Brain Stimulation for Aphasia

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Disclosures

- I have no financial disclosures
- I am collaborating with Soterix Medical, Inc. on a clinical trial of transcranial direct current stimulation for aphasia, funded by NIH.

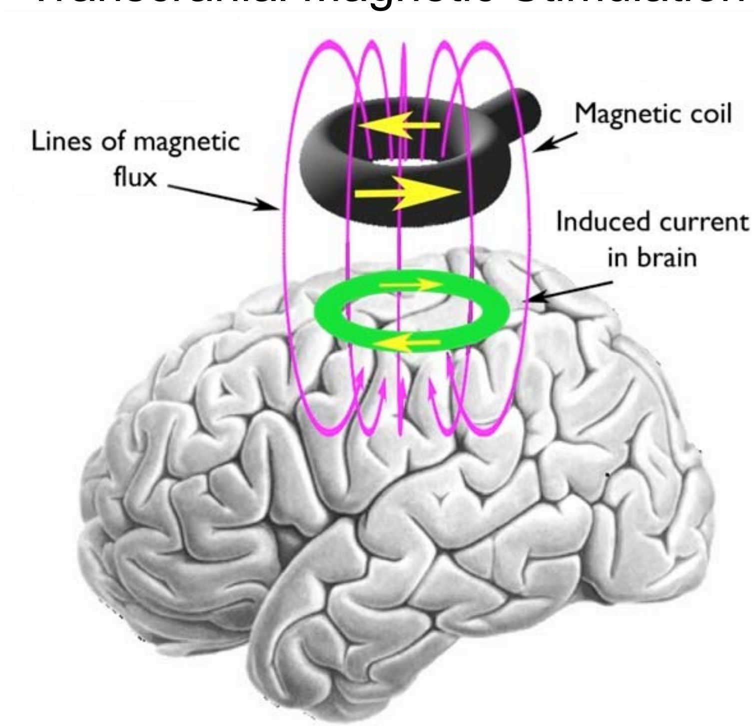
Outline

- Non-invasive brain stimulation techniques
- Brain basis of aphasia recovery (to guide new treatments)
- Evidence so far on non-invasive brain stimulation for aphasia
  - TMS
  - tDCS
  - Results of a new tDCS trial

Neuromodulation

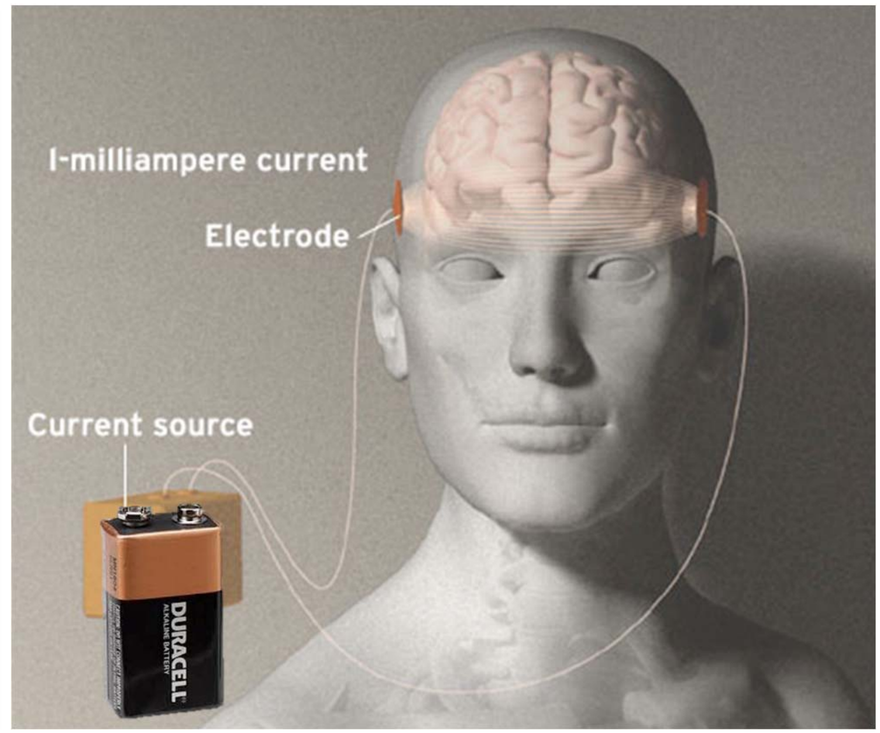
rTMS

Transcranial Magnetic Stimulation



tDCS

Transcranial Direct Current Stimulation

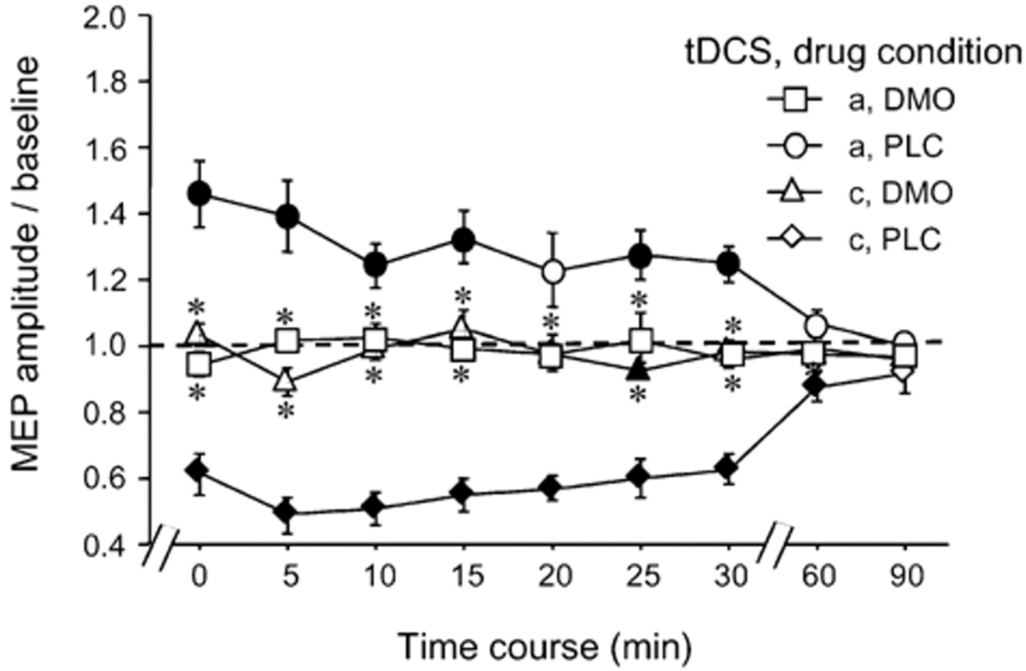


Medications

Speech-Language Therapy

rTMS and tDCS Commonalities

- Increase or decrease cortical excitability
- Effects last minutes-hours after stimulation
- Repeated sessions have long-term effects



Nitsche et al., 2003

rTMS vs. tDCS Differences

rTMS	tDCS
• Makes neurons fire	• Alters the probability of neurons firing
• Focal, precise anatomical effect	• Anatomically wide effect
	• Cheaper
	• Simpler
• Patient must stay still	• Can move during Tx
• Noisy	• Silent
• Small risk of seizure	• No serious adverse events

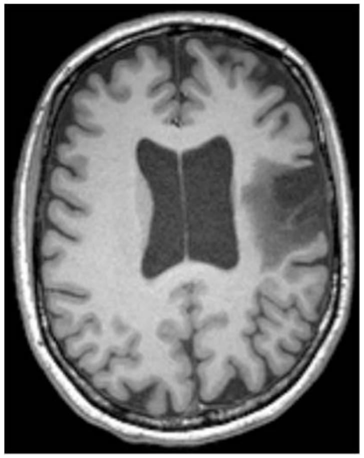
How? When? Where? Who? Why?

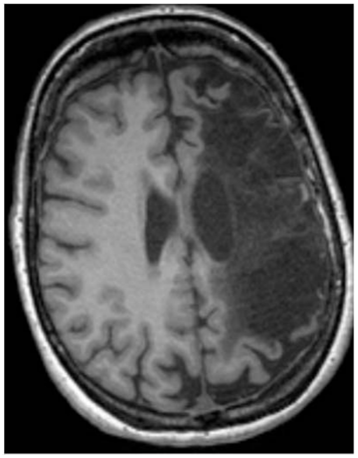
Understanding the brain basis of aphasia recovery will (hopefully) help to guide the treatment approach.

Recovery from aphasia (weeks- years)

- Depends on
  - Resolution of remote dysfunction
  - Strategic shifts
  - Brain plasticity

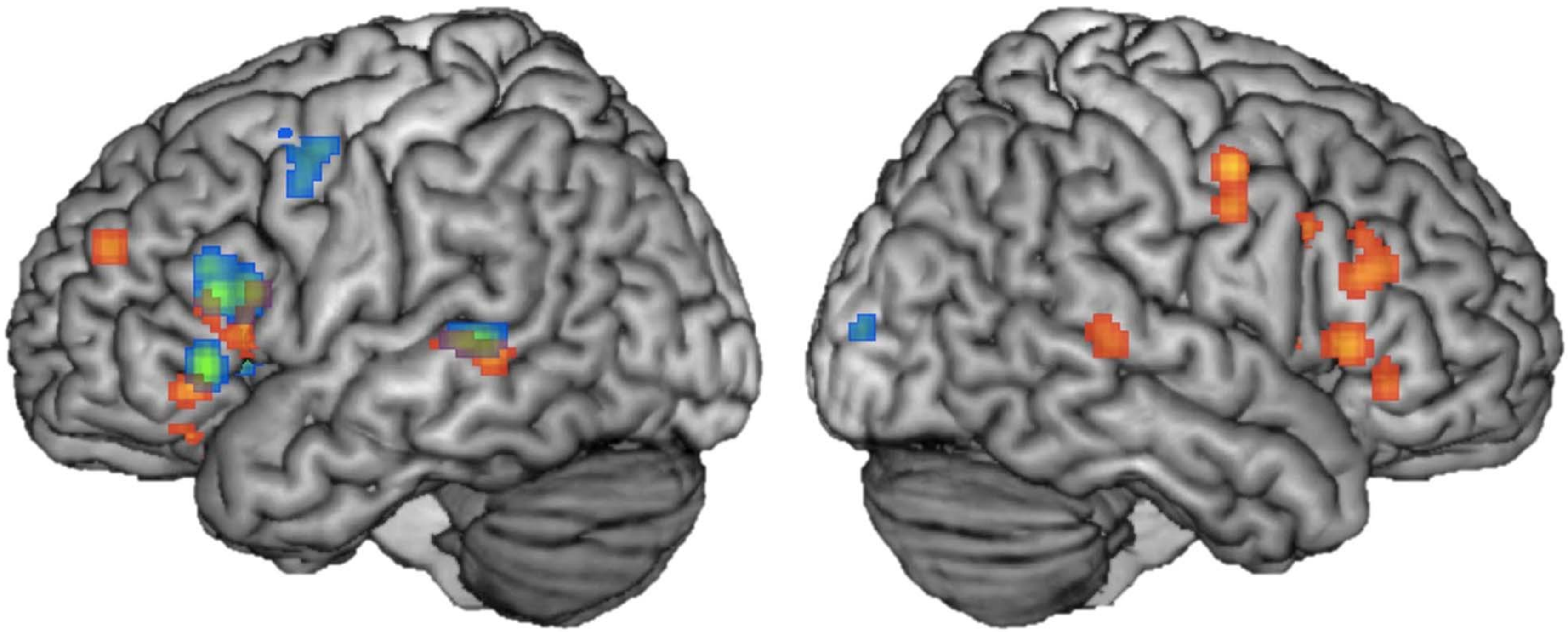
  (Strategic shifts and Brain plasticity: Influenced by experience)
- Constrained by
  - Lesion size and location
  - Health of the rest of the brain





Bilateral Language Activity in Chronic Post-Stroke Aphasia

12 studies: 106 patients, 129 controls

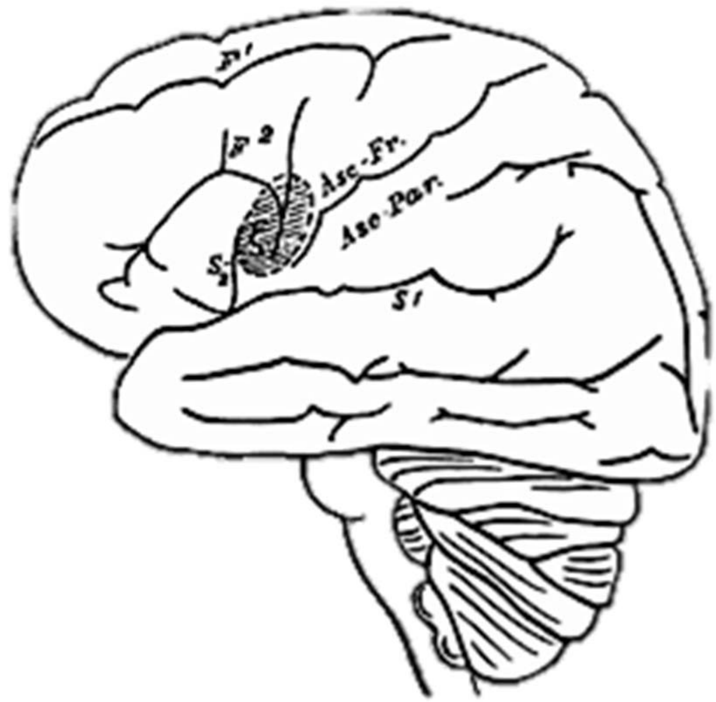


Controls
Aphasia

Turkeltaub et al., Neurology, 2011

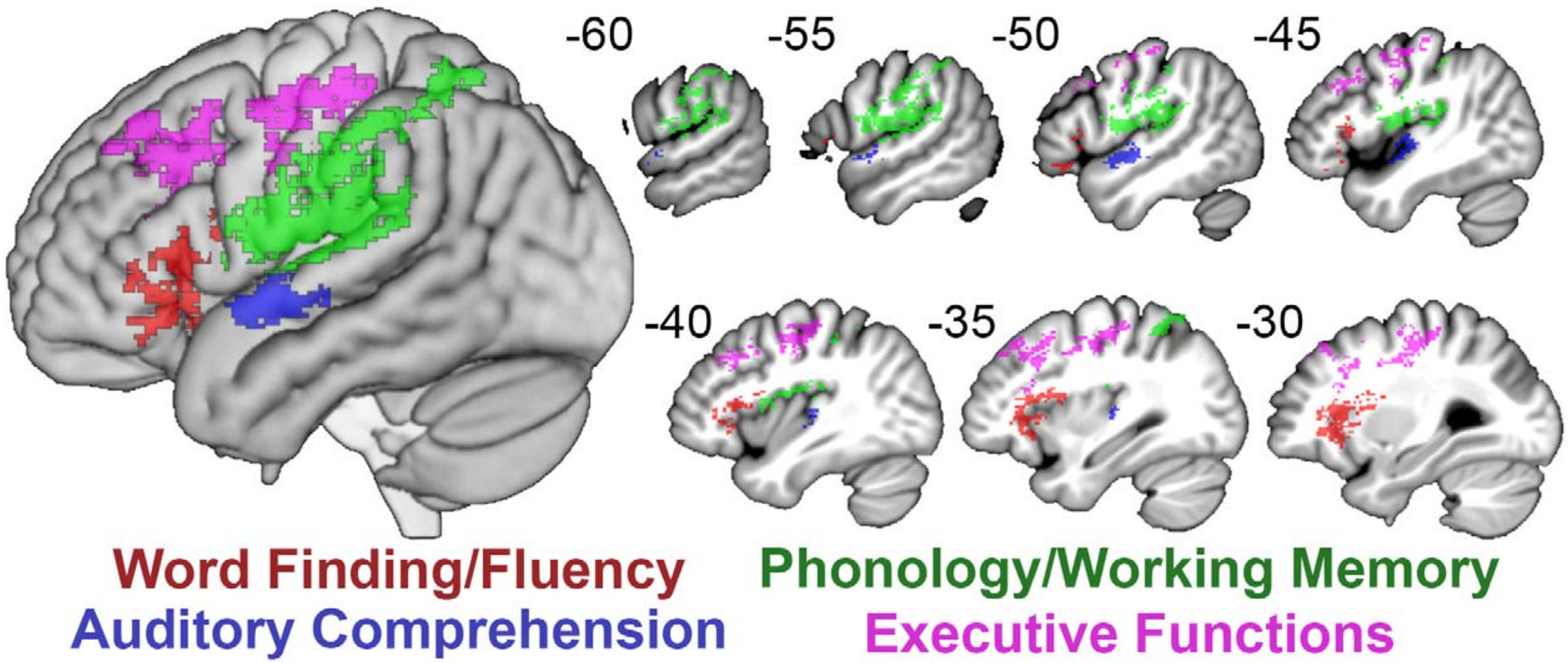
The roles of the two hemispheres in aphasia recovery

- Left Hemisphere
  - Sparing of language networks
  - Perilesional compensation (Fridrikkson et al, 2010)
- Right Hemisphere
  - Compensation (Barlow 1877, Basso 1989, Blasi 2002, Xing 2015)
  - Inefficiency, dysfunction or interference (Naeser 2005, Postman-Caucheteux et al., 2010)
  - Domain general cognitive functions (Geranmayeh et al., 2014)
  - Mixed roles (Saur 2006, Turkeltaub 2011, Anglade 2014, others)



Barlow, 1877

Language is not one thing



Lacey et al., 2017

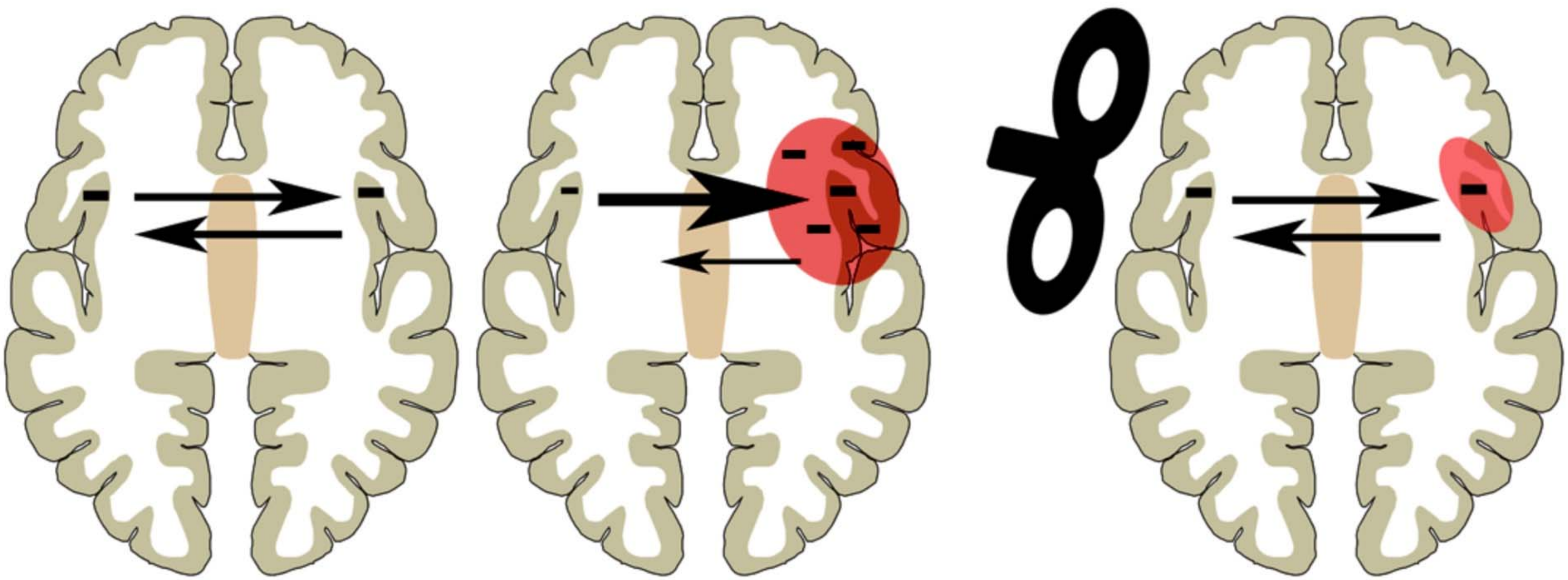
Different brain regions may be recruited by different mechanisms

- Right M1-mouth activity and Right STS activity relate to good naming outcomes
- Right motor cortex recruited for naming when left motor cortex is damage (Skipper-Kallal et al., 2017a)
- Right STS recruitment is blocked by left STS damage (Skipper-Kallal et al., 2017b)

Emerging Consensus

- Native left hemisphere networks are best
- Most efficient available networks
  - Perilesional cortex in small strokes
- Right hemisphere can compensate to some degree
  - Varies by specific language function
  - May be more important in the subacute period
- Multiple biologically and behaviorally driven mechanisms of change

Framework guiding rTMS Treatments: Interhemispheric Inhibition Model



Mutual transcortical inhibition

Unopposed inhibition after unilateral injury

Exogenous manipulation restores inhibitory equilibrium

Figure courtesy of Roy Hamilton

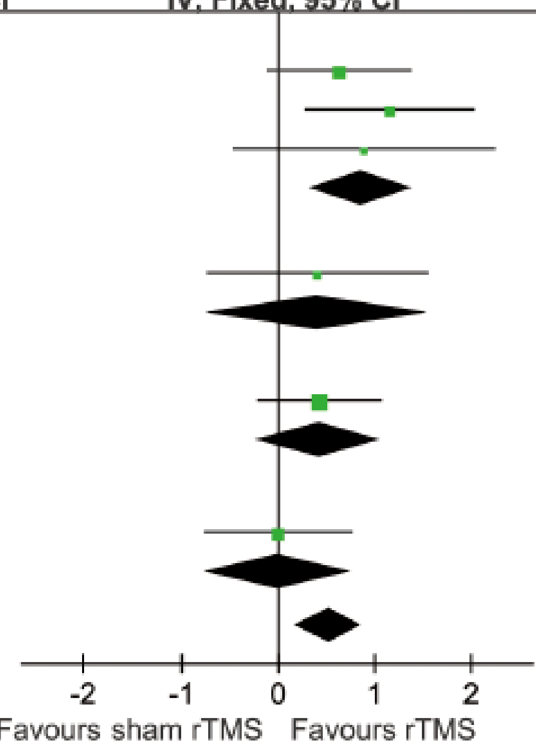
Randomized double-blind trials of inhibitory TMS to right IFG

Total N = 139

Study or Subgroup	Real rTMS Mean	Real rTMS SD	Real rTMS Total	Sham rTMS Mean	Sham rTMS SD	Sham rTMS Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AAT naming subtest								
Heiss WD 2013	6.1	6.35	15	2.4	4.89	14	21.0%	0.63 [-0.12, 1.38]
Thiel A 2013	6.67	3.33	13	1.67	5	11	15.3%	1.16 [0.28, 2.04]
Weiduschat N 2011	26.67	6.15	6	15.75	16.28	4	6.4%	0.89 [-0.47, 2.25]
Subtotal (95% CI)			**34**			**29**	**42.7%**	**0.86 [0.33, 1.38]**
BNT								
Barwood CHS 2013	6.83	15.4	6	0.34	14.15	6	8.9%	0.41 [-0.74, 1.55]
Subtotal (95% CI)			**6**			**6**	**8.9%**	**0.41 [-0.74, 1.55]**
BDAE naming subtest								
Seniow J 2013	34.7	30.68	19	20.7	33.36	19	28.4%	0.43 [-0.22, 1.07]
Subtotal (95% CI)			**19**			**19**	**28.4%**	**0.43 [-0.22, 1.07]**
CPNT accuracy of naming								
Waldowski K 2012	2.15	2.58	13	2.16	3.46	13	20.0%	-0.00 [-0.77, 0.77]
Subtotal (95% CI)			**13**			**13**	**20.0%**	**-0.00 [-0.77, 0.77]**
Total (95% CI)			**72**			**67**	**100.0%**	**0.52 [0.18, 0.87]**

Heterogeneity: $Chi^2 = 4.28$, df = 5 (P = 0.51); $I^2 = 0\%$
Test for overall effect: Z = 2.99 (P = 0.003)
Test for subgroup differences: $Chi^2 = 3.48$, df = 3 (P = 0.32), $I^2 = 13.9\%$

Std. Mean Difference IV, Fixed, 95% CI

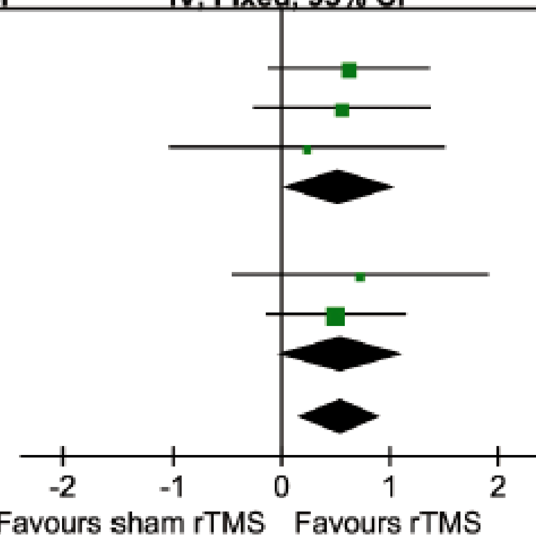


Ren et al., 2014

TMS Effect on Repetition and Writing

A

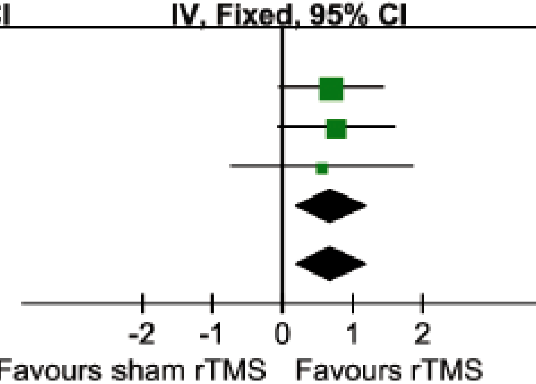
	Real rTMS			Sham rTMS				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
ATT repetition subtest									
Heiss WD 2013	3.5	3.44	15	1.3	3.43	14	25.6%	0.62 [-0.13, 1.37]	
Thiel A 2013	3.11	3.56	13	1.11	3.33	11	21.2%	0.56 [-0.26, 1.38]	
Weiduschat N 2011	15.67	27.24	6	10	4.16	4	8.8%	0.24 [-1.04, 1.51]	
Subtotal (95% CI)			**34**			**29**	**55.6%**	**0.54 [0.03, 1.04]**	
BDAE repetition subtest									
Barwood CHS 2013	1.84	2.45	6	0	2.22	6	10.2%	0.73 [-0.46, 1.91]	
Seniow J 2013	4.8	4.22	19	2.4	5.15	19	34.2%	0.50 [-0.15, 1.15]	
Subtotal (95% CI)			**25**			**25**	**44.4%**	**0.55 [-0.02, 1.12]**	
Total (95% CI)			**59**			**54**	**100.0%**	**0.54 [0.16, 0.92]**	



Heterogeneity: Chi² = 0.38, df = 4 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.81 (P = 0.005)
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.97), I² = 0%

B

	Real rTMS			Sham rTMS				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
ATT writing subtest									
Heiss WD 2013	4.7	4.35	15	2.1	2.65	14	46.7%	0.70 [-0.06, 1.45]	
Thiel A 2013	4.94	4.44	13	1.94	2.78	11	37.8%	0.77 [-0.07, 1.60]	
Weiduschat N 2011	13.17	11.02	6	6.5	9.98	4	15.6%	0.57 [-0.74, 1.87]	
Subtotal (95% CI)			**34**			**29**	**100.0%**	**0.70 [0.19, 1.22]**	
Total (95% CI)			**34**			**29**	**100.0%**	**0.70 [0.19, 1.22]**	



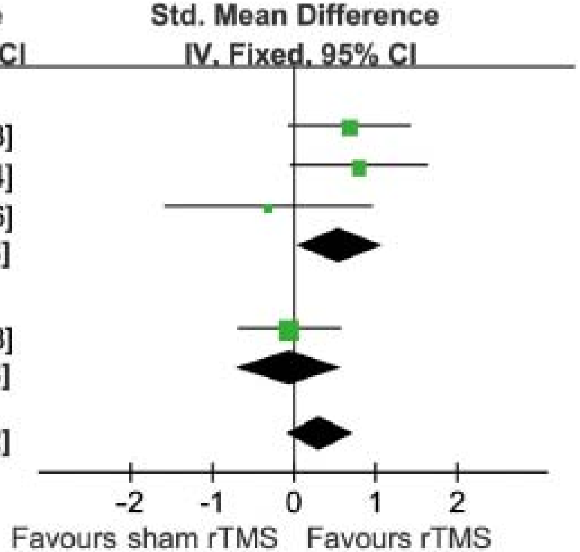
Heterogeneity: Chi² = 0.07, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.68 (P = 0.007)

Ren et al., 2014

TMS Effect on Comprehension

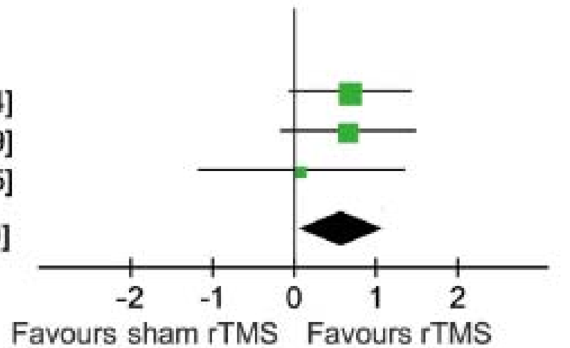
Study or Subgroup	Real rTMS Mean	Real rTMS SD	Real rTMS Total	Sham rTMS Mean	Sham rTMS SD	Sham rTMS Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AAT comprehension subtest								
Heiss WD 2013	4.4	3.7	15	1.8	3.72	14	28.2%	0.68 [-0.07, 1.43]
Thiel A 2013	4.45	3.33	13	1.66	3.44	11	22.6%	0.80 [-0.04, 1.64]
Weiduschat N 2011	10.17	11.37	6	15.5	20.34	4	9.8%	-0.31 [-1.59, 0.96]
Subtotal (95% CI)			**34**			**29**	**60.6%**	**0.56 [0.05, 1.08]**
BDAE comprehension subtest								
Seniow J 2013	19.4	20.44	19	20.6	19.81	19	39.4%	-0.06 [-0.69, 0.58]
Subtotal (95% CI)			**19**			**19**	**39.4%**	**-0.06 [-0.69, 0.58]**
Total (95% CI)			**53**			**48**	**100.0%**	**0.32 [-0.08, 0.72]**

Heterogeneity: $Chi^2 = 4.43$, df = 3 (P = 0.22); $I^2 = 32\%$
Test for overall effect: Z = 1.56 (P = 0.12)
Test for subgroup differences: $Chi^2 = 2.23$, df = 1 (P = 0.14), $I^2 = 55.1\%$



Study or Subgroup	Real rTMS Mean	Real rTMS SD	Real rTMS Total	Sham rTMS Mean	Sham rTMS SD	Sham rTMS Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Token test								
Heiss WD 2013	3.7	3.7	15	1.1	3.67	14	45.9%	0.69 [-0.07, 1.44]
Thiel A 2013	3.61	3.61	13	1.11	3.72	11	37.9%	0.66 [-0.17, 1.49]
Weiduschat N 2011	3.66	5.2	6	3.25	2.36	4	16.2%	0.08 [-1.18, 1.35]
Total (95% CI)			**34**			**29**	**100.0%**	**0.58 [0.07, 1.09]**

Heterogeneity: $Chi^2 = 0.70$, df = 2 (P = 0.71); $I^2 = 0\%$
Test for overall effect: Z = 2.22 (P = 0.03)
Test for subgroup differences: Not applicable



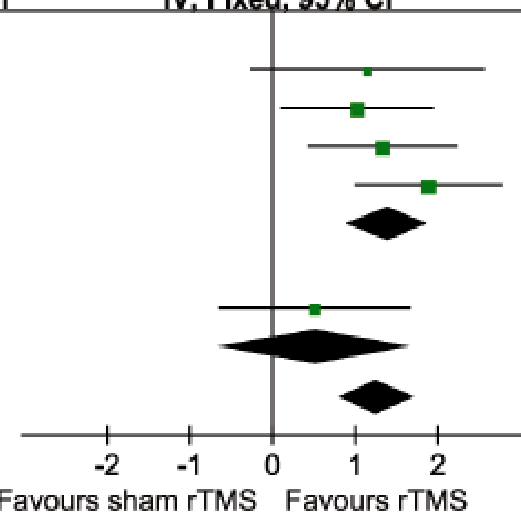
Ren et al., 2014

TMS Effect on Overall Severity

	Real rTMS			Sham rTMS				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
The global ATT score								
Weiduschat N 2011	19.83	8.2	6	8.5	9.95	4	10.1%	1.15 [-0.27, 2.57]
Hartmann A 2013	22.8	12.36	11	9.4	12.79	10	24.0%	1.02 [0.10, 1.95]
Thiel A 2013	23.6	12.15	13	7.55	11	11	25.1%	1.33 [0.43, 2.23]
Heiss WD 2013	22.4	1.77	15	8.6	10.06	14	25.4%	1.89 [0.99, 2.79]
Subtotal (95% CI)			**45**			**39**	**84.8%**	**1.39 [0.90, 1.88]**
The global BDAE score								
Barwood CHS 2013	18.5	36.68	6	0.17	28.73	6	15.2%	0.51 [-0.65, 1.67]
Subtotal (95% CI)			**6**			**6**	**15.2%**	**0.51 [-0.65, 1.67]**
Total (95% CI)			**51**			**45**	**100.0%**	**1.26 [0.80, 1.71]**

Heterogeneity: Chi² = 3.79, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 5.44 (P < 0.00001)
Test for subgroup differences: Chi² = 1.86, df = 1 (P = 0.17), I² = 46.3%

Std. Mean Difference
IV, Fixed, 95% CI

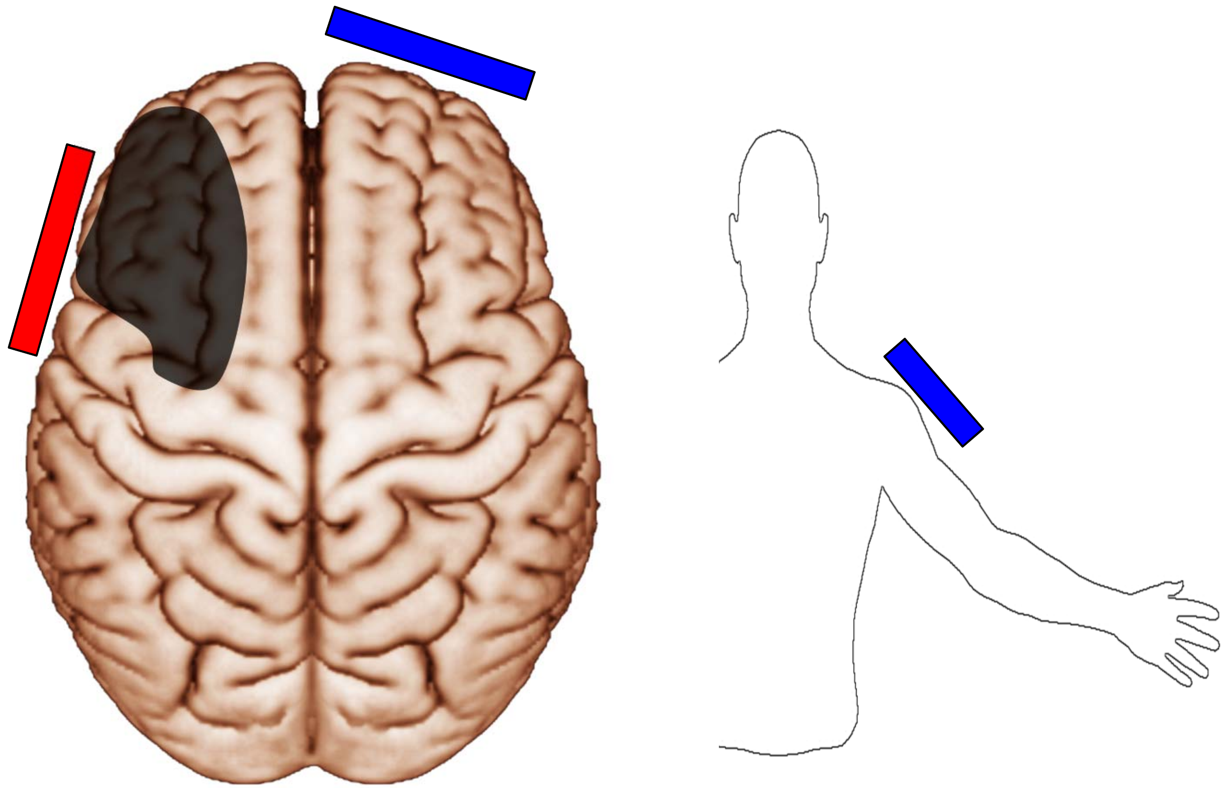


Ren et al., 2014

Limitations of TMS data

- Insufficient evidence for functional communication (i.e., measures of daily life communication)
- Mechanism of effect of right IFG inhibition is unclear

tDCS approaches
Left inferior frontal anodal stimulation

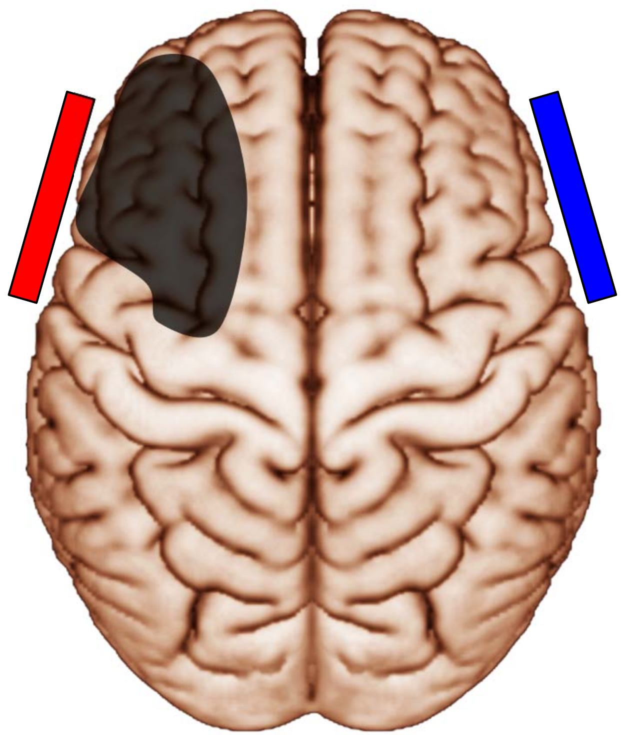


= anode (excitation)

= cathode (inhibition?)

tDCS approaches

Bi-frontal or left lateralizing frontal



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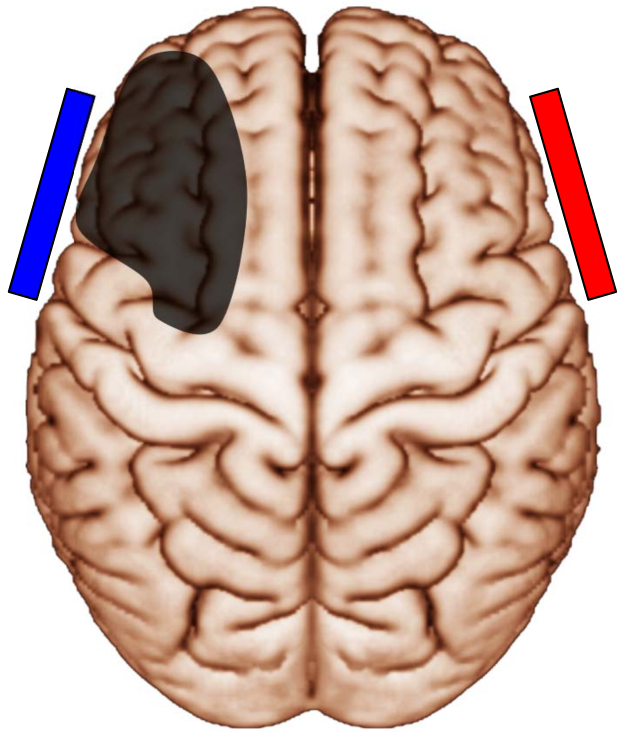
tDCS approaches
Bi-frontal or right lateralizing frontal



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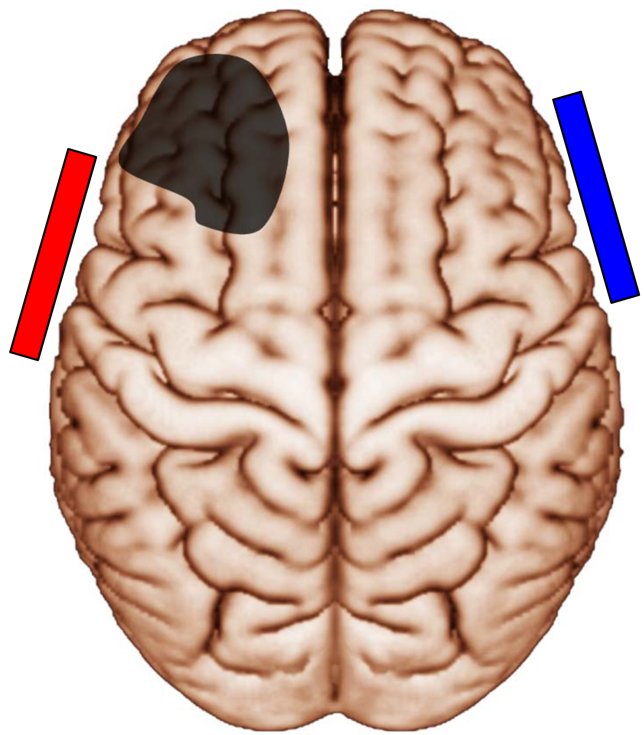
= cathode (inhibition?)

tDCS approaches
Individually targeted



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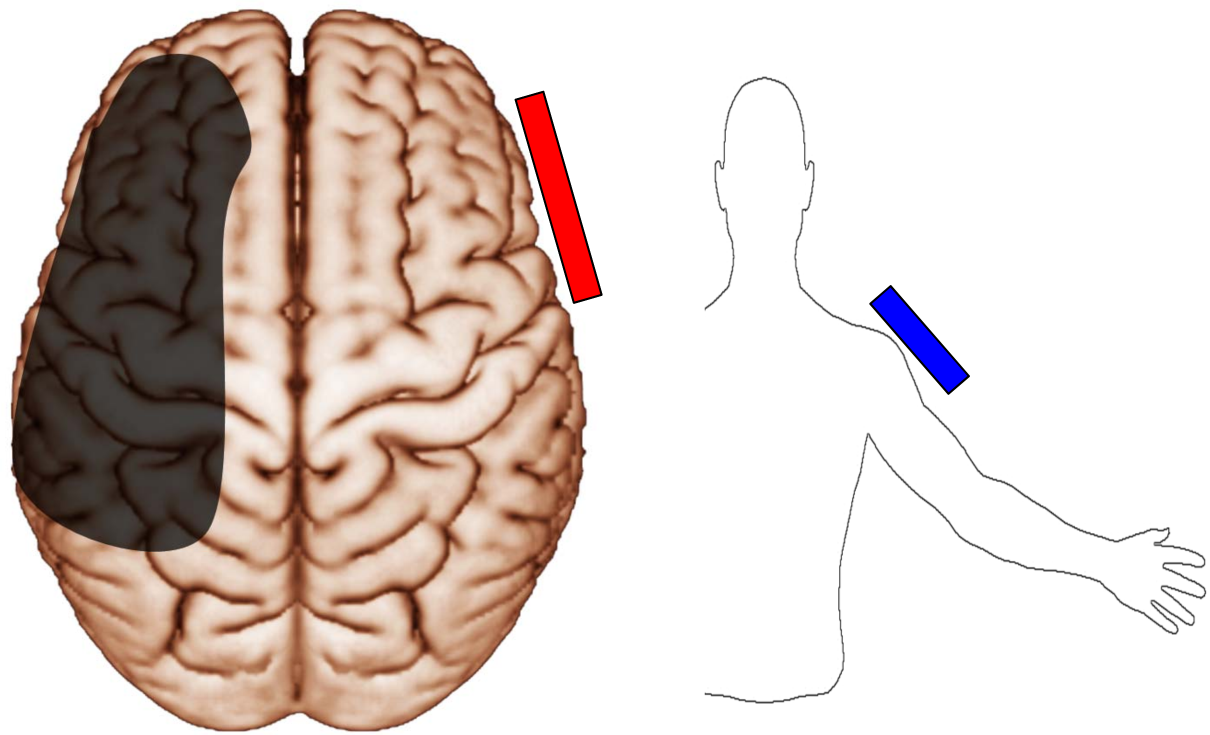
tDCS approaches
Individually targeted



= anode (excitation)

= cathode (inhibition?)

Lots of small studies

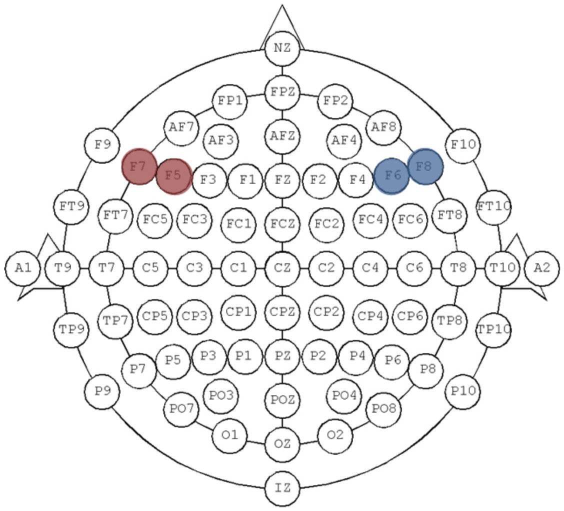
Table 1 (*continued*)

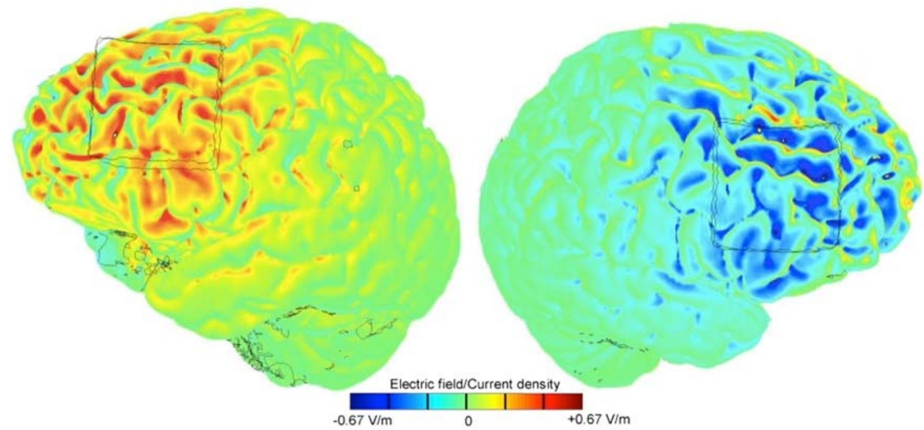
Articles	Number and type of patients	Target	Control condition	Stimulation polarity and intensity	Duration and number of sessions	Results
Polanowska et al. [25]	24 (post-acute stroke/non-fluent aphasics: 2–24 weeks after stroke)	LIFG	sham	Anodal 1 mA	10 min, 15 sessions (followed by 45 min of picture naming task)	Improvement in naming accuracy and naming response time in both groups (A-tDCS and Sham).
Polanowska et al. [26]	37 (post-acute stroke/non-fluent aphasics: 2–24 weeks after stroke)	LIFG	sham	Anodal 1 mA	10 min, 15 sessions (followed by 45 min of picture naming task)	Improvement in the BDAE in both groups (A-tDCS and Sham) both at post-treatment and at 3 months follow-up.
Marangolo et al. [20]	12 (chronic stroke/non-fluent aphasics: 5–84 months after stroke)	LIFG Left Wernicke's area	sham	Anodal, 1 mA	20 min, 10 sessions (during conversational therapy)	Improvement in content units, verbs and sentences production after tDCS over LIFG at post- treatment and at 1 month follow-up.
Marangolo et al. [21]	12 (chronic stroke/non-fluent aphasics: 6–74 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG	sham	Anodal and Cathodal, 2 mA	20 min, 10 sessions (during repetition task)	Improvement in repetition accuracy and response time for syllables, words and sentences (on trained and untrained stimuli) after bihemispheric tDCS at post-treatment and at 1 week follow-up.
Marangolo et al. [22]	8 (chronic stroke/non-fluent aphasics: 12–84 months after stroke)	LIFG Left Wernicke's area	sham	Anodal, 1 mA	20 min, 5 sessions (during verb naming)	Improvement in verb naming after A- tDCS over the LIFG at post-treatment and at 1 month follow-up.
Lee et al. [48]	11 (chronic stroke/6 non-fluent and 5 fluent aphasics: 8–180 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG Single tDCS, LIFG	no no	Anodal and Cathodal, 2 mA Anodal, 2 mA	30 min, 1 session (during picture naming task)	Improvement in naming response time in the BNT after bihemispheric tDCS, no significant improvement after single tDCS. Improvement in naming accuracy after bihemispheric and single tDCS. No follow-up
Fiori et al. [17]	7 (chronic stroke/non-fluent aphasics: 9–84 months after stroke)	LIFG, Left Wernicke's area	sham	Anodal, 1 mA	20 min, 5 sessions (during noun and verb naming)	Improvement in noun naming after A-tDCS over left Wernicke's and in verb naming after A-tDCS over LIFG at post-treatment and at 1 and 4 weeks follow-up.
Cherney et al. [30]	1 (chronic stroke/non-fluent aphasic: 204 months after stroke)	Right Wernicke area	no	Cathodal, 1 mA	13 min, 30 sessions (during SLT)	Improvement in WAB AQ and in auditory comprehension at post- treatment.
You et al. [37]	21 (post-acute stroke/non-fluent aphasics: 16–38 days after stroke)	Left or right Wernicke's area	sham	Anodal over left Wernicke's area or cathodal right Wernicke's area, 2 mA	30 min, 10 sessions (during SLT)	Improvement in auditory verbal comprehension after C-tDCS at post-treatment. No follow-up.
Vines et al. [39]	6 (chronic stroke/non-fluent aphasics: 15–120 months after stroke)	RIFG	sham	Anodal, 1.2 mA	20 min, 3 sessions (during MIT)	Improvement in verbal fluency after A-tDCS at post-treatment. No follow-up
Marangolo et al. [58]	3 (chronic stroke/non-fluent aphasics: 7–48 months after stroke)	LIFG	sham	Anodal, 1 mA	20 min, 5 sessions (during repetition task)	Improvement in syllables and words repetition after A- tDCS at post-treatment and at 2 months follow-up Improvement in different language subtests.
Jung et al. [38]	37 (post-acute/chronic stroke: average 221 days after stroke)	RIFG	no	Cathodal, 1 mA	30 min, 10 sessions (during SLT)	Improvement in the WAB AQ. No follow-up.
Kang et al. [36]	10 (chronic stroke/8 non-fluent and 2 fluent aphasics: 6 − 181 months after stroke)	RIFG	sham	Cathodal, 2 mA	20 min, 5 session (during word-retrieval training)	Improvement in naming accuracy in the BNT at 1 h following the last C-tDCS session, no changes after sham. No follow-up.
Fridriksson et al. [18]	8 (chronic stroke/fluent aphasics: 10–150 months after stroke)	Left posterior cortex	sham	Anodal, 1 mA	20 min, 5 sessions (during picture naming)	Improvement in naming accuracy after A-tDCS at post-treatment and at 3 weeks follow-up.
Floel et al. [67]	12 (chronic stroke/9 non-fluent aphasics and 3 fluent aphasics: 14–260 months after stroke)	Right temporo-parietal cortex	sham	Anodal, Cathodal, 1 mA	20 min, 3 sessions (2 × 1 h/day of computer-assisted naming)	Improvement in naming accuracy after A-tDCS at post-treatment and at 2 weeks follow-up.
Fiori et al. [16]	3 (chronic stroke/non-fluent aphasics: 21–71 months after stroke)	Left Wernicke's area	sham	Anodal, 1 mA	20 min, 5 sessions (during SLT)	Improvement in naming accuracy and response time after A-tDCS at post-treatment and at 3 weeks follow-up.

(*continued on next page*)

Marangolo, 2017

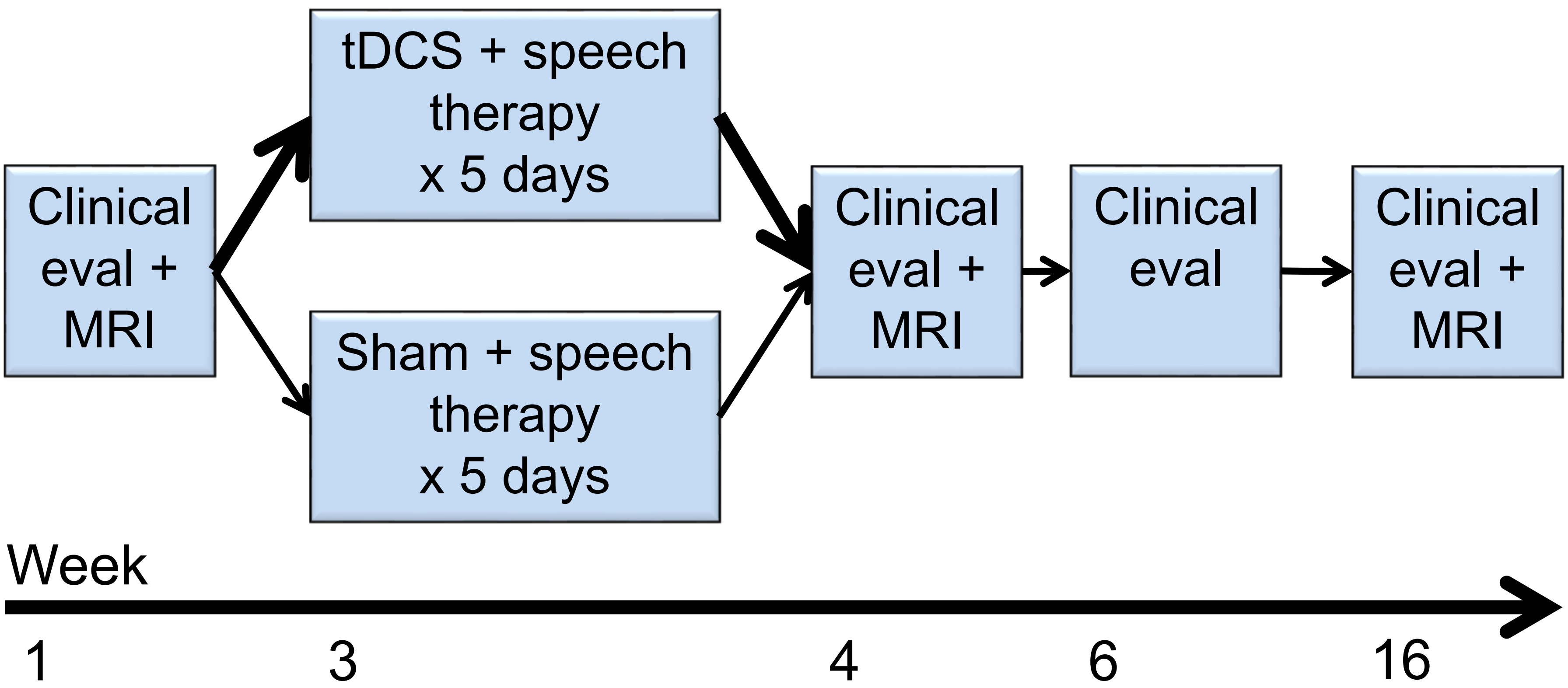
tDCS trial in chronic aphasia





- Phase II randomized double-blind sham-controlled trial
  - Real vs. sham tDCS (2:1) with speech therapy
  - > 6 months post-stroke (broad inclusion)
  - Funded by Doris Duke Charitable Foundation and the National Center for Advancing Translational Sciences via the GHUCCTS

Study Design



Prespecified Primary Outcome Measure = WAB Naming and Word Finding

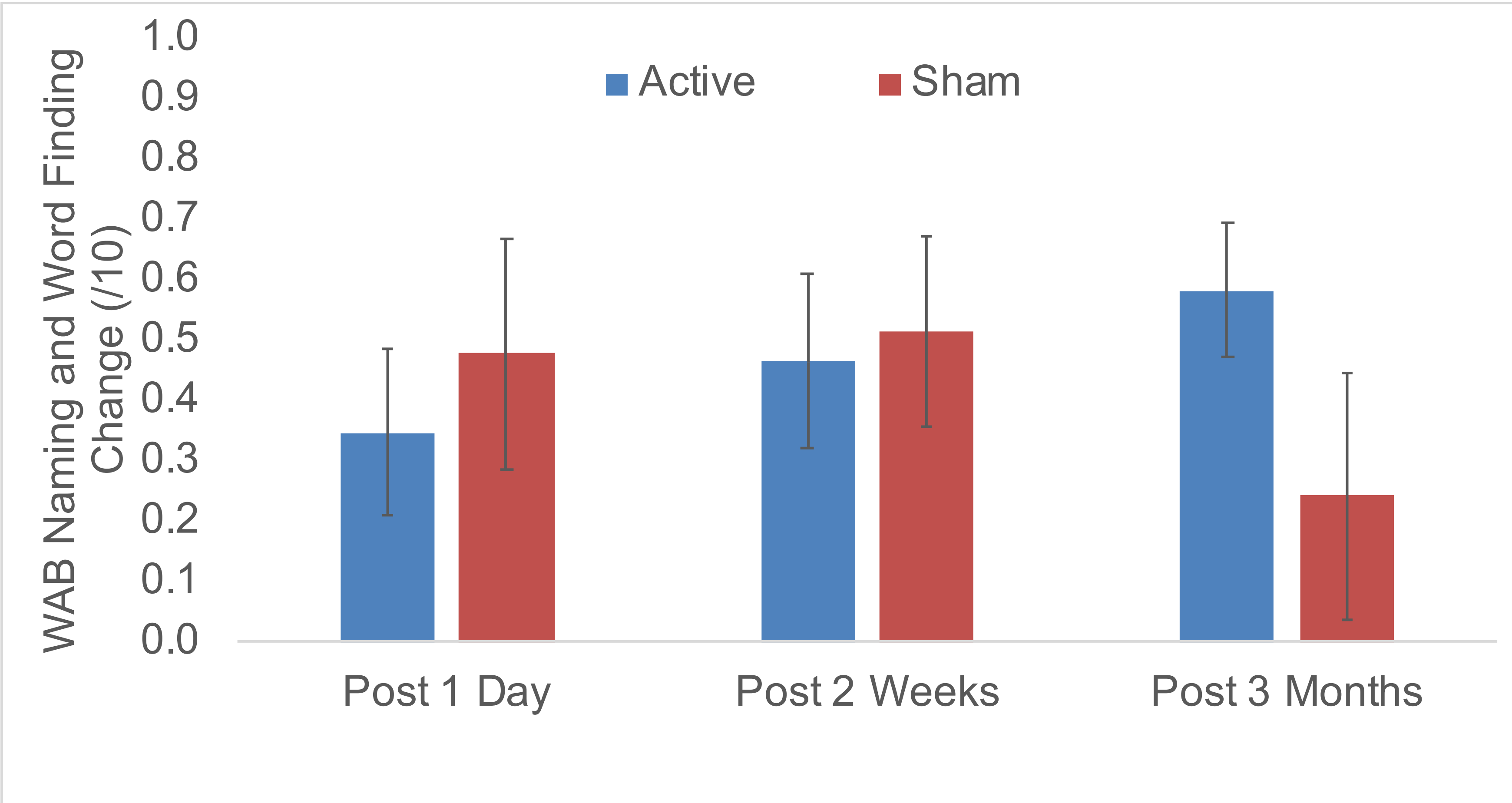
Participants

	Active tDCS (N=24)	Sham tDCS (N=14)	Diff
Age (yrs)	60.2 (10.9)	60.1 (8.6)	P=.97
Sex	16M, 8 F	9M, 5F	P>.99
Time since Stroke (mo)	55.1 (44.0)	44 (26.9)	P=.51
WAB AQ (/100)	66.3 (21.1)	65.1 (26.8)	P=.88
WAB N&WF (/10)	6.1 (2.9)	6.1 (3.0)	P=.99
PNT (%)	53.6 (29.9)	53.6 (39.2)	P>.99
Written PNT (%)	21.8 (16.25)	25.5 (21.7)	P=.57

Also matched on lesion size, apraxia, education

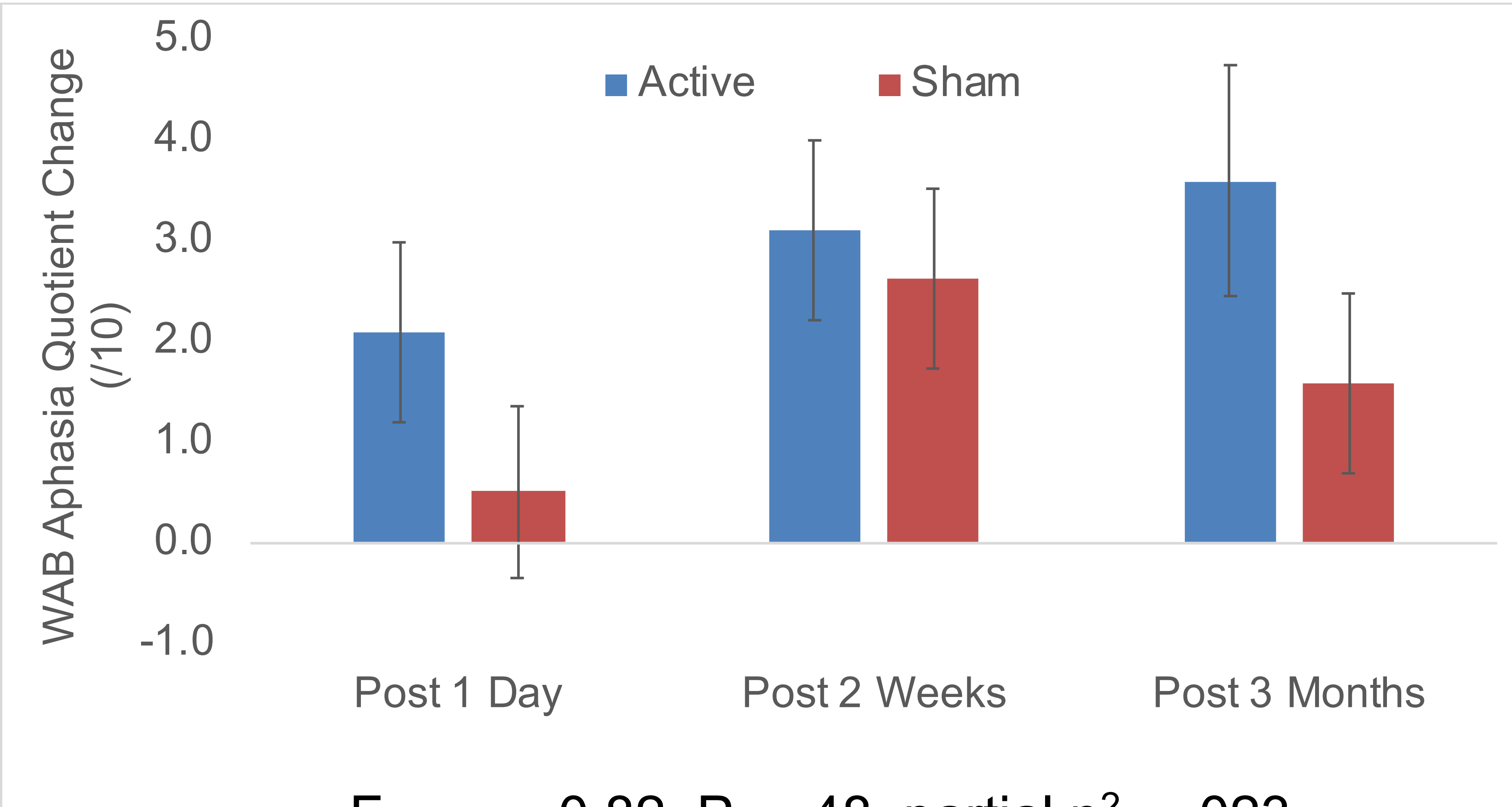
No serious Adverse Events
1 drop out (active tDCS, unclear reason, came to 2 week follow up only)

WAB Naming and Word Finding



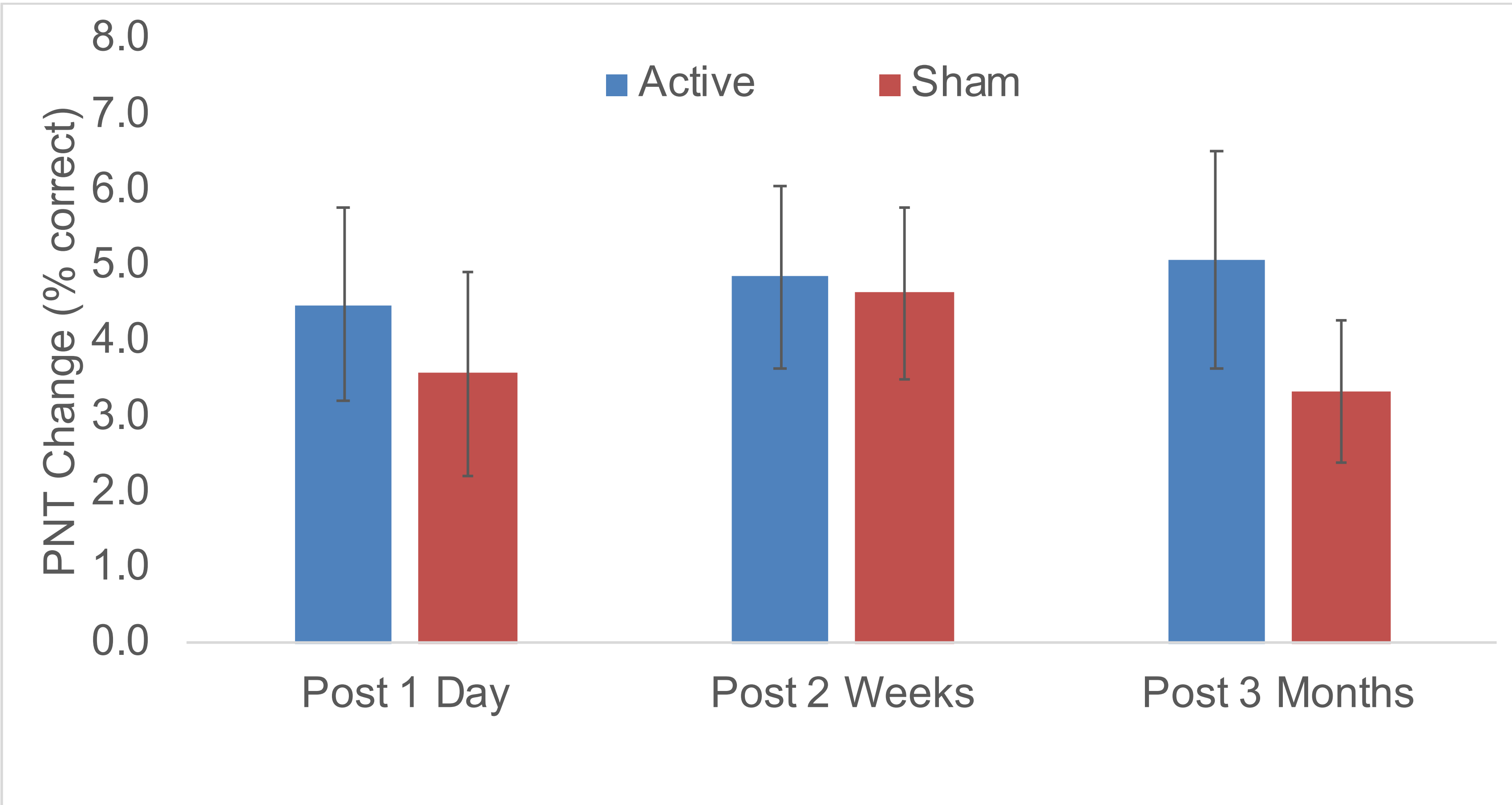
$F_{(3,105)} = 1.78$, $P = .16$, partial $\eta^2 = .048$

WAB Aphasia Quotient



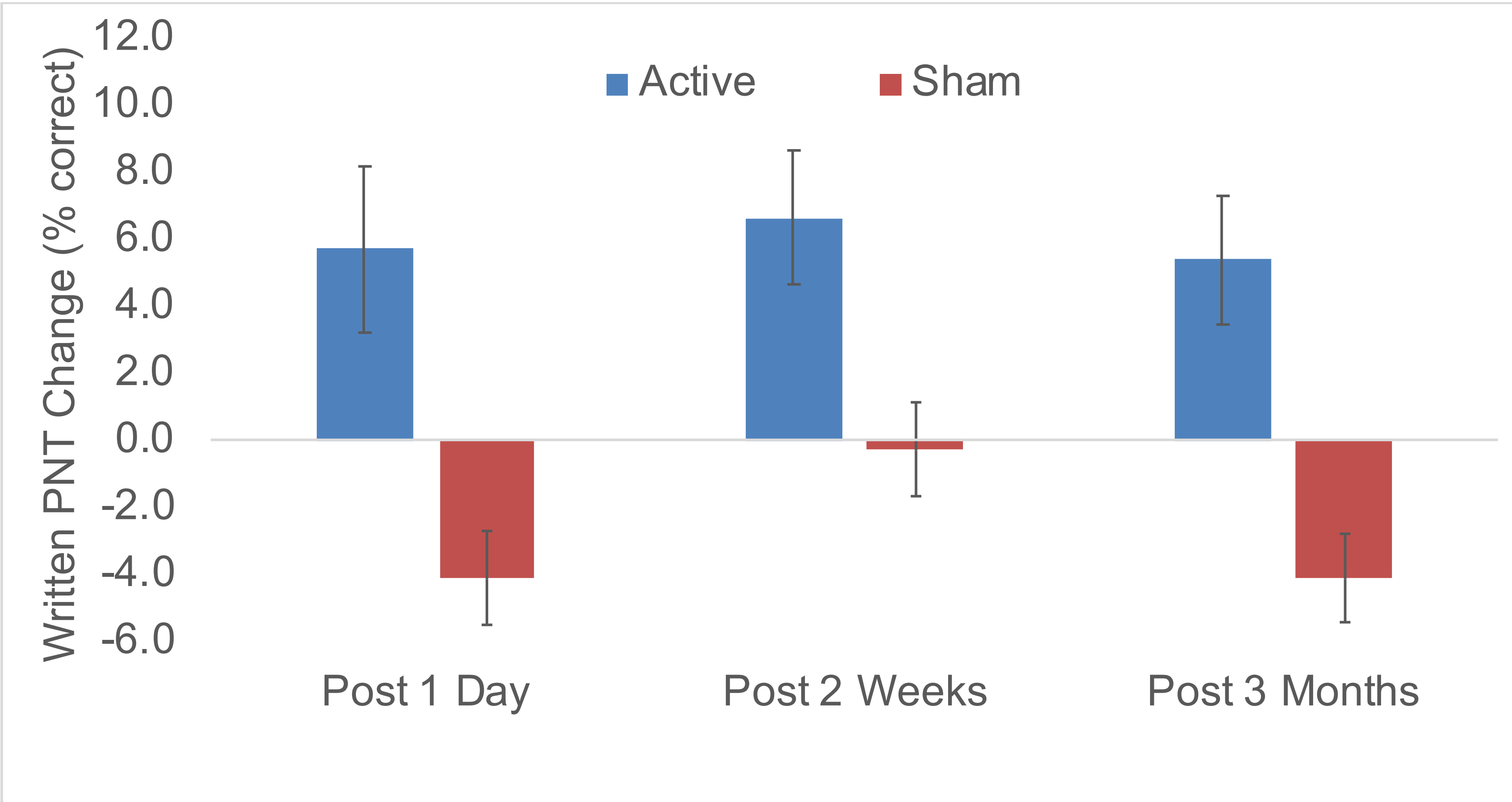
$F_{(3,105)} = 0.82$, $P = .48$, partial $\eta^2 = .023$

Spoken Naming



$F_{(3,105)} = 0.28$, $P = .84$, partial $\eta^2 = .008$

Written Naming



N=34, $F_{(3,96)} = 4.68$, $P = .004$, partial $\eta^2 = .128$

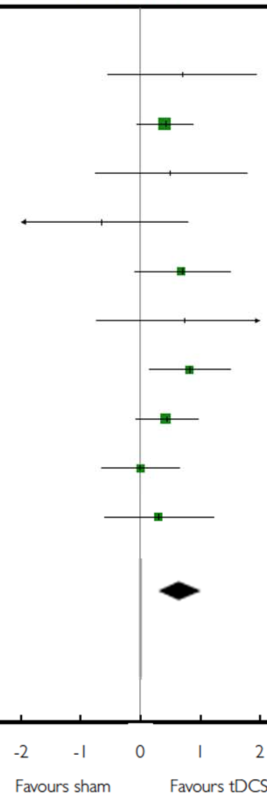
tDCS Effect on Noun Naming Post-tDCS

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Fiori 2013 (1)	4	8.8 (5.7)	3	0 (0)			Not estimable
Flöel 2011 (2)	8	90.1 (10.1)	4	69.8 (46.7)		3.6 %	0.70 [-0.55, 1.94]
Fridriksson 2018 (3)	34	13.9 (14)	40	8.2 (13.8)		26.4 %	0.41 [-0.06, 0.87]
Kang 2011 (4)	5	3.8 (5.8)	5	1.4 (1.9)		3.5 %	0.50 [-0.77, 1.77]
Marangolo 2013b (5)	4	7.5 (17.4)	4	20 (15.6)		2.6 %	-0.66 [-2.12, 0.80]
Meinzer 2016 (6)	13	27.9 (14.9)	13	16.7 (16.4)		8.9 %	0.69 [-0.10, 1.49]
Monti 2008a (7)	4	1.33 (1.83)	4	0.13 (0.83)		2.6 %	0.73 [-0.74, 2.21]
Polanowska 2013 (8)	18	11.8 (6.16)	19	7.3 (4.55)		12.4 %	0.82 [0.14, 1.49]
Spielmann 2016 (9)	26	6.5 (3.78)	32	4.7 (4.37)		20.5 %	0.43 [-0.09, 0.96]
Turkeltaub 2017 (10)	23	2.8 (5.48)	14	2.8 (20.48)		12.8 %	0.0 [-0.66, 0.66]
You 2011 (11)	14	9.1 (12.3)	7	5.4 (10.3)		6.8 %	0.30 [-0.61, 1.22]
Total (95% CI)	**153**		**145**			**100.0 %**	**0.42 [0.19, 0.66]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.86$, df = 9 (P = 0.75); $I^2 = 0.0\%$

Test for overall effect: Z = 3.49 (P = 0.00048)

Test for subgroup differences: Not applicable



Elsner et al., 2019

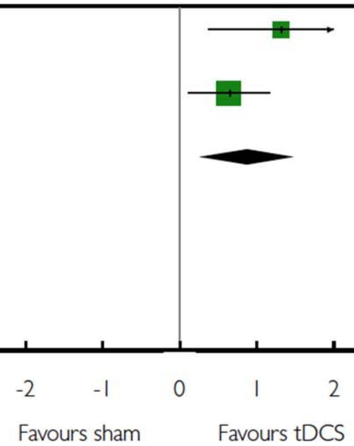
tDCS Effect on Noun Naming at Follow-Up

Study or subgroup	tDCS N	tDCS Mean(SD)	Sham N	Sham Mean(SD)	Weight	Std. Mean Difference IV,Random,95% CI
Meinzer 2016 (1)	11	24.3 (11.6)	11	8.7 (11.2)	32.4 %	1.32 [0.38, 2.26]
Spielmann 2016 (2)	26	12.5 (3.78)	32	10.6 (1.88)	67.6 %	0.65 [0.12, 1.18]
Total (95% CI)	**37**		**43**		**100.0 %**	**0.87 [0.25, 1.48]**

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 1.47$, df = 1 (P = 0.23); $I^2 = 32\%$

Test for overall effect: Z = 2.77 (P = 0.0056)

Test for subgroup differences: Not applicable



Elsner et al., 2019

Other notes from the meta-analysis

- Moderate quality of evidence for naming
- No effect on functional communication
- No significant effect of stimulation site/polarity
- No significant effect of aphasia type
- Analysis of naming at follow-up did not include several papers for unclear reasons
- “Current evidence does not support the routine use of tDCS for aphasia after stroke.”

Elsner et al., 2019

Summary of Findings

- Negative trial
- Small to medium effects
  - Not clinically significant
- Largest effect was on written naming
- Variance in treatment group suggests individual differences

Recent positive developments

- Increasing sample sizes
  - Meinzer et al., 2016 (n=26)
  - Polanowska et al., 2013 (n=37)
  - Fridriksson et al., 2018 (n>60)
  - Turkeltaub et al., forthcoming (n=38)
  - Hillis, Tsapkini, Sebastian, in progress
- Multi-site RCTs
  - NORTHSTAR, completed enrollment (?)
  - TEASER, in progress (planned n = 58)
- Brain imaging pre and post

Needed areas of investigation for tDCS and rTMS

- Larger multi-site studies
- Systematic parameter exploration
  - Electrode placement
  - Polarity and intensity
  - Length of treatment
  - Timing (after stroke and in relation to therapy)
  - Stimulation- Therapy pairings
  - → individualized treatment approach
- Brain imaging measures to understand biological mechanisms of effect
- Clinically meaningful outcome measures

Conclusions

- rTMS and tDCS are both promising
- Both appear to be safe
- Efficacy not clearly established yet
- More research needed
  - Understanding brain basis of aphasia recovery
  - Understanding mechanisms of effect
  - Optimizing treatment protocols
  - Test for clinically meaningful effects

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