Methodological considerations for tDCS

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Review

A technical guide to tDCS, and related non-invasive brain stimulation tools

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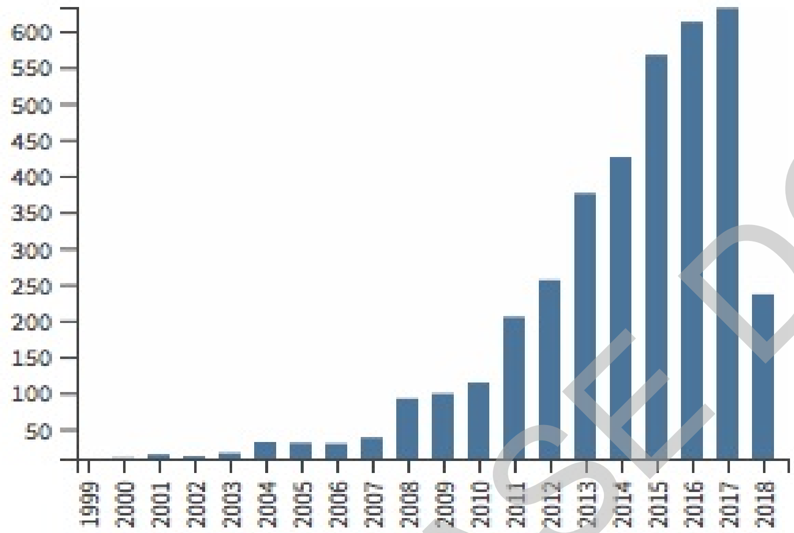
Motivation



- tDCS is increasingly applied
- Seemingly simple tool
- Inappropriate use can lead to frustrating results
- Not all practically relevant information readily available

Overview

- Devices and application
- Protocols
- Physiological effects
- Functional effects in healthy humans and patients

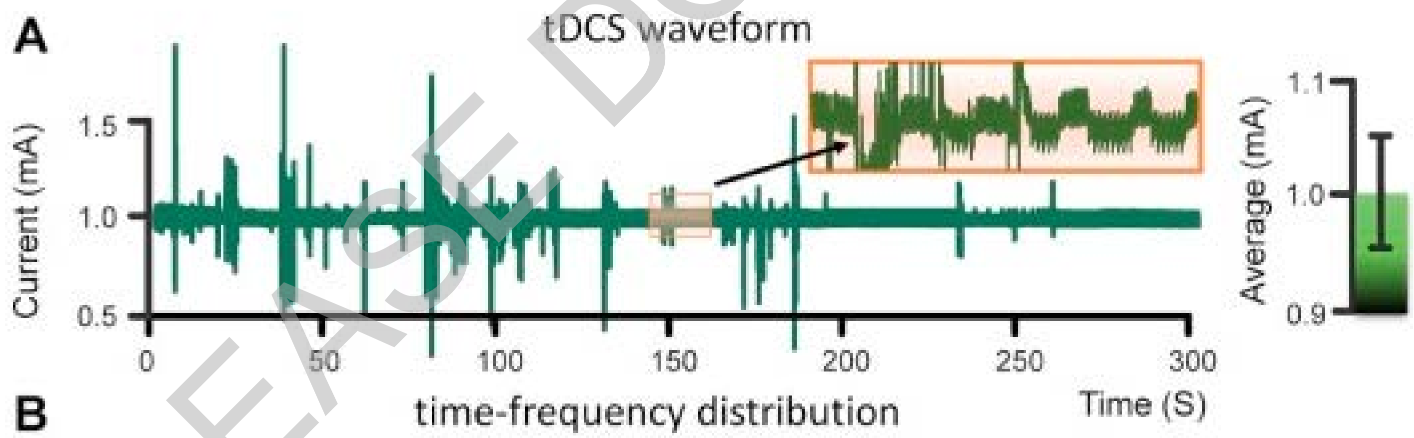
Devices I

Devices II

✓ Numerous CE-certified devices available

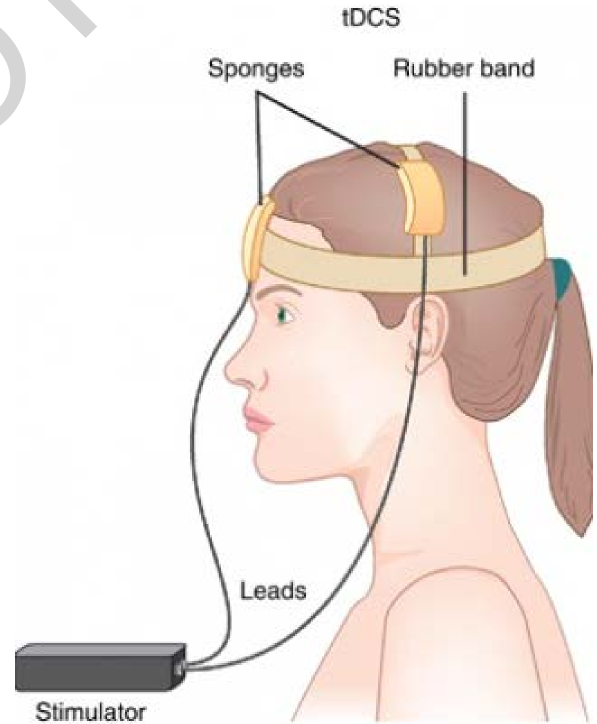
✓ Different characteristics (MRI-suited, multiple channel, wireless, simultaneous EEG, home-use units, range of stimulation modes)

✓ test for appropriate current flow!

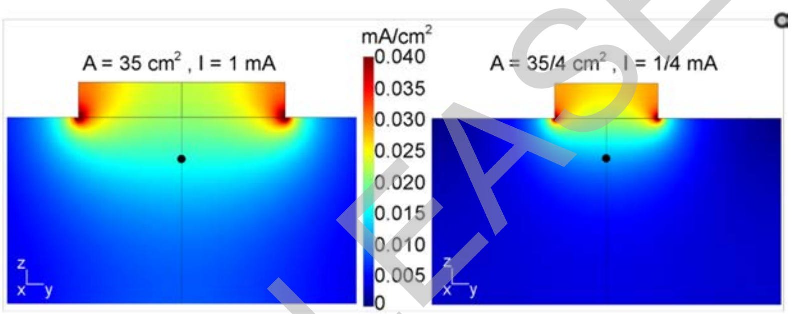


Salimpour et al. 2016

Electrodes - Types



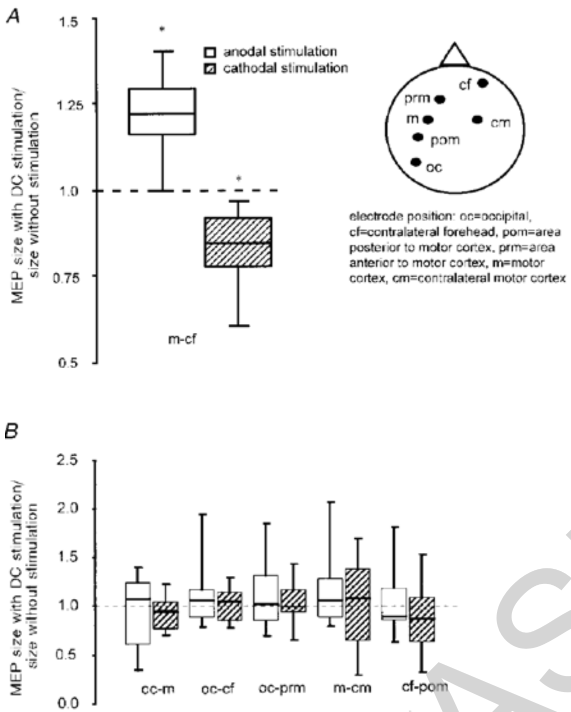
Electrodes – Contact Medium

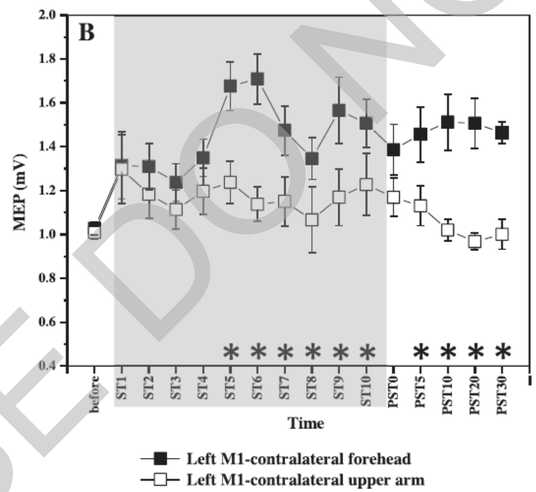


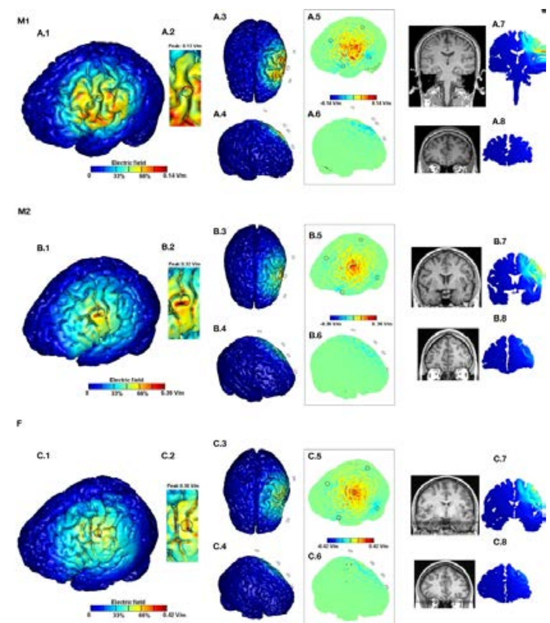
- Saline and cream are suitable
- Saline: not too wet and not too dry...
- Cream: sufficiently thick film
- Electrode shape and distance are relevant

Miranda et al. 2009, Palm et al. 2014

Electrodes – Placement I





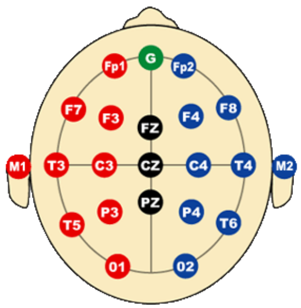


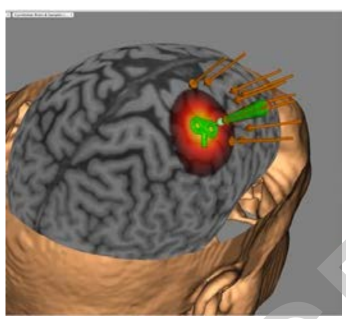
Nitsche & Paulus 2000

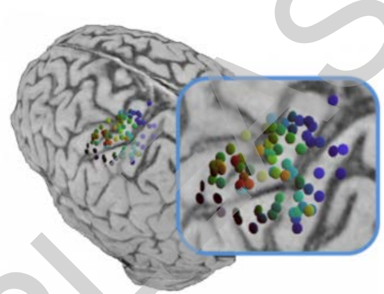
Moliadze et al. 2010

Datta et al. 2012

Electrodes – Placement II



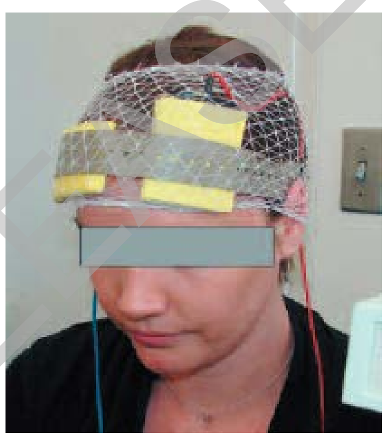




- Standard systems (e.g. 10 20 EEG)
- Neuronavigation (MRI-based)
- Physiology-based

Electrodes – Placement III



- Not too tight
- Not too loose
- Not too wet
- Not too dry
- Constant position
- Not too close

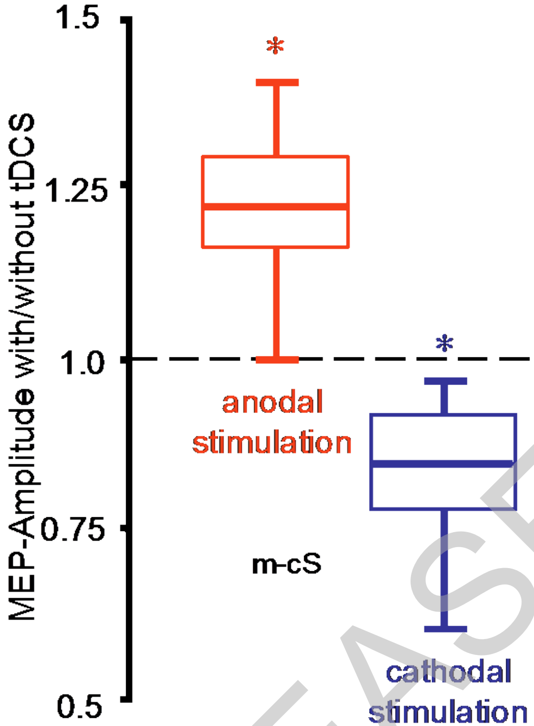
Conclusions - Devices

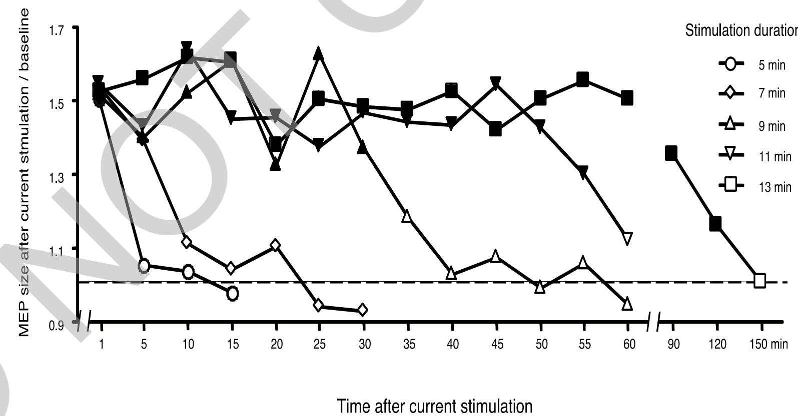
- Different devices for different needs available
- Make sure that stimulators deliver current as expected!
- Electrodes come in different shapes and designs
- Saline solution and cream/gel suited
- Take care for constant and correct positioning!

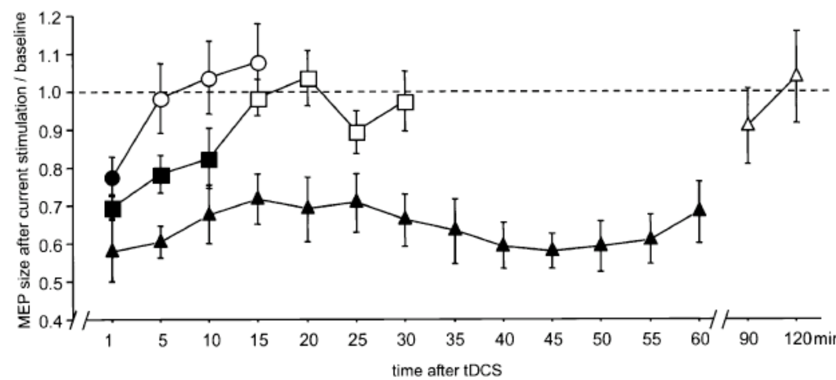
Stimulation protocols

- Stimulation duration and intensity
- Focality of stimulation
- Blinding
- Safety

Stimulation duration





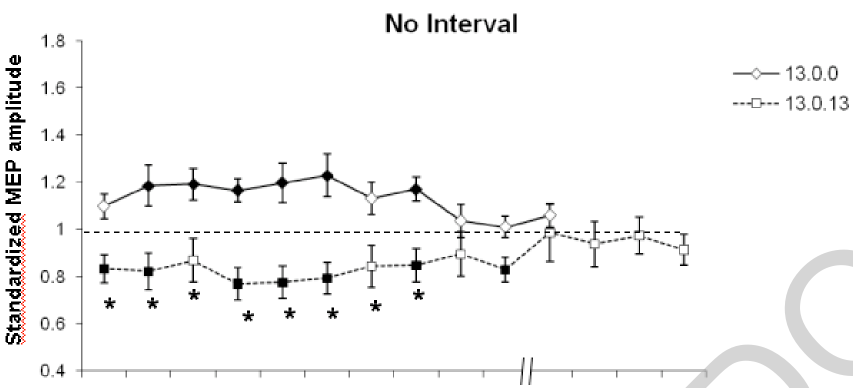


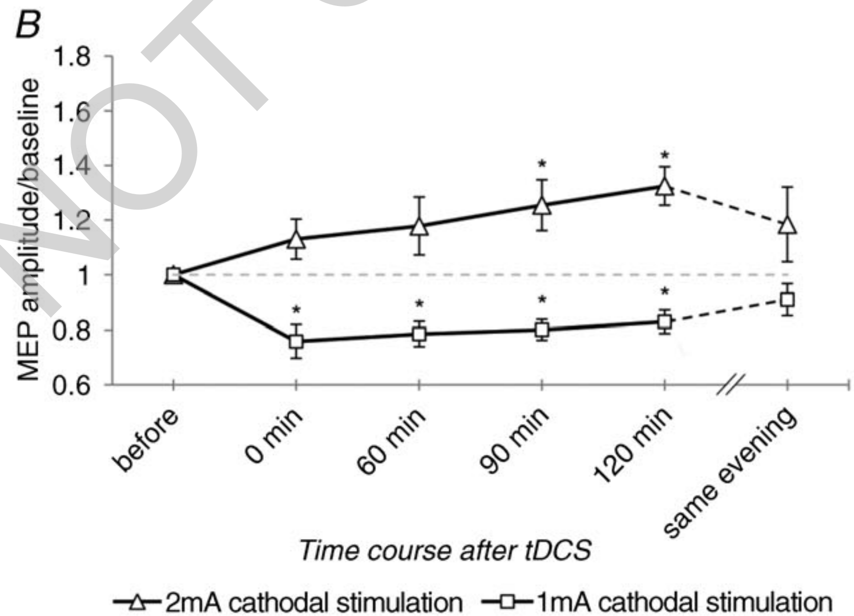
4 seconds

5-13 min

Nitsche & Paulus 2000, 2001, Nitsche et al. 2003

Stimulation duration and intensity





13 vs 26 min anodal tDCS

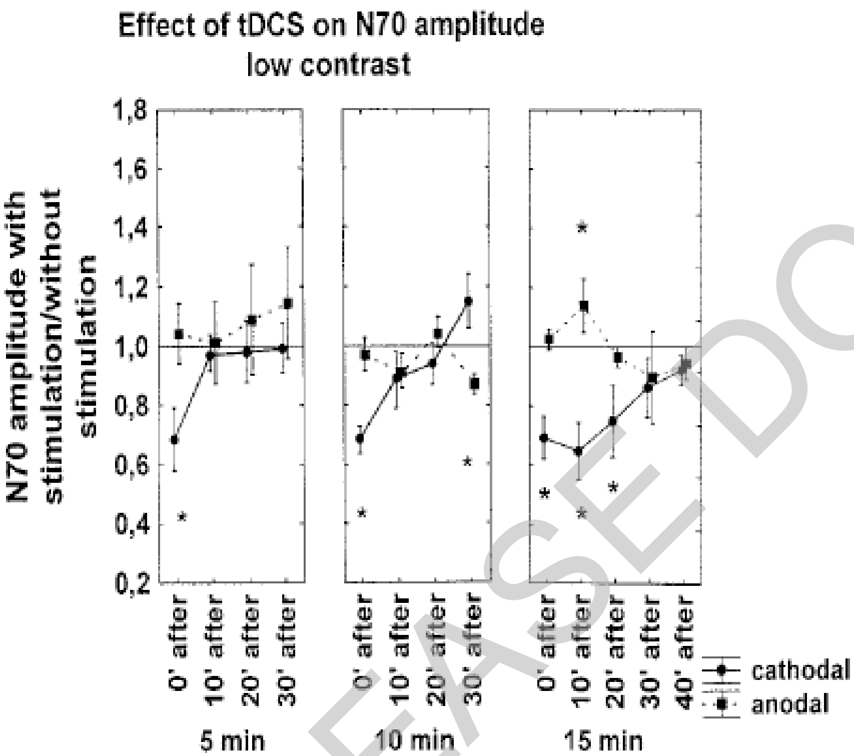
1 vs 2 mA cathodal tDCS

Longer and stronger is not always better

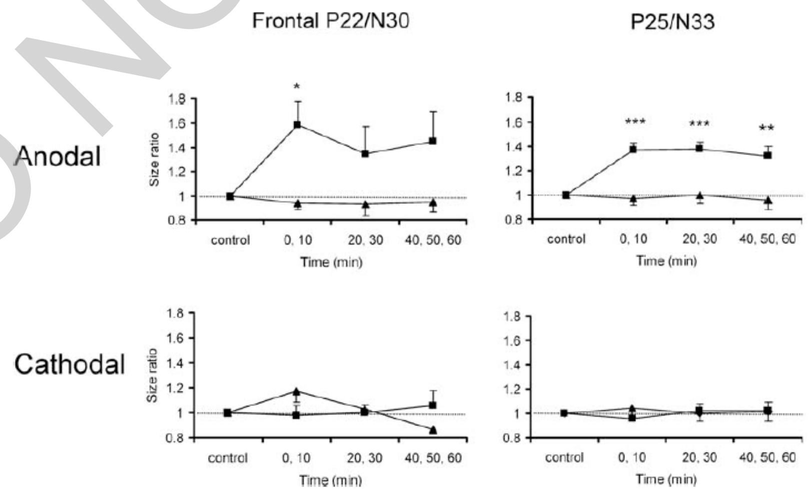
Batsikadze et al. 2013, Monte-Silva et al. 2013

Transferability to other cortices?

Visual cortex

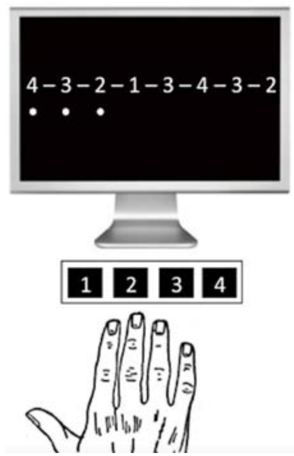


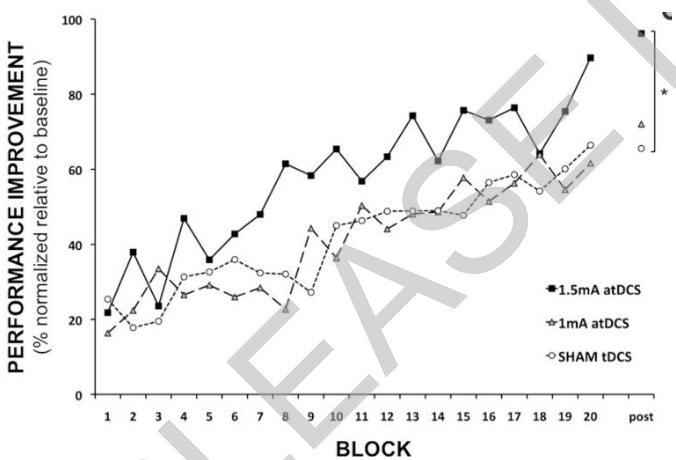
Somatosensory cortex

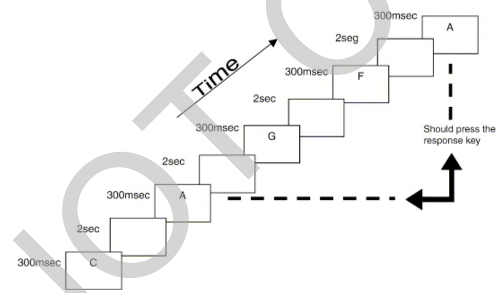


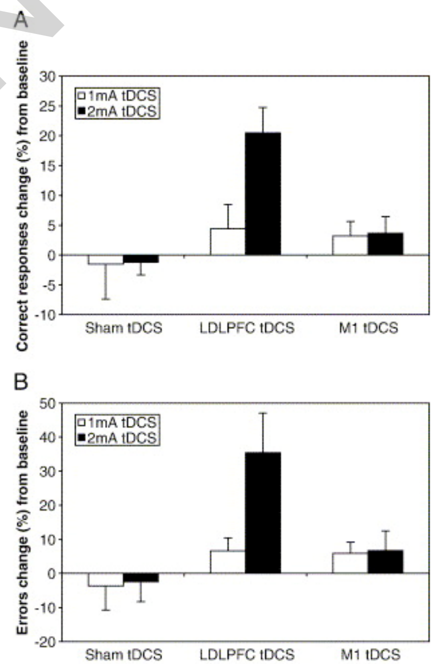
Antal et al. 2004, Matsunaga et al. 2004

Shaping effects of tDCS by systematic protocol adaptation







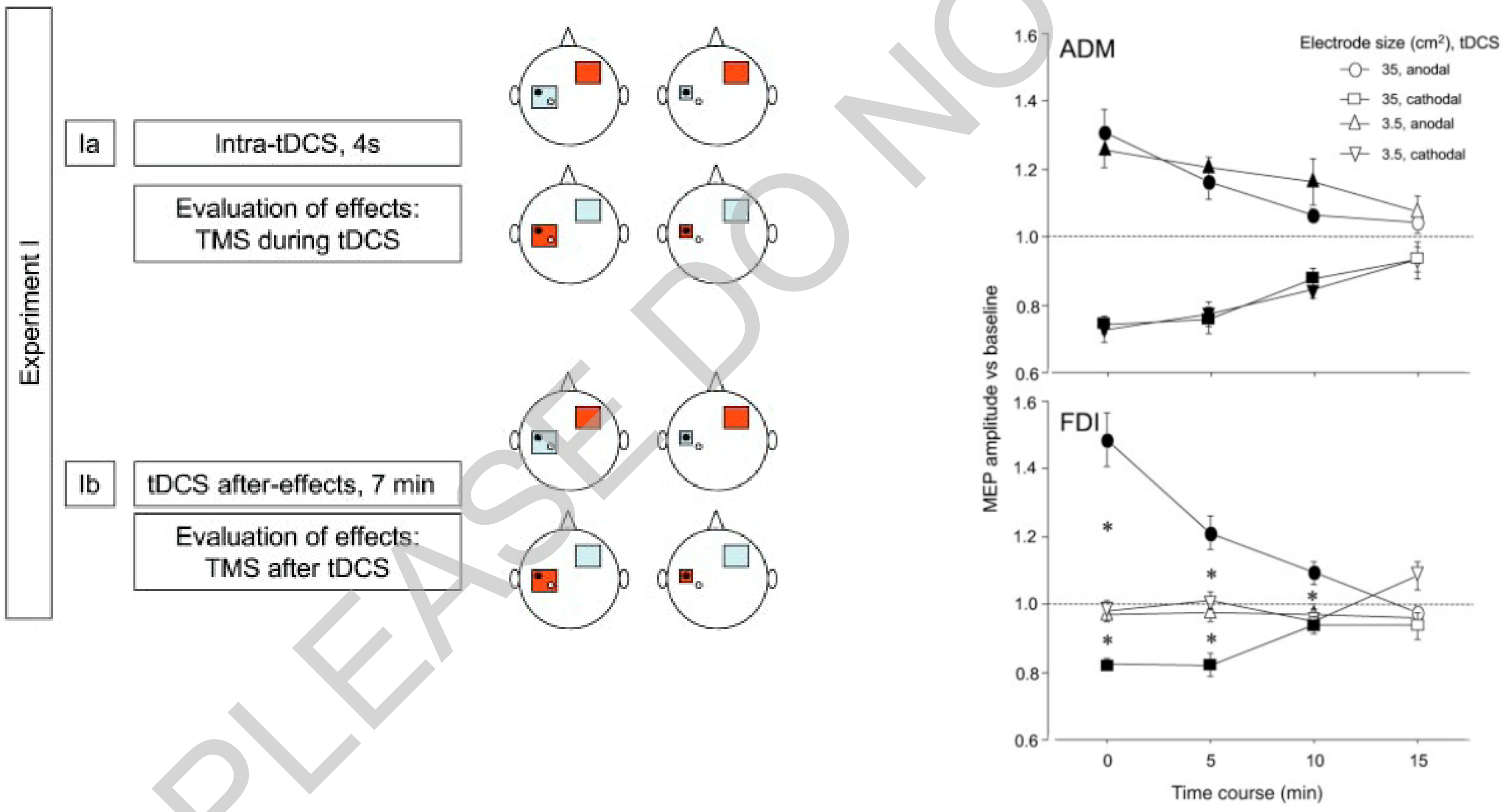


Cuypers et al. 2013, Boggio et al. 2006

Conclusion Protocols I

- Protocols inducing acute and after-effects available
- Longer and stronger stimulation does not always increase efficacy
- Repetition can result in bidirectional interference effects
- Not identical effects in all areas
- Titration of effects preferable for new areas

Focalizing by reducing the size of the stimulation electrode



Focalizing by use of an extracephalic return electrode?

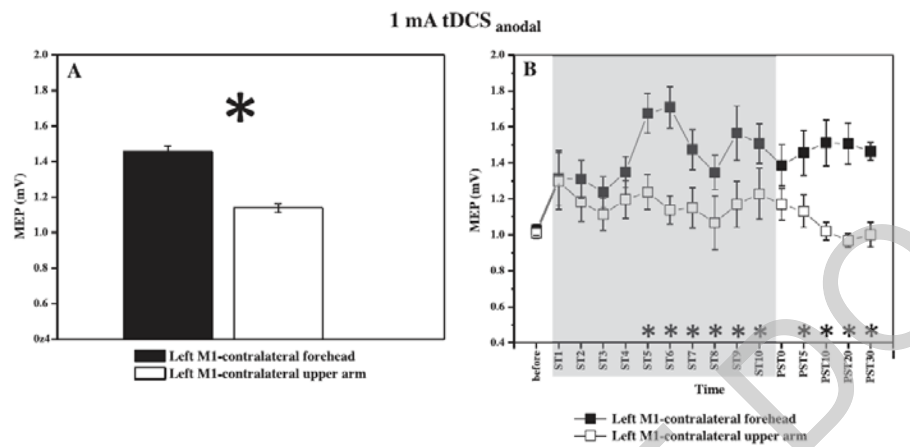


Fig. 1. *Left M1 – contralateral forehead vs. Left M1 – contralateral upper arm.* (A) Comparison of the 1 mA $tDCS_{anodal}$ induced effects on cortical excitability using the *Left M1 – contralateral forehead vs. Left M1 – contralateral upper arm* electrode montage. The bar graph shows the mean MEP value from ST1 to PST30, averaged over 9 subjects. Error bars indicate standard errors. An asterisk indicates $P < 0.05$. (B) The figure shows mean amplitudes of MEPs and their SEMs during 10 min of stimulation and up to 30 min after stimulation (9 subjects). Significantly increased MEPs were observed in Left M1- contralateral forehead montage at the ST5-ST10 and PST5-PST30 time points compared to the corresponding time points using the *Left M1 – contralateral upper arm montage* ($P < 0.05$).

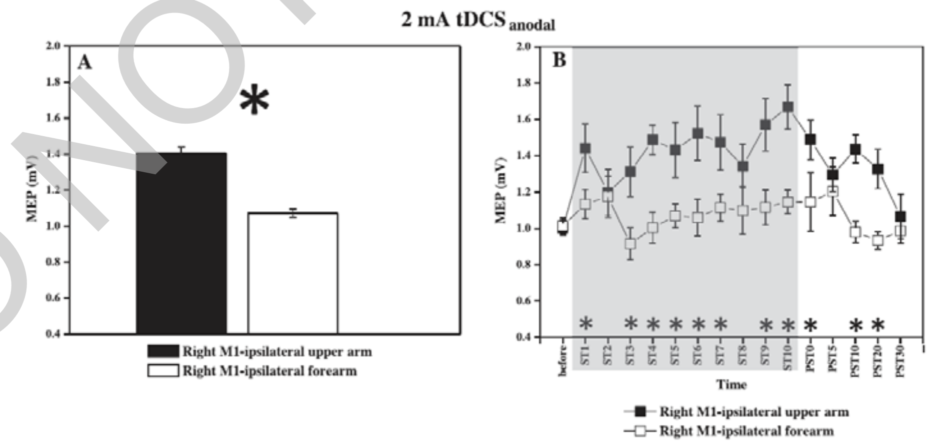
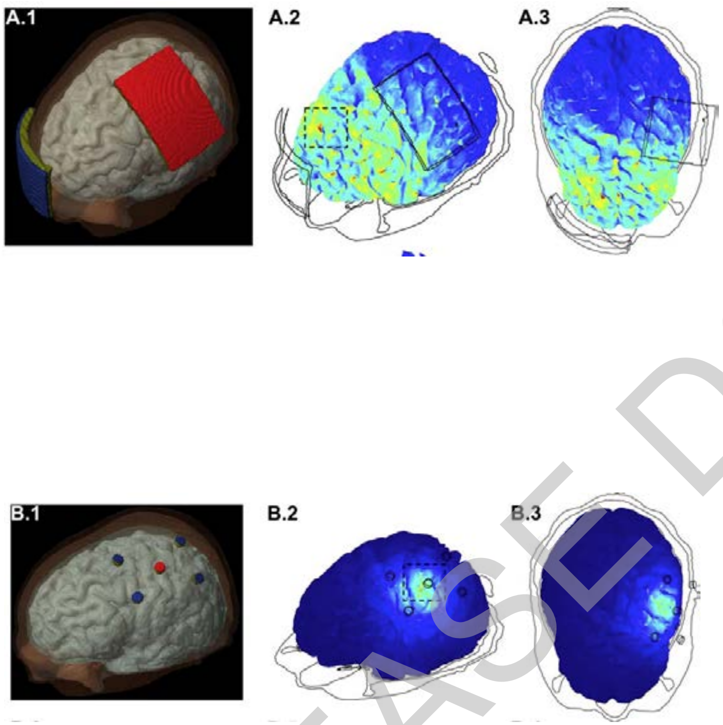
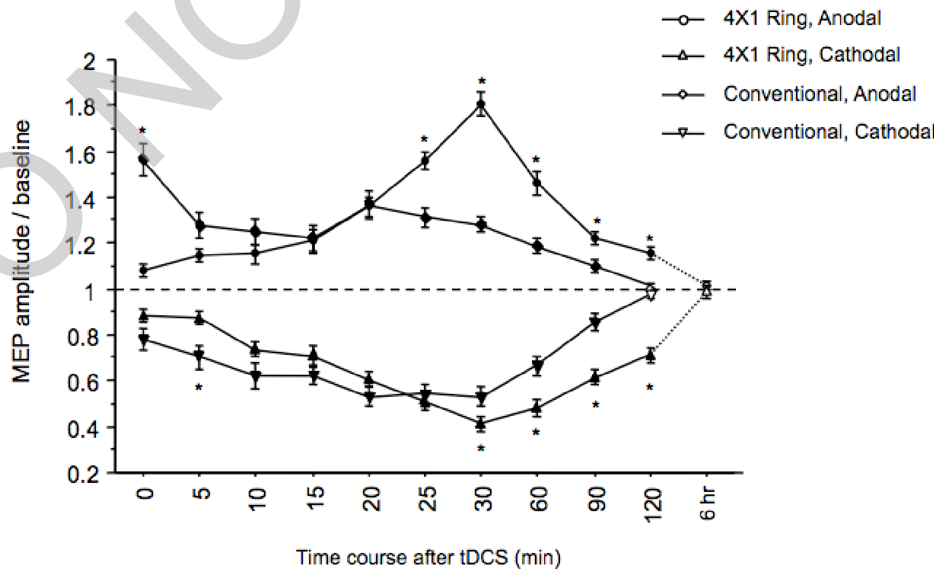


Fig. 4. *Right M1 – ipsilateral upper arm vs. Right M1 – ipsilateral forearm.* (A) Comparison of the 2 mA $tDCS_{anodal}$ induced effects on cortical excitability using the Right M1-ipsilateral upper arm vs. Right M1-ipsilateral forearm electrode montage. The bar graph shows the mean MEP value from ST1 to PST30, averaged over 7 subjects. Error bars indicate standard errors. An asterisk indicates $P < 0.05$. (B) The figure shows mean amplitudes of MEPs and their SEMs during 10 min and after stimulation up to 30 min. (7 subjects). Significantly increased MEPs were observed in *Right M1 ipsilateral upper arm montage* at the ST1, ST3-ST7, ST9-ST10, PST0, and PST10-PST20 time points compared to the corresponding time points using the *Right M1 – ipsilateral forearm montage* ($P < 0.05$).

Moliadze et al. 2010

Focalizing by modification of electrode shape?





Kuo et al., 2013

Enhanced focality (?)

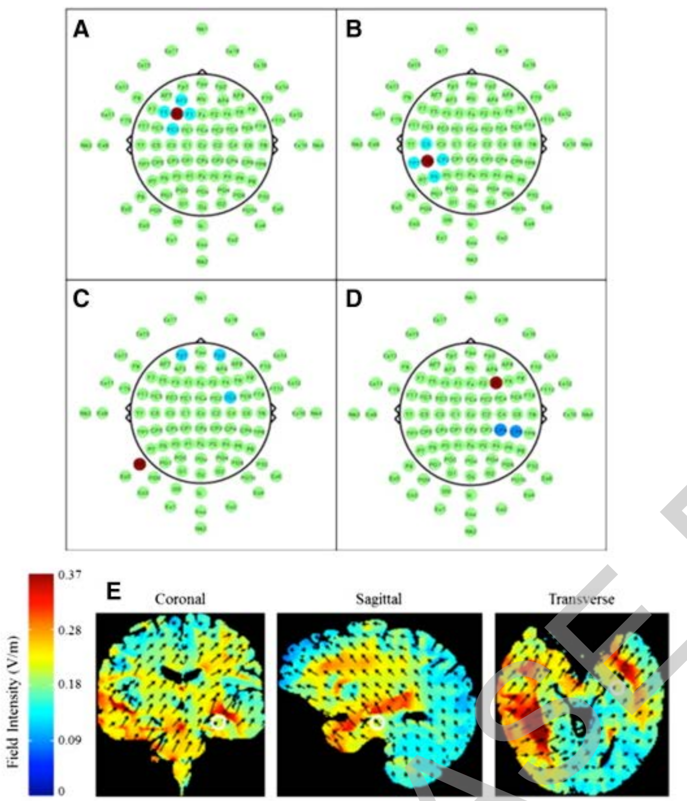


Fig. 1.
Montages used during stimulation, derived from HDExplore™ and HDTargets™ software: A, anodal stimulation to the LDLPFC (anode: F3; cathodes: AF3, F5, FC, FC3). B, Anodal stimulation to the PT (anode: Cp5; cathodes: C5, TP7, Cp3, P5). C, Electrode configuration resulting in anodal stimulation of the LMTL (anode: P9; cathodes: Fp1, Fp2, FC4); D, sham montage (anode: F4; cathodes: Cp4, Cp6). E, Model simulation using HDExplore™ of the pattern of current strength associated with the LMTL montage designed to maximally stimulate the left hippocampus.

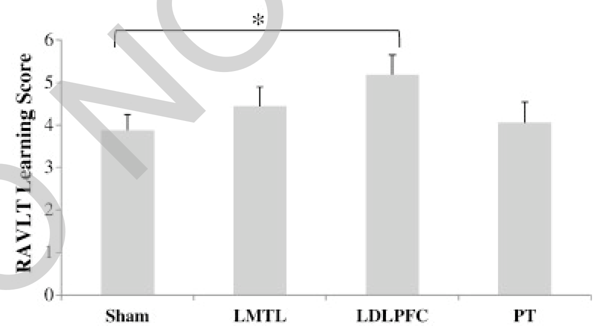
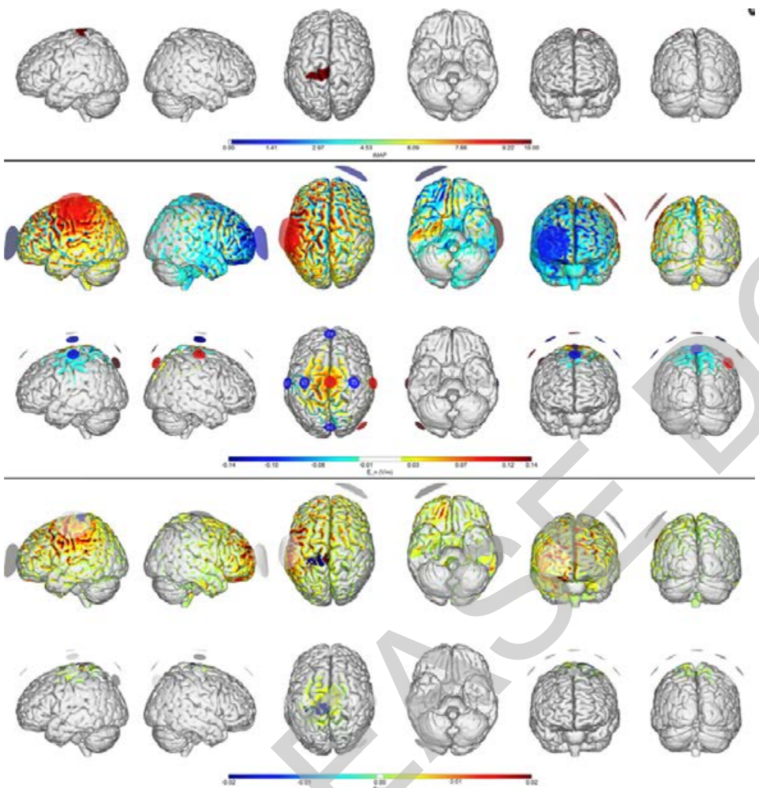


Fig. 3.
Verbal learning scores, as calculated by the difference between final and initial blocks of the Rey's Auditory Verbal Learning Test (RAVLT), for each stimulation condition.*p < .05.

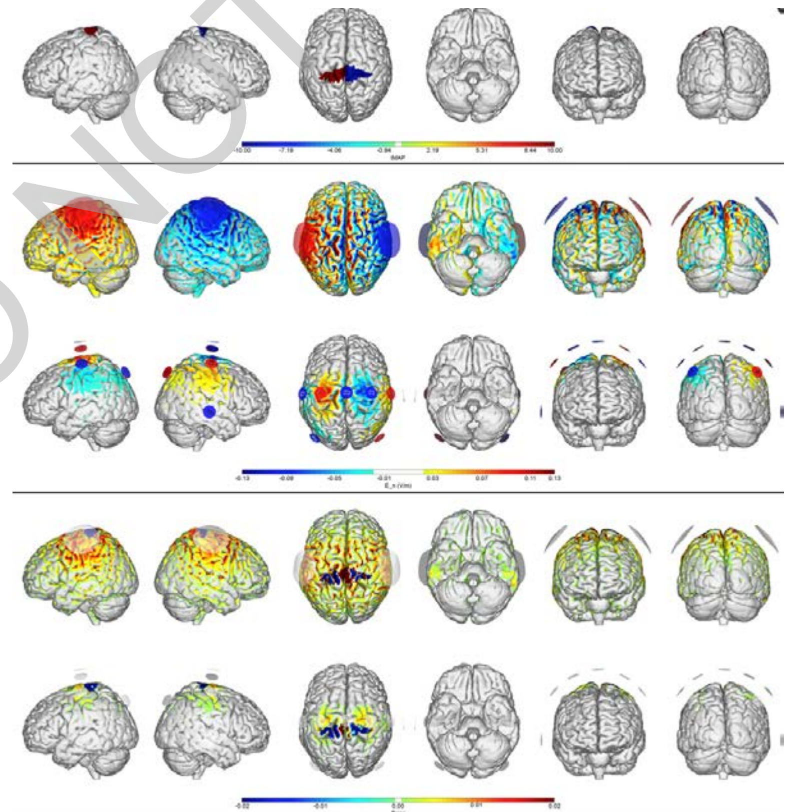
Nikolin et al., 2015

New multi-electrode approach

„monopolar“

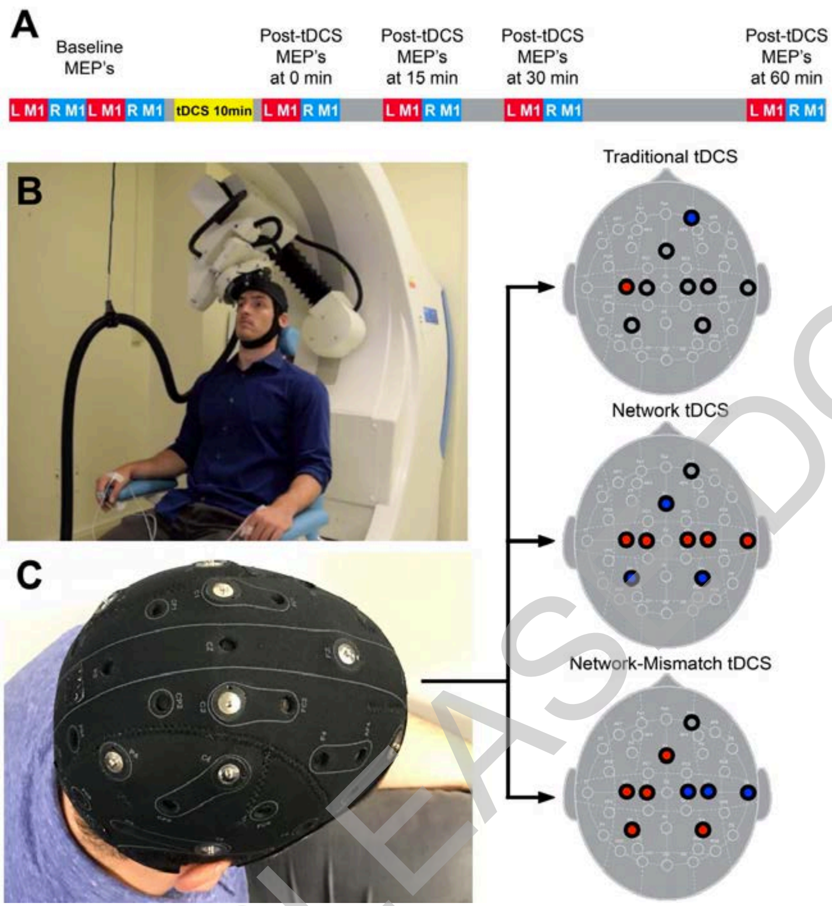


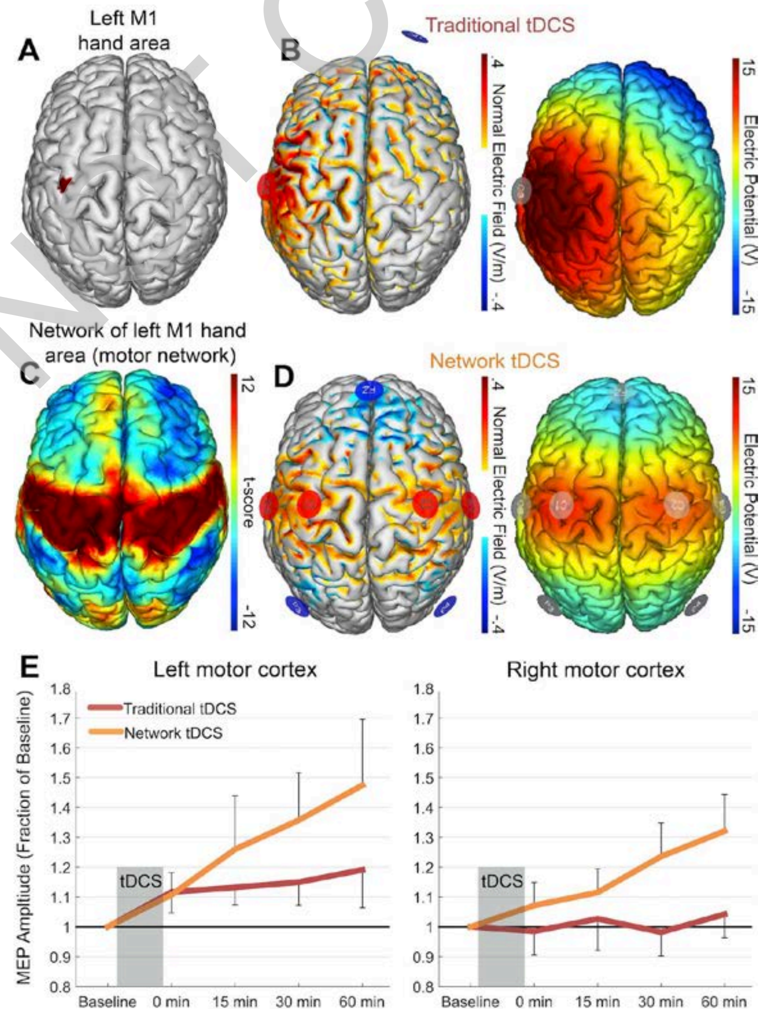
„bipolar“



Ruffini et al. 2015

Increasing the efficacy of tDCS by network stimulation





Fischer et al., 2017

Conclusion Protocols II

- Focality of tDCS can be increased
- ...by altering electrode size
- ...by altering electrode configuration
- ...by altering electrode position
- Application-dependent usefulness
- Physiological alterations induced by these alternative protocols not sufficiently explored so far in each case

Blinding of stimulation

- Ramping of stimulation
- Reliable blinding at 1 mA
- Might be not reliable for stronger stimulation
- Might be not reliable for repetitive sessions
- Reduction of tingling sensation by local anesthetics
- Active control

- Specific stimulators with coded stimulation
- One experimenter only conducts stimulation
- Reduction of stimulation-generated erythema with ketoprofen

Safety vs tolerability

Safety: induction of structural or functional *damage*

Tolerability: unintended or uncomfortable effects without damage

Safety and tolerability of tDCS I

- No NSE enhancement
- No brain edema
- No structural damage

Adverse effects of tDCS during stimulation in different groups of participants

Participants	Tingling			Itching sensation			Burning sensation			Pain			Headache			Fatigue			Difficulties in concentrating		
	N	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity
Migraine patients	6	66.7	1.67 ± 0.82	1	11.1	2.0 ± 0	2	22.2	2.0±1.41	1	11.1	2.0 ± 0	1	11.1	1.0 ± 0	4	44.4	2.5 ± 1.29	0	0	0
Post-stroke patients	2	33.3	1.0 ± 0	1	16.7	1.0 ± 0	0	0	0	1	16.7	1.0 ± 0	1	16.7	3.0 ± 0	2	33.3	2.5 ± 2.12	1	16.7	4.0 ± 0
Tinnitus sufferers	8	80	1.13 ± 0.35	1	10	1.0 ± 0	3	30	1.0 ± 0	0	0	0	0	0	0	3	30	1.33 ± 0.58	1	10	1.0 ± 0
Patients total	16	64	1.31 ± 0.60	3	12	1.33 ± 0.58	5	20	1.4 ± 0.89	2	8	1.5 ± 0.70	2	8	2.0 ± 1.41	9	36	2.11 ± 1.27	2	8	2.5 ± 2.12
Healthy subjects	56	72.7	1.86 ± 0.86	28	36.4	1.63 ± 0.74	17	22.7	1.65 ± 0.93	14	18.2	1.4 ± 0.74	3	3.9	1.0 ± 0	27	35.1	2.19 ± 1.08	9	11.7	1.56 ± 0.88
Participants total	72	70.6	1.74 ± 0.84	31	30.4	1.6 ± 0.72	22	21.6	1.59 ± 0.91	16	15.7	1.41 ± 0.71	5	4.9	1.4 ± 0.89	36	35.3	2.17 ± 1.11	11	10.8	1.73 ± 1.10

Participants	Nervousness			Changes in visual perception			Unpleasant sensation			Visual sensation, associated with the start/end of the stimulation		Difference between stimulations		Others			
	N	%	Mean intensity	*N*	%	Mean intensity	*N*	%	Mean intensity	*N*	%	*N*	%	*N*		*N*	
Migraine patients	1	11.1	1.0 ± 0	0	0	0	2	22.2	1.0 ± 0	3	33.3	4	44.4	–		–	
Post-stroke patients	0	0	0	0	0	0	1	16.7	1.0 ± 0	1	16.7	1	16.7			–	
Tinnitus sufferers	0	0	0	0	0	0	0	0	0	0	0	1	10	1	Drowsiness	–	
Patients total	1	4	1.0 ± 0	0	0	0	3	12	1.0 ± 0	4	16	6	24	1	Drowsiness	–	
Healthy subjects	4	5.2	1.0 ± 0	0	0	0	15	19.5	1.29 ± 0.47	7	9.1	11	14.3	1	Drowsiness	1	Nausea
Participants total	5	4.9	1.0 ± 0	0	0	0	18	17.7	1.24 ± 0.44	11	10.8	17	16.7	2	Drowsiness	1	Nausea

Nitsche et al. 2003, 2004, Poreisz et al. 2007

Safety and tolerability of tDCS II

Brain Stimulation ■■ (2016) ■■–■■

Contents lists available at ScienceDirect

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Brain Stimulation

journal homepage: www.brainstimjrnl.com

Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016

Marom Bikson [a,*], Pnina Grossman [a], Chris Thomas [a], Adantchede Louis Zannou [a], Jimmy Jiang [a], Tatheer Adnan [a], Antonios P. Mourdoukoutas [a], Greg Kronberg [a], Dennis Truong [a], Paulo Boggio [b], André R. Brunoni [c], Leigh Charvet [d], Felipe Fregni [e], Brita Fritsch [f,g], Bernadette Gillick [h], Roy H. Hamilton [i,j,k], Benjamin M. Hampstead [l,m], Ryan Jankord [n], Adam Kirton [o], Helena Knotkova [p,q], David Liebetanz [r], Anli Liu [s], Colleen Loo [t], Michael A. Nitsche [r,u,v], Janine Reis [f,g], Jessica D. Richardson [c,w,x], Alexander Rotenberg [y,z], Peter E. Turkeltaub [aa,ab], Adam J. Woods [ac]

This review updates and consolidates evidence on the safety of transcranial Direct Current Stimulation (tDCS). Safety is here operationally defined by, and limited to, the absence of evidence for a Serious Adverse Effect, the criteria for which are rigorously defined. This review adopts an evidence-based approach, based on an aggregation of experience from human trials, taking care not to confuse speculation on potential hazards or lack of data to refute such speculation with evidence for risk. Safety data from animal tests for tissue damage are reviewed with systematic consideration of translation to humans. Arbitrary safety considerations are avoided. Computational models are used to relate dose to brain exposure in humans and animals. We review relevant dose–response curves and dose metrics (e.g. current, duration, current density, charge, charge density) for meaningful safety standards. Special consideration is given to the- oretically vulnerable populations including children and the elderly, subjects with mood disorders, epilepsy, stroke, implants, and home users. Evidence from relevant animal models indicates that brain injury by Direct Current Stimulation (DCS) occurs at predicted brain current densities (6.3–13 A/m2) that are over an order of magnitude above those produced by conventional tDCS. To date, the use of conventional tDCS protocols in human trials (≤40 min, ≤4 milliamperes, ≤7.2 Coulombs) has not produced any reports of a Serious Adverse Effect or irreversible injury across over 33,200 sessions and 1000 subjects with repeated sessions. This includes a wide variety of subjects, including persons from potentially vulnerable populations.

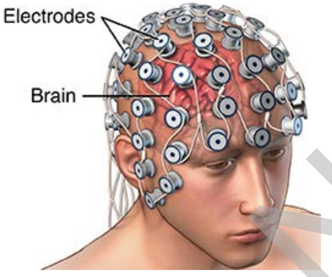
Conclusion - Safety and tolerability of tDCS

- Well tolerated, no serious adverse effects
- Applies to conventional protocols
- Side effects can be monitored by tDCS questionnaires (e.g. Poreisz et al. 2007)
- Side effects like skin burns reported caused by inappropriate application

Monitoring physiological effects of tDCS - preconditions

- Participants in relaxed, stable state
- Test session might help
- Avoid unintended interference effects in case of multiple sessions
- Avoid interference effects between stimulation and monitoring method

Monitoring physiological effects of tDCS - methods

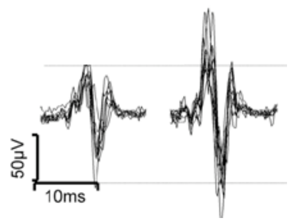


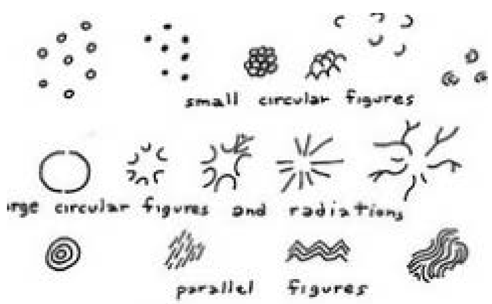
- Cortical excitability
- Motor evoked potentials
- Visual phosphenes
- TMS-EEG

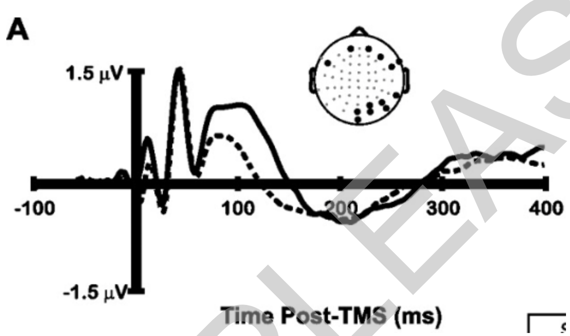
- Cortical activity
- Resting EEG
- EP
- ERP

- Cortical activity
- Functional MRI
- BOLD
- ASL
- MRS
- Structural MRI

Monitoring physiological effects of tDCS - TMS

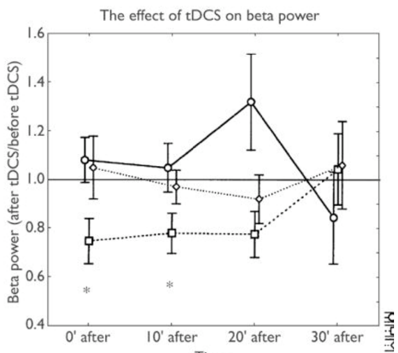


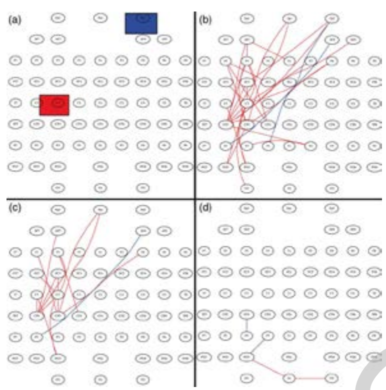


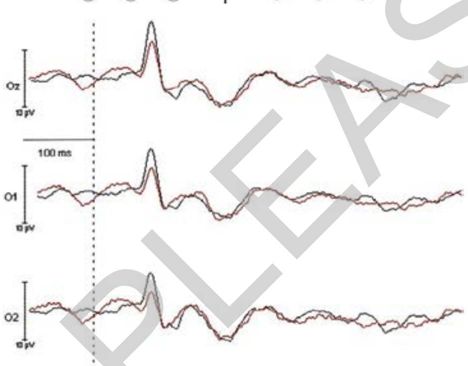


- Reliable hot spot and coil position
- Reliable baseline
- Constant state throughout experiment
- Sufficient number of stimuli (20 or more)
- No muscle activity before TMS
- TMS EEG over regions which do not induce relevant muscle contraction

Monitoring physiological effects of tDCS - EEG



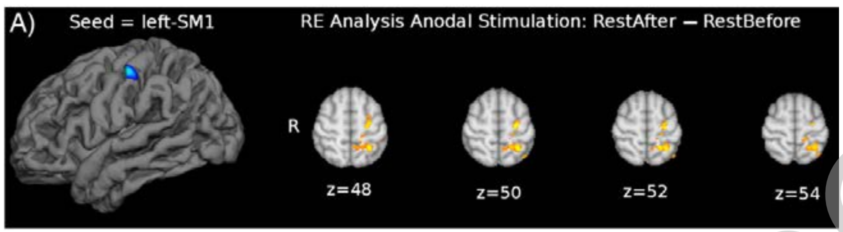


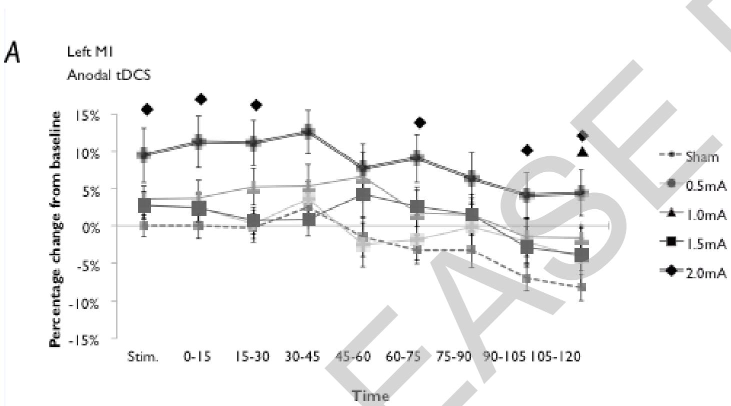


- Online or offline
- Online: cave artifacts, no EEG electrodes under stimulation electrodes
- Offline: cave conductivity alterations at former tDCS electrode positions
- Solution: integrated approaches with recording/stimulation electrodes

Polania et al. 2011, Antal et al. 2004

Monitoring physiological effects of tDCS - MRI





- Online or offline
- Online: cave artifacts, MRI-suited tDCS system required
- Offline: tDCS outside scanner will cause delay, and enhance „noise“ due to altered head position
- No saline-moisted sponges (will get dry)
- Mark electrode positions with oil capsules
- Cables parallel to magnet bore
- Sufficient sample size

Polania et al. 2011, Jamil et al. submitted

Conclusion - Monitoring physiological effects of tDCS

- Couple of methods are available
- Different temporal and spatial sensitivity
- Different restrictions with regard to areas
- Specific considerations to be followed to receive reliable results

Functional effects in healthy humans - Rationale

stimuli

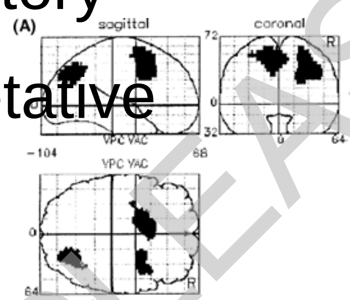
- visual
- auditory
- somatosensory
- gustatory
- olfactory
- vegetative

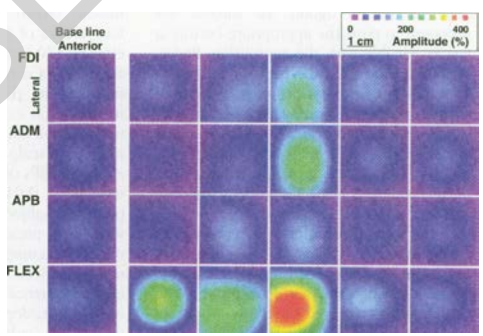
perception

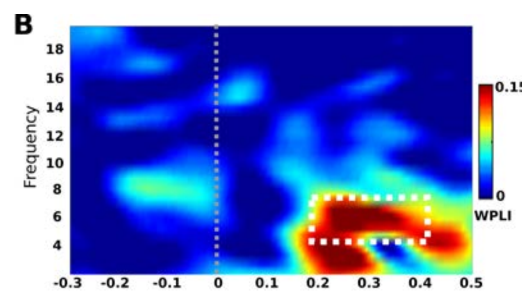
behaviour

motor activity

cognition, motivation, emotion







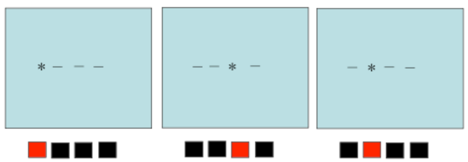
Honda et al. 1998, Pascual-Leone et al. 1994, Polania et al. 2012

Functional effects in healthy humans – relevant factors

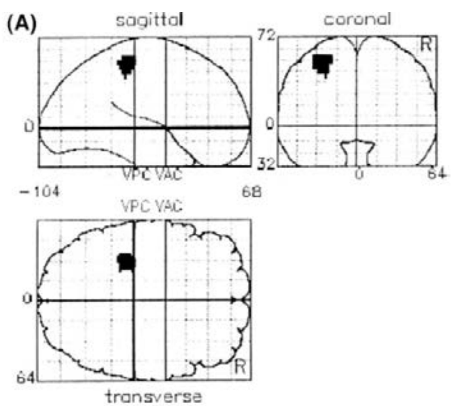
- Timing of stimulation
- Stimulated area
- Type of task
- Bottom vs ceiling effects

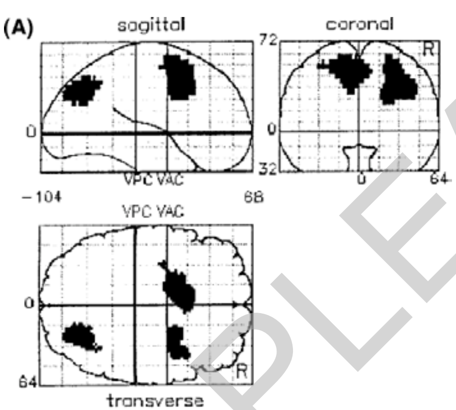
Timing and area of stimulation

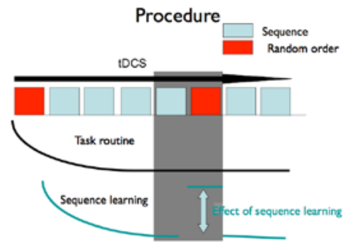
Serial reaction time task (SRTT)

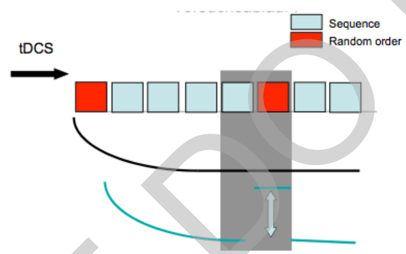


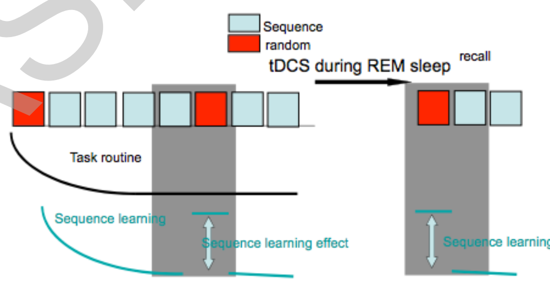
12 stimuli, 10 times repetition per block

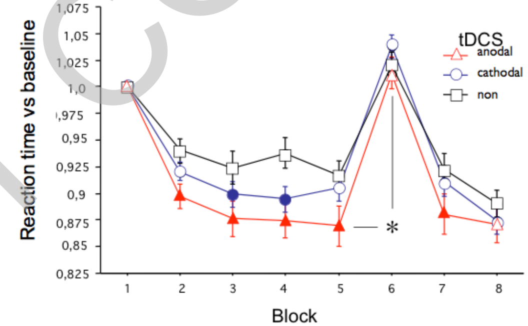


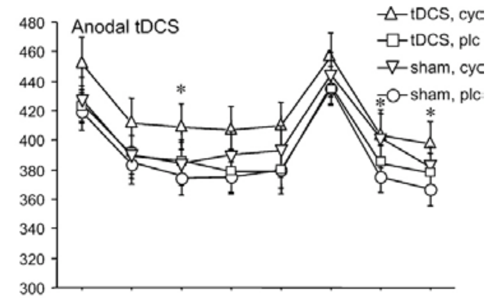


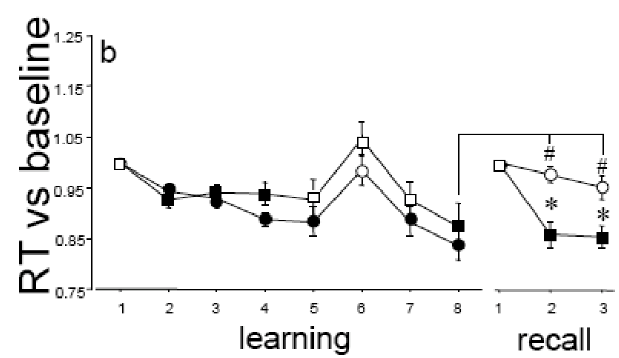






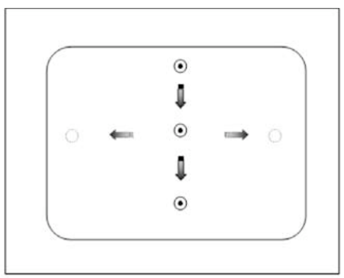


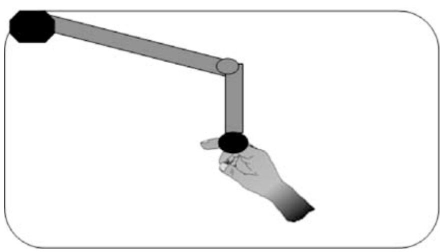


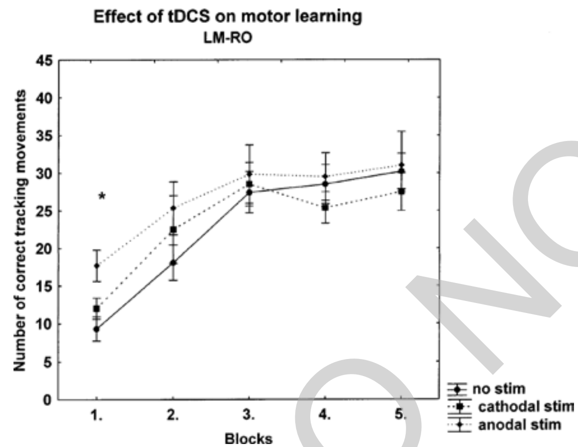


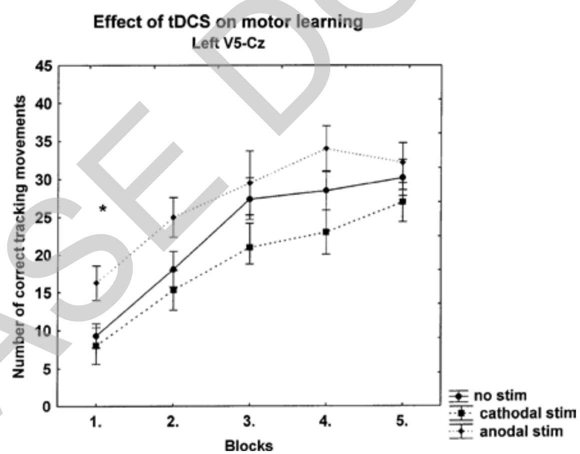
Kuo et al. 2008, Nitsche et al. 2003, 2010

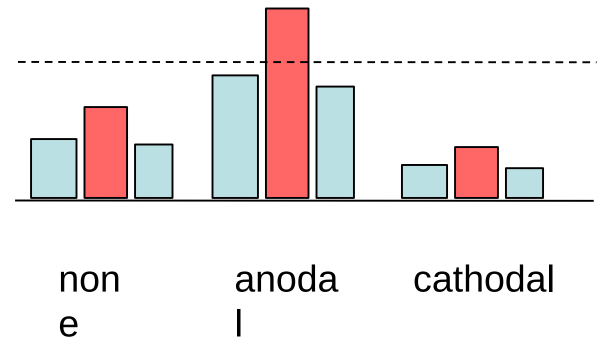
Task characteristics I





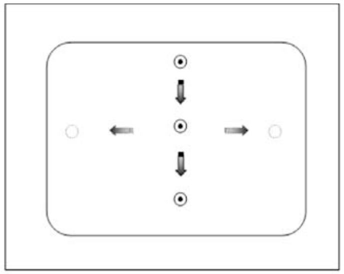


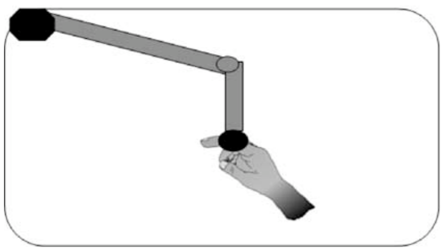


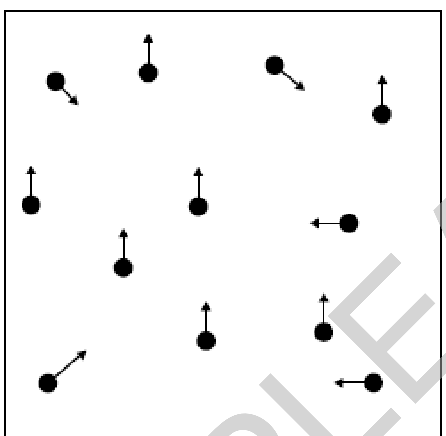


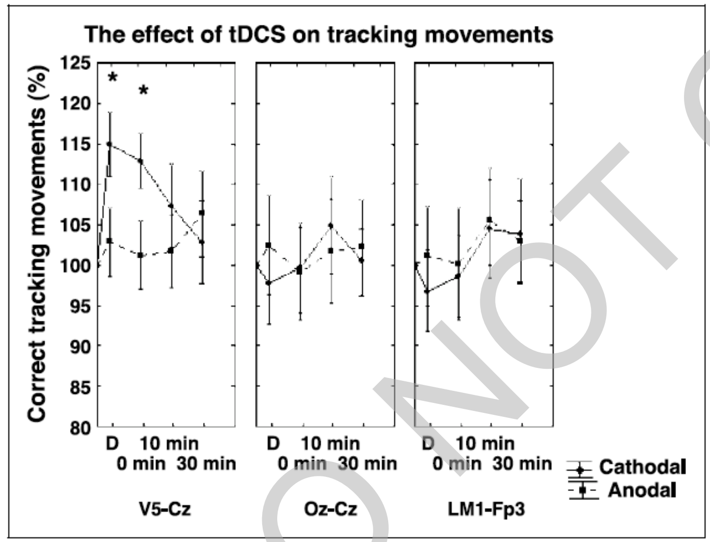
Antal et al. 2004a,b

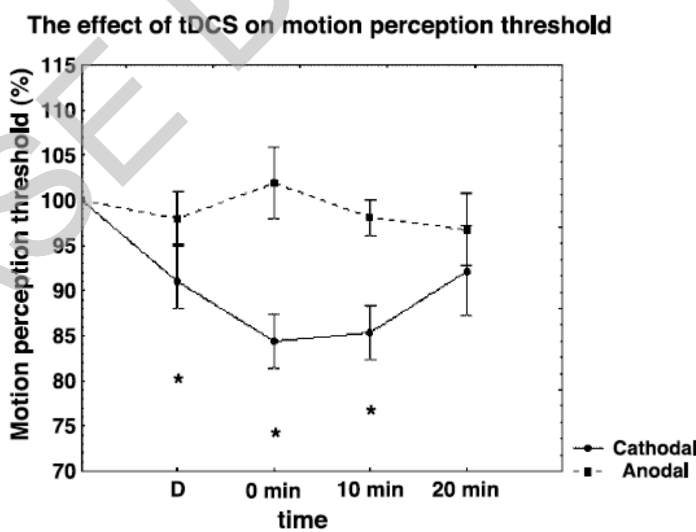
Task-characterisitics II

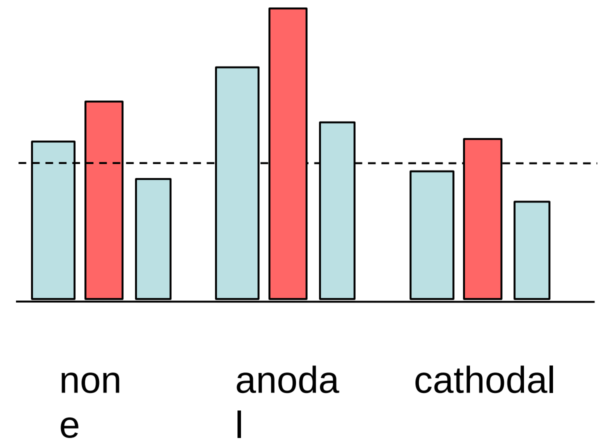






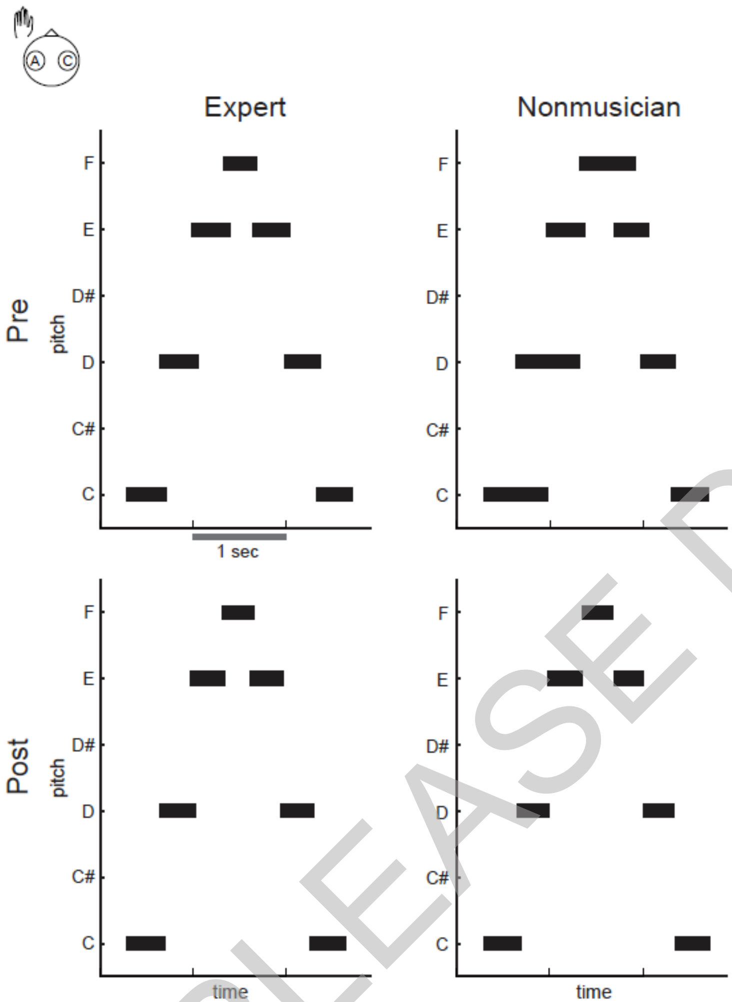


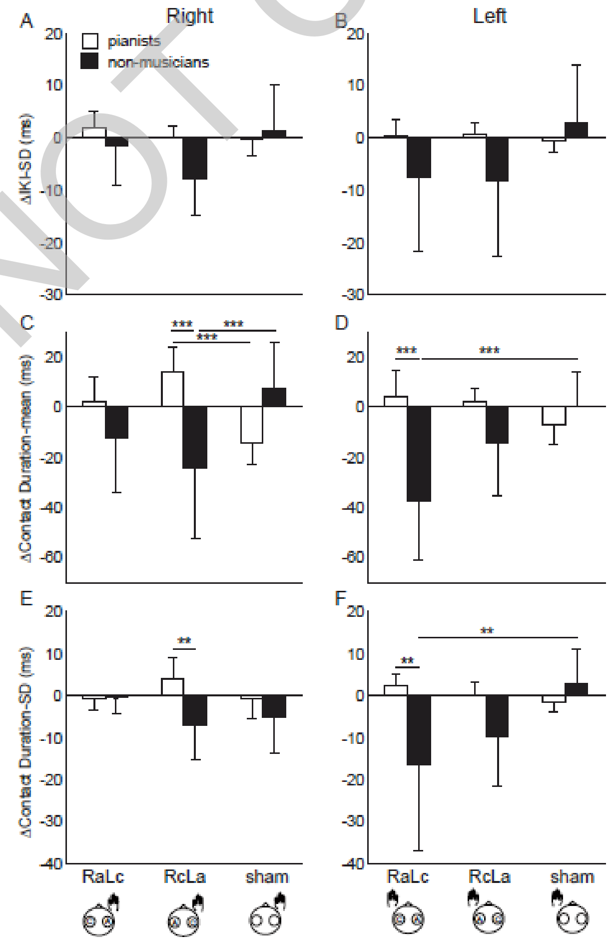




Antal et al. 2004a,b

Ceiling effect – level of expertise





Furuya et al., in 2014

Functional effects in healthy humans

- Timing and area of stimulation should be adjusted to task-related physiology
- Task specifics affect stimulation impact
- Task should not be prone to bottom or ceiling effects
- Relatively fragile neuromodulatory effects; enhancing efficacy by repetition, and titration?

Functional effects in patients

Common rationale: Restitution of disturbed activity/excitability

Article

Examining Transcranial Direct-Current Stimulation (tDCS) as a Treatment for Hallucinations in Schizophrenia

Jerome Brunelin, Ph.D.
Marine Mondino, M.Sc.
Leila Gassab, M.D., Ph.D.
Frederic Haesebaert, M.D.
Lofti Gaha, M.D., Ph.D.
Marie-Françoise Suaud-Chagny, Ph.D.
Mohamed Saoud, M.D., Ph.D.
Anwar Mechri, M.D., Ph.D.
Emmanuel Poulet, M.D., Ph.D.

Objective: Some 25%–30% of patients with schizophrenia have auditory verbal hallucinations that are refractory to antipsychotic drugs. Outcomes in studies of repetitive transcranial magnetic stimulation suggest the possibility that application of transcranial direct-current stimulation (tDCS) with inhibitory stimulation over the left temporo-parietal cortex and excitatory stimulation over the left dorsolateral prefrontal cortex could affect hallucinations and negative symptoms, respectively. The authors investigated the efficacy of tDCS in reducing the severity of auditory verbal hallucinations as well as negative symptoms.

Method: Thirty patients with schizophrenia and medication-refractory auditory verbal hallucinations were randomly allocated to receive 20 minutes of active 2-mA tDCS or sham stimulation twice a ...

ode was placed over the left dors... prefrontal cortex and the catho... the left temporo-parietal cortex.

Results: Auditory verbal halluci... were robustly reduced by tDC... tive to sham stimulation, with a... diminution of 31% (SD=14; d=1.5... CI=0.76–2.40). The beneficial ef... hallucinations lasted for up to 3 ... The authors also observed an ar... tion with tDCS of other symptoms... sured by the Positive and Negati... drome Scale (d=0.98, 95% CI=0.2... especially for the negative and pos... mensions. No effect was observed on the dimensions of disorganization or grandiosity/excitement.

Conclusions: Although this study is limited by the small sample size, the results show promise for treating refractory auditory verbal hallucinations and other ...

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PAIN® 154 (2013) 1274–1280

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Motor and parietal cortex stimulation for phantom limb pain and sensations

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[b] Neuropsychological Laboratory, IRCCS Istituto Auxologico Italiano, Milano, Italy
[c] Department of Rehabilitation, Azienda Ospedaliera Carlo Poma, Mantova, Italy
[d] Laboratory of Neuromodulation, Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, MA, USA

Effect of Transcranial Brain Stimulation for the Treatment of Alzheimer Disease: A Review

Raffaele Nardone,[1,2] Jürgen Bergmann,[3] Monica Christova,[4] Francesca Caleri,[2] Frediano Tezzon,[2] Gunther Ladurner,[3] Eugen Trinka,[1] and Stefan Golaszewski[1,3]

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[2] Department of Neurology, Franz Tappeiner Hospital, Via Rossini 5, 39012 Meran/o, Italy
[3] Neuroscience Institute, Christian Doppler Clinic, 5020 Salzburg, Austria
[4] Department of Physiology, Medical University of Graz, 8010 Graz, Austria

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Effects of dual transcranial direct current stimulation on post-stroke unilateral visuospatial neglect

...Sunwoo [a,1], Yun-Hee Kim [b,*], Won Hyuk Chang [a,2], Soojin Noh [a,3], ...Jin Kim [c,4], Myoung-Hwan Ko [d,5]

...ment of Physical and Rehabilitation Medicine, Stroke and Cerebrovascular Center, Samsung Medical Center, Sungkyunkwan University School of ..., 50 Irwon-dong, Gangnam-gu, Seoul, 135-710, Republic of Korea

Bihemispheric tDCS enhances language recovery but does not alter BDNF levels in chronic aphasic patients

Paola Marangolo[a,b,*], Valentina Fiori[b], Francesca Gelfo[b,c], Jacob Shofany[b], Carmelina Razza..., Carlo Caltagirone[b,c] and Francesco Angelucci[b,*]

[a] Facoltà di Medicina, Università Politecnica Marche, Ancona, Italy
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[c] Dipartimento di Medicina dei Sistemi, Università degli studi di Roma "Tor Vergata", Roma, Italy

ELSEVIER

Brain Stimulation

Volume 6, Issue 4, July 2013, Pages 696–700

Restorative Neurology and Neuroscience xx (20xx) x–xx
IOS Press

Transcranial Direct Current Stimulation (tDCS)/Transcranial Alternating Current Stimulation (tACS)

Transcranial Direct Current Stimulation for Treatment of Refractory Childhood Focal Epilepsy

Narong Auvichayapat [a,1], Alexander Rotenberg [b,2], Roman Gersner [b,2], Sudarat Ngodklang [c,1], Somsak Tiamkao [d,1], Wichittra Tassaneeyakul [e,2], Paradee Auvichayapat [c,1]

Impact of transcranial direct current stimulation on fatigue in multiple sclerosis

Catarina Saiote[a], Thomas Goldschmidt[a,b], Charles Timäus[a], Martijn D. Steenwijk[b], Alexander Opitz[a], Andrea Antal[a], Walter Paulus[a] and Michael A. Nitsche[a,*]

[a] Department of Clinical Neurophysiology, University Medical Center, Georg-August University Göttingen, Göttingen, Germany
[b] Department of Radiology and Nuclear Medicine, Neuroscience Campus Amsterdam, VU University Medical Center, Amsterdam, The Netherlands

Clinical Study

Polarity Specific Suppression Effects of Transcranial Direct Current Stimulation for Tinnitus

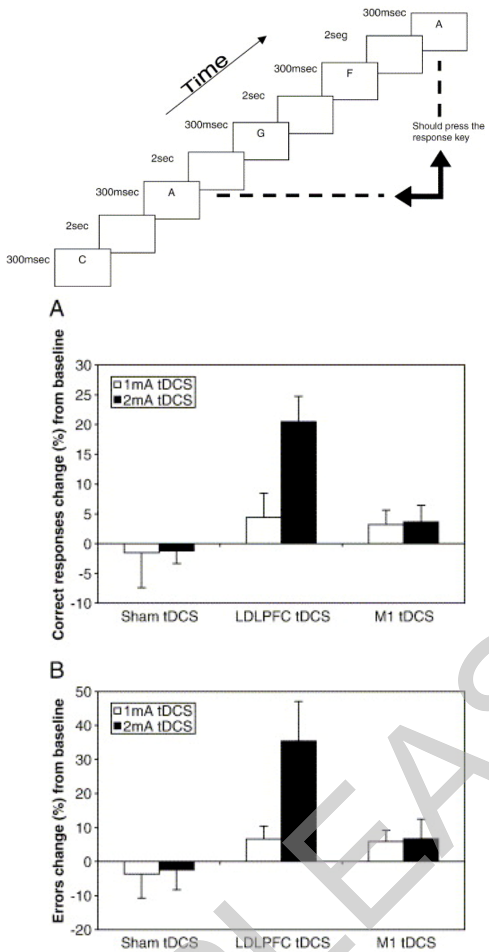
Kathleen Joos,[1,2] Dirk De Ridder,[3,4] Paul Van de Heyning,[2,5] and Sven Vanneste[2,6]

[1] Department of Neurosurgery, University Hospital Antwerp, 2650 Edegem, Belgium
[2] Department of Translational Neuroscience, Faculty of Medicine, University of Antwerp, 2650 Edegem, Belgium
[3] Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, Dunedin 9054, New Zealand
[4] BRAI²N & TRI, Sint Augustinus Hospital, 2610 Wilrijk, Belgium
[5] Department of Otorhinolaryngology and Head & Neck Surgery, University Hospital Antwerp, 2650 Edegem, Belgium
[6] School of Behavioral and Brain Sciences, The University of Texas at Dallas, TX 75235, USA

Flöel 2014, Kuo et al. 2014

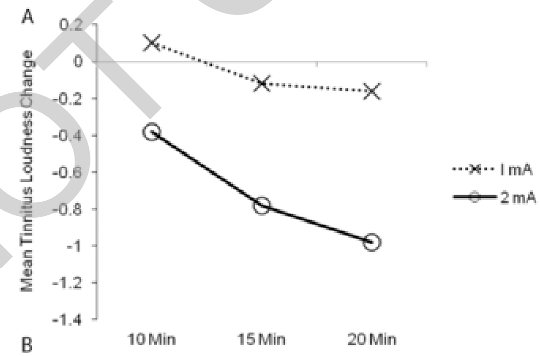
Maximizing effects - titration

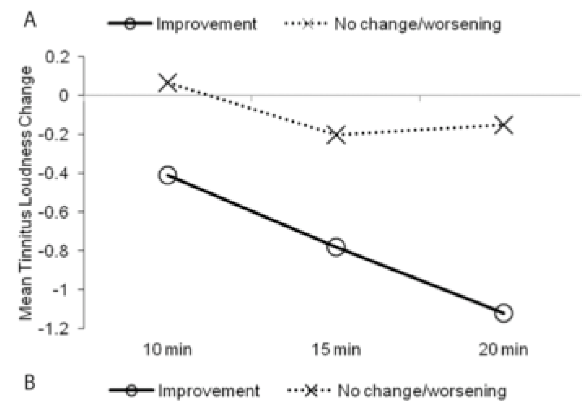
PD - Intensity



Batsikadze et al. 2013, Boggio et al. 2006

Tinnitus - duration

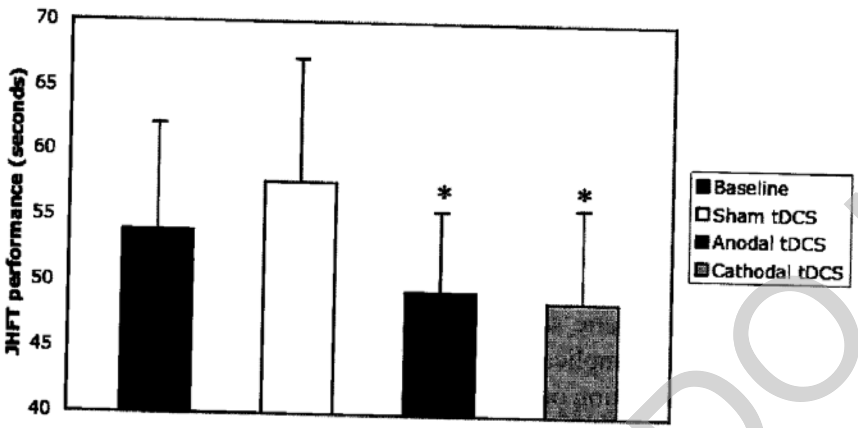




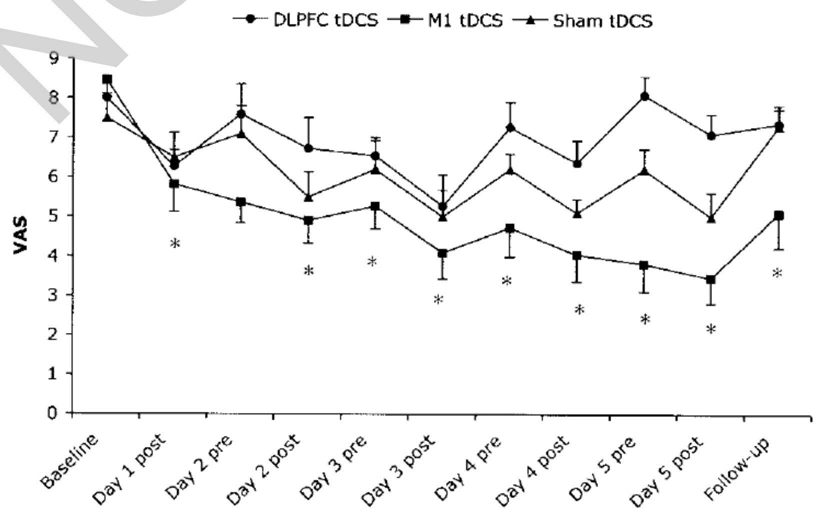
Shekhawat et al. 2013

Maximizing effects - repetition

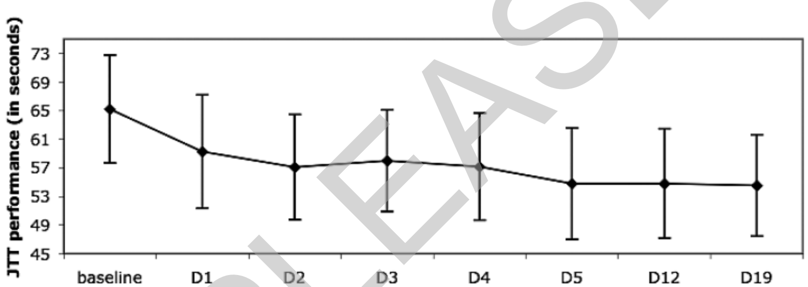
Stroke



Fibromyalgia

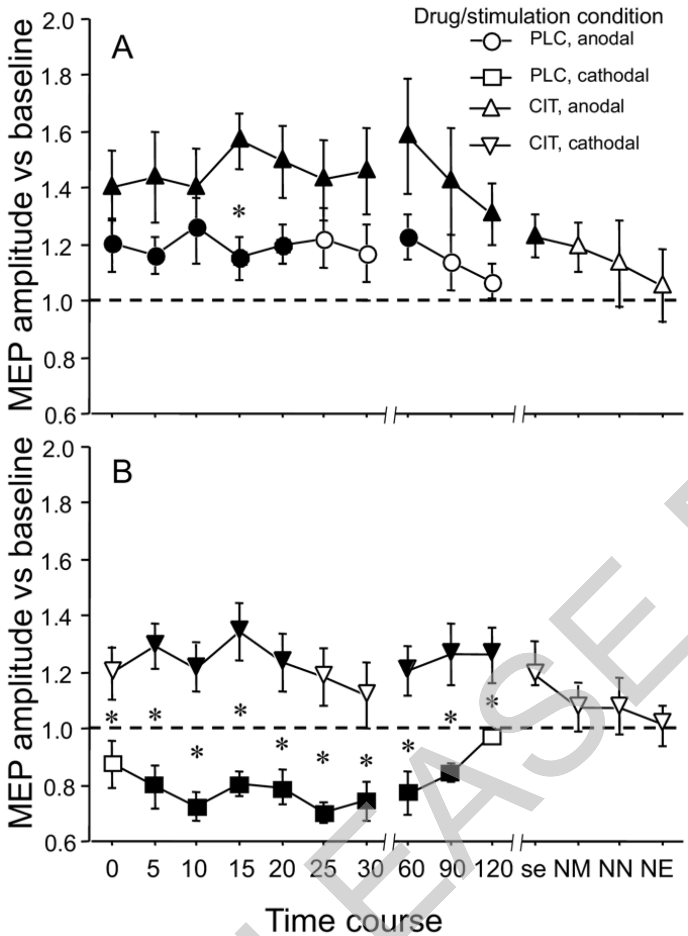


Once daily repetition



Boggio et al. 2007, Fregni et al. 2006

Maximizing effects – combination



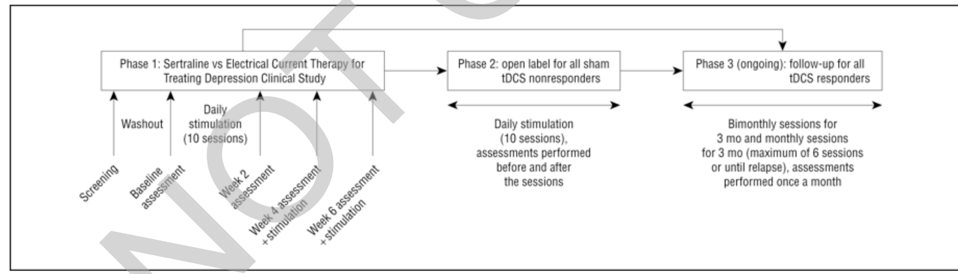


Table 1. Montgomery-Asberg Depression Rating Scale Scores at Different Times

	Baseline	Week 2		Week 4		Week 6	
Group or Factor	**Mean (SD)**	**Mean (SD)**	**% (SD)[a]**	**Mean (SD)**	**% (SD)[a]**	**Mean (SD)**	**% (SD)[a]**
Group							
Sham tDCS and placebo	30.76 (5.31)	21.37 (10.06)	−30.2 (30.7)	22.56 (9.50)	−24.1 (36.1)	24.73 (8.65)	−18.2 (29.0)
Sham tDCS and sertraline	30.50 (6.81)	22.10 (11.50)	−28.9 (30.1)	22.83 (11.03)	−25.2 (34.5)	21.67 (13.14)	−29.8 (36.7)
Active tDCS and placebo	30.76 (5.78)	20.53 (9.59)	−34.0 (26.8)	19.33 (10.41)	−37.9 (29.5)	19.07 (12.21)	−39.5 (34.2)
Active tDCS and sertraline	30.73 (6.72)	15.53 (7.90)	−48.5 (23.5)	15.70 (7.98)	−46.9 (25.7)	13.17 (8.46)	−55.6 (27.3)
P value[b]	.99	.01		.01		<.001	
Factor							
No sertraline	30.76 (5.51)	20.95 (9.70)	−32.1 (28.6)	20.95 (10.02)	−31.0 (33.3)	21.90 (10.88)	−28.8 (33.3)
Sertraline	30.61 (6.71)	18.81 (10.32)	−38.7 (28.6)	19.27 (10.20)	−36.1 (32.5)	17.14 (11.77)	−42.7 (34.8)
P value[b]	.89	.25		.36		.03	
No tDCS	30.63 (6.10)	21.73 (10.71)	−29.6 (30.9)	22.70 (10.21)	−24.7 (34.8)	23.20 (11.14)	−24.0 (33.3)
tDCS	30.75 (6.22)	18.03 (9.02)	−41.2 (25.6)	17.52 (9.38)	−42.4 (27.9)	16.11 (10.83)	−47.6 (31.7)
P value[b]	.91	.04		.003		.001	

Nitsche et al. 2009

Brunoni et al. 2012

Functional effects in patients - specifics

- Parameters such as stimulation intensity, duration, repetition and combination can be adjusted to optimize effects
- The brain state of patients differ, and should be taken into account

Concluding remarks

- Although seemingly simple to apply, tDCS studies require careful planning and conduction
- Technical aspects of the intervention are often not taken sufficiently in account
- Design aspects are critical for successful conduction
- As neuromodulatory interventions, plasticity-inducing NIBS might be especially vulnerable to protocol problems
- Most of the aspects discussed here are not specific to tDCS, but apply also to other NIBS protocols, and neuromodulatory interventions.