

Large-scale trials in neuropsychiatry

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Aims

- To overview all, completed and ongoing, large-scale ($n > \sim 100$) trials in neuropsychiatry using tDCS
- To compare the upcoming trials with all RCTs performed so far (regardless of sample size) Aparicio, Brunoni, 2016
- Data discussed focused on: *Anode and Cathode electrode position; Dose parameters (current, number of sessions, session duration); Study design; and Long term follow up.*

Completed trials

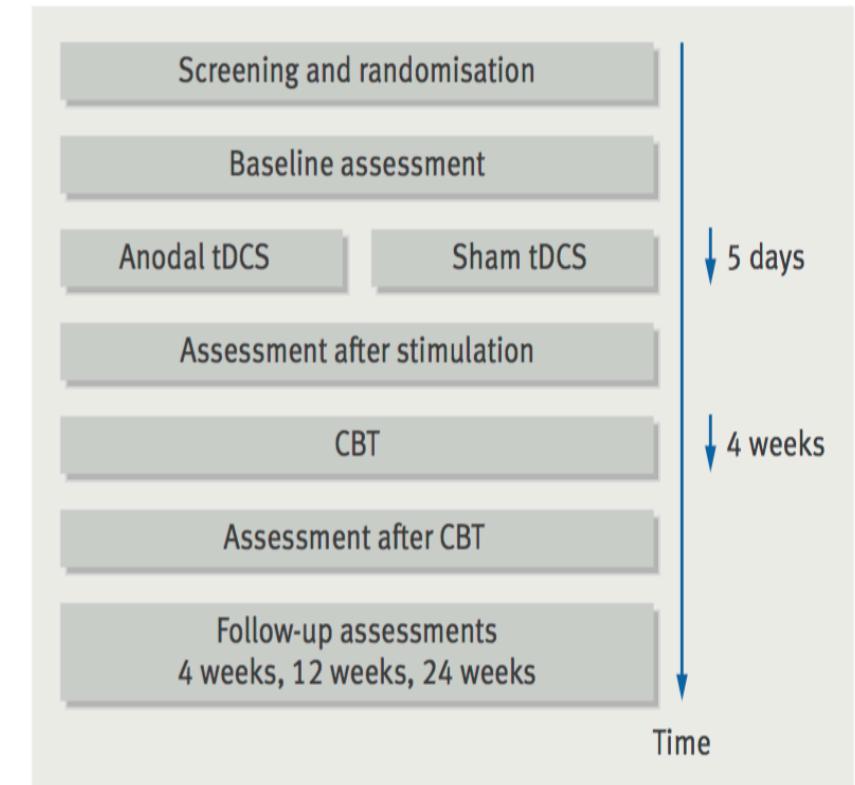
Author (year)	Disorder	n	Design	Other interventions	Treatment	A / C	Pure placebo	Follow-up	Results
Brunoni et al. (2013)	MDD	120	Factorial	Sertraline	2mA/30min/1 2d	F3/F4	Yes	6 weeks	Positive
Hesse et al. (2011)	Stroke	96	3-arm	Robot arm-training	2ma/20min/3 0d	A-lesioned or C- nonlesioned	No	12 weeks	Negative
Luedtke et al. (2015)	Chronic low back pain	135	2-arm	CBT for pain	2mA/20min/5 days	C3/rSO	No	5 days	Negative

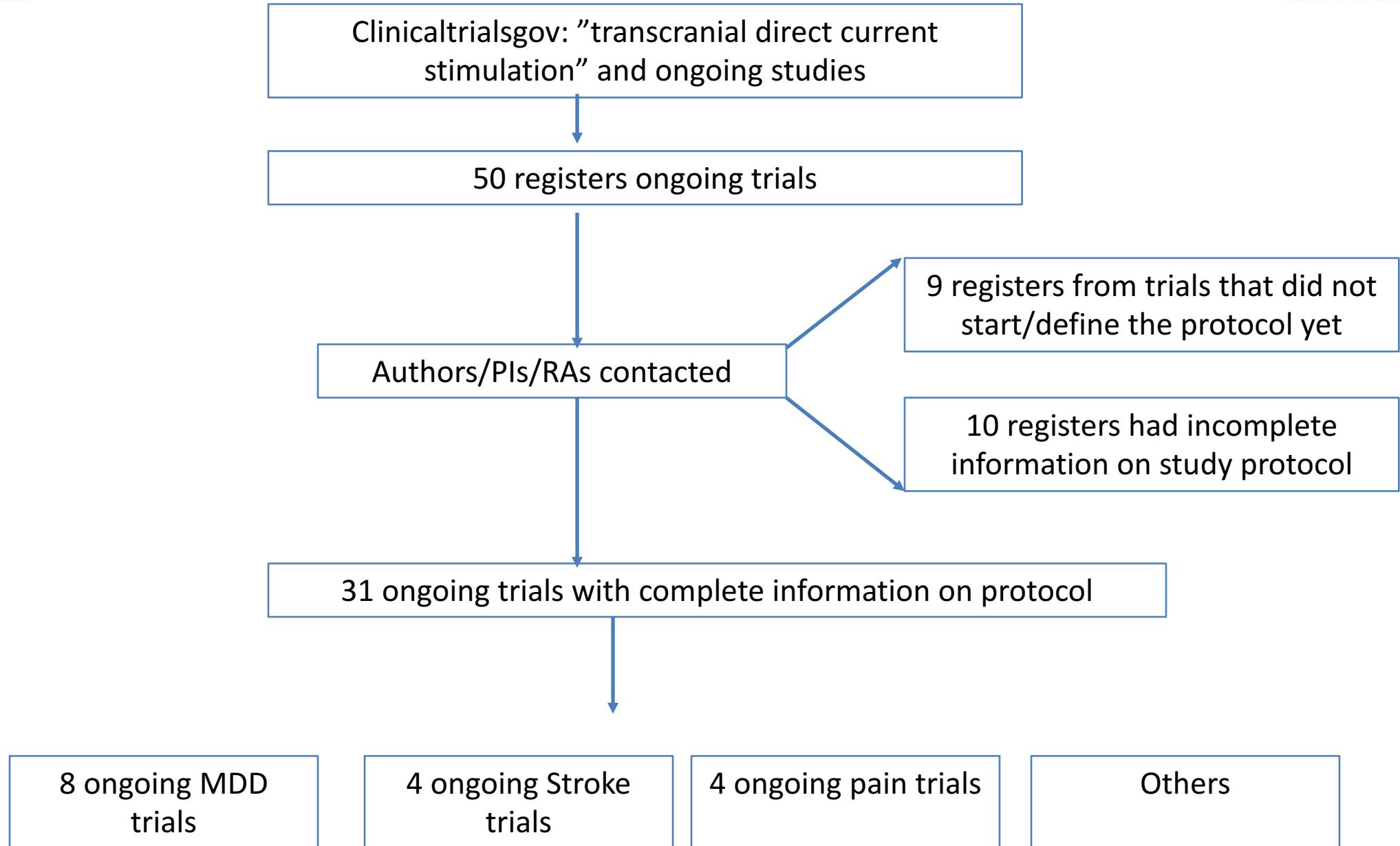
Negative results

- Hesse et al. (2011)
- → No pure placebo (all pts received Arm training) --> Ceiling effect
- → No A-lesioned / C- non-lesioned group
- → Small sample size (estimated ES of 1)

Negative results

- Luedtke et al. (2015)
- Only 5 days of stimulation
- No pure placebo (ceiling effects)
- Small sample sizes (ES of 0.75)





Upcoming studies - Depression

PI	Country	NCT	n	Design	Outcome	Follow-up	Parameters	Other Interventions	Anode	Cathode
Brunoni ("ELECT-TDCS")	Brazil	1894815	245	3-arm: tDCS vs. escitalopram vs. placebo	HDRS	10 w	2mA/30min/22 sessions	Escitalopram 20mg/d	left DLPFC	right DLPFC
Bajbouj	Germany	2633449	192	2-arm: tDCS + CBT vs. sham + CBT	MADRS	30w	1-2mA/30 min/ 12 sessions	Group CBT therapy, 60 min (tDCS from 10-40m)	left DLPFC	right DLPFC
Haffen ("STICODEP") MDD/BD	France	1644747	96 MDD/ 24 BD	2-arm: tDCS + TAU vs. Sham tDCS + TAU	HDRS-21	24w	2mA/30 min/10 sessions	TAU	left DLPFC	right DLPFC
Padberg ("DepressionDC")	Germany	2530164	152	2-arm: tDCS + SSRI vs. Sham tDCS + SSRI	MADRS	24w	2mA/30min/24 sessions	SSRI	left DLPFC	right DLPFC
Loo	Australia	1974076	135	2-arm: tDCS + CBT vs. sham + CBT	MADRS	3w	.	CBT	.	.
Taiminen ("DEPTDCS2014")	Finland	2521883	120	2-arm: tDCS + TAU vs. Sham tDCS + TAU	MADRS	24w	2mA/30 min	TAU	left DLPFC	right DLPFC
Loo and Chan	Australia/Singapore	1346306	120	2-arm: two active interventions	MADRS	4w	2.5mA/30 min/20-30 sessions	TAU	left DLPFC	F8 vs. extracephalic
Lee (Ybrain company)	S Korea	2657980	96	2-arm: Yband (YDT-201N) vs. Sham-Yband (YDT-201N)	MADRS	6w	2mA/30 min/10 sessions	TAU	left DLPFC	right DLPFC

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Upcoming studies - Stroke

PI	Country	NCT	Condition	n	Design	Outcome	Follow-up	Parameters	Other Intervention	Anode	Cathode
Hummel	Austria	909714	Stroke - Paresis	250	2-arm : tDCS + training vs. sham + training	FMS	48 w	anodal / 20min	Upper extremity training	.	.
Shin	S Korea	2422225	Stroke - Dysphagia	120	4 arm: Sham vs. Bipolar over motor area vs. Anodal/Cathodal simulation over motor area vs. Single Anode stimulation	Dysphagia Outcome and Severity Scale(DOSS)	4 weeks	1.5mA/20 min/30 sessions	Not described	Affected Pharyngeal motor cortex	Non-affected cortex or SO area
Kumar	United States	1919112	Stroke - Dysphagia	99	3-arm: high dose anodal tDCS vs. Low dose anodal tDCS vs. Sham	PAS	3 weeks	2mA/20 minutes/ 10 or 5 sessions	swallowing exercises	C3/T3 or C4/T4 over the unaffected hemisphere	contralateral SO
Hesse	Germany	2395874	Stroke - Aphasia	96	2-arm: active vs. sham + Speech Therapy	Goodglass-Kaplan communication scale (GKS)	6 weeks	2mA/20 minutes/30 sessions	ST	Homologous speech area (TACS) in the right hemisphere or on the speech area perilesional in the left hemisphere	Contra laterally

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Upcoming studies:

Pain

PI	Country	NCT	n	Condition	Design	Outcome	Follow-up	Parameters	Other Interventions	Anode	Cathode
Fregni	USA	2487966	132	Phantom Limb Pain	Factorial: tDCS vs. Mirror therapy	VAS for pain	13-14w	2mA/20min/10days	Mirror Therapy	M1	rSO
Borckardt	USA	2241967	120	Post-operative pain	4-arm: tDCS full dose vs. tDCS half dose vs. tDCS minimal dose vs. Sham tDCS	opioid use	3d	4 sessions vs. 2 sessions vs. 1 session	TAU	.	.
Fregni	USA	1599767	120	SCI - Chronic Pain	2-arm: tDCS vs. Sham tDCS	Change in Pain Scale	24w	2mA/20min/15 sessions	tDCS only	M1	cSO
Brill	Israel	1220323	100	Chronic pain	2-arm: tDCS vs. Sham tDCS	Pain relief	3w	2mA/20min/5 sessions	TAU	M1	.

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Fregni	USA	1599767	120	SCI - Chronic Pain	2-arm: tDCS vs. Sham tDCS	Change in Pain Scale	24w	2mA/20min/15 sessions	tDCS only	M1	cSO
Brill	Israel	1220323	100	Chronic pain	2-arm: tDCS vs. Sham tDCS	Pain relief	3w	2mA/20min/5 sessions	TAU	M1	.

Upcoming studies: Substance dependence

PI	Disorder	Country	NCT	n	Design	Outcome	Follow-up	Parameters	Other Intervention	Anode	Cathode
Trojak	Alcohol dep	France	2505126	340	2-arm: tDCS vs. Sham tDCS	Alcohol consumption and heavy drinking	24 weeks	13:20:13/5 sessions	TAU	.	.
Lerman	Smoking (>10 cig per day)	USA	2624284	130	3-arm: sham tDCS vs. 1mA dose tDCS vs. 2mA dose tDCS	time to first cigarette in the resist smoking paradigm	12 days	1 mA or 2 mA/20 min/3 sessions	TAU	F3	rSO
Claus	Smoking (>10 cig per day)	USA	2534454	100	2x2: AAT vs tDCS	Cigarettes per Smoking Day	1 week	2 mA		F10	Left shoulder

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Trojak	Alcohol dep	France	2505126	340	2-arm: tDCS vs. Sham tDCS	Alcohol consumption and heavy drinking	24 weeks	13:20:13/5 sessions	TAU	.	.
Lerman	Smoking (>10 cig per day)	USA	2624284	130	3-arm: sham tDCS vs. 1mA dose tDCS vs. 2mA dose tDCS	time to first cigarette in the resist smoking paradigm	12 days	1 mA or 2 mA/20 min/3 sessions	TAU	F3	rSO
Claus	Smoking (>10 cig per day)	USA	2534454	100	2x2: AAT vs tDCS	Cigarettes per Smoking Day	1 week	2 mA		F10	Left shoulder

Upcoming studies: Cognition

PI	Country	NCT	Disorder	n	Design	Outcome	Follow-up	Parameters	Other Intervention	Anode	Cathode
Mulsant	Canada	2386670	MCI/MDD	375	2-arms: tDCS + CR vs. Sham tDCS + sham CR	Change in cognitive scores over time	60 months	2mA/30 min/40 sessions	CR exercises online at home	Fz	Iz
Valentin, Carmona	Brazil	2549560	Postoperative Cognitive Dysfunction	138	2 arms: tDCS vs. Sham tDCS	Cognitive enhancement	18 months	2mA/20 min/8 sessions	tDCS only	Left DLPFC	Right DLPFC
Martin	Australia	1653431	MCI	100	2 arms: tDCS vs. Sham tDCS	California Verbal Learning Test II	.	2mA/30 min/15 sessions	tDCS only	F3	F8
Hampstead	USA	2155946	Mild Cognitive Impairment/Alzheimer's Disease	100	active/sham tDCS + Memory Rehab or reminiscence training	Functional MRI and Cognitive Tasks	3 months	.	Memory rehabilitation Reminiscence training	no info	no info

Upcoming studies:

Cognition

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Upcoming studies: other psychiatric / neurologic disorders

PI	Country	NCT	Disorder	n	Design	Outcome	Follow-up	Parameters	Other Intervention	Anode	Cathode
Brunelin	France	2652832	Depression and Schizophrenia	200	ECT vs. rTMS vs. tDCS (MDD) or tDCS vs. rTMS (Schizo)	Serum BDNF levels	variable	2mA/20 min/10 sessions	rTMS or ECT	left DLPFC	no info
Vicari	Italy	2382497	AN and BED	160	tDCS vs. sham	EDI-3	6 weeks	1mA/20 min/18 sessions	TAU	F3	F4
Gluck	USA	739362	Obesity	148	2-arms: tDCS vs. Sham tDCS	Weight loss and appetite	6 weeks	2mA/40 min/12 sessions	Behavioral Weight Loss Treatment	left DLPFC	rSO
Poulet (STIM'ZO)	France	2744989	Schizophrenia	138	2 -arms: tDCS vs. Sham tDCS	Responders (PANNS)	6 months	2mA/20 min/10 sessions	TAU	F3/FP1	T3/P3
Hampstead	USA	2442843	PTSD	105	3-arms: tDCS vs. Sham tDCS vs. Combat controls	fc-fMRI	4 weeks	2mA/20 min/10 sessions	TAU	.	.
Valiengo	Brazil	2535676	Schizophrenia	100	2-arms: tDCS vs. Sham tDCS	Change in subscale of PANSS	12 weeks	2mA/20 min/10 sessions	TAU	F3	T3/P3
Kimberley	USA	2180139	Dystonia	96	2 x2 : M1 vs. Cerebellar tDCS	Cervical Dystonia Questionnaire	1 week	2mA / 4 sessions	tDCS only	M1 or Cerebellar	Contralaterally

Upcoming studies: other psychiatric / neurologic disorders

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Vicari	Italy	2382497	AN and BED	160	tDCS vs. sham	EDI-3	6 weeks	1mA/20 min/18 sessions	TAU	F3	F4
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Kimberley	USA	2180139	Dystonia	96	2 x2 : M1 vs. Cerebellar tDCS	Cervical Dystonia Questionnaire	1 week	2mA / 4 sessions	tDCS only	M1 or Cerebellar	Contralaterally

Comparison

Published vs. upcoming

		n of studies	sample size	Intensity	Duration	n of sessions	Follow-up	A/C Position
MDD	Previous	9	44 (31)	1.7 (0.4)	23.7 (4.8)	10.3 (4.8)	<i>6 week (max)</i>	<i>F3/F4 or rsO</i>
	Upcoming	8	147 (48)	2.1 (0.4)	30	15.8 (7.1)	<i>Most >10w</i>	<i>F3/F4</i>
Pain	Previous	11	44 (33)	2	20	5.9 (2)	<i>Usually <3w</i>	<i>M1/cSO</i>
	Upcoming	11	118 (11)	2	20	9 (4.5)	<i>3-24 w</i>	<i>M1/cSO</i>
Stroke	Previous	21	33.4 (23.7)	1.6 (0.4)	20.7 (8.1)	11 (6)	<i>6 weeks (max)</i>	<i>A in affected and/or C in un-affected</i>
	Upcoming	3	141 (73)	1.8 (0.2)	20	23 (11)	<i>3 – 48w</i>	<i>Idem</i>
Other neuro	Previous	12	27 (9)	2	21 (3.2)	6.6 (2.2)		
	Upcoming	5	162 (120)	2	23.7 (7.5)	16.7 (16)		
Other psych	Previous	9	27 (8.7)	2	19 (2.3)	7.2 (3.6)		
	Upcoming	9	158 (75)	1.7 (0.4)	22.8 (6.7)	13.5 (14.4)		
Total	Previous	64	35.4 (23)	1.8 (0.3)	21 (5)	8.5 (4.7)		
	Upcoming	31	147 (69)	1.9 (0.3)	23.8 (5.9)	14.7 (11.7)		

Final remarks

- Large number of upcoming trials (n=31) and patients (4567)
- MDD, stroke and pain are the most investigated conditions.
- Most protocols use the same parameters compared to previous trials (A/C, dose, session duration), although more sessions are being delivered and the follow-up period is longer.
- Therefore, upcoming clinical trials are based on generally the same premises of tDCS mechanisms of action used in pilot studies.
- Some upcoming trials exploring the effects of tDCS combined/compared to other intervention(s), the effects of different dose intensities or the effects of different electrode positions on the outcome.

- Thank you!
- Andre Brunoni
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