Cognitive Enhancement with tCS

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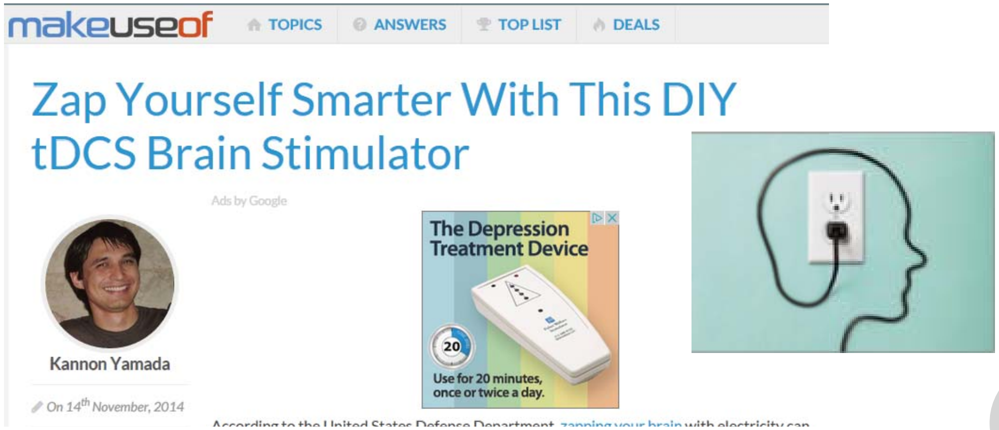
BA CNBS Berenson-Allen Center For Noninvasive Brain Stimulation

Boston, 27th June 2019

VE RI TAS HARVARD

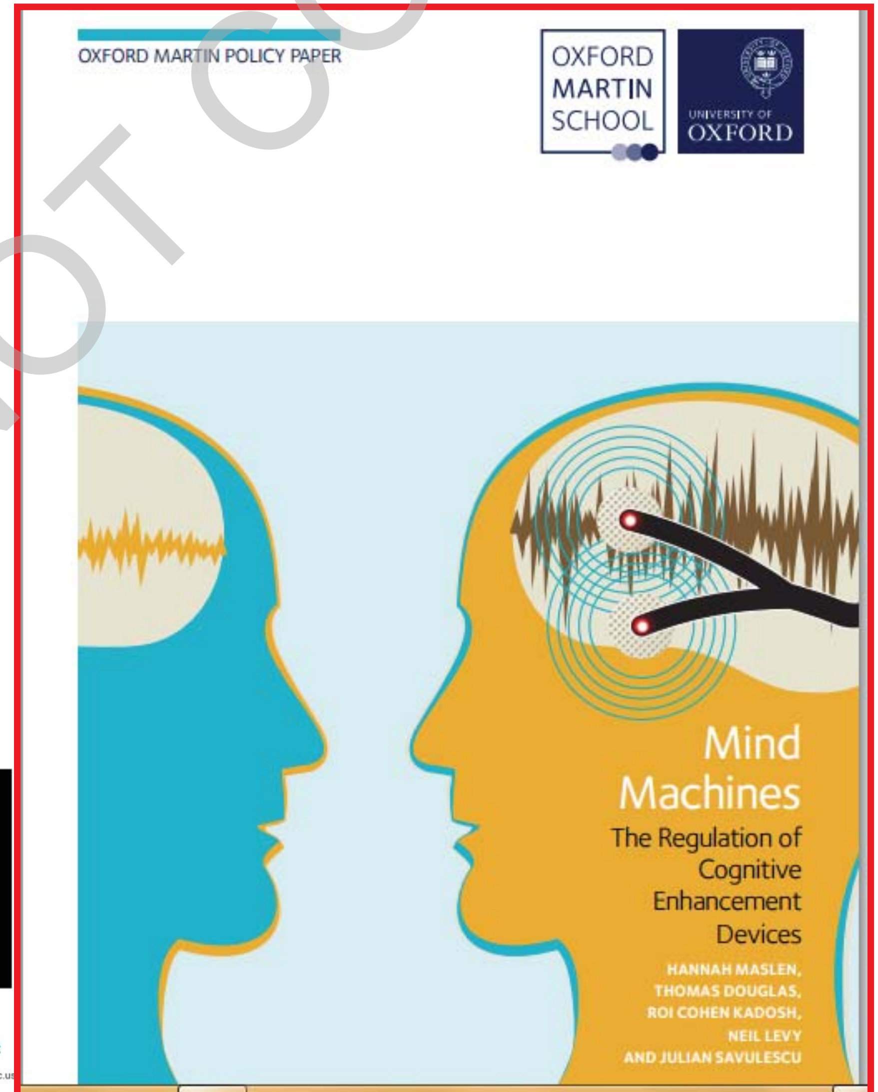
DIY cognitive enhancement..

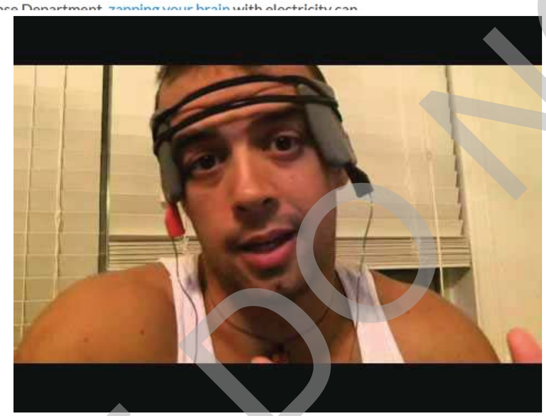

makeuseof
TOPICS ANSWERS TOP LIST DEALS

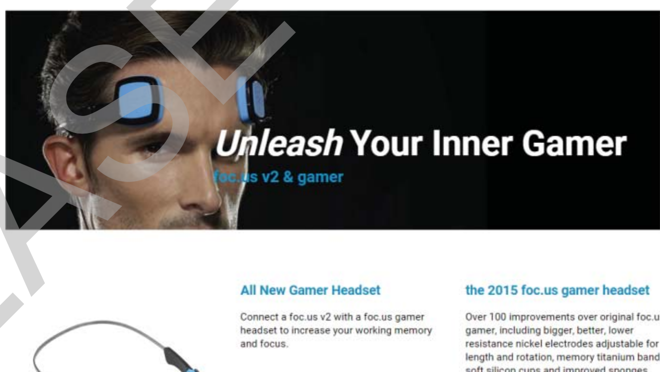
Zap Yourself Smarter With This DIY tDCS Brain Stimulator

Kannon Yamada

On 14th November, 2014







The Atlantic

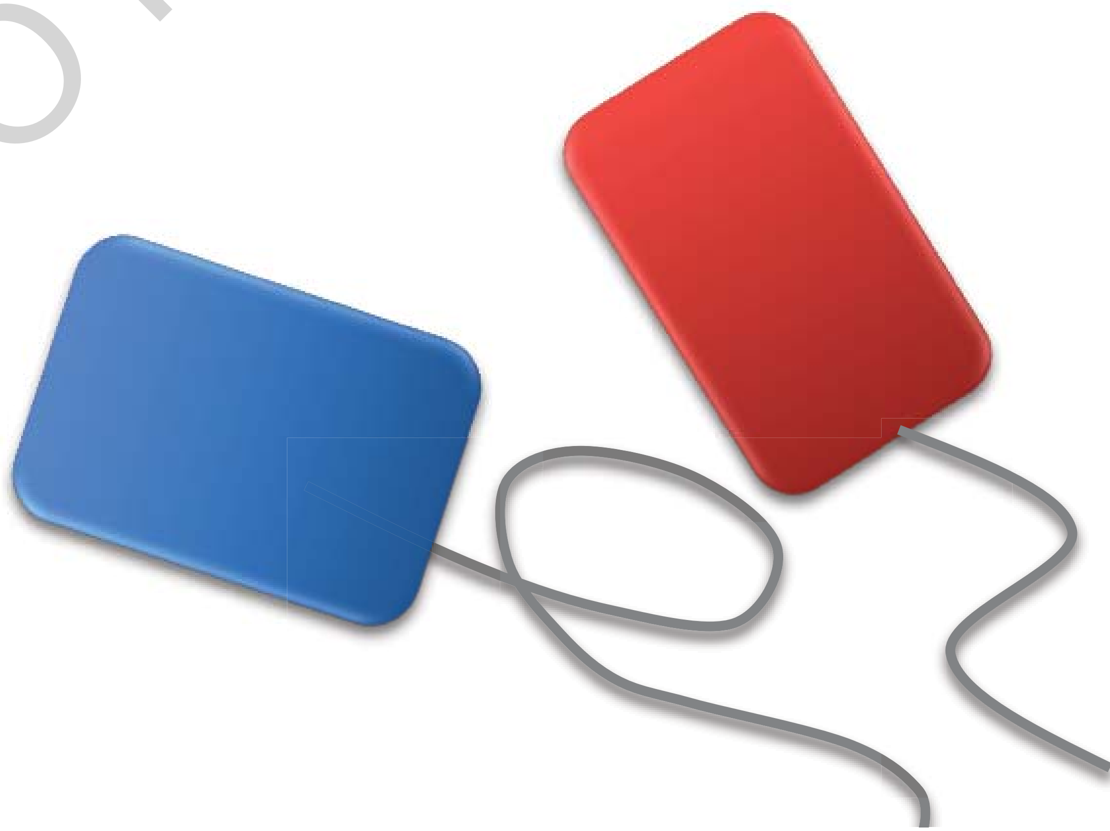
SEPTEMBER 2014

Prepare to Be Shocked

Four predictions about how brain stimulation will make us smarter

Outline

- tCS effects: theories & controversies
- Net-zero sum theory (?)
- Trait – Dependency of tCS effects
- tCS targeting → Networks



Why-What-Where-How Neuroenhancement

Physical activity

- unspecific effects on metabolism and nutrients
- Requires commitment and time (elderly..)

Drugs (modafinil, memantine)

- Side effects
- unspecific effects **(all brain)**

Dietary regimen

- Same as physical activity

Neuroenhancement

Brain training

- Effect on specific functions
- *Effect size is usually small..*

Transcranial Current Stimulation (tCS)

- Cheap
- Less commitment
- Wearable
- Easy to use
- Stand-alone intervention OR add-on (enhancer)
- More focal (→ modeling)

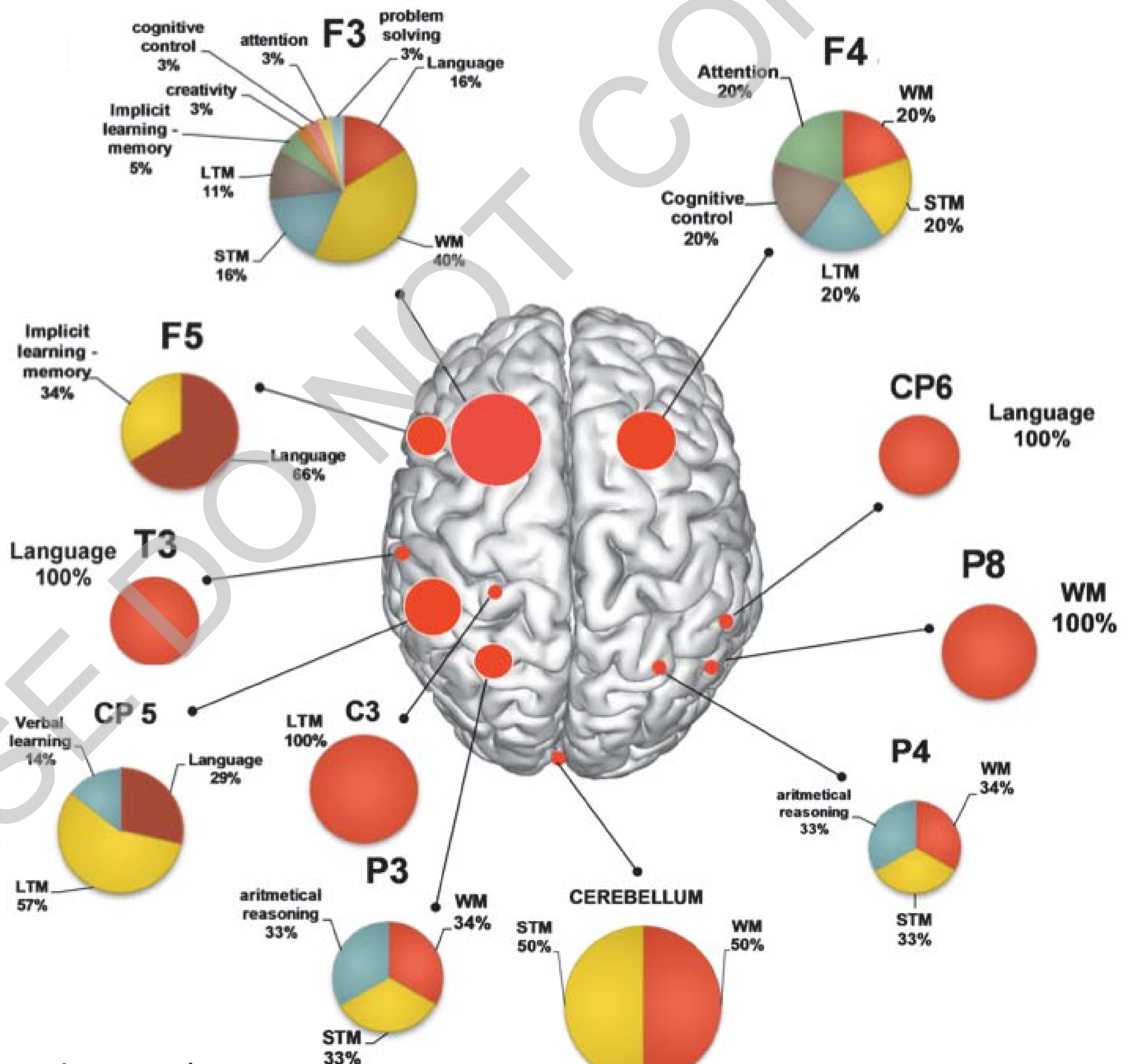
Special issue in Current Opinion in Behavioural Sciences 2016

Cognitive Enhancement with tDCS

Santarnecchi et al. 2015, Curr. opin. in Behav. Sc.

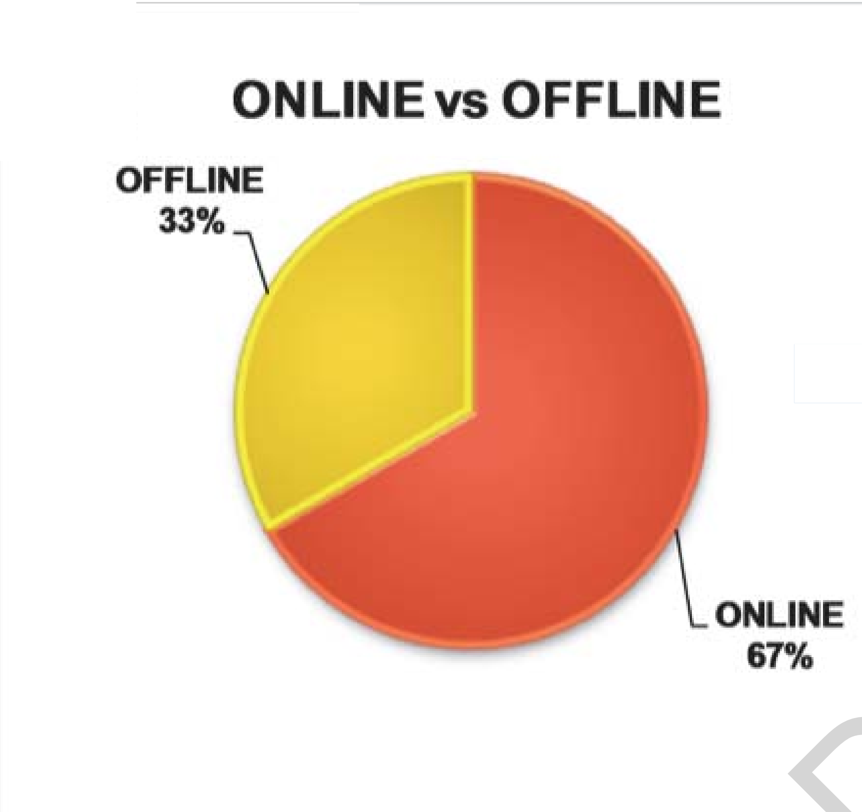
Reviewed ~ 100 studies

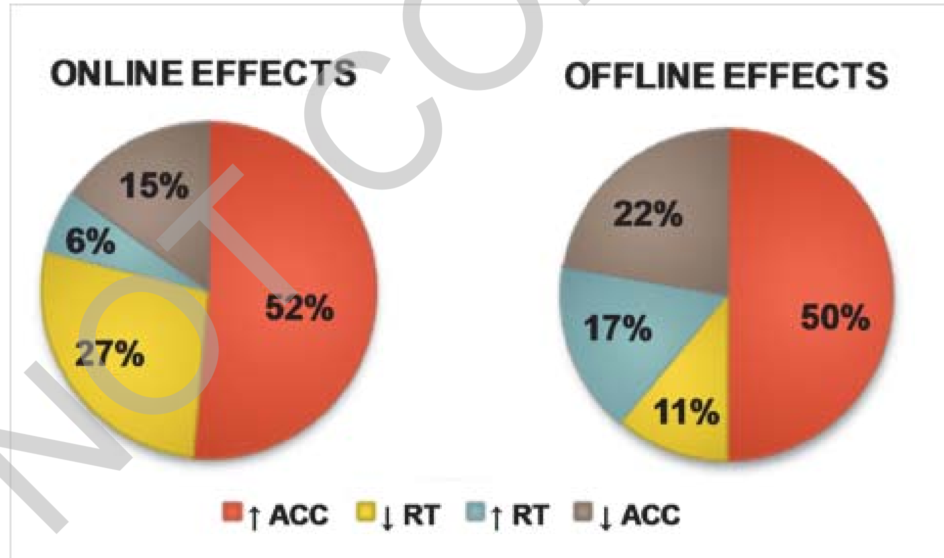
- tDCS (anodal, cathodal)
- healthy participants
- age 18-55
- Sham-controlled

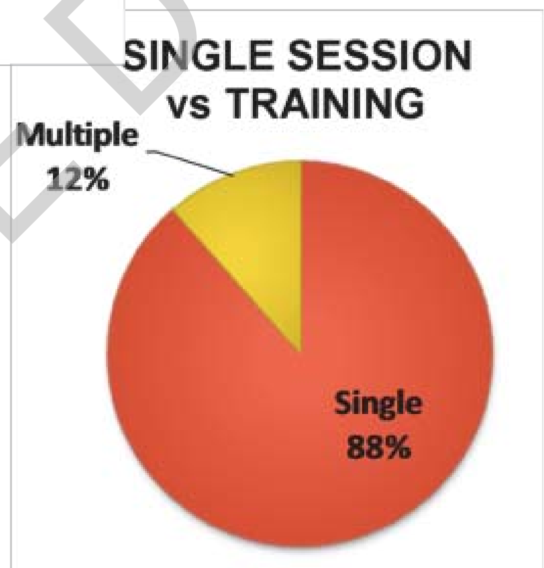


(Coffman et al., 2014; Horvath et al., 2015)

Single session vs training; online-offline…







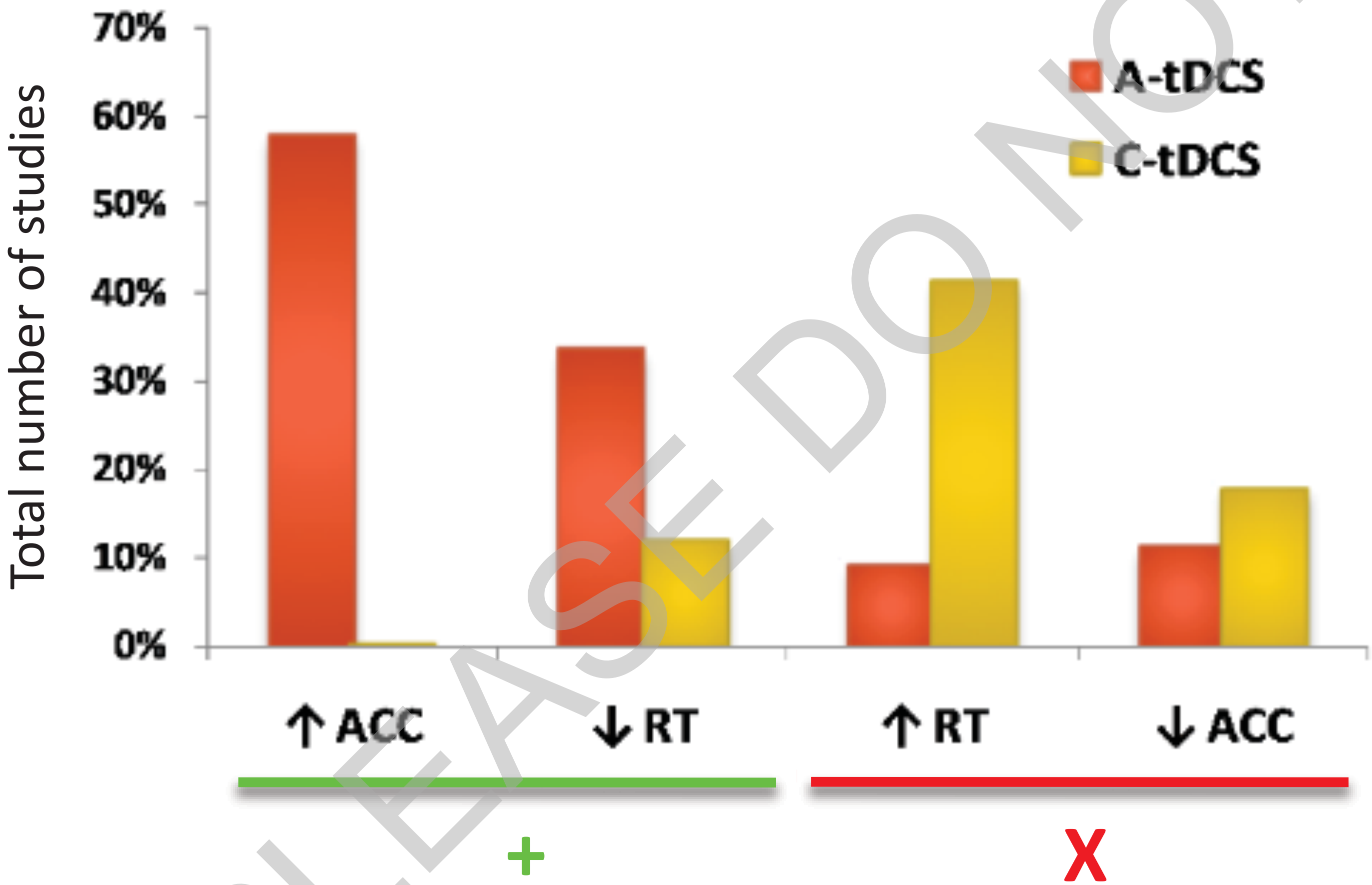
?

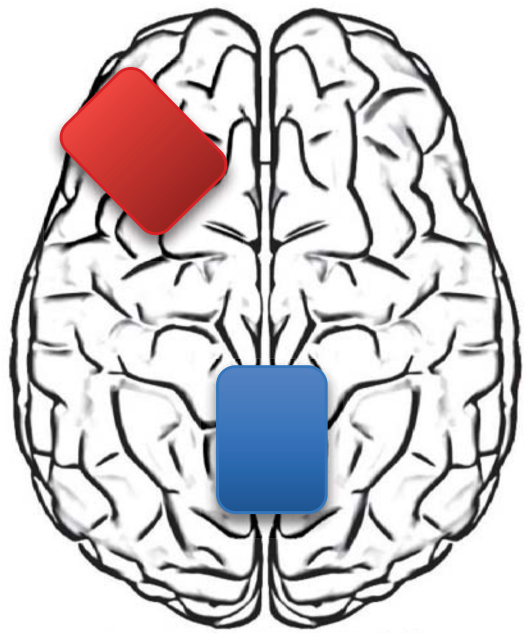
Santarnecchi et al. 2015, Curr. opin. in Behav. Sc.

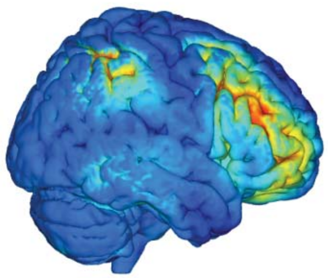
Polarity specific Effects?

Santarnecchi et al. 2015, Curr. opin. in Behav. Sc.

Is **anodal** tDCS more effective? Is **cathodal** tDCS detrimental?

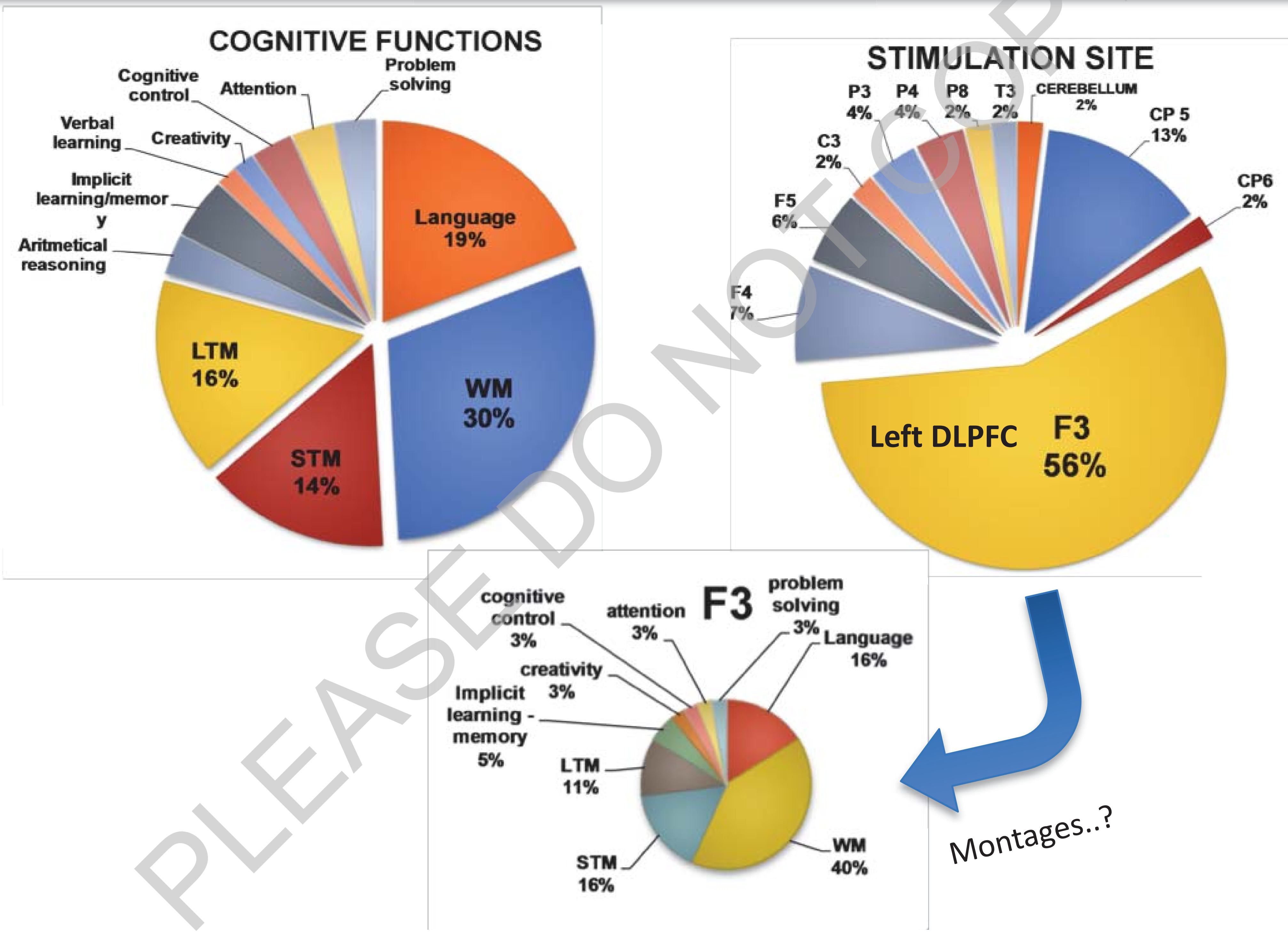






Modeling

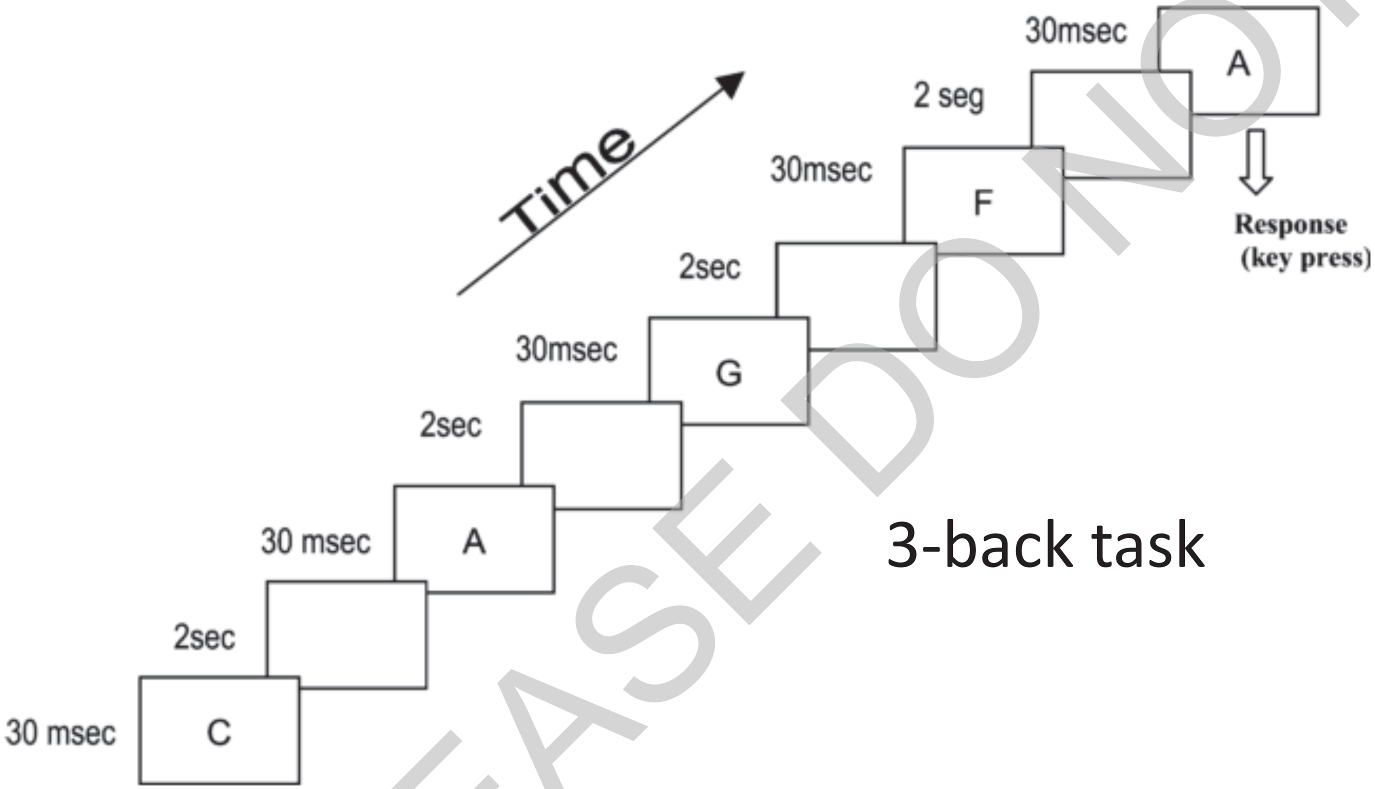
Non-specific effects?



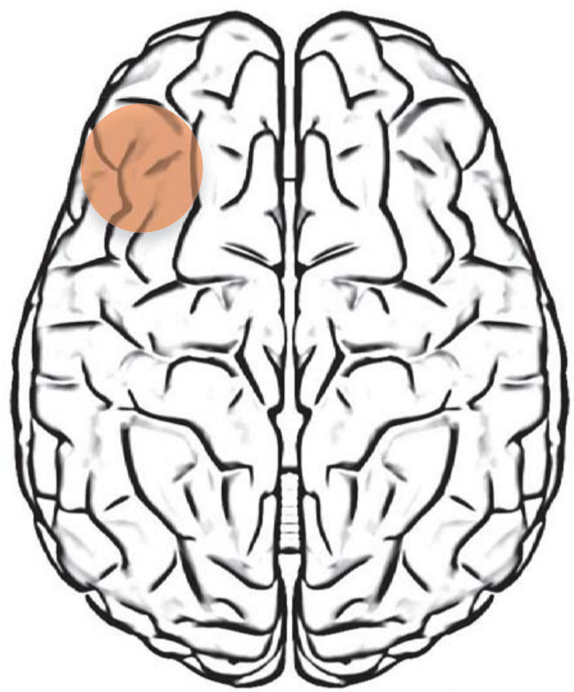
Montages..?

Enhancement of Working Memory

- The N-back working memory task (Fregni et al., 2005)



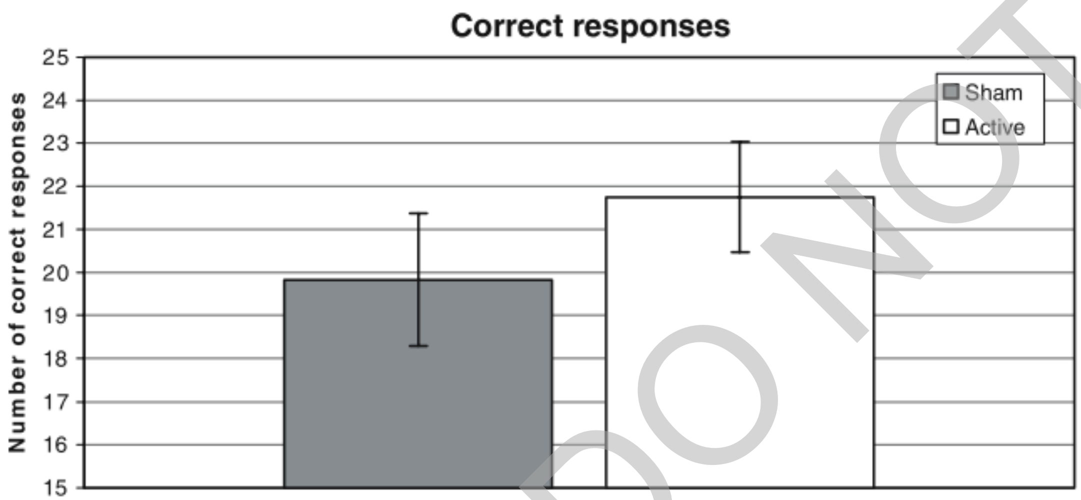
3-back task

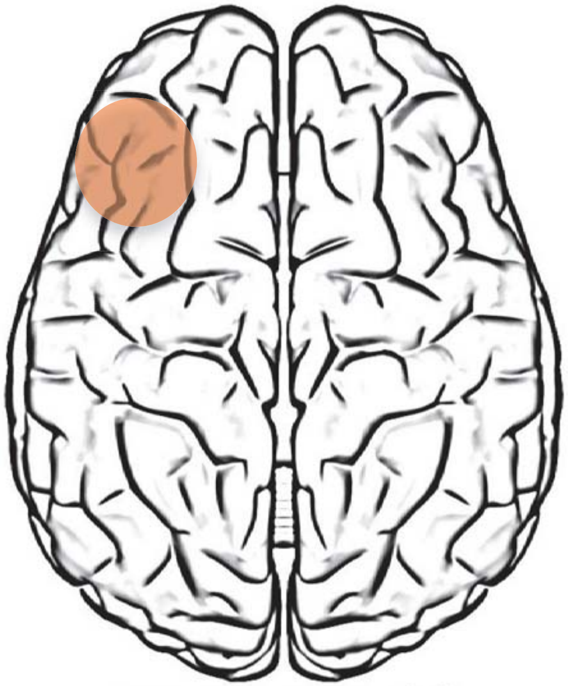


Key region: dorsolateral prefrontal cortex

Enhancement of Working Memory

- **Anodal tDCS of left DLPFC enhances performance on 3-back working memory task** (Fregni et al., 2005)

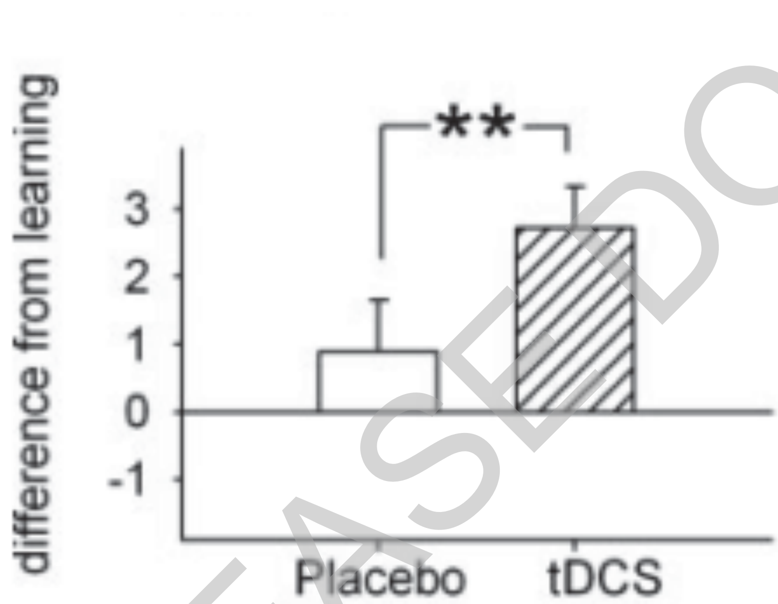


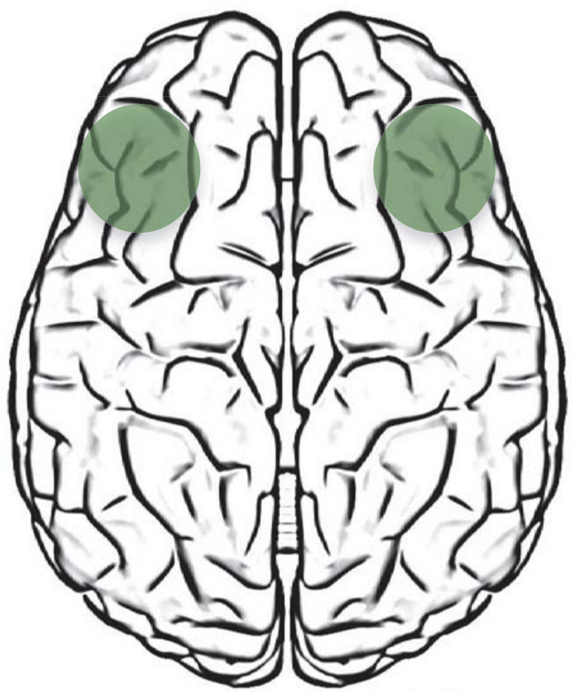


- **Anodal tDCS of the left DLPFC, combined with N-back working memory task, enhances digit span** (Andrews et al., 2011)
  - Neither tDCS nor N-back testing alone was sufficient

Enhancement of Explicit Learning

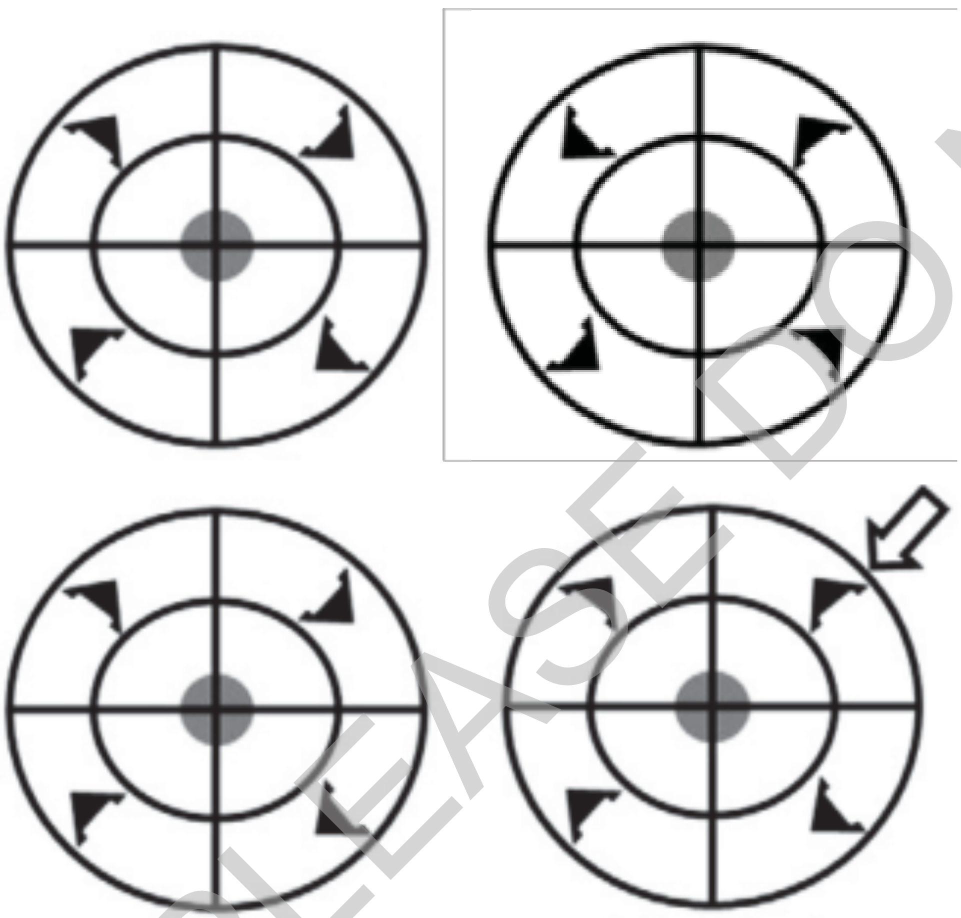
- **Enhancement of explicit learning consolidation during sleep (Marshall et al., 2004)**
  - List of words presented to subjects during the day
  - Anodal tDCS of bilateral DLPFC during slow wave sleep
  - Enhanced recall of word list

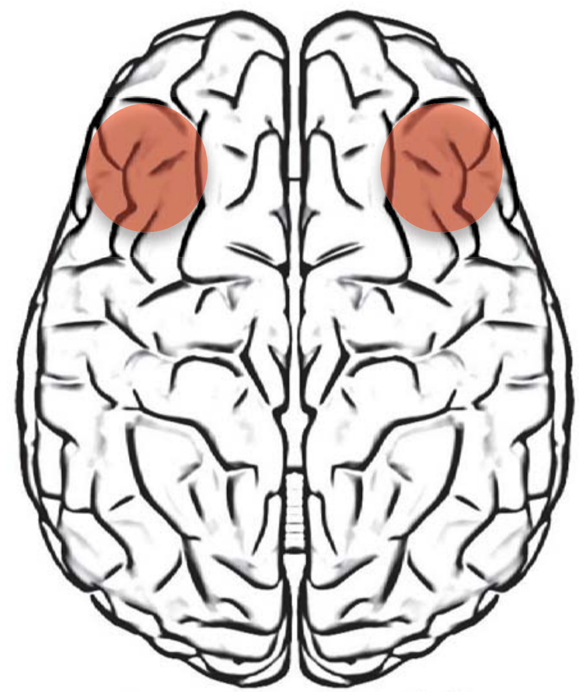




Enhancement of Attention

- Visual Attention Task: Air Traffic Control (Nelson et al., 2014)

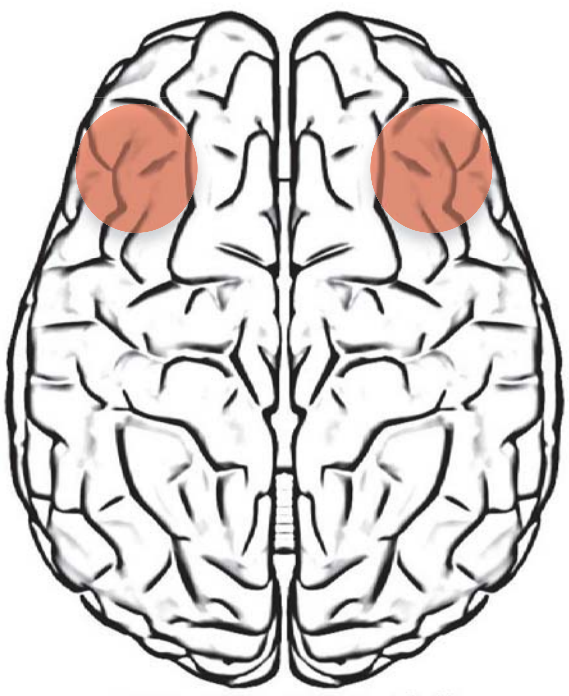




Enhancement of Attention

- With sham tDCS, attention decreases over time (Nelson et al., 2014)
  - Lower target detection rate
  - Slower reaction times
  - Reduction in cerebral blood flow velocity

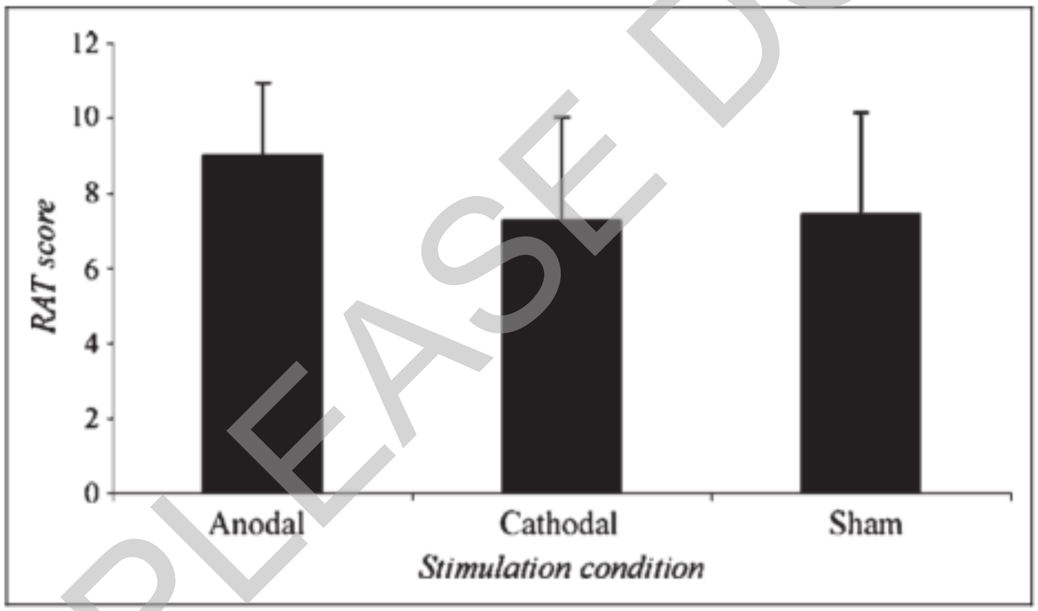
- Anodal tDCS of DLPFC (left or right) enhances attention
  - Higher target detection rate
  - Maintained blood flow velocity
  - Increased cerebral oxygenation

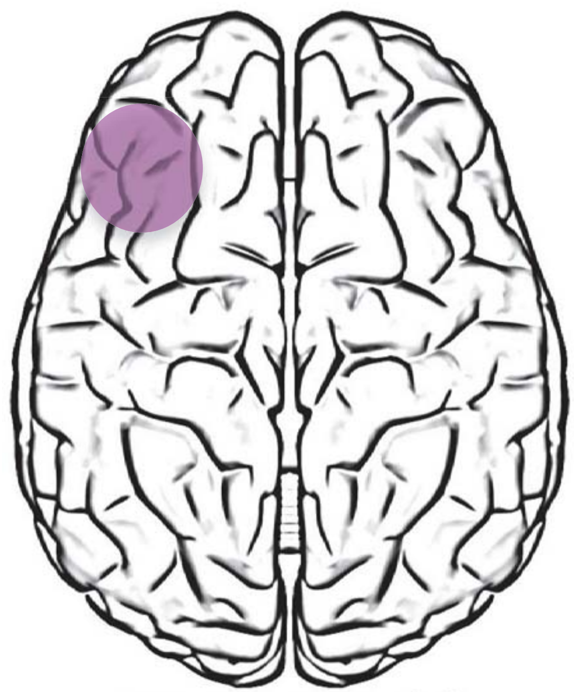


Enhancement of Complex Cognition: Eureka!

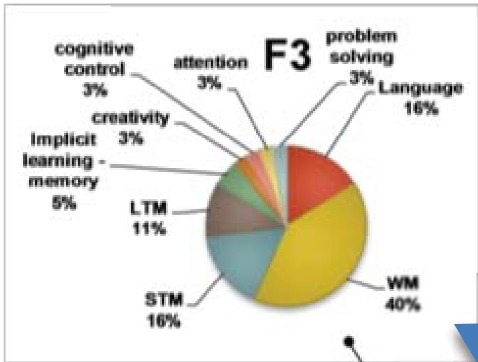
- **Remote associates test** (Cerruti & Schlaug, 2009)
  – Given 3 words, have to find a word associated with all 3
  – E.g., “Child, Scan, Wash” → “Brain”

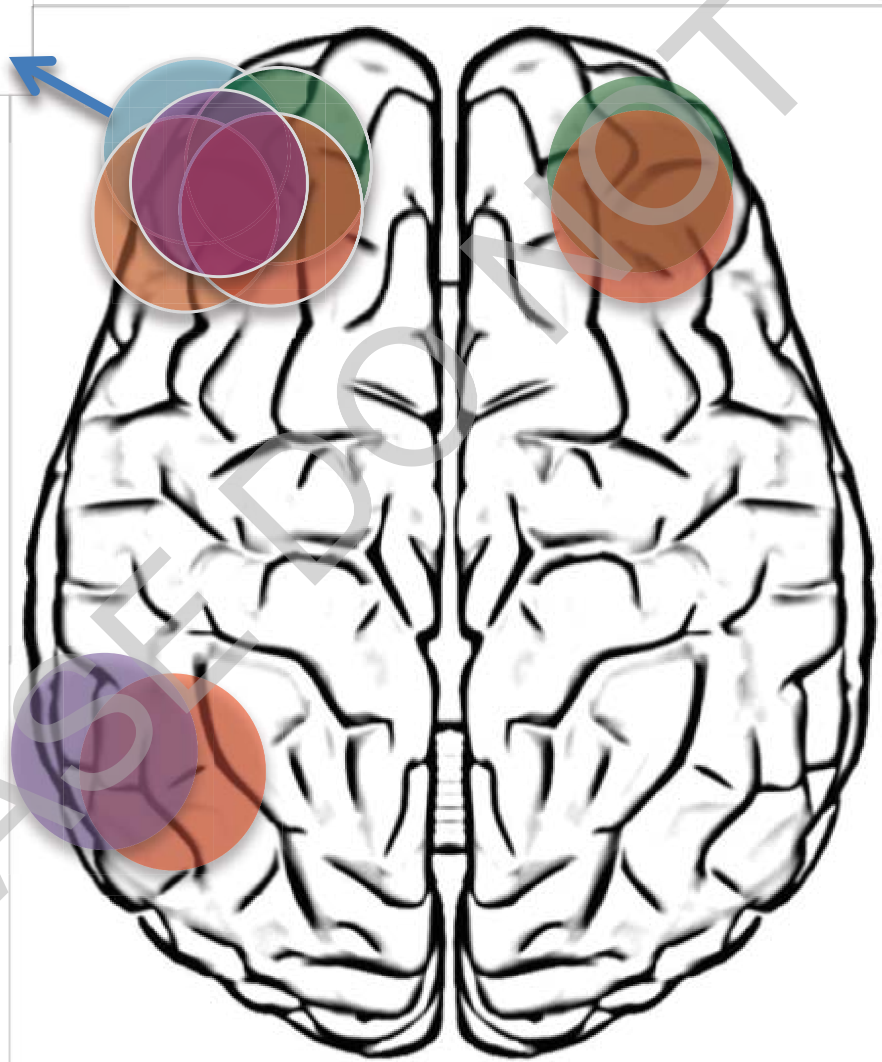
- Anodal tDCS of the left DLPFC enhances performance





Overlapping effects and stimulation sites..





Implicit Learning

Explicit Learning

Working Memory

Motor Learning

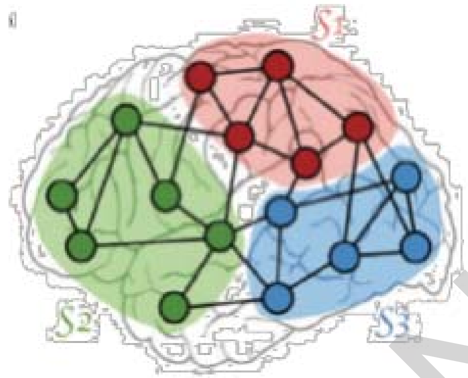
Attention

Language

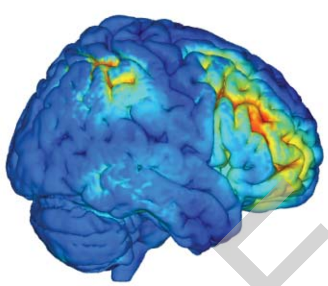
Complex Cognition

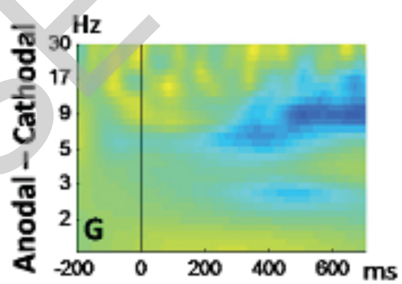
1) Stimulating Different Networks?

- Stimulation of DLPFC as a "*Gate*" to other regions/networks

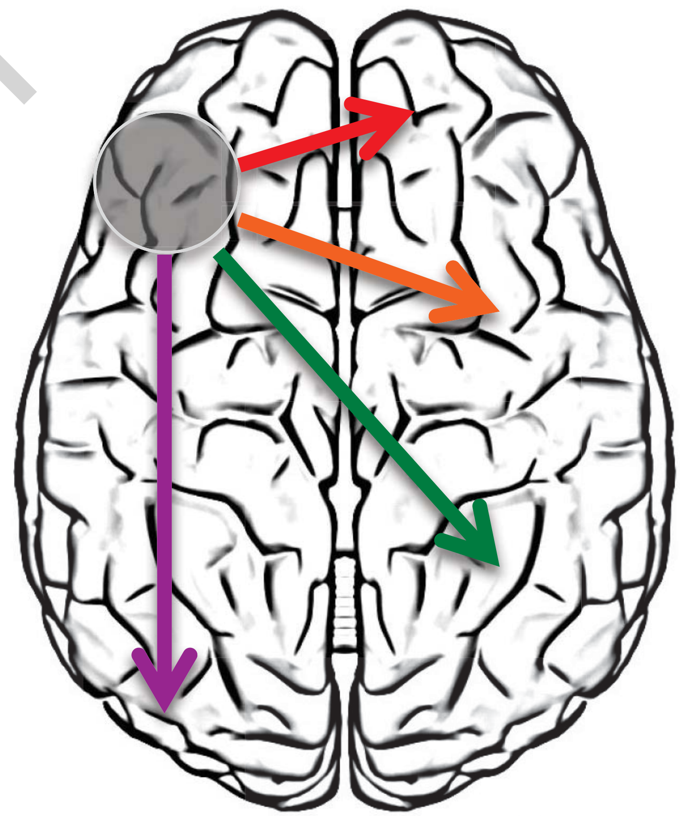


- tDCS can alter functional connectivity between brain regions (Coffman et al., 2014), as demonstrated with fMRI and EEG





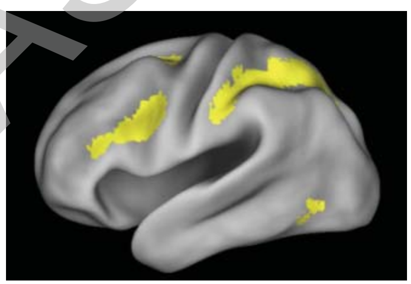
Zahele et al. 2011 (EEG)



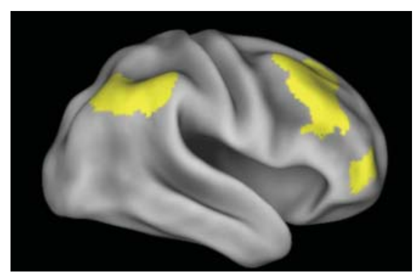
2) Stimulating Overlapping Cognitive Skills?

- Enhancement of explicit learning with tDCS correlates with enhancement of **attention** (Coffman et al., 2012)
- Enhancement of **working memory** with tDCS mediated by enhancement of selective **attention** (Gladwin et al., 2012)
- Learning (memory acquisition/consolidation) linked to **working memory** and **attention** (Coffman et al., 2014)

Common denominator → Improvement of **attention**, therefore reaction times, and filtering ability, working memory, etc…..



Left Executive Control

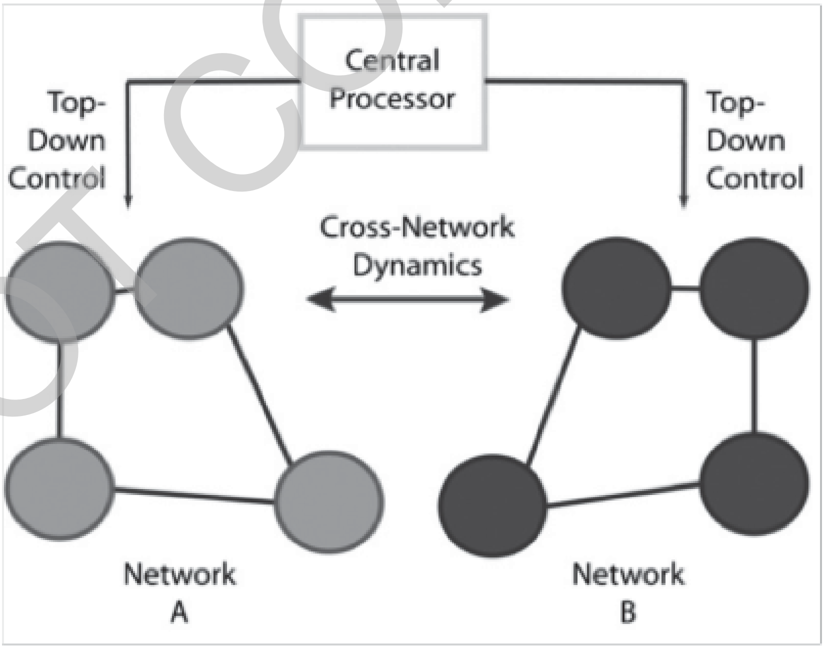


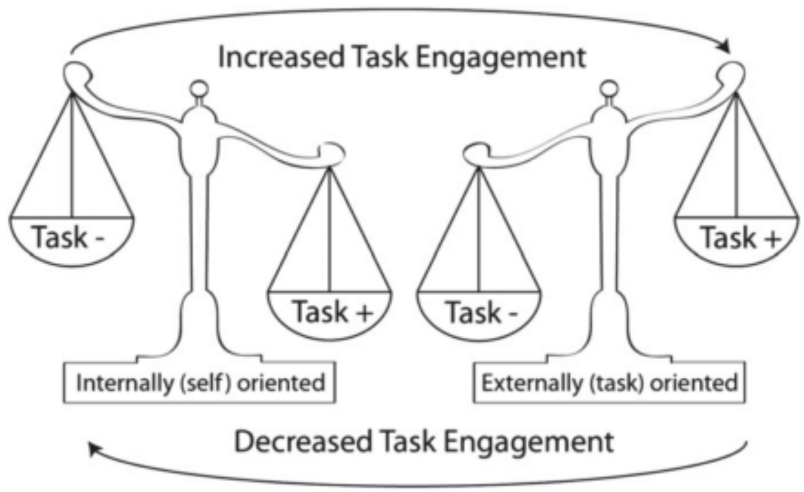
Right Executive Control

Net Zero Sum effect?

tDCS effects → Net zero-sum?

- Net zero-sum derived from notion of conservation of energy
- A gain in function is accompanied by an equal loss of function
- Is brain enhancement a zero-sum game?
  – Distribution of processing power
  – Example: Trade-offs (e.g. speed-accuracy)





Brem et al., 2014

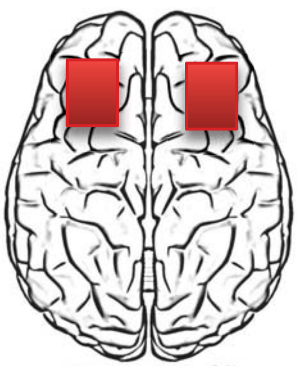
Evidence for Zero-Sum?

Iuculano & Cohen Kadosh, 2013

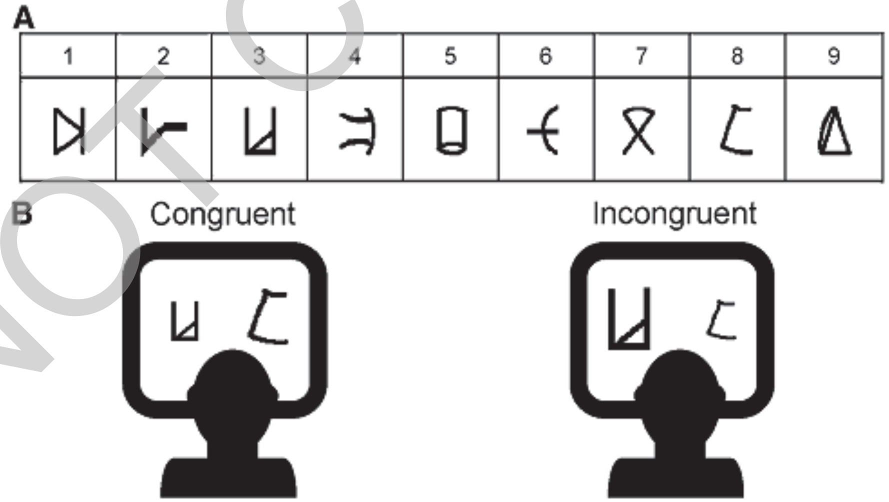
Study of numerical learning in healthy participants.

6 Days of training combined with:

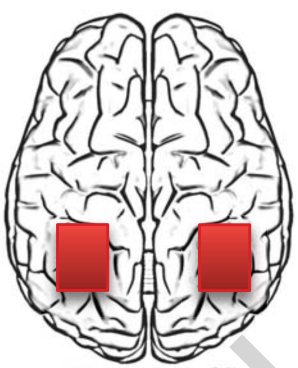
1) tDCS over Dorsolateral Prefrontal Cortex



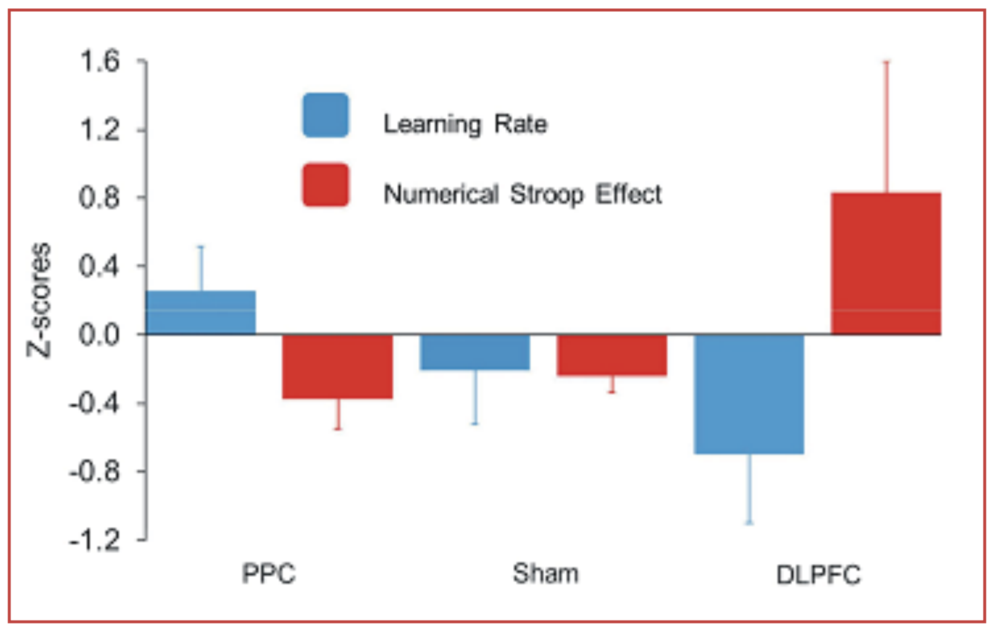
Enhance Automaticity



2) tDCS over Posterior Parietal Lobe



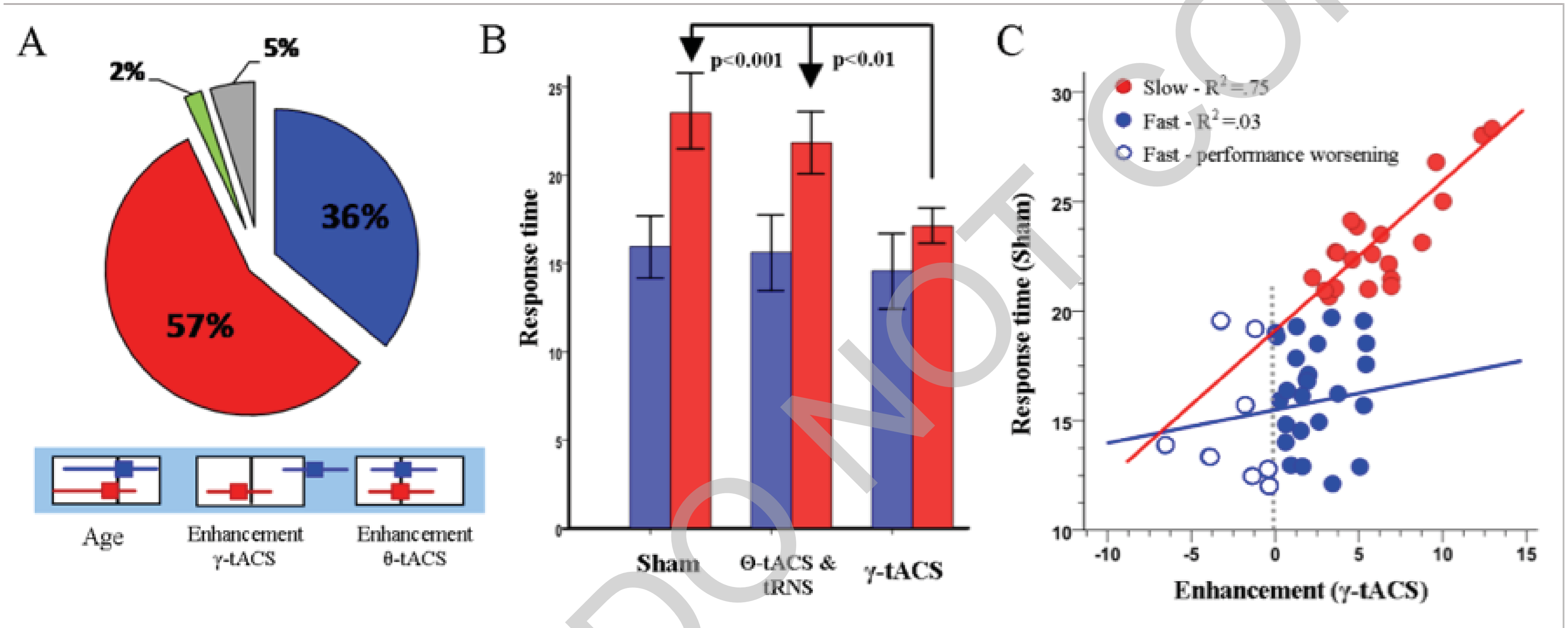
Enhance Learning



Trait Dependency

Trait Dependecy of tCS effects: Fluid Intelligence

Santarnecchi et al., 2015



• Effect of tES reflect **individual differences** → "Phenotype", related to pre-existing oscillatory patterns (higher/lower gamma?)

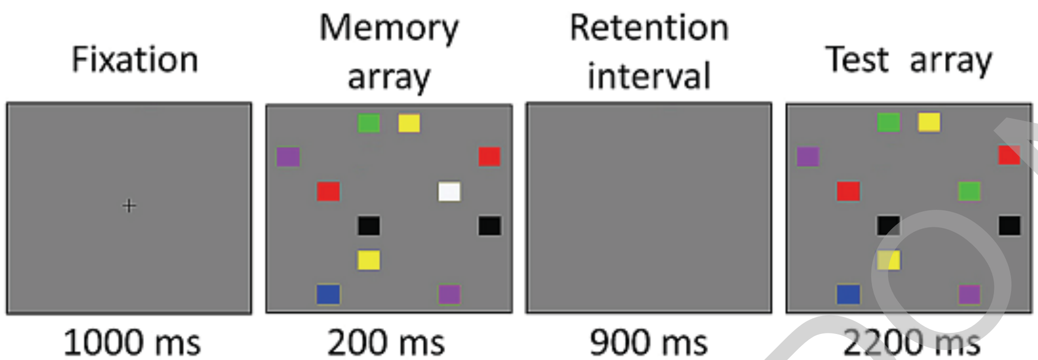
• Important for the **personalization of tES protocol** and for the **ethical evaluation** of cognitive enhancement interventions.

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

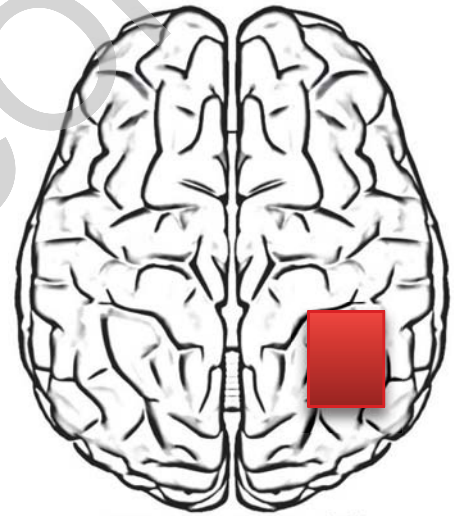
Trait Dependency of tCS effects: Working Memory

Unleashing Potential: Transcranial Direct Current Stimulation over the Right Posterior Parietal Cortex Improves Change Detection in Low-Performing Individuals

Philip Tseng,[1]* Tzu-Yu Hsu,[1,2]* Chi-Fu Chang,[1] Ovid J.L. Tzeng,[1,2,3] Daisy L. Hung,[1,2] Neil G. Muggleton,[1,4] Vincent Walsh,[4] Wei-Kuang Liang,[1] Shih-kuen Cheng,[1] and Chi-Hung Juan[1]

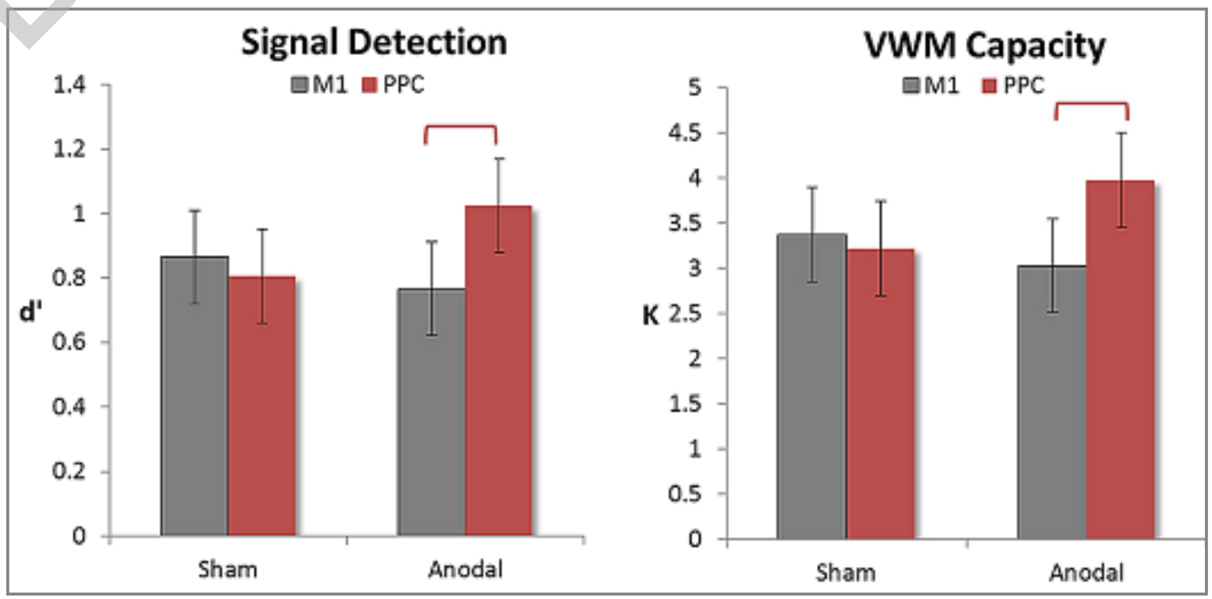


Change Detection Task
(visual short term memory)

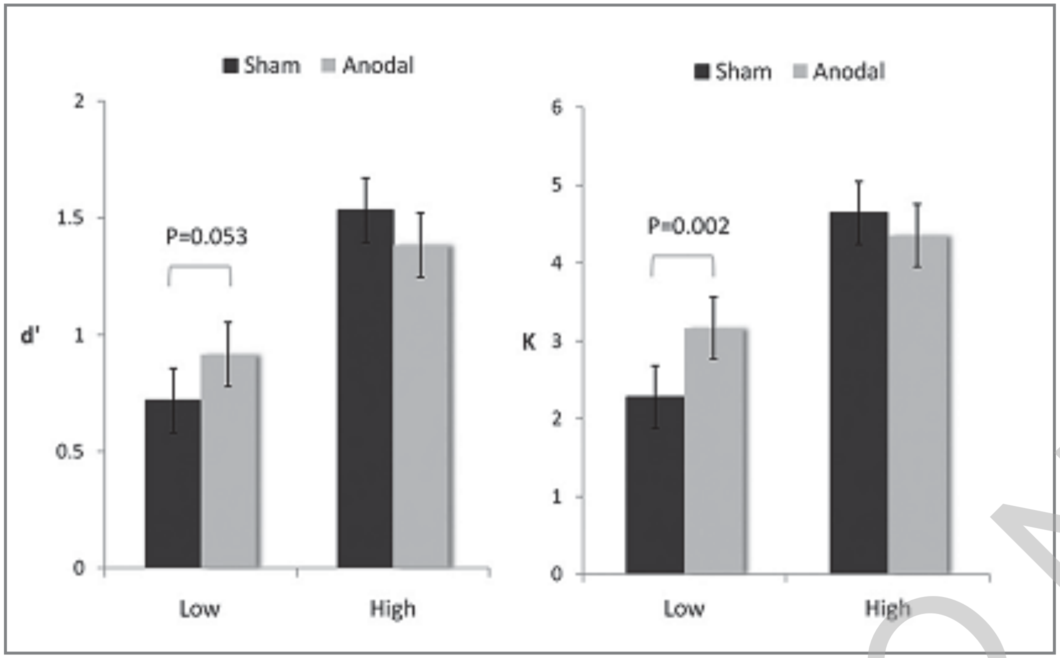


Right Posterior Parietal cortex **Anodal** tDCS

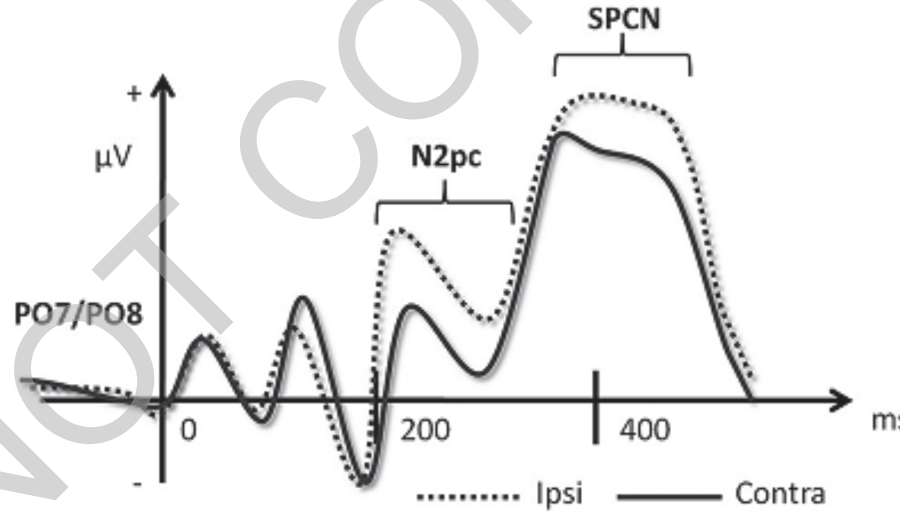
EEG recording during the task



Trait Dependency of tCS effects



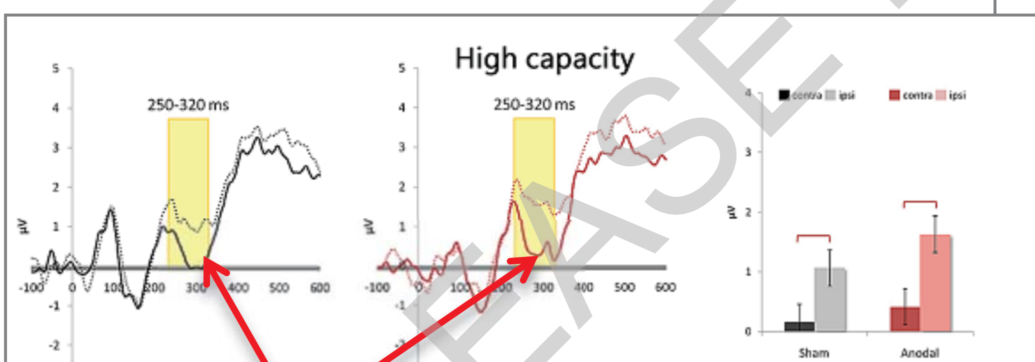
Low and High Baseline performers

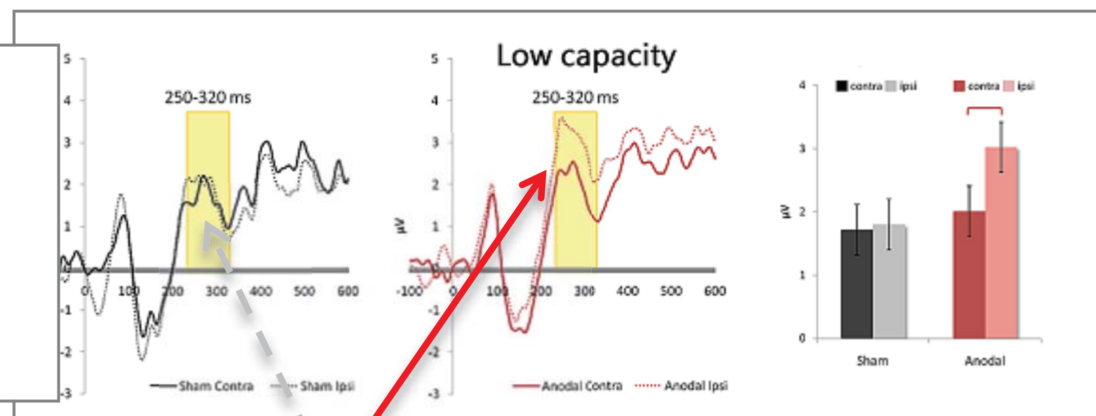


Performance indexes

N2pc= Negative parietal contralateral wave (200ms)

SPCN=Sustained parietal contralateral negativity





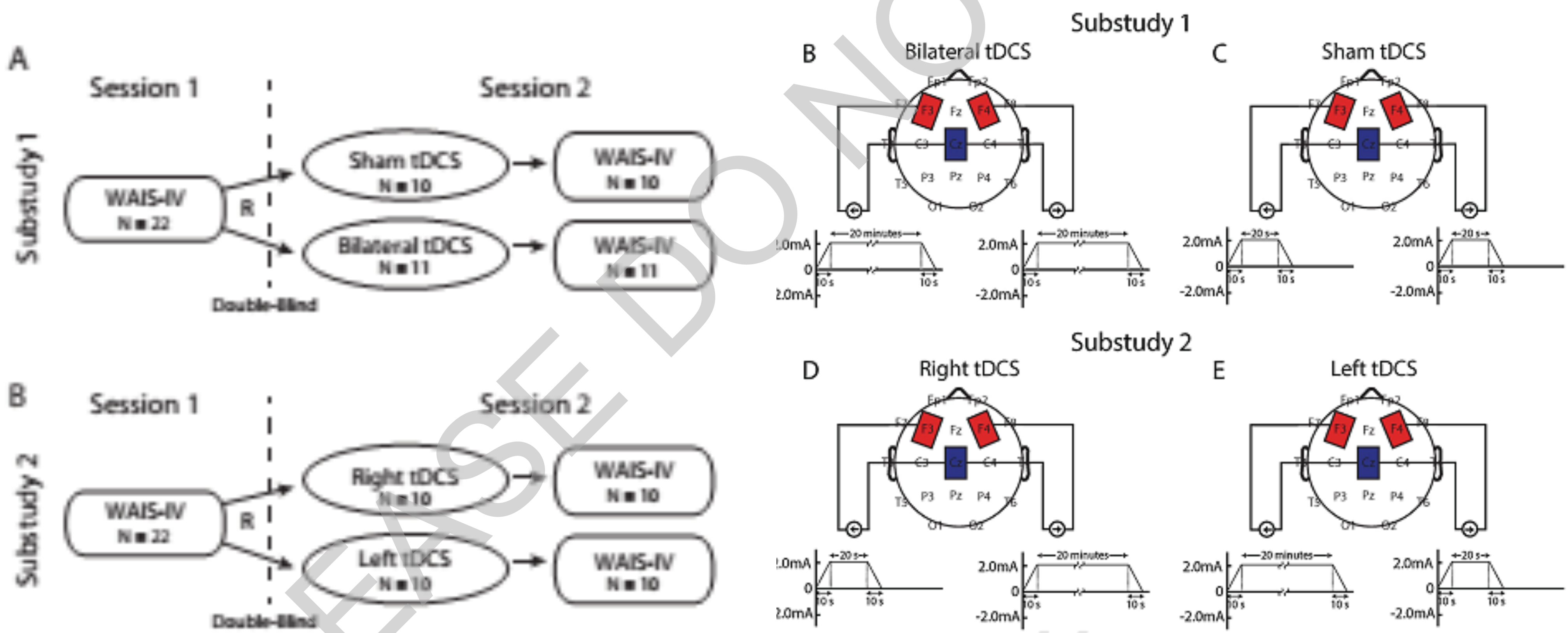
High performers at baseline cannot push their physiological limit → Higher Intensity?

Timing, State dependency and Network Targeting

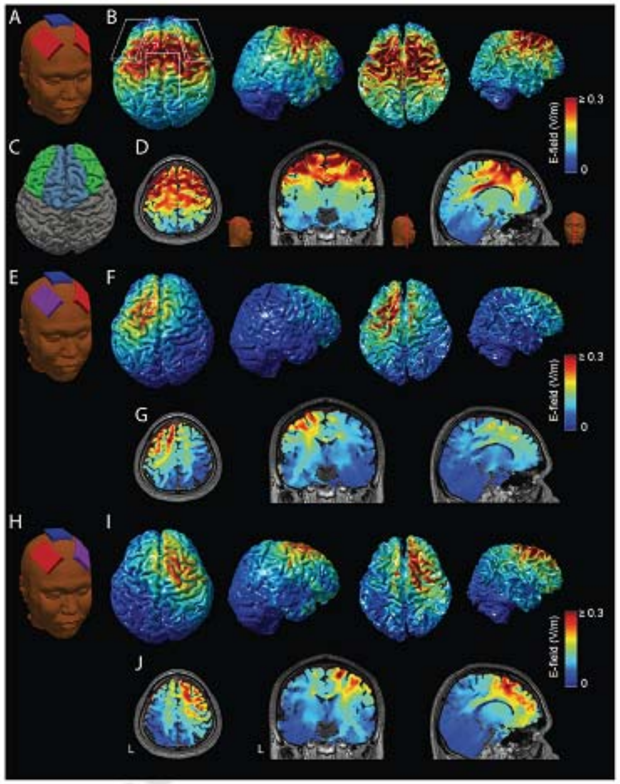
State-Dependency: Can tDCS alone increase intelligence?

Sellers et al. 2015

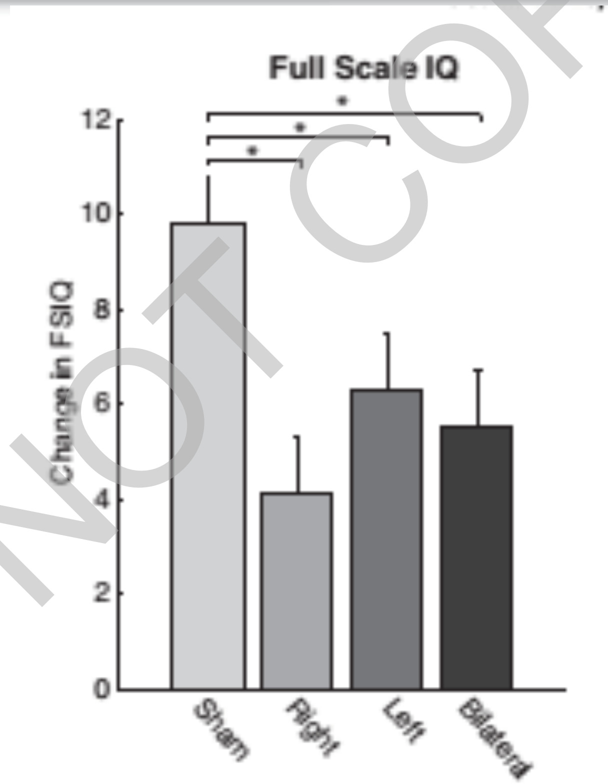
Intelligence Quotient assessment Day 1 → **tDCS (20')** → **Intelligence Quotient assessment Day 2**



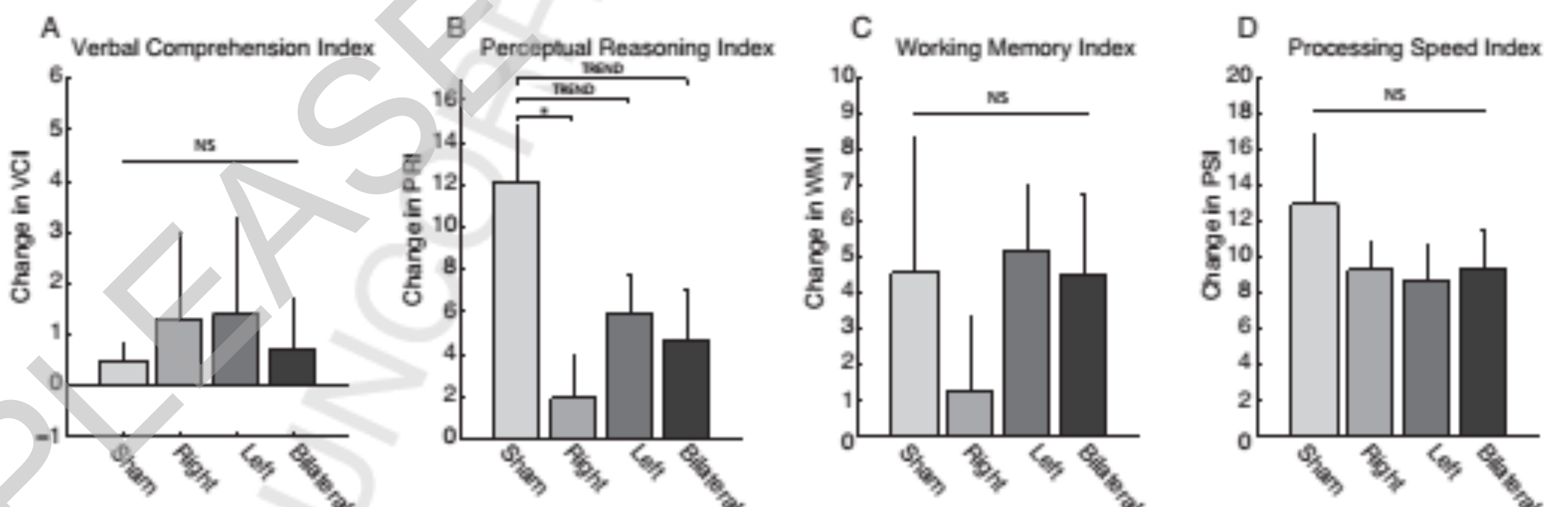
tDCS decreases IQ?



Modeling of electric fields



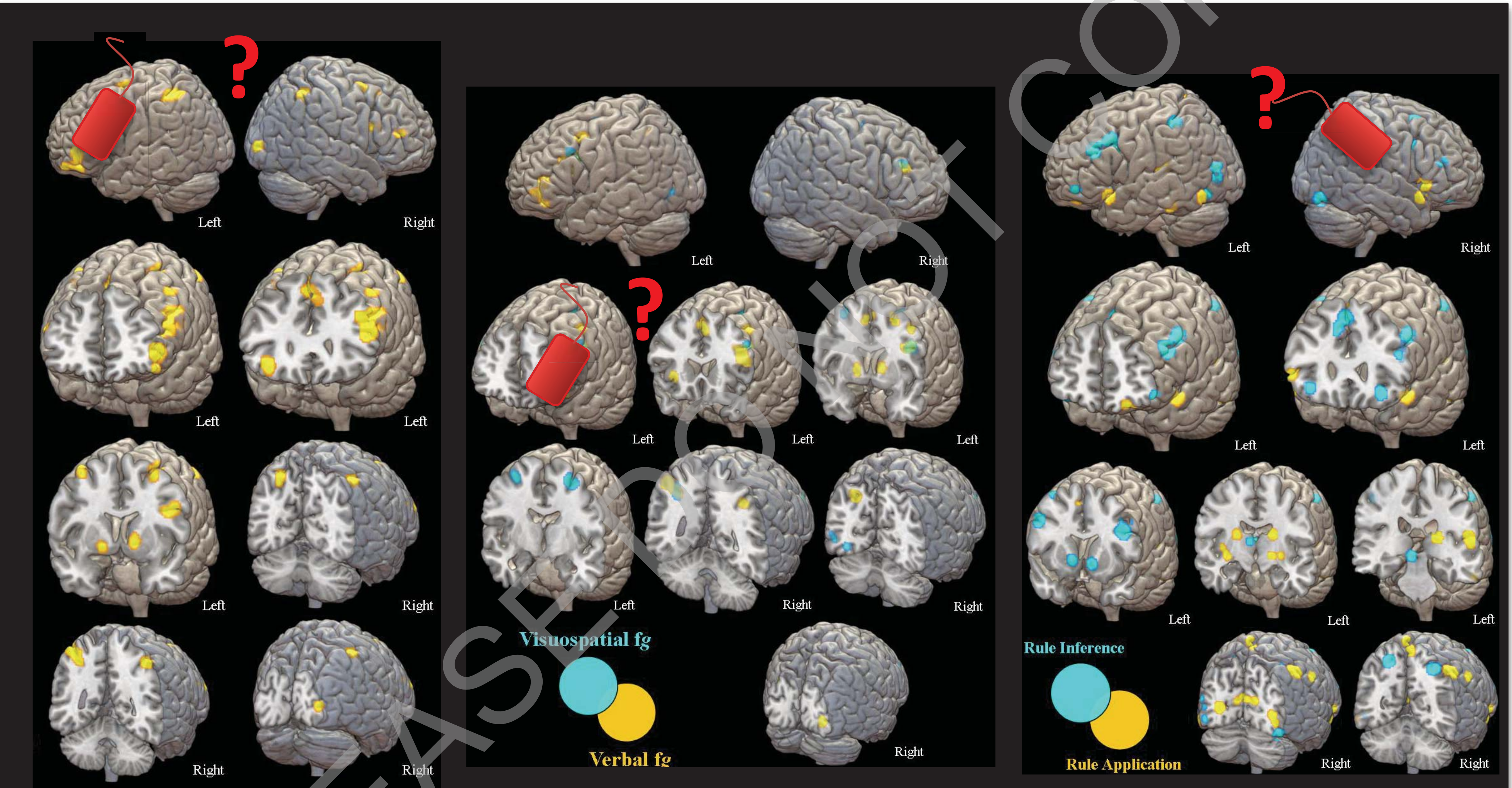
Effect on Intelligence Quotient



Effect on specific indexes of cognitive performance

Cognitive networks

Santarnecchi et al., 2018



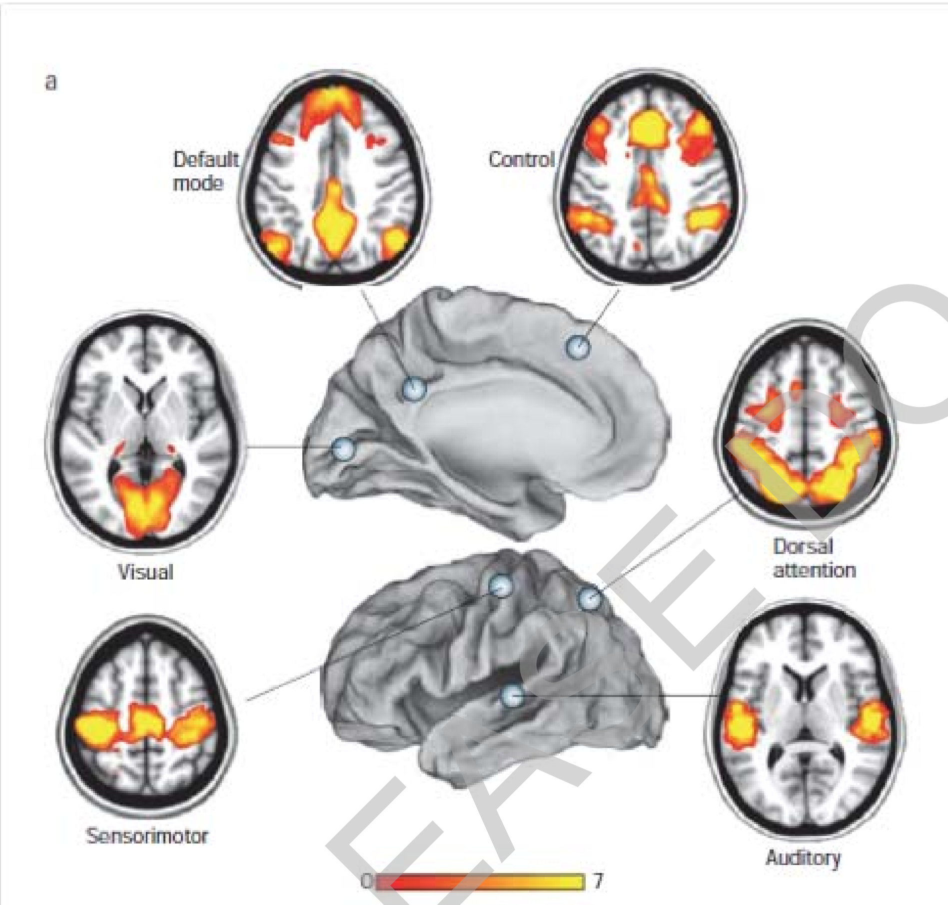
Fluid Intelligence
(20 functional units)

Verbal and Visuospatial
Fluid Intelligence

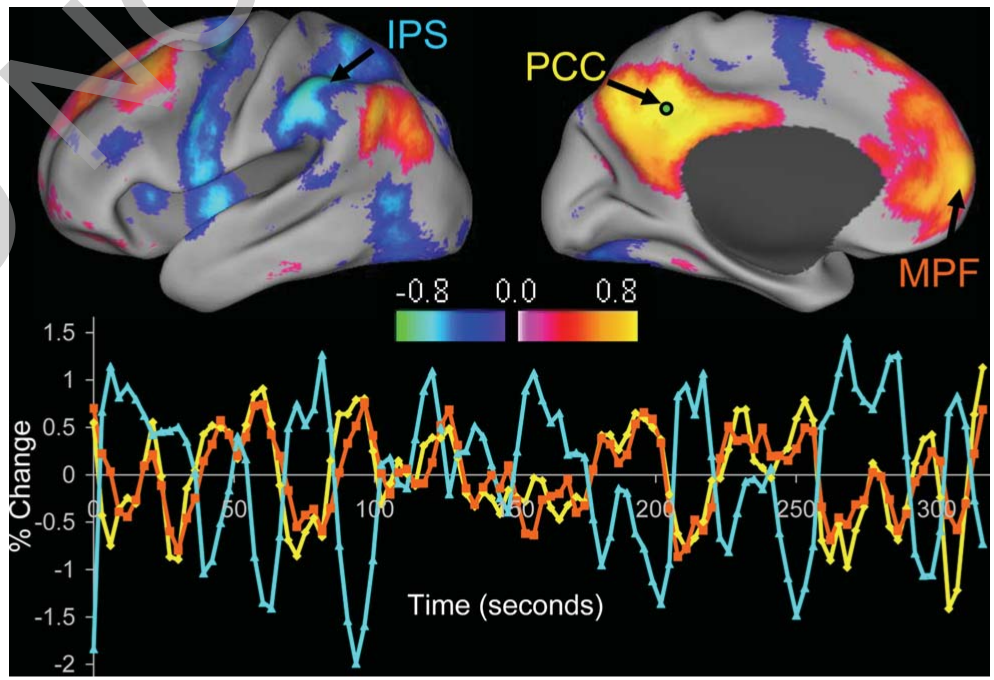
Processing stages
- Rule Inference
- Rule Application

Brain connectivity

- Brain is organized in distinct networks (Zhang et al 2010)
- Negatively correlated networks (Fox et al., 2005)



Resting-State Networks

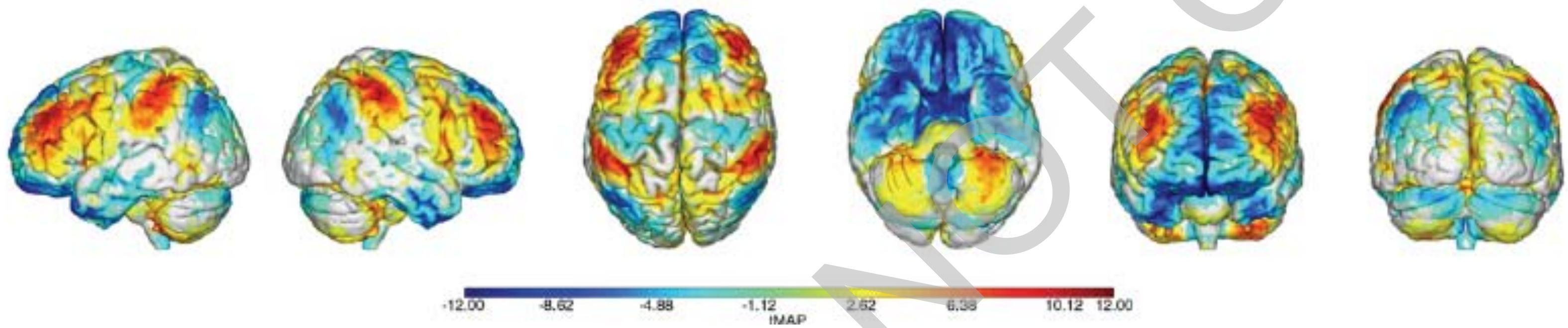


Task positive and Default Mode Networks

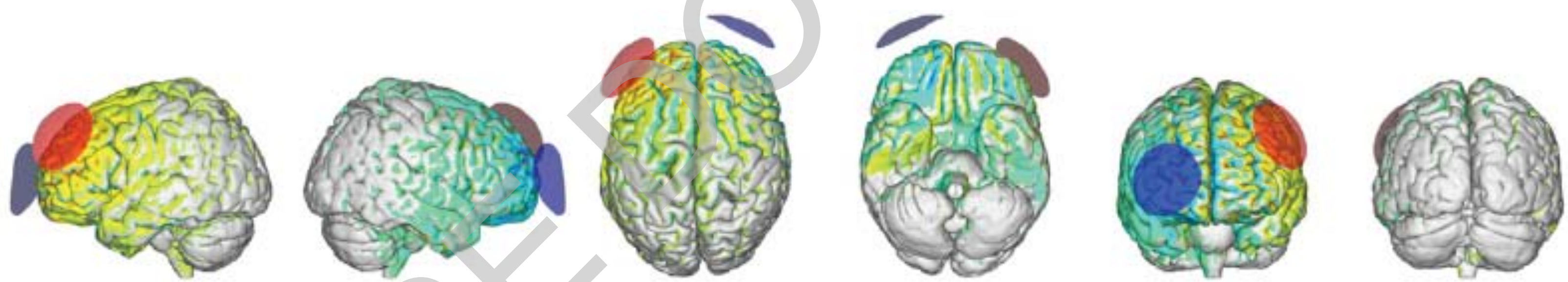
fMRI-based Multifocal tCS

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

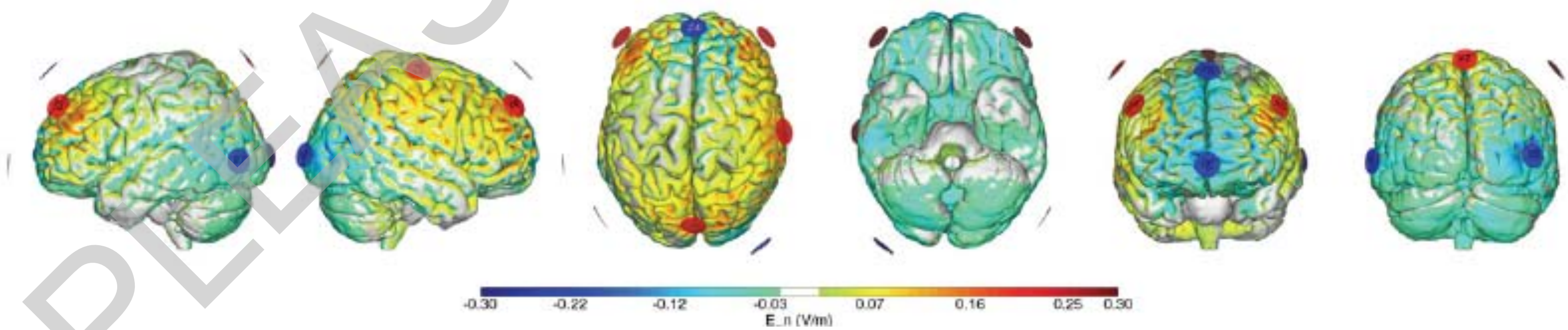
Ruffini et al. 2013



fMRI activation map

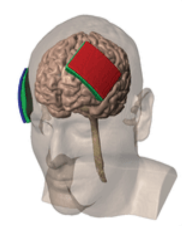


tES solution with 2 electrodes

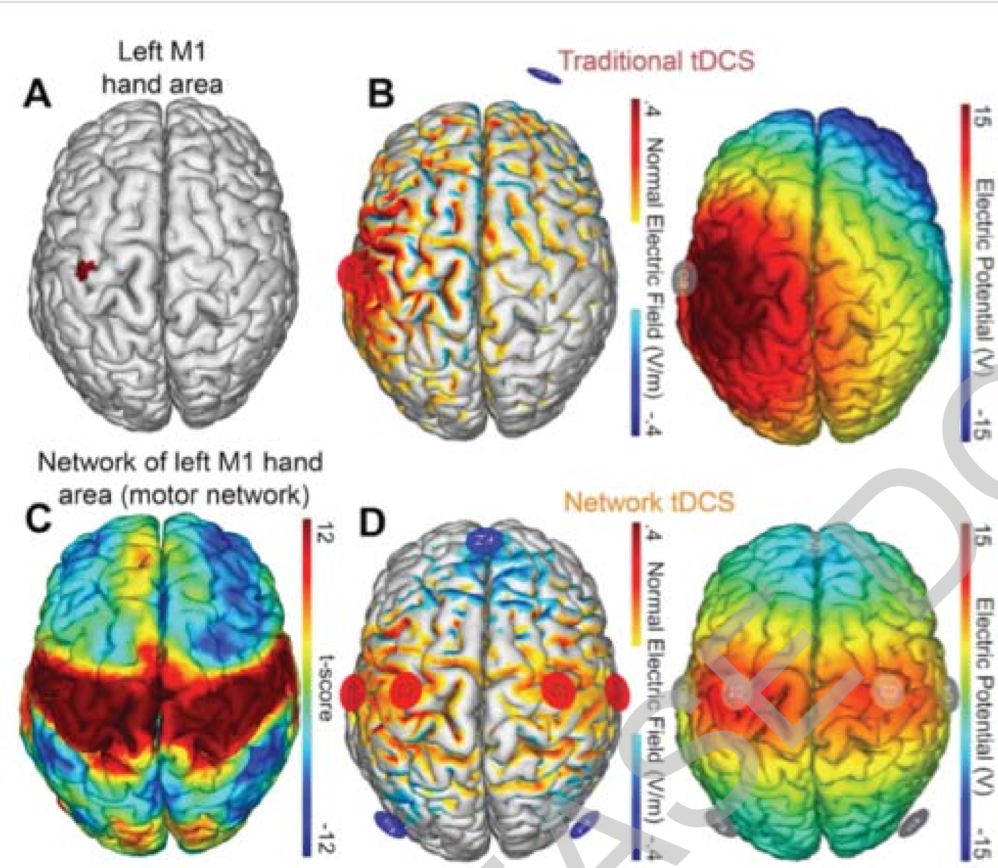


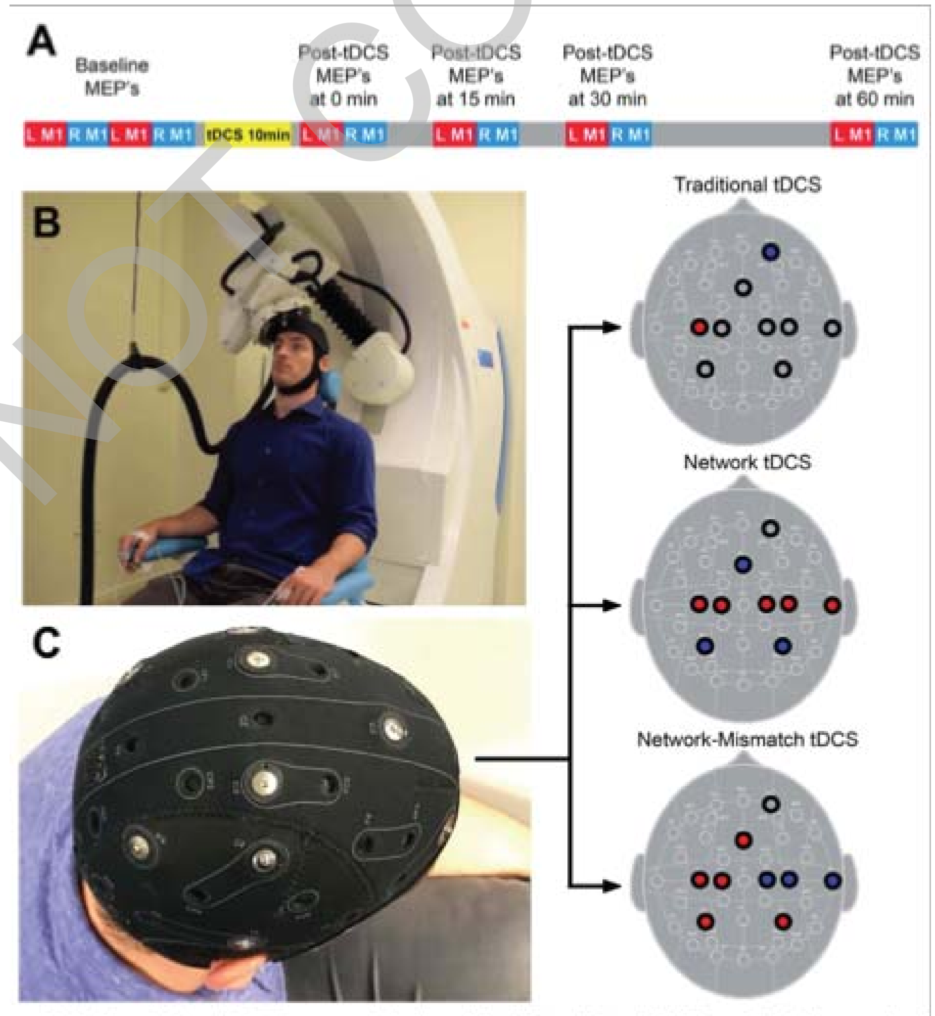
Multifocal tES solution with 8 electrodes

Bifocal vs Multifocal tDCS: effect on Cortical Excitability



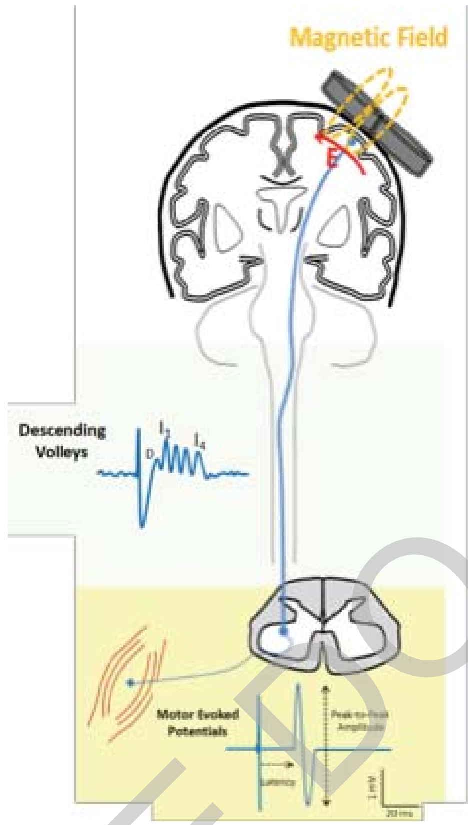
Fischer et al. 2016, Neuroimage





How to measure tCS effects: changes in corticospinal excitability

Measure evoked brain responses using TMS



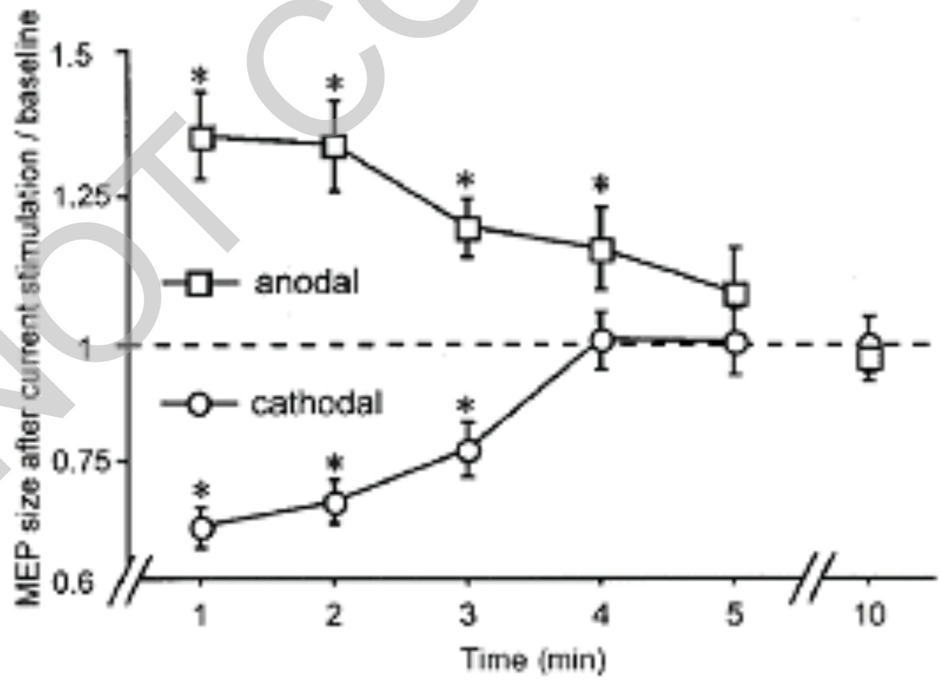


Figure adapted from Nitsche & Paulus, 2000

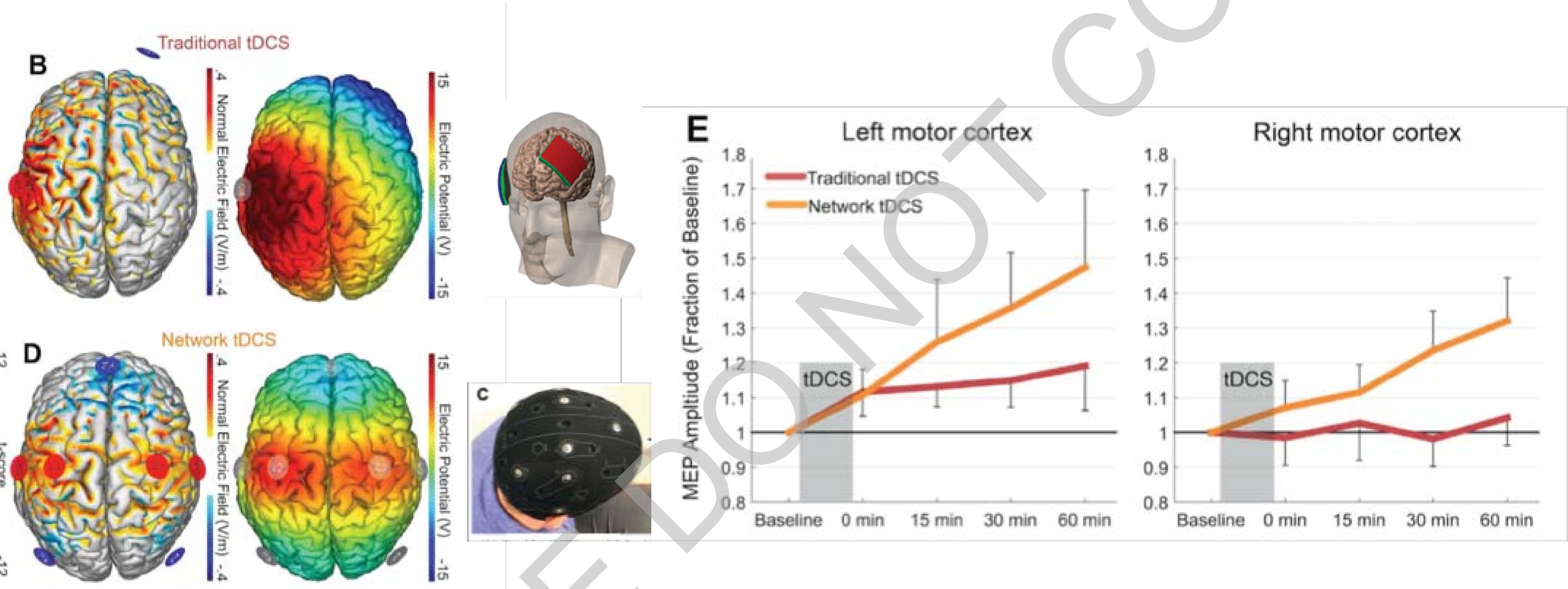
First evidence of tDCS after effect from **Nitsche and Paulus, 2000**

Changes in cortical excitability assessed using TMS-EMG,

anodal tDCS increases excitability, **cathodal** tDCS decreases excitability

Bifocal vs Multifocal tDCS

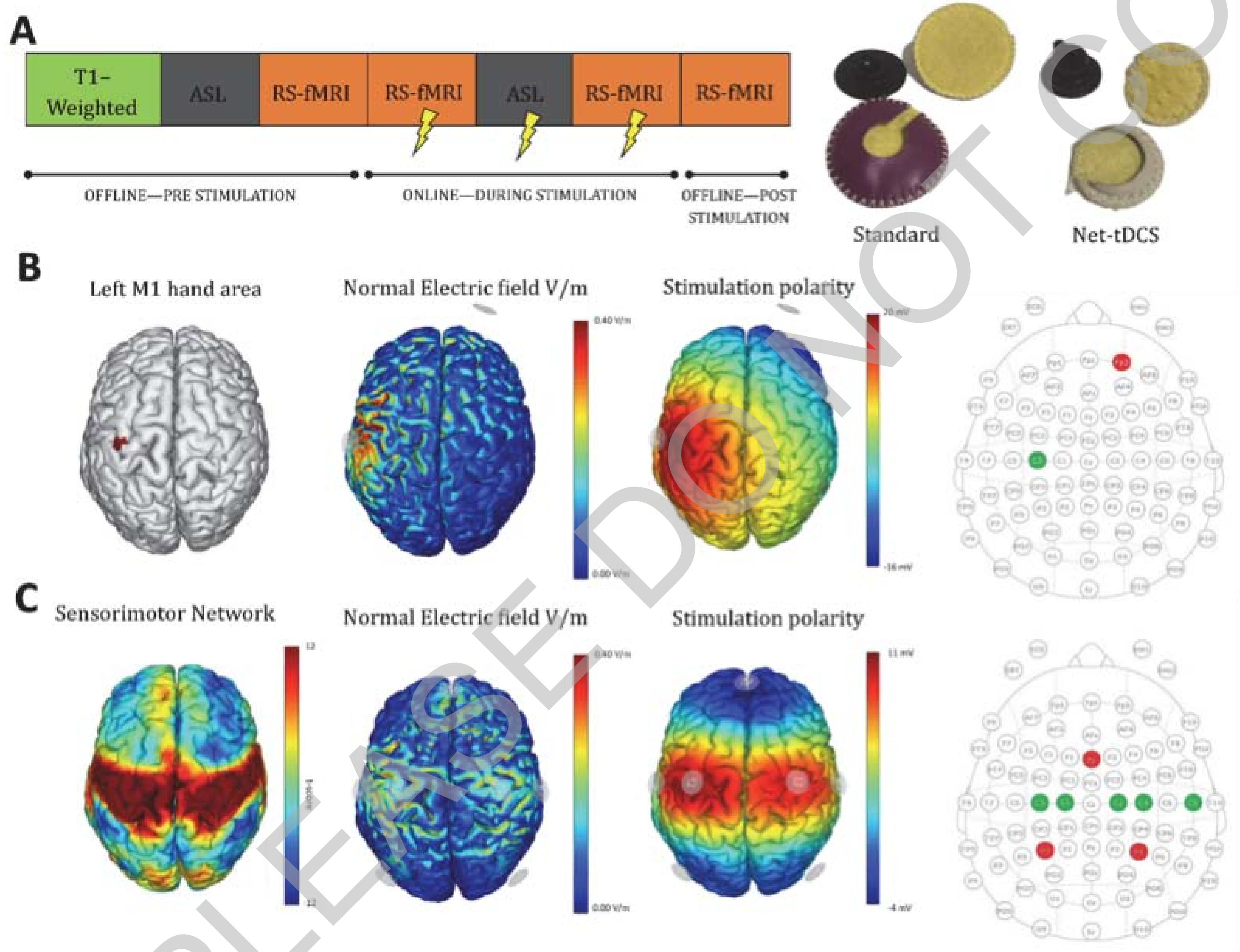
Fischer et al. 2016, Neuroimage



Change in cortical Excitability during and after tDCS

Bifocal vs Multifocal tDCS: Effect on fMRI connectivity

Mencarelli et al., under revision



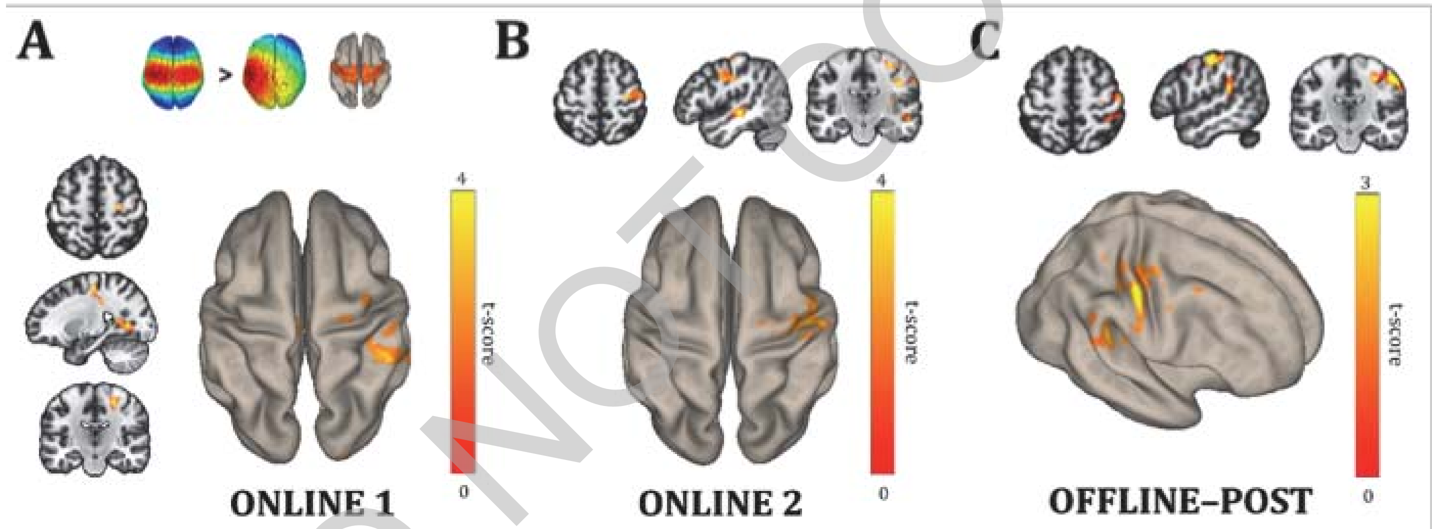
Lucia Mencarelli

Francesco Neri

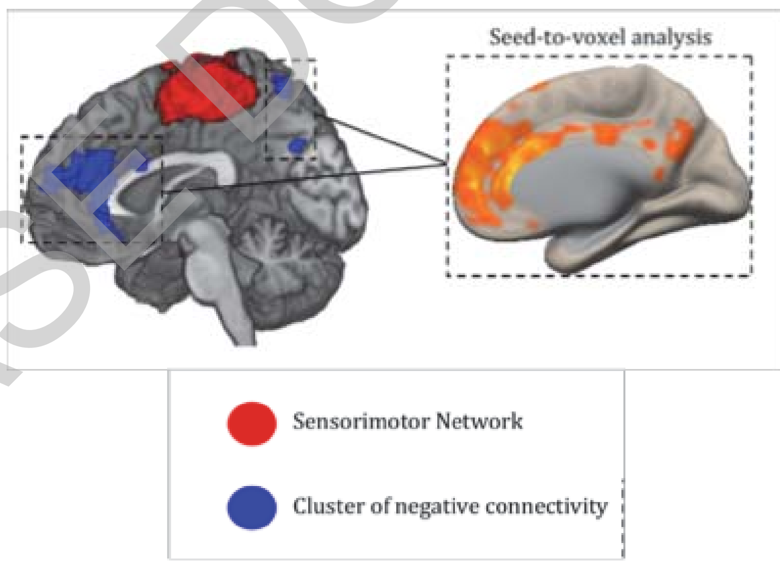
Bifocal vs Multifocal tDCS: effect on fMRI connectivity

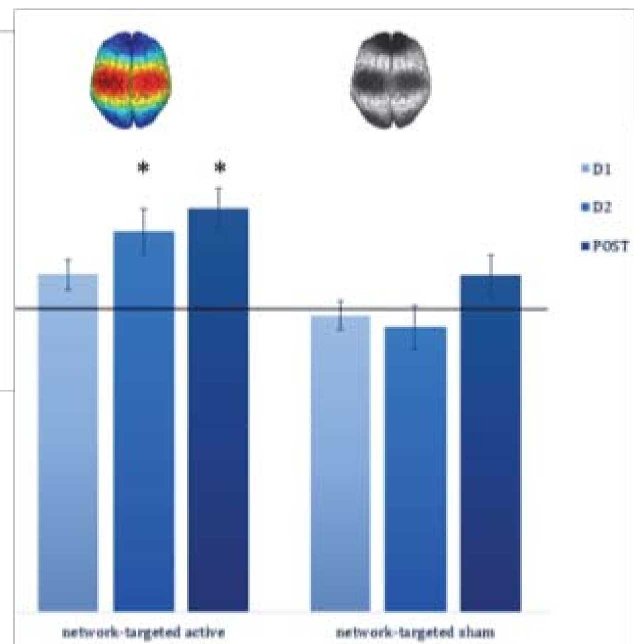
Mencarelli et al., under revision

Within-Network Effect



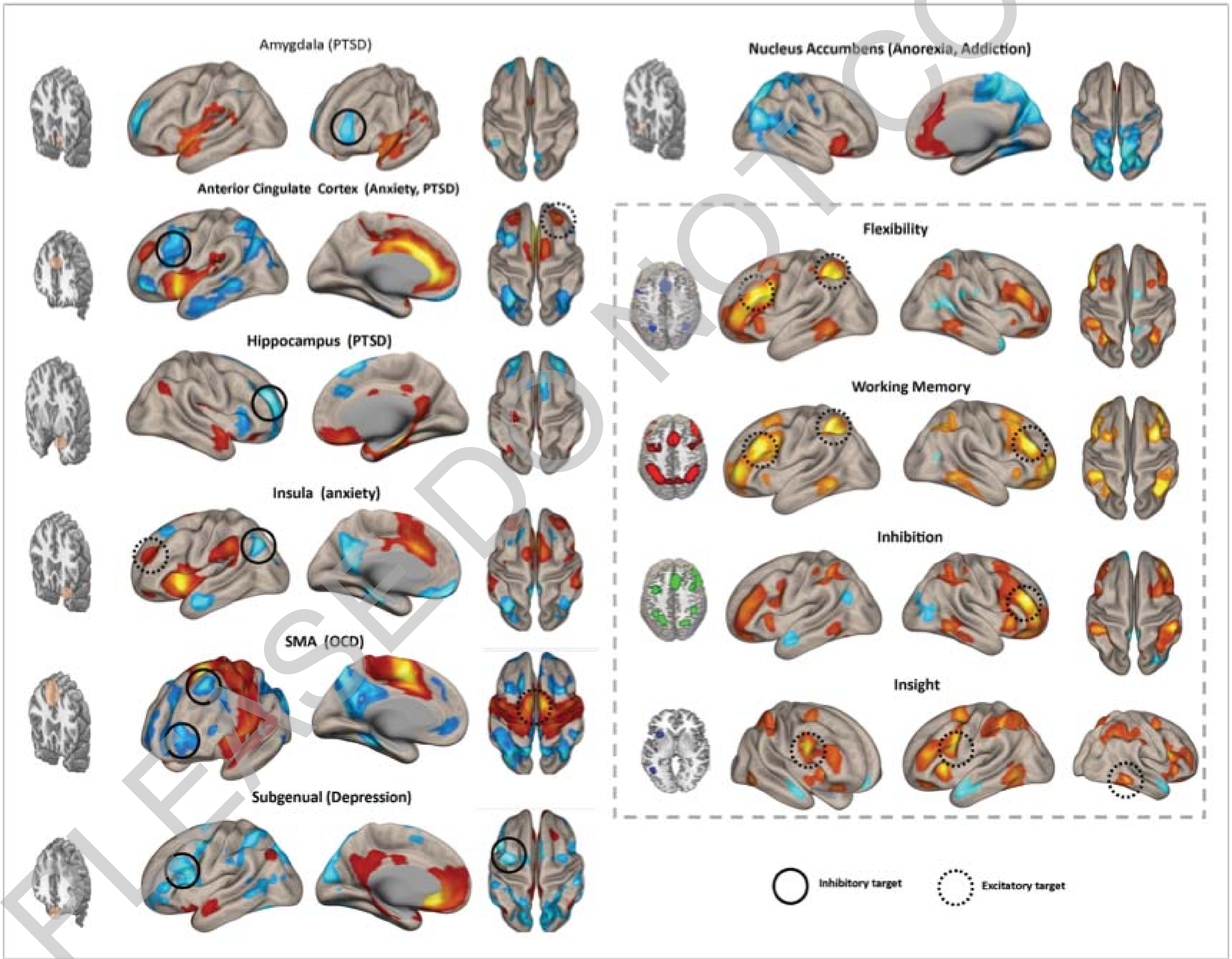
Network-to-Network Effect





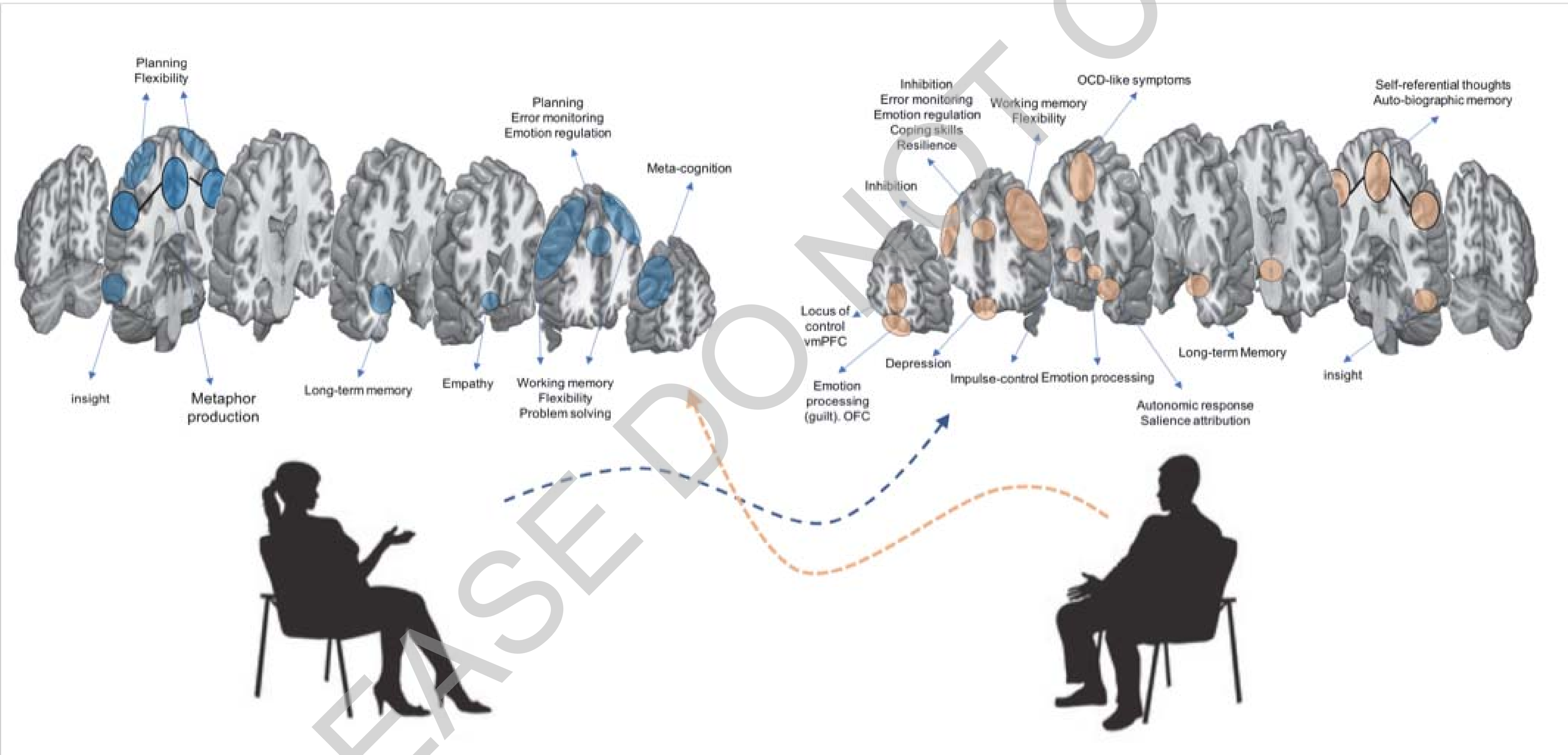
Towards Network-based targeting for clinical applications

Ruffini, Wendling, Sanchez, Santarnecchi
Current Opinion in Biomedical Engineering 2018



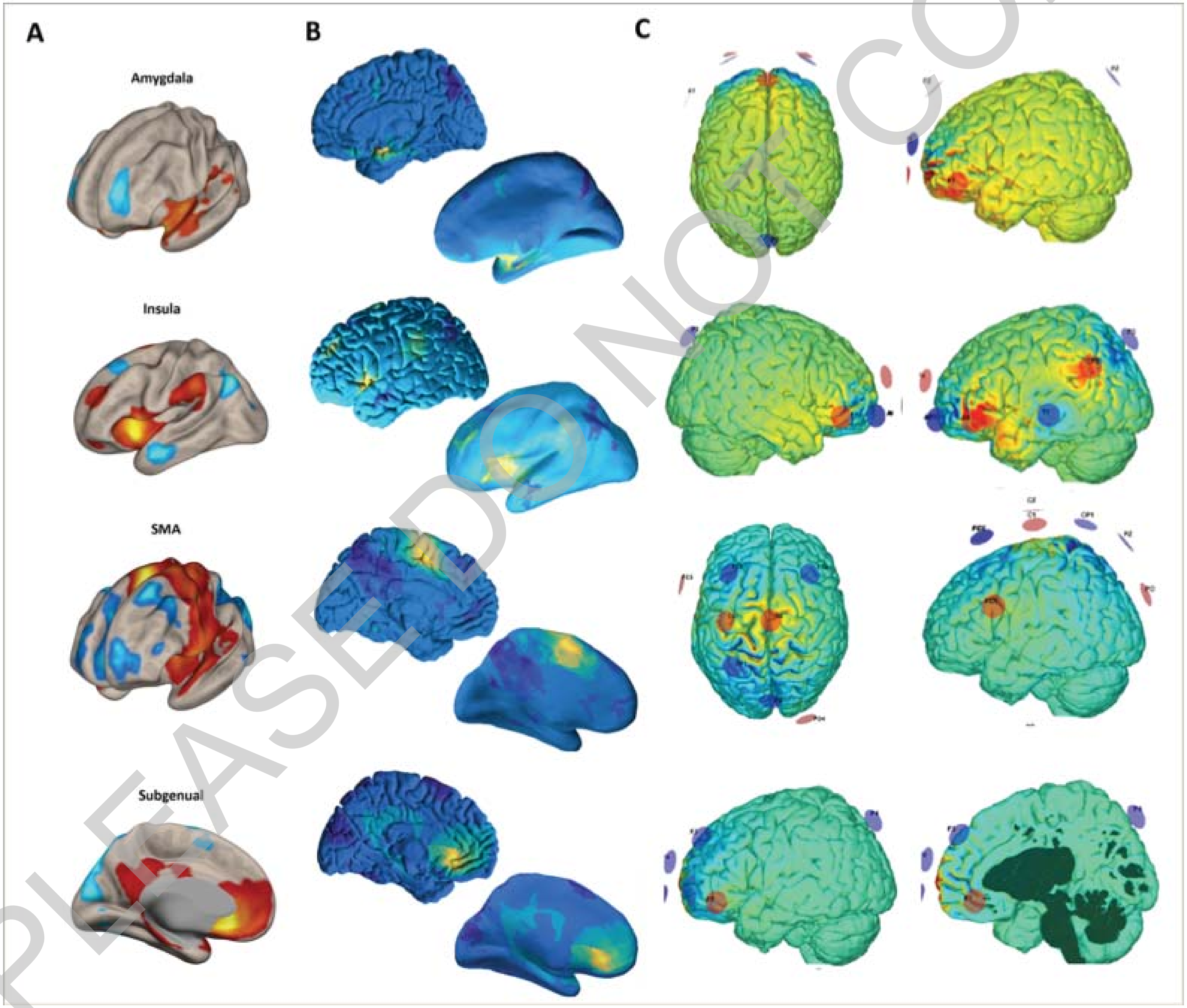
Combine tCS with Psychotherapy

Pachorek et al., submitted



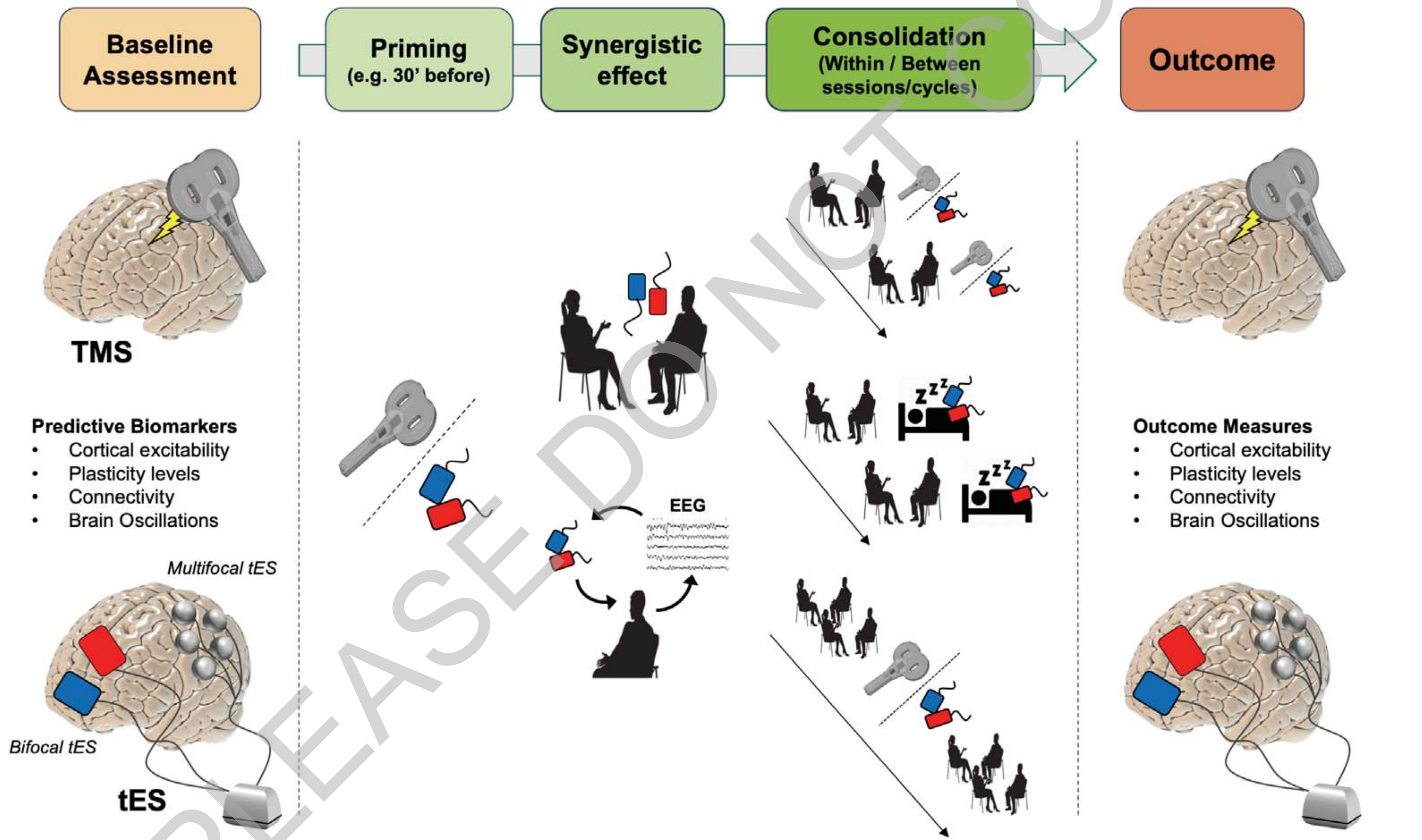
Multichannel tCS targeting connectivity patterns

Pachorek et al., submitted

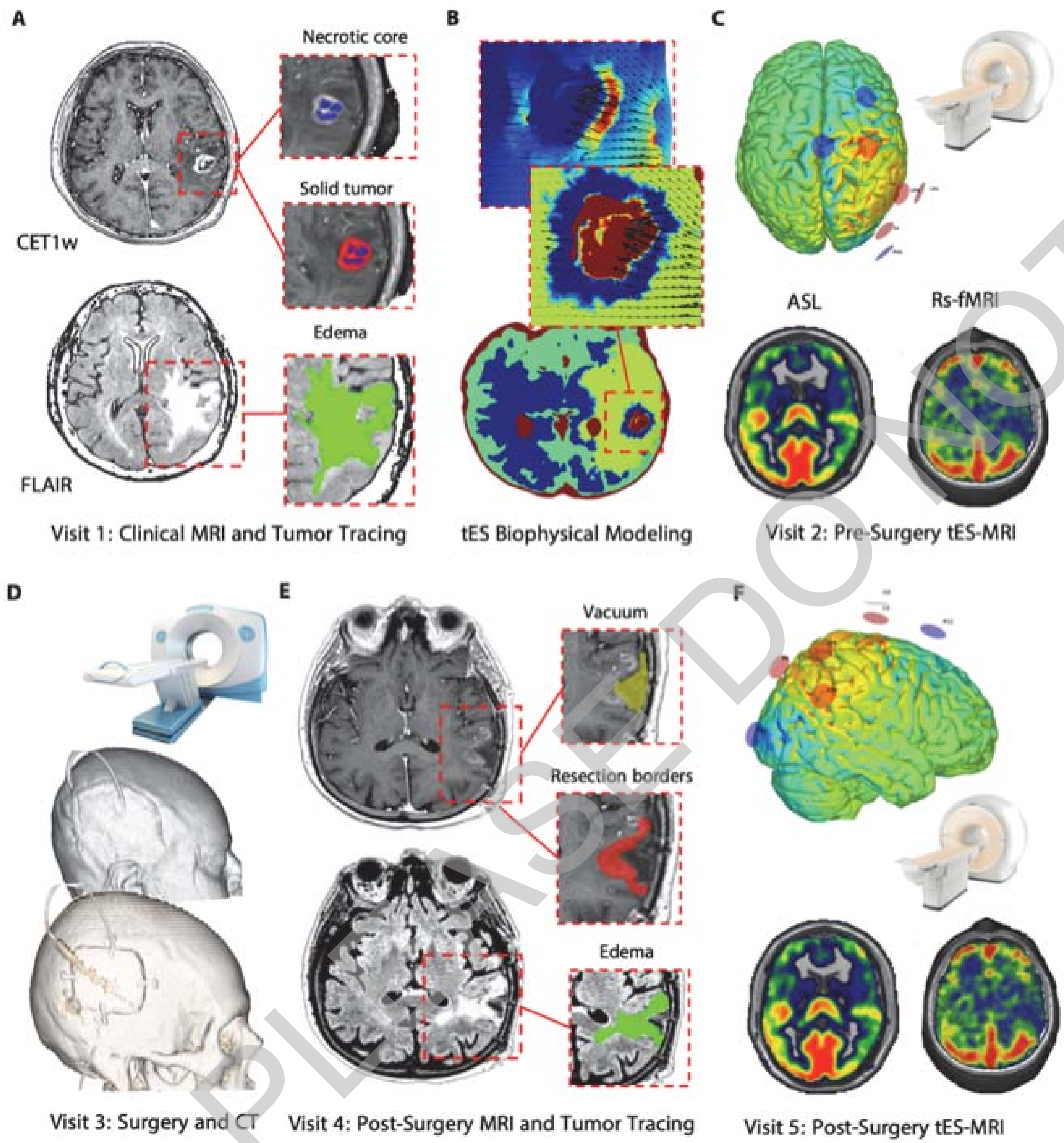


Combine tCS with Psychotherapy: Timing

Pachorek et al., submitted



Safety & Feasibility of Multifocal tDCS in Glioblastoma and Metastasis

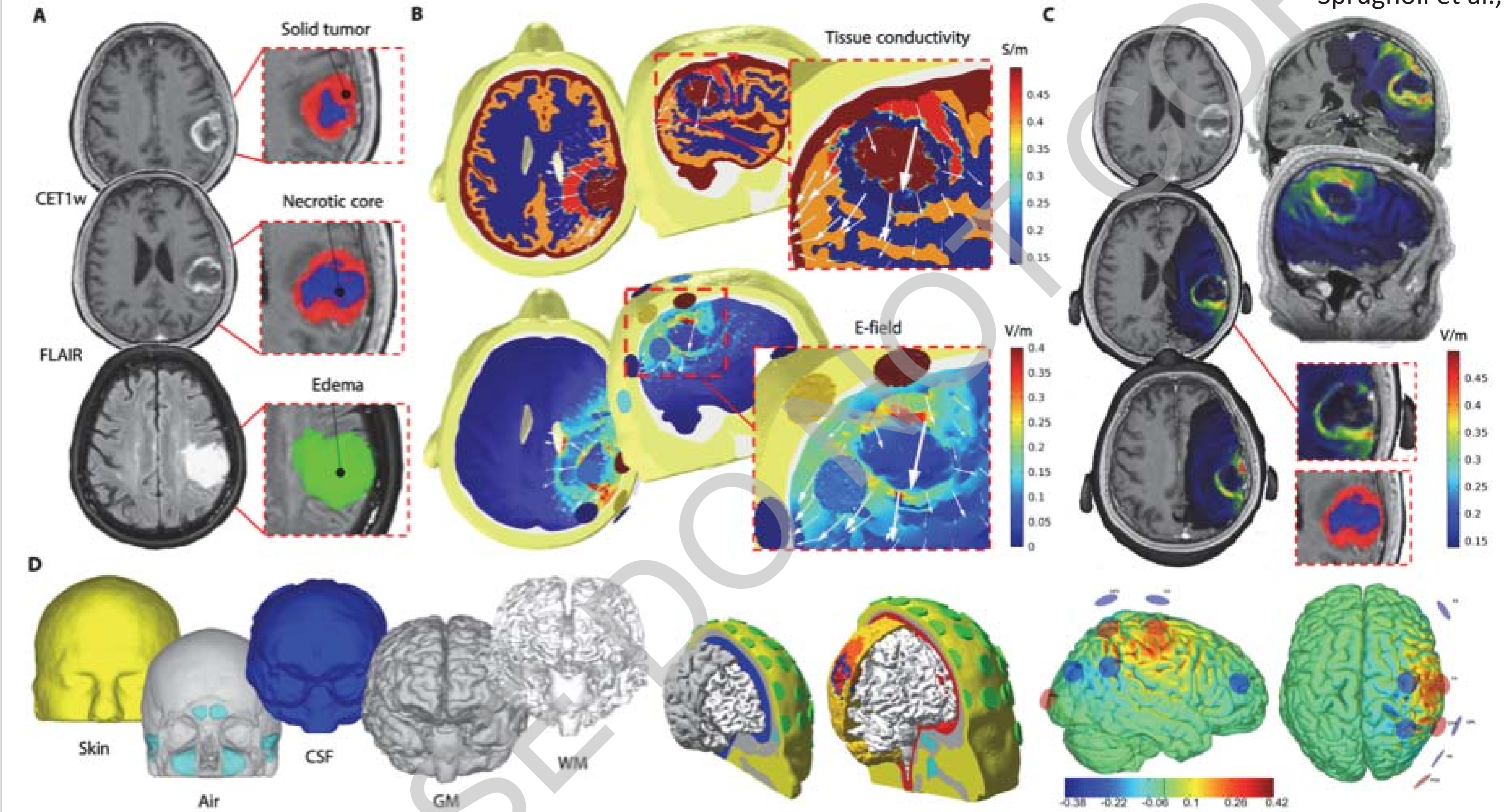


Sprugnoli et al., accepted

Experimental Design. (**A**) Patients underwent a clinical MRI in order to define and characterize the brain tumor, including standard and CET1w, T2w, FLAIR, ASL and resting-state fMRI images. Regions of Interest (ROIs) were defined by parcellating the solid component as the necrotic core of the tumor (metastasis in this example) using CET1w sequences, and the edema surrounding the tumor by using FLAIR images. (**B**) Conductivity values were assigned to each ROIs as well as to healthy brain tissue according to existing literature (lower panels), then E-field distribution of current was calculated (upper panel). (**C**) The personalized multielectrode solution maximizing the E-field on the solid-edema interface was selected. The experimental session was planned 3-5 days preceding the surgical intervention and multichannel tES was performed inside the MRI scanner by means of an MRI-compatible brain stimulation device. The stimulation session included the acquisition of (i) T1w, FLAIR, ASL and rs-fMRI sequences before tES, (ii) rs-fMRI and ASL during tES, and (iii) FLAIR images after tES. (**D**) Roughly 1 week after the pre-surgery MRI, patients underwent neurosurgery with subsequent histological classification and immediate post-surgery CT acquisition. (**E**) Finally, one month after neurosurgery, selected patients underwent a new MRI acquisition and ROIs segmentation in order to perform a second MRI-tES session (**F**), aiming at evaluating the safety and feasibility of applying tES after neurosurgery. Additional modeling based also on CT scan was performed to account for the effects of skull defects created by craniotomy. This was important to ensure safety and to study/quantify changes in electric field distribution in the presence of skull breaches.

Biophysical modeling of Pre-Surgical data and Montage Optimization

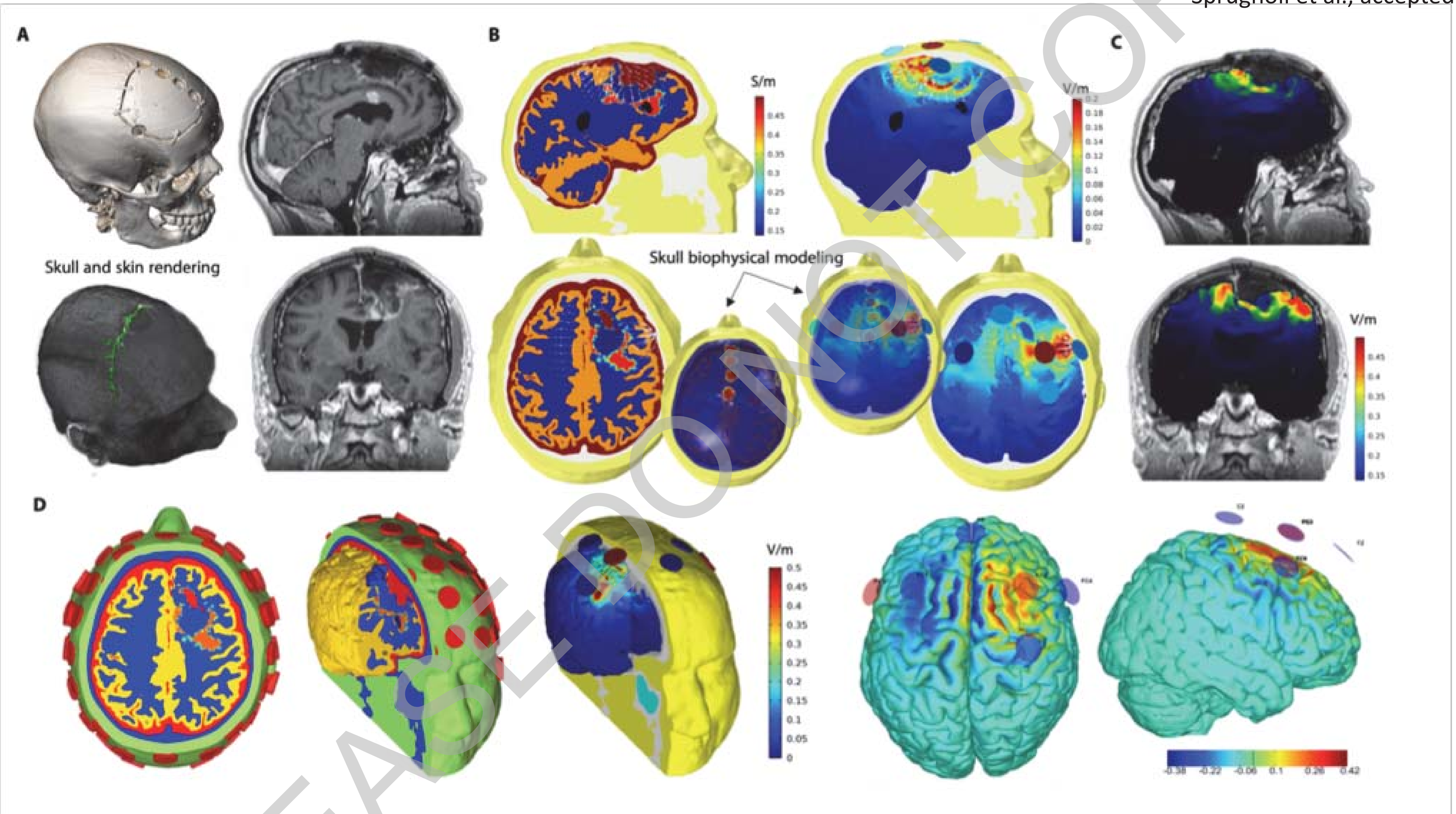
Sprugnoli et al., accepted



Tumor Tracing, Modeling and Optimization. (**A**) MRI images were manually segmented by two independent investigators using MRIcro software and 3DSlicer. Following the RANO recommendations, the solid part (red) of the tumor (GBM in this example) as well as the necrotic core (blue) were identified on CET1w images. The edema (green) was segmented using FLAIR images. In the post-surgery phase, T2 TSE scans were used in order to correctly identify the vacuum created by the surgical intervention. (**B**) Conductivity values were assigned to each ROIs as well as to healthy brain tissue according to existing literature: grey and white matter, CSF, skin, skull. A multi-electrode solution maximizing stimulation over the edema-solid tumor interface was identified for each patient, with the corresponding E-field distribution calculated on patients' head models (B, lower panel). Resulting E-field was overlaid onto individual anatomical T1w scans, showing specificity of the tES solution targeting the solid tumor (**C**). (**D**) T1w MRI of the subject was segmented into multiple tissue classes using MARS, the SPM-8 segmentation toolbox and FreeSurfer (left). Models of PITRODE electrodes (cylinders, 1 cm radius) were placed in the scalp positions corresponding to the 10/10 EEG system (green circles, center). A genetic algorithm was then used to estimate the best multi-electrode solution among those possible using 32 positions on the scalp (center), with the final personalized tES montage including up to 8 electrodes (right).

Biophysical modeling of Post-Surgical data and Montage Optimization

Sprugnoli et al., accepted



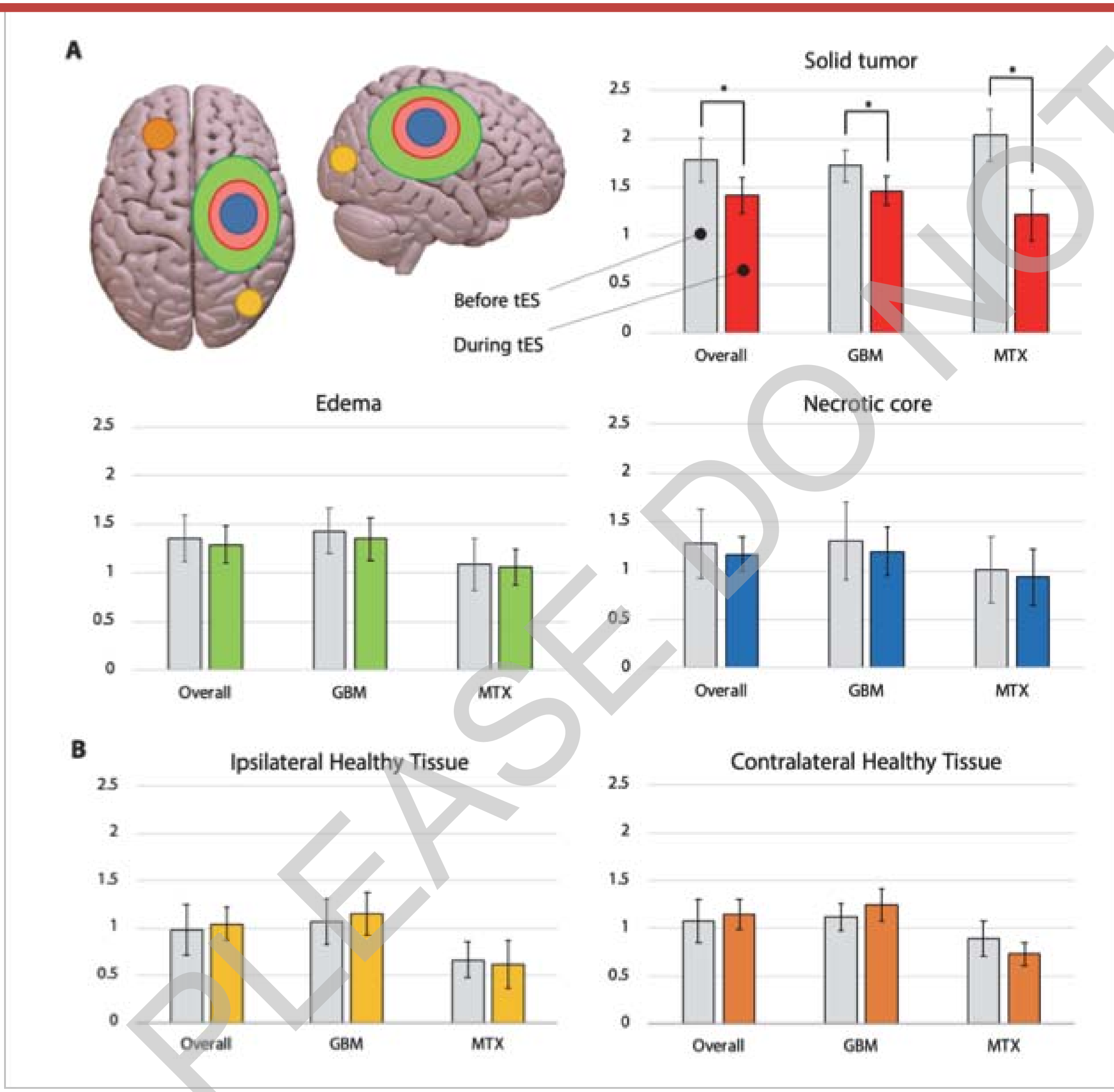
Post-surgical modeling. (**A**) Structural MRI and CT images were used to model the impact of tES after surgery (shown: complete resection of a GBM). Ad-hoc ROIs and 3D renderings were created for both skull breaches and metallic clips that could respectively favor current shunting and affect electrodes positioning. (**B**) New tissue conductivity values were derived by assigning skull defects a conductivity equal to that of the CSF (left), and the amount of current (i.e. E-field) shunting through them was estimated (right). (**C**) A new multi-electrode stimulation solution was implemented to maximize stimulation over the resection borders, showing high spatial specificity and control of induced E-field. (**D**) In details, new geometries of the different head tissues (healthy ones and ROIs) were computed after surgery, leading to a new optimized montage maximizing the current on the surgical borders.

RESULTS: Reduction of intratumoral perfusion (solid part)

Sprugnoli et al., accepted

Science Advances AAAS

1) No Adverse Events or Side Effects, neither Pre- nor Post- surgery
2) Selective Decrease of Intratumoral perfusion during stimulation (~-36%)



Perfusion changes. (**A**) Significant reduction in white matter-corrected CBF was observed in the solid tumor during stimulation for both patients with GBM and MTX ($p < 0.001$), as compared to no changes in the edema ($p < 0.328$) and necrotic core ($p < 0.294$). (**B**) Control ROIs in the contra- and ipsilateral hemispheres to each tumor did not show significant changes in CBF.

Controversy about efficacy

Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS)

Jared Cooney Horvath*, Jason D. Forte, Olivia Carter

- Included every study of the cognitive effects of tDCS among healthy adults (59)
- Cognitive tasks must be used by 2 or more groups
- Included only studies of single session tDCS
- Spanned executive function, memory, language, and other
- No significant effects of any.

A few studies in each category (~3) ? **Small sample size** ? **Anodal & Cathodal tDCS**

Thank you

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