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Guidelines on safety and application of tDCS

Low intensity transcranial current stimulation: Safety, ethical, legal regulatory and application guidelines

Antal A, Alekseichuk I, Bikson M, Brockmöller J, Brunoni AR, Chen R, Cohen LG, Bowthwaite G, Ellrich J, Flöel A, Fregni F, Goerge MS, Hamilton R, Haueisen J et al.
2017 - Clinical Neurophysiology, Volume 128, NO. 9

OBJECTIVE

To review the safety and potential side effects of tDCS in humans and recommendations for safe use in clinical practice

METHODOLOGY

Systematic hazard analysis side effects in transcranial current stimulation studies (in total 18000 stimulation sessions in healthy people, neurological and psychiatric patients). Inclusion of studies up to 2016

RESULTS

Assessment	*Results*
Safety	- (tDCS) in humans is considered safe on the basis of this study
	- side effects in the elderly, pregnant women, children are not different from those typical of adult study participants
	- long-term effects in children/adolescents have not been sufficiently investigated
Side effects	- moderate side effects requiring action are rare and not clearly caused by tDCS
	- mild side effects without need for action: headache, tiredness after stimulation, slight tingling or burning sensation at the stimulation site
	- moderate side effects: skin burns due to improper application of the electrodes
	- no reports of serious side effects
	- no reported cognitive or perceptual side effects
	- no reported seizures demonstrably attributable to tDCS
Injuries	- risk of injury can be minimized by: - selection and preparation of the electrode - correct placement of the electrodes, specifically the position and contact with skin (through saline paste or sponges with sufficient saline solution)

RECOMMENDATIONS

Training	- sufficient training of users in safety precautions and the attaching of electrodes
Patient Suitability	- comprehensive background information on patient before therapy in an intake consultation assessing contraindications and risks
Device technology	- use devices which are verified in scientific research
	- do not use homemade or uncertified equipment
Protocol	- comply with maximum stimulation levels and duration alongside correct electrode application

CONCLUSION

This analysis shows that standardized applications of tDCS can be safely performed within the limits of the clinically approved and common intensity of max. 1 - 2 mA and max. 20 - 30 minutes with correct application of the electrodes. For all practitioners, instruction in handling the electrodes and the protocols is necessary.

Depression

Trial of Electrical Direct-Current Therapy versus Escitalopram for Depression

Brunoni AR, Moffa AH, Sampaio-Junior B, Borrione L, Moreno ML, Fernandes RA, Veronezi BP, Nogueira BS, Aparicio LVM, Razza LB,Chamorro R, Tort LC, Fraguas R, Lotufo PA, Gattaz WF, Fregni F, Benseñor IM; 2017 – The New England Journal of Medicine, Volume 376

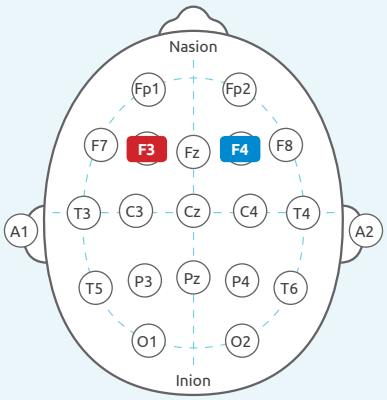
OBJECTIVE Influence of tDCS or escitalopram (SSRI) on depression

PROCEDURE Placebo group: placebo escitalopram + placebo stimulation;
Escitalopram group: escitalopram + placebo stimulation
tDCS group: escitalopram + active stimulation

METHODOLOGY Double-blind study (RCT) with 202 depressed patients (55 placebo, 75 escitalopram, 72 tDCS)

PARAMETERS

Stim. intensity	2 mA
Duration	30 minutes
Anode	F3
Cathode	F4
Size of electrode	35 cm^2
Treatment	5 times a week (first 3 weeks) after that 1 x weekly (7 weeks)
Scope of treatment	22 sessions
Assessment	HDRS-17, MADRS



10-20 System

RESULTS

Assessment	*Placebo group*	*Escitalopram group*	*tDCS group*
HDRS-17	reduction of HDRS scores compared pre-post by **5.8 ± 7.9 points**	reduction of HDRS scores compared pre-post by **11.3 ± 6.5 points**	reduction of HDRS scores compared pre-post by **9.0 ± 7.1 points**
		** Escitalopram was significantly better than placebo [Difference: 5.5, 95% CI, 3.1 zu 7.8, P<.001]	* tDCS was significantly better than placebo [Difference: 3.2, 95% CI, 0.7 zu 5.5, P=.01]
		* slight superiority of Escitalopram over tDCS [Difference: 2.3, 95% CI, -4.3 zu -0.4, **P=.02**]	
		** in the 10th week, the response rate was significantly higher (reduction by >50% to baseline) in tDCS and escitalopram than in placebo stimulation	
MARDS	reduction of MARDS scores compared pre-post by **6.6 ± 9.3 points**	reduction of MARDS scores compared pre-post by **13.4 ± 9.3 points**	reduction of MARDS scores compared pre-post by **11.0 ± 9.4 points**
		** Escitalopram was significantly better than placebo [Difference: 6.8, 95% CI, 5.4 zu 10.6, P<.001]	** tDCS was significantly better than placebo [Difference: 4.4, 95% CI, 2.1 zu 7.2, P=.006]
		* slight superiority of Escitalopram over tDCS [Difference: -2.4, 95% CI, -5.7 zu -1.1, **P=.04**]	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This study shows that patients with moderate or severe depression (and existing anxiety disorder) can be successfully treated with tDCS. For classic pharmacological treatment, tDCS was shown to be a successful alternative in this study.

Depression - Stroke

Effect of transcranial direct current stimulation of stroke patients on depression and quality of life

Tae-Gyu A, Soo-Han K, Ko-Un K
2017 – The Journal of Physical Therapy Science, Volume 29

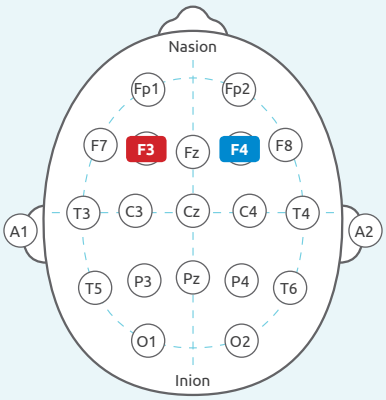
OBJECTIVE Effect of tDCS of DLPFC in patients with post-stroke depression

PROCEDURE Placebo group: conventional occupational therapy + placebo stimulation;
Verum group: conventional occupational therapy + active stimulation

METHODOLOGY Controlled study of 40 patients with post-stroke depression (20 control group, 20 tDCS group)

PARAMETERS

Stim. intensity	2 mA
Duration	30 minutes
Anode	F3
Cathode	F4
Size of electrode	35 cm^2
Treatment	1 x daily (for four weeks)
Scope of treatment	20 sessions
Assessment	BDI, SS-QOL



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
BDI	- no significant change in the depressive symptoms from pre 39.0 ± 4.6 to post: 37.8 ± 6.1	* significant improvement of depressive symptoms from pre 38.8 ± 4.7 to post: 16.8 ± 4.6
SS-QOL	- no significant change in quality of life from pre 154.3 ± 18.3 to post: 162.1 ± 18.7	* significant improvement of depressive symptoms from pre 152.1 ± 16.9 to post: 167.7 ± 25.7

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show the positive effect of tDCS on the DLPFC in patients after stroke. Twenty treatments reduced the depressive symptoms by half (BDI scores) and improved quality of life.

Depression

Transcranial direct current stimulation in depressive disorders

Aust S, Palm U, Padberg F, Bajbouj M
2015 – Nervenarzt – Review, Ausgabe 12/2015

Der Nervenarzt

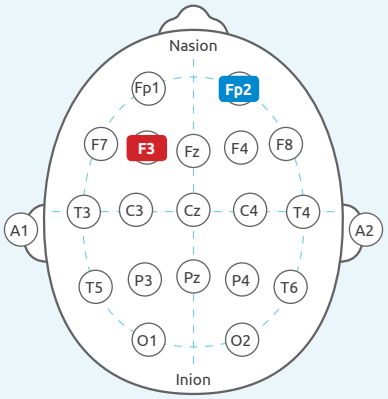
OBJECTIVE Efficacy of tDCS to reduce depressive disorders

PROCEDURE Placebo group: placebo stimulation; active group: active stimulation

METHODOLOGY Review: 6 randomized controlled studies involving 294 patients

PARAMETER

Stim. intensity	2 mA
Duration	20-30 minutes
Anode	F3
Cathode	Fp2
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	10-15 sessions
Assessment	HAMD, MADRS, BDI



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
HDRS-17	- no significant differences	* **significant improvement in therapy-resistant patients by 40-47%**
MARDS	- no significant differences	* significant improvement * treatment combining combining drug and tDCS showed great success (tDCS + sertraline)

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The review reports on the positive effect of tDCS in depressed patients - tDCS enhances activation in DLPFC. Neurological rehabilitation research points to a targeted use of tDCS to reduce depressive disorders.

Depression

Concurrent Cognitive Control Training Augments the Antidepressant Efficacy of tDCS: A Pilot Study

Segrave RA, Arnold S, Hoy K, Fitzgerald P
2014 – Brain Stimulation, Volume 7

BRAIN STIMULATION

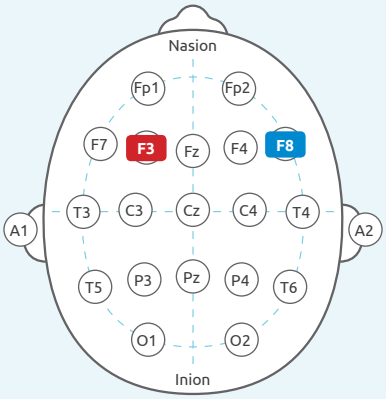
OBJECTIVE Clinical effects of tDCS in combination with computer-assisted cognitive training in depressive symptoms

PROCEDURE Placebo group: cognitive training + placebo stimulation; active group: cognitive training + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** Double-blind study

PARAMETERS

Stim. intensity	2 mA
Duration	24 minutes
Anode	F3
Cathode	F8
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	5 sessions
Assessment	MARDS, BDI, Two-Back



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
MARDS	* MARDS scores decreased [P=0.02]	- decreased MARDS scores [P=0.06]
	- after follow-up, MARDS scores decreased and were similar to the baseline	** after **follow-up, clear and increasing improvement in MARDS scores [P<0.001]**
BDI	** BDI scores decreased [P=0.006]	- no significant changes [P>0.05]
	- after follow-up, BDI scores decreased and were similar to the baseline	** after **follow-up, clear and increasing improvement in the BDI scores [P=0.004]**
Two-back (accuracy)		* higher accuracy [P=0.02]
Two-back (responsiveness)	** responsiveness increased over time, in all [positive: $F_{(3,69)}$=7.93, P=0.001; neutral: $F_{(3,69)}$=10.16, P<0.001; negative: $F_{(3,69)}$=13.25, P<0.001]	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This study shows that tDCS can reduce depressive symptoms. Additional cognitive training (attention training) can effectively reduce depression and increase alertness in a short period of time.

Addiction - Overview

A Review of Brain Stimulation Methods to Treat Substance Use Disorders

Coles AS, Kozak K, George TP
2018 – American Journal on Addictions, Volume 27

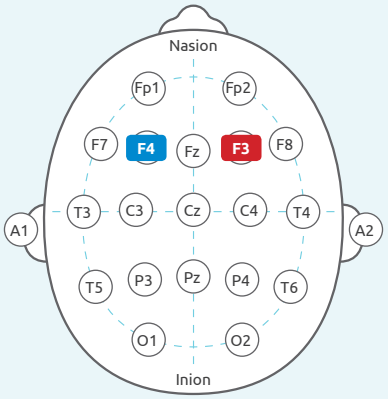
The American Journal on Addictions

OBJECTIVE Review of the clinical efficacy of various stimulation methods (rTMS, tDCS, DBS) for addiction disorders

METHODOLOGY Systematic analysis of studies published between 2000 and 2017 in peer-reviewed journals; test participants had diagnoses of an addiction disorder according to DSM IV and DSM V, respectively

GENERAL RESULTS REGARDING tDCS

Stim. intensity	mostly 2 mA
Duration	20 minutes
Effect sizes	medium to large after several sessions
Anode	different positions, often lDLPFC
Cathode	different positions, often rDLPFC
Session number	various sessions (5-10) are recommended
Primary / secondary objective	addiction or consumption; recurrence quote
Outcome	effectiveness of tDCS comparable to effectiveness of rTMS



10-20 System

RESULTS tDCS STUDIES WITH MULTIPLE SIMILAR SESSIONS tDCS 2 MA, 20 MINUTES

Substance	*Total number of participants*	*Results*
Alcohol	137	- craving and / or recurrence rate significantly changed with cathodal stimulation of the left DLPFC
Tobacco	76	- mixed results on anodal stimulation of the left DLPFC - significant reduction in craving and / or consumption in cathodal stimulation of the left DLPFC
Cocaine	60	- significant reduction in craving versus baseline and placebo group - no difference in anxiety, depressive symptoms and cognitive performance

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This analysis shows that short-term treatment with tDCS leads to a decrease in craving in different types of substance-related dependencies. The recurrence rate and thus the consumption itself are in some cases significantly reduced. The best results are achieved by stimulating the DLPFC.

Addictive disorders - Alcohol addiction

Multiple Sessions of Transcranial Direct Current Stimulation (tDCS) Reduced Craving and Relapses for Alcohol Use: A Randomized Placebo-Controlled Trial in Alcohol Use Disorder

Klauss J, Anders QS, Felippe LV, Nitshe MA, Nakamura-Palacios EM
2018 – frontiers in Pharmacology, Volume 9

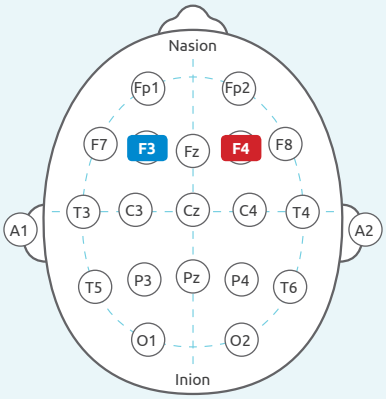
OBJECTIVE Efficacy of repetitive bilateral tDCS over the DLPFC in alcoholics

PROCEDURE Placebo group: placebo stimulation; active group: active stimulation

METHODOLOGY Double-blind study (RTC) with alcoholics (placebo group, active group) in a specialist hospital for addiction sufferers

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	F4 (DLPFC)
Kathode	F3 (DLPFC)
Size of electrode	35 cm^2
Treatment	every two days
Scope of treatment	10 sessions
Assessment	OCDS (addiction pressure), abstinence



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Recurrence	- 72.2% of the patients relapsed within 3 months of therapy	- 27.3% of the patients relapsed within 3 months of therapy
	difference between the groups (relapse) is significant (p=0.01)	
OCDS	- mean dropped from 3.82 (at the beginning) to 2.46 (in the follow-up) - small effect size (0.32)	- mean dropped from 5.25 (at the beginning) to 1.56 (in the follow-up) - big effect size (1.07)
	- no significant difference pre-post	- no significant difference pre-post
	significant difference before treatment to follow-up	
	significant group differences	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The study shows that bilateral stimulation of the DLPFC can significantly reduce the probability of both recurrence and craving. At the time of follow-up, three quarters of the test participants remained abstinent after the stimulation therapy. In the placebo group approximately only a quarter of the participants remained abstinent. It is therefore understood that tDCS can support the long-term success of treatment.

Addictive disorders - Cocaine addiction

A randomized placebo-controlled trial of targeted prefrontal cortex modulation with bilateral tDCS in patients with crack-cocaine dependence

Batista E, Klauss J, Fregni F, Nitsche MA, Nakamura-Palacios EM
2015 – International Journal of Neuropsychopharmacology, Volume 18

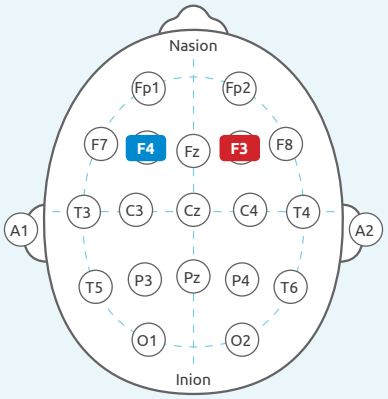
OBJECTIVE Clinical effects of repetitive bilateral tDCS on DLPFC in cocaine addiction

PROCEDURE Placebo group: placebo stimulation; active group: active stimulation

METHODOLOGY Double blind study (RTC) with 36 crack cocaine addicts (19 placebo group, 17 verum group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	F4 (DLPFC)
Cathode	F3 (DLPFC)
Size of electrode	35 cm^2
Treatment	1 x daily, every second day
Scope	5 sessions
Assessment	HAM-D, HAM-A, WHOQOL, Craving



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Craving	-	* active group and placebo group differ significantly in terms of craving (group and treatment: [F(1,33)=5.29, P=.028, partial η^2=0.14]
	-	* craving scores decreased linearly from baseline to last treatment [linear regression: 4.412 - 0.617X, r2=0.058, F(1,66)=4.089, P=.047]
HAM-D	-	* significant change in HAM-D values within the group (P=.04)
HAM-A	-	* opposite results: values of the active group decrease, values of the placebo group increase (P=.03)
WHOQOL	-	* significant differences between groups in WHOQOL: (Q1: P=0.31 & Q2: P=0.48)

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The craving scores were lower after bilateral repetitive tDCS. The active group, compared to the placebo group, is significantly different in terms of anxiety, quality of life and health. The values of the active group improved in post and follow-up.

Schmerzen - Fibromyalgie

Anodal transcranial direct current stimulation over the left dorsolateral prefrontal cortex modulates attention and pain in fibromyalgia: randomized clinical trial

Silva AF, Zortea M, Carvalho S, Leite J, da Silva Torres IL, Fregni F, Caumo W; 2017 – Nature, Volume 7

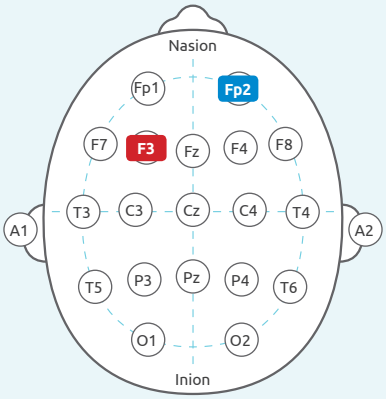
OBJECTIVE Efficacy of tDCS on patients with fibromyalgia and cognitive deficits

PROCEDURE Placebo group: Go/No-go task + placebo stimulation;
active group: Go/No-go task + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** Single blind study (RCT) with 40 patients with fibromyalgia (20 placebo group, 20 active group)

PARAMETERS

Stimulationsstärke	1 mA
Duration	20 minutes
Anode	F3
Cathode	Fp2
Size of electrode	35 cm^2
Treatment	1 x weekly
Scope	2 sessions
Assessment	ANT, HPTh, HPTo, Go/No-go task



10-20 System

RESULTS

Assessment	
ANT	* significant group difference; active group compared to placebo group achieved higher orientation values in ANT after stimulation [F(1, 70.0)=4.189; P=0.044]
	* significant group effect; active group compared to placebo group achieved higher levels in executive function in ANT after stimulation [F(1, 49.11)=7.94; P=0.007]
	* active group compared to placebo group performed significantly better than placebo group in congruent target condition without cue and spatial cues [P=0.040; P=0.020]
HPTh	* active group showed a **significant improvement of 4.95% of the heat pain threshold** compared to the placebo group [P=0.03]
HPTo	* active group showed a **significantly higher tolerance of 3.6% to heat pain compared** to the placebo group [P=0.03]
Go/No-go Task	- no significant effects

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show that only after a few stimulation sessions in combination with a Go/No-go training can increase the neural network for attention in orientation and executive function. Stimulation of the DLPFC can be used as an additional stimulation site adjacent to M1 to reduce pain in patients with fibromyalgia.

Pain - Migraine

Transcranial direct current stimulation (tDCS) and its influence on analgesics effectiveness in patients suffering from migraine headache

Przeklasa-Muszynska A, Kocot-Kepska M, Dobrogowski J, Wiatr M, Mika J
2017 - Pharmacological Reports, Volume 69

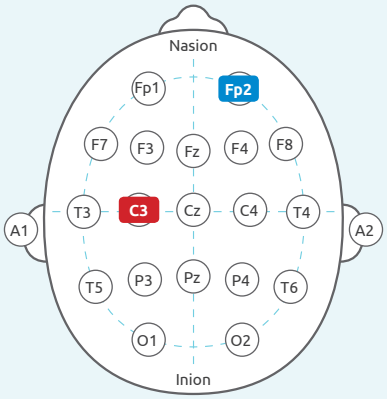
OBJECTIVE Effect of tDCS on drug consumption and pain in migraine patients

PROCEDURE Control group: pharmacological therapy
Active group: active stimulation and pharmacological therapy

METHODOLOGY Single blind study (RCT) with 50 migraine patients with and without aura (20 control group, 30 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	C3
Cathode	Fp2
Size of electrode	35 cm^2
Treatment	2-3 times a week
Scope	10 sessions
Assessment	duration of migraine, migraine seizures, drug use, pain intensity of migraine (NRS)



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Duration of migraine	- no significant reduction - with and without aura	*** with aura: reduced from 24 hours to 10 hours *** without aura: reduced from 25 to 8.5 hours
Migraine seizures	- no significant reduction - with and without aura	** with aura: from 7 days a month to 4 days a month ** without aura: from 7 days a month to 4 days a month
Drug consumption	- no significant reduction (Analgesic) with and without aura	** Analgesic consumption: with aura a **reduction of 49%** * Analgesic consumption: without aura a **reduction of 72%**
	- no significant reduction (Triptane) with and without aura	** Triptans: with Aura a **reduction of 58%** * Triptans: without aura a **reduction of 59%**
Pain intensity of migraine (NRS)	*** after the 10th treatment, the groups differed quite significantly from each other	
	reduction in pain intensity with aura by 12,5%	**reduction in pain intensity with aura by 36%**
	reduction in pain intensity without aura by 10%	**reduction in pain intensity without aura by 40%**

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This study demonstrates the well-tolerated and effective use of tDCS in migraine patients. The pain intensity of the migraine, the migraine seizures, the migraine duration as well as drug consumption were significantly reduced by 10 treatments.

Pain - Chronic pain

Anodal transcranial direct current stimulation for chronic pain in the elderly: a pilot study

Concerto C, Al Sawah M, Chusid E, Trepal M, Taylor G, Aguglia E, Battaglia F
2016 - Aging – Clinical and Experimental Research, Volume 28

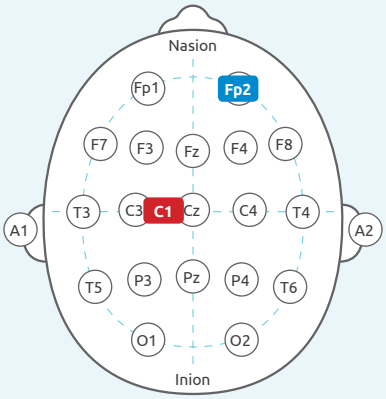
OBJECTIVE Efficacy of anodal tDCS on the motor cortex to relieve chronic pain and depression

PROCEDURE Experimental group: pharmacological therapy + active stimulation

METHODOLOGY Uncontrolled study: 10 patients with chronic pain

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	C1/C2 (contralateral to the pain side)
Cathode	Fp1/Fp2 (contralateral to the anode)
Size of electrode	25 cm^2
Treatment	1 x daily
Scope	5 sessions
Assessment	VAS for pain, FFI, PASS-20, drug use, HDRS



10-20 System

RESULTS

Assessment	*Active group*
VAS for pain	*** improvement of chronic pain by 36.9% after last treatment [P<0.0001], 42,4% one week after the last stimulation [P<0.0001]
	** significant improvement of chronic pain by 21.6% after last treatment four weeks after the last stimulation [P<0.006]
FFI	*** improved foot function by 36.8 % after the last stimulation [P<0.0001], 25.2% one week after the last stimulation [P<0.0001], 23.2% four weeks after the last stimulation [P<0.0001]
PASS-20	*** anxiety related to potential pain decreased by 18.2% after stimulation [P<0.0001], 15.5% one week after the last stimulation [P<0.0001], 12.7% four weeks after the last stimulation [P<0.0001]
Drug consumption	*** significantly reduced consumption of painkillers in follow-up [P<0.0002, P<0.0043]
HDRS	- no significant changes over time

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The study shows that anodal tDCS of the motor cortex can significantly reduce pain and is long lasting. The normalization of impaired activity in the pain-processing network has increased the quality of life of chronic pain patients.

Pain - Stroke

Analgesic effect of transcranial direct current stimulation on central post-stroke pain

Sea-Hyun B, Gi-Do K, Kyung-Yoon K
2014 – The Tohoku Journal of Experimental Medicine, Volume 234

Tohoku Journal of Experimental Medicine

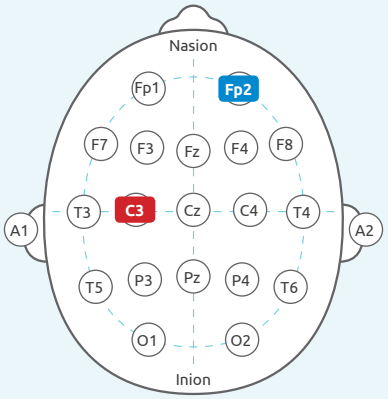
OBJECTIVE Effect of tDCS on the analgesic effects in patients after stroke

PROCEDURE Placebo group: Placebo stimulation
Active group: active stimulation

METHODOLOGY Single blind study (RCT) with 14 patients after stroke with central pain (7 placebo group, 7 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	C3/C4-contralateral to the pain side
Cathode	Fp1/Fp2-contralateral to the anode
Size of electrode	35 cm^2
Treatment	3 x times a week
Scope of treatment	3 weeks
Assessment	VAS for pain, skin temperature measurement, quantitative sensory measurements



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
VAS for pain	- no significant change pre: 4.28, post: 4.14	* significant pain reduction Pre: 4.92 and post: 3.14 [P<.05]
Skin temperature	- no significant change pre: 0.94, post: 0.82	* significant reduction of temperature pre: 0.96, post: 0.49 [P<.05]
Quantitative sensory measurement	- no significant change in cold perception: pre: 24.71, post: 25.09	* significant change in cold perception: pre: 24.71, post: 25.09 [P<.05]
	- no significant change in heat perception: pre: 7.36, post: 36.99	* significant change in heat perception: pre: 38.19, post: 35.93 [P<.05]
	- no significant change in cold pain threshold pre: 13.57, post: 13.80	** significant change in cold pain threshold pre: 12.24, post: 14.03 [P<.001]
	- no significant change in threshold for heat pain pre: 48.01, post: 48.16	* significant change in threshold for heat pain pre: 48.07, post: 47.7

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results demonstrate the effectiveness of tDCS in reducing pain in post stroke patients. The threshold for feeling cold and cold pain as well as for feeling warmth and heat pain changed sustainably.

Pain - Multiple Sclerosis

Effects of anodal transcranial direct current stimulation on chronic neuropathic pain in patients with multiple sclerosis

Mori F, Codeà C, Hajime K, Monteleone F, Buttari F, Fiore S, Bernardi G, Koch G; 2010 - The Journal of Pain, Volume 11

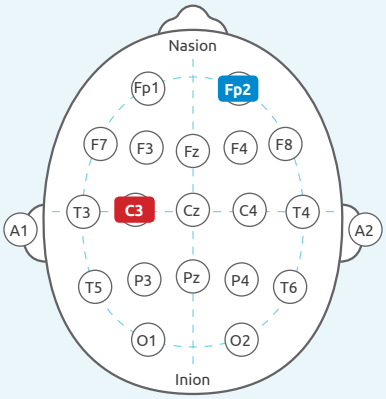
OBJECTIVE Efficacy of daily tDCS (on consecutive days) to reduce chronic pain in multiple sclerosis patients

PROCEDURE Placebo group: Placebo stimulation;
Active group: active stimulation

METHODOLOGY Double-blind study (RCT) with 19 drug-resistant multiple sclerosis patients with neuropathic pain (9 placebo group, 10 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	C3/C4-contralateral to the pain side
Cathode	Fp1/Fp2-contralateral to the anode
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	5 sessions
Assessment	VAS for pain, SF-MPQ, MSQOL-54, BDI, VAS for anxiety



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
VAS for pain	-	** pain reduction after the fifth day compared to the first [baseline, day 1, day 2, day 3, day 4, day 5: F=9.03, P<.001]
	-	* significant differences from day three compared to baseline by 51.7% ± 10.3, day four at baseline by 43.9% ± 11,5 and day five at baseline by 45.5% ± 11,0
SF-MPQ	-	* subjective pain perception decreased after the first week and remained low [every: P<.05]
MSQOL-54	-	* significant effects time (group x time interaction) -> significant differences persisted until follow-up
BDI	-	• no significant differences
VAS for anxiety	-	• no significant differences

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results show the effectiveness of tDCS for the reduction of neuropathic pain in multiple sclerosis patients (significant reduction of pain in active group). A small amount of stimulation is enough to improve pain perception and quality of life in MS patients.

Motor disorders - Stroke

Constraint-Induced Movement Therapy Combined with Transcranial Direct Current Stimulation over Premotor Cortex Improves Motor Function in Severe Stroke: A Pilot Randomized Controlled Trial

Andrade SM, Batista LM, Nogueira LLRF, de Oliveira EA, de Carvalho AGC, Lima SS, Santana JRM, de Lima ECC, Fernández-Calvo B; 2017 – Rehabilitation Research and Practice, Volume 2017

Rehabilitation Research and Practice

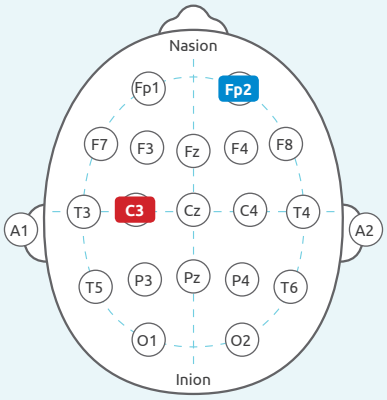
OBJECTIVE Effects of daily tDCS in combination with CIMT on motor rehabilitation in patients after stroke

PROCEDURE Placebo group: motor training + placebo stimulation;
Active group: motor training + active stimulation

METHODOLOGY Double blind study (RCT) with 60 patients after stroke (20 placebo group, 20 active group (M1), 20 active group (PMC))

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	C3 / C4 or 2.5 cm anterior to C3 / C4 (same hemisphere as lesion)
Cathode	Fp1 / Fp2 (contralateral to the anode)
Size of electrode	16 cm^2
Treatment	5 times a week
Scope of treatment	10 sessions
Assessment	BI, UEFM, MAS, BBT, MRC



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
BI	* smaller effect size in placebo group [δ = -. 14, P = .01]]	* stronger effect size in PMC and M1 groups [PMC: δ = -. 83, P = .02; M1: δ = -. 64, P = .01]
	* significant differences between the groups [x2 = 11.41, df = 2, P = .01]	
UEFM	* improvement placebo group, pre-post within the group from 20 to 24 [z = 0.44, P = .01]	* improvement group M1, pre-post within the group from 20 to 29 [z = -2.04, P = .01]
		* PMC improvement, pre-post within the group from 21 to 33 [z = -2.86, P = .02]
	* PMC showed greatest improvement in motor recovery compared to M1 [z = -2.01; P = .04] and placebo [z = -2.36; P = .03]	
MAS	* reduction of spasm in placebo stimulation, pre-post from 18 to 15 [z=-1.16, P=.03]	* reduction of spasm in M1, pre-post from 17 to 11 [z=-1.94, P=.01]
		* reduction of spasm in PMC, pre-post from 16 to 7 [z=-2.87, P=.02]
	* PMC greatest reduction of spasm compared to M1 [z=-2.12; P=.02] and placebo stimulation [z=-2.51; P=.04]	
BBT und MRC	- no significant improvement in placebo group, pre-post [p>0.05]	- no significant improvement in M1, pre-post [p>0.05]
		* significant improvement in PMC, pre-post from 1 to 7 [z=-2.98, P=.02] and [z=-3.01, P=.03]

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The study shows that the combined use of CIMT and tDCS leads to significantly greater effects of motor rehabilitation than the isolated use of CIMT. It shows that the stimulation of the premotor cortex (PMC) can cause greater increases in performance than the stimulation of the motor cortex (M1). The stimulation of the premotor area can be a good alternative to standard stimulation of the M1.

Motor disorders - Stroke

Ipsilesional anodal tDCS enhances the functional benefits of rehabilitation in patients after stroke

Allman C, Amadi A, Winkler AM, Wilkins L, Filippini N, Kischka U, Stagg CJ, Johansen-Berg H; 2016 – Science Translational Medicine, Volume 8

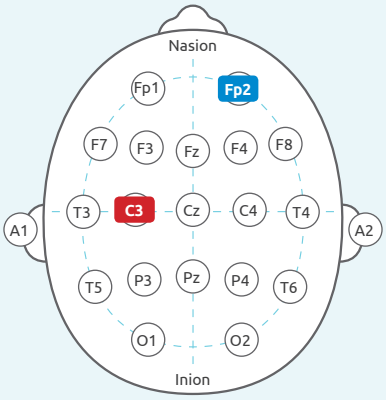
OBJECTIVE Effect of tDCS with Motor Training on Patients after Stroke

PROCEDURE Placebo group: motor training + placebo stimulation;
Active group: motor training + active stimulation

METHODOLOGY **Combination of tDCS and motor training:** double-blind study (RCT) with 24 patients after stroke (13 placebo group, 11 active group)

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes stimulation + 40 minutes motor training
Anode	C3 / C4 (same hemisphere as lesion)
Cathode	Fp1 / Fp2 (contralateral to the anode)
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	9 sessions
Assessment	ARAT, WMFT, UEFM und MRT



10-20 System

RESULTS

Assessment	*Placebo-Gruppe*	*Active group*
ARAT	-	* significant improvement in ARAT [P=.031] compared with placebo group
WMFT	-	* significant improvement [P=.037] compared to the placebo group
UEFM	-	* UEFM showed no significance compared to the placebo group [P=.329]
MRT	- no significant activation patterns in the fMRI	* fMRI studies show increased activity of the active group in restricted hand movement in ipsilateral premotor and motor areas
	* MRI measurements of the active group show **volume increase of grey matter** after tDCS in the premotor and motor cortex compared to the placebo group	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This study shows that the combination of tDCS with motor training promotes neuronal plasticity. The significant long-term changes (follow-up) in the active group show the good possibility of combining tDCS with existing motor therapy. This suggests that motor cortex stimulation can produce plasticity and achieve greater effects than motor training without tDCS.

Motor disorders - Stroke

Bihemispheric-tDCS and Upper Limb Rehabilitation Improves Retention of Motor Function in Chronic Stroke: A Pilot Study

Goodwill AM, Teo W, Morgan P, Daly RM, Kidgell DJ
2016 – Frontiers in Human Neuroscience, Volume 10

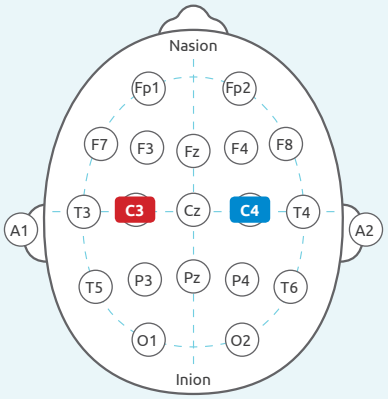
OBJECTIVE Effect of anodal tDCS on upper extremity motor rehabilitation and corticospinal plasticity

PROCEDURE Placebo group: motor training + placebo stimulation;
Active group: motor training + active stimulation

METHODOLOGY Combination of tDCS and motortraining: double-blind study (RCT) with 15 chronic stroke patients (7 placebo groups, 8 active groups)

PARAMETER

Stim. intensity	1,5 mA
Duration	20 minutes
Anode	C3/C4 (same hemisphere as lesion)
Cathode	C3/C4 (contralateral to the anode)
Size of electrode	25 cm^2
Treatment	3 times a week
Scope of treatment	9 sessions
Assessment	MAS, grip strength, tardieu, corticospinal excitability, intracortical inhibition



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
MAS	** significant improvement in pre-post in both groups: placebo group: by 43%; **active group: by 62%** [df=2, both P<0.001]	
	- in follow-up (after 3 weeks) motor function decreased to 21% [Forest Chi-Square=77.21, df=2, P=0.08]	** improvements were maintained in **follow-up (after 3 weeks), or increased to 64%** [Chi-Square forest=13.25, df=2, P<0.001]
Grip strength	- no significant differences	
Tardieu Scale	* significantly small increase in the Tardieu Scale in the wrist [x2 = 6.56, P = 0.02]	- no significant differences
	- no significant group differences in the elbow and spasticity	
Corticospinal excitability: AMT	- no significant differences	

Corticospinal excitability: MEPs (paretic arm)	- no significant changes in triggering MEPs (% M_{MAX}) pre-post, by 12% [Forest Chi-Square=0.86, df=2, P=0.36]	** significantly easier triggering of MEPs ** (% M_{MAX}) pre-post, by 46% [Forest Chi-Square=37.49, df=2, P<0.001]
	** in follow-up (after 3 weeks), MEPs (% M_{MAX}) were more easily released by 38% [Wald Chi-Square=37.49, df=2, P<0.001]	** in follow-up (after 3 weeks), MEPs (% M_{MAX}) were more easily released by 38% [Forest Chi-Square=37.49, df=2, P<0.001
	- no significant changes in MEPs in the non-paretic arm	
Corticospinal excitability: Laterality Index (LI)	- no significant changes	** **increased excitability, shift of LI from 0.6 to 0.3,** pre-post [Forest Chi-Square = 14.80, df=2, P<0.001]
	- no significant changes	* in follow-up (after 3 weeks) the shift of the LI remained constant [Forest Chi-Square=14.80, df=2, P=0.03]
Intrakortikale Inhibition: CSP, (non-paretic arm)	- no significant changes	* **significant increase in CSP by 33%,** pre-post [Forest Chi-Square=8.16, df=2, P=0.01]
	- no significant changes	* in follow-up (after 3 weeks) the increase was maintained, 24% [Forest Chi-Square=8.16, df=2, P=0.04]
Intracortical inhibition: SICI	- no significant changes	- no significant changes
	* in follow-up (after 3 weeks), **SICI in the active group increased by 27%** compared to placebo [Forest Chi-Square=7.08, df=2, P=0.04]	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION

This study demonstrates in detail the improvement of motor function of the upper limb after a tDCS stroke in combination with motor training. The increased hemispheric balance as well as improved corticospinal plasticity in the ipsilasional and contralesional M1 proves to be an important rehabilitation process for the recovery of motor functions after stroke.

Motor disorders - stroke

Anodal tDCS combined with radial nerve stimulation promotes hand motor recovery in the acute phase after ischemic stroke

Sattler V, Acket B, Raposo N, Albucher JF, Thalamas C, Loubinoux I, Chollet F, Simonettra-Moreau M;
2015 – Neurorehabilitation and Neural Repair, Volume 29

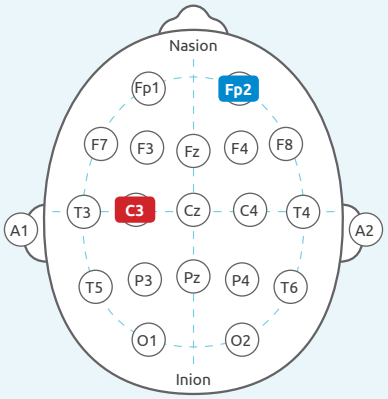
OBJECTIVE Effect of tDCS and FES on the functional restoration of aromotory in patients after stroke in the acute phase

PROCEDURE Placebo group: active FES + placebo stimulation (tDCS);
Active group: active FES + active stimulation (tDCS)

METHODOLOGY **Combination of tDCS and FES:** Double-blind study (RCT) with 20 patients after stroke with mild to moderate motor deficits (10 placebo, 10 active)

PARAMETERS

Stim. intensity	1-2 mA
Duration	13 minutes stimulation + 13 minutes FES
Anode	C3/C4 (same hemisphere as lesion)
Cathode	Fp1/Fp2 (contralateral to the anode)
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	5 sessions
Assessment	JHFT, Hand Dynamometer, Nine Hole, Peg Test, Hand Tapping Test, ULFM, TMS (MEP)



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
JHFT	* significant improvement (baseline follow-up), reducing time to perform JHFT	* significant improvement (baseline follow-up), Reducing the time to perform JHFT, **day 5: 6 sec faster; day 15: 23 sec more quickly; day 30: 24 seconds faster**
	-	* **significantly improved motor performance after follow-up compared to the placebo group [day 15: P=.03; Day 30: P=.01]**
DYN	- no significant changes	
9HPT	- no significant changes	
HTap	- no significant changes	
ULFM	*** significant temporal improvement in follow-up; improved hand and finger extension	*** **significant temporal improvement in follow-up, improved hand and finger extension**
TMS	- no significant changes regarding AMT and RMT	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the combined therapy of tDCS and FES show an improvement of the tDCS group in the follow-up (JHFT). Specifically, the functionality of the hand improved, which has a positive effect on the activities of daily life. tDCS in combination with FES can be used for motor rehabilitation.

Motor disorders - Parkinson's

Transcranial direct current stimulation associated with gait training in Parkinson's disease: A pilot randomized clinical trial

Coast-Ribeiro A, Maux A, Bosford T, Aoki Y, Castro R, Baltar A, Shirahige L, Moura Filho A, Nitsche MA, Monte-Silva K; 2016 – Developmental Neurorehabilitation, Volume 0

DEVELOPMENTAL NEUROREHABILITATION

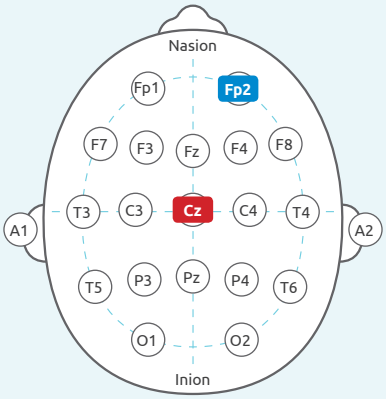
OBJECTIVE Efficacy of tDCS with gait training on functional mobility in Parkinson's patients

PROCEDURE Placebo group: gait training + placebo stimulation;
Active group: gait training + active stimulation

METHODOLOGY **Combination of tDCS and gait training:** double blind study (RCT) with 22 Parkinson's patients (11 placebo group, 11 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	13 minutes stimulation + 30 minutes gait training
Anode	Cz (2 cm anterior)
Cathode	Fp2 (contralateral to the affected side)
Size of electrode	35 cm^2
Treatment	3 x times a week
Scope of treatment	10 sessions
Assessment	TUG, gait speed, cadence, UPDRS, UL-MT, BBS, PDQ-39



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
TUG, walking speed	* significant improvements, both TUG and gait speed improved significantly **in post, but were no longer significant in follow-up**	* significant improvements, both parameters TUG and gait speed improved significantly in the post test, **these improvements remained significant in the follow-up** [gait speed: z=-2,184, P=.05; TUG: t=2.223, P=.05]
Cadence	* significant changes	
UPDRS	* significant changes	
UL-MT	* significant changes	
BBS	* significant changes	
PDQ-39	* significant changes	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The result of the combined therapy of tDCS and gait training initially showed no difference to the control group, both groups improved significantly. In follow-up (1 month), only the positive effects of gait training + tDCS remain sustainable. This means that tDCS in combination with gait training prolongs and stabilizes the effects.

Cognitive deficits - Working memory - Additional study

tDCS-induced episodic memory enhancement and its association with functional network coupling in older adults

Antonenko D, Hayek D, Netzband J, Grittner U, Flöel A
2019 – nature, Scientific Reports, Volume 9

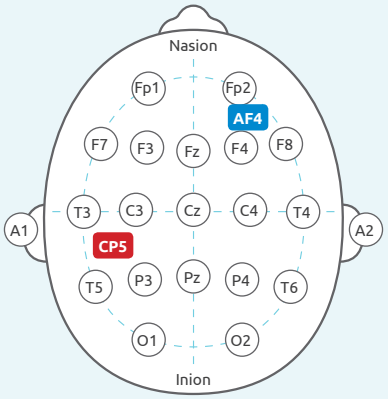
OBJECTIVE Effect of tDCS over the left temporo-parietal cortex on episodic memory in the elderly

PROCEDURE Learning picture-word pairs combined with placebo or active stimulation

METHODOLOGY **tDCS during memory-related learning tasks**: 34 healthy older people with normal cognitive functions

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	CP5
Cathode	AF4 (right supraorbital)
Size of electrode	anode: 35 cm^2, cathode: 100 cm^2
Treatment	5 learning blocks, stimulation during the first 4 blocks
Scope of treatment	2 sessions (per person 1 active / 1 placebo)
Assessment	accuracy, learning curve, response time, BOLD



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Accuracy of task fulfilment	- significantly better performance with number of training blocks	** significantly better performance with number of training blocks (P=0.002)
		* significantly better performance in retrieving the learning after completing the learning blocks (P=0.014)
Learning curve		* steeper learning curve (P=0.014)
Reaction time	- response time shorter with number of training blocks	*** response time shorter with number of training blocks (P <0.001)
	- no significant difference placebo vs. active group	
BOLD	- better performance with initially higher connectivity between temporo-parietal region and hippocampus	
		- better learning progress with initially higher connectivity

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The study shows that tDCS also produces significant improvements in cognitive performance in the elderly. Steeper learning curves and better memory performance are achieved. The effectiveness is better with higher existing connectivity between learning-relevant brain regions.

Cognitive deficits - Additional study

Augmentation of working memory training by transcranial direct current stimulation (tDCS)

Ruf SP, Fallgatter AJ, Plewnia C
2017 – Nature, Volume 7

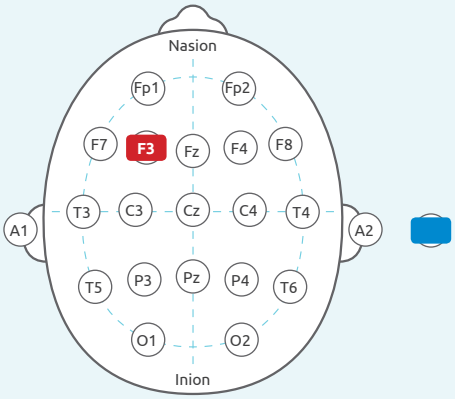
OBJECTIVE Influence of tDCS on the working memory performance

PROCEDURE Placebo group: working memory training + placebo stimulation;
Active group: working memory training + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** single blind study (RCT) with 71 subjects (23 placebo group, 24 congruent group, 24 incongruent group)

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	F3 (verbal tasks), F4 (spatial tasks)
Cathode	contralateral shoulder, deltoid muscle
Size of electrode	anode: 35 cm²
Treatment	1 x daily
Scope of treatment	3 sessions
Assessment	verbal n-back, spatial n-back



10-20 System

RESULTS

Assessment	
Effects during training (verbal and spatial n-back)	*** high performance increase in active group (congruent) compared to placebo [$\beta_{\text{session x congruent vs sham}}$ =1.00, SE=0.27, z=3.66, P<0.001]
	** after two stimulations (second day) marked **increase in performance of the active group** compared active to the placebo group [t(45)=3.29, P=0.002]
Effects after follow-up (verbal and spatial n-back)	* active group (congruent) showed greater increase in performance in follow-up than placebo group [$\beta_{\text{congruent vs sham}}$ =2.02, SE=1.01, t(48)=2.01, P=0.050]
	** active group (congruent) showed **significantly better performance level** in follow-up than placebo group [t(33)=2.96, P=0.006]
Transfer effects	** patients with lower performance (baseline) benefited more from stimulation [$\beta_{\text{baseline x congruent vs sham}}$ =0.74, SE=0.25, t(65)=-3.00, P=0.004]

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This study showed that stimulation of the DLPFC can increase working memory performance. The cognitive training accompanied by tDCS can also improve non-trained tasks through transfer effects. The improvement in working memory performance can last up to 9 months. Patients with lower initial performance benefit most from the combined use.

Cognitive deficits - Traumatic brain injury

Concomitant use of transcranial direct current stimulation and computer-assisted training for the rehabilitation of attention in traumatic brain injured patients: Behavioral and neuroimaging results

Sacco K, Galetto V, Dimitri D, Geda E, Perotti F, Zettin M, Geminiani GC
2016 – Frontiers in Behavioral Neuroscience, Volume 10

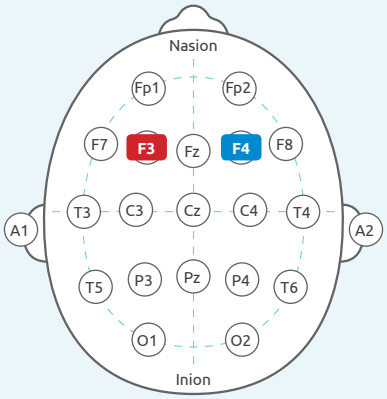
OBJECTIVE Efficacy of tDCS and cognitive training on shared attention and neural activity

PROCEDURE Placebo group: computer-based training + placebo stimulation;
Active group: computer-aided training + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** single blind study (RCT) with 32 patients after craniocerebral trauma (16 placebo group, 16 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes (+30 minutes cognitive training)
Anode	DLPFC (Läsionsseite)
Cathode	DLPFC (contralateral to the anode)
Size of electrode	35 cm^2
Treatment	2 x times a day
Scope of treatment	10 sessions
Assessment	TEA, rBANS, BDI, AES, MRT



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
TEA	- no significant differences	*** significantly better in pre-post [faster reaction time: t=3.41, P=0.004; Omission error: t=4.49, P<0.0001] **improvements remained until follow-up**
rBANS	-	- no significant differences
BDI	-	- no significant differences
AES	-	- no significant differences
MRT	-	** reduction of activity in the right cingulate gyrus

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION After computer-assisted cognitive therapy + tDCS, abnormal cortical activity normalized only in the active group. In addition, significant, sustained improvements in shared attention and responsiveness have been demonstrated.

Cognitive deficits - Multiple Sclerosis

Neuroenhancement through cognitive training and anodal tDCS in multiple sclerosis

Mattioli F, Bellomi F, Stampatori C, Capra R, Miniussi C
2016 – Multiple Sclerosis Journal, Volume 22

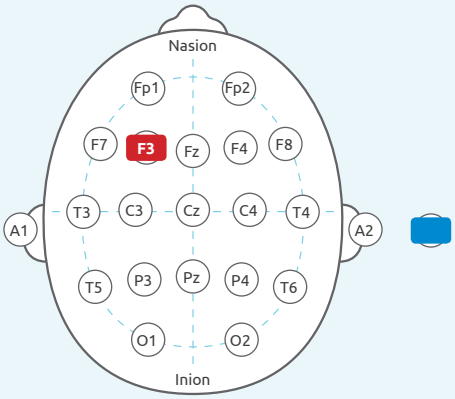
OBJECTIVE Effect of tDCS with cognitive training on attention performance

PROCEDURE Placebo group: cognitive training + placebo stimulation;
Active group: cognitive training + active stimulation

METHODOLOGY **Combination of tDCS and Cognitive Training:** Double blind study (RCT) with 20 Multiple Sclerosis patients (10 placebo group, 10 verum group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	left DLPFC (F3)
Cathode	shoulder (right)
Size of electrode	25 cm²
Treatment	1 x daily
Scope of treatment	10 sessions
Assessment	SDMT, PASAT, WCST



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
SDMT	* after 10 days of active group is significantly better than placebo group [P=.019]	
PASAT 2	-	* significant improvement
	* significantly better effects in the active group (active group compared with placebo group): follow-up baseline [PASAT 2: P=.015; WCST P=.035]	
PASAT 3	* significant improvement	
WCST	after 10 days active group is significantly better than placebo group: ** total error [P=.003] ** perseverative responses [P=.035] ** perseverative errors [P=.043] ** non-perseverative errors [P=.009]	
difficulty	-	* faster achievement of higher difficulty levels [P=.02]

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION tDCS in combination with cognitive training improves attention and information processing in multiple sclerosis patients. In the active group, the significant results are sustainable (follow-up). The stimulation increases the activation of the neuron populations, which could lead to stronger response to therapy.

Cognitive deficits - Parkinson's

Mild cognitive impairment in Parkinson's disease is improved by transcranial direct current stimulation combined with physical therapy

Manenti R, Brambilla M, Benussi A, Rosini S, Cobelli C, Ferrari C, Petesi M,
Orizio I, Padovani A, Borroni B, Cotelli M; 2016 – Movement Disorders, Volume 31

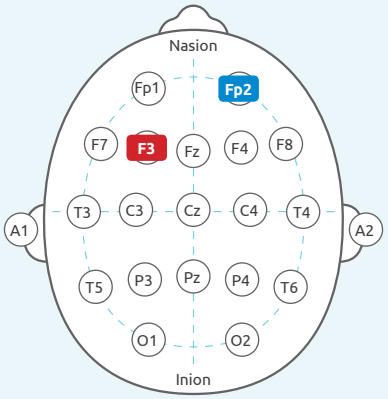
OBJECTIVE Effect of tDCS and exercise training in Parkinson's patients on motor and cognitive performance

PROCEDURE Placebo group: exercise training + placebo stimulation;
Active group: exercise training + active stimulation

METHODOLOGY **Combination of tDCS and exercise training**: double blind study (RCT) with 20 Parkinson's patients (10 placebo group, 10 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	25 minutes
Anode	DLPFC (F3/F4: contralateral to the affected side of the body)
Cathode	Fp2/Fp1 (contralateral to the anode)
Size of electrode	35 cm^2
Treatment	1 x daily
Scope of treatment	10 sessions
Assessment	motor function tests, PD-CRS, verbal fluency, TMT



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Motor tests	*	both groups improved in the motor tests (e.g. balance)
PD-CRS	-	- results improved in post test [P = .003], **this effect remained stable in follow-up**
Verbal word liquid	-	- improved in the post test [P=.002] and **remained sustainable significantly in the follow-up** [P=.005]
TMT-B	-	- less time was needed to complete the test - [P=.002], **also in follow-up**

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show a significant increase in cognitive performance parameters through the combination of tDCS and exercise training. The motor performance increased significantly in both groups, the memory and attention performance improved only in the active group.

Cognitive deficits - Stroke

The effects of transcranial direct current stimulation on cognition in stroke patients

Yun GJ, Chun MH, Kim BR
2015 – Journal of Stroke, Volume 17

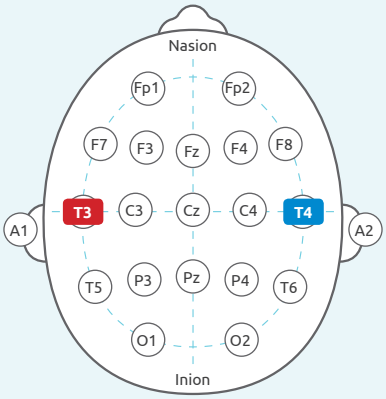
OBJECTIVE Efficacy of tDCS on cognitive abilities in post stroke patients

PROCEDURE Placebo group: cognitive training + placebo stimulation;
Active group: cognitive training + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** double blind study (RCT) with 45 stroke patients (15 placebo group,15 active group (FT-AS left), 15 active group (FT-AS right))

PARAMETERS

Stim. intensity	2 mA
Duration	30 minutes
Anode	T3
Cathode	T4
Size of electrode	25 cm^2
Treatment	1 x daily
Scope of treatment	15 sessions
Assessment	K-MBI, K-MMSE, BDST, FVST, VeLT-R



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
K-MMSE	* significant improvements in pre-post comparison	
BDST (backwards visual)	-	* significant improvements in pre-post comparison
FVST (forward visual span)	-	* significant improvements in pre-post comparison
VeLT-R (verbal learning test - delayed recall)	-	* significant improvements in pre-post comparison
K-MBI	* significant improvements in pre-post comparison	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION Stimulation of the T3 region improved memory. The working memory performance only increased in the active group.

Neglect - Stroke

The Effect of Transcranial Direct Current Stimulation on Neglect Syndrome in Stroke Patients

Yi YG, Chun MH, Do KH, Sung EJ, Kwon YG, Kim DY
2016 – Annals of Rehabilitation Medicine, Volume 40

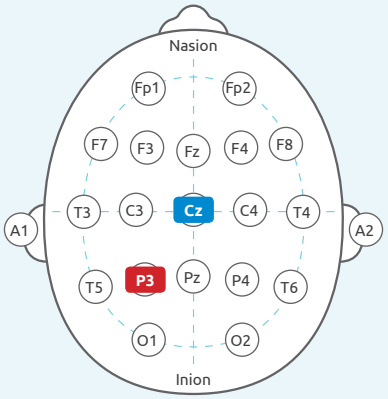
OBJECTIVE Effect of tDCS with conventional occupational therapy on visuo-spatial attention and post-stroke function with neurological neglect

PROCEDURE Placebo group: conventional therapy + placebo stimulation;
Active group: conventional therapy + active stimulation

METHODOLOGY **Combination of tDCS and cognitive training:** single blind study (RCT) with 30 left-sided neglect patients (10 placebo group, 20 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	30 minutes
Anode	P3 or P4
Cathode	Cz
Size of electrode	25 cm^2
Treatment	1 x daily
Scope of treatment	15 sessions
Assessment	MVPT, SCT, LBT, CBS, K-MBI, FAC



10-20 System

RESULTS

Assessment	*Results*
MVPT	* both groups improved significantly pre-post
	* significantly greater improvement in the active group (from pre: 8.2 ± 6.8 to post: 14.8 ± 5.8) to the placebo group (from pre: 8.3 ± 5.2 to post: 10.3 ± 5.5) [P=0.014]
SCT	* both groups improved pre-post
LBT	* both groups improved pre-post
	* significantly greater improvement in the active group (from pre: 27.3 ± 18.6 to post: 12.5 ± 13.0) to the placebo group (from pre: 26.0 ± 13.2 to post: 19.0 ± 12.3) [P=0.016]
CBS	* both groups improved pre-post
	* significantly greater improvement in the active group (from pre: 16.2 ± 6.4 to post: 10.0 ± 6.2) to the placebo group (from pre: 16.0 ± 9.7 to post: 12.3 ± 10.8) [P=0.013]
K-MBI	* both groups improved pre-post
FAC	* both groups improved pre-post

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show that the anodal or cathodal tDCS of PPC (P3/P4) can be combined to support the existing therapy to increase visuo-spatial attention in neglect patients.

Dysphagia - Stroke

Randomized Trial of Transcranial Direct Current Stimulation for Poststroke Dysphagia

Suntrup-Krueger S, Ringmaier C, Muhle P, Wollbrink A, Kemmling A, Hanning U, Claus I, Warnecke T, Teismann I, Pantev C, Dziewas R; 2018 – Annals of Neurology, Volume 83

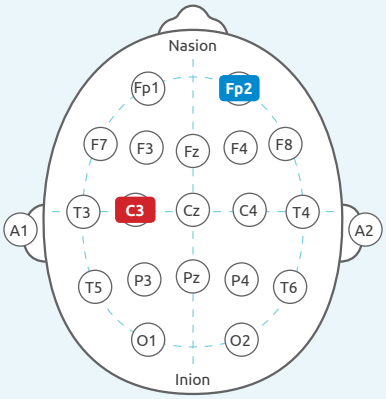
OBJECTIVE Effect of repeated tDCS in combination with swallowing on the dysphagia severity

PROCEDURE Placebo group: swallowing + placebo stimulation;
Active group: swallowing + active stimulation

METHODOLOGY Double-blind study (RCT) with 59 patients after stroke (30 placebo group; 29 verum group)

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	contralesional: from Cz 3.5 cm lateral and 1 cm anterior: ~ C3 or C4 (in brain stem infarction: ~ C4)
Cathode	Fp1 / Fp2 (contralateral to the anode)
Size of electrode	35 cm^2 anode, 100 cm^2 cathode
Treatment	4 times a week
Scope of treatment	4 sessions
Assessment	FEDSS, MEG, DSRS, FOIS, Dysphagia limit



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
FEDSS	* significant improvement (baseline post) [P=.027]	** significant improvement (baseline post) [P<.001]
	***significantly greater improvement, 1 FEDSS point in active group (83.3%) compared to placebo group (36.7%) average improvement 1.3 vs. 0.4 FEDSS points [η2=0.208, P<.0005]**	
MEG	- no significant changes	* significant increase in swallow-related event-related desynchronization (baseline post, 13-30Hz)
DSRS	** significant improvement in verum group compared to placebo group [P=.001]	
FOIS	* significant improvement in placebo group compared to active group [P=.041]	
Dysphagia limit	* significant improvement in active group compared to placebo group [P=.018]	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The study shows that tDCS provides additional benefits over conventional dysphagia therapy currently practiced. tDCS can be used to achieve faster and greater progress in acute dysphagia patients.

Aphasia - Stroke

Repetitive sessions of tDCS to improve naming in post-stroke aphasia: Insights from an individual patient data (IPD) meta-analysis

Rosso C, Arbizu C, Dhennain C, Lamy JC, Samson Y
2018 – Restorative Neurology and Neuroscience (IOS Press), Volume 36

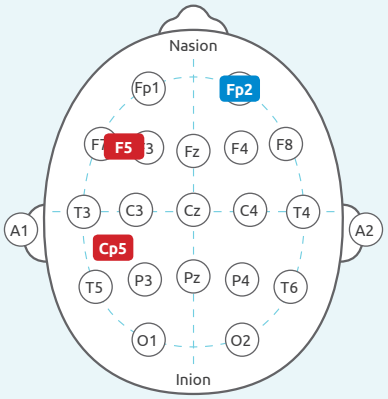
OBJEKTIVE Effectiveness of tDCS + naming training based on individual patient data

PROCEDURE Placebo group: naming training + placebo stimulation;
tDCS group: naming training + active stimulation

METHODOLOGY meta-analysis with 68 aphasics (87 active-placebo comparisons)

PARAMETERS

Stim. intensity	1-2 mA
Duration	20 minutes
Anode	F5 or Cp5
Cathode	Fp2
Size of electrode	35 cm^2
Scope of treatment	>5 sessions
Assessment	naming accuracy



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
naming accuracy	*** significant improvement in naming accuracy by 25% (± 37%) (P<.0001)	*** **significant improvement in naming accuracy by 35%** (± 34%) (P<.0001)
	*** the stronger the improvement in the placebo group, the greater the improvement in the tDCS group [r=0.993, 95% CI: 0.896-0.954, R2= 87%, P<.0001]	
		* frequency of treatment: **repeated stimulation (more than five) increases the effects of treatment** (P<.02)
		- anodal stimulation of the left temporoparietal flap most effective
	* for all severity grades of aphasia (mild / moderate / severe), greater enhancements can be achieved with active stimulation compared to placebo stimulation (P =.01, P=.002, P=.01)	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION This meta-analysis shows that the combination of tDCS + naming task can lead to greater progress. The stimulation amount should exceed 5 treatments and should be done on the temporoparietal lobe.

Aphasia - Stroke

Electrical stimulation of the motor cortex enhances treatment outcome in post-stroke aphasia

Meinzer M, Darkow R, Lindenberg R, Flöel A
2016 – Brain – A Journal of Neurology, Volume 139

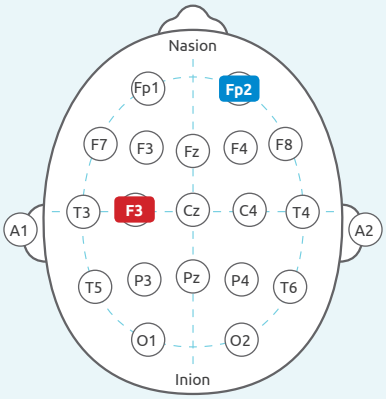
OBJEKTIVE Effect of tDCS on language proficiency in patients with chronic aphasia after stroke

PROCEDURE Placebo group: naming training + placebo stimulation;
Active group: naming training + active stimulation

METHODOLOGY **Combination of tDCS and naming training:** double-blind study (RCT) with 26 patients after stroke (13 placebo group, 13 active group)

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	C3
Cathode	Fp2
Size of electrode	Anode: 35cm², Cathode: 100 cm²
Treatment	2 times a day, 4 days a week
Scope of treatment	2 weeks, 16 sessions
Assessment	Naming Test, CETI, PCQ



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Naming Test	* significant improvement on trained objects in post and follow-up	* significant improvements in trained objects [P=.08] and **significantly better than the control group in follow-up (6 months)** [P=.01]
	* significant improvement in untrained objects, in follow-up no significant improvements (basline follow-up)	*** significant improvements in trained objects [P=.0009] and **significantly better than control group in follow-up (6 months)** [P<.01]
CETI (Communicative Effectiveness Index)	* significant	* significantly **higher than placebo group** after pre-post [P=.037] and in follow-up [P=.055]
PCQ (Partner Communication Questionnaire)	* significant	* significantly **higher than placebo group** in pre-post [P=.06] and follow-up [P=.03]

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results show the positive effects of the combination of tDCS and verbal training in chronic aphasia. Progress is achieved in a short period of time. Stimulation on C3 combined with naming training improved speech ability. A transfer into the everyday life could be proven, whereby the quality of life of the patients increased.

Aphasia - Stroke

Differential involvement of the left frontal and temporal regions in verb naming: A tDCS treatment study

Fiori V, Di Paola M, Oliveri M, Caltagironne C
2013 – Restorative Neurology and Neuroscience, Volume 31

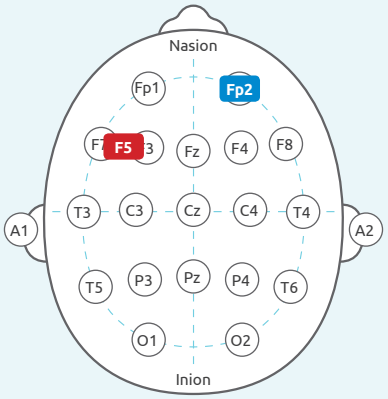
OBJECTIVE Effect of tDCS on verbal retrieval performance in aphasics

PROCEDURE Placebo setting: naming training + placebo stimulation;
Verum setting: naming training + active stimulation

METHODOLOGY **Combination of tDCS and naming training:** Uncontrolled study in 7 patients with left hemispheric stroke

PARAMETERS

Stim. intensity	1 mA
Duration	20 minutes
Anode	F5
Cathode	Fp2
Size of electrode	35cm²
Treatment	1 x daily
Scope of treatment	15 sessions
Assessment	Naming Test



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Naming Test	- no significant improvement	** significant improvement: 33% correct name [P = .004]
		*** significant improvement pre-post: 40% correct name [P = .000]
		after 5 days: 54% correctly named and recognized (baseline = 14%)
		in follow-up: performance at 44% (remained constant)

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show that tDCS + verbal training is a good therapeutic combination. The stimulation of the Broca area shows good effects in aphasia patients.

Aphasia - Dementia

Inferior parietal transcranial direct current stimulation with training improves cognition in anomic Alzheimer's disease and frontotemporal dementia

Roncero C, Kniefel H, Service E, Thiel A, Probst S, Chertkow H;
2017 – Alzheimer's & Dementia: Translational Research & Clinical Interventions, Volume 3

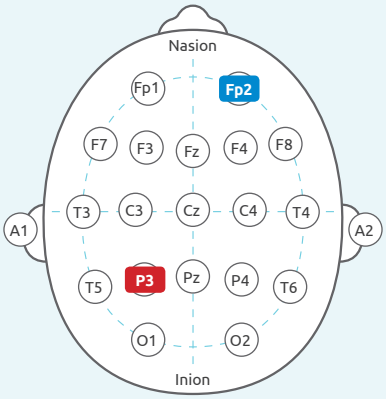
OBJECTIVE Impact of tDCS and language training on naming performance

PROCEDURE Placebo group: naming training + placebo stimulation;
Active group: naming training + active stimulation

METHODOLOGY **Combination of tDCS and naming training:** double blind study (RCT) with 10 dementia patients (AD or FTD); crossover design

PARAMETERS

Stim. intensity	2 mA
Duration	30 minutes
Anode	P3
Cathode	Fp2
Size of electrode	35cm²
Treatment	once a day, every other day
Scope of treatment	10 sessions
Assessment	Naming Test, Digit Span, Interviews



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
Naming Test	* trained objects: significant improvement: baseline - last stimulation: 19% improvement	* trained objects: significant improvement: baseline - last stimulation: 40% improvement
	non-trained objects: * in direct comparison: baseline results are the same for both groups, after two weeks: significantly different (t (9)=3.07, P<.05)	
Digit Span	- baseline 11.38 (SE=1.98)	- baseline 11.75 (SE=1.01)
	- similar baselines [t(7)=0.31, P=.77]	
	- after two weeks to 9.38 (SE = 1.52)	- after two weeks to 12.75 (SE=1.39)
	* significantly different after two weeks [t (7) = 4.34, P<0.1]	
Interview	- no significant improvement	* **7/10 relatives reported significant improvements in behavior**

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of the study show the positive effects of parietal lobe stimulation on the naming performance. Through the combination of language training and tDCS the effect of the therapy can be strengthened. In addition, stimulated patients were better able to cope with the increased level of semantic processing.

Schizophrenia

Effects of transcranial direct current stimulation on working memory and negative symptoms in schizophrenia: a phase II randomized sham-controlled trial

Gomes JS, Trevizol AP., Ducos DV., Gadelha A, Ortiz BB, Fonseca AO, Akiba HT, Azevedo CC, Guimaraes LSP, Shiozawa P, Cordeiro Q, Lacerda A, Dias AM;
2018 – Schizophrenia Research: Cognition, Volume 12

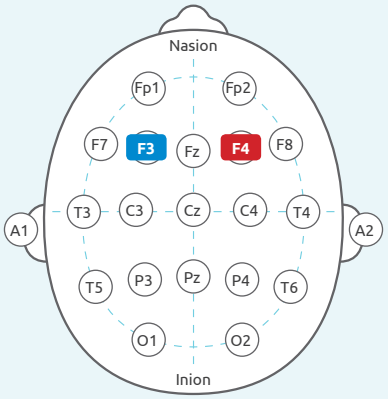
OBJECTIVE Effect of multiple tDCS in schizophrenia patients

PROCEDURE Placebo group: placebo stimulation;
Active group: active stimulation

METHODOLOGY Double-blind study (RCT) with 24 patients with schizophrenia (12 placebo group, 12 verum group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	F3 (left DLPFC)
Cathode	F4 (right DLPFC)
Size of electrode	25cm²
Treatment	5 times a week
Scope of treatment	10 sessions
Assessment	PANSS, cognitive assessment



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
PANSS-Negative symptoms	reduction of baseline to last intervention: 0.17; remained constant until the FU	reduction of baseline to last intervention: 3.83; remained constant until FU
PANSS-General symptoms	reduction of baseline to last intervention and FU by 0.83 points	reduction of baseline to last intervention and FU by 10.75 points
PANSS-Total symptoms	reduction of baseline to last intervention and FU by 0.59 points	reduction of baseline to last intervention and to the FU by 6 points
cognitive Assessment	* time effect for working memory, processing speed, visual learning, problem solving	

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results of this study recommend the therapeutic use of tDCS in schizophrenia sufferers. Multiple tDCS applications significantly reduced the negative symptoms.

Acoustic hallucinations - Schizophrenia

Examining transcranial direct current stimulation (tDCS) as a treatment for hallucinations in schizophrenia

Brunelin J, Mondino M, Gassab L, Haesebaert F, Gaha L, Suaud-Chagny MF, Saoud M, Mechri A, Poulet E; 2012 – The American Journal of Psychiatry, Volume 169

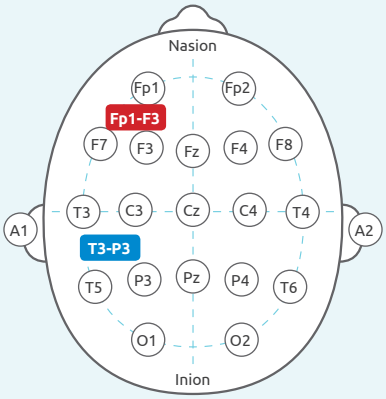
OBJECTIVE Efficacy of tDCS in schizophrenia sufferers with severe auditory hallucinations

PROCEDURE Placebo group: placebo stimulation;
Active group: active stimulation

METHODOLOGY Double-blind study (RCT) with 30 patients with acoustic hallucinations in schizophrenia (15 placebo group, 15 active group)

PARAMETERS

Stim. intensity	2 mA
Duration	20 minutes
Anode	F1 - F3
Cathode	T3 - P3
Size of electrode	35cm²
Treatment	2 times a day
Scope of treatment	10 sessions
Assessment	AHRS, PANSS



10-20 System

RESULTS

Assessment	*Placebo group*	*Active group*
AHRS	- AHRS improved by 8%	*** after 5 days, a large effect in the active group compared to the placebo group, [df=1.58, p<.0001] (6 months) relapse
	-	*** HRS improved by 31% (after 5 days)
	- effect on AHRS persisted after 1 month (3%) and after 3 months (5%)	*** effect in AHRS increased after one month (36% [t=-4.48, p <.0001]) and also after three months (38% [t=-4.58, p<.0001])
Craving	- slight reduction of negative symptoms PANSS from 82.8 to 80.5	* significant reduction in negative symptoms PANSS from 76.9 to 66.9 compared to the placebo group [P=.01]

Significance Scores: * P<0.05; ** P<0.01; *** P<0.001

CONCLUSION The results show that auditory hallucinations in schizophrenics can be significantly reduced after 10 tDCS treatments. The improvement continued until follow-up (3 months) and improved the quality of life of patients. In addition, the stimulation caused a reduction of the negative symptoms (PANSS).

Abbreviation	test procedure
AES	Apathy Evaluation Scale
AHRS	Auditory Hallucination Rating Scale
AMT	Active Motor Threshold
ANT	Attention Network Test
ARAT	Action Research Arm Test
BBS	Mountain Balance Scale
BBT	Box and Block Test
BDI	Beck Depression Inventory
BDST	Backward Digit Span Test
CBS	Catherine Bergego Scale
CATI	Communicative Effectiveness Index
CSP	Cortical Sildent Period
DSRS	Dysphagia Severity Scale
DYN	Hand Dynamometer
Dysphagia-limit	Dysphagia Maximum intake (H2O), without ingestion or aspiration
FAB	Frontal Assessment Battery
FAC	Functional Ambulation Classification
FEDSS	Fiber Optic Endoscopic Dysphagia Severity Scale
FFI	Foot Function Index
FOIS	Functional Oral Intake Scale
FVST	Forward Visual Span Test
HAMA	Hamilton Anxiety Scale
HAMD	Hamilton Depression Scale
HDRS	Hamilton Depression Rating Scale
HPTH	Heat Pain Threshold
HPTo	Heat Pain Tolerance
HTap	Hand Tapping Test
JHFP J	ebsen and Taylor Hand Function Test
K-MBI	Korean Modified Barthel Index
LBT	Line Bisection Test
LI	Laterality Index
MARDS	Montgomery-Åsberg Depression Rating Scale
MEG	Modified Ashworth Scale
MEP	Motor Evoked Potential
MMSE	Mini-Mental State Examination

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MRC	Medical Research Council
MSQOL-54	Multiple Sclerosis Quality of Life-54
MVPT	Motor-Free Visual Perception Test
NRS	Numerical Rating Scale
OCDS	Obsessive Compulsive Drinking Scale
PANSS	Positive and Negative Syndrome Scale
PASAT 2	Paced Auditory Serial Addition Task 2
PASAT 3	Paced Auditory Serial Addition Task 3
PASS-20	Pain Anxiety Symptoms Scale-20
PCQ	Partner Communication Questionnaire
PD-CRS	Parkinson's Disease Cognitive Rating Scale
PDQ-39	Parkinson's Disease Questionnaire-39
rBANS	Repeatable Battery for the Assessment of the Neuropsychological Status
RCT	Randomized Controlled Trial
SCT	Star Cancellation Test
SDM	Symbol Digit Modality Test
SF-MPQ	Short-form McGill Pain Questionnaire
SICI	Short-Interval Intracortical Inhibition
SS-QOL	Stroke-specific Quality of Life
TEA	Test for the Examination of Attention
TMT-B	Trail Making Test -Part B
TUG	Timed Up and Go Test
UEFM	Upper Extremity Fugl-Meyer
ULFM	Upper Limb Fugl-Meyer
UL-MT	Upper Limb Motor Task
UPDRS	Unified Parkinson's Disease Rating Scale
VAS	Visual Analog Scale
VeLT-R	Verbal Learning Test-delayed Recall
WCST	Wisconsin Card SortingTest
WHOQOL	Quality of Life of the World Health Organization
WMFT	Wolf Motor Function Test
9HPT	Nine Hole Peg Test

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