

### Overview



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- 3. Orthogonal versus Parallel Montages
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### Brief Historical Background

- ► Therapeutic application of electrical currents to the skull: Scribonius Largus Compositiones Medicae
- early XIX century: Giovanni Aldini electrical stimulation of exposed cortex of decapitated criminals
- ▶ 1874- Bartholow- electrical stimulation of exposed brain of a patient with a cancerous erosion of the skull bone
- ▶ 1896- Cerletti- introduction of electroconvulsive therapy

Brief Historical Background-TMS

- XX Century- Penfield and the Montreal procedure
- ▶ 1985- Barker, Jalinous and Freeston- TMS
- ▶ 1996- Pascual-Leone- modulatory effects of TMS in depression

### Brief Historical Background-tDCS

- ▶ 1960's and 1970's brain polarization
- ▶ 1962- increased alertness and mood improvement in healthy volunteers- Bindman, Lippold and Readfern
- ▶ 1974- improvement in depression- Nias & Shapiro

tDCS- modern developments

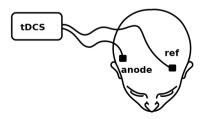
- ▶ 1998- 2000- Priori in Italy and Nitsche in Germany
- ► TMS probing confirmed changes in cortical excitability as after-effects of a tDCS session
- many studies on normal physiology and in pathological conditions



#### Current flow and tDCS results

Outcomes of transcranial direct current stimulation (tDCS) are influenced by the current flow between the electrodes (Rawji et al., 2018) [11]

To target the motor cortex (M1), the conventional tDCS montage calls for a large (e.g. 5x5 cm) anode electrode to be positioned over the M1 hotspot of the right hand, while a large cathode electrode is placed over the right supra-orbital area (Woods et al., 2016) [12]





State of the Art-2008

Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, Antal A, Paulus W, Hummel F, Boggio PS, Fregni F, Pascual-Leone A. Transcranial direct current stimulation: state of the art 2008. Brain stimulation. 2008 Jul 1;1(3):206-23.[8]



Nitsche et al., 2008

Transcranial direct current stimulation (tDCS) of different cortical areas has been shown, in various studies, to result in modifications of perceptual, cognitive, and behavioral functions.[8]



Increasing focality- Nitsche et al, 2008

Increasing focality of tDCS can be achieved by: (1) reducing electrode size, but keeping current density constant, for the electrode that is intended to affect the underlying cortex; (2) increasing the size, and thus reducing current density, of the electrode, which should not affect the underlying cortex; or (3) using an extracephalic reference. Each of these approaches implies methodologic differences that might lead to qualitatively different effects of the stimulation.[8]



Interesting results with conventional tDCS

Grippe TC, Brasil-Neto JP, Boechat-Barros R, Cunha NS, Oliveira PL. Interruption of epilepsia partialis continua by transcranial direct current stimulation. Brain Stimul. 2015 Nov 1;8(6):1227-8.

[3]



- female patient, 20 years old
- ▶ 5 years before: tonic-clonic generalized seizures with aura: intense headache and perioral paresthesiae
- began CBZ, 200 mg b.i.d.
- seizure pattern changed to partial motor seizures of the right arm
- began epilepsia partialis continua of the left arm
- ► EEG: bilateral epileptiform activity in fronto-centro-parietal areas, with spikes mostly over the right hemisphere
- using CBZ 1200 mg/day, clobazam 20 mg/day, and topiramate 300 md/day
- persistent myoclonic jerks of the left hand

- rTMS at 1 Hz and 5 % of threshold
- round coil- clockwise current targeting the right hemisphere
- 300 pulses, no effect
- coil flipped, and more 300 pulses targeting the left hemisphere
- no response

- one week after, tDCS was carried out
- cathode over C4, 2 mA; anode over contralateral supra-orbital region
- duration of 20 min
- as soon as tDCS was turned on: complete cessation of left hand jerks
- after tDCS, jerks returned
- 4 new consecutive sessions were carried out, always with the same result
- subjective improvement even between tDCS sessions



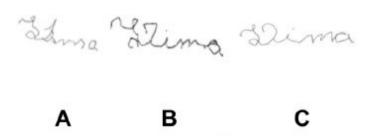
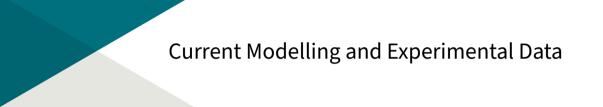


Figure 1. Improvement in handwriting after ipsilateral tDCS. The patient wrote the word "Lima" after the second (A), third (B) and fourth (C) tDCS sessions. Before tDCS she was not able to write.



## Current Modelling and Experimental Data Kuo et al. 2013



- ► The authors compared the effects of conventional anodal and cathodal motor cortex stimulation on subsequent MEPs with those produced by 4X1 high definition anodal and cathodal tDCS
- Both anodal and cathodal stimulation induced the expected increase and decrease in M1 excitability
- ▶ High definition tDCS induced more gradual and prolonged after-effects [6]

### Current Modelling and Experimental Data Leiros Costa et al., 2013 [2]





## Current Modelling and Experimental Data Hogeveen et al., 2016



Hogeveen, J., Grafman, J., Aboseria, M., David, A., Bikson, M., Hauner, K. K. (2016). Effects of high-definition and conventional tDCS on response inhibition. Brain stimulation, 9(5), 720-729. [5]

## Current Modelling and Experimental Data Hogeveen et al., 2016



Bayesian estimation of the effects of HD- and conventional tDCS to IFC relative to control site stimulation demonstrated enhanced response inhibition for both conditions. No improvements were found after control task (CRT) training in any tDCS condition.[5]

### Orthogonal versus Parallel Montages

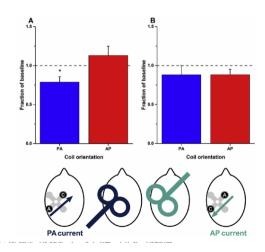
## Orthogonal versus Parallel Montages Rawji et al. 2018



- Current flow models predicted that the orthogonal electrode montage produces consistently oriented current across the hand region of M1 that flows along cortical columns, while the parallel electrode montage produces non-uniform current directions across the M1 cortical surface [11]
- ➤ TMS with a monophasic pulse that induces an electric current flowing from approximately posterior to anterior across the central sulcus (perpendicular to the line of the individual's central sulcus at that point) evokes MEPs (PA-TMS-MEPs) that have a shorter latency and lower threshold than stimulation with an anterior-posterior induced current (AP-TMS-MEPs). [11][1]

### Orthogonal versus Parallel Montages Rawji et al. 2018

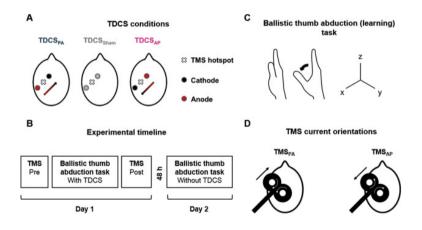




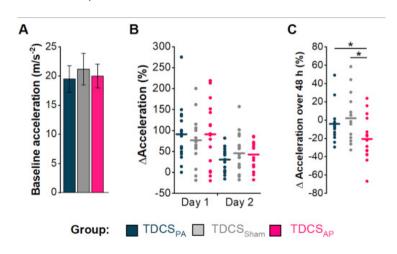


- ► The authors applied tDCS during the practice of a ballistic movement task to test whether it affected learning or the retention of learning 48h later.
- ► TDCS electrodes were oriented perpendicular to the central sulcus and two current orientations were used (posterior-anterior, tDCSPA; and anterior-posterior, tDCSAP)
- ▶ Directional tDCSAP impaired the retention of learning on the ballistic movement task compared to tDCSPA and a sham condition [4]











...the retention of learning on a ballistic motor task appeared to be affected by AP, but not PA, directed current flow. [4]

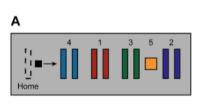
# Orthogonal versus Parallel Montages Iannone et al. submitted

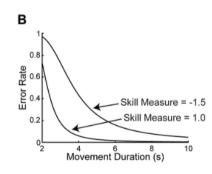


- ➤ 30 subjects practiced the sequential-visuomotor-isometric-pinch-force-task (SVIPT) while under conventional, high-definition or sham tDCS over M1
- ► 10 subjects in each group

# Orthogonal versus Parallel Montages Iannone et al, submitted







# Orthogonal versus Parallel Montages Iannone et al, submitted



Focal tDCS led to greater motor skill performance in between-day retention but had no effect during training sessions

## Orthogonal versus Parallel Montages Mikonnen, 2020



- ► Interindividual variability of predicted EFs increased with EF focality for conventional M1- contralateral forehead and 4X1 HD montages.
- 4X1 HD-tDCS was found to have the highest EF focality and greatest variability. [7]

# Orthogonal versus Parallel Montages Mikonnen, 2020



Bipolar HD montages targeting the region between two small electrodes... produced EF magnitudes comparable to those of 4X1 HD-TDCS, with a minor decrease in focality and lower interindividual variability.

— Mikkonen et al, Brain Stimulation 13 (2020) 117-124 [7]

### **Latest Systematic Review**

### **Latest Systematic Review**



Parlikar et al, 2021- a Review

Parlikar, R., Sreeraj, V. S., Shivakumar, V., Narayanaswamy, J. C., Rao, N. P., Venkatasubramanian, G. (2021). High definition transcranial direct current stimulation (HD-tDCS): A systematic review on treatment of neuropsychiatric disorders. Asian Journal of Psychiatry, 102542.[9]

HD-tDCS in Neurological Disorders [9]

- three randomized, controlled trials
- ▶ intensity of stimulation: tolerance is comparable across 1mA-3 mA
- strong sham arm advisable to avoid placebo effects
- different effects of HD-tDCS and conventional montages? uniform parameters are needed



HD-tDCS in Neurological Disorders [9]

All six studies, out of which three were randomized trials, showed significant outcomes with HD-tDCS. There is sufficient evidence to support the tolerability of HD-tDCS in these studies, but to ascertain its beneficial effects, certainly, more exploration is warranted. [9]



Results of a Systematic Review of HD-tDCS [9]

- more HD-tDCS studies are necessary
- experiments with bipolar orthogonal montages provide neurophysiological insights[11] [4][7]



Afterthought: Is focality really all that important?

- ▶ tDCS is capable of modulating localized neuronal networks as well as subcortical structures and cortico-subcortical connections [10]
- this is a physiological phenomenon and not merely due to electric field spread
- certain montages may show clear clinical benefits even though the exact mechanisms at play might not be completely clear

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