a similar task.

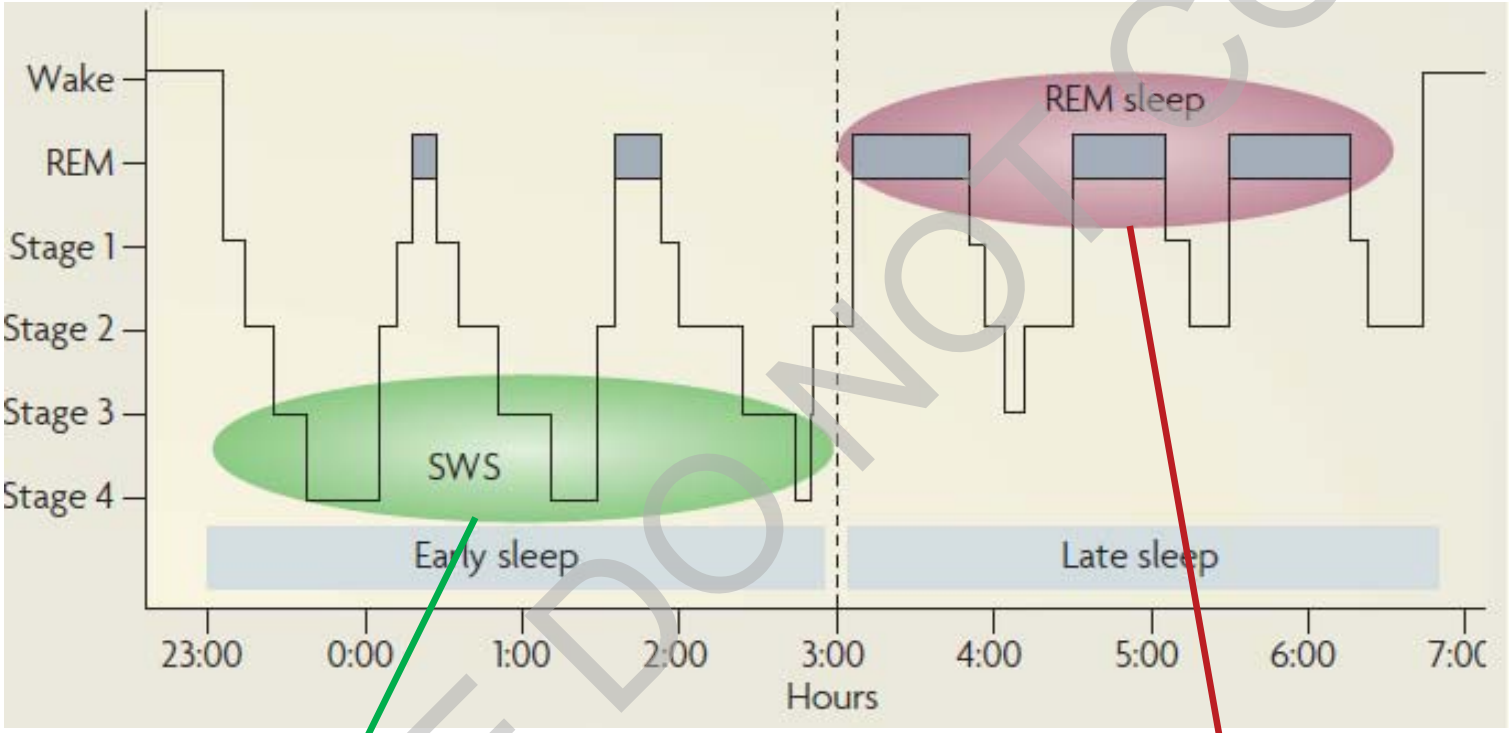
- No effects during Loop, Acceleration, Pursuit

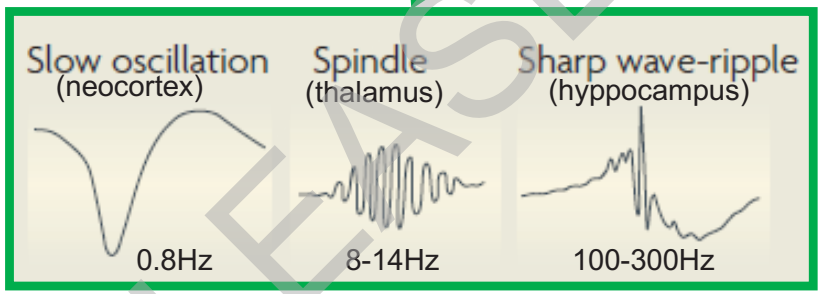
tACS and Cognition

Memory Consolidation

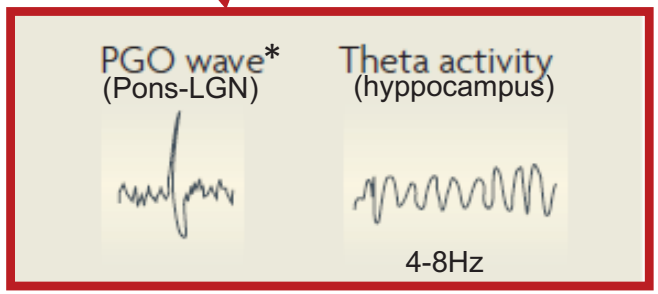
Rationale

Sleep Architecture





Declarative memory



Non- Declarative memory

for further reading see Diekelmann, 2010

* PGO: ponto-geniculooccipital

Memory Consolidation

Design

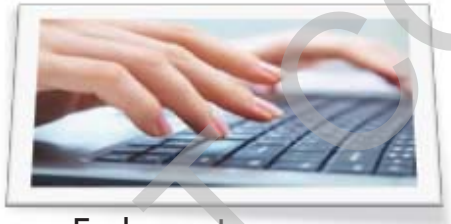
Marshall et al., Nature 2006

Declarative memory

Paired Associated Learning Task

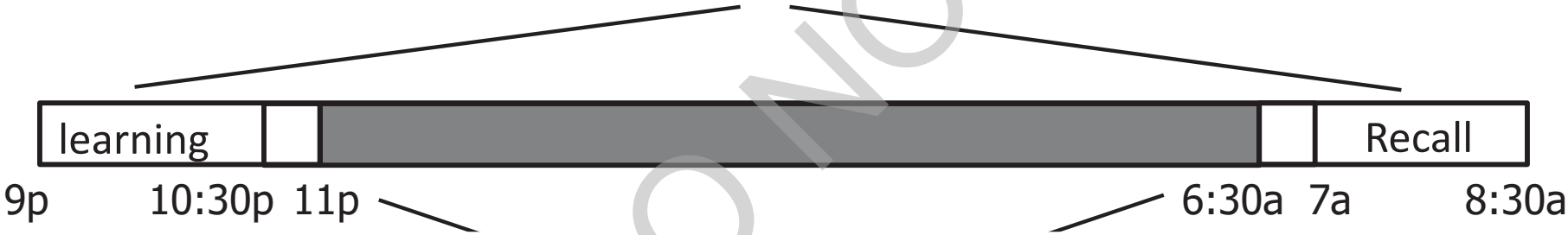
46 word pairs

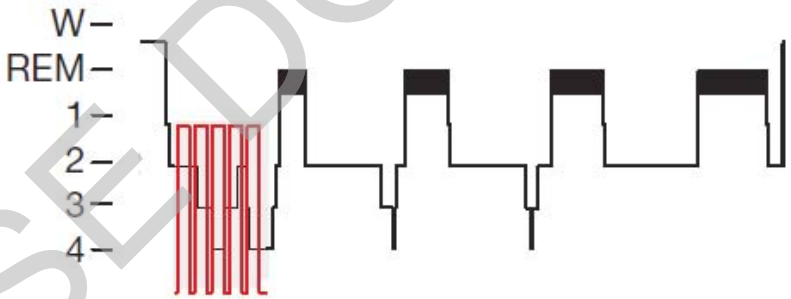
Finger Sequence Tapping Task



5-element sequences
(e.g. 4-2-3-1-4) in 30s

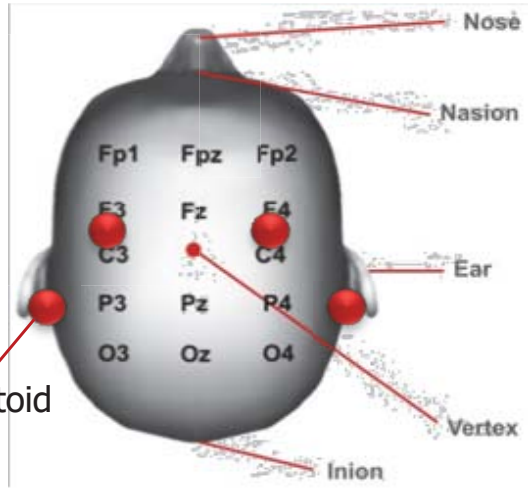
Non-declarative memory





W, wake; 1–4, sleep stages 1–4

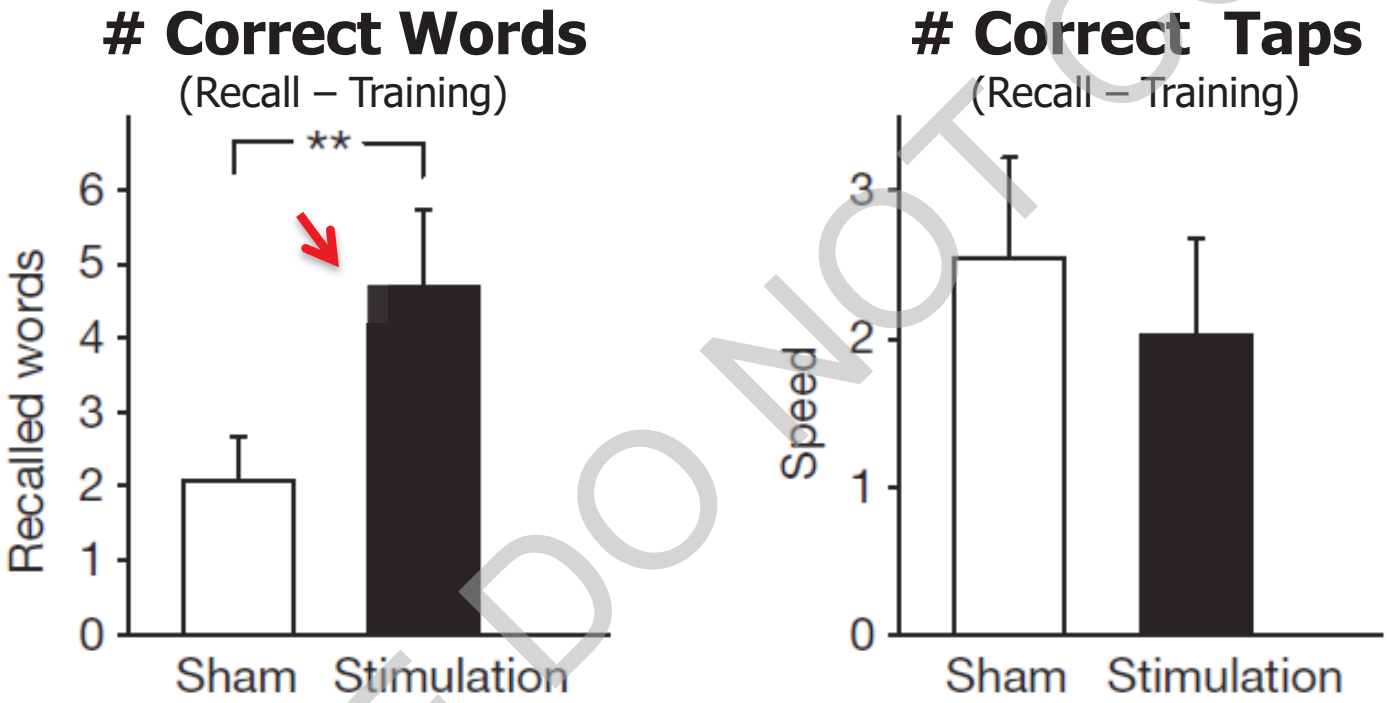
Electrodes	F3-Mastoid , F4-Mastoid (diam=1cm)
Current	0.75Hz, ~0.33A , 5min/1min ON/OFF
Subjects	13 Healthy



Memory Consolidation

Marshall et al., Nature 2006

Results



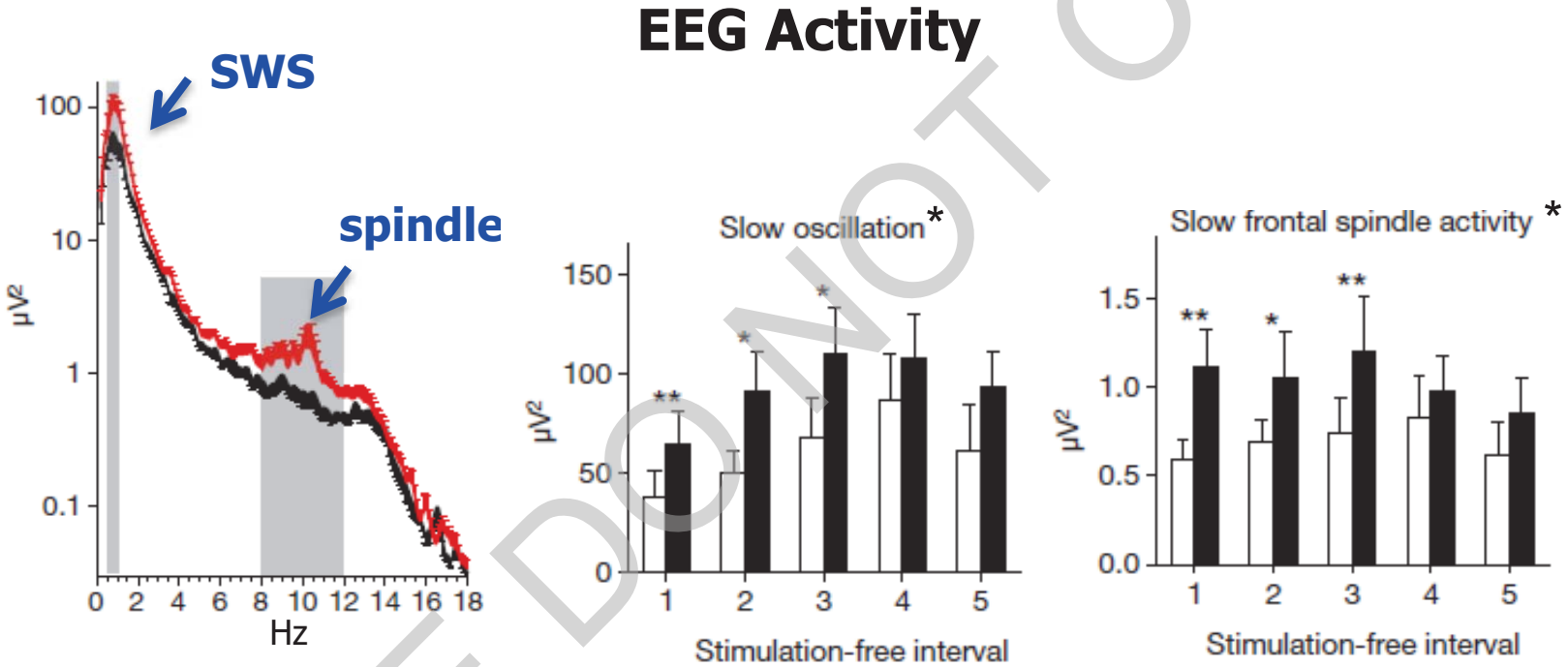
- Bilateral 0.75Hz frontal- tACS during early sleep selectively enhances hippocampus-dependent retention of declarative memory

**P < 0.01

Memory Consolidation

Marshall et al., Nature 2006

Results



- tACS entrained SWS and spindle power spectra in the prefrontal region

* Bands for slow oscillations (0.5–1 Hz) ; Bands for spindle oscillations (8-12 Hz)

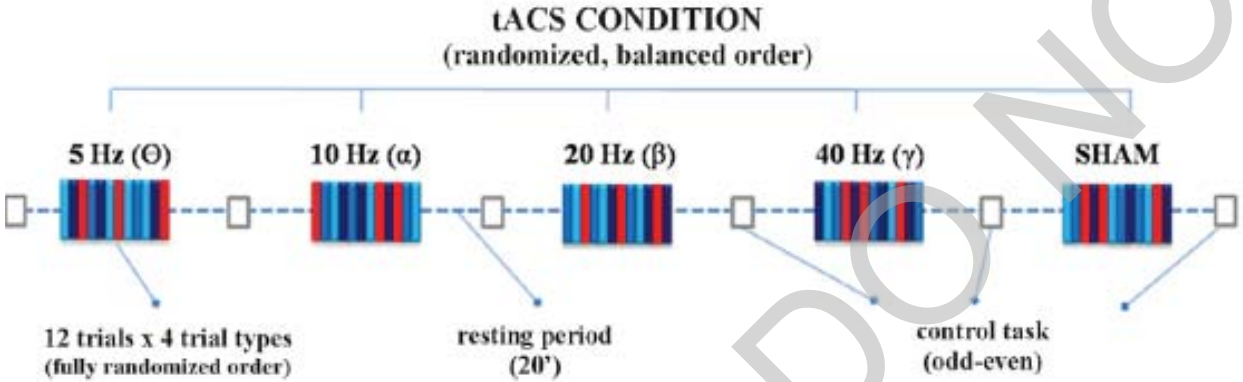
Fluid Intelligence – Abstract Reasoning

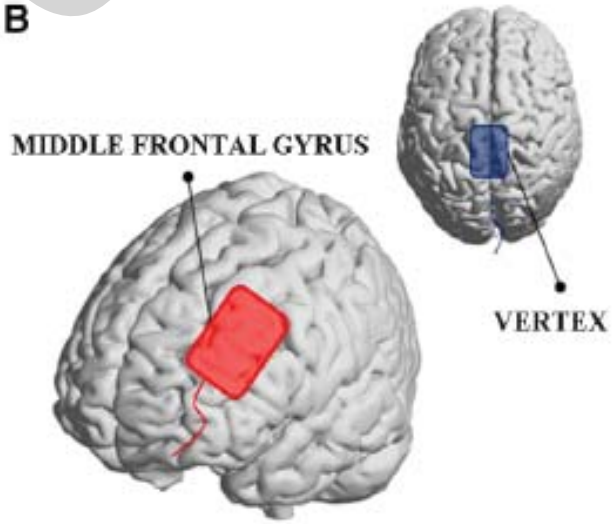
Santarnecchi et al., Curr. Biology 2013

Question

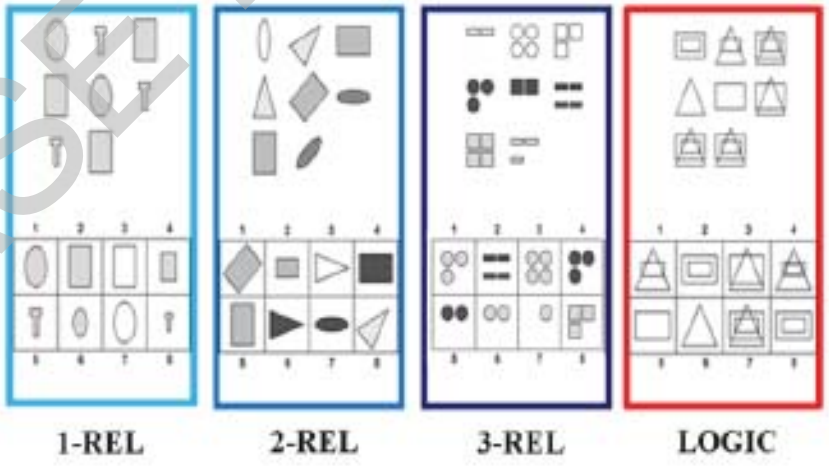
- Does tACS enhance Intelligence-related processing in a frequency and trial specific manner? Is prefrontal gamma an epiphenomenon?

Design





Stimulation sites



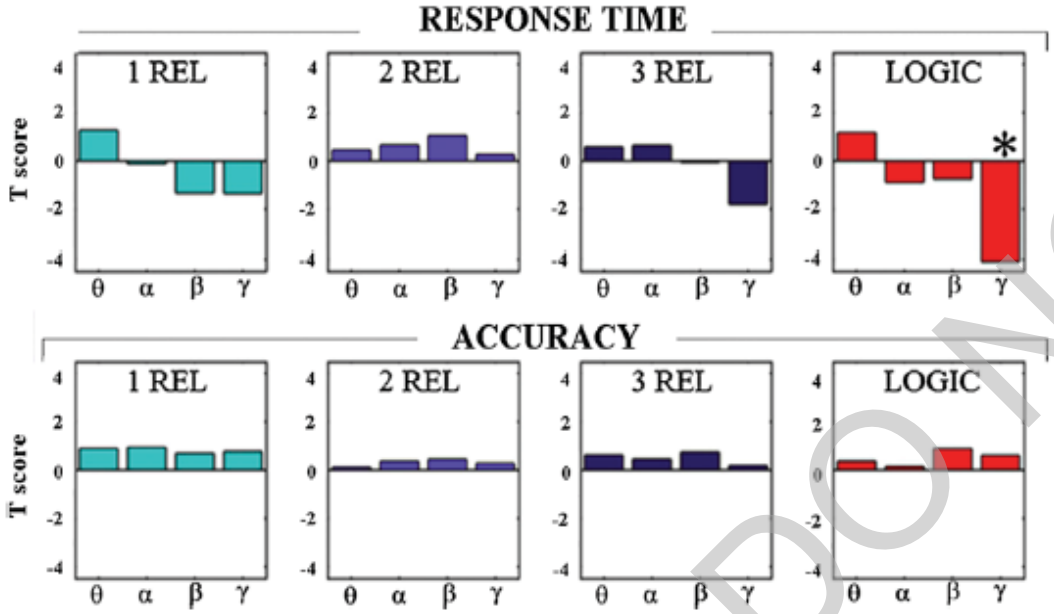
Logical and Relational Reasoning Stimuli

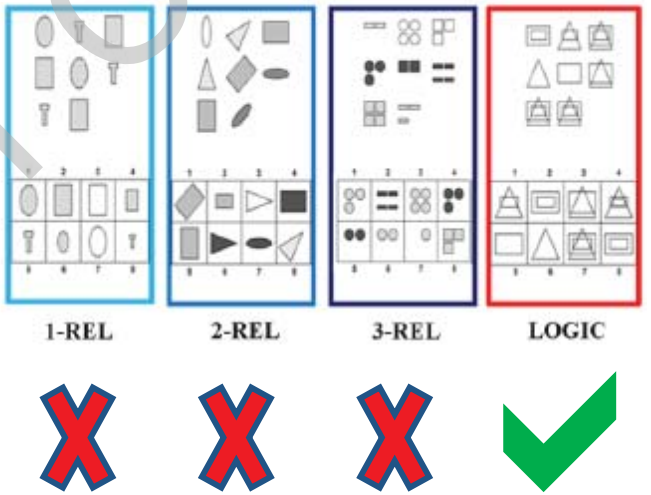
N=24; tACS 1.250mA

Fluid Intelligence

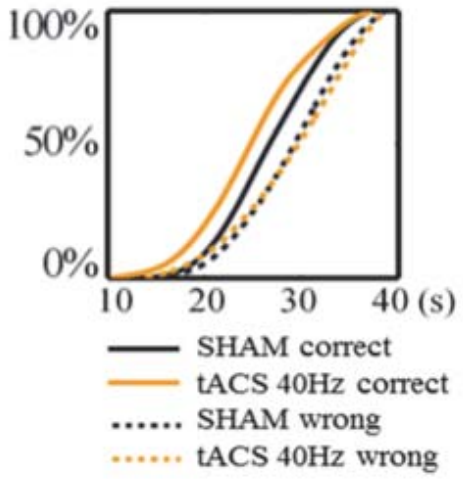
Results

Santarnecchi et al., Curr. Biology 2013





- **Decrease of *Correct* trials *Response Time*** during **gamma-tACS**
- Selective effect for **Logic trials**.
- First evidence of a "causal" Role of gamma-oscillations in higher-order cognition.

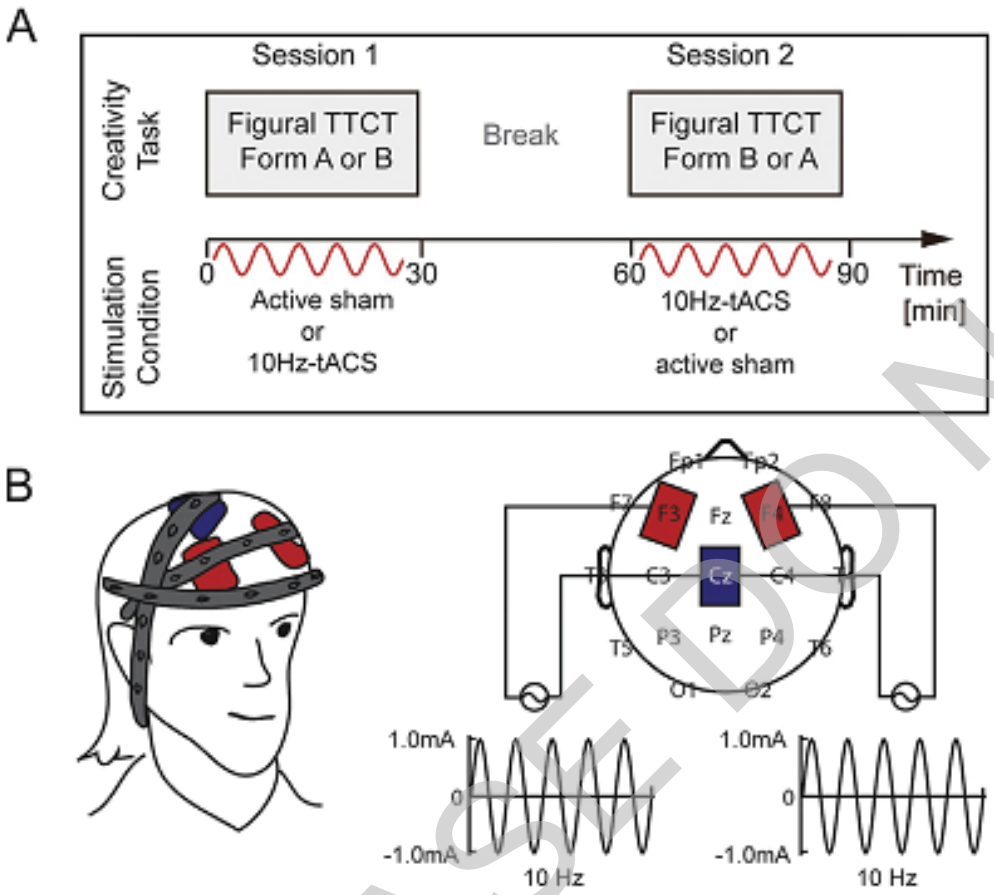


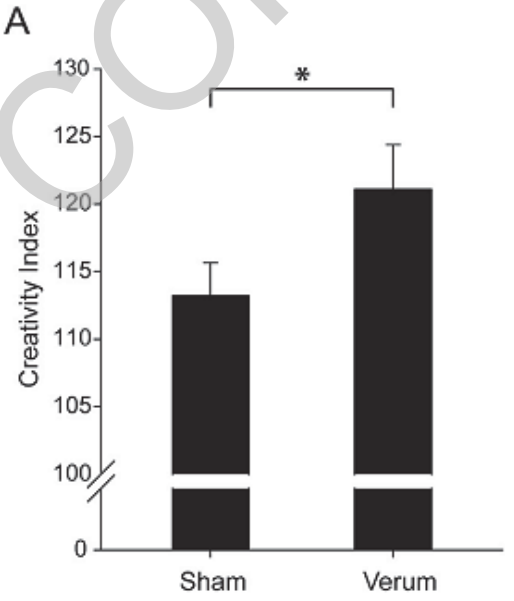
No modulation of speed-accuracy tradeoff

Creativity

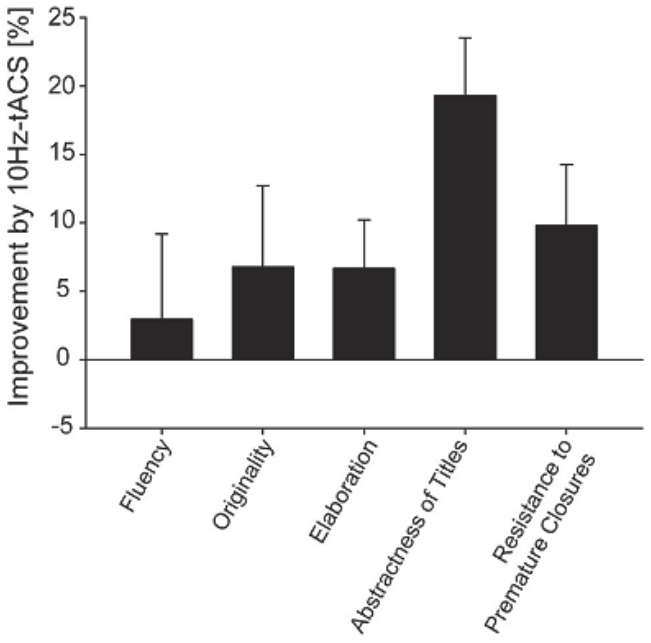
Design and Results

Lustenberger et al., Cortex 2015





10Hz tACS effect on a Creativity Index

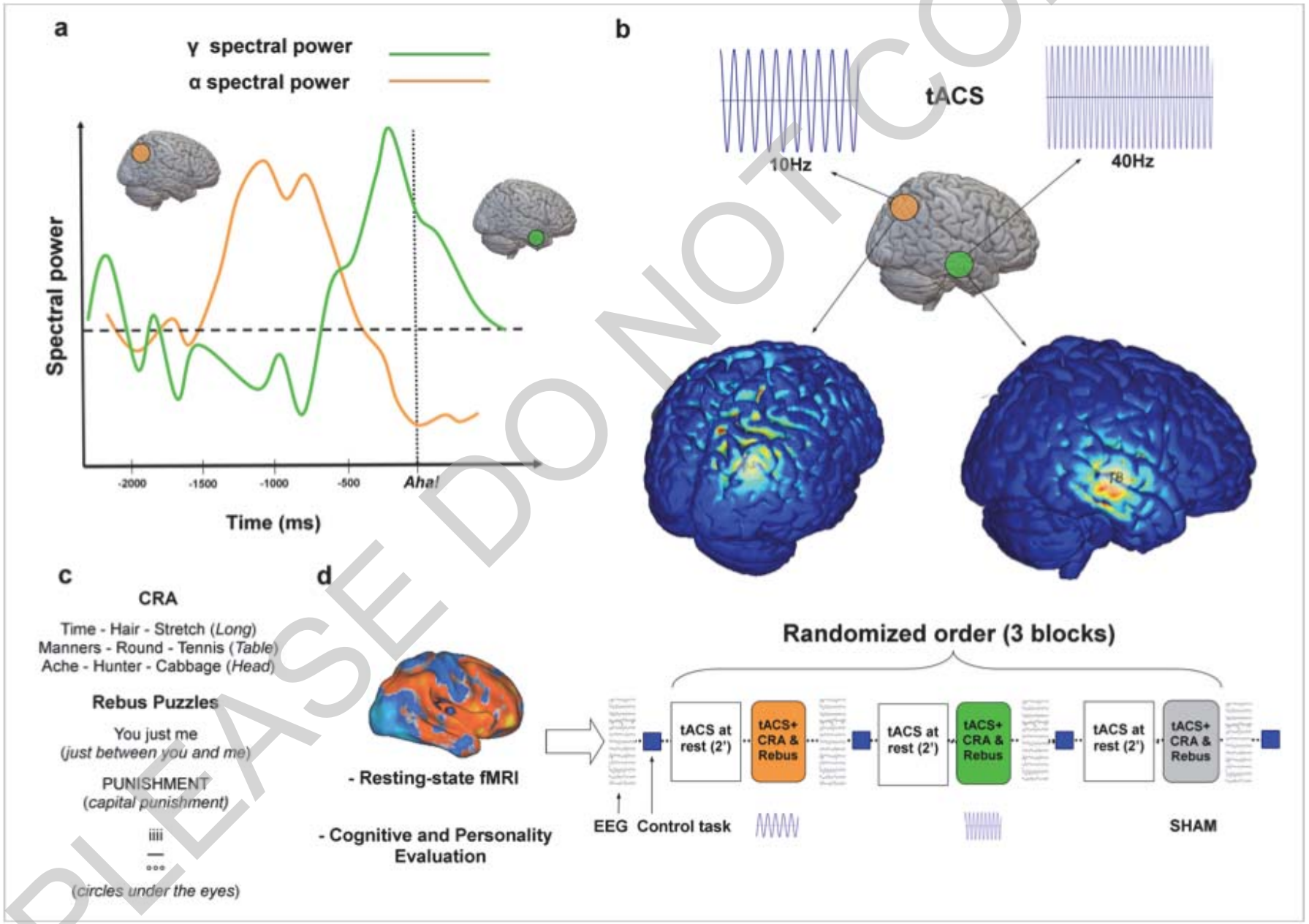


- Torrance Test of Creative Thinking (TTCT)
- In-phase tACS over the prefrontal lobes
- Sham, 10Hz and 40Hz tACS

Inducing *Eureka!* moments

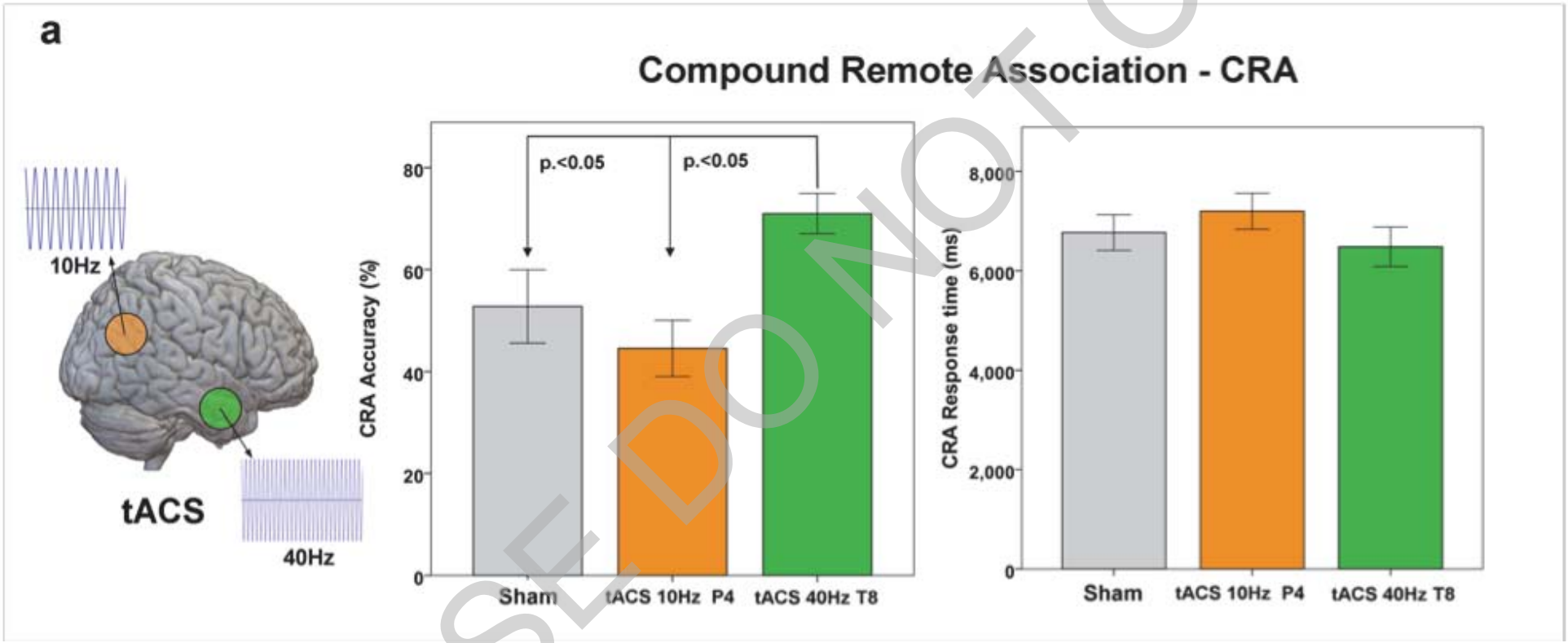
Santarnecchi et al., 2019 Scientific Reports

Giulia Sprugnoli



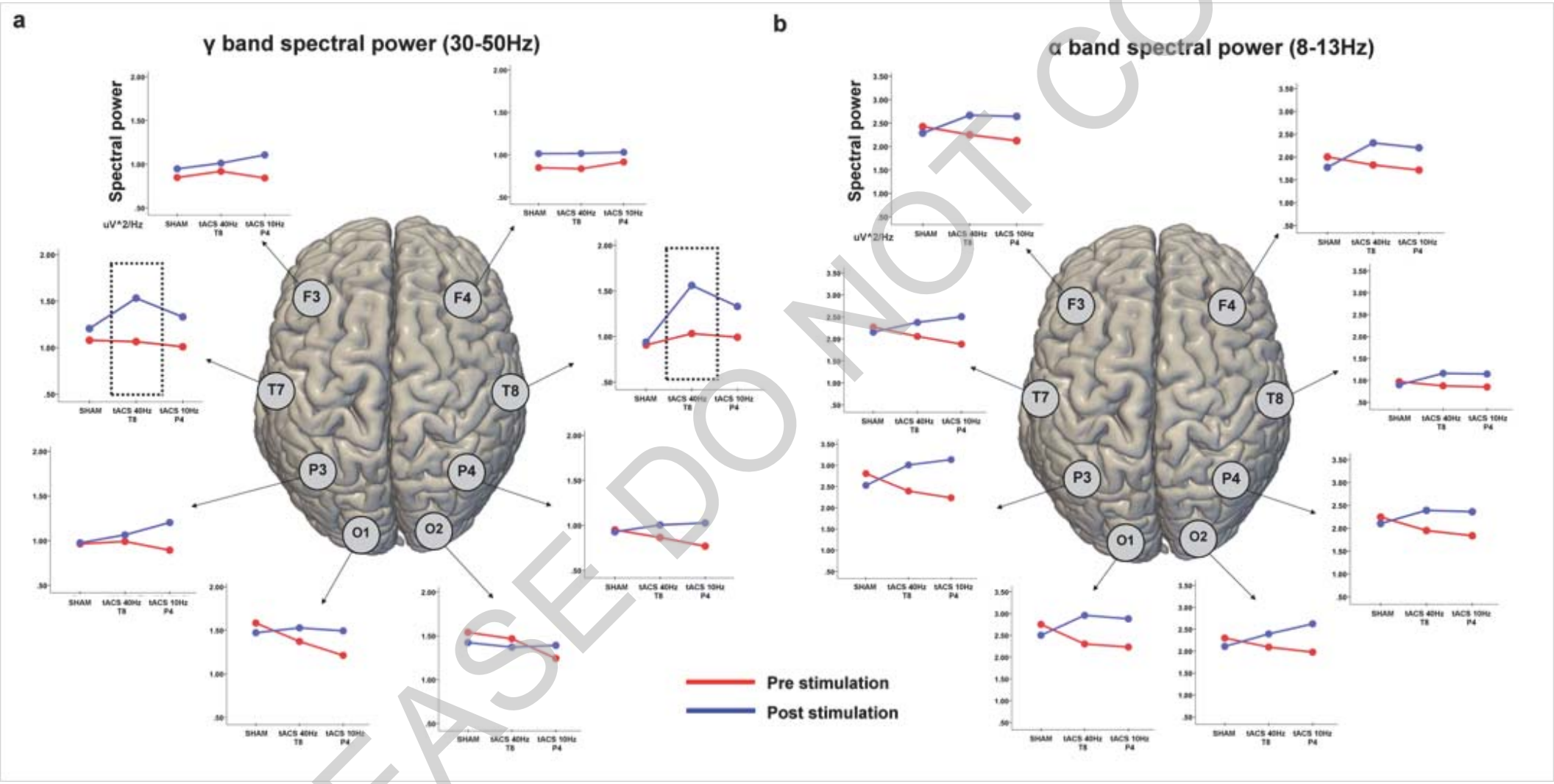
Behavioral Effects

Santarnecchi et al., 2019 Scientific Reports



Increase in Gamma spectral power

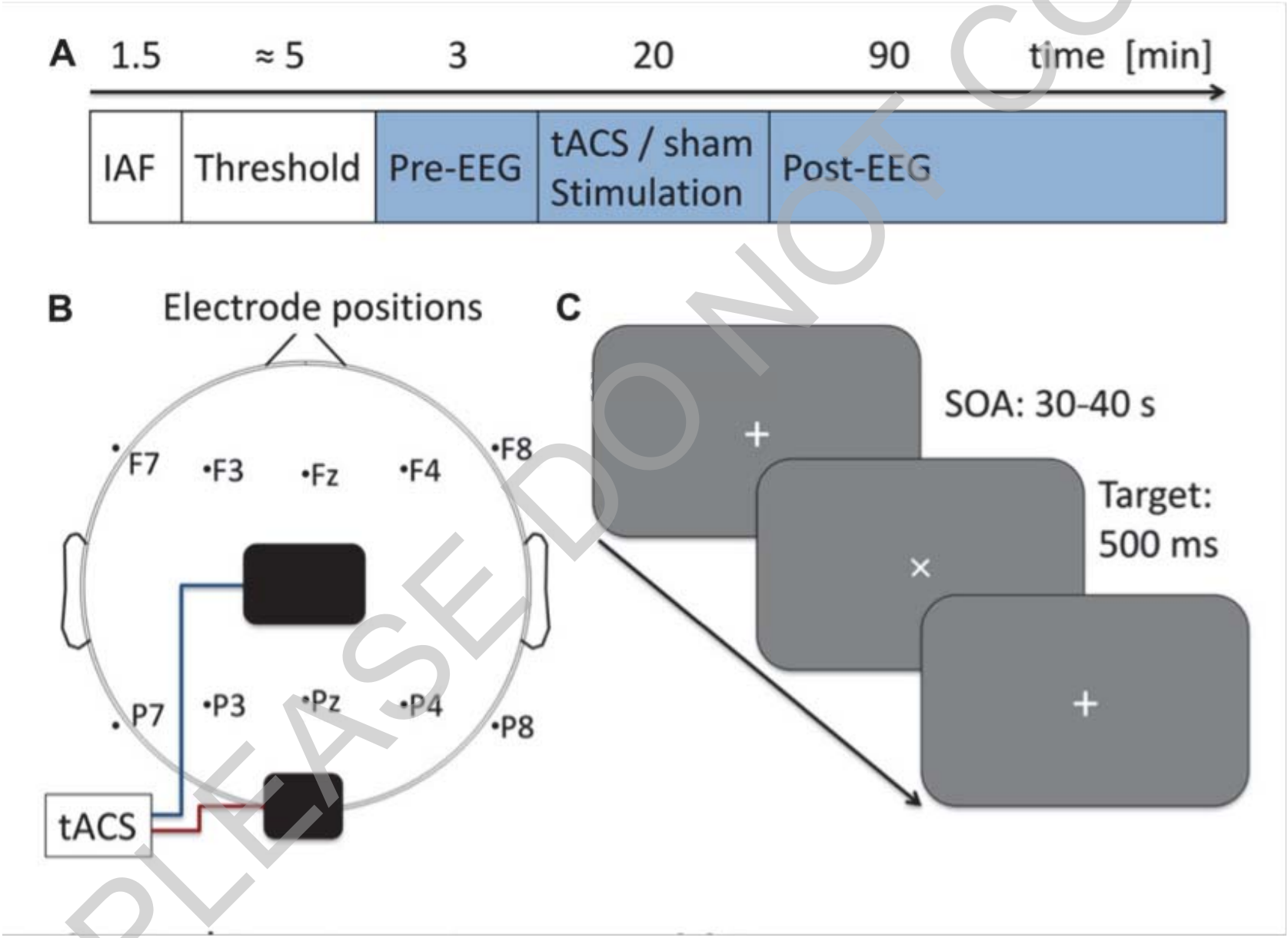
Santarnecchi et al., 2019 Scientific Reports



tACS: long lasting after effects?

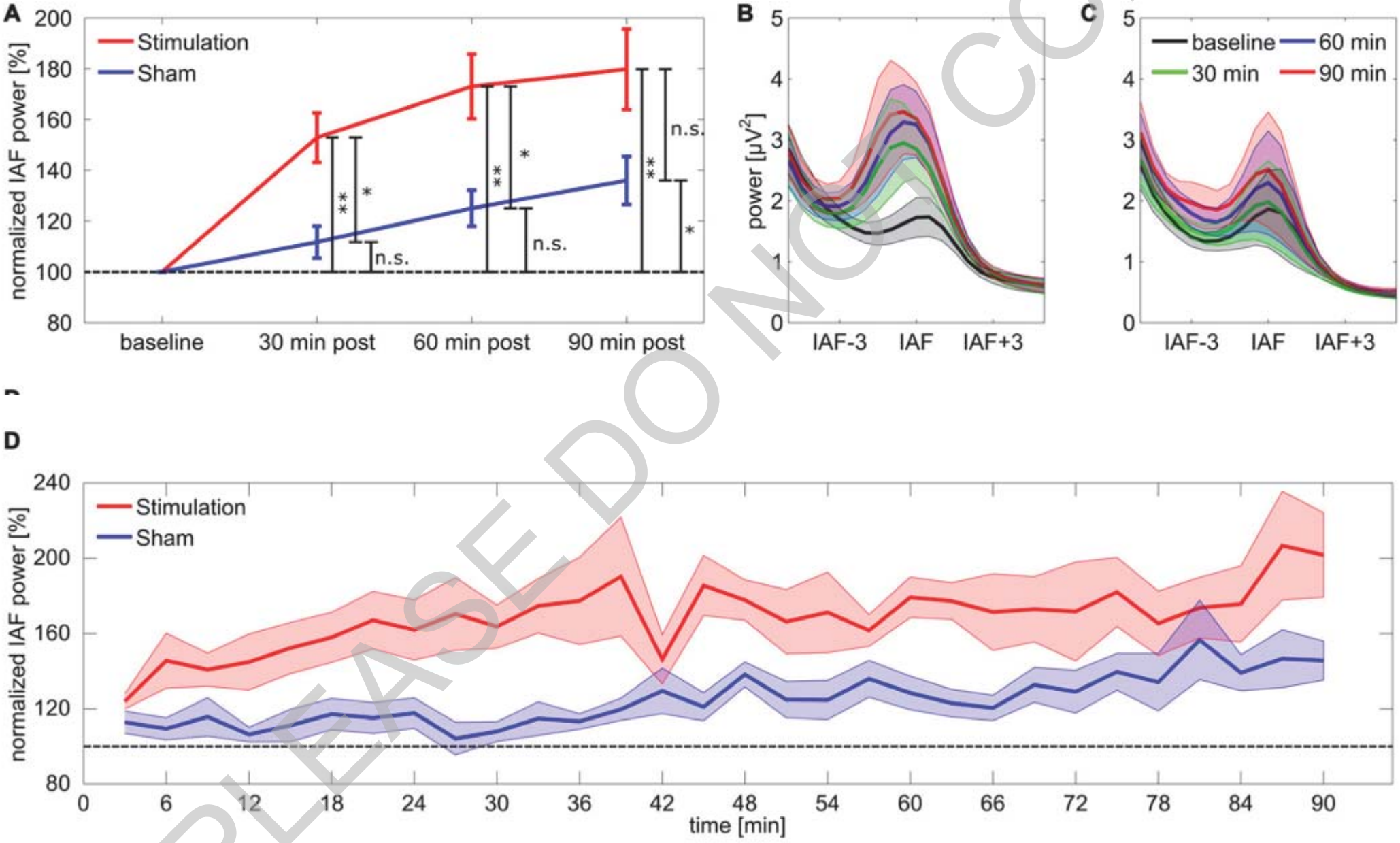
tACS targeting Alpha oscillations

Kasten et al. 2016, Frontiers Human Neuroscience



Results

Kasten et al. 2016, Frontiers Human Neuroscience

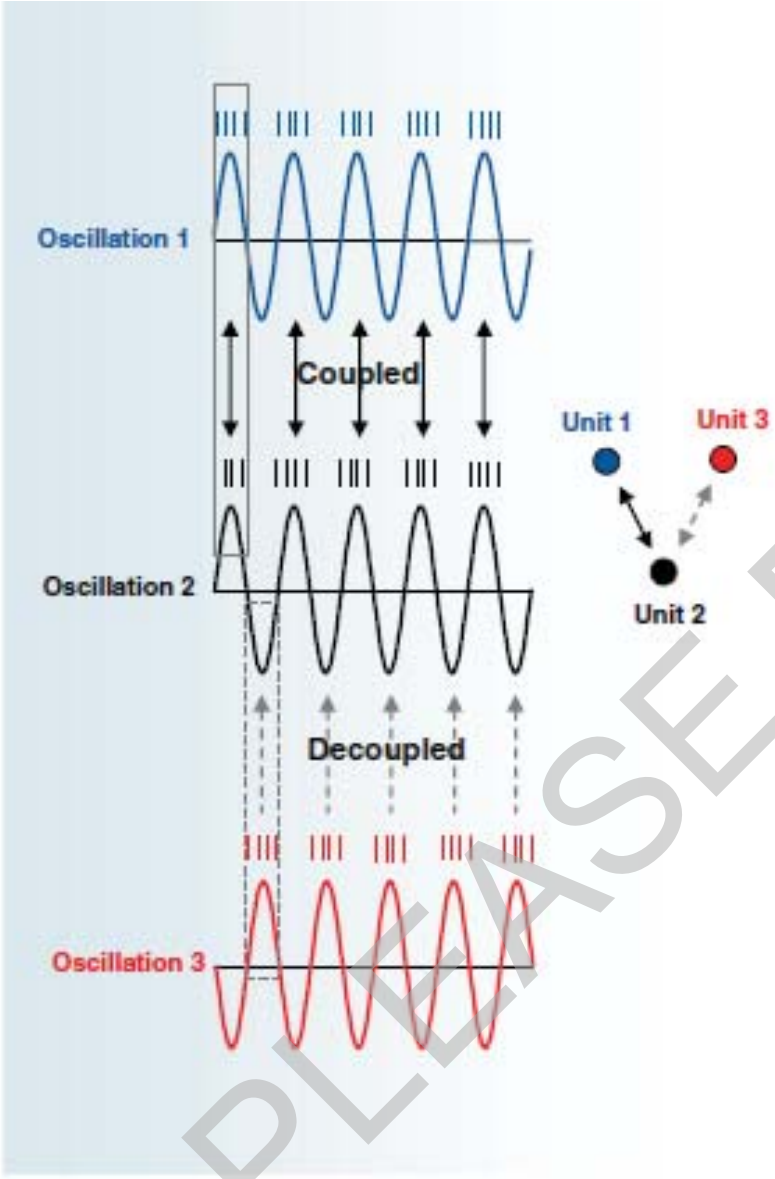


Phase-Related Modulation by tACS

Oscillatory pattern and periodicity in behaviour

Canolty, Science 2005

"Communication-through-coherence" Theory



- Communication being facilitated when two oscillatory populations are **aligned to their high excitability phases.**

- **Effective communication relies on spikes** from the sending population reaching the receiving population **at a phase of high excitability.**

- **Changes in synchronization** between distant brain areas (possibly reflecting communication) **are systematically related to task performance**.

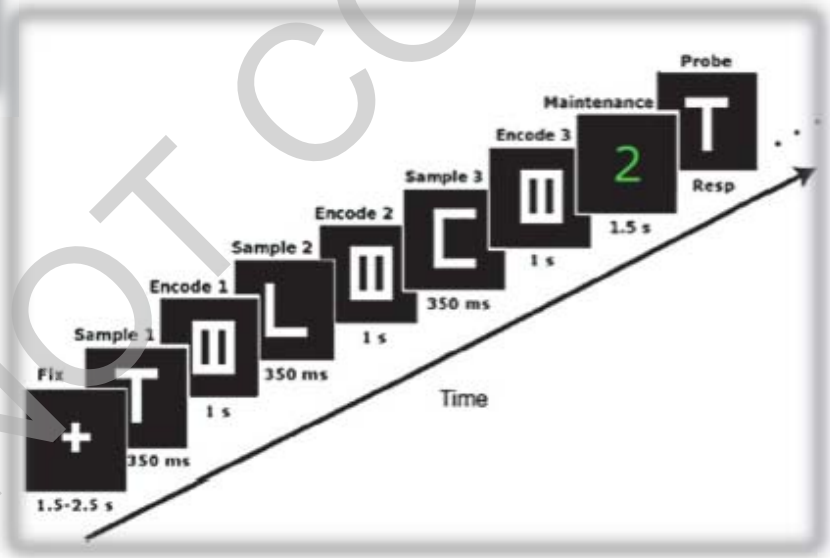
tACS and Phase Coupling: Working Memory

The Importance of Timing in Segregated Theta Phase-Coupling for Cognitive Performance

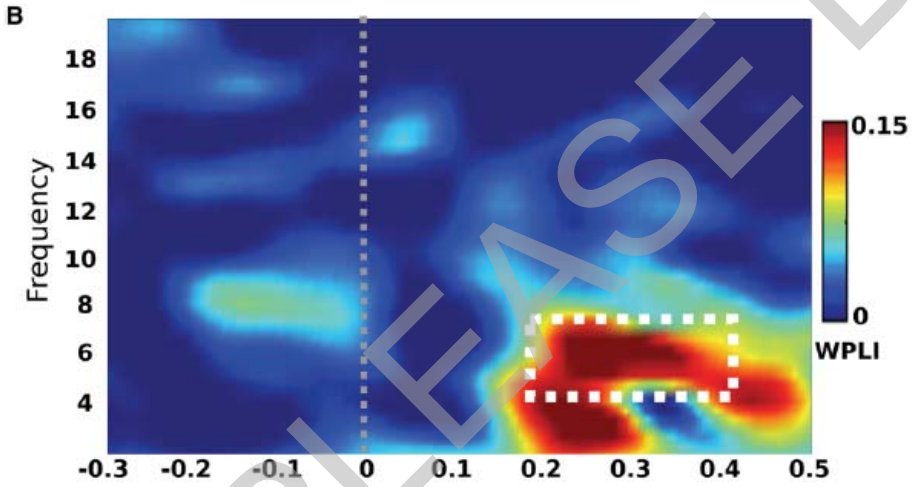
***Polania* et al., Curr. Bio 2012**

Question

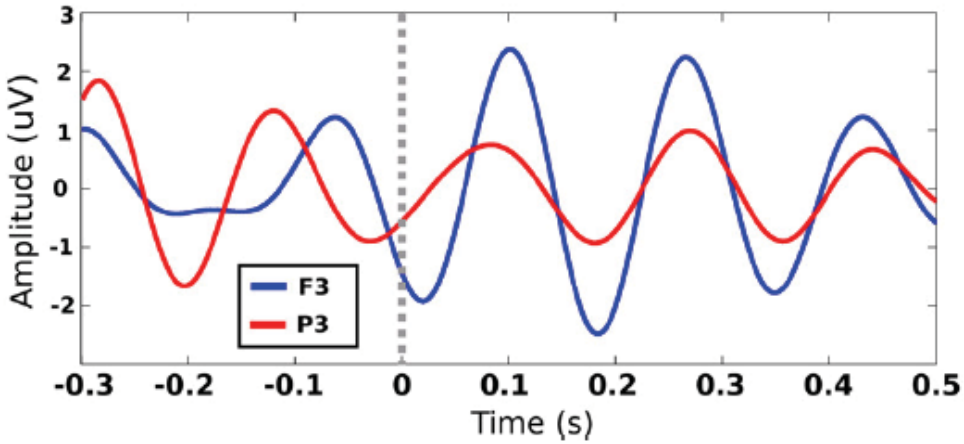
- Can we modulate synchronization during working memory processing? Does it matters?



Sternberg Working memory task



Fronto-parietal Phase-lag

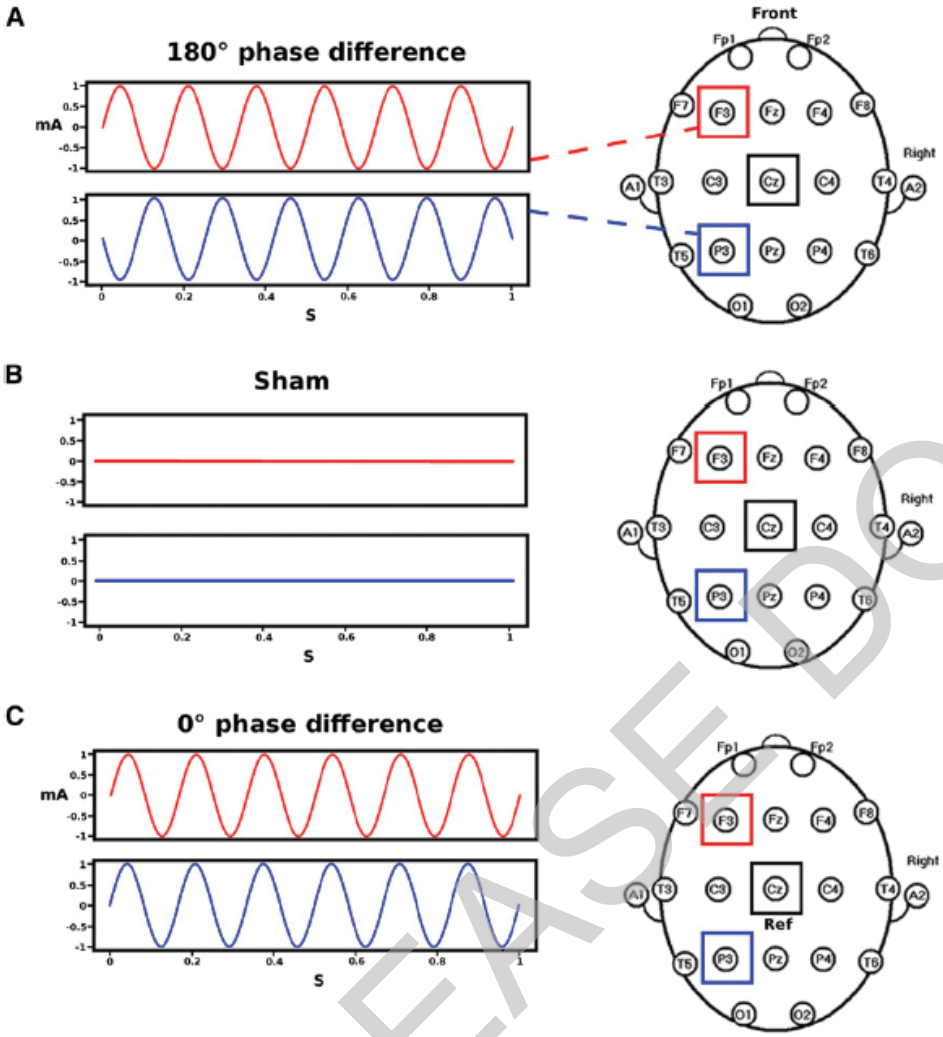


Band-pass 6 +/- 1 Hz

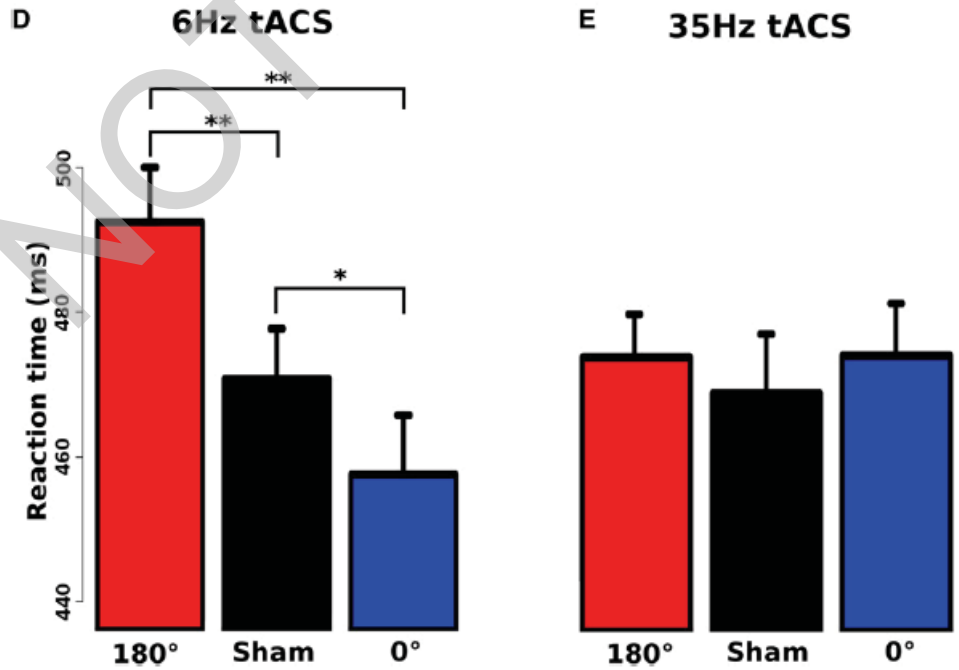
tACS and Phase Coupling: Working Memory

Design and Results

Polania et al., Curr. Bio 2012



Online tACS protocol



WM performance

State Dependency of tACS

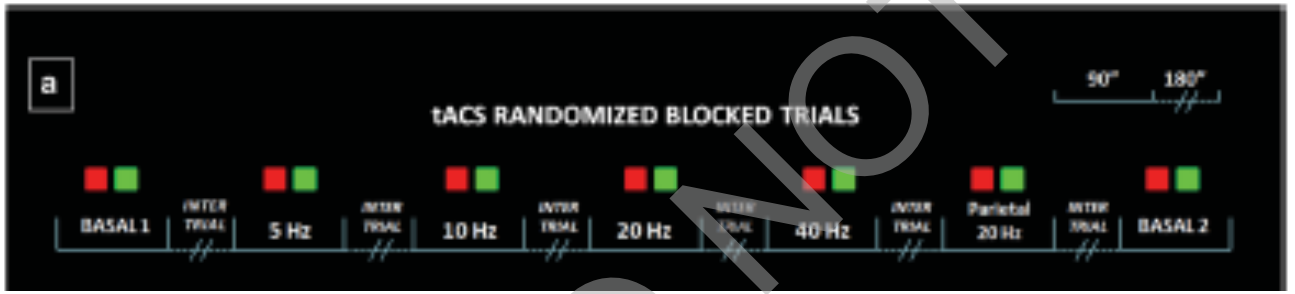
State Dependency: Motor Imagery

State-Dependent Effects of Transcranial Oscillatory Currents on the Motor System: What You Think Matters

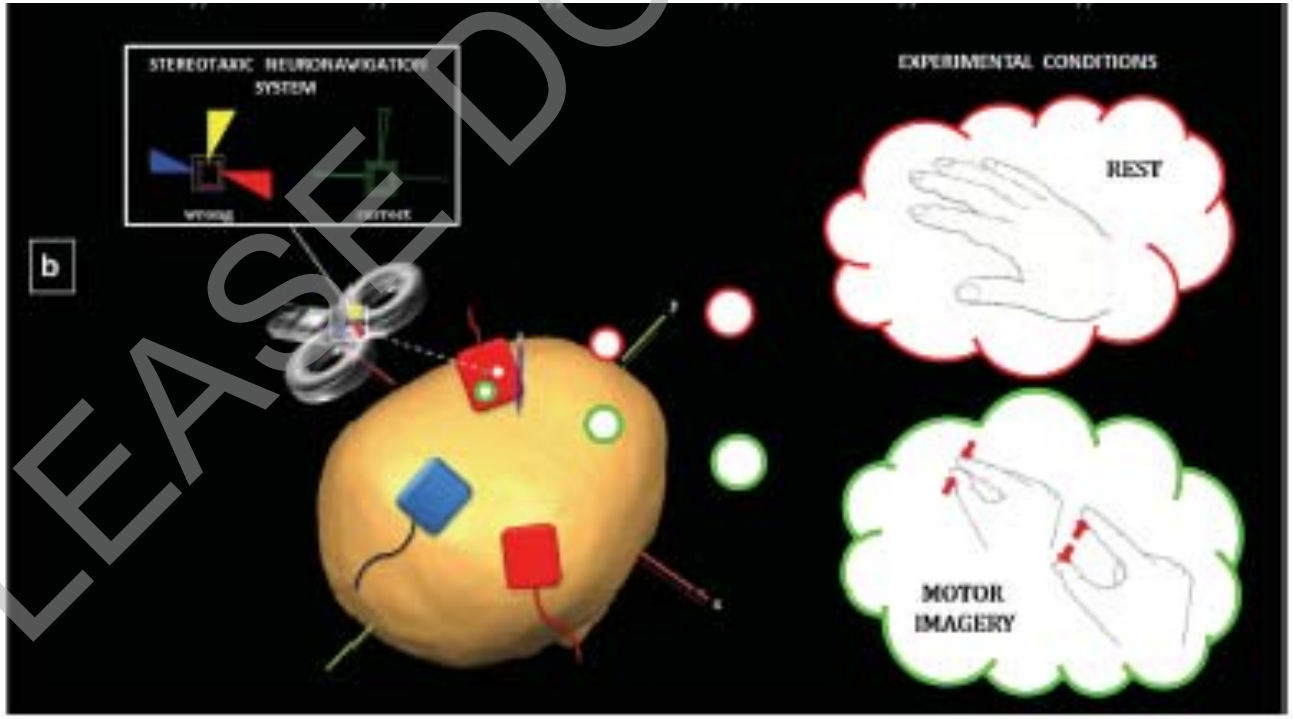
Feurra et al., 2013,
Journal of Neuroscience

Question

- Does the effects of tACS depend on brain state?



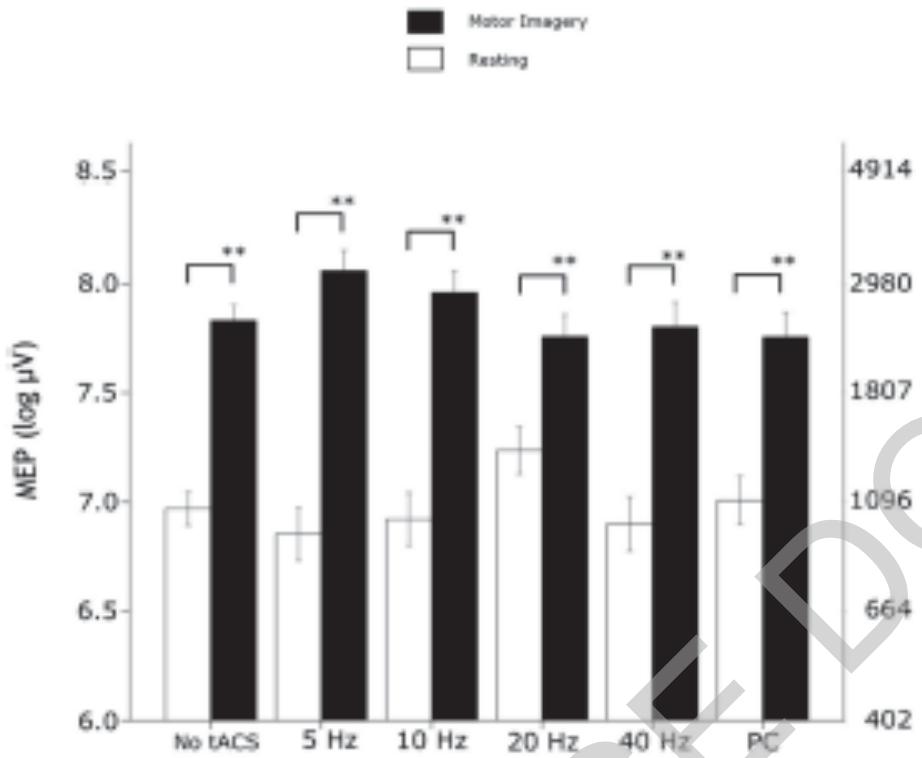
N=18, tACS= 1mA (peak-to-peak).



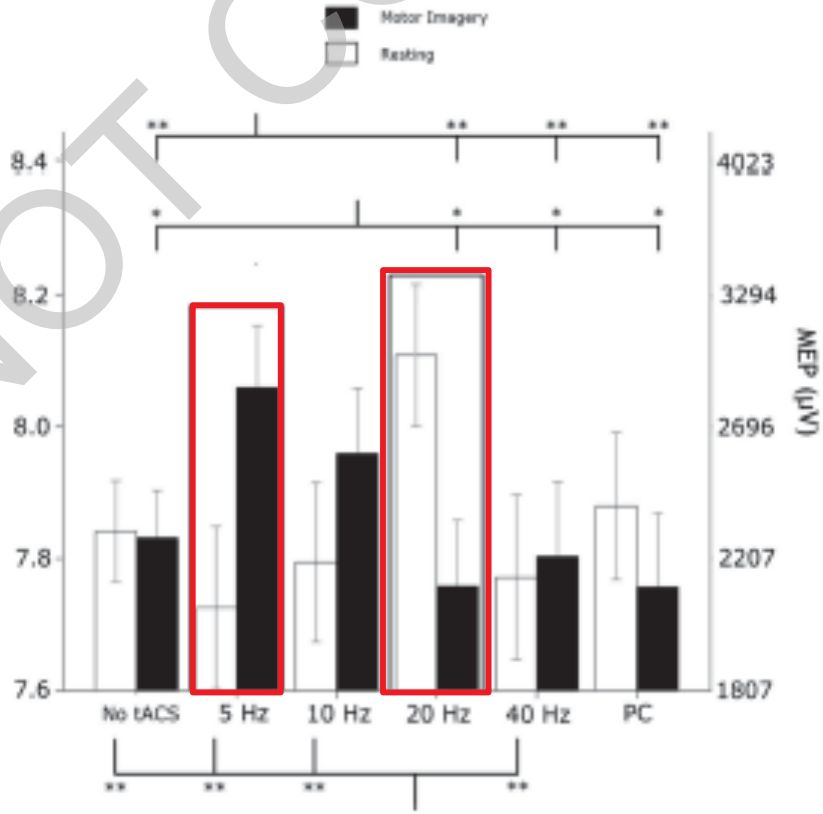
State Dependency

Results

Feurra et al., 2013,
Journal of Neuroscience



Consistent increase of MEP size during Motor Imagery versus the quiescence state, regardless of the type of tACS applied.



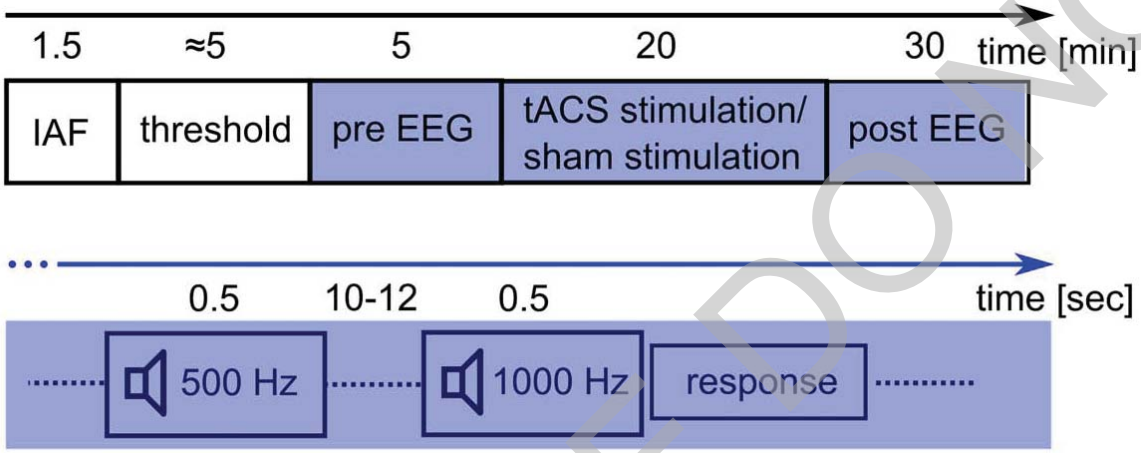
Dissociation between tACS (5 Hz) and-tACS (20 Hz), after removing the average facilitatory main effect of motor imagery

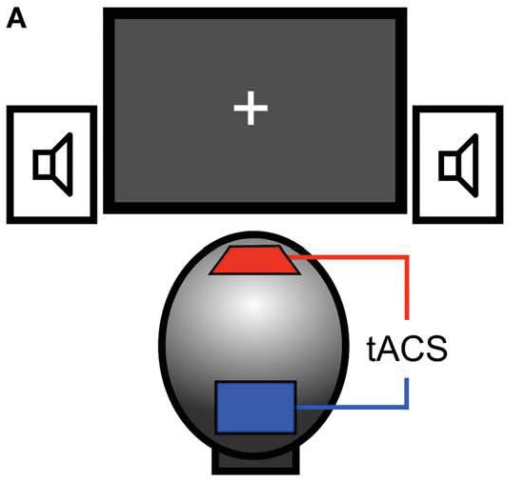
State Dependency

Orchestrating neuronal networks: sustained after-effects of transcranial alternating current stimulation depend upon brain states

Neuling et al., 2013

- **Does the after-effects of tACS depend on the endogenous power of oscillations?**





Exp. 1: 19 sbjs, 20' tACS at Individual Alpha frequency*, **Eyes Open**

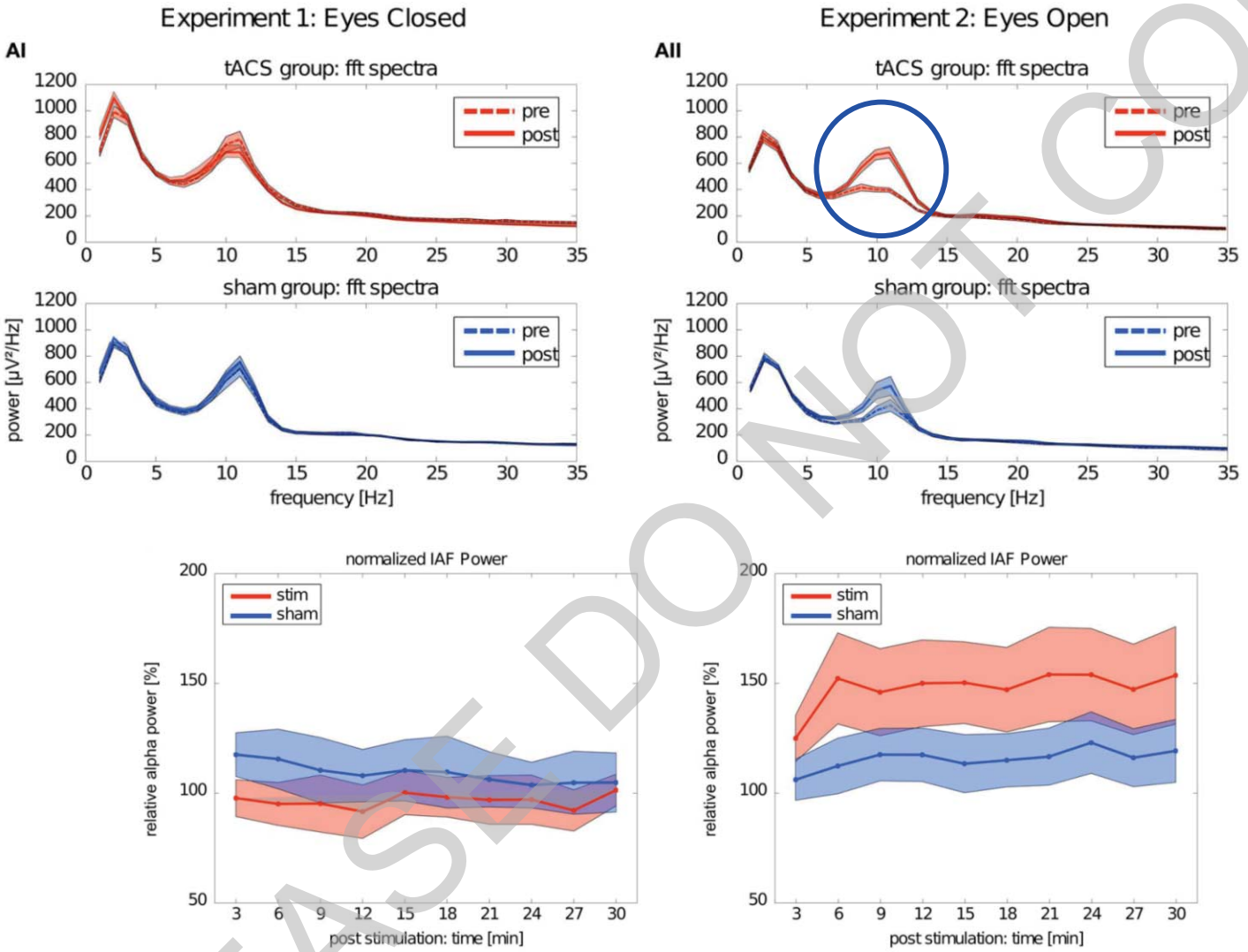
Exp. 2: 29 sbjs 20' tACS at Individual Alpha frequency*, **Eyes Closed**

*power peak in the alpha range (8–12Hz)

State Dependency

Results

Neuling et al., 2013



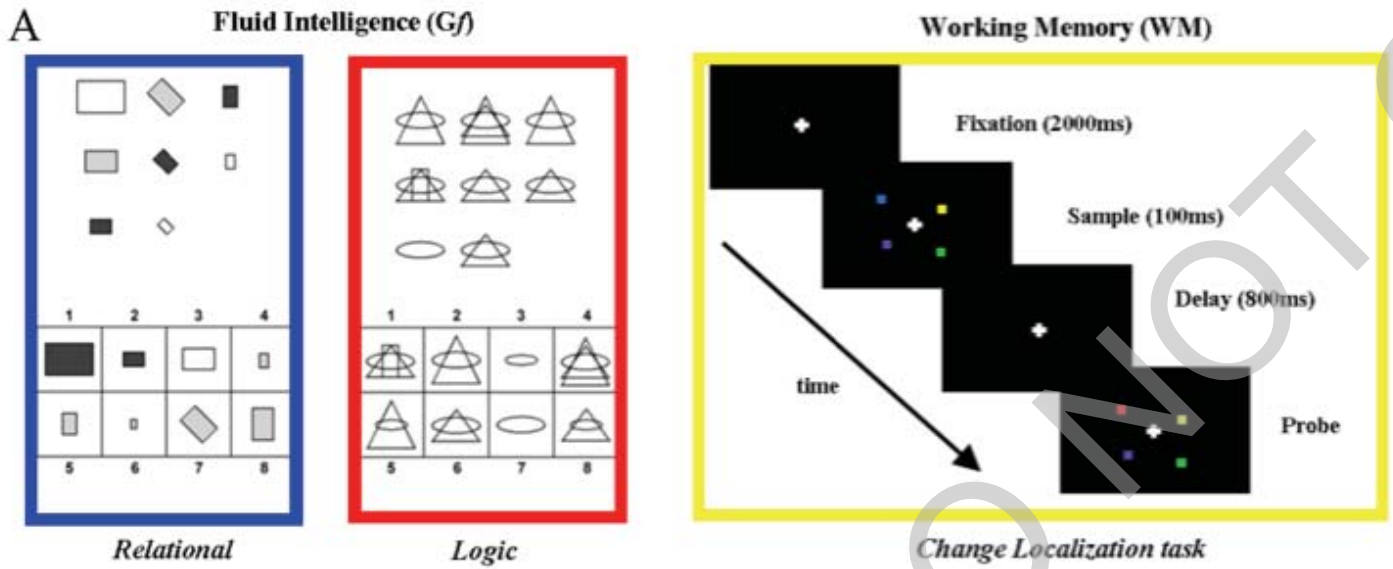
tACS effect depend on brain states During the stimulation…

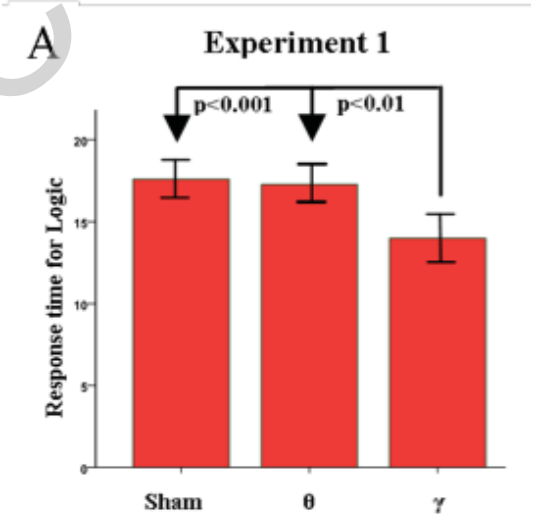
- Alpha reaches a plateau during Eyes Closed condition?

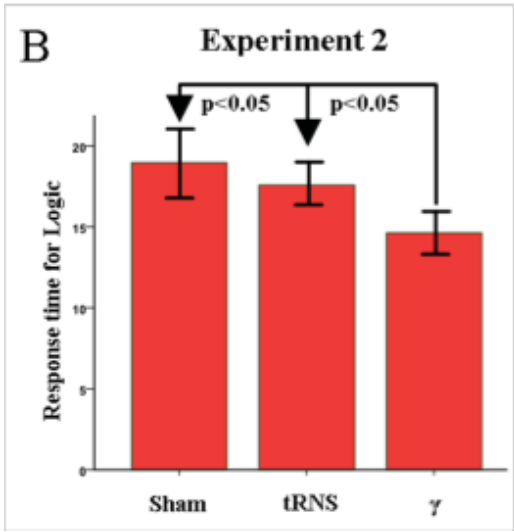
Trait-dependency?

Individual differences in response to tACS?

Santarnecchi et al., 2016







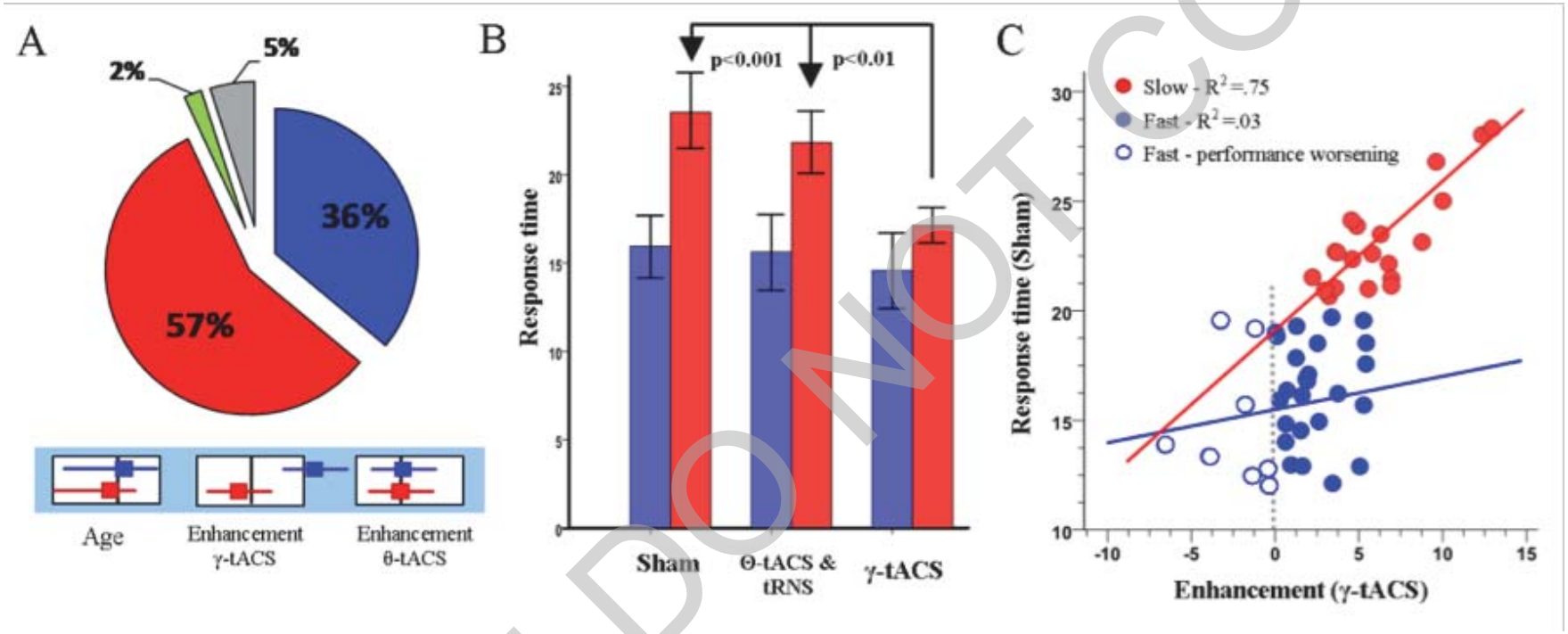
Compared tACS and tRNS effect in both fluid intelligence and Working memory tasks.

N=58
tACS=*1.0 mA,*
tRNS=*1.0 mA*

Replicated previous finding

Individual differences in response to tACS?

Santarnecchi et al., 2016



- **individual differences in the response to tACS**
- **Relevant for the ethical evaluation of cognitive enhancement intervention**

tACS=*1.0 mA,* **tRNS**=*1.0 mA*

State-Trait dependency

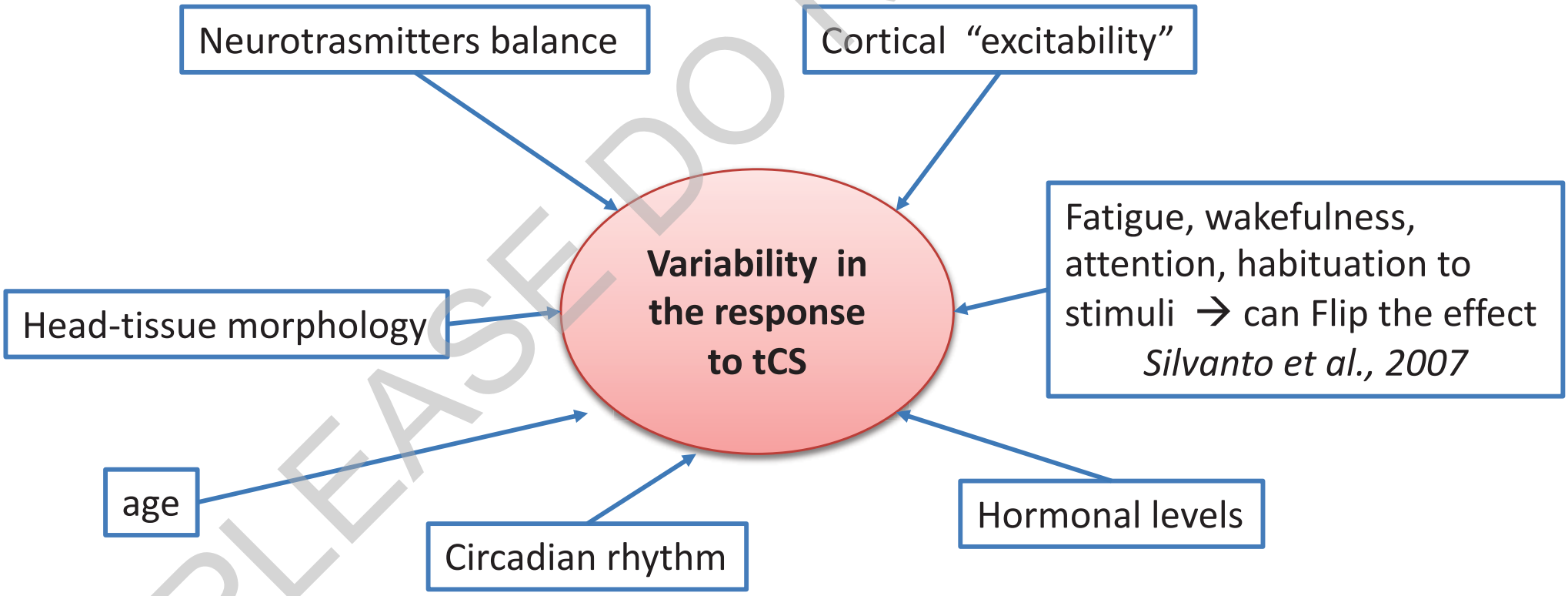
frontiers in
SYSTEMS NEUROSCIENCE

REVIEW ARTICLE
published: 24 February 2014
doi: 10.3389/fnsys.2014.00025

Not all brains are created equal: the relevance of individual differences in responsiveness to transcranial electrical stimulation

Beatrix Krause* and Roi Cohen Kadosh

Department of Experimental Psychology, University of Oxford, Oxford, UK



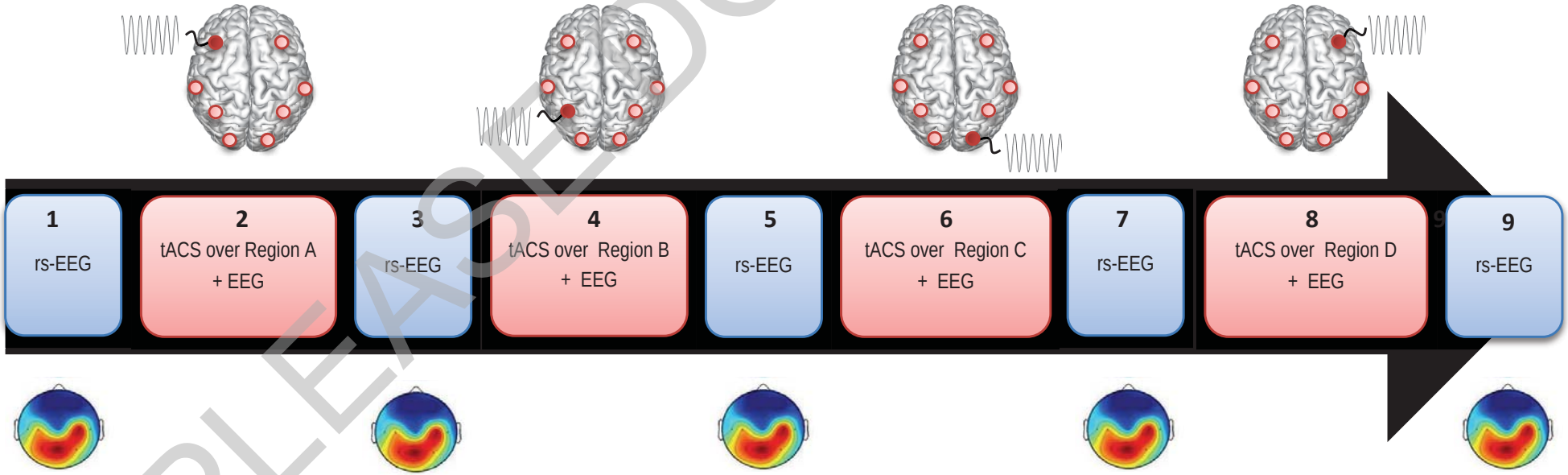
Trait dependency

BROAD INSTITUTE

Perturbation-based Physiologic Biomarkers by means of Non-Invasive Brain Stimulation and EEG

- tACS @ multiple frequency bands (theta, alpha, beta, gamma) & TMS-EEG
- over multiple different locations
- EEG recording Before, During and After stimulation

Look for region-specific responses, also depending on frequency of stimulation



Therapeutic Potential of tACS

Tremor Suppression?

Rationale

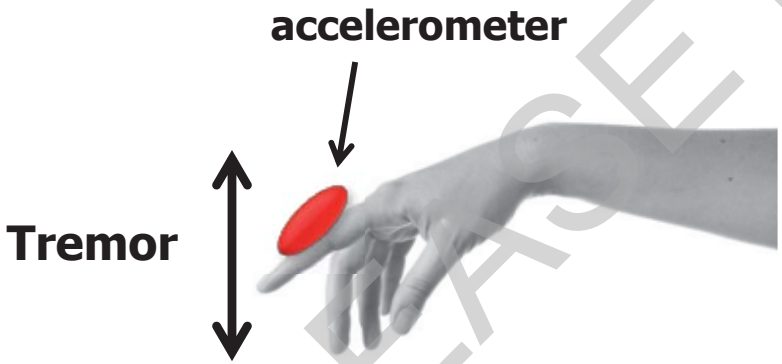
Brittain et al., Curr. Bio 2013

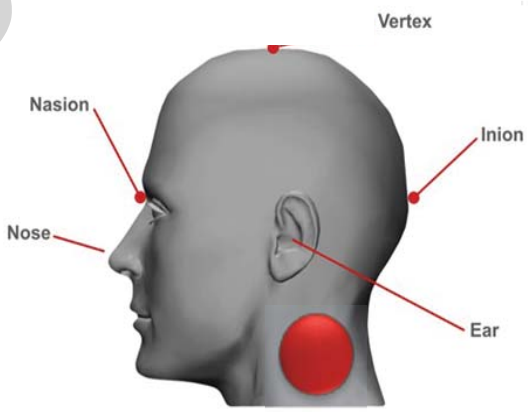
- Can tACS reduce tremor in PD patients?

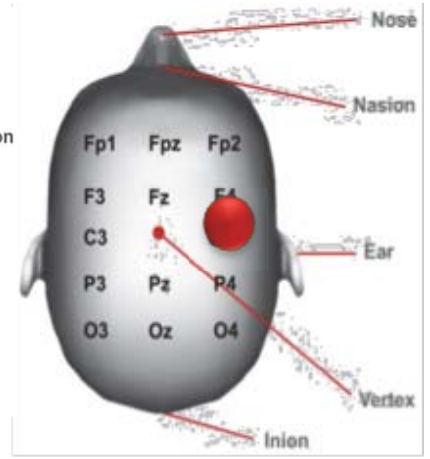
Design

Closed-loop tACS – tremor phase (accelerometer)

Tremor amplitude (accelerometer)

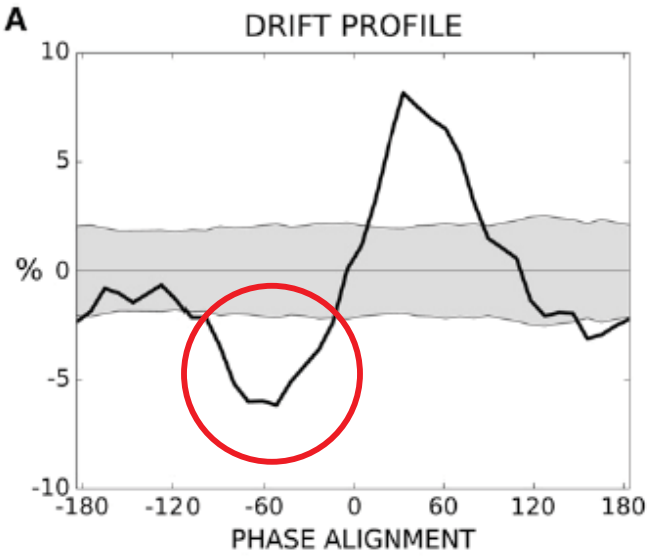




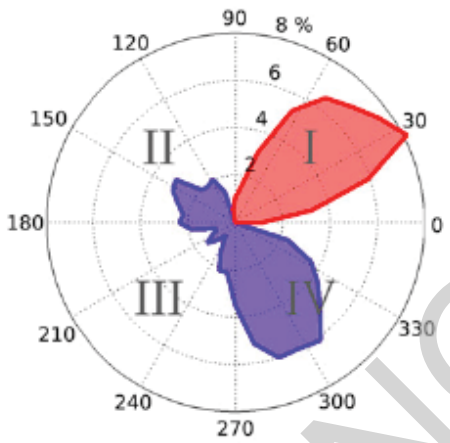


Tremor Suppression?

Brittain et al., Curr. Bio 2013



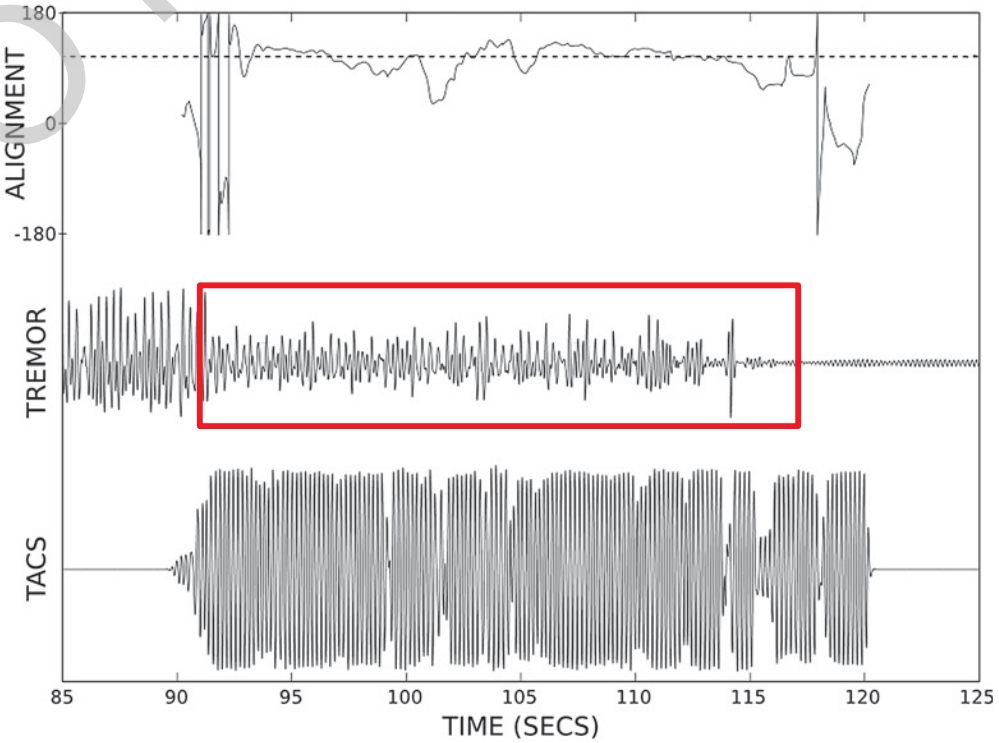
Polar Map



Tremor Excitation

Tremor Suppression

Identification of the optimal Phase-Delay for tremor suppression



Phased-locked tACS reduced tremor by up to 50%

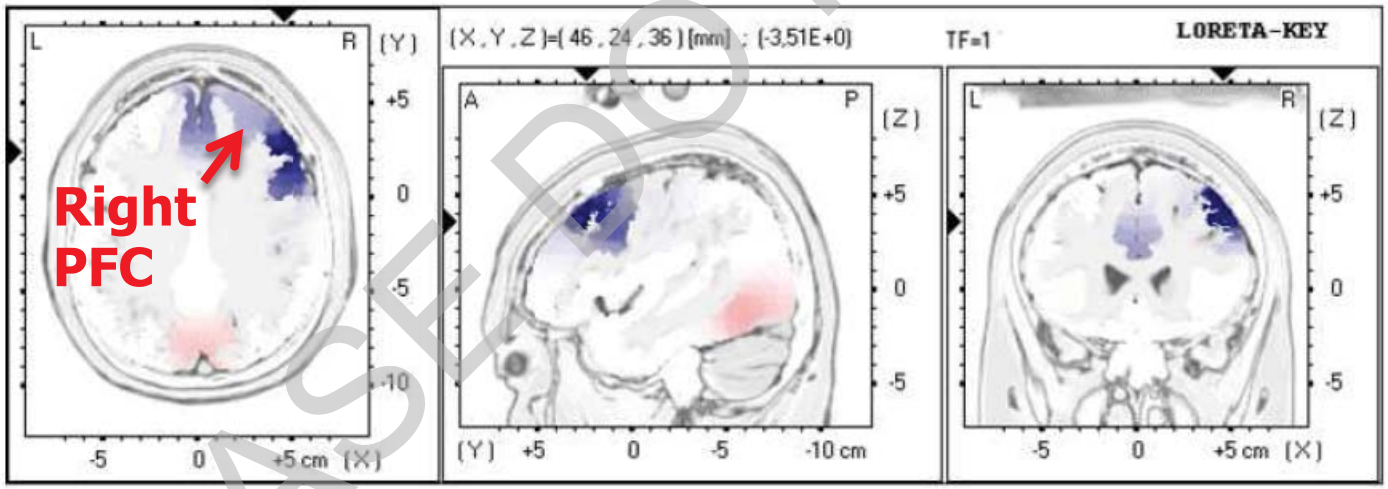
Treating Tinnitus?

Rational

- **tDCS** (left temporal or bifrontal) **reduces tinnitus intensity** (e.g. Song 2012)
- Patients with tinnitus have **lower alpha activity (10Hz)** on right Prefrontal Cortex

tACS!

Mean Alpha Spectrum



Red: high distress > low distress Blue: high distress < low distress

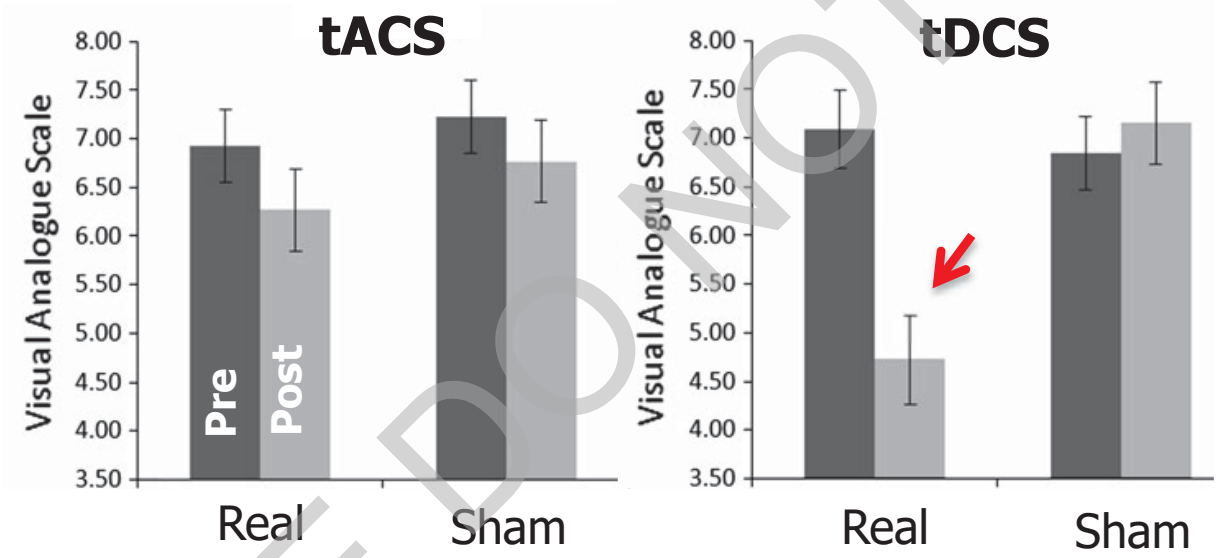
Measured with EEG and Low Resolution Electromagnetic Tomography (LORETA)

Treating Tinnitus? No..

Results

Vanneste et al., 2013 (RCT)

Tinnitus Intensity Rating



- **left-right DLPFC tACS** in the alpha "band" was **not effective as tDCS** in reducing tinnitus intensity (and annoyance).

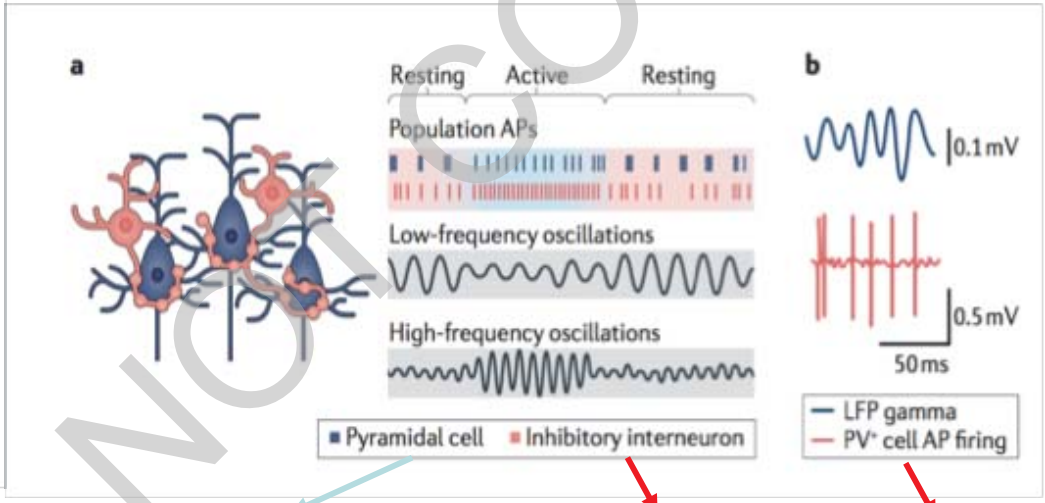
Alzheimer's Disease, Interneuron pathology and Gamma Oscillations

Network abnormalities and interneuron dysfunction in Alzheimer disease

Jorge J. Palop[1,2] *and Lennart Mucke*[1,2]

Abstract | The function of neural circuits and networks can be controlled, in part, by modulating the synchrony of their components' activities. Network hypersynchrony and altered oscillatory rhythmic activity may contribute to cognitive abnormalities in Alzheimer disease (AD). In this condition, network activities that support cognition are altered decades before clinical disease onset, and these alterations predict future pathology and brain atrophy. Although the precise causes and pathophysiological consequences of these network alterations remain to be defined, interneuron dysfunction and network abnormalities have emerged as potential mechanisms of cognitive dysfunction in AD and related disorders. Here, we explore the concept that modulating these mechanisms may help to improve brain function in these conditions.

Palop 2016, *Nature Review*

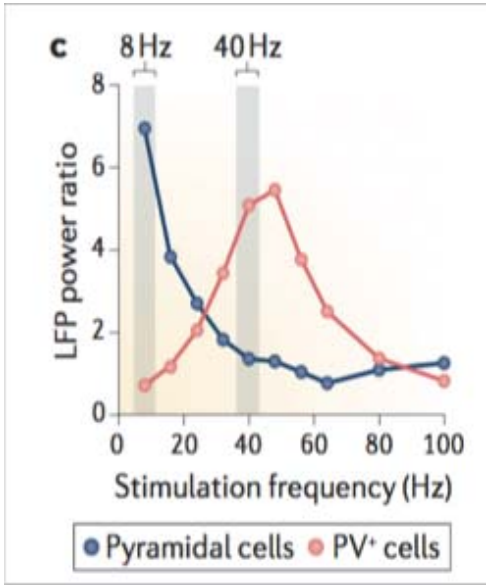


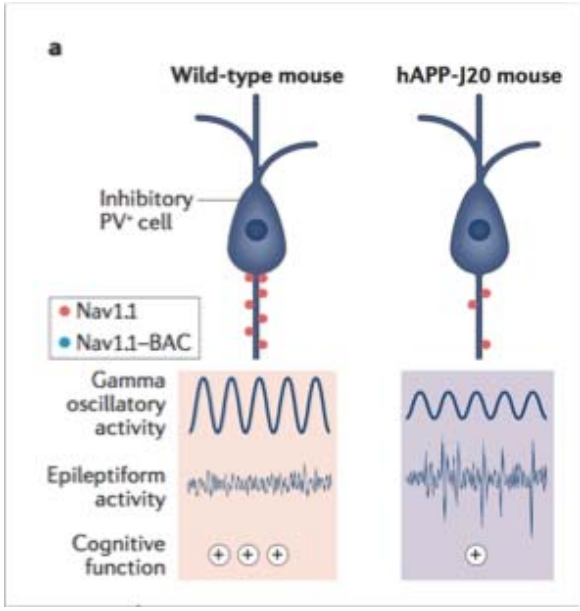
Excitatory (Glutamatergic)

Inhibitory (GABAergic)

PV+: Parvalbumin positive Interneurons

In FAD mice (lines hAPP-J20, Tg2576, APP23, *APOE4*-KI and APP/PSEN1dE9) (Supplementary information S1 (table)), gamma oscillatory activity is altered[107,172,191–193], suggesting that these animals have deficits in interneuron function. hAPP-J20 mice have brief peaks of increased gamma power and long periods of decreased gamma power[172,192]. Similar abnormal fluctuations in gamma power occur in Tg2576 mice[191].

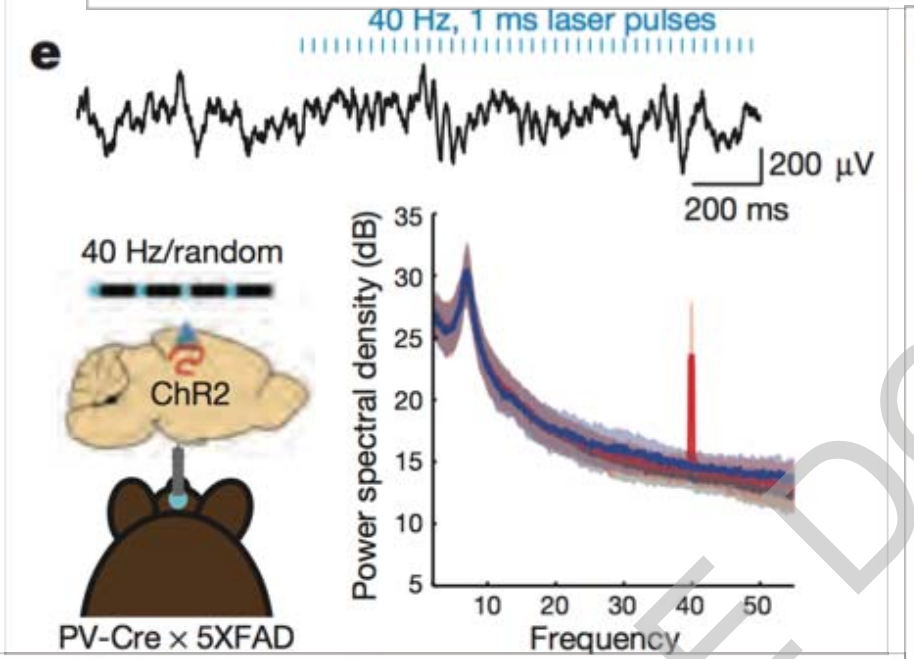




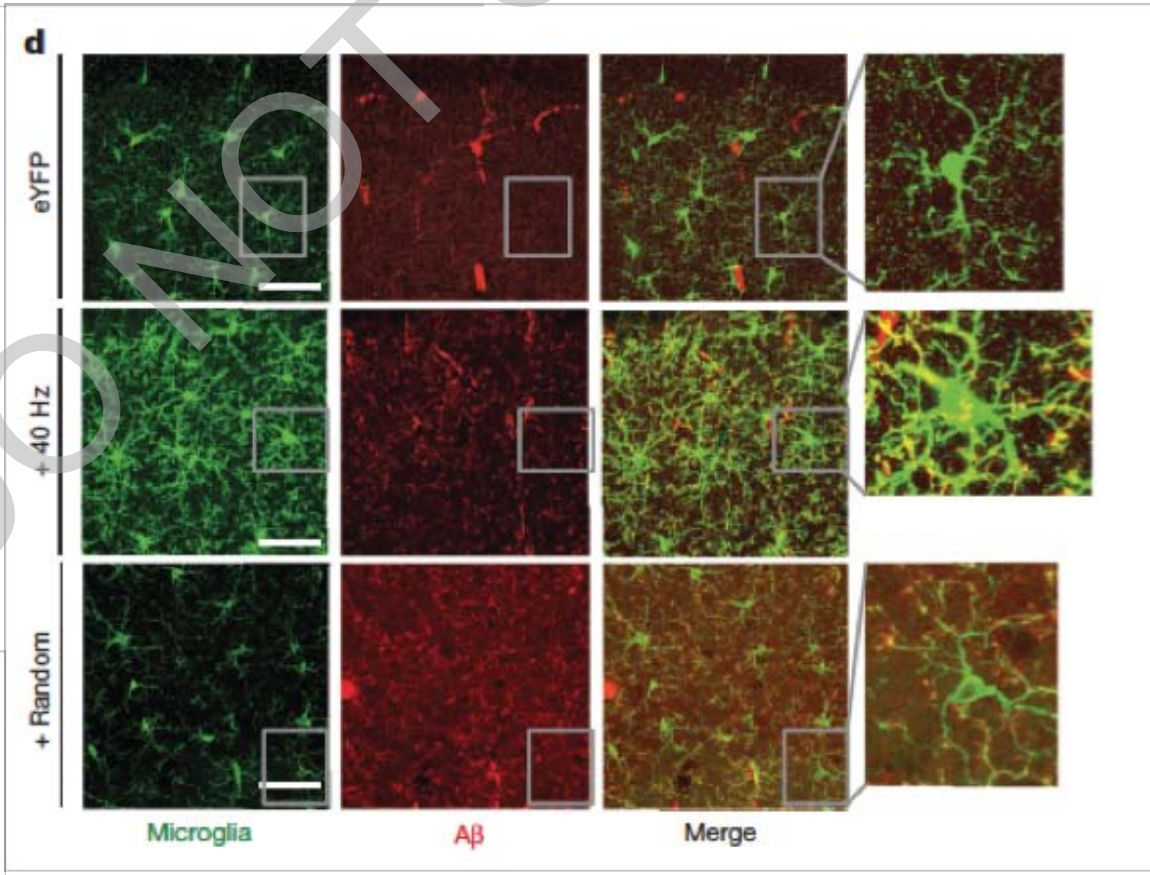
Increased Amyloid-β via Induction of Gamma Activity

Gamma frequency entrainment attenuates amyloid load and modifies microglia

Hannah F. Iaccarino[1,3*], Annabelle C. Singer[2,3,4*], Anthony J. Martorell[1,3], Andrii Rudenko[1,3], Fan Gao[1,3], Tyler Z. Gillingham[1,3], Hansruedi Mathys[1,3], Jinsoo Seo[1,3], Oleg Kritskiy[1,3], Fatema Abdurrob[1,3], Chinnakkaruppan Adaikkan[1,3], Rebecca G. Canter[1,3], Richard Rueda[1,3], Emery N. Brown[1,3,5,6], Edward S. Boyden[2,3,4] & Li-Huei Tsai[1,3,7]



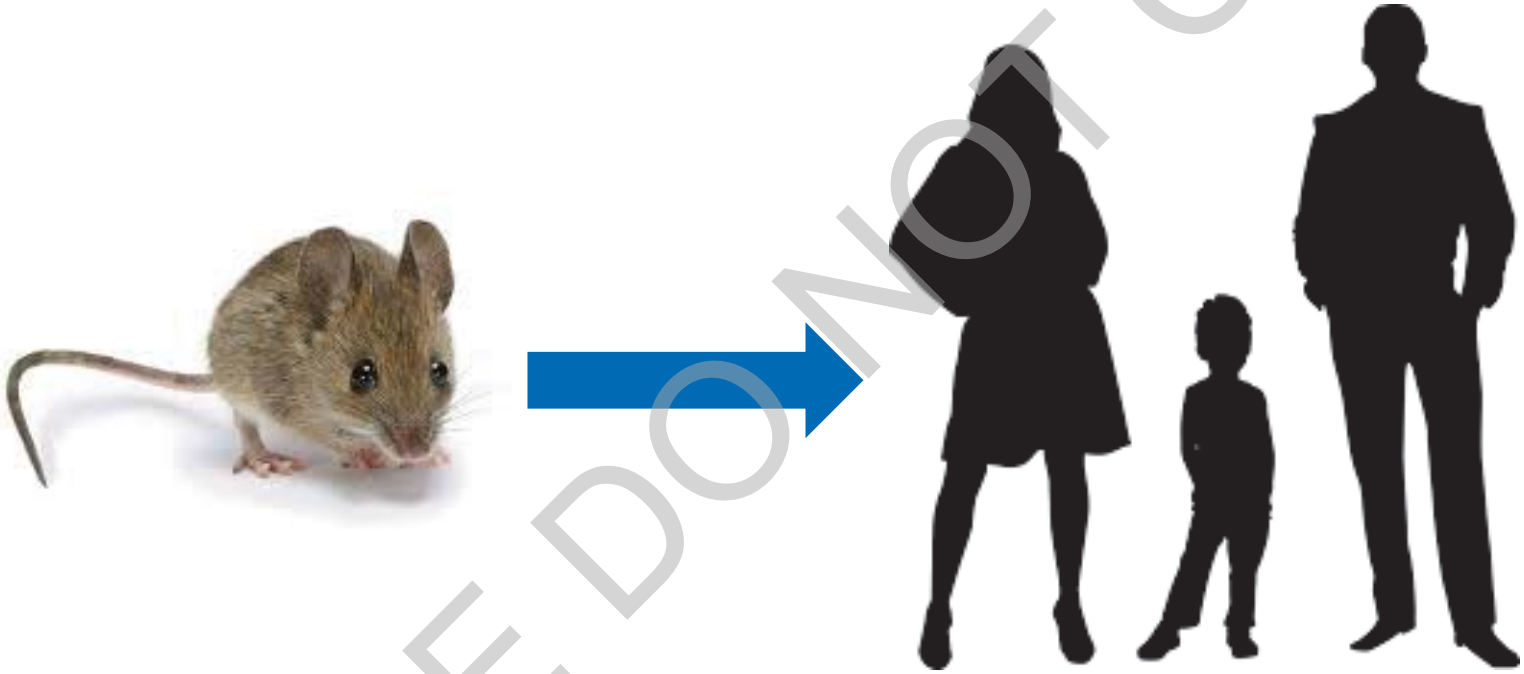
High-frequency visual stimulation in the gamma band in rats



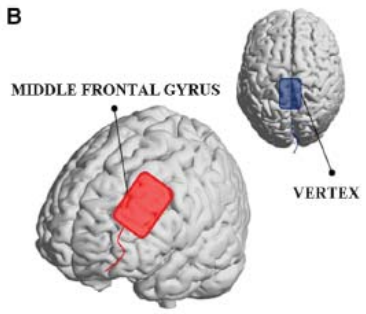
Twice as many microglia in the 40 Hz group compared with the eYFP and random control groups

Decrease in hippocampal amyloid-ß after 40Hz stimulation visible at Immunohistochemistry

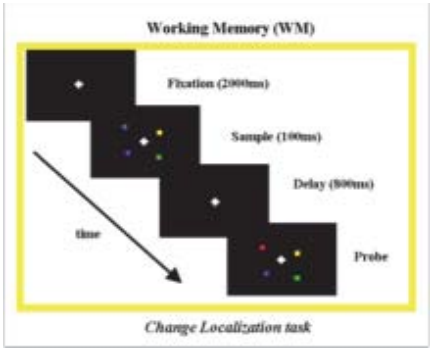
The challenge of translation



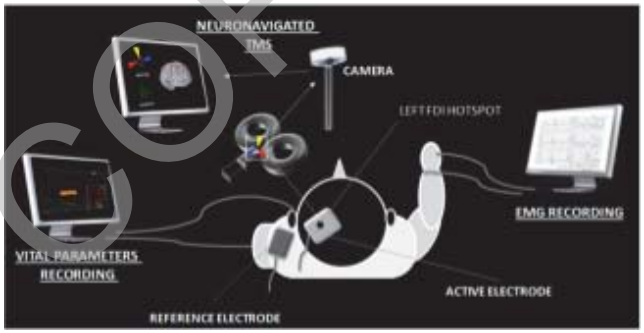
HOW: Extensive experience with tACS and frequency-specific modulation



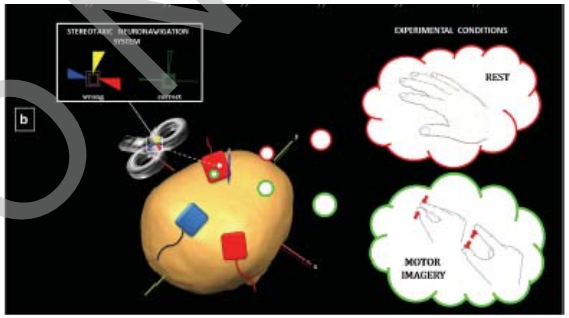
Santarnecchi et al. 2013
Abstract reasoning



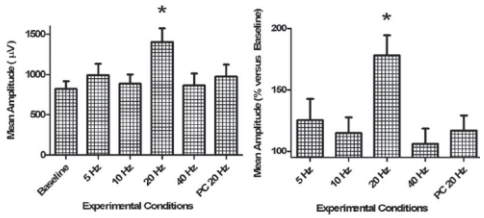
Santarnecchi et al. 2015
Working memory



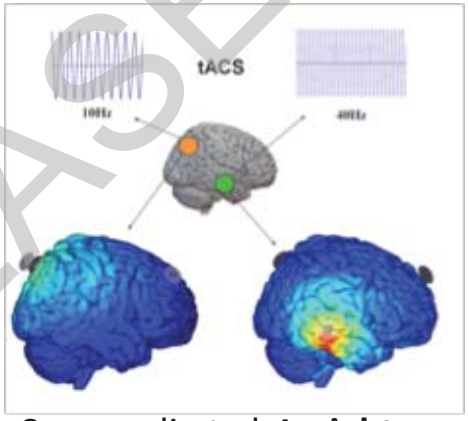
Santarnecchi et al. 2014
Cortical excitability



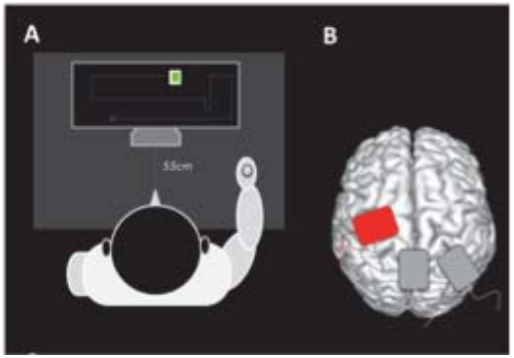
Feurra et al. 2011
Motor imagery



Feurra et al. 2011
Cortico-spinal excitability

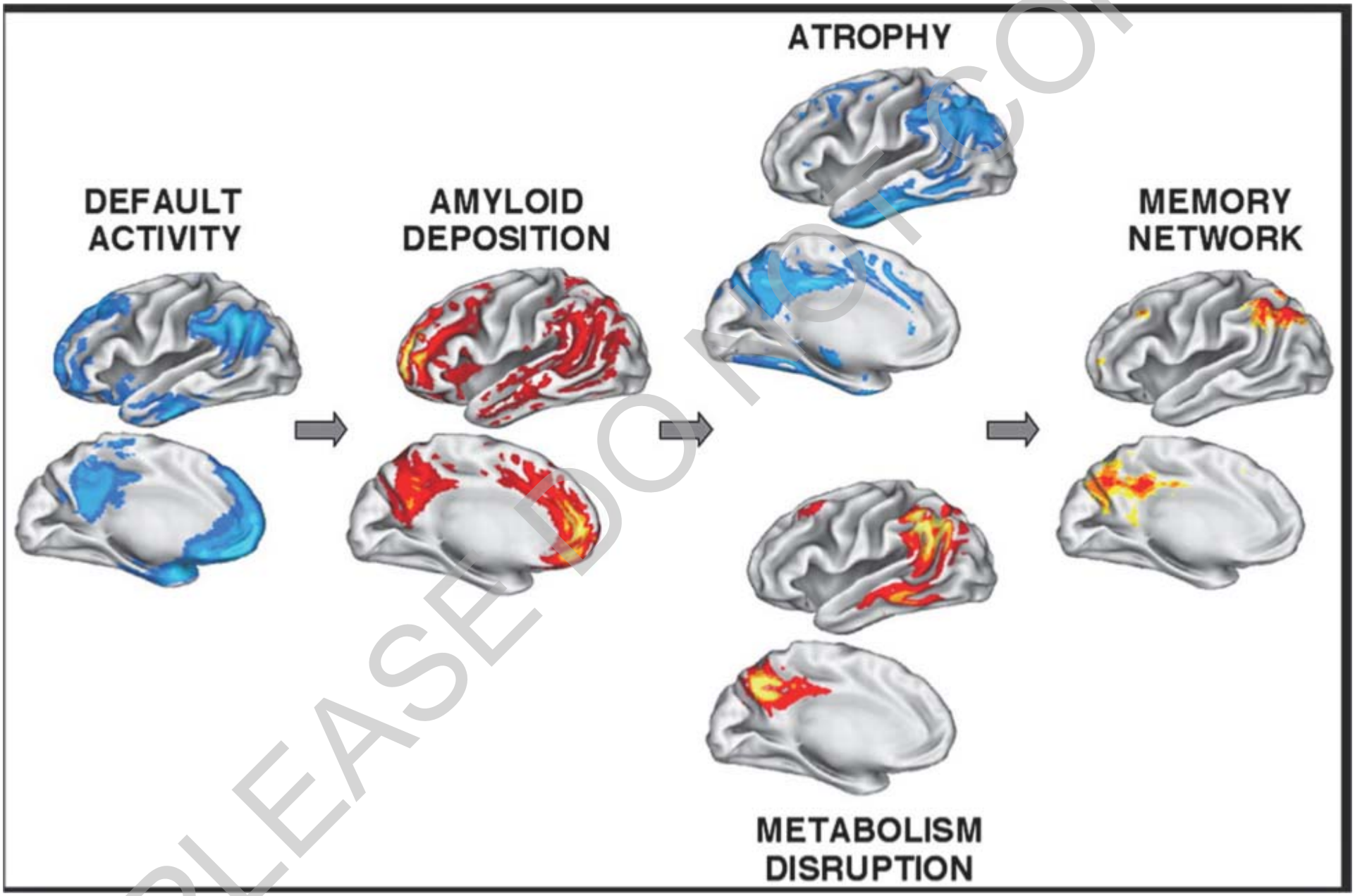


Sprugnoli et al. **Insight**

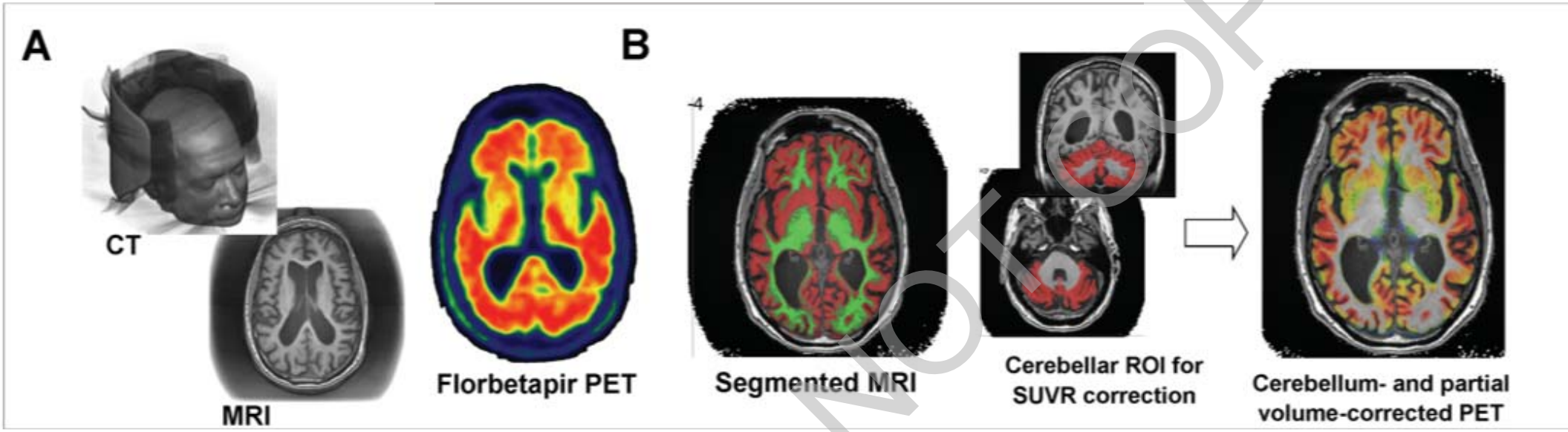


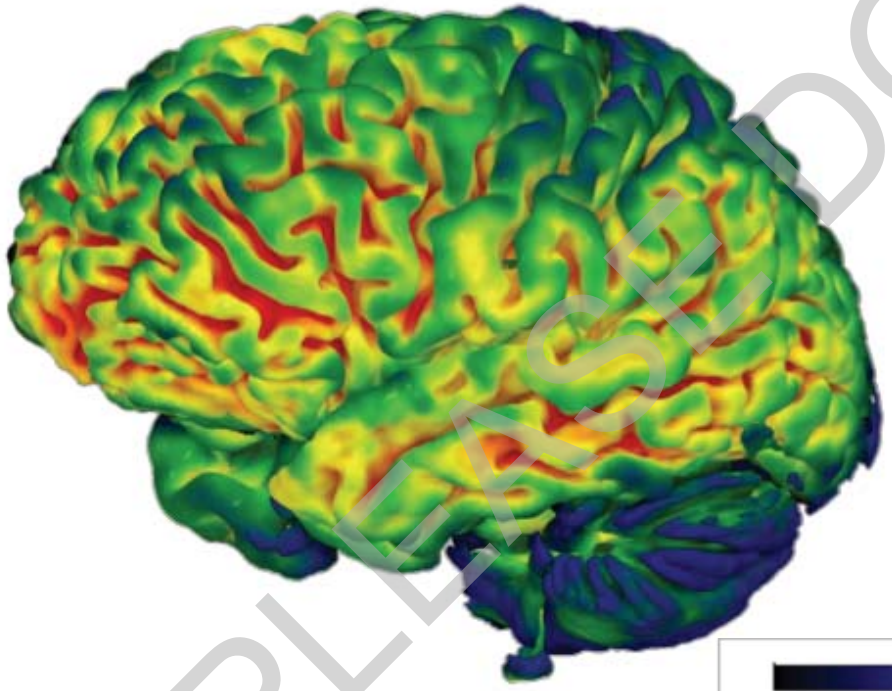
Santarnecchi et al. 2017
Visuo-motor coordination

WHERE: potential targets

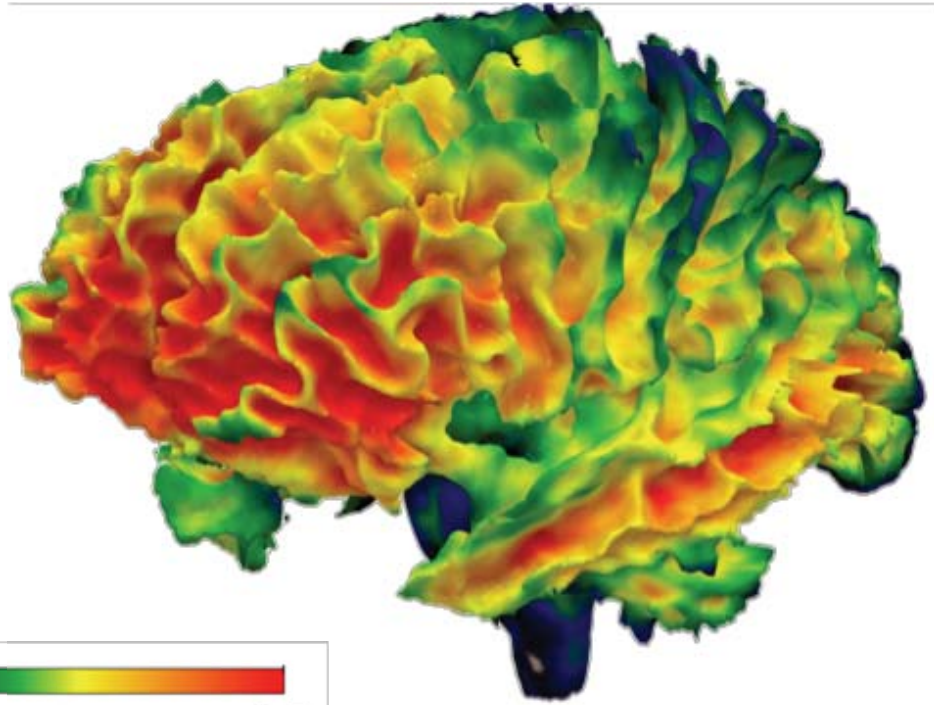


Ad-Hoc PET analysis pipeline



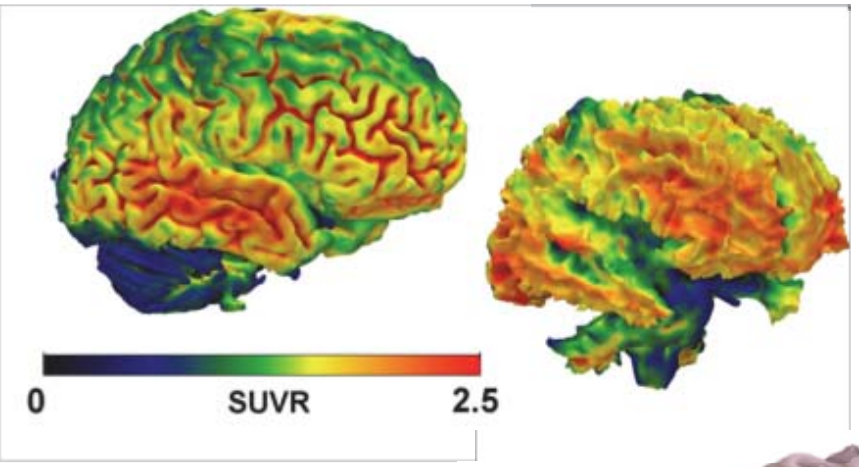


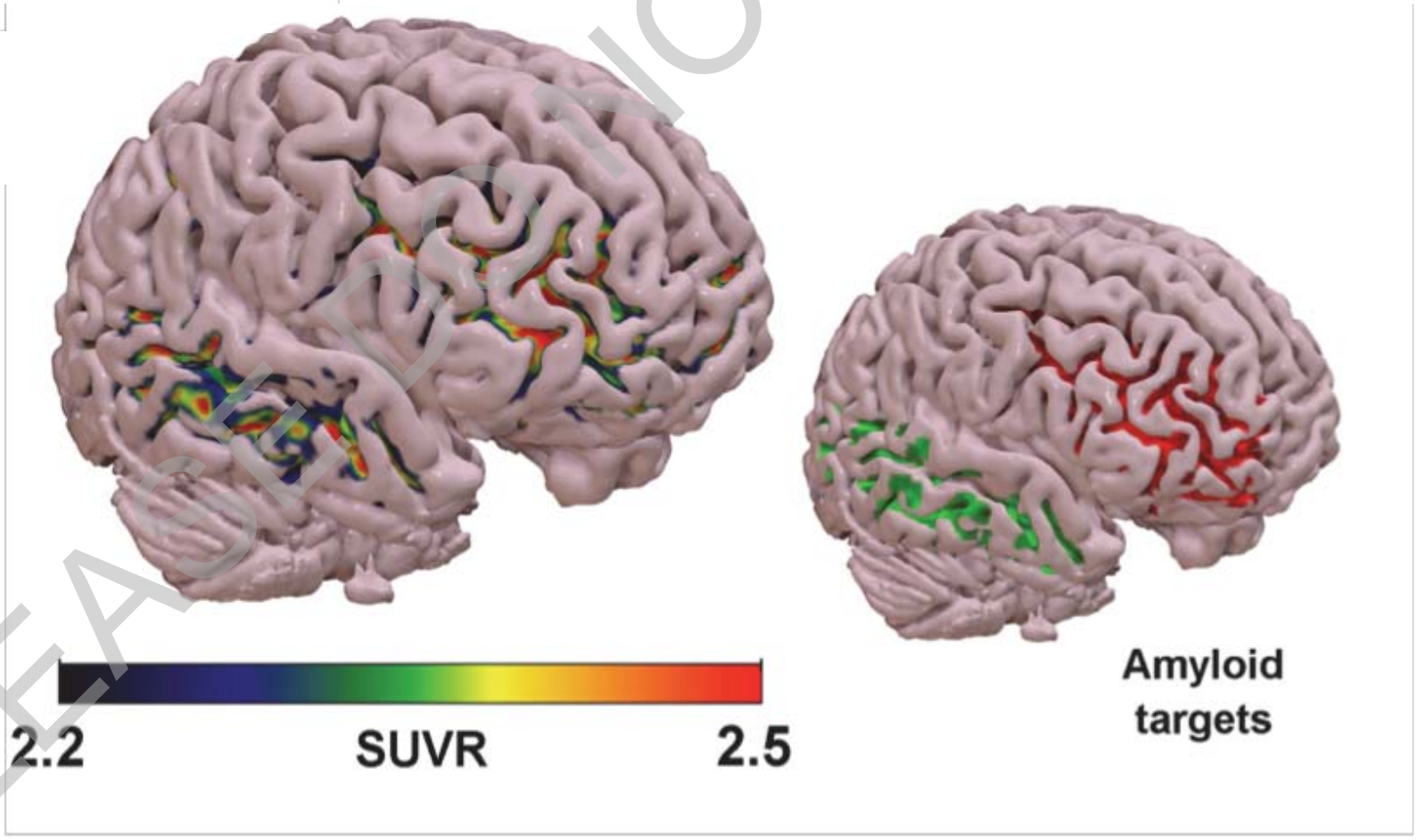
PET-MRI Grey matter amyloid deposition



White matter amyloid deposition

Individualized Amyloid-β targets

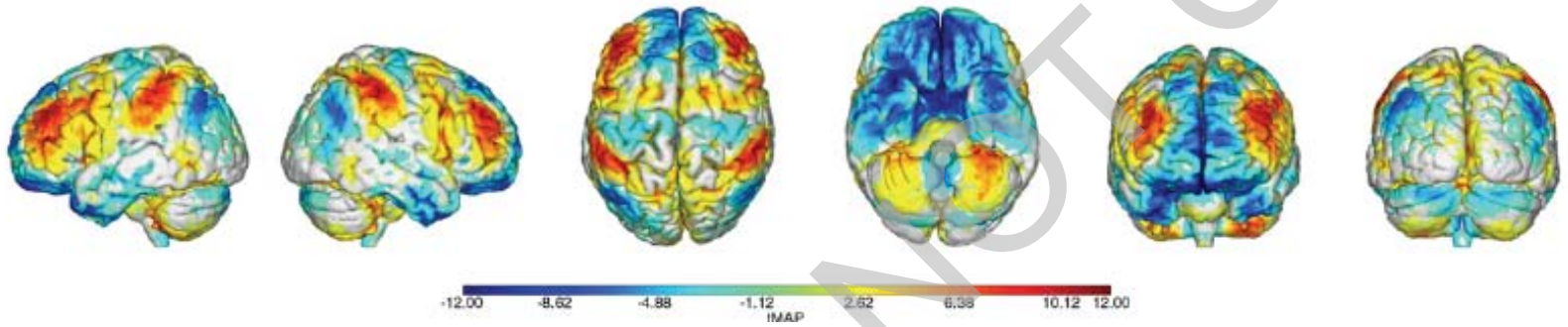




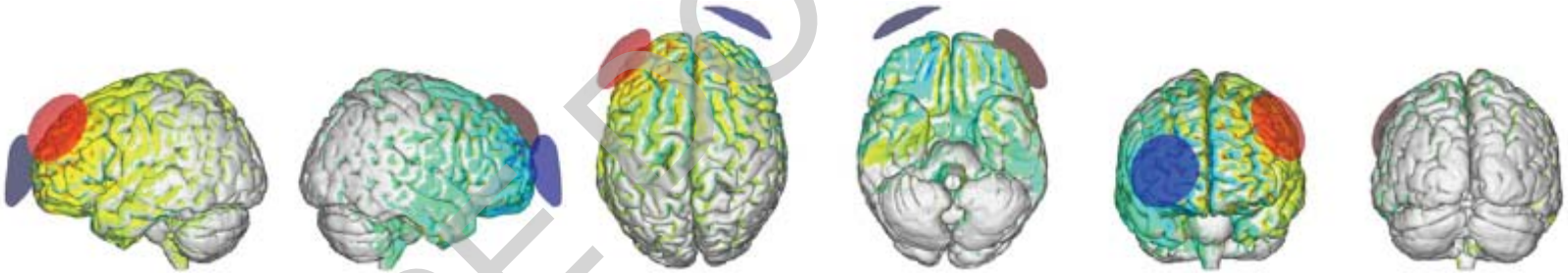
HOW TO ENGAGE MULTIPLE REGIONS: Multifocal tCS

Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields

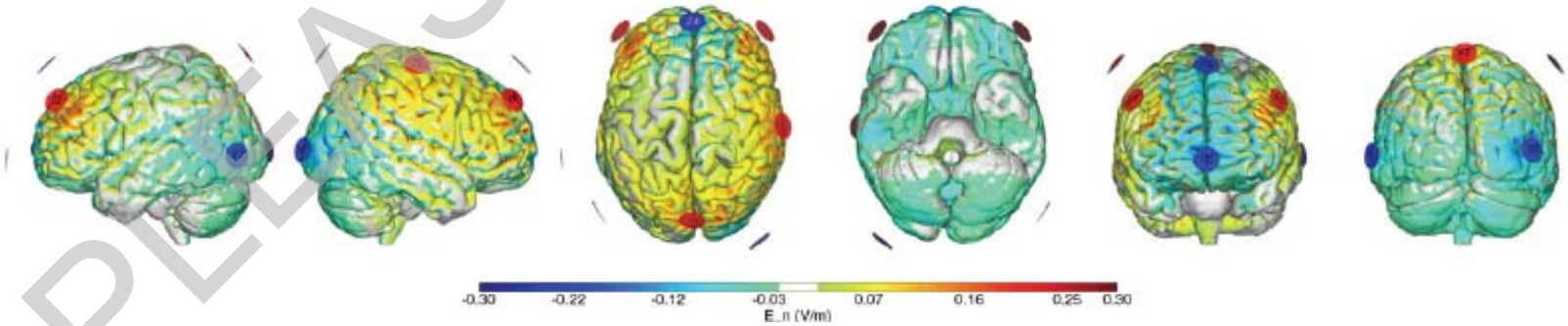
Ruffini et al. 2013



fMRI activation map

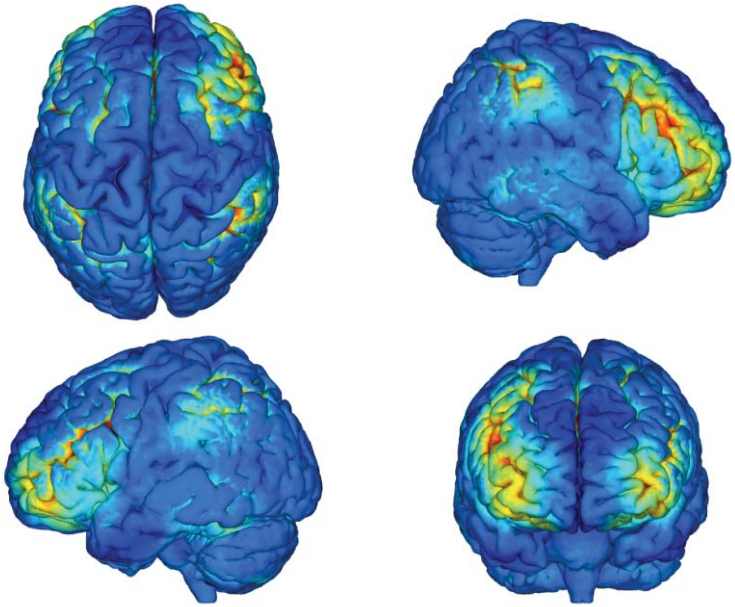


tCS solution with 2 electrodes

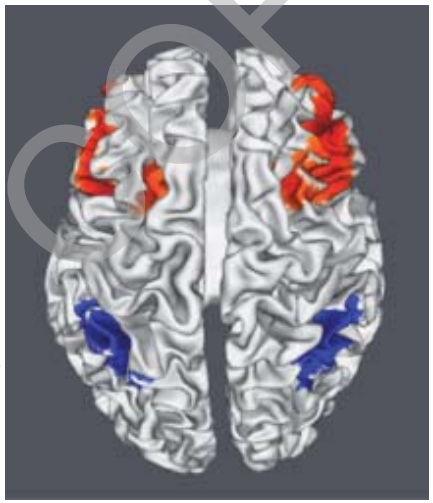


Multifocal tCS solution with 8 electrodes

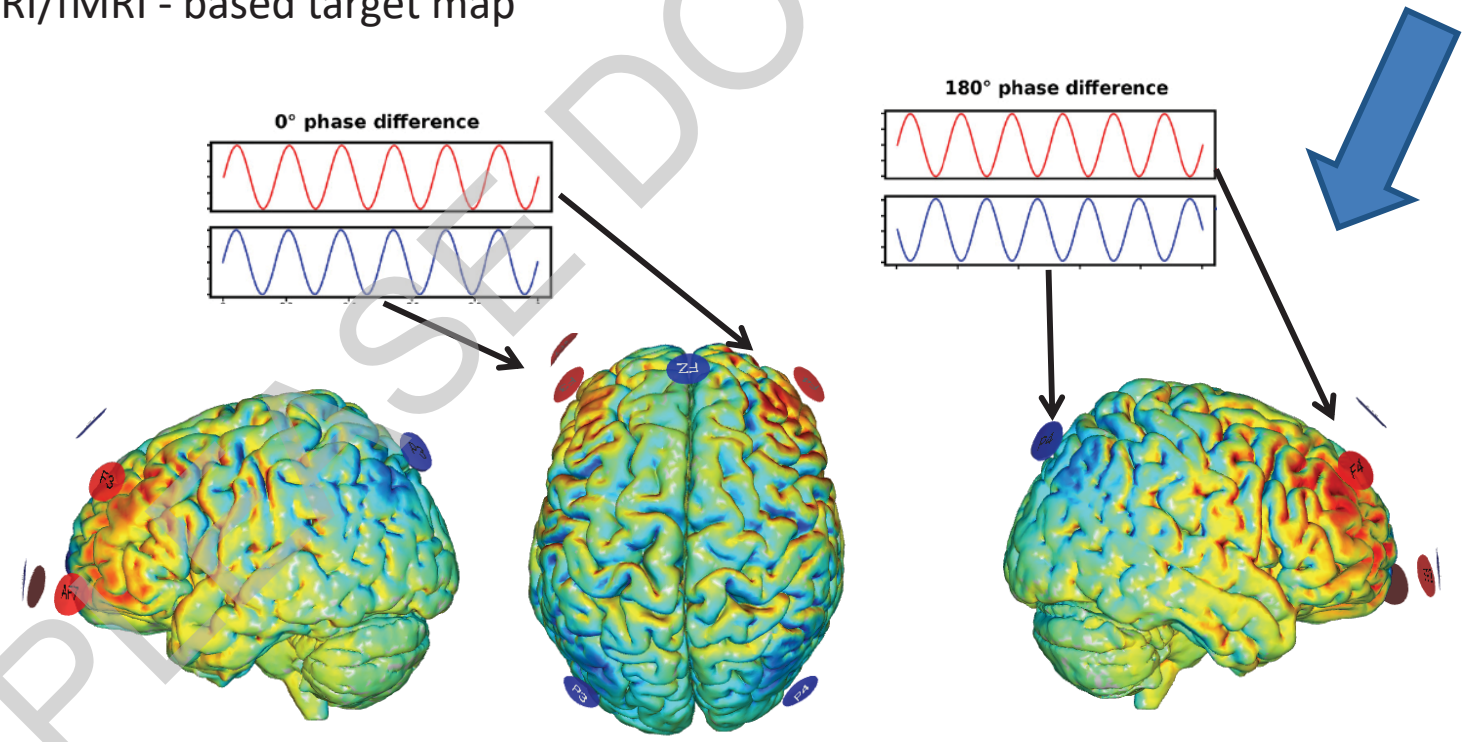
fMRI-EEG based Multifocal tACS



MRI/fMRI - based target map



Targets for Fronto-Parietal Synchronization



Personalized tACS treatment in mild-to-moderate Alzheimer's patients

First ***Safety-Feasibility*** trial at BIDMC funded by the **Chief Academic Officer** (CAO) Award 2017

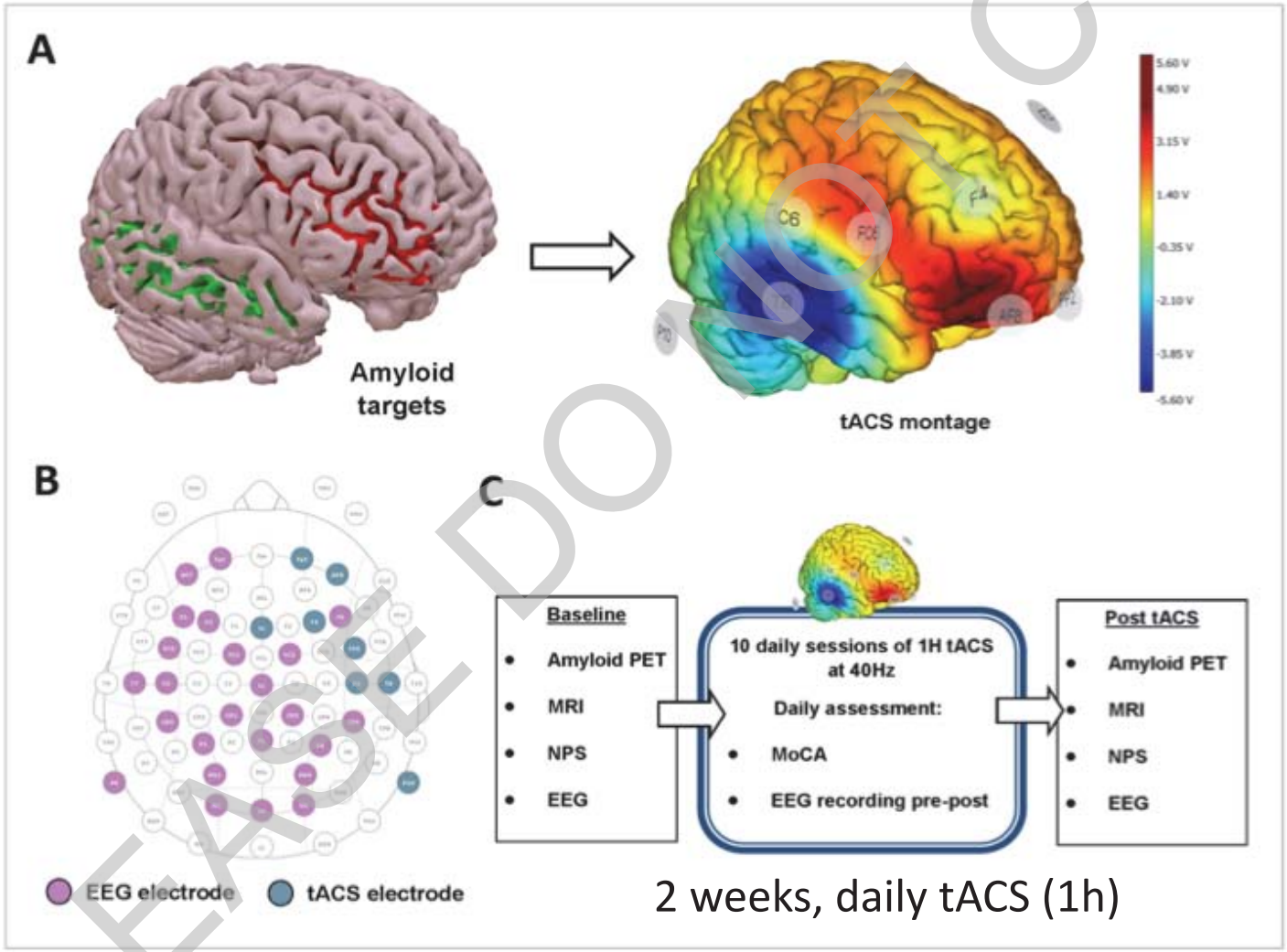
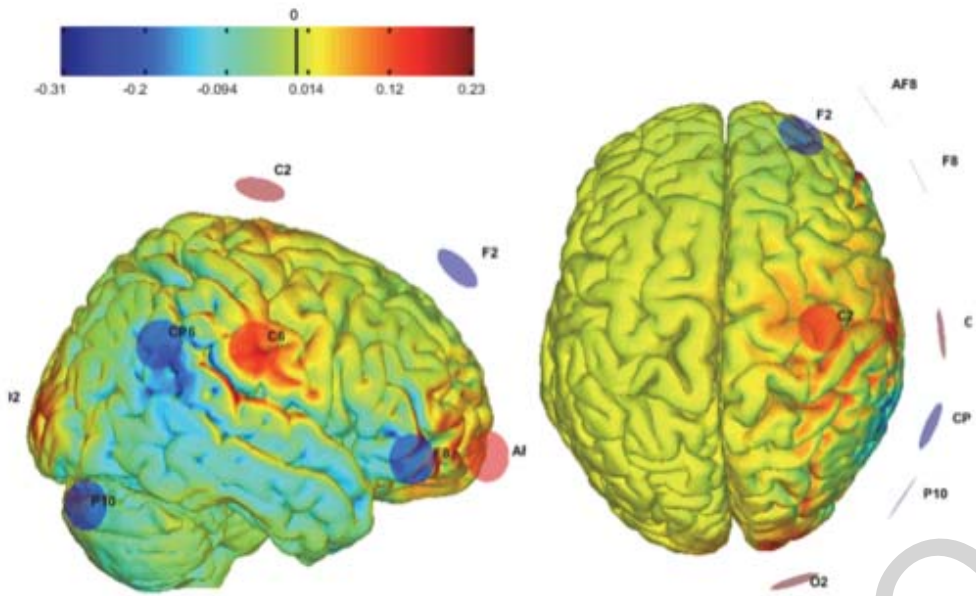
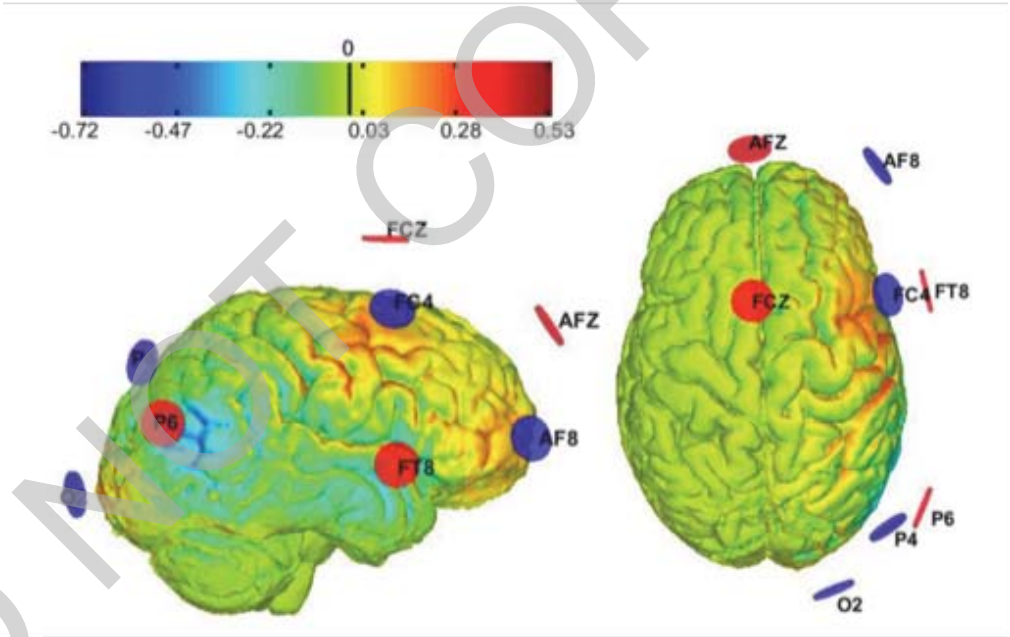
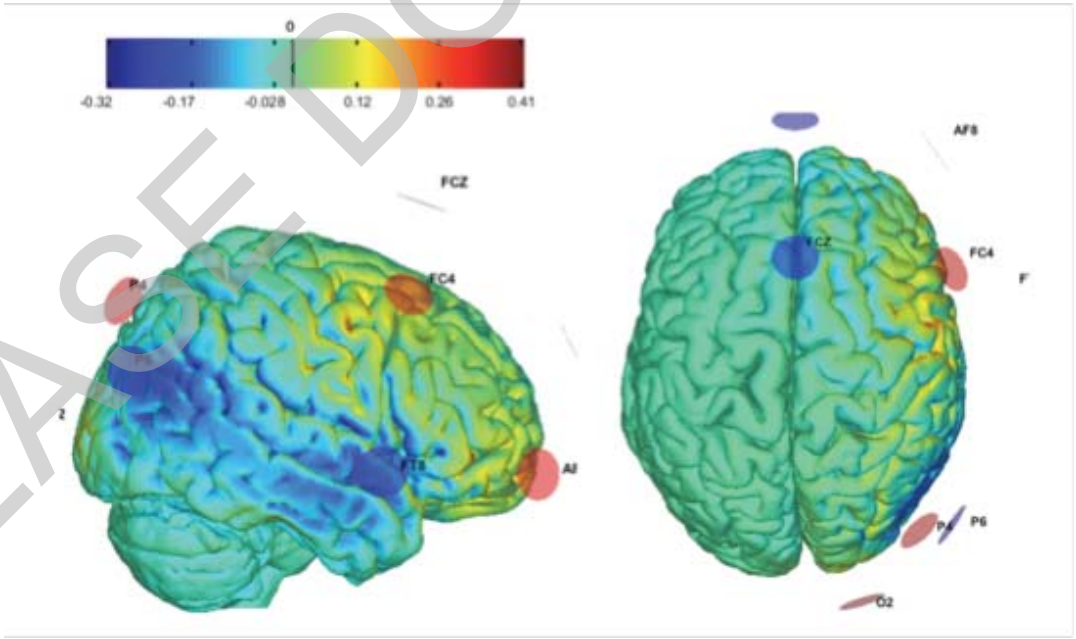


Figure 9. Target selection. PET targets are used to optimize a multi-electrode tACS template aimed at maximizing the electric field in the target regions, while minimizing it over the rest of the brain. The Red-Blue field represents instantaneous polarity of tACS at a given time point; during stimulation, the field alternates across the two stimulated regions at the stimulation frequency (i.e. 40Hz) (A). The resulting stimulation template included 8 stimulating electrodes, combined with 24 EEG electrodes used for monitoring cerebral activity before/after tACS (B). The patient underwent a multidimensional baseline assessment, followed by 2 weeks of 1 hr-long daily tACS at 40Hz and repeated assessment (C).

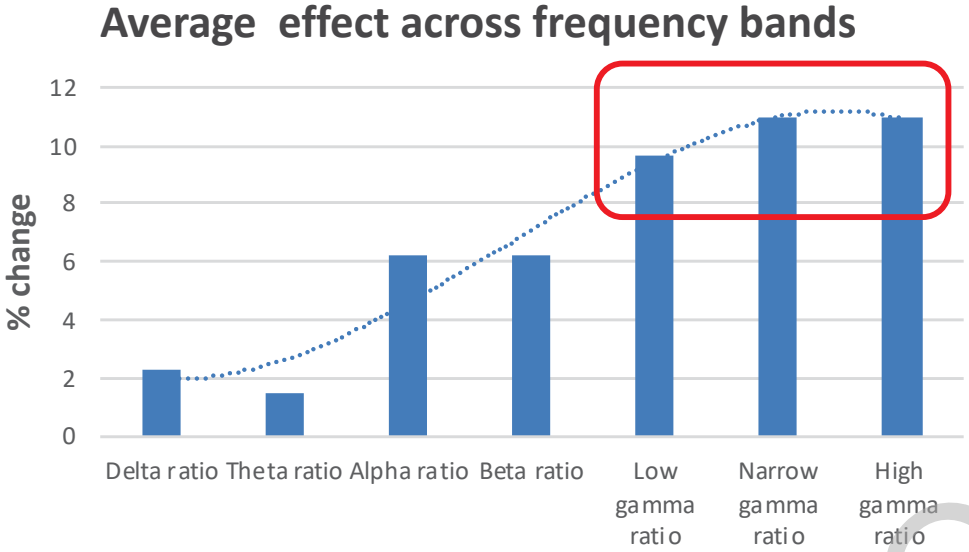
Personalized tACS montages

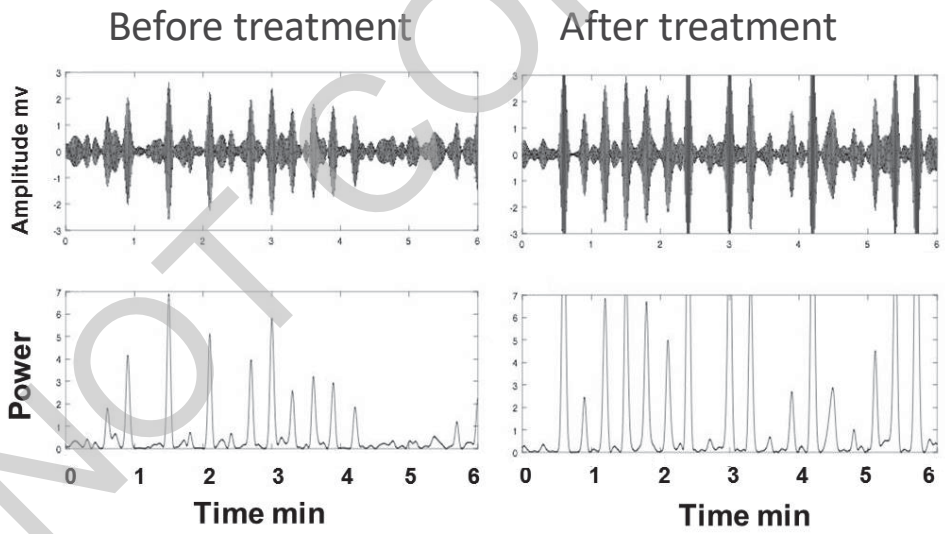


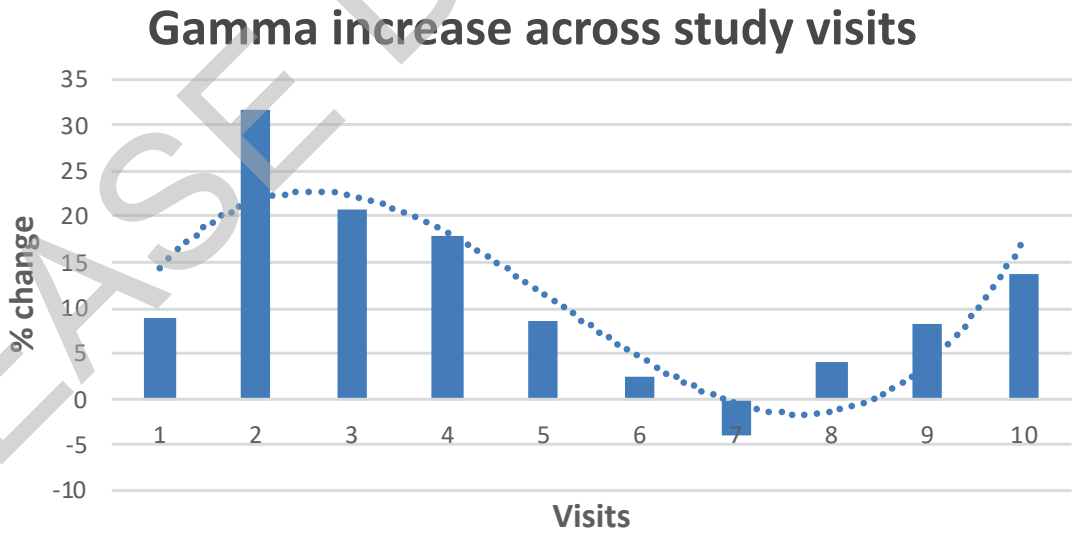




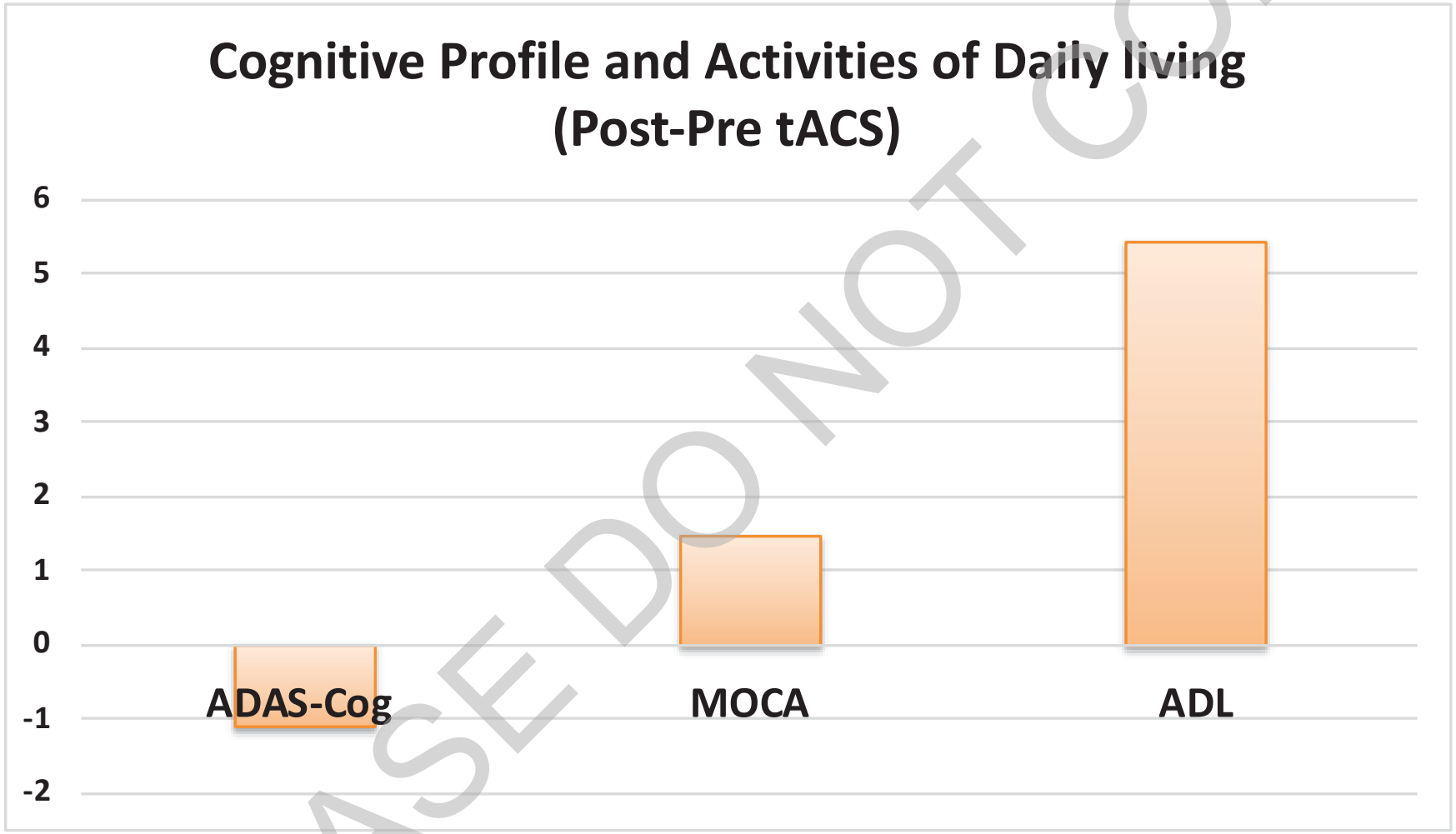
Preliminary results: Effect on Gamma Oscillations (EEG spectral power)



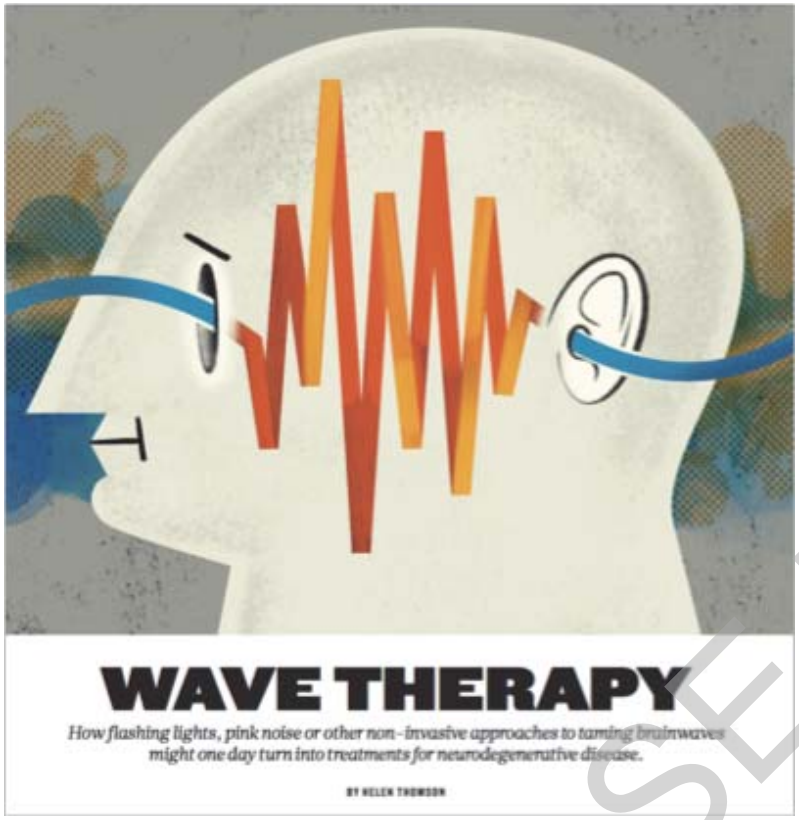




Preliminary Results: Cognition



Follow-up Clinical trial in Alzheimer's funded by DARPA



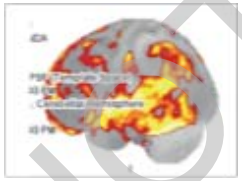
WAVE THERAPY

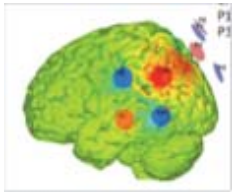
How flashing lights, pink noise or other non-invasive approaches to taming brainwaves might one day turn into treatments for neurodegenerative disease.

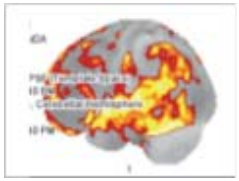
BY HELEN THOMSON

Nature, February 2018

4 weeks, daily tACS (1h)







- Consent
- Screening

- Medical exam
- Clinical evaluation
- Neurological exam
- Neuropsychological exam
- Blood tests
- MRI:
  - resting-state fMRI
  - perfusion MRI (ASL)
  - DTI
  - anatomical
- EEG
- TMS-EEG
- TMS-Plasticity
- tACS-EEG
- Genetics (saliva sample)
- PET – Aβ/TAU/Microglia
- Lumbar Puncture (optional)

tACS

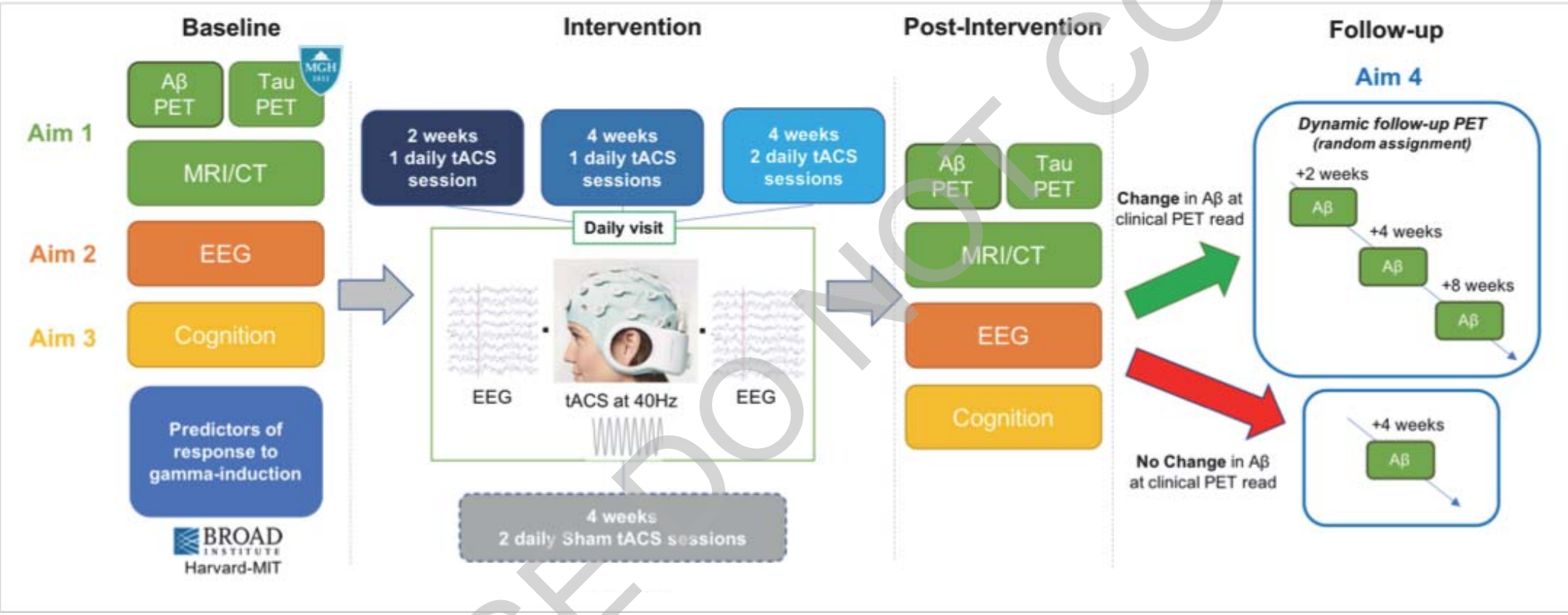
- EEG before, during, after intervention
- Safety evaluation after each session

- Medical exam
- Clinical evaluation
- Neurological exam
- Neuropsychological exam
- Blood tests
- MRI:
  - resting-state fMRI
  - perfusion MRI (ASL)
  - DTI
  - anatomical
- EEG
- TMS-EEG
- TMS-Plasticity
- tACS-EEG
- PET – Aβ/TAU/Microglia
- Lumbar Puncture (optional)

T0 T1 T2 T3

Daily tACS intervention and repeated Amyloid, Tau and Microglia PET imaging

R01 trial (starting May 2019)



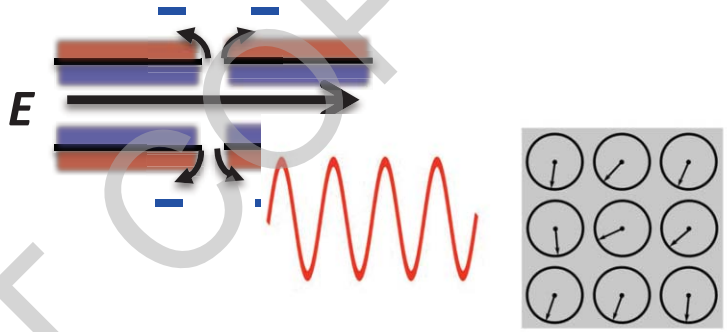
Double blind, sham controlled study

AIMS: Dose – Response and long-lasting effects

Summary

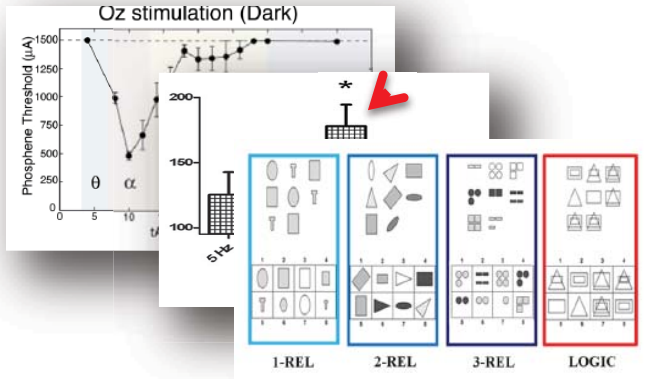
Principles of tACS

- Oscillations
- Endogenous Resonance



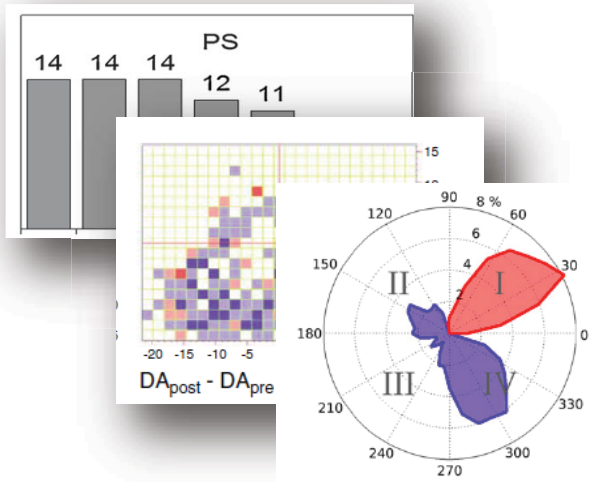
tACS probe oscillatory neural activities

- Perception (vision, tactile)
- Cortico-Spinal Excitability
- Cognition (Intelligence, memory, risk-taking,...)



Potential therapeutic tool

- Tremor, Alzheimer..



What else??

Temporal Interference tACS for "Non-Invasive Deep Brain Stimulation" (R01 at BIDMC)

Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields

Nir Grossman • David Bono • Nina Dedic [16] • Suhasa B. Kodandaramaiah [16] • Andrii Rudenko • Ho-Jun Suk • Antonino M. Cassara • Esra Neufeld • Niels Kuster • Li-Huei Tsai • Alvaro Pascual-Leone • Edward S. Boyden [17] • Show less • Show footnotes

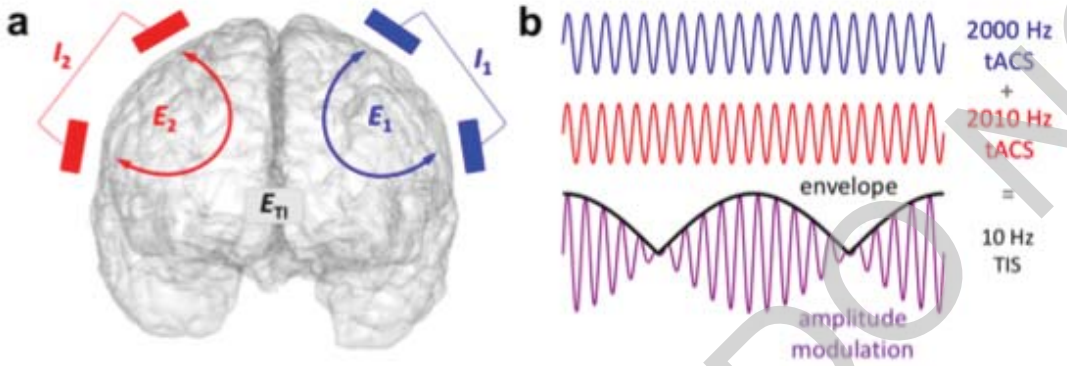


Figure 1: Concept of temporal interference stimulation. **a)** Example arrangement of the two pairs of stimulating electrodes on the scalp, each supplying an oscillating current and producing an oscillating electric field. The intersection of the two fields produces an amplitude-modulated field $\vec{E}_{TI}$. Note that it is not required for the two sets of electrodes to be on opposite sides of the head. **b)** Illustration of two high-frequency oscillations and their sum, which is an amplitude-modulated oscillation with a carrier frequency equal to the average frequency of the inputs and an envelope oscillating at the difference frequency.

Prospects for transcranial temporal interference stimulation in humans: a computational study

Sumientra Rampersad[a], Biai Roig-Solvas[a], Mathew Yarossi[a,b], Praveen P. Kulkarni[c], Emiliano Santarnecchi[d], Alan D. Dorval[e], Dana H. Brooks[a]

[a]Department of Electrical and Computer Engineering, Northeastern University, Boston, USA
[b]Department of Physical Therapy, Movement and Rehabilitation Science, Northeastern University, Boston, USA
[c]Center for Translational Neuro-imaging, Northeastern University, Boston, USA
[d]Berenson-Allen Center for Noninvasive Brain Stimulation, Harvard Medical School, Boston, USA
[e]Department of Biomedical Engineering, University of Utah, Salt Lake City, USA

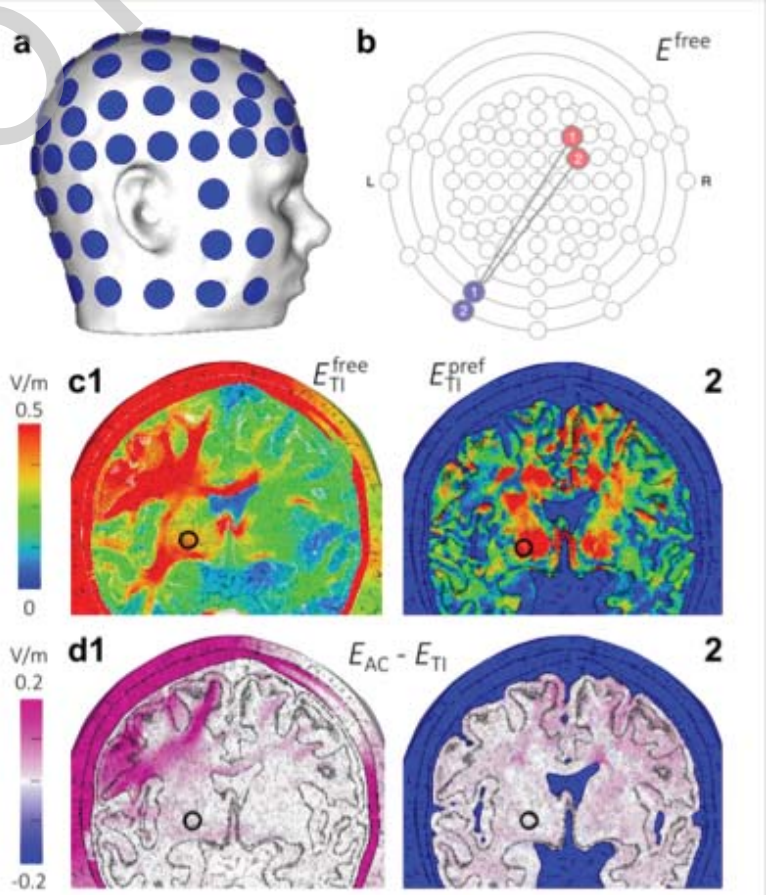


Figure 10: Study 3 – Optimization of four-electrode tTIS in the right pallidum. **a)** Model with all 88 electrodes used in the optimization. **b)** Electrode configuration

tACS to synchronize brain oscillations in Aging

MENU

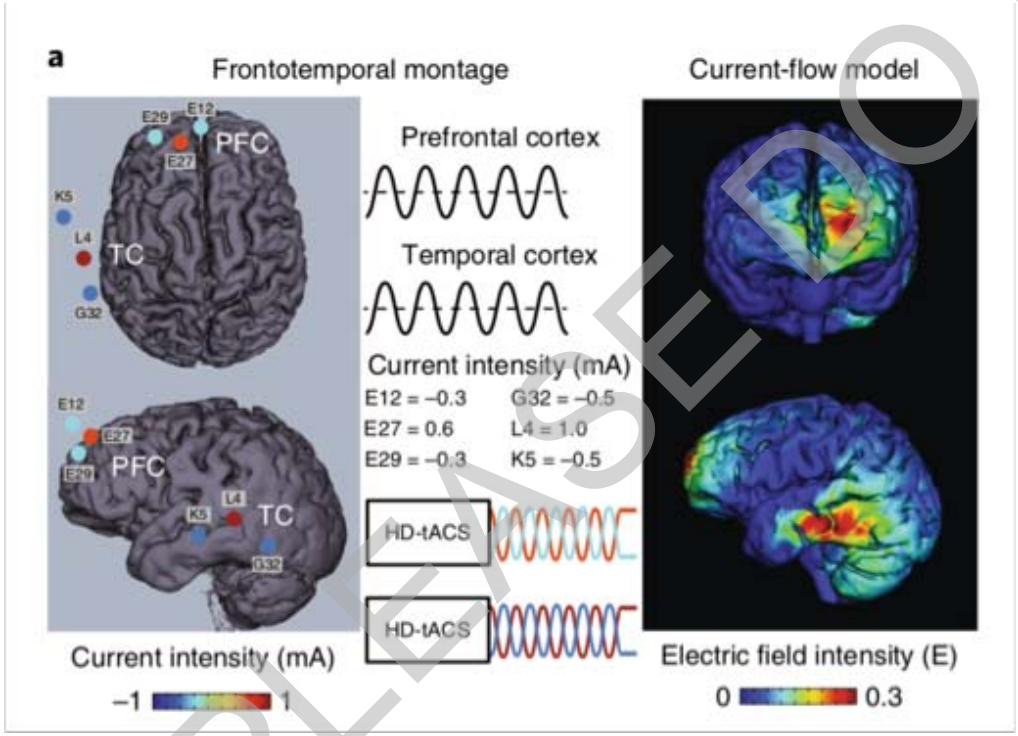
nature neuroscience

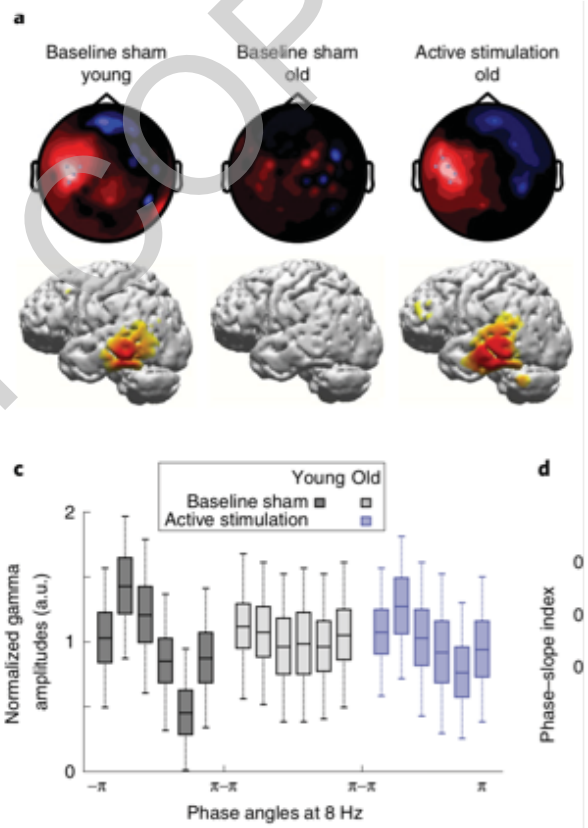
Article | Published: 08 April 2019

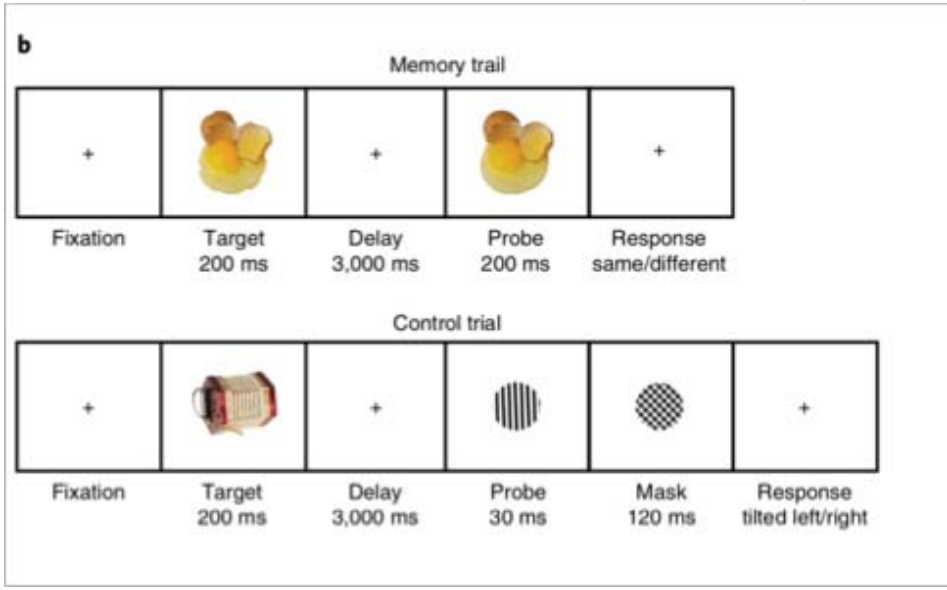
Working memory revived in older adults by synchronizing rhythmic brain circuits

Robert M. G. Reinhart & John A. Nguyen

Nature Neuroscience **22**, 820–827 (2019) | Download Citation







tACS and Cross-Frequency Coupling

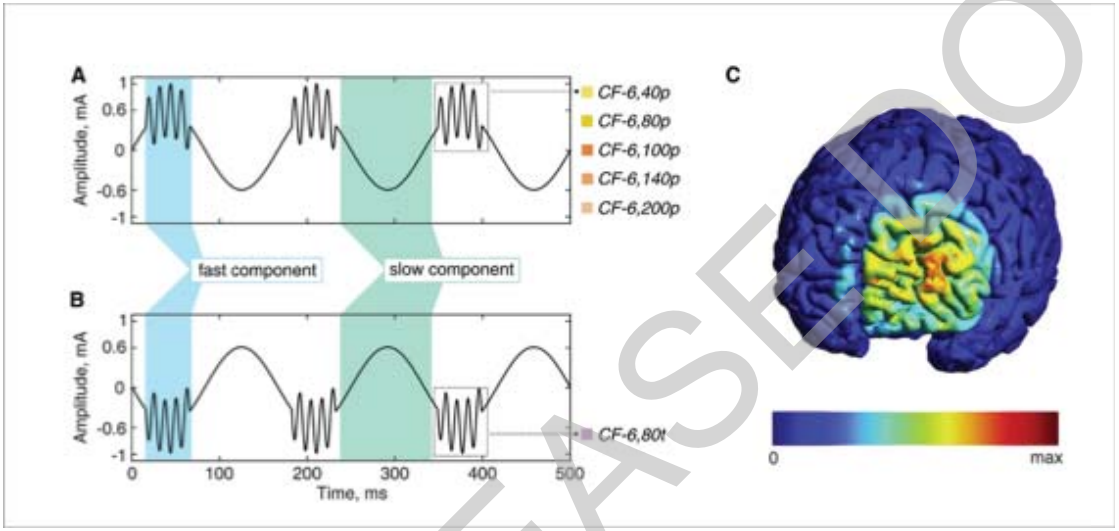
Current Biology

Spatial Working Memory in Humans Depends on Theta and High Gamma Synchronization in the Prefrontal Cortex

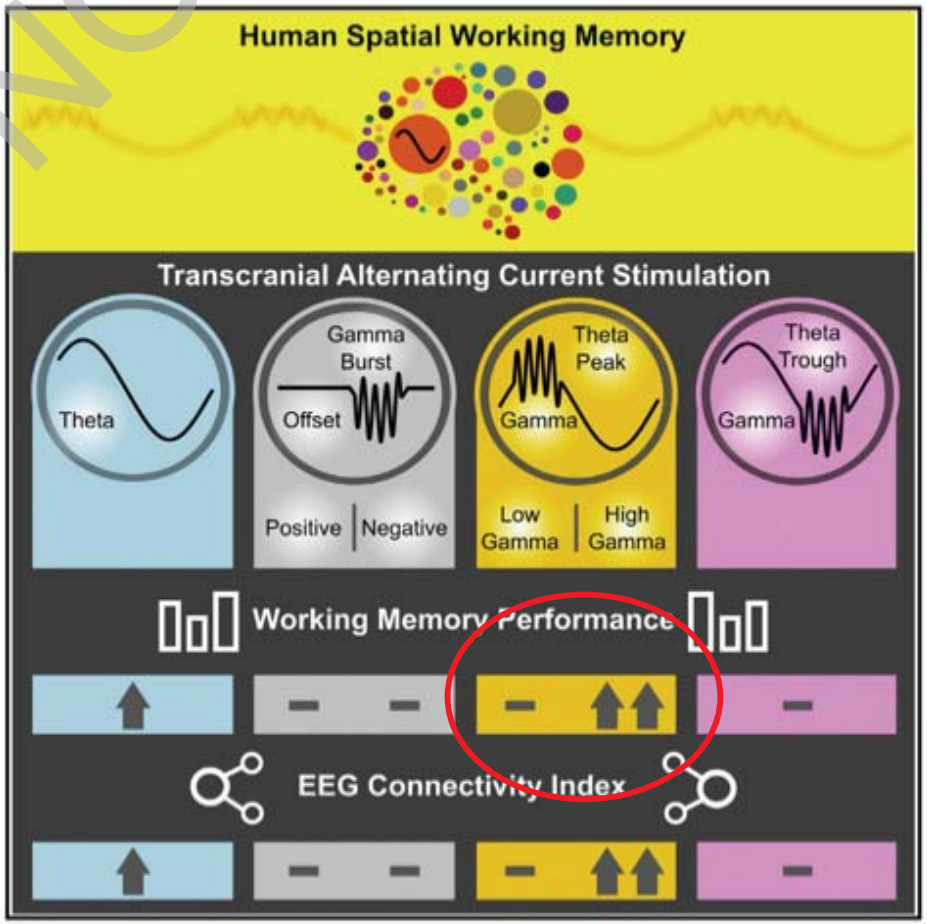
Authors

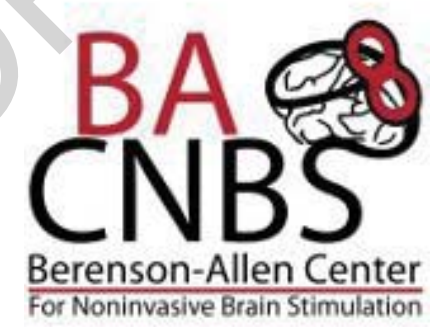
Ivan Alekseichuk, Zsolt Turi, Gabriel Amador de Lara, Andrea Antal, Walter Paulus

tACS to induce Theta-Gamma coupling



Graphical Abstract





Thank you for your attention!

esantarn@bidmc.harvard.edu