Using non-invasive brain stimulation in the treatment of chronic post-stroke aphasia: a preliminary analysis of TMS as a supplement to constraint-induced language therapy

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Background

- Aphasia, an acquired loss of language abilities, affects nearly 30% of individuals with strokes and nearly 1 million Americans (see NINDS.NIG.gov)
- Non-invasive brain stimulation to the right inferior frontal gyrus (IFG) has been used as a supplementary tool to speech language therapy with lasting and enhanced benefits in language-based tasks (Martin et al., 2004, Naeser et al., 2005, Nissim et al. 2020)
- The efficacy of TMS remains unclear due to the lack of large-scaled, controlled randomized clinical trials
- This research reports preliminary findings from a randomized clinical trial assessing the efficacy of TMS as a supplement to CILT

Aims

- Demonstrate that Transcranial Magnetic Stimulation (TMS) paired with Constraint Induced Language Therapy (CILT) will improve language performance more than sham TMS and CILT

Methods

- Double-blind, randomized in a 2:1 ratio to TMS with CILT or sham TMS with CILT
- One Hz TMS at 90% motor threshold delivered to the right IFG for 20 minutes in 10 sessions over 2 weeks; CILT language therapy will be provided for 60-90 minutes after each TMS session
- Change (>5) from baseline in the Western Aphasia Battery Aphasia Quotient (WAB-AQ) at 3- and 6-months post-treatment will serve as the primary outcome measure

Screening Visit	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Treatment 1-10	Follow-up 1	Follow-up 2 & 3	Follow-up 4, 5, 6
Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6-16	Visit 17	Visit 18-19	Visit 20-22
-Informed Consent -Inclusion/Exclusion Criteria -Demographics History -Medical History -Medical Intake -Geriatric Depression Scale	-WAB -PNT -Pyramids and Palm Trees -Communication Confidence Scale -CILT baseline	-WAB -Ruff Figural Fluency Test -Word and non-word repetition -Cinderella Story -CILT baseline	-Leftover Testing -Baseline will continue into 4th and 5th visits if necessary	-MRI/CAT scan	Real or Sham TMS (20 min, 1hz at 90% MT) + CILT	-CILT probe	3-months: -same as Baseline 1 & 2	6-months: -same as Baseline 1 & 2 -MRI scan
120 minutes	120-180 minutes	120-180 minutes	60-180 minutes	120 minutes	90-120 minutes	60 minutes	120-180 minutes	120-180 minutes

Figure 1. Overview of study visit structure

Demographics & Study Criteria

Inclusion:
-Human subjects with a single left hemisphere cerebral infarct
-WAB-AQ scores between 85-20
-Suffered infarction >6mo prior to study
-Give informed consent

Exclusion:
-Multiple infarcts
-History of substance abuse
-Previous head trauma
-Psychiatric illness
-Chronic exposure to medications affecting CNS
-History suggestive of dementia

Subject ID	Sex	Age at Enrollment	Years of Education	Months Post-Stroke	Baseline WAB Aphasia Classification
1	Male	53	12	30	Broca's
2	Male	60	14	95	Anomic
3	Male	76	16	131	Wernicke's
4	Male	55	12	98	Broca's
5	Male	58	16	15	Conduction
6	Female	69	12	52	Broca's
7	Male	58	13	19	Global
8	Male	63	14	183	Broca's
9	Male	57	20	13	Conduction

Table 1. Demographic of Patients

Results

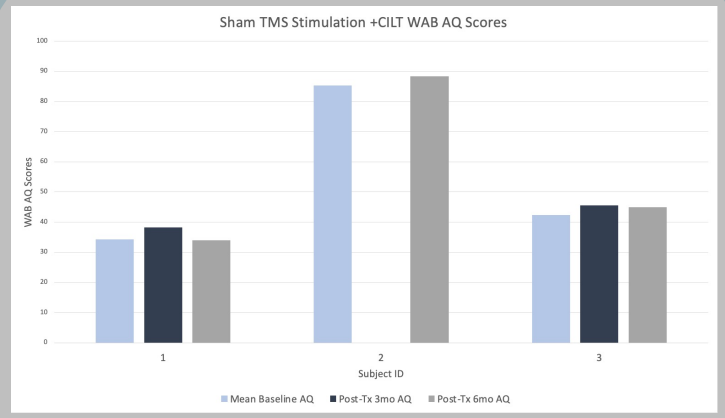

Figure 2. Bar graph showing WAB performance at baseline, 3-mo post-treatment, and 6-mo post-treatment for sham TMS+CILT group. * indicates a patient with significant improvement in performance (criterion: >5 increase). No individuals demonstrated significant aphasia improvement..

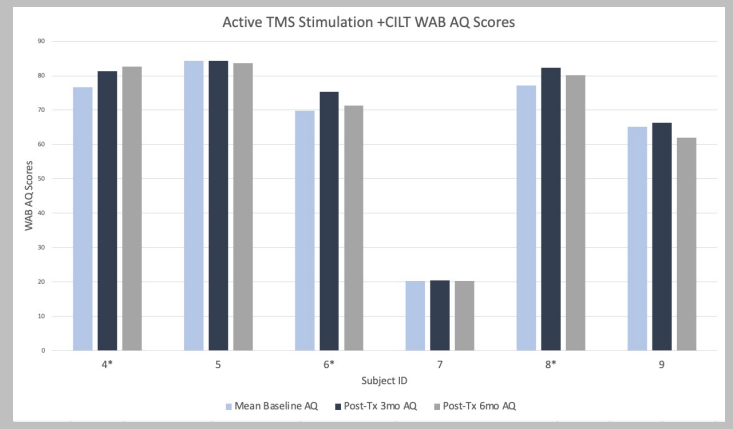

Figure 3. Bar graph showing WAB performance at baseline, 3-mo post-treatment, and 6-mo post-treatment for active TMS+CILT group. * indicates a patient with significant improvement in performance (criterion: >5 increase). Subjects 4, 6, and 8 demonstrated significant aphasia improvements.

WAB-AQ Sub-scores

Sham group WAB sub-scores				
Subject ID		Mean Baseline	3-month Follow-up	6-month Follow up
1	Spontaneous Speech	6	7	7
	Comprehension	4.975	5.55	4.6
	Repetition	2.35	2.4	2.1
	Naming	3.8	4.2	3.3
	AQ	34.25	38.3	34
2	Spontaneous Speech	15		15
	Comprehension	9.85		10
	Repetition	9		9.2
	Naming	8.85		10
	AQ	85.4		88.4
3	Spontaneous Speech	9	9	10
	Comprehension	4.7	5.9	4.8
	Repetition	1.2	1.4	1.8
	Naming	6.3	6.5	5.9
	AQ	42.4	45.6	45

Table 2. WAB AQ sub-scores for sham TMS+CILT group.

Active group WAB sub-scores				
Subject ID		Mean Baseline	3-month Follow-up	6-month Follow up
4	Spontaneous Speech	12	14	15
	Comprehension	9.6	9.8	9.7
	Repetition	7.8	8.1	7.8
	Naming	8.95	8.8	8.8
	AQ	76.7	81.4	82.6
5	Spontaneous Speech	19	19	19
	Comprehension	8.45	8.7	8.6
	Repetition	6.3	5.7	5.3
	Naming	8.4	8.8	8.9
	AQ	84.3	84.4	83.6
6	Spontaneous Speech	13	15	12
	Comprehension	8.7	9.1	9.05
	Repetition	5.3	6	6.7
	Naming	7.9	7.6	7.9
	AQ	69.8	75.4	71.3
7	Spontaneous Speech	3	3	3
	Comprehension	6.725	7.2	7.15
	Repetition	0.35	0	0
	Naming	0	0	0
	AQ	20.15	20.4	20.3
8	Spontaneous Speech	14.5	15	15
	Comprehension	9.85	10	9.5
	Repetition	5.5	7.7	6.9
	Naming	8.7	8.5	8.7
	AQ	77.1	82.4	80.2
9	Spontaneous Speech	14	15	14
	Comprehension	7.9	8.1	7.8
	Repetition	4.55	3.6	3.6
	Naming	6.15	6.5	5.6
	AQ	65.2	66.4	62

Table 3. WAB AQ sub-scores for active TMS+CILT group.

Analysis

- All individuals scored higher at the 3-mo post-treatment timepoint than their mean baseline scores
- In the sham TMS+CILT group, no individuals had a >5 increase in WAB-AQ scores, indicating a variable response to CILT alone
- Response to TMS was variable in the active TMS+CILT group, with 3 out of 6 active participants showing significant improvements in WAB-AQ scores
- Severity at baseline may be a factor determining response to TMS; individuals with moderate severity (baseline AQ's 60-80) seem to be more likely to respond compared to patients with more severe aphasia
- Patients with less severe aphasia may be less likely to respond because there is less "room" for improvement, characteristic of the "ceiling effect."

Conclusion

- Collectively, this data supports the efficacy of TMS as a supplemental tool to Constraint Induced Language Therapy in the treatment of chronic post-stroke aphasia
- A larger sample size is needed to conduct a more in-depth statistical analysis and explore the influence of factors such as age, infarct location, aphasia severity, and time since stroke onset.
- Future work will look at fMRI imaging and robust machine learning techniques to identify changes in the strengths of connections between nodes in the language network to address the effects of TMS and CILT on brain organization that are associated with beneficial response to treatment.

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