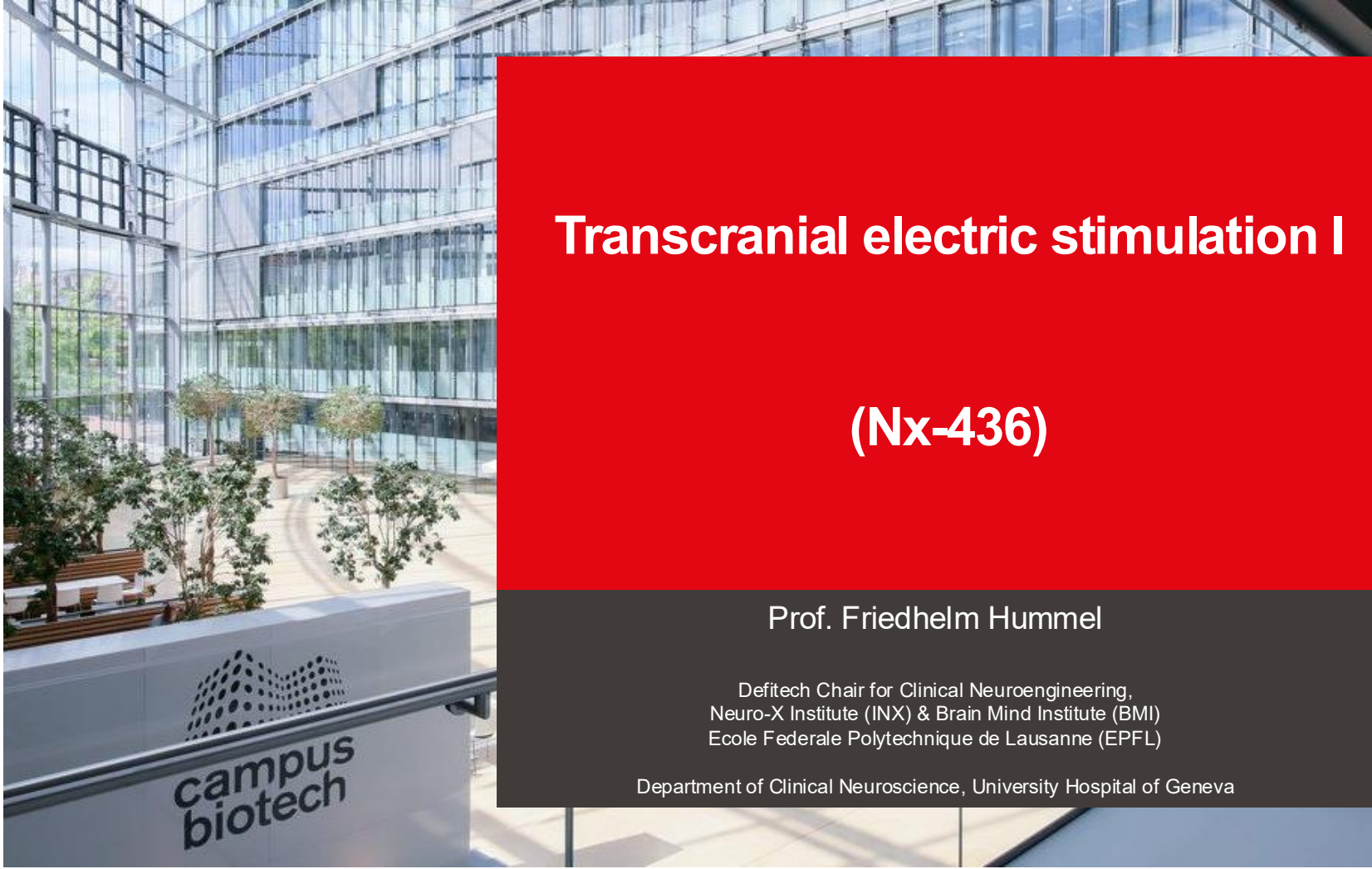
EPFL

Neuro X Institute



Transcranial electric stimulation I

(Nx-436)

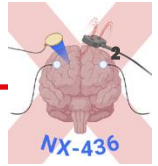
Prof. Friedhelm Hummel

Defitech Chair for Clinical Neuroengineering,
Neuro-X Institute (INX) & Brain Mind Institute (BMI)
Ecole Federale Polytechnique de Lausanne (EPFL)

Department of Clinical Neuroscience, University Hospital of Geneva

Nx-436
05/11/2025

Overview



Three main tES methods for cortical stimulation

- transcranial Direct Current Stimulation (tDCS)
- transcranial Alternating Current Stimulation (tACS)
- transcranial Random Noise Stimulation (tRNS)

Concepts and Mechanims of these tES methods

Applications

Challenges/Limitations

Optimization

Home-based self-appliction

The vision: **Neuromodulation**

Scribonius largus (43-48 AC)

Modifed from Sabatowski *et al.* 1999

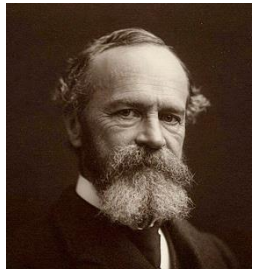
Neuroplasticity

….is the ability of neural networks in the brain

- to change through growth/degradation, dys-/connection (reorganization)
  - from individual synapsis, neurons to
  - whole brain network changes
- thought to be exclusively apparent in the developing brain
- apparent through lifespan

Anatomist MV Malacarne (1744-1816)

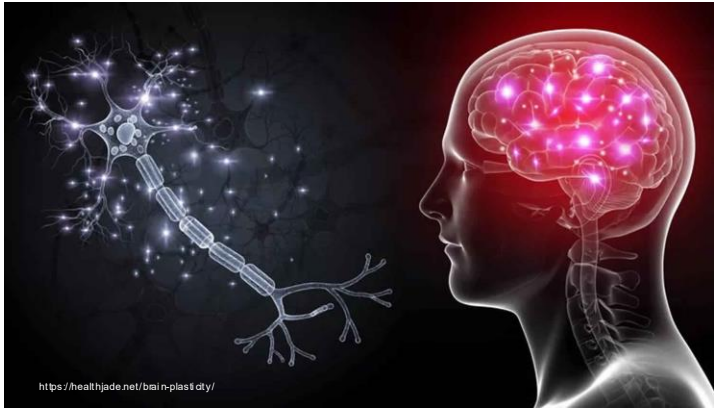
…exps demonstrating neuroplasticity (18th century)



Psychologist W James (1742-1910)

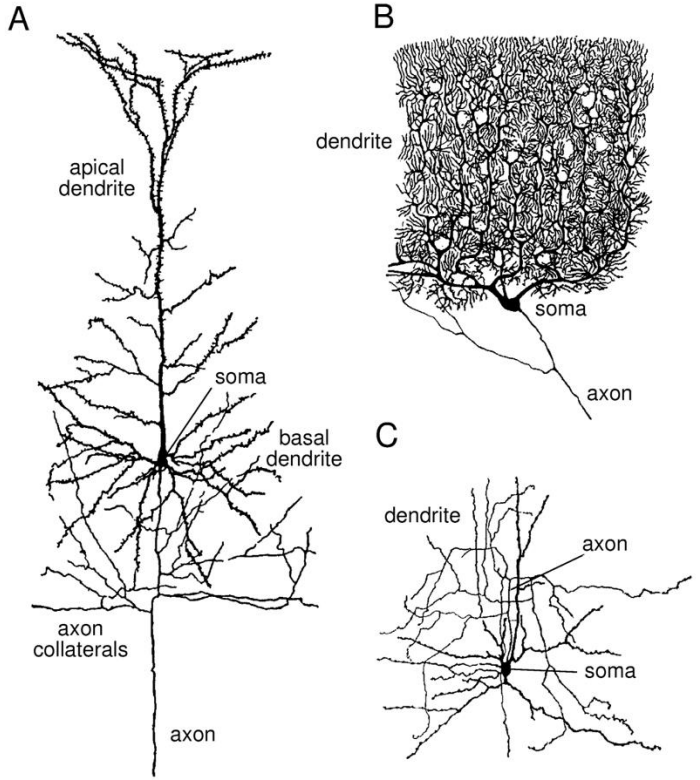
… term / concept first mentioned (19th century)

Neuroplasticity

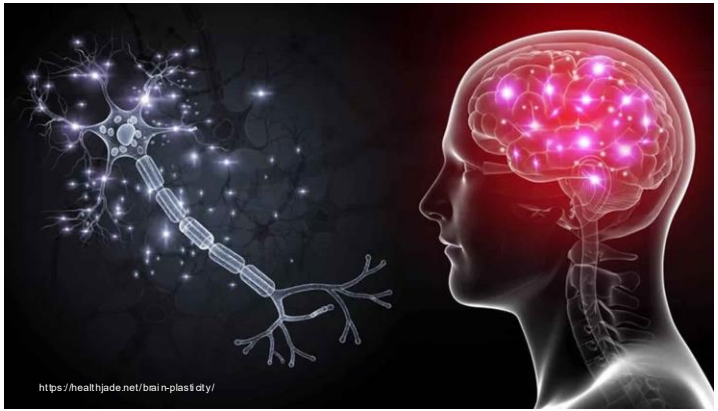


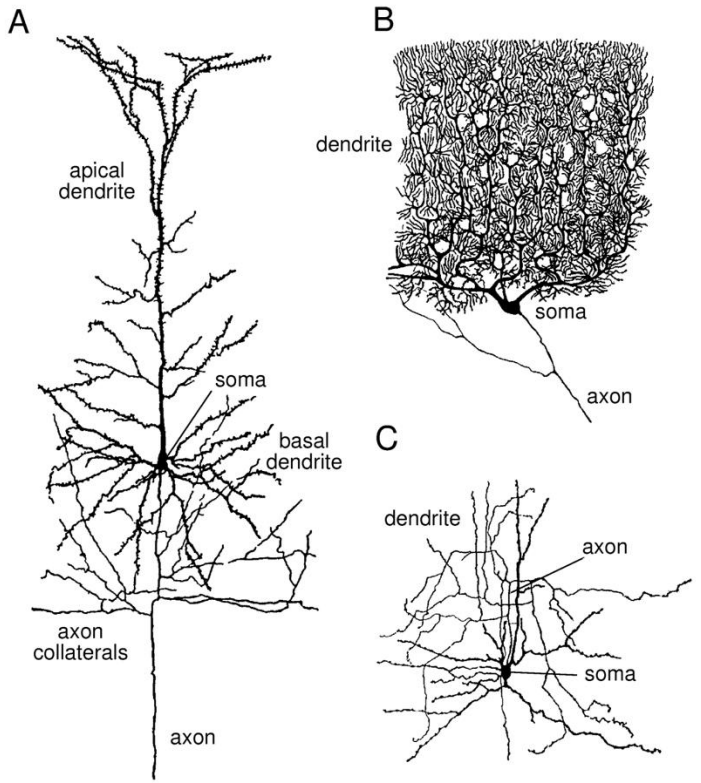
In the cortex more than 10^9 neurons

Each neuron up to 10^4 synapses



Neuroplasticity

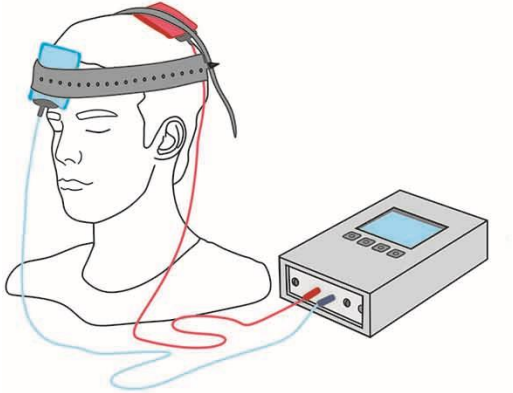




In the cortex more than 10^9 neurons

Each neuron up to 10^4 synapses

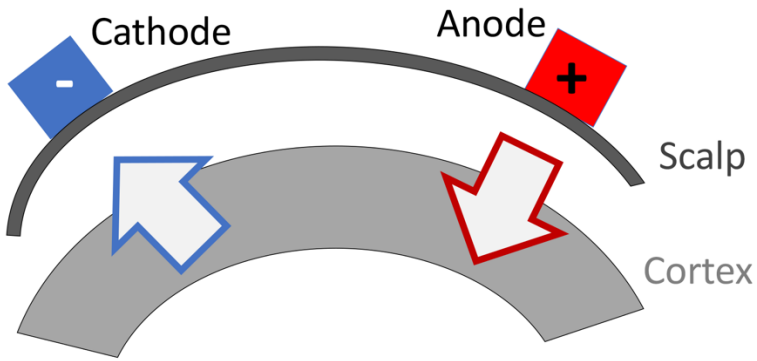
Electric stimulation can impact on these mechanisms



Transcranial Direct Current Stimulation (tDCS)

Neuromodulation with tDCS: Mechanism of action

tDCS changes the resting membrane potential of local neurons at the targeted area of the brain



e.g., for review Hummel & Cohen (2006), Wessel et al (2015), LeFaucheur et al. (2015), Antal et al. (2020), Biksom et al. (2021)

Neuromodulation with tDCS: Mechanism of action

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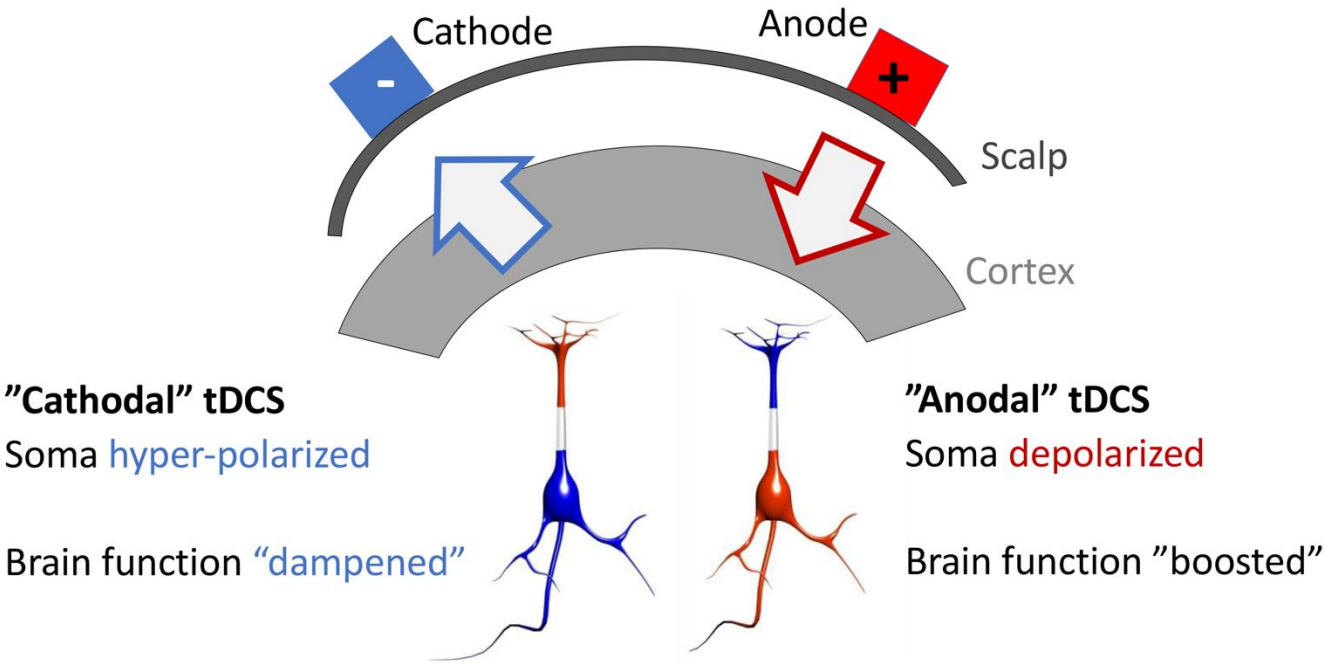

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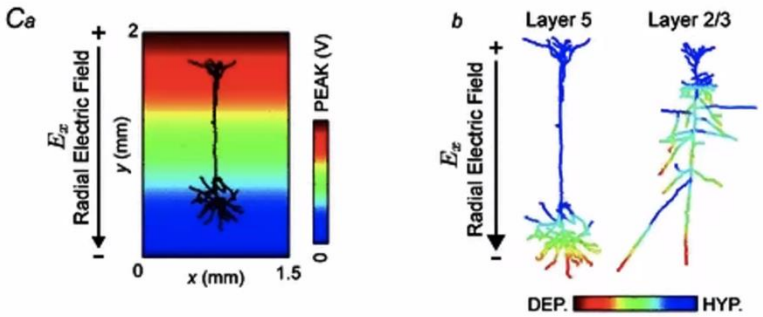
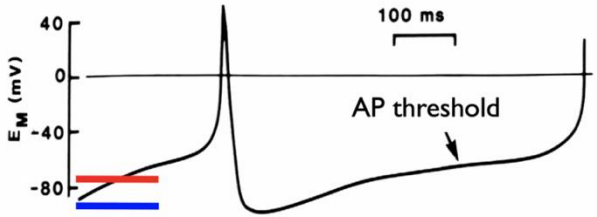


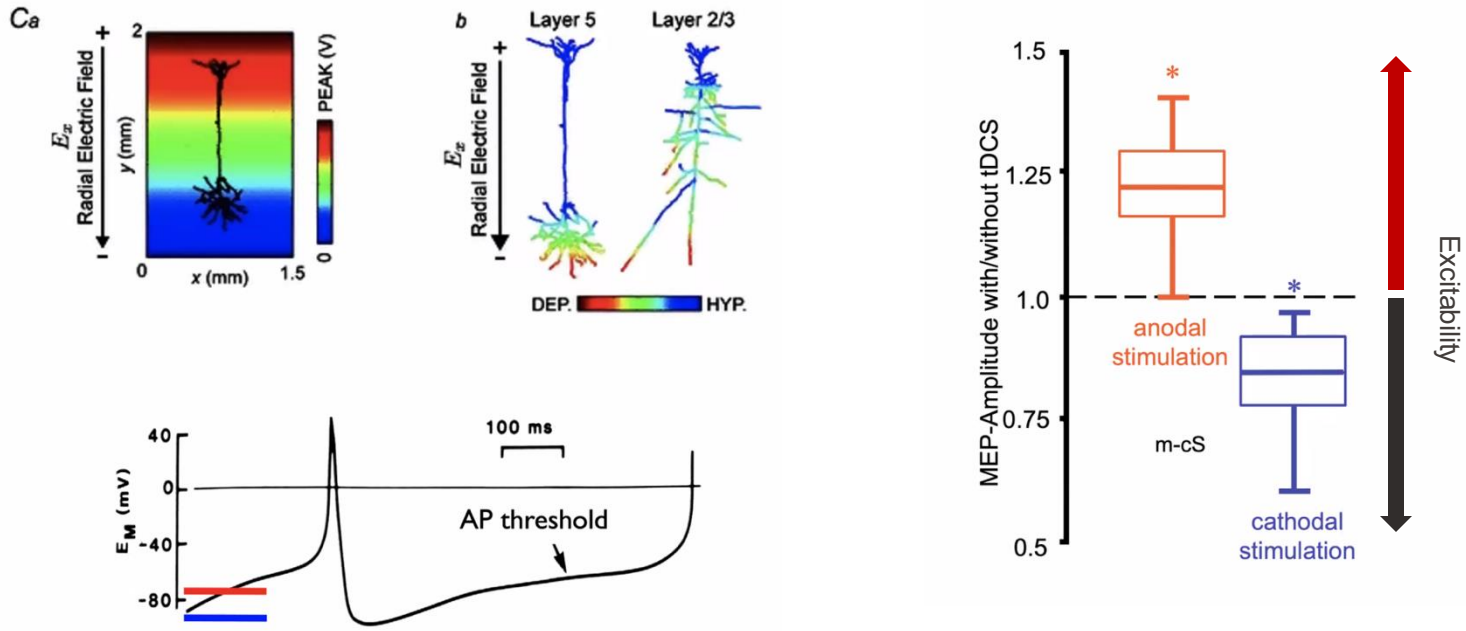
Polarization profile of a layer 5 pyramidal neuron in a radially directed uniform electric field indicating soma depolarization (red) corresponds to apical dendrite hyperpolarization (blue)



During tDCS, the resting membrane potential is depolarized or hyperpolarized by the inflow (positive/negative) of the current.

Rahman et al (2013), Kronberg et al. (2020), Biksom et al. (2021)

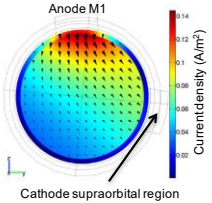
Neuromodulation with tDCS: Mechanism of action

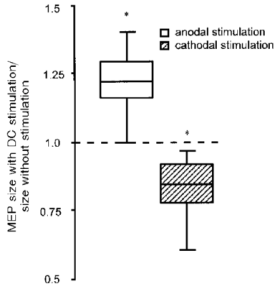


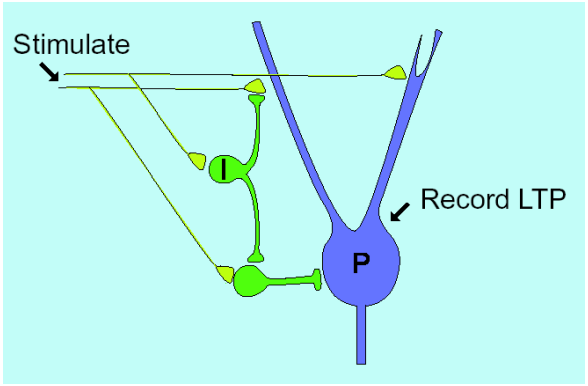
Polarity specific effects of tDCS

Nitsche & Paulus (2000), Rahman et al (2013), Kronberg et al. (2020), Biksom et al. (2021)

Neuromodulation with tDCS: Mechanism of action



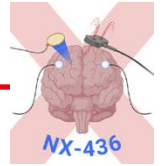




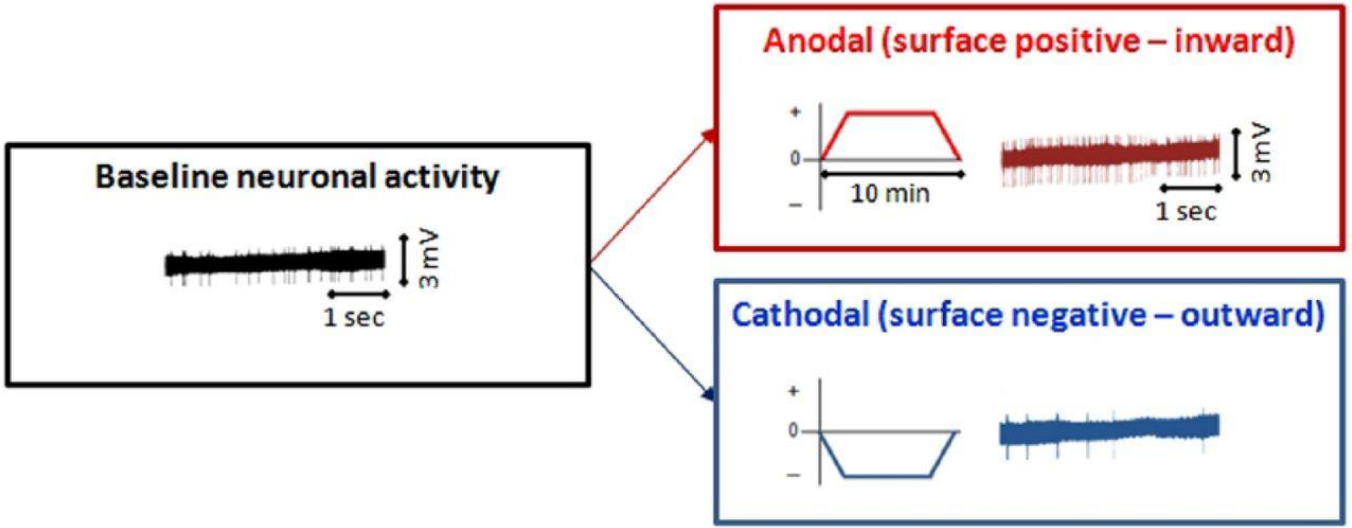
long-term potentiation

- Modulates synaptic efficacy, cortical excitability
- Modulates Neuroplasticity
- Effects are inhibitory or excitatory
- After effects minutes to hours (up to 120min)
- Modulates resting membrane potentials
- Influences Glutamate-ergic, GABA-ergic neurotransmission (pharmacological studies, GABA MRS, dp TMS)

Hallett, Nature (2000); Hummel & Cohen, Curr Op Neurol (2005); Hummel & Cohen, Lancet Neurol (2006)

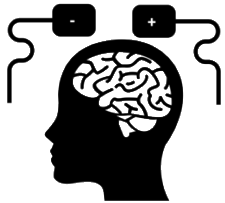


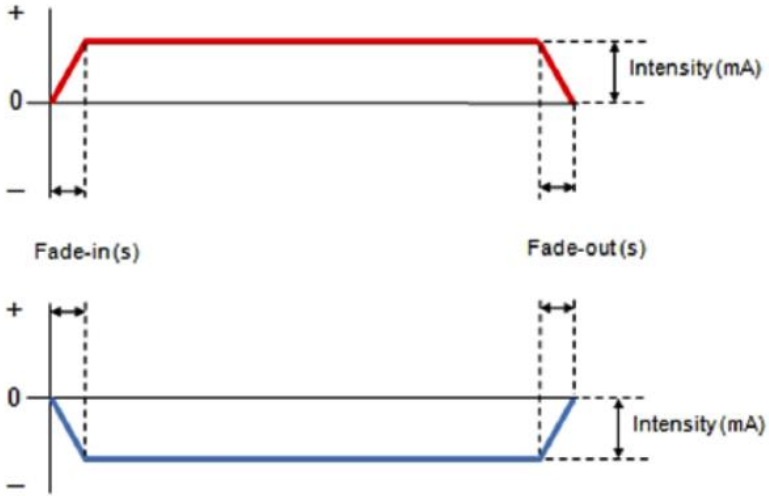
Transcortical direct current polarization (respectively anodal-positive and cathodal-negative) is able to modify the spontaneous activity of a neuron in the visual cortex of a cat.



Adapted from Fertonani & Miniussi Neuroscientist (2016)

Neuromodulation with tDCS





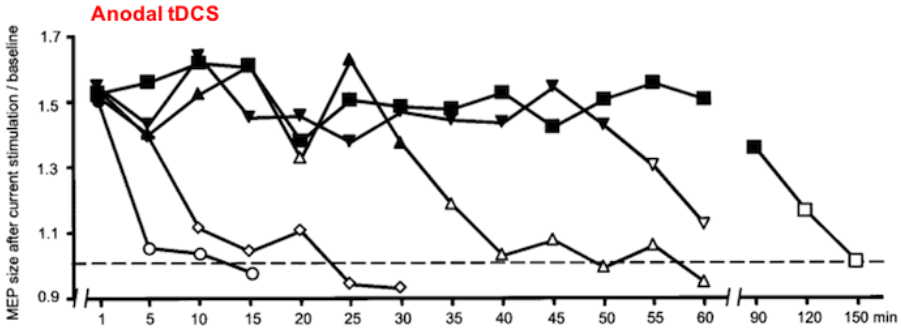
Anodal tDCS

Cathodal tDCS

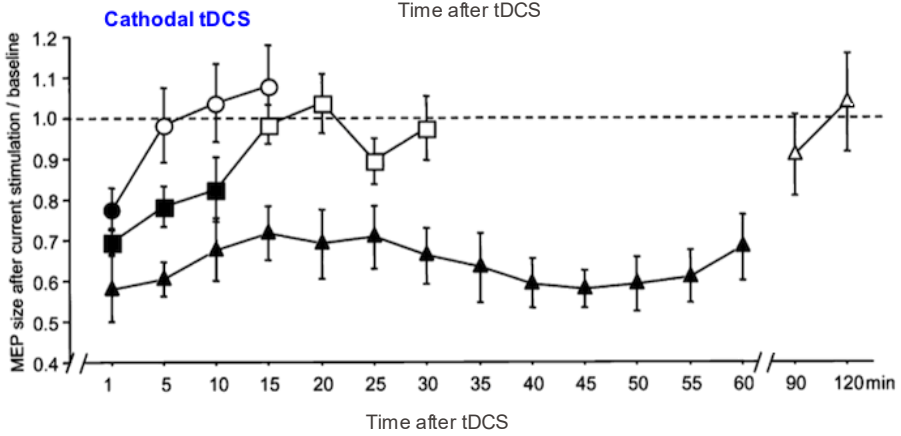
To avoid uncomfortable perceived sensations at the skin the currents are slowly faded-in and faded-out. Provides also good placebo (sham) control.

Neuromodulation with tDCS: Duration of effects

tDCS after-effects depends on the time of stimulation



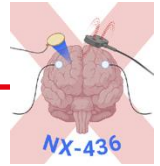
tDCS duration:
Circles - 5 min
Diamonds - 7 min
Upward triangles - 9 min
Downward - triangles - 11 min
Squares - 13 min



tDCS duration:
Circles - 5 min
Squares - 7 min
Triangles - 9 min

Nitsche et al (2001) *Neurology*, Nitsche et al. (2003) *Clinical Neurophysiology*

tDCS



Relatively imple and fairly cost-effective neuromodulation technique!

Potential for wide application in translational/clinical field

- Stroke
- Depression
- Pain

Relevant human studies performed

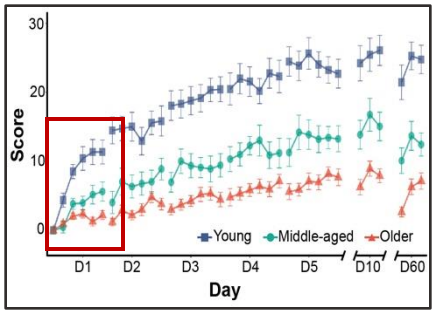
Neuromodulation of Motor learning

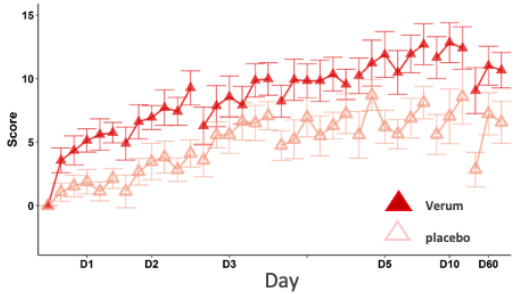
SCIENCE ADVANCES | RESEARCH ARTICLE

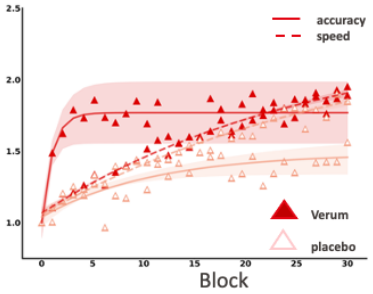
NEUROSCIENCE

Dissecting motor skill acquisition: Spatial coordinates take precedence

Pablo Maceira-Elvira[1,2]†, Jan E. Timmermann[3]†, Traian Popa[1,2]‡, Anne-Christine Schmid[1,2]‡, John W. Krakauer[4], Takuya Morishita[1,2], Maximilian J. Wessel[1,2,5], Friedhelm C. Hummel[1,2,6]*

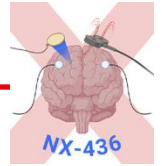






Maceira-Elvira *et al.* (2024) npj learning

Non-invasive brain stimulation (NIBS): Stroke Rehabilitation



doi:10.1093/brain/awh369 *Brain* (2005), **128**, 490–499

Effects of non-invasive cortical stimulation on skilled motor function in chronic stroke

Friedhelm Hummel,[1,2] Pablo Celnik,[1] Pascal Giraux,[1] Agnes Floel,[1] Wan-Hsun Wu,[1] Christian Gerloff[2] and Leonardo G. Cohen[1]

Rapid Review

Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke?

Friedhelm C Hummel, Leonardo G Cohen

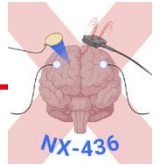
Lancet Neurol 2006; 5: 708–12

REVIEWS

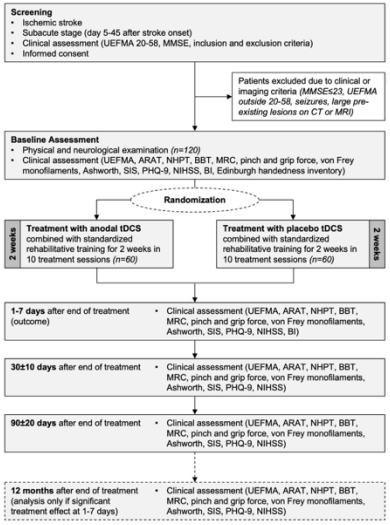
Modulation of brain plasticity in stroke: a novel model for neurorehabilitation

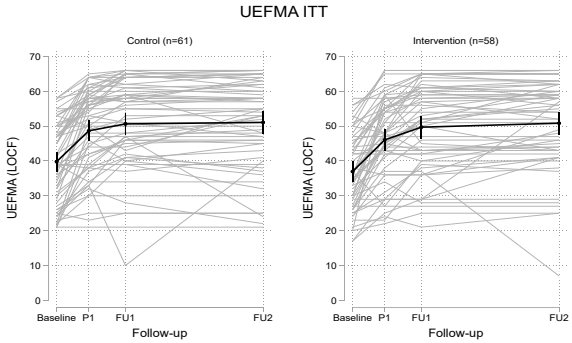
Giovanni Di Pino, Giovanni Pellegrino, Giovanni Assenza, Fioravante Capone, Florinda Ferreri, Domenico Formica, Federico Ranieri, Mario Tombini, Ulf Ziemann, John C. Rothwell and Vincenzo Di Lazzaro

Heterogeneous results

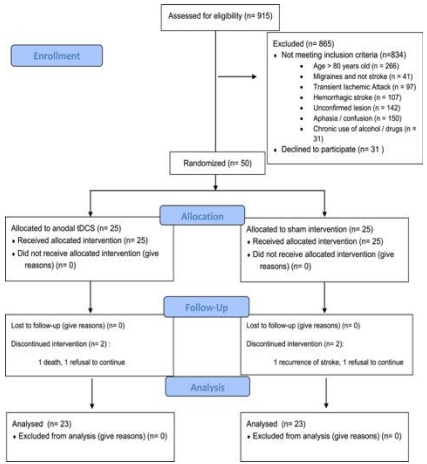


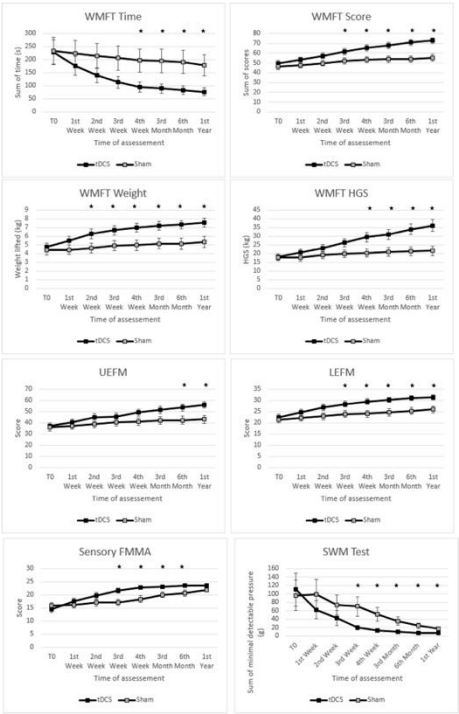
Stroke





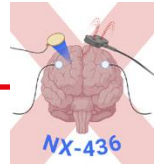
The NETS Trial Collaboration Group* (2024) Lancet Reg Healthy





Bornheim *et al.* (2020) BrainStimulation

Heterogeneous results



Depression

Original Article FREE

April 2013

The Sertraline vs Electrical Current Therapy for Treating Depression Clinical Study

Results From a Factorial, Randomized, Controlled Trial

Andre R. Brunoni, MD, PhD; Leandro Valiengo, MD; Alessandra Baccaro, BA; et al

» Author Affiliations | Article Information

JAMA Psychiatry. 2013;70(4):383-391. doi:10.1001/2013.jamapsychiatry.32

THE LANCET

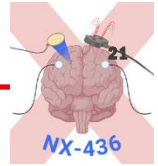
ARTICLES | VOLUME 402, ISSUE 10401, P545-554, AUGUST 12, 2023 Download Full Issue

Transcranial direct current stimulation as an additional treatment to selective serotonin reuptake inhibitors in adults with major depressive disorder in Germany (DepressionDC): a triple-blind, randomised, sham-controlled, multicentre trial

Gerrit Burkhardt, MD • Ulrike Kumpf, MD • Alexander Crispin, MD • Stephan Goerigk, PhD • Elisabeth Andre, PhD • Christian Plewnia, MD • et al. Show all authors

Published: July 03, 2023 • DOI: https://doi.org/10.1016/S0140-6736(23)00640-2 • Check for updates

Heterogeneous results

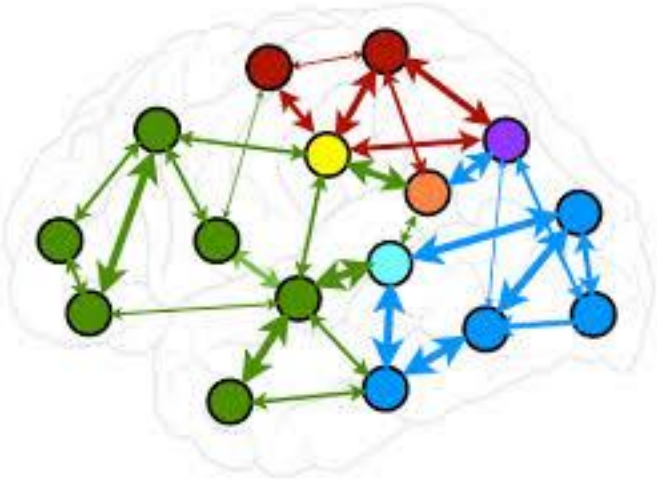


Phenotyping needed

- **individual anatomy (Skull, brain)**
    - targeting
    - intensity of stimulation (fixed vs personalized)
- **state of the brain**
- **genetic background** (e.g., BDNF polymorphisms)
- **external factors** (daytime, smoking, drugs, gender, hormonal level)

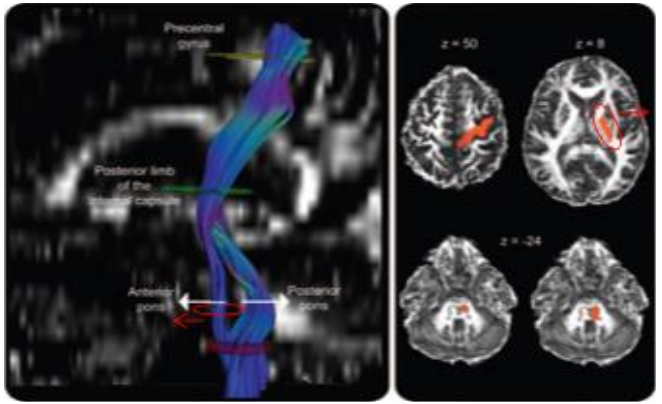
Stratification by structural damage / remaining structural connectivity

Stimulation target selection based on structural / functional connectivity

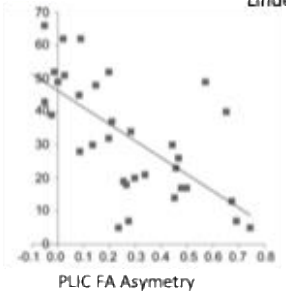


Stratification by structural damage / remaining structural connectivity

Cortico-spinal tract (CST)

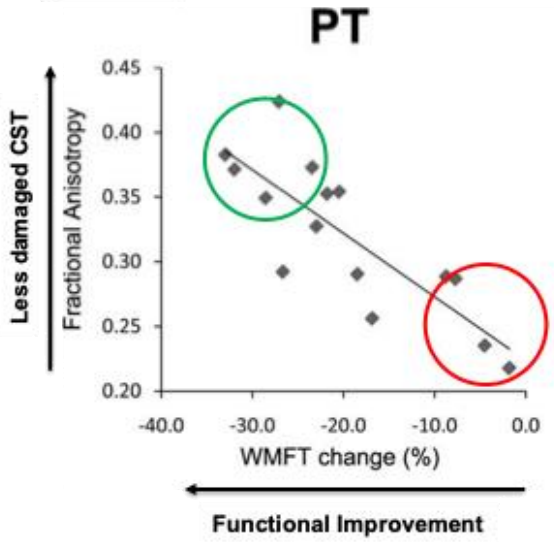


Lindenberg et al. (2010)



UEFMS

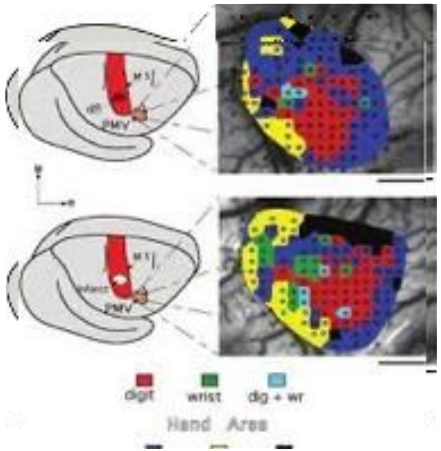
5 days of bihemispheric tDCS + PT/OT

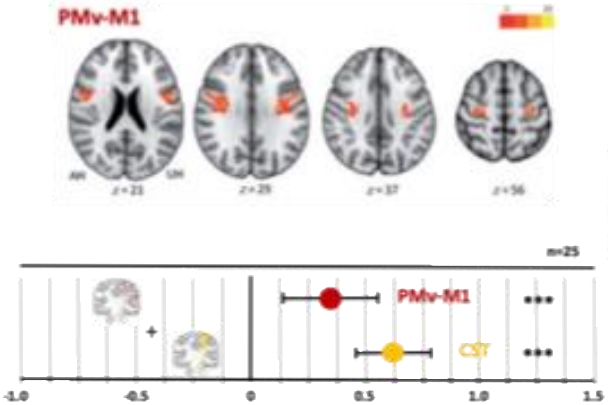


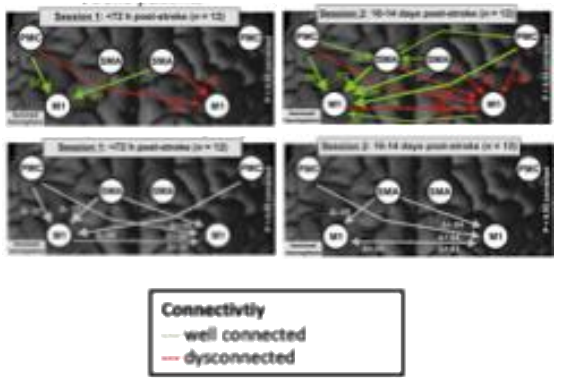
Alternative targets for NIBS: brain stimulation vPM

Animal model (monkeys):
Reorganisation in PMv, taking over function from M1 (Frost et al. 2003).

Structural and functional MR-based imaging: Points towards the involvement of the PMv-M1 interaction for recovery (Schulz, Koch et a. 2015; Rehme et al. 2011).

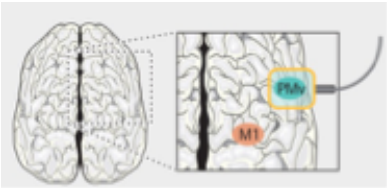






Structural integrity between **PMv** and **M1** is associated with the **degree** of recovered function, **additional** to structural integrity of the **CST**!

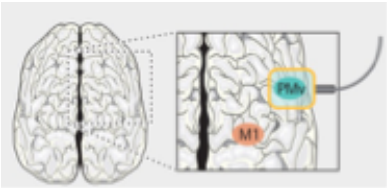
Alternative targets for NIBS: brain stimulation vPM



Motor training combined with anodal tDCS to the PMv of the lesioned hemisphere in chronic stroke patients.

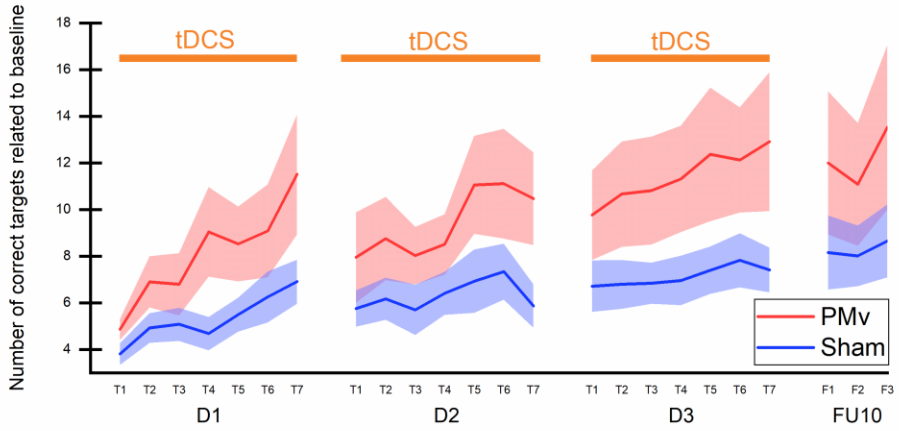
N = 20 chronic stroke patients, Double-blind, sham-controlled, parallel design, Sequential grip force modulation task

Alternative targets for NIBS: brain stimulation vPM



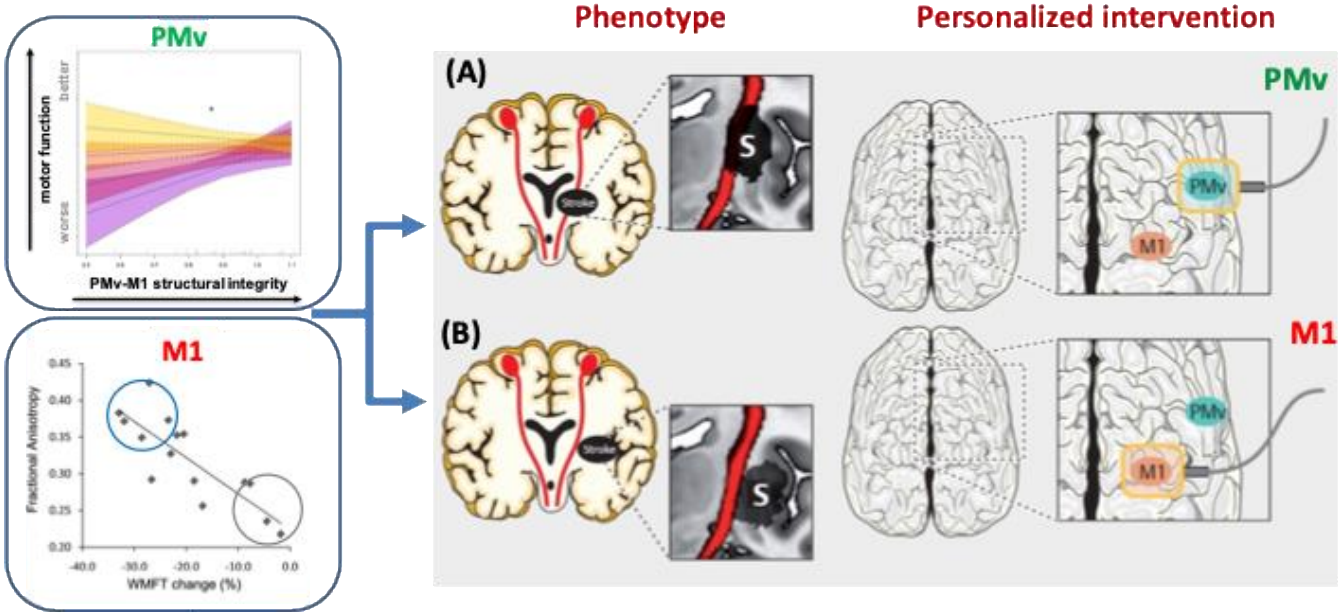
Motor training combined with anodal tDCS to the PMv of the lesioned hemisphere in chronic stroke patients.

N = 20 chronic stroke patients, Double-blind, sham-controlled, parallel design, Sequential grip force modulation task



the more **impaired** the **CST** the more **improved** patients from **tDCS** to the **PMv**

Towards biomarkers of phenotyping: treatment stratification



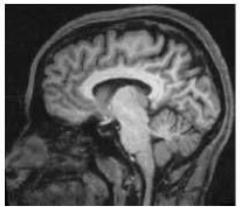
(A) CST **significantly** lesioned	(B) CST **mildly** lesioned
Limited answer to M1 NIBS Strong answer to PMv NIBS	Strong answer to M1 NIBS Limited answer to PMv NIBS

Koch & Hummel (2017) *Current Opinion in Neurology*, Morishita & Hummel (2017) *Current Behavioral Neuroscience Reports*

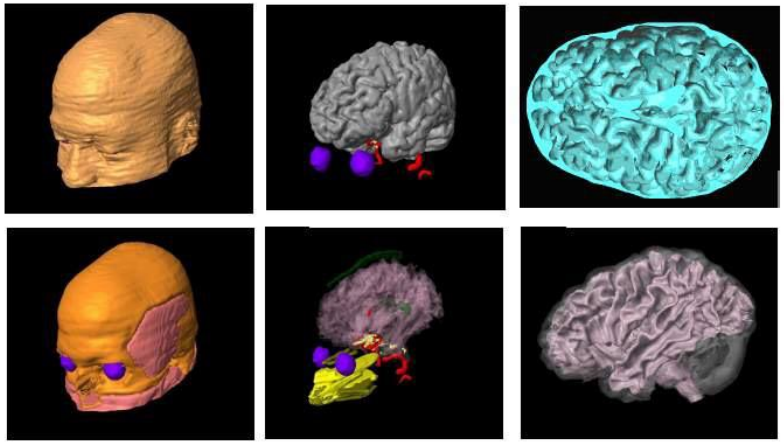
Optimization

Segment tissues (skin, skull, CSF, brain) in model

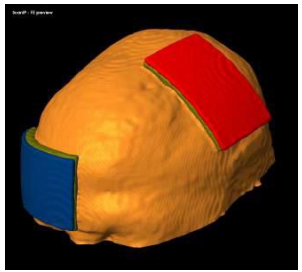
Individualized high resolution MRI



High-resolution 3T MRI scans at 1 mm X 1 mm X 1 mm pixel spacing



Place electrodes (in model), predict current flow



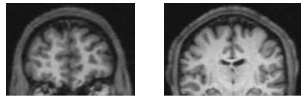
Individual electrode placement for each subject/patient to achieve most accurate and strong current delivery

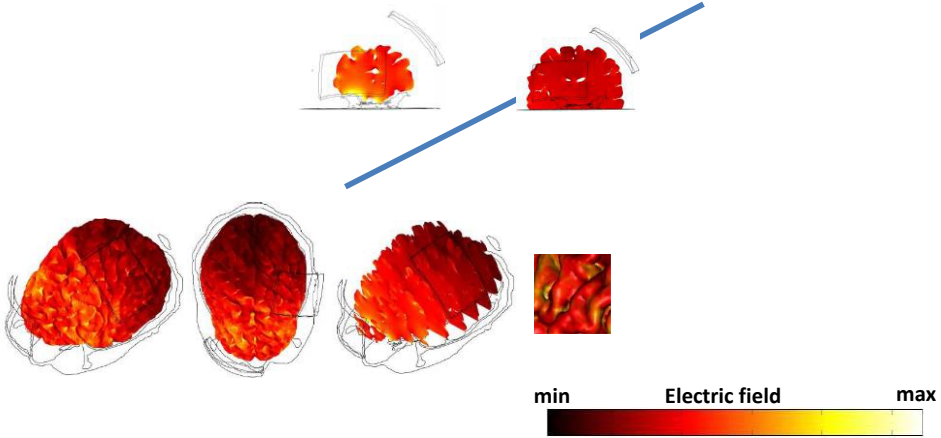
Datta et al. (2009), Biksom et al. (2021), Hartwigsen et al (2015)

Optimization

Classical

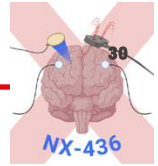
Individual anatomy - MRI





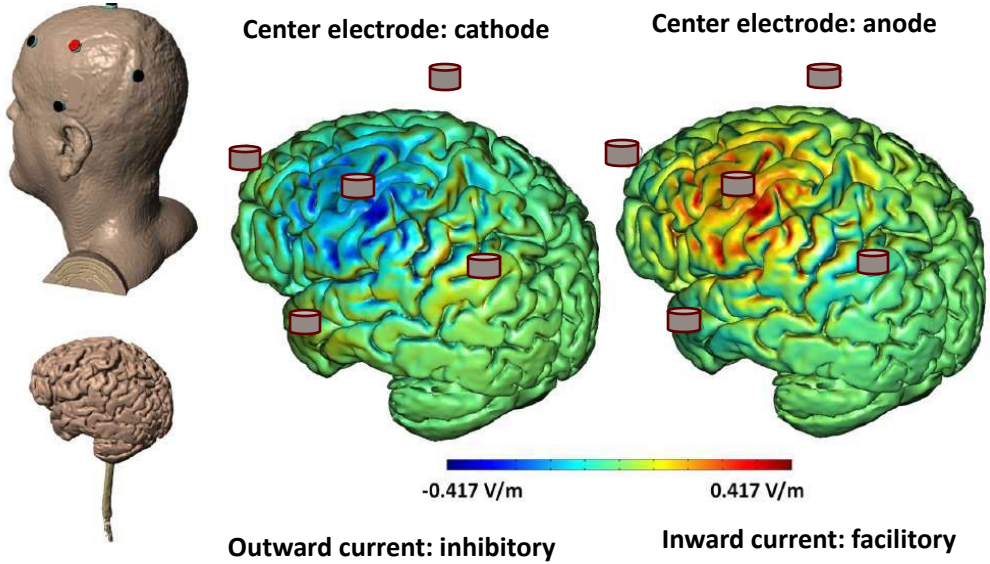
Datta et al. (2009), Biksom et al. (2021)

Optimization



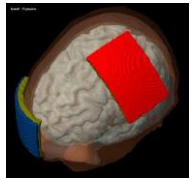
5 small “HD” electrodes (4+1)

- Center electrode over target determines polarity 4 return electrodes
- “Ring” radius determines modulation area



Datta et al. (2009), Biksom et al. (2021)

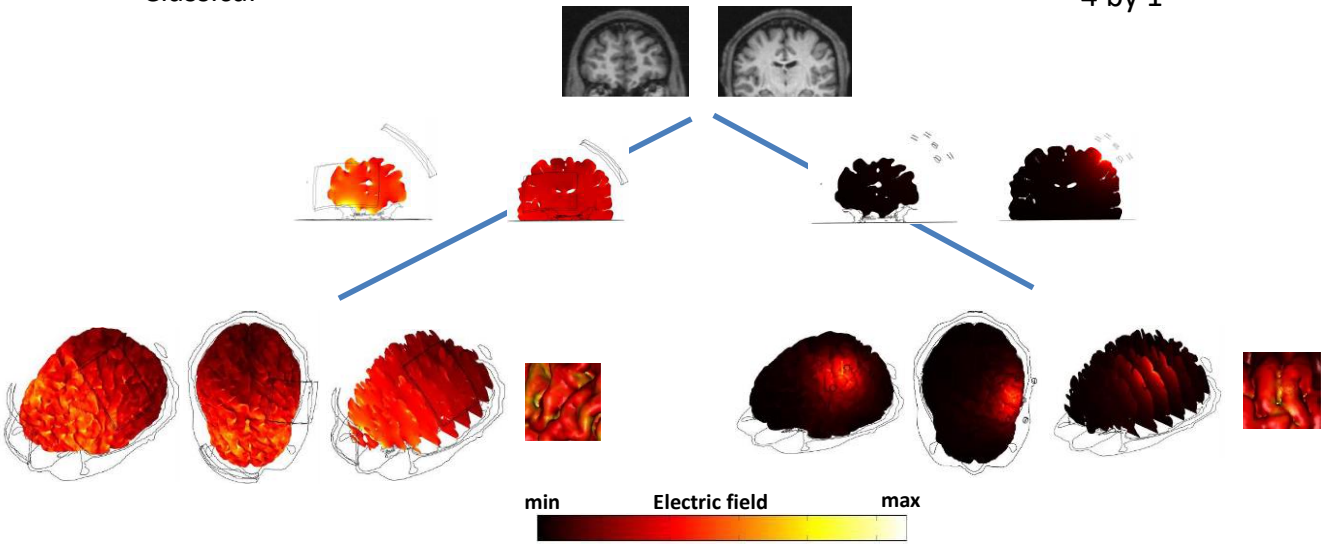
Optimization – better focality



Classical

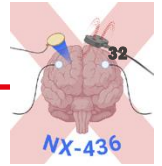
Individual anatomy - MRI

4 by 1



Datta et al. (2009), Biksom et al. (2021)

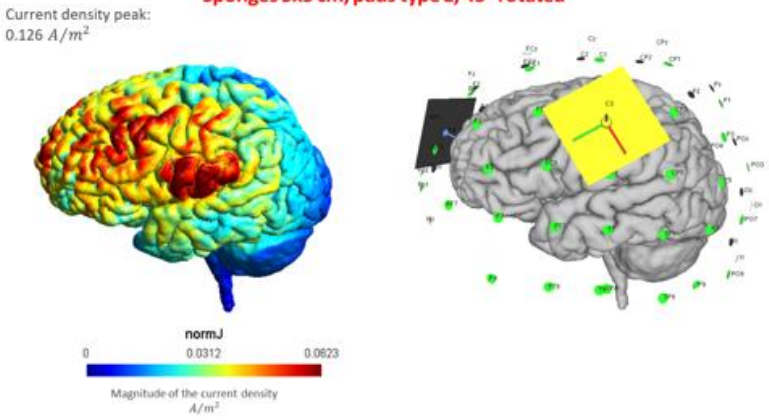
Optimization



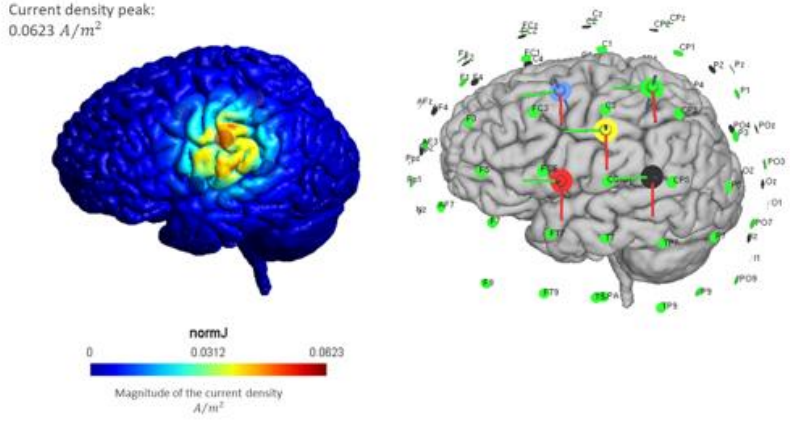
Simulations, modelling allow
- better reach of the target
- with envisaged intensity

Multi-electrode application
- higher topographic resolution
- better on-target and less off-target stimulation

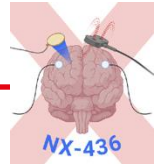
Gold-standard montage on C3-F4, 1mA
Sponges 5x5 cm, pads type E, 45° rotated



4x1 montage, anode close to C3, 1mA



Transcranial Direct Current Stimulation



- **What It Is**:

  tDCS is a non-invasive brain stimulation technique that applies a constant, low-intensity direct current to modulate neuronal activity and cortical excitability.

- **Mechanism of Action**:

  Delivers a steady electrical current through electrodes on the scalp, which can increase (anodal stimulation) or decrease (cathodal stimulation) the excitability of targeted brain regions.

- **Application**:

  Electrodes are strategically placed over specific brain areas associated with motor, cognitive, or emotional processing to enhance or suppress neural activity.

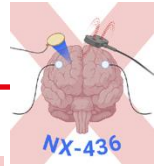
- **Purpose**:

  - Studied for enhancing cognitive functions such as learning, memory, attention, and language skills.

  - Applied in motor rehabilitation, especially in stroke patients, to improve motor function.

  - Investigated for treating neuropsychiatric conditions like stroke, depression, anxiety, chronic pain, and schizophrenia.

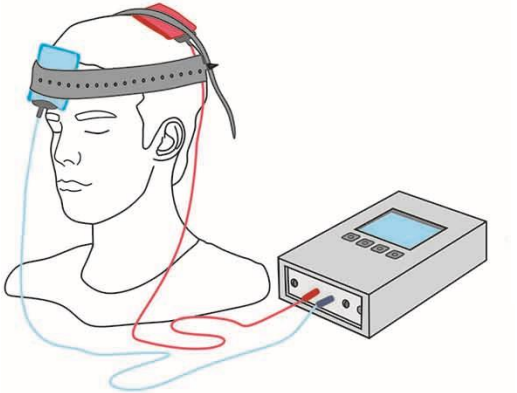
Transcranial Direct Current Stimulation

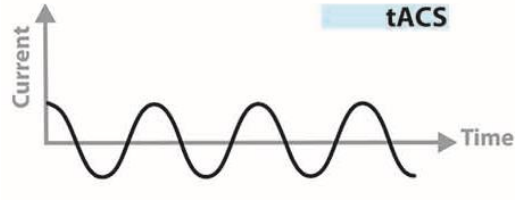


- **Advantages**:
  - Non-invasive, safe, and typically painless with few reported side effects.
  - Can be applied to specific brain regions (cortex) for targeted modulation.
  - Often used as an adjunct to cognitive or physical training for potentially enhanced outcomes.
- **Limitations**:
  - Effects can be subtle and vary significantly between individuals
  - Mechanisms of action are still being investigated, and the optimal dosage, timing, and duration of effects are not fully established.
- **Side Effects**:

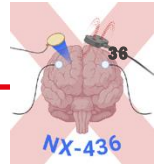
  Usually mild, tingling, itching, or redness (electrode); more intense side effects are rare.
- **Research Status**:

  Widely used in research, with an expanding body of studies supporting its potential in neurorehabilitation and neuropsychiatric treatment, though further validation is needed for consistent clinical application.





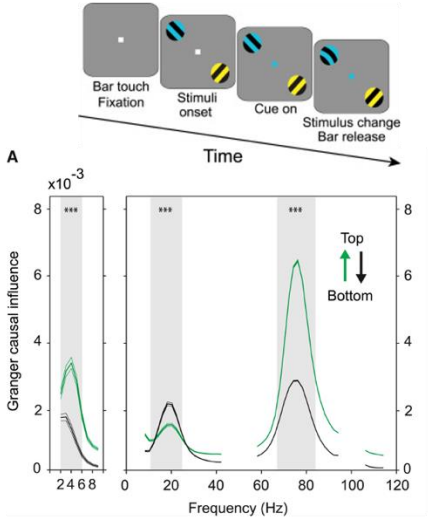
Transcranial Alternating Current Stimulation (tACS)



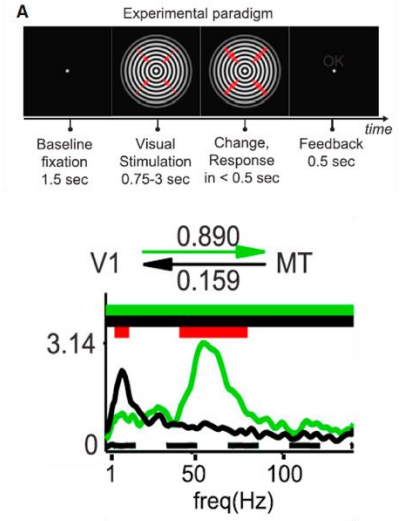
Brain communication by oscillatory activity

Can oscillatory activity be entrained by non-invasive brain stimulation?

Oscillatory activity to implement cognition

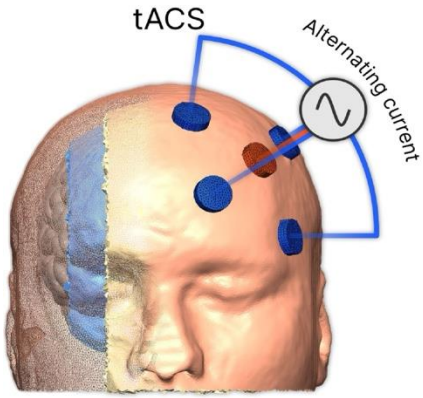


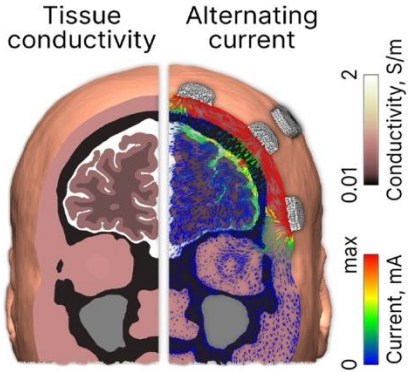
Bastos et al., 2015

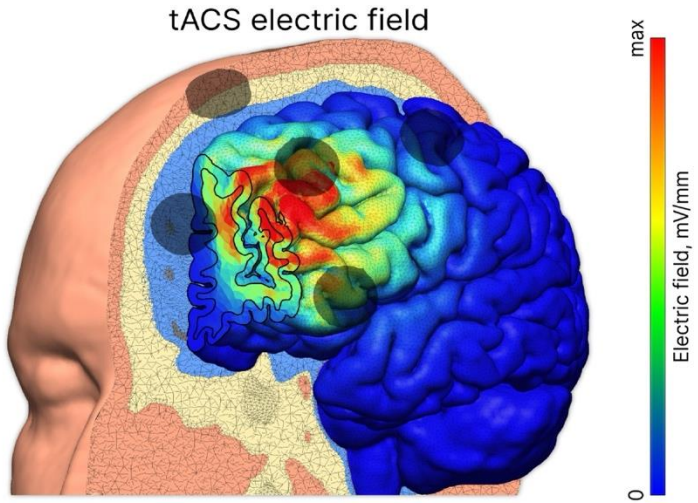


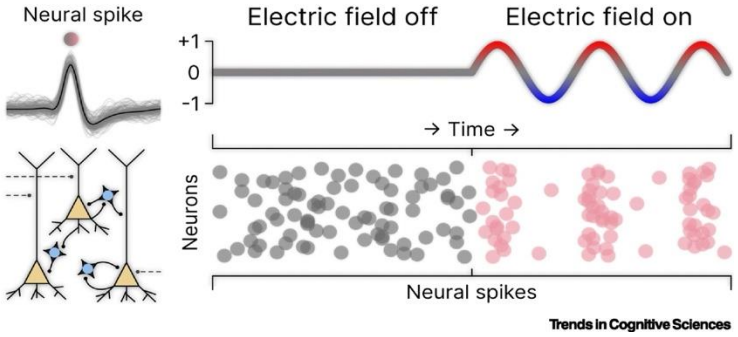
Michalareas et al., 2016

tACS



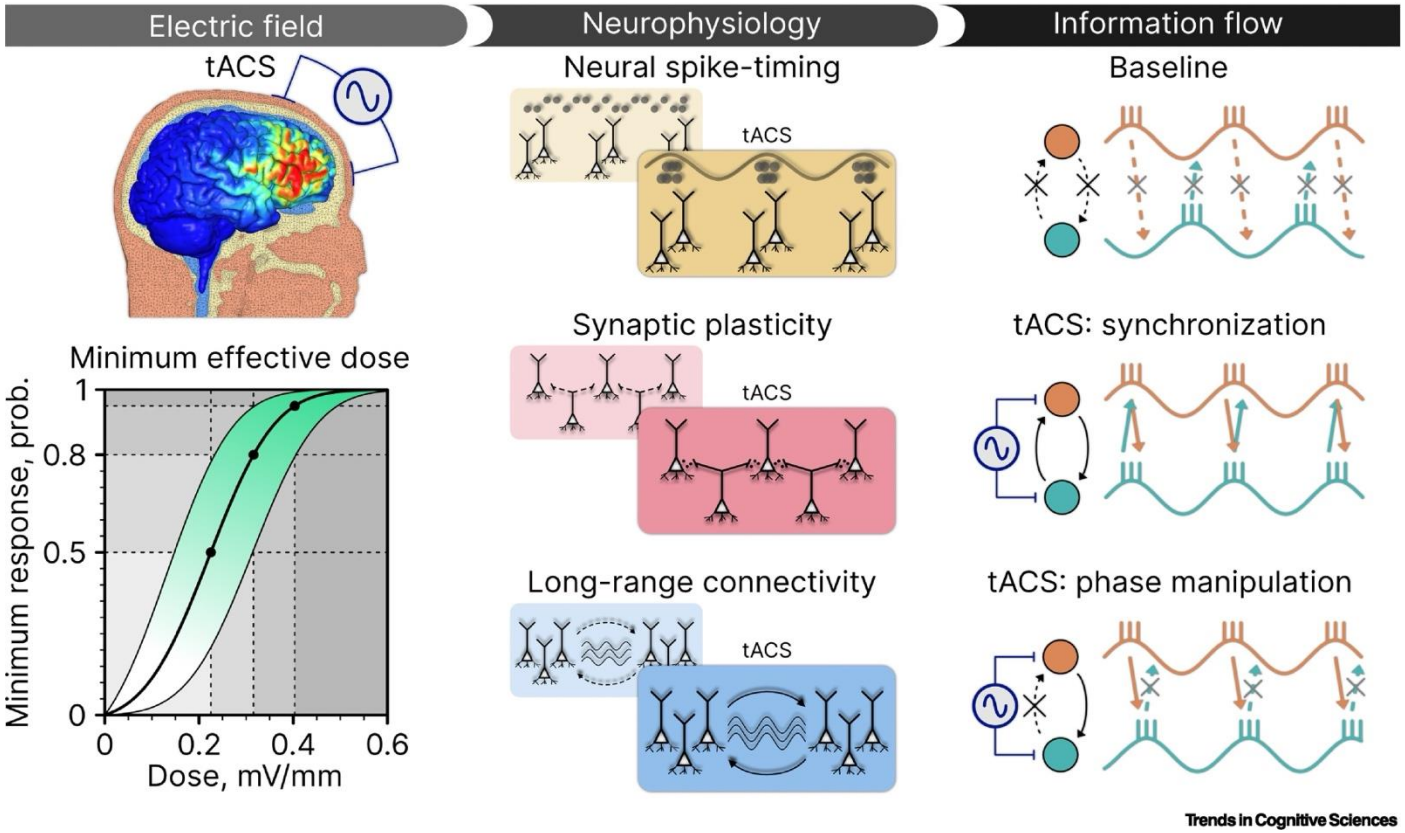






Wischnewski et al. 2023 TICNS

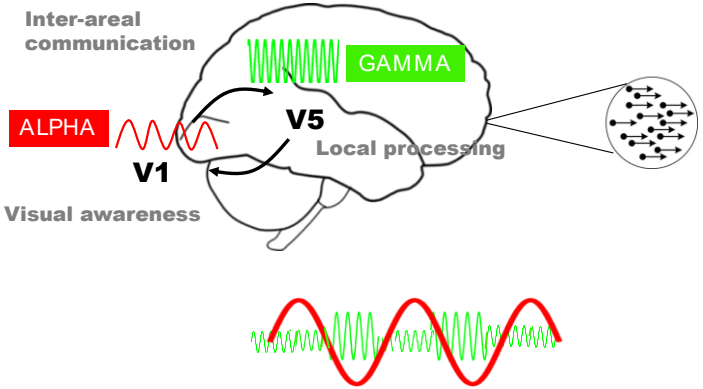
tACS



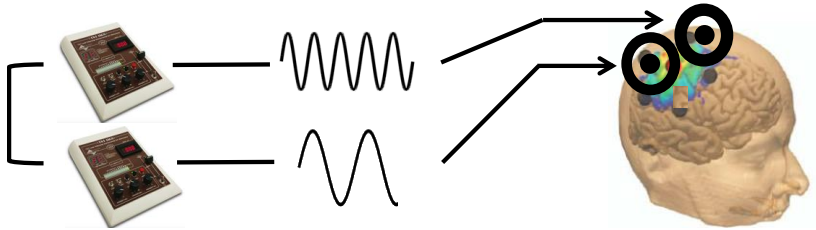
Wischnewski et al. 2023 TICNS

Entrain oscillatory activity by tACS

Brain processes information based on oscillatory interactions

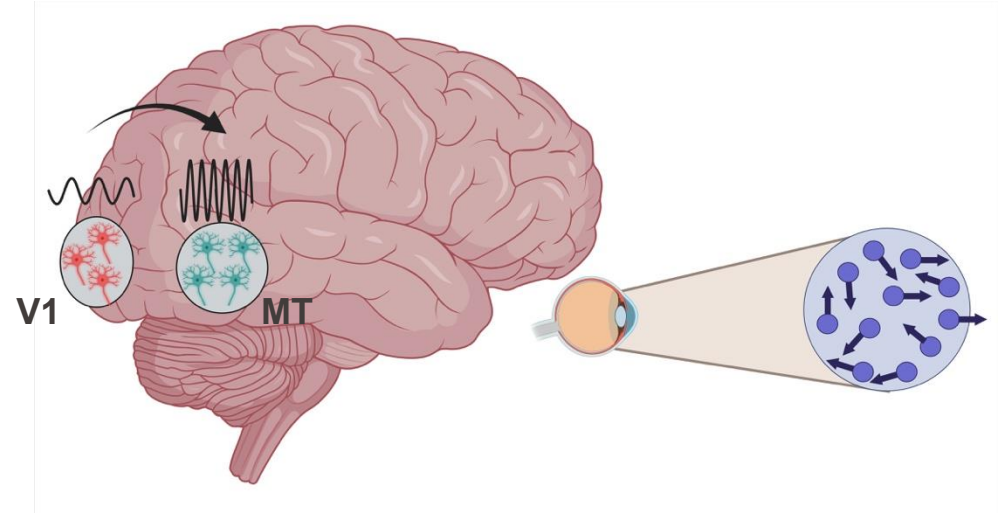


NIBS to support or mimic these oscillatory interactions

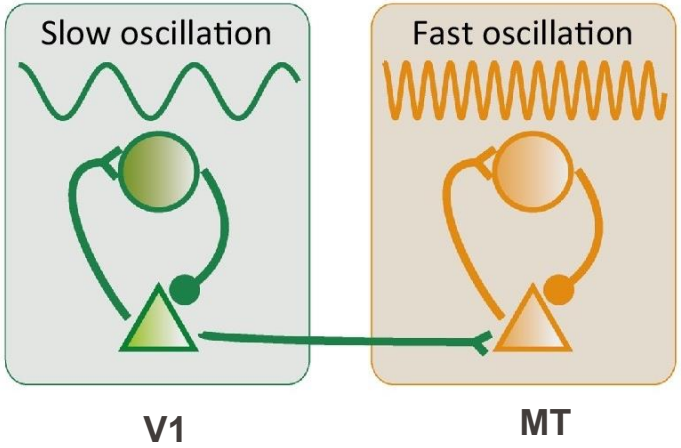


Raffin & Hummel (2018) *Neuroscientist*

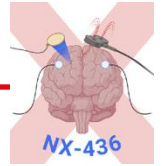
Orchestrated neuromodulation – interregional interactions

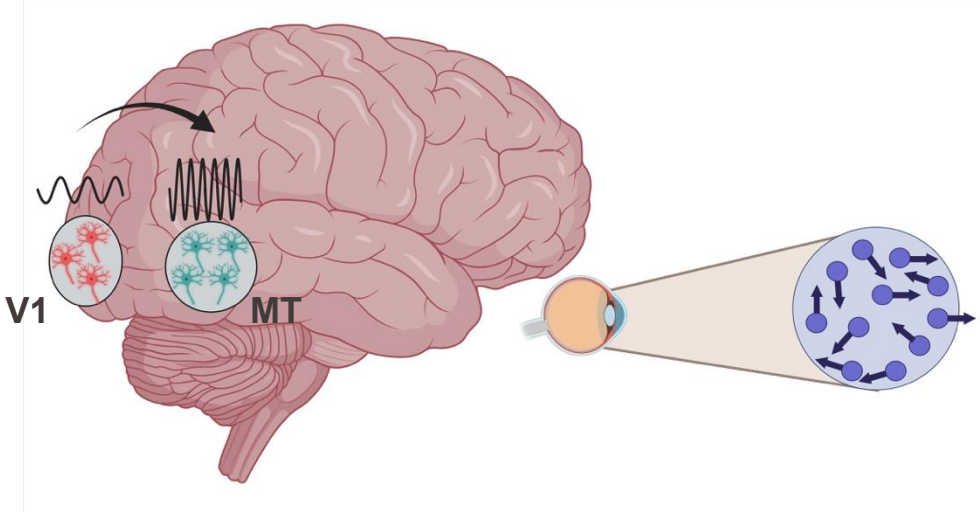


Inter-regional interactions

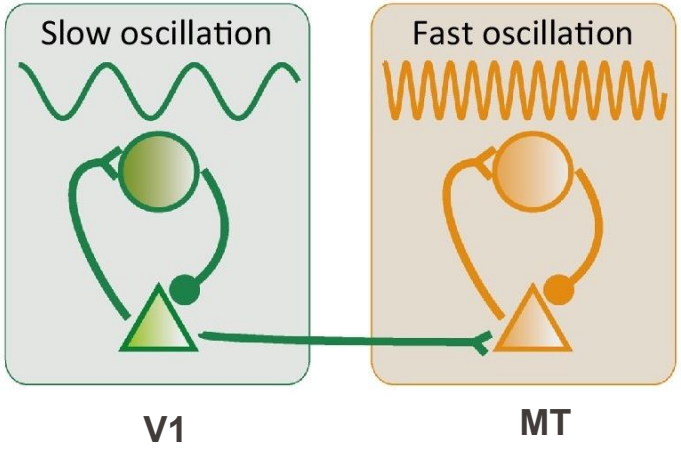


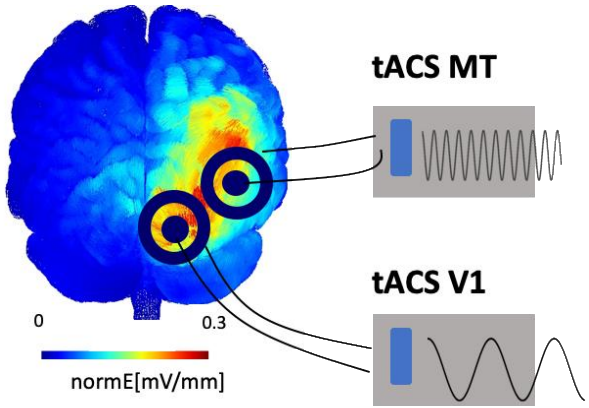
Orchestrated neuromodulation



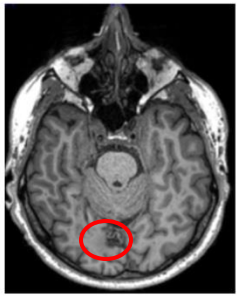


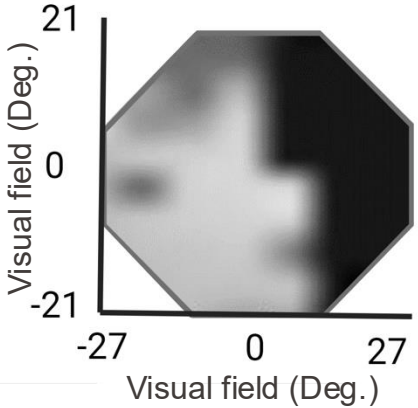
Inter-regional interactions

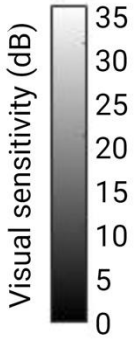




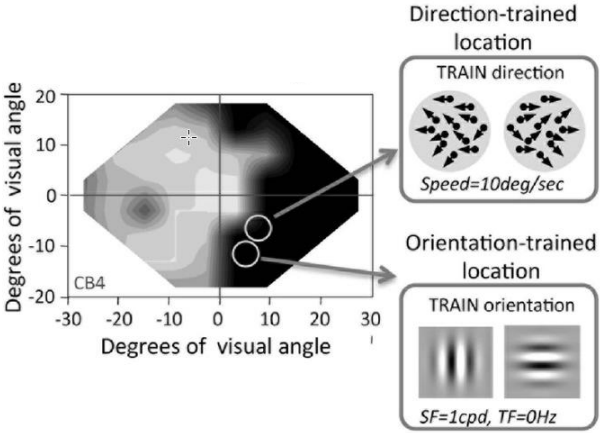
Target patients – Hemianopia

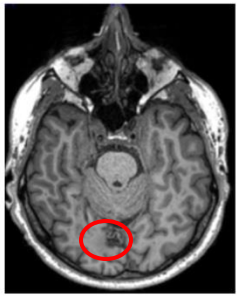


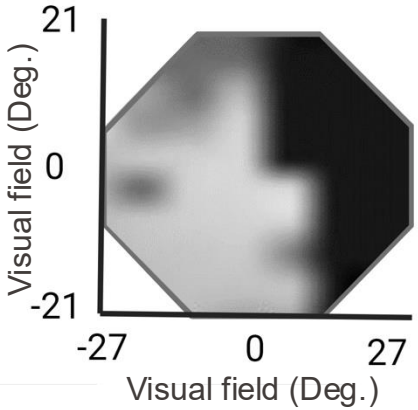


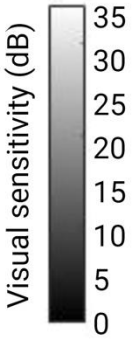


Target patients – Hemianopia

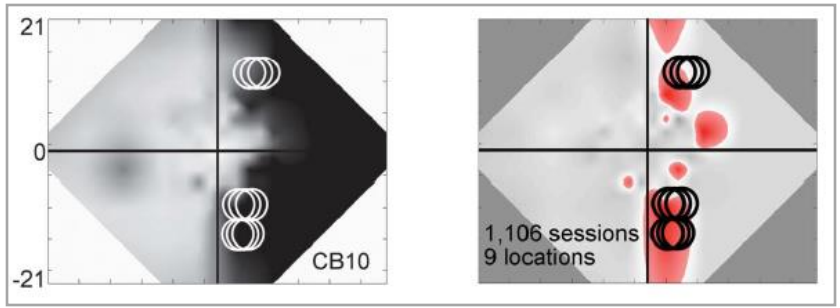






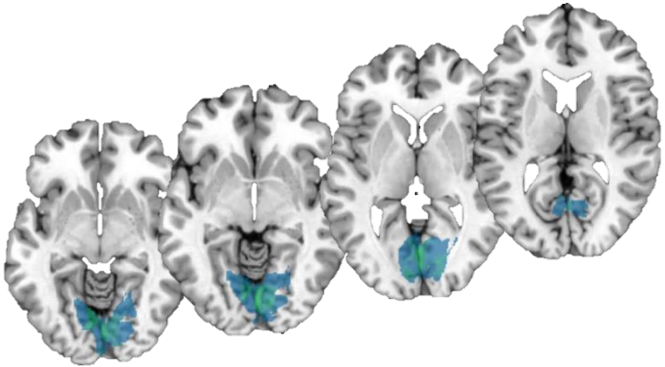


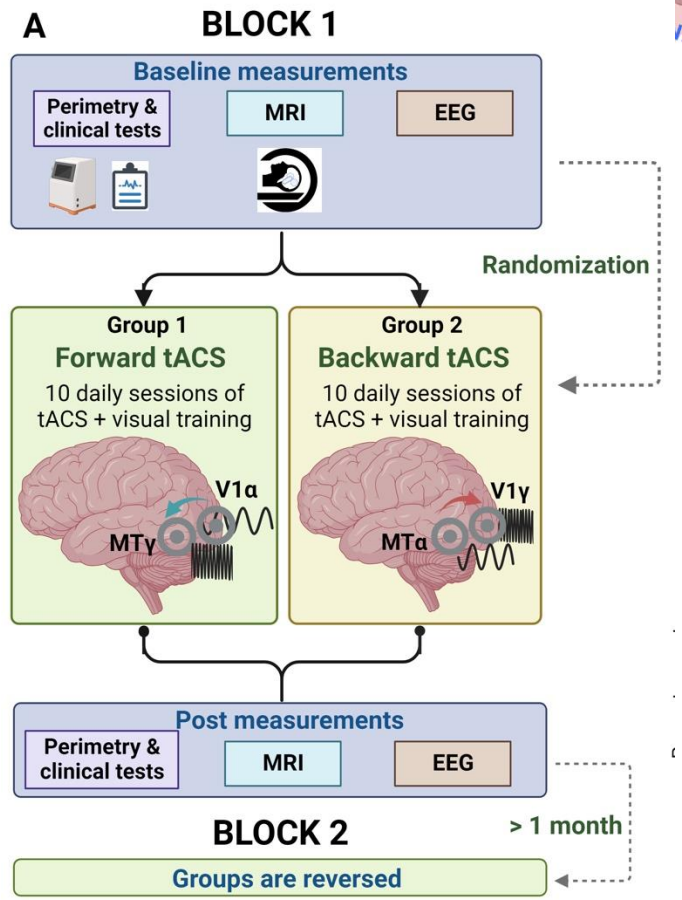
Extensive training over months



Cavaunaugh and Huxlin *et al., 2017*, Neurology

Re-Orchestrate 4 Vision Trial



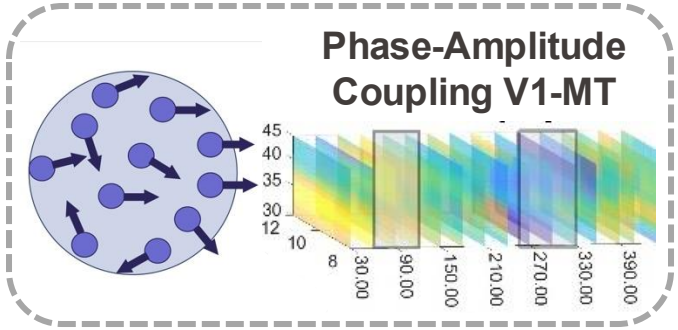


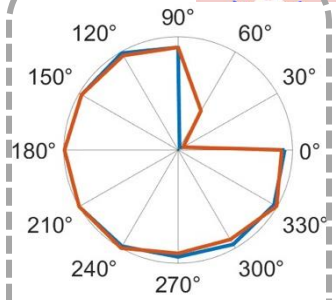
Raffin *et al.*, (**in press**) Brain

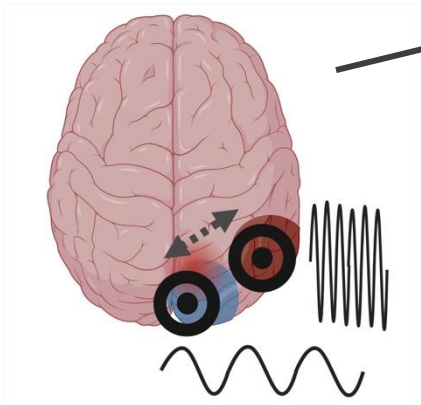
Re-Orchestrate 4 Vision Trial

- **Orchestrated neuromodulation** combined with visual **training** led to significant **reduction** of visual **deficits** in stroke patients

- Treatment **effects** were achieved in **10 sessions** over 2 weeks whereas **without neuromodulation**, training of **several months** is required for comparable effects (Cavaunaugh *et al.*, 2017)







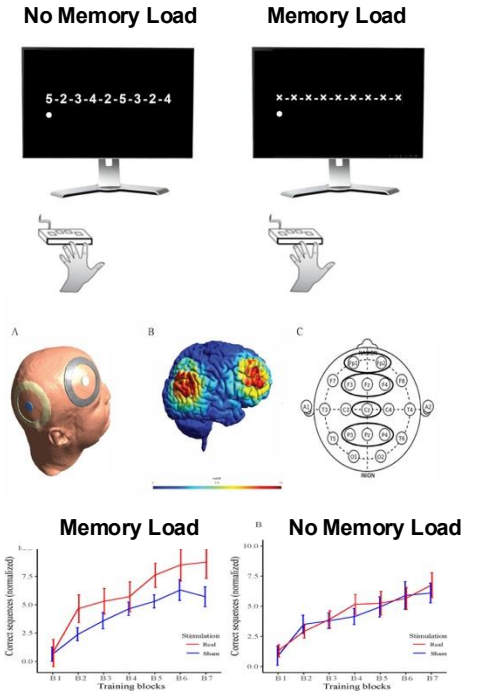
Raffin *et al.*, (**in press**) Brain

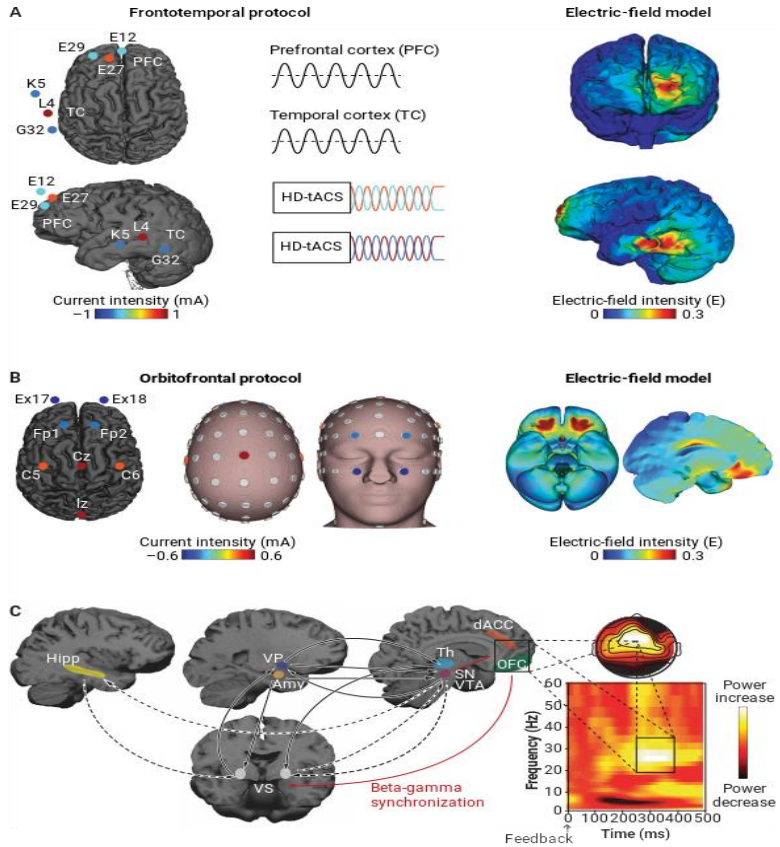
Orchestrated neuromodulation – interregional interactions

Contents lists available at ScienceDirect
Brain Stimulation
journal homepage: http://www.journals.elsevier.com/brain-stimulation

Targeting the frontoparietal network using bifocal transcranial alternating current stimulation during a motor sequence learning task in healthy older adults

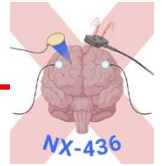
L.R. Draaisma [a, b], M.J. Wessel [a, b, c], M. Moyne [a, d], T. Morishita [a, b], F.C. Hummel [a, b, d, *]





Reinhart et al 2022 Science

Transcranial Alternating Current Stimulation



- **What It Is:**

tACS is a non-invasive brain stimulation technique that uses a weak, oscillating electrical current to modulate brain activity by entraining neural oscillations at specific frequencies.

- **Mechanism of Action**:

Applies sinusoidal (alternating) currents through electrodes placed on the scalp, with frequencies tailored to target specific brain wave oscillations (e.g., alpha, beta, gamma), which may enhance synchronization and functional connectivity in the brain.

- **Application**:

Electrodes deliver stimulation to specific brain regions associated with cognitive and motor functions, emotional regulation, or sensory processing.

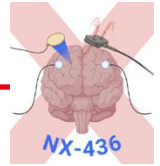
- **Purpose**:

- aims to modulate brain rhythms associated with various functions (e.g., alpha waves for relaxation, beta waves for attention and focus).

- investigated for enhancing cognitive functions such as memory, attention, and problem-solving.

- explored as a potential therapy for psychiatric and neurological conditions, including depression, anxiety, and chronic pain.

Transcranial Alternating Current Stimulation



• **Advantages**:

- Non-invasive and typically well-tolerated, with a relatively low risk of side effects.

- Allows frequency-specific stimulation, providing targeted modulation of brain networks.

- Combination with other therapies (e.g., cognitive training, medication)

• **Limitations**:

- The precise effects can vary across individuals and may depend on the location and duration of stimulation.

- Mechanisms of action still not fully understood, research is ongoing to refine stimulation protocols.

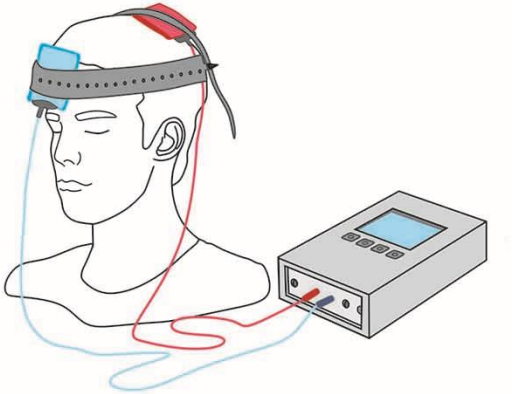
- Mostly used in research settings, with limited regulatory approval for clinical applications.

• **Side Effects**:

Usually minimal, including mild tingling or discomfort under the electrodes, but effects are temporary.

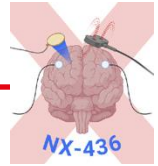
• **Research Status**:

Actively studied in neuroscience and clinical research, promising applications in cognitive enhancement and treatment of neuropsychiatric disorders



Transcranial Random Noise Stimulation (tRNS)

transcranial Random Noise Stimulation (tRNS)



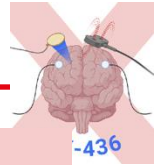
Underlying concept:

- tRNS adds **random electrical "noise"** to neuronal populations.
- this noise can **enhance neural signal transmission** through a process called **stochastic resonance** — weak subthreshold signals become detectable when a moderate level of noise is added
- the result is **increased cortical excitability** and **facilitated synaptic plasticity**, promoting learning and performance.

Mechanistic summary:

- *Random noise current → membrane potential fluctuations → higher probability of neuronal firing*
- *Improved signal-to-noise ratio → enhanced information processing*
- *Cumulative plastic effects → short- and long-term performance gains*

transcranial Random Noise Stimulation (tRNS)



Schematic Overview

Power Source:

Typically a battery, often housed within a portable control box.

Control Unit/Stimulator:

A device that generates the specific tRNS waveform (random frequencies, usually between 0.1 and 640 Hz, with a mean current of zero) and allows the user to adjust intensity (e.g., peak-to-peak amplitude up to 2 mA) and duration.

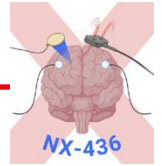
Functional Diagram

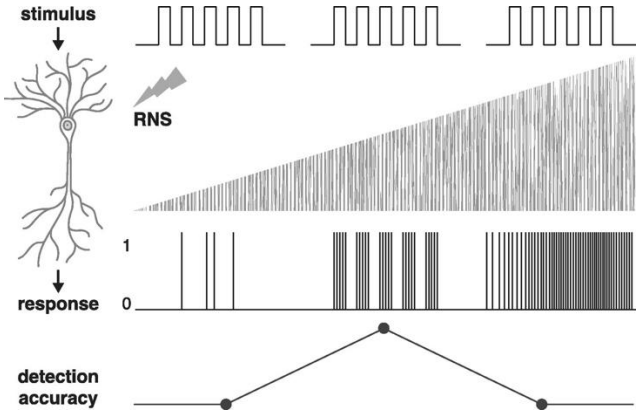
1.Current Generation: The control unit produces a "white noise" alternating current (AC) waveform, meaning the power spectral density is constant across a range of frequencies

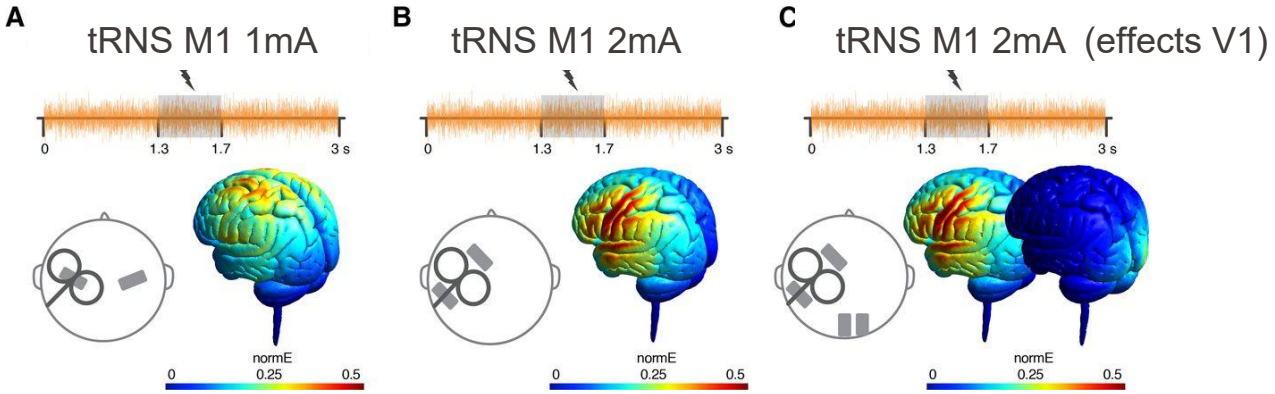
2.Current Delivery: This current is sent through the lead wires to the two (or more) electrodes positioned on specific scalp locations, often determined using the international 10-20 EEG system for targeting specific brain regions (e.g., left vs. right dorsolateral prefrontal cortex).

3.Neuromodulation: The constantly changing polarity and random frequency current modulates neuronal excitability, making neural signal transmission more efficient, a phenomenon related to stochastic resonance.

transcranial Random Noise Stimulation (tRNS)



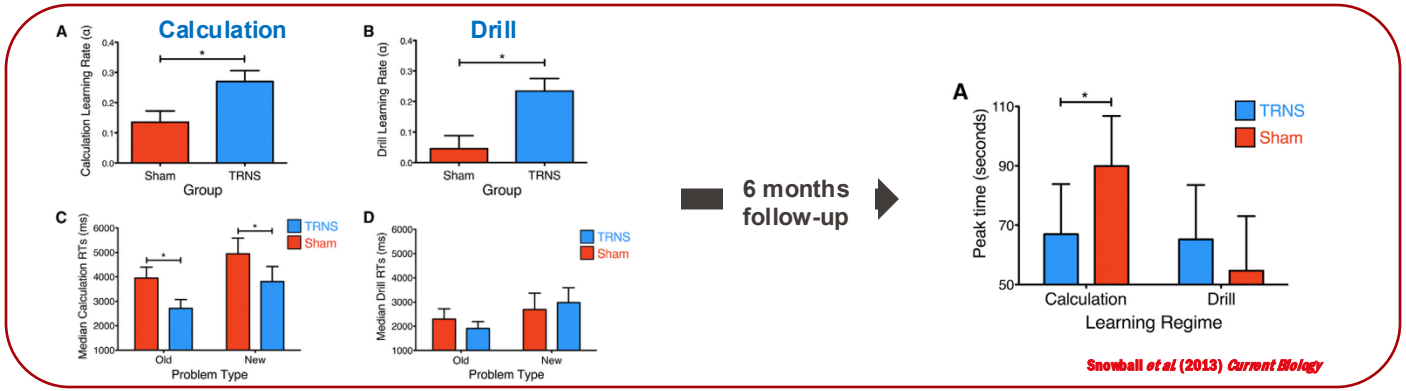




Potok et al (2021) *J Nsc*

Examples of application of NIBS: Cognitive tasks

- University students
- Memorization of mathematical facts (e.g. 2x17 = 34) and more complicated calculations (e.g., 32–17+5)
- tRNS prefrontal cortex



Examples of application of NIBS: Cognitive tasks

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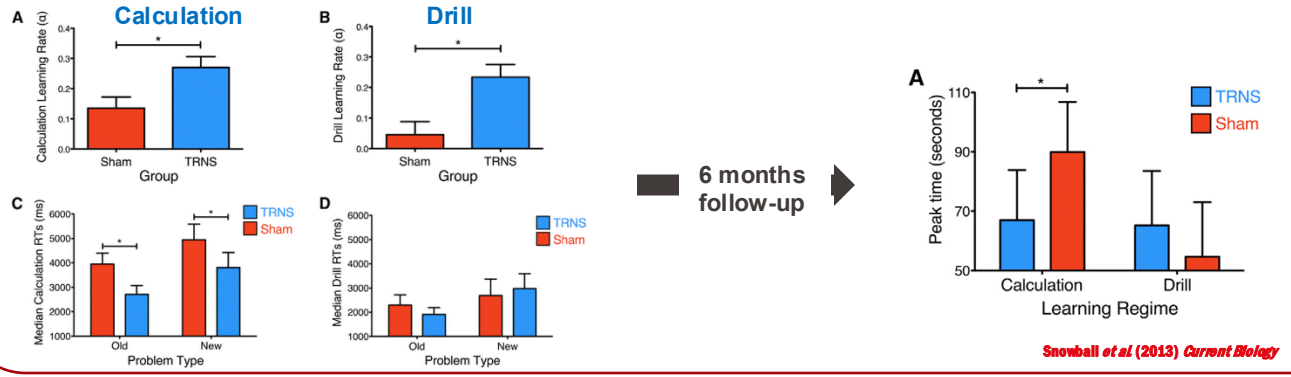
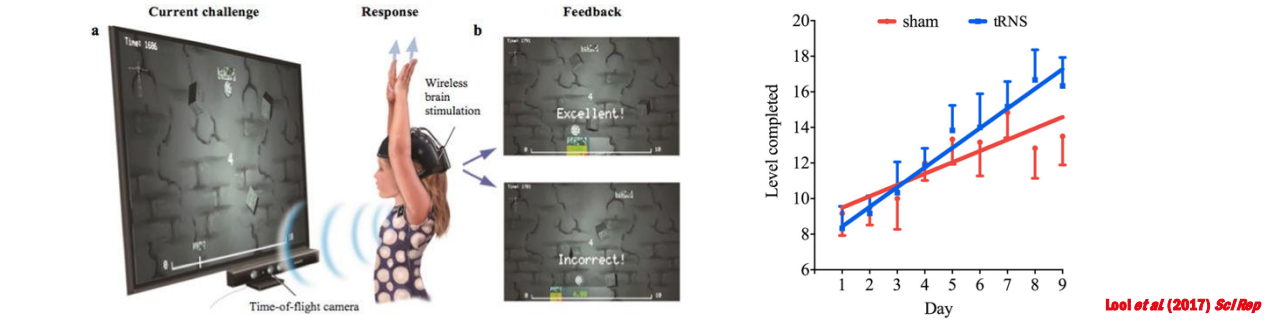


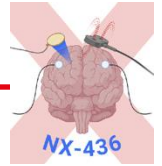
Snowball *et al.* (2013) *Current Biology*

- Children with mathematical learning disabilities (**MLD**)
- Arithmetic training
- tRNS prefrontal cortex bilat.



Looi *et al.* (2017) *Sci Rep*

transcranial Random Noise Stimulation (tRNS)



What It Is: tRNS is a non-invasive brain stimulation technique that applies random electrical noise to the scalp to modulate brain activity.

Mechanism of Action:

- Delivers alternating currents with randomly fluctuating frequencies (usually between 0.1 and 640 Hz), producing a “noise” effect that can enhance cortical excitability and plasticity.
- A hallmark feature of stochastic resonance (SR) is that signal processing can benefit from added noise.

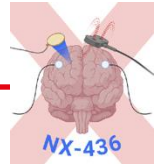
Application:

Electrodes placed on the scalp deliver the stimulation over targeted brain regions, often for cognitive or motor enhancement.

Purpose:

- Used to improve cognitive functions (e.g., memory, attention, learning).
- Applied in motor recovery and neurorehabilitation, particularly in stroke patients.
- Potentially beneficial for managing symptoms of neuropsychiatric conditions like depression, schizophrenia, and ADHD.

transcranial Random Noise Stimulation (tRNS)



Advantages

- Non-invasive, painless, and safe when used correctly.

- Can be used as an adjunct to other therapies (e.g., cognitive training, physical therapy).

Limitations:

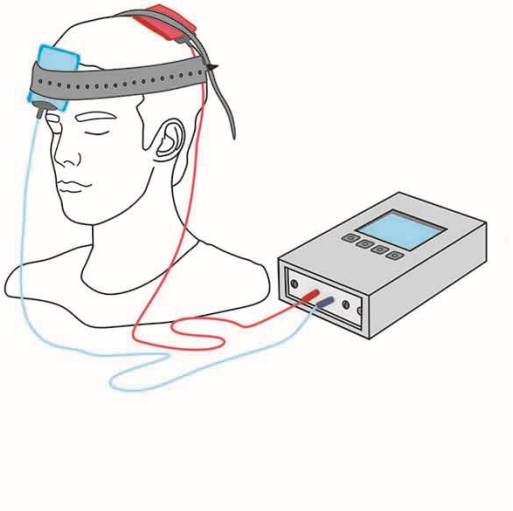
- Effects can be variable depending on the individual and the specific brain region targeted.

- The exact mechanisms are not fully understood, and further research is needed to establish standardized protocols.

- Currently experimental, with limited regulatory approval for therapeutic use.

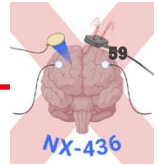
Side Effects:

- Generally mild, including tingling, itching, or discomfort under the electrodes.



Home-based self-application

Home-based, self-application



Can non-invasive brain stimulation be applied at home?

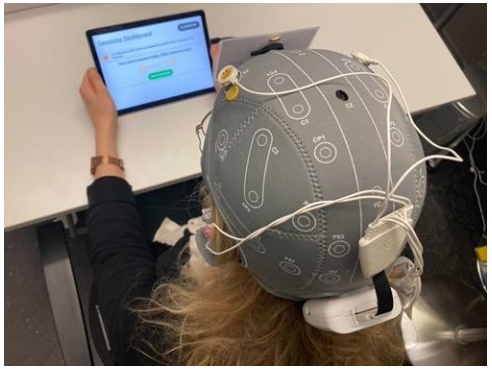
Home-based, self-application

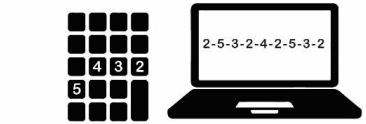
§ Ensure repeated and high-frequency treatment exposure

§ Promote a larger outreach

§ Comfort of the setting is beneficial especially for patient population

§ Stimulation settings and parameters are remotely controlled and supervised to warrant safety





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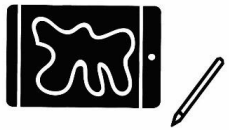


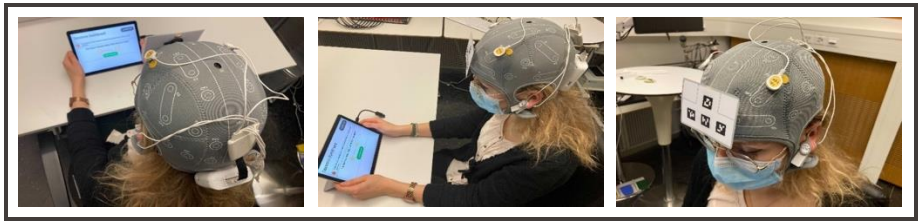
C

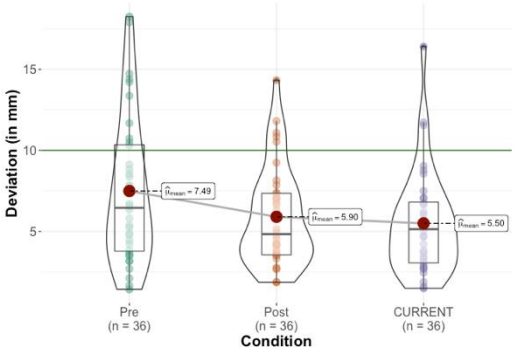
Open challenges:

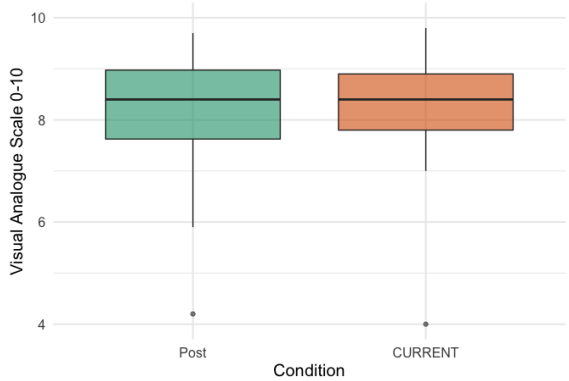
- How to ensure correct stimulation electrode placement?
- Safety
- Combining with training/treatment

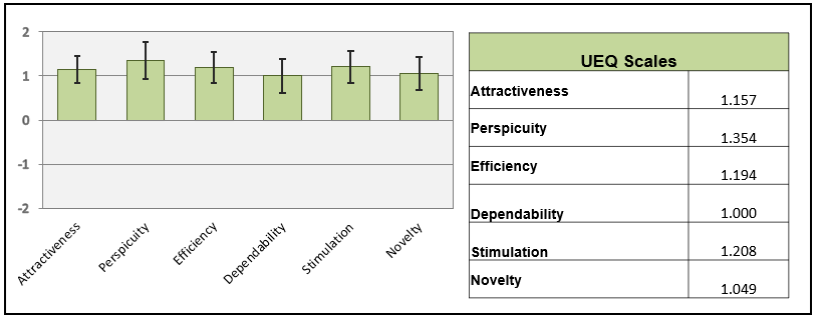
Maceira *et al.* (2020) BrainStimulation

Home-based, self-application – correct delivery







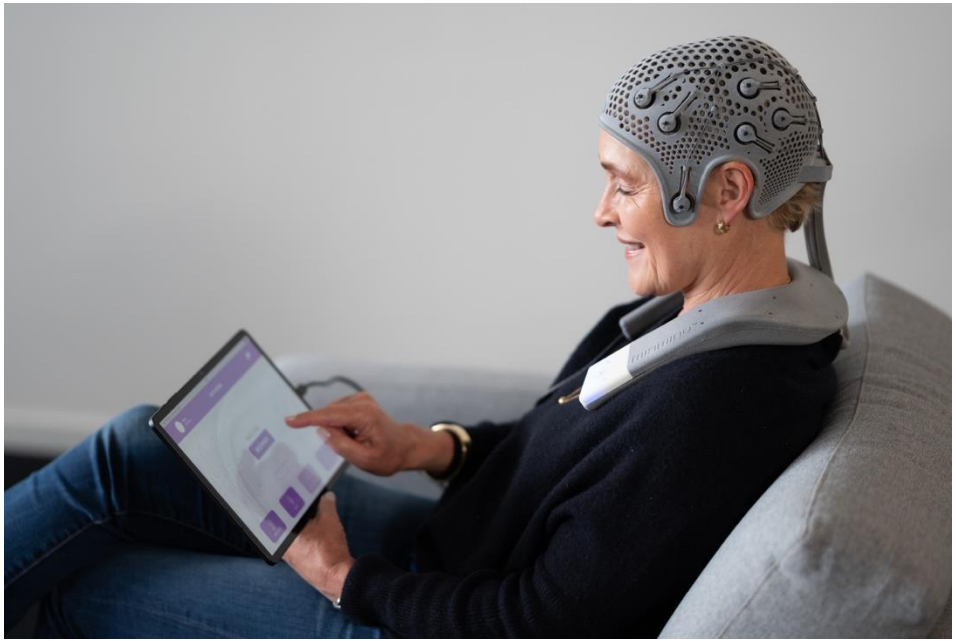


UEQ Scales	
Attractiveness	1.157
Perspicuity	1.354
Efficiency	1.194
Dependability	1.000
Stimulation	1.208
Novelty	1.049

Windel *et al*., 2023 Clin Neurophys

Home-based, self-application – correct delivery

Individualized 3D printed electrode cap



https://bottneuro.ch

Home-based, self-application – correct delivery

DISCOVER project

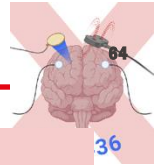
- Multi-site, double-blind, sham controlled trial
- tDCS + cognitive control videogame
- Target: alleviate depressive symptoms in MDD patients

Collaborators:
UNIGE – Prof. Daphne Bavelier
HUJI - Dr. Mor Nahum
EPFL – Prof. Friedhelm Hummel

Clinical sites:
LMU - Prof. Frank Padberg
RSU - Prof. Elmars Rancans
Hadassah Medical Center - Prof. Omer Bonne

Windel *et al.* (2023) Clin Neurophys; Dechantsreiter et al. (2022)

Home-based, self-application – Core requirements



Patient safety by design

Hard limits on dose: current, current density (via minimum electrode area), session duration, ramp-up/down, and lockouts between sessions.
Automatic impedance check & live monitoring (abort or auto-adjust if impedance too high; clear user feedback).
Skin protection: shaped electrodes/sponge cartridges, even pressure via cap/strap, single-use or limited-use consumables, gel/saline dosing guidance, contact-loss detection.
Fail-safe behavior: watchdogs, safe shutdown on faults, battery and charger safety, over-temperature protection.
Contraindication screening built into onboarding (implants, epilepsy history, pregnancy policy per protocol, dermatologic issues at sites).

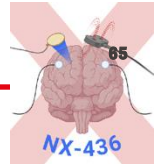
Usability & human factors (self-application)

Placement made foolproof: pre-positioned cap/helmet with printed landmarks, keyed color-coded connectors, “cannot plug it wrong.”
On-device guidance: step-by-step animated/app wizard; pass/fail checks before start; large, unambiguous indicators.
One-button start once checks pass; no parameter editing by the patient.
Accessible UI: readable fonts, haptics/tones, localization; designed per **IEC 62366** human-factors principles.

Clinician control & adherence

Prescription-locked protocols (pre-programmed by clinician; cryptographically signed).
Scheduling & lockouts (e.g., max N sessions/week; minimum inter-session interval).
Remote disable / modify ability; **adherence dashboard** with session logs, impedance traces, reasons for aborts.
In-app symptom & AE check-ins before/after each session.

Home-based, self-application – Core requirements



Sensing, QA and logs

Complete audit trail: timestamped device firmware version, protocol ID, delivered dose, impedance/time curves, alerts.
Self-test on power-up; calibration checks; firmware update mechanism with rollback.
Optional add-ons: heart-rate/PPG for comfort monitoring; simple pain/itch VAS capture.

Connectivity, privacy, and security

Secure comms (BLE/Wi-Fi with strong encryption; mutual auth).
Data minimization + **consent management**; GDPR-/HIPAA-grade storage in the cloud or clinical server.
Offline mode tolerance with later sync; no session if protocol is expired or revoked.

Materials & biocompatibility

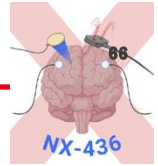
Compliance for all skin-contact parts.
Robust, cleanable textiles/caps; replacement schedule for sponges/electrodes clearly defined.

Regulatory & standards pathway (baseline)

Clinical workflow integration

Patient selection & training module (brief remote session or in-clinic teach-back).
Starter kit: device, cap/positioning aid, pre-wet sponges/gel, mirror or camera alignment aid, quick card.
Support: in-app chat/FAQ, alert routing (e.g., skin irritation, headache) to the clinical team with simple triage rules.

Summary tES – to know



I. 3 main methods for cortical stimulation (tDCS, tACS, tRNS) with different properties and underlying mechanism

II. Subthreshold stimulation with limited topographic resolution and depth

III. Easy to apply

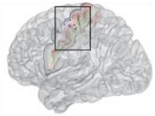
IV. Good side effect and blinding profile

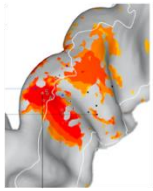
V. Well feasible in human / clinical studies

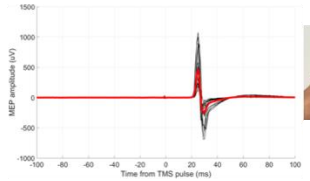
VI. Clinical trial examples

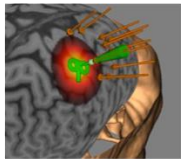
VII. Heterogeneity and respective sources of heterogeneity

VIII. Home-based self-application









Thank you for your attention!