Evaluating the Efficacy of Transcranial Alternating Current Stimulation (tACS) combined with Speech Therapy for Cantonese-Speaking Individuals with Post-Stroke Aphasia: A Randomized Controlled Trial

YU Ka Yee, Tina

Faculty of Education, The University of Hong Kong

Supervised by

Professor Anthony Pak-Hin KONG

Mr. Chester Yee-Nok CHEUNG (PhD. Student)

Academic Unit of Human Communication, Learning, and Development
Faculty of Education, The University of Hong Kong

Abstract

Aphasia affects one-third of post-stroke patients, severely impacting their communication and quality of life. While speech therapy (ST) is the primary treatment, its effectiveness is limited, particularly when used alone. Recent research has been investigating the integration of Non-invasive brain stimulation (NIBS) into ST for better rehabilitation outcomes. However, many of them adopt a one-size-fits-all method, regardless of the variations in individual patient profiles or specific conditions. Transcranial alternating current stimulation (tACS), as one of the NIBS, is little if not none, being studied in Hong Kong, targeting Cantonese-speaking individuals. Therefore, this randomized controlled trial (RCT) investigates the effectiveness of combining tACS with intensive speech therapy for Cantonese-speaking individuals with post-stroke aphasia, comparing generalized, individualized, and sham stimulation protocols to identify the optimal strategy for diverse patient needs.

Ten participants were randomly assigned to one of three groups: Generalized-Connectomic tACS (GC), Individualized-Connectomic tACS (IC), or Sham stimulation (SH). Over a two-week intervention, participants underwent 10 sessions of ST combined with tACS, followed by pre- and post-treatment evaluations of language outcomes (Cantonese Aphasia Battery - Aphasia Quotient; discourse measures) and neurological changes (dysfunctome scores).

Findings revealed that all groups demonstrated improvements in language measures, with the IC group showing the most substantial gains in CAB scores ($BF_{10} = 15.34$). Neurological changes were inconclusive, though individualized protocols exhibited potential for network modulation. Despite limitations in sample size and patients' heterogeneity, this study provides preliminary evidence for the potential of tACS in aphasia rehabilitation. Future studies with larger sample sizes, more diverse participant groups, and refined methodologies are necessary to determine whether tACS improves language outcomes and if individualized protocols outperform generalized ones.

Table of Contents

1. Introduction

About one-third of all patients who suffer a stroke develop aphasia (Gronberg et al., 2020) worldwide. It most commonly occurs due to an occlusion in the middle cerebral artery (MCA) territory (Fridriksson et al., 2018), resulting in changes to functional brain connectivity and disrupting normal patterns of neural oscillations (Gobbo & Marini, 2025). Patients with aphasia (PWA) have a higher chance of in-hospital mortality, extended hospital stays, and increased disability lasting from 28 days up to 2 years (Flowers et al., 2016), affecting their quality of life. Speech therapy, as supported by multiple RCTs and meta-analyses of its effectiveness (Brady et al., 2016) is, however, usually not incorporated with modern tools for additional support.

Non-invasive brain stimulation (NIBS) refers to various tools designed to alter neural activity through the scalp. A systematic review by Williams et al. (2023) revealed the beneficial effects of using NIBs to facilitate the recovery of PWA, with Transcranial Direct Current Stimulation (tDCS) being the most frequently used technique, and over three-quarters of existing studies employed a uniform stimulation protocol for all participants. However, there are various subtypes of aphasia, such as Broca's aphasia and Wernicke's aphasia using the Boston Classification System, which may limit the therapy outcome due to the heterogeneity. This concern is confirmed by the review, which pointed out that several authors attributed the high levels of inter-individual response variability in their studies to the diverse characteristics of their participants. That is to say, a one-size-fits-all stimulation protocol may not elicit the greatest effects of application of NIBs.

Transcranial alternating current stimulation (tACS) is defined as the external application of oscillating electrical currents (Antal & Paulus, 2013). It is also a novel, non-invasive neuromodulation method that modulates brain oscillations (Yang et al., 2024). Findings on the effectiveness of tACS for poststroke patients are overall positive and promising. Yang et al. (2024) found that the use of tACS has been linked to enhanced overall functional recovery, improvements in sensorimotor impairment, aphasia, and hemispatial neglect. Specifically, a study found that the naming ability, verbal fluency, and overall language function in a PWA were improved by applying amplitude-modulated tACS between Broca's area and its right hemisphere counterpart, and the improvement was maintained for over a month (Omae et al., 2024).

However, as mentioned, there is a lack of research studied the effectiveness of individualized tACS compared with tDCS, plus a specific focus on the Cantonese-speaking population in Hong Kong. Therefore, the impact of tACS needs to be further examined to provide evidence on the suitability of utilising tACS as an aphasia treatment and to cope with the heterogeneity of PWA. Therefore, this research aims to evaluate the effectiveness of the tACS in improving communication skills for Cantonese-speaking PWA in Hong Kong. The research questions are:

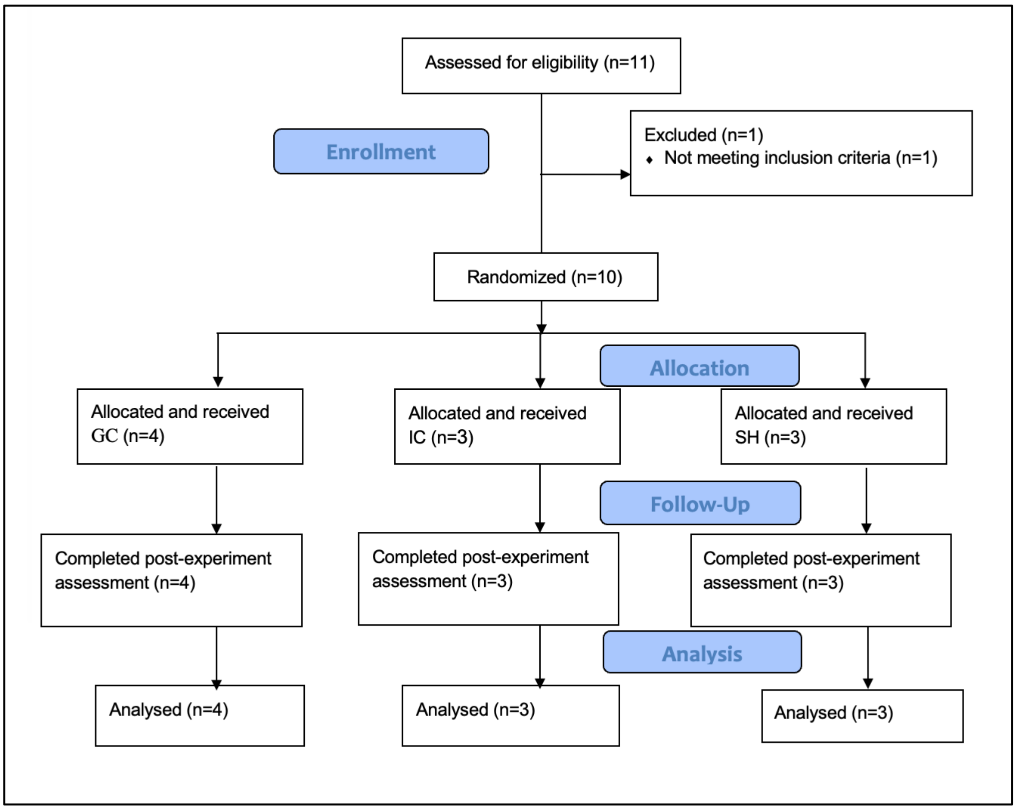
RQ1. Does tACS combined with speech therapy improve speech and language outcomes in PWA compared to speech therapy alone (sham condition)?

RQ2. How do individualized tACS protocols, tailored to dysfunctome profiles, compare to generalized tACS protocols in enhancing speech and language recovery in PWA?

2. Method

This study employed a randomized controlled trial (RCT) design with double-blinding procedures; neither the participants nor the 6 trained student clinicians knew which group the subjects belonged to. Group allocation was known exclusively to 2 researchers who were not involved in scoring the assessment.

FIGURE 1: CONSORT 2010 Flow Diagram



2.1 Participants

A total of 11 participants were recruited for this study during the summer of 2025. Inclusion criteria include (a) first-ever left-hemispheric stroke, (b) age 18-70 years old, (c) native in Cantonese, (d) at least 6 months after stroke onset, (e) right-handed (f) no contraindications for tACS, such as history of seizures, implanted medical devices (g) no history of developmental or acquired diseases affecting cognitive or language abilities. Exclusion criteria include (a) clinically not diagnosed as aphasia by the Cantonese Aphasia Battery (CAB; Yiu, 1992), (b) Global aphasia, and (c) severe comprehension or cognitive impairment hindering the ability to follow instructions. One participant was excluded because his baseline CAB score exceeded the diagnosis threshold.

TABLE 1: The characteristics of the 10 participants

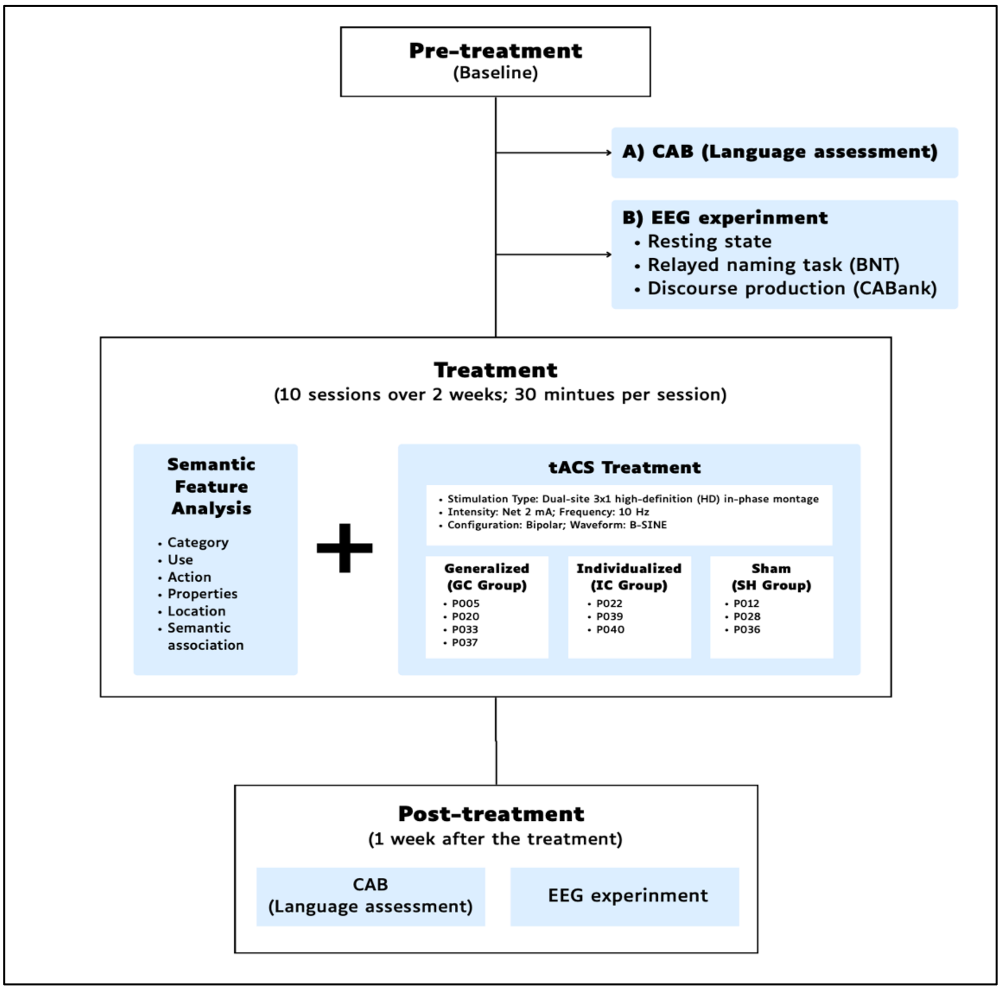
ID	Sex	Age	Education (years)	Post_onset (months)
P005	F	48	17	57
P012	F	63	11	39
P020	F	45	11	63
P022	M	33	16	25
P028	M	64	16	184
P033	F	64	6	17
P036	M	64	6	28
P037	M	58	13	16
P039	F	60	16	40
P040	M	59	16	13

2.2 Design and Procedure

Before the intervention began, 10 participants were randomly allocated into three groups: 4 received Generalized-Connectomic tACS (GC), 3 received Individualized-Connectomic tACS (IC), and 3 received Sham tACS (SH). The 6 student clinicians were all trained and learned how to use and score different tests.

The experiment has three phases: pretreatment, treatment, and posttreatment. Regarding the pretreatment phase, all participants underwent an electroencephalogram (EEG) assessment that included (a) a resting state, (b) a delayed naming task using items from Chinese adaptation of the Boston Naming Test (BNT; Cheung et al., 2004), and (c) a discourse production task using the Cantonese Aphasia Bank (CABank; Kong & Law, 2019) to measure brain activity and establish baseline neural profiles. Additionally, participants' speech and language abilities were evaluated using selected components of CAB, including spontaneous speech, auditory verbal comprehension, repetition, and naming. CAB's score is the primary measure of this study. During the treatment phase, the participants completed 10 days of intensive speech therapy sessions over 2 weeks, with each session lasting 30 minutes. Speech therapy was conducted simultaneously with tACS treatment. As for the post-treatment phase, all participants returned for follow-up assessment one week after completing the 10-day intervention protocol. This assessment mirrored the pretreatment evaluation, consisting of both an EEG recording and administration of the CAB to measure treatment-related changes in neural activity and language function. All 10 participants completed the pre-assessment, 10 intensive intervention sessions, and the post-assessment.

FIGURE 2: Flowchart of the treatment procedures



2.3 Electroencephalogram (EEG) scan

This study utilized PsychoPy to design and execute the experimental tasks. Curry 8 was used for EEG recording and processing.

2.3.1 Data acquisition

This study utilized the BrainVision actiCHamp amplifier paired with BrainVision actiCAP snap 64 electrodes, configured according to the international 10-20 EEG system. Two additional electrodes were placed over the left superior and inferior orbicularis oris muscles to record electromyographic signals associated with physiological movements during speech, using a bipolar surface electromyogram (EMG) setup. Before the EEG experiment, Easycap HiCl Electrolyte-Gel was applied to each channel for better electrode conductivity, and the impedances were kept below 33 kΩ. The whole EEG setup process was assisted by one researcher and one student clinician.

Once the setup was complete, EEG signals were recorded as the participant performed three tasks in the recording room. The presentation was manually controlled by a student clinician positioned next to the participant. The first resting state task consisted of a 2-minute eye-open scan, during which the participant was asked to relax and focus on a central point on a screen, followed by a 2-minute eye-closed wakefulness scan. Subsequently, the delayed naming task was administered, where the participant silently viewed an image for 4 seconds before a sound signal prompted them to name the object. They had up to 20 seconds to respond, and the next image was displayed only after the participant responded. This task consisted of a total of 30 trials (5 practice trials and 25 actual trials). Following this was the discourse production task, where participants were asked to describe the picture displayed on the screen. Each discourse prompt had a maximum duration of 3 minutes, with a total of 7 prompts: two single-picture descriptions, two sequential-picture descriptions, one procedural discourse, and two well-known narratives. The countdown began only after the participant had viewed the picture and indicated readiness.

As EEG signals typically range up to 100 Hz, the brain signals were recorded at a rate of 512 samples per second to avoid aliasing. Bandpass filtering with a range of 0.1-100 Hz was applied to reduce noise and remove artifacts.

2.3.2 Data processing

The collected EEG data were first imported into the EEGLAB toolbox (Delorme & Makeig, 2004) in MATLAB version 9.14 (The MathWorks Inc., 2022). Event markers, such as stimulus timings and channel locations, were then integrated into the dataset. Down-sampling was performed to reduce the sampling rate to 250 Hz to reduce computational load. The EEG signals underwent bandpass filtering with cut-off frequencies of 0.1–40 Hz to remove low-frequency drifts and high-frequency noise. Channels exhibiting excessive noise or artifacts were identified through visual inspection and corrected using spherical interpolation (Perrin et al., 1987).

Subsequently, Independent Component Analysis (ICA) was performed, followed by component classification using the ICLabel plugin in EEGLAB. Components labeled as "eye," "muscle," or "channel noise" with a probability greater than 50% and components showing higher-than-majority correlation with EMG signals recorded from lip muscles (Porcaro et al., 2015) were rejected. Cleaned EEG data was reconstructed into channel space, visually inspected to ensure signal quality, and converted to an average reference to minimize bias.

Afterwards, EEG signals were filtered into six frequency bands: Delta (1–4 Hz), Theta (4–7 Hz), Alpha (8–12 Hz), Low-Beta (15–20 Hz), High-Beta (21–30 Hz), Low-Gamma (31–40 Hz). Signals were segmented into 4-second intervals, and any segments exceeding ±50 µV were excluded.

Connectivity matrices were then constructed in sensor space, where each electrode was treated as a node and connections between electrodes formed edges. Phase Locking Value (PLV), calculated using in-house MATLAB routines, served as the connectivity measure. A 64 × 64 matrix was generated for each frequency band per individual.

2.4 Dysfunctome-based targeting

Each participant's dysfunctome was identified using EEG data collected during the delayed naming task in pre-intervention, as suggested by Cheung et al. (2025), that a naming task reliably engages language-related networks, and a "naming-predictive" dysfunctome may provide precise targets for stimulation. Their research has demonstrated that the network hubs in the dysfunctome positively correlate with naming performance.

For participants in the IC group, stimulation targets were tailored to their unique connectivity profiles. The edge with the highest priority was determined using two key metrics: (a) high connectivity strength, which identifies intact network hubs that are functionally important within the dysfunctome, and (b) high centrality metrics, which pinpoint edges that act as critical “bottlenecks” in the network structure (e.g., edges with high centrality). The two nodes connected by the chosen edge served as individualized stimulation targets for dual-site tACS.

For participants in the GC and SH groups, standardized stimulation targets were determined using only centrality metrics (b). Specifically, the two nodes connected by the edge with the highest centrality were selected as standardized stimulation targets. The location of the stimulating electrodes, as detailed in Table 2, corresponded to these target nodes.

2.5 Transcranial Alternating Current Stimulation (tACS)

Soterix Medical MxN-9 HD tES stimulator (Soterix Medical, New York, USA) was used to deliver the 30-minute tACS for each patient. The stimulation was delivered through circular Ag/AgCl electrodes with a radius of 1 cm and a conductivity of 5.99×10^7 S/m. A conductive gel was applied to maintain electrode impedance at or below 10 kΩ. This study employed a dual-site 3 x 1 HD electrode montage and a bipolar configuration with a B-SINE waveform, delivering a net intensity of 2 mA at a frequency of 10 Hz for 30 minutes. In detail, two simulating electrodes were positioned at target nodes to synchronize activity. Three return electrodes surrounded each stimulating electrode at the nearest channels. As required by the hardware system, one extra reference electrode was placed at Cz, remained inactive, and was away from the stimulation montage. Both stimulating electrodes are set to positive polarity for dual-site in-phase stimulation. Electrodes were positioned at P7 and FC4 for the generalized and control groups, while the individualized group received customized electrode placement based on participant-specific dysfunctome profiles (see Table 2).

During the experiment, participants in the generalized and individualized groups received real tACS, while those in the control group received sham tACS. Concerning the Sham

Stimulation Protocol, the stimulator was increased to 1 mA intensity for the first 30 seconds to mimic the sensation of stimulation and immediately reduced to a negligible intensity (e.g., 0.02 mA) for the remainder of the session. The ramp-up and ramp-down process was repeated during the last minute of the session. This is called the “fade-in, short-stimulation, fade-out” (FSF), which is effective for blinding participants (Ambrus et al., 2012).

TABLE 2: Location of the stimulating and returning electrodes in tACS

Group	**ID**	**Stimulating Electrodes** (+ polarity, 1 mA for each site)	**Surrounded Returning Electrodes** (– polarity, 0.33 mA for each site)	**Treatment Method**
Generalized (GC)	P005	P7 & FC4	P7: [PO7, CP5, TP9] FC4: [C4, F2, F6]	Real tACS
	P020			
	P033			
	P037			
Sham (SH)	P012			Sham tACS
	P028			
	P036			
Individualized (IC)	P022	P5 & FC4	P5: [PO3, CP3, TP7] FC4: [C4, F2, F6]	Real tACS
	P039	P7 & F4	P7: [PO7, CP5, TP9] F4: [FC4, AF4, F8]	
	P040	P5 & FC4	P5: [PO3, CP3, TP7] FC4: [C4, F2, F6]	

2.6 Speech Therapy

Semantic feature analysis (SFA) was the therapy technique used in this study. It is proven to consistently improve naming accuracy for trained items in people with aphasia, with positive effects observed across various study designs (Efstratiadou et al., 2018; Quique et al., 2019). This approach involves breaking down a target word into its semantic features, such as its appearance, function, and category, to assist individuals in retrieving the word from memory. Training items were carefully tailored to match the participant's skill level, and all picture stimuli were found from online picture banks.

FIGURE 3: Example of an SFA chart

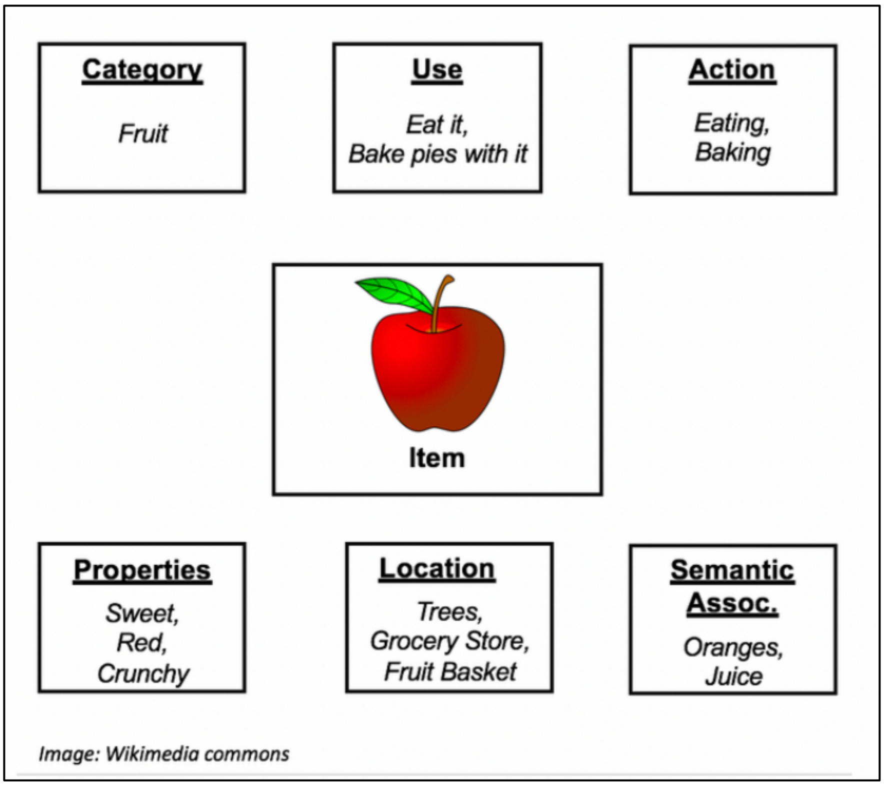


Image: Wikimedia commons

2.7 Outcome measures

A total of 7 measures were used in this study, collected at 2 time points (pre- and post-treatment). The primary measure, CAB scores, is reported as Aphasia Quotient (AQ), which is calculated using 5 sections in CAB: Spontaneous Speech (Information), Spontaneous Speech (Fluency), Comprehension, Repetition, and Naming. The cut-off for diagnosing aphasia is <96.4/100, with 8 types of aphasia that can be identified.

Participants' discourse production in CABank was assessed using the following measures: Information Content Units (ICU), ICUs per minute (ICU_min), Main Concepts (MC), and Accurate and Correct Main Concepts per Minute (AC_min). The "per minute" calculation is crucial for normalization and providing a more nuanced understanding of participants' improvements in processing abilities over time. The scores for these measures were manually derived by a single student clinician through the replay of participants' audio recordings.

In addition to these linguistic measures, neurological outcomes were evaluated using the dysfunctome, which represents the average weight of edges in the network. This measure offered insight into participants' brain connectivity and its relationship to their language recovery.

2.8 Statistical Data Analysis

Pre- and post-treatment comparisons between time and condition were conducted using Bayesian statistics in JASP (JASP Team, 2025 Version 0.95.1) to assess improvements in neurological and language outcome measures. Bayesian repeated measures ANOVA was first carried out to detect any time or time-condition interaction effects, and paired t-tests were then used to identify time effects across conditions. One-way ANOVA and post-hoc tests were performed for specific group comparisons.

3. Results

No unanticipated events occurred during the experiment. All except one participant (ID: P005) reported pain while receiving tACS.

A series of Bayesian model comparisons was first conducted to evaluate the effects of "Time-condition interaction" on 7 measures. The model included random slopes for repeated measures factors and accounted for subject-level variability. A) The null model serves as the baseline, includes subject-level random effects, and suggests that the interaction between "Time" and "Condition" does not significantly improve model fit. B) The full Model ("Time + Condition + Time × Condition") tests whether the pattern or amount of improvement in the outcomes over time differs significantly across the three conditions: GC, IC & SH.

In this study, the Bayes Factor (BF_{10}, alternative over null) was chosen as the primary metric because it provides a direct, continuous measure of evidence for the tested (alternative) model relative to the null hypothesis (Schönbrodt & Wagenmakers, 2018). Unlike p-values, which only indicate whether the data are inconsistent with the null hypothesis, BF_{10} quantifies the degree to which the data support one model over another.

We interpreted BF_{10} using conventional heuristics:

- $BF_{10} < 1$: Evidence favors the null model.
- $BF_{10} > 1$: Evidence favors the alternative model: BF_{10} between 1 and 3 reflects only weak evidence; $BF_{10} > 3$ represents moderate evidence, and $BF_{10} > 10$ represents strong evidence.

To ensure clarity and focus, other metrics used in Bayesian model comparison (e.g., P(M), P(M|data)) were excluded from the results to streamline the presentation.

3.1 Language outcomes

3.1.1 Primary analysis

The results analyzed using Bayesian Repeated Measures ANOVA in JASP are summarized below (see Table 4). It indicates that participants in all three conditions show improvement across all language measures from pre-experiment to post-experiment. Across all language measures (see Table 5), the BF_{10} values of the **full model** for 5 out of the 6 measures (excluding BNT) indicate weak to moderate evidence for an interaction effect between time and condition, with ICU (per min) showing the strongest evidence (BF_{10} = 4.734).

TABLE 3: Mean and standard deviation across language and neurological measures

Time	Cond.		AQ		BNT		ICU		ICU (per min)		MC		AC (per min)		Dysf.	
		N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pre	GC	4	77.43	4.288	35.5	22.11	58.75	19.99	8.306	1.875	55.75	22.66	1.753	0.694	0.315	0.217
	IC	3	73.87	10.792	43	14.42	71.33	17.62	8.174	1.249	69.67	14.36	1.408	0.609	0.180	0.171
	SH	3	67.9	13.501	49.33	11.55	27	20.07	4.555	5.009	23.33	20.23	0.44	0.39	0.333	0.121
Post	GC	4	79.45	3.87q7	38.5	25.83	73.75	32.62	9.503	1.881	64.75	28.35	1.721	0.747	0.298	0.139
	IC	3	79.27	11.568	50	17.09	79.33	23.16	9.099	1.727	75.67	17.24	1.764	0.689	0.187	0.145
	SH	3	68.07	10.289	50.67	11.06	39.67	21.46	4.773	4.339	35.67	26.56	1.135	0.568	0.207	0.038

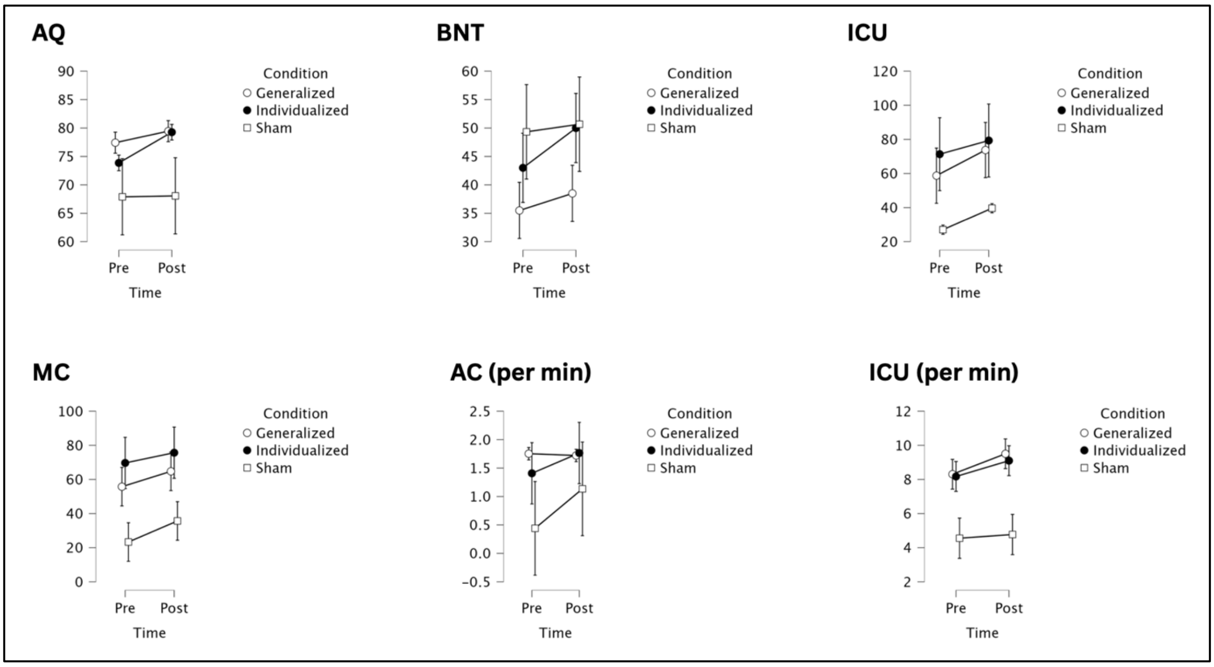
Note: Cond.: Condition; AQ: Aphasia Quotient; BNT: Boston Naming Test; ICU: Information Content Units; ICU (per min): Information Content Units per minute; MC: Main Concepts; AC (per min): Accurate and Correct Main Concepts per minute; Dys.: Dysfunctome

TABLE 4: Bayesian repeated measures ANOVA: Model comparison across 7 measures

Model Comparison	AQ	BNT	ICU	ICU (per min)	MC	AC (per min)	Dysfuntome
				BF_{10} (error %)			
Null model	1	1	1	1	1	1	1
Time + Condition + Time ✻ Condition	2.077 (0.7)	1.148 (2.196)	3.632 (2.018)	4.734 (2.8)	3.407 (2.4)	2.758 (1.5)	0.261 (1.5)

Note. All models include subject, and random slopes for all repeated measures factors.

FIGURE 4: Descriptive plots based on language measures by groups



Note. the 95% credible intervals are shown as **error bars** extending vertically from each data point.

3.1.2 Paired sample t-test

Bayesian paired sample t-tests were conducted for all 10 participants to evaluate pre- and post-intervention differences across six measures, with additional analyses performed separately for the three experimental conditions (GC, IC, and SH). The results are shown below (see Table 6). From the condition-specific results, the individualized condition (IC) demonstrated the greatest evidence for post-treatment improvement in 2 primary measures: AQ (BF_{+0} = 15.34) and BNT (BF_{+0} = 3.825). Notably, the BF_{10} for AQ in the IC group was significantly higher than in the GC (BF_{+0} = 2.963) and SH (BF_{+0} = 0.492) groups.

In contrast, participants in the SH group demonstrated the strongest evidence for improvement in ICU (BF_{+0} = 18.629). However, this improvement did not persist when ICU was measured for efficiency per minute (BF_{+0} = 0.718), suggesting the increase in total ICU was likely due to participants spending more time on the discourse task after the intervention, rather than efficiency gains. This pattern may be explained by their relatively low baseline ICU score (27) compared to the IC (71.33) and GC (58.75) groups, giving them more room for improvement and making it easier to produce more ICU overall.

In contrast, participants in the IC and GC groups demonstrated stronger evidence for improvement in ICU per minute (IC: BF_{+0} = 3.459; GC: BF_{+0} = 4.350) than in total ICU alone (IC: BF_{+0} = 1.137; GC: BF_{+0} = 2.295). This suggested that these two groups achieved real efficiency improvement, as they produced more ICUs pre-intervention within the same amount of time.

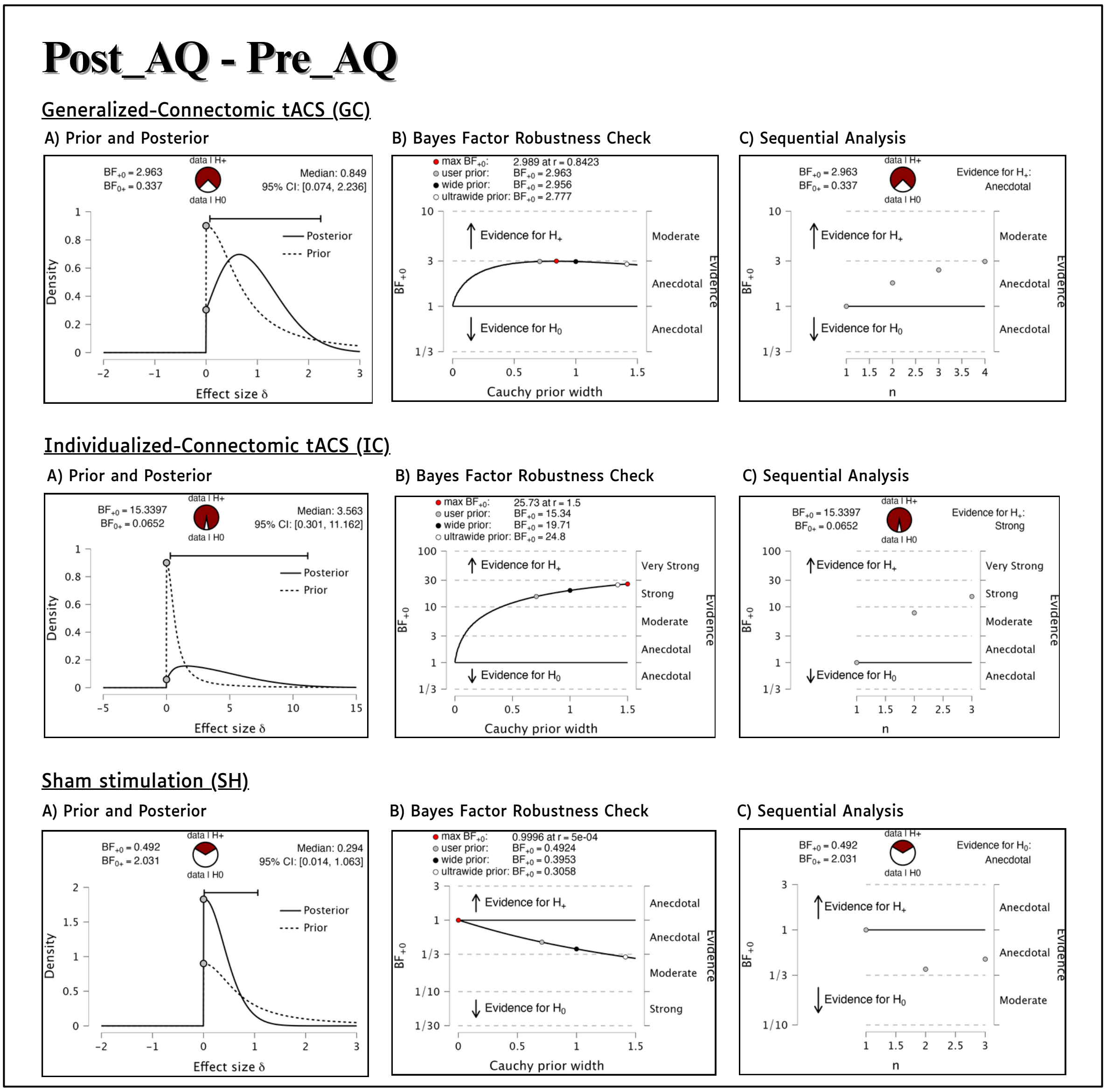
TABLE 5: Bayes factors for Bayesian paired sample t-tests across six measures with and without filters by condition

Measure 1	Measure 2	BF_{+0} (All)	BF_{+0} (GC)	BF_{+0} (IC)	BF_{+0} (SH)
Post_AQ	Pre_AQ	5.373	2.963	15.340	0.492
Post_BNT	Pre_BNT	5.484	1.310	3.825	0.677
Post_ICU	Pre_ICU	20.527	2.295	1.137	18.629
Post_ICU_min	Pre_ICU_min	17.575	4.350	3.459	0.718
Post_MC	Pre_MC	18.112	1.848	1.205	3.598
Post_AC_min	Pre_AC_min	3.537	0.300	2.011	2.657

Note. For all tests, the alternative hypothesis specifies that Measure 1 is greater than Measure 2. For example, Post_AQ is greater than Pre_AQ. The error % is less than 1.

The supplementary figure below provides a detailed visualization of the Bayesian paired samples T-test results for the primary measure (AQ) across three conditions

FIGURE 5: Inferential plots of paired sample t-test for AQ (across GC, IC, and SH)



3.1.3 Interaction effect follow-up: One-Way ANOVAs

Six one-way Bayesian ANOVA t-tests were conducted to examine pre-post differences in scores (e.g., post AQ score minus pre AQ score) across three conditions: generalized (n=4), individualized (n=3), and sham (n=3). As shown in Table 7, the analyses did not reveal significant differences between conditions (BF_{10} <1), possibly due to the small sample size.

However, post hoc comparisons, presented in Table 8, yielded notable findings. For the "Generalized V.S. Individualized" comparison, moderate evidence for a group difference was observed in AQ (BF_{10} =3.050; GC's mean = 2.025, IC's mean =5.4), weak evidence in AC (per min) (BF_{10} =1.779; GC's mean =-0.031, IC's mean =0.356), while no evidence was observed across other measures (BF_{10} <1). In the "Generalized vs. Sham" comparison, moderate evidence was found for a difference in AC.min (BF_{10} =2.806; GC's mean =-0.031, SH's mean =0.694). Finally, for the "Individualized vs. Sham" comparison, only weak evidence for a difference was observed in AQ (BF_{10} =1.539) and BNT (BF_{10} =1.053).

TABLE 6: Six One-Way ANOVAs and followed Post Hoc Tests across conditions (GC, IC, SH)

Dependent Variable	BF_{10}
Pre-Post AQ Difference	0.654
Pre-Post BNT Difference	0.704
Pre-Post ICU Difference	0.444
Pre-Post ICU_min Difference	0.853
Pre-Post MC Difference	0.456
Pre-Post AC_min Difference	0.452

Note. For all tests, the error % is less than 1.

Post Hoc Comparisons	**Bayes Factors (*BF*10,U) of Pre-Post Difference**					
	AQ	BNT	ICU	ICU_min	MC	AC_min
Generalized V.S. Individualized	**3.050**	0.839	0.621	0.590	0.573	**1.779**
Generalized V.S. Sham	0.679	0.583	0.556	1.113	0.585	**2.806**
Individualized V.S. Sham	1.539	1.053	0.636	0.935	0.742	0.749

Note. The posterior odds have been corrected for multiple testing by fixing to 0.5 the prior probability that the null hypothesis holds across all comparisons (Westfall, Johnson, & Utts, 1997). Individual comparisons are based on the default t-test with a Cauchy (0, r = 1/sqrt(2)) prior. The "U" in the Bayes factor denotes that it is uncorrected. The error % is less than 1%.

TABLE 7: Additional descriptive statistics for pre-post AQ and AC_min differences

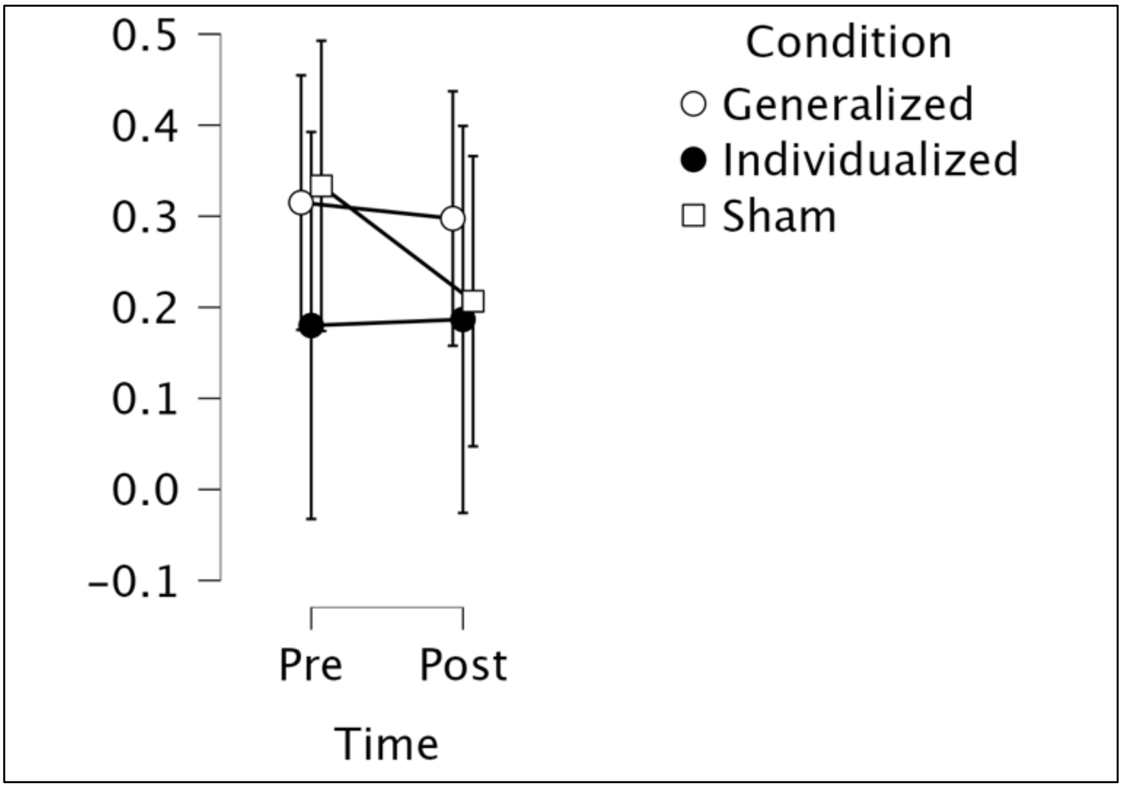
	Group	N	Mean	SD	95% Credible Interval
Pre-Post AQ Difference	Generalized	4	2.025	1.646	-0.594 - 4.644
	Individualized	3	5.400	0.781	3.46 - 7.340
	Sham	3	0.167	3.819	3.460 - 7.340
Pre-Post AC_min Difference	Generalized	4	-0.031	0.096	-0.185 - 0.122
	Individualized	3	0.356	0.307	-0.406 - 1.118
	Sham	3	0.694	0.469	-0.470 - 1.858

3.2 Neurological outcomes

Dysfuntome scores were collected at two time points (pre- and post-intervention). As shown in Table 4, only participants in the Individualized Condition (IC) group demonstrated improvement, with scores increasing from 0.180 to 0.187. In contrast, both the Generalized

Condition (GC) and Sham (SH) groups exhibited declines in scores. However, the Bayesian analysis yielded inconclusive results. The evidence for the Interaction ($BF_{10} = 0.261$) favored the null hypothesis. Additional data would be required before drawing any conclusions.

FIGURE 6: Descriptive plots based on dysfunctome scores

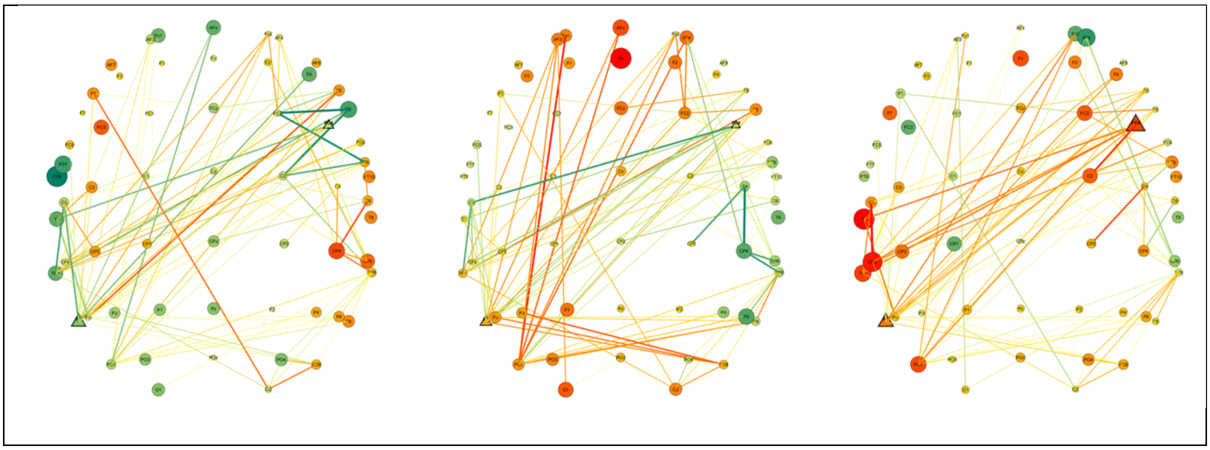


Note. the 95% credible intervals are shown as **error bars** extending vertically from each data point.

The graph below (see Graph 1) visually represents how the strength of individual brain regions (nodes) and the connections between them (edges) have changed following tACS treatment. Compared with the other 2 groups, the IC group appears to show the most pronounced overall increases in both node strength and edge weight for the target regions. The GC group exhibits a more mixed pattern of changes, and the SH group shows a united decrease signal (red elements) specifically for the stimulation targets, although some localized regions show increases.

GRAPH 1: Group-level post-treatment changes within dysfunctome

a) Individualized (IC)	b) Generalized (GC)	c) Sham (SH)



Note. The size and depth of color of these nodes indicate the percentage change in node strength after the treatment. Green colours signify post-treatment increases in node strength or edge weight, and red colours signify post-treatment decreases. The triangle node marks the stimulation target.

4. Discussion

This study investigated whether combining tACS with ST could enhance language recovery in post-stroke aphasia patients. Specifically, we compared a novel IC tACS protocol, tailored to each participant's dysfunctome profile, with GC and SH tACS. In summary, we found that the IC group produced the strongest evidence for post-treatment improvements in two key language measures: AQ (BF_{+0} = 15.34) and BNT (BF_{+0} = 3.825). Importantly, the evidence for improvement in AQ was significantly stronger in the IC group compared to both the GC (BF_{+0} = 2.963) and the SH (BF_{+0} = 0.492) groups.

Although Bayesian one-way ANOVA of pre-post difference scores found no significant differences between groups, the post hoc tests found moderate to weak evidence for the IC group outperforming the GC (AQ: BF_{10} = 3.050; AC_min: BF_{10} = 1.779) and SH groups (AQ: BF_{10} = 1.539).

The non-significant results in Bayesian one-way ANOVA likely stems from three factors: (1) Variance in pre-language scores, as participants started with differing baseline abilities that influenced their potential for improvement; (2) High score variability in the Sham condition, where post-treatment scores showed a wider range compared to GC and IC conditions, reducing the ability to detect effects; and (3) Inadequate statistical power due to the small sample size (n=10), with only 3–4 participants per condition, limiting the sensitivity of Bayesian analyses.

4.1 Interpretation of Language Outcomes

Overall, the analysis supports the post-intervention improvement regardless of the conditions (see Table 5). This aligns with existing evidence, as systematic reviews and meta-analyses have shown that using SFA as an ST method yields significant gains in naming trained items for the majority of PWA, with small to moderate effect sizes overall (Efstratiadou et al., 2018; Quique et al., 2019).

4.1.1 RQ1: The impact of tACS combined with ST on language outcomes in PWA

Our findings provide preliminary evidence supporting the efficacy of tACS combined with ST in enhancing language recovery for PWA. Regarding our primary language outcome measure (CAB), Bayesian paired sample t-tests revealed strong evidence supporting post-treatment improvement in AQ scores after IC, anecdotal evidence after GC, and no evidence after SH (IC: BF_{+0} =15.340; GC: BF_{+0} =2.963; SH: BF_{+0} = 0.492). Additionally, both active stimulation conditions demonstrated stronger evidence for improvement in ICU per minute (IC: BF_{+0} = 3.459; GC: BF_{+0} = 4.350).

These findings align with the limited but growing body of research exploring tACS applications in aphasia rehabilitation. A recent review by Gobbo and Marini (2025) identified only three experimental studies applying tACS coupled with ST in aphasia rehabilitation, which all employed standardized stimulation approaches rather than individualized protocols. They identified the stimulation nodes using fMRI ROI-guided or subjective functional magnetic images. Xie et al. (2022) reported significant improvements across multiple language domains when 6 Hz tACS over the left supplementary motor area was combined with ST. Similarly, Keator (2022) demonstrated significantly increased word production during 7 Hz in-phase high-density tACS delivered over left language regions compared to sham conditions. Garnier et al. (2022), despite non-significant results likely due to small sample size (n=10), observed promising trends with up to 40% improvement in naming performance during high gamma tACS.

Despite methodological variations across these studies (e.g., differences in study design and stimulation parameters), the consistency in positive outcomes strengthens our hypothesis that tACS combined with ST may enhance language recovery beyond what can be achieved with ST alone. However, we acknowledge that the evidence base remains preliminary as there are only a limited number of high-quality controlled studies in this field. Therefore, while our findings and those of others point in a promising direction, definitive conclusions about long-term outcomes and the generalizability of tACS combined with ST still require further research.

4.1.2 RQ2: Individualized Versus Generalized tACS protocols: Enhancing speech and language recovery

As discussed, among the 3 conditions, the IC condition is proven to have the strongest evidence for post-intervention improvement for the primary measure (AQ: BF_{+0} = 15.34). Post hoc analyses further supported this advantage, revealing weak to moderate evidence favoring IC over GC for both AQ (BF_{10} = 3.050) and AC per minute (BF_{10} = 1.779).

The potential superiority of personalized stimulation approaches has been documented in the broader neurostimulation literature. Studies by Zoefel et al. (2020) and Wilsch et al. (2018) pointed out that customizing parameters, such as electrode placement and frequency to match individual neural activity patterns, may enhance therapeutic outcomes compared to one-size-fits-all methods. While no previous studies have implemented tailored tACS protocols specifically for aphasia rehabilitation, meta-analyses in cognitive domains suggest that interventions using current flow models or adjustments based on individual neurophysiology typically yield greater cognitive benefits (Grover et al., 2023).

Given our current understanding that language processing involves a complex network spanning classical cortical areas (e.g., Broca's and Wernicke's), subcortical structures, and the cerebellum, all forming extensive cortico-subcortical-cerebellar circuits that modulate both language and cognitive functions (Bulut & Hagoort, 2024; Siqi et al., 2025). It seems reasonable to hypothesize that personalized stimulation approaches targeting these individualized neural networks would yield greater benefits for PWA than standard ones as well.

To our knowledge, this study represents the first application of individualized current tACS protocols for aphasia treatment. There is a paucity of direct head-to-head studies comparing individualized and generalized tACS protocols in PWA. Additionally, the field lacks consensus on fundamental aspects of stimulation, including optimal frequency parameters, electrode placement, session duration, and effective edge prioritization methods for targeting neural networks. Therefore, while the results are promising, as only two pieces of evidence for group differences (IC vs. GC) and no significant differences were observed in the other four language measures, current evidence in this study does not definitively establish whether IC tACS protocols outperform GC protocols in supporting speech and language recovery in PWA. Further studies should continue to explore similar or alternative methodologies, work toward identifying optimal priority indicators for individualized target selection.

4.2 Neurological Changes and Network Modulation

No significant time or interaction effect was found for participants' dysfunctome scores when performing 2-way ANOVA ($BF_{10} = 0.606$; $BF_{10} = 0.261$). However, we found that dysfunctome scores only increase in the Individualized Condition (IC; n = 0.007), and they decrease more prominently in the Sham group (SH: n = -0.126) compared to the Generalized Condition (GC; n = -0.017). Additionally, the dysfunctome graph illustrates a distinct reduction in node strength and edge weight for the targeted regions within the Sham group, which is not observed in the other groups (see Graph 1).

Interestingly, similar findings were reported by Cheung et al. (2025), who demonstrated that individualized tACS targeting weakened connector hubs facilitates network reorganization and improves global network properties in post-stroke aphasia. Their study suggested that dysfunctome restoration may not be directly associated with language facilitation, but rather, broader network reorganization plays a significant role. The reduction in node strength and edge weight observed in the Sham group aligns with the lack of network modulation reported in their sham condition. While the mechanisms driving these changes remain unclear, the findings further support the potential importance of individualized targeting approaches in promoting functional network changes for PWA.

4.3 Limitations

4.3.1 Time Constraint

This study was conducted over three months, from mid-May to late August, and therefore does not address the long-term effectiveness of tACS. A follow-up session is planned, and the resulting data will be analyzed in a separate study led by my supervisor, Mr. Chester Yee-Nok Cheung.

4.3.2 Small Sample Size

This study has inadequate statistical power due to its small sample size (n=10). the data indicate improvements in language measures across both generalized and individualized conditions over time, but the small sample sizes within each group (n =4 for GC, n =3 for IC, and n =3 for SH) restrict the study's capacity to produce significant results in Bayesian analysis and therefore to answer the 2 research questions.

4.3.3 Participants' Heterogeneity

Though the 10 participants in this study are all Cantonese-speaking individuals, they differ in terms of age (33–64 years), education levels (6–17 years), post-onset duration (13–184 months), aphasia type (e.g., Broca's, Anomic, Wernicke), and severity (CAB AQ scores: 52.7–83.8). These differences may not only limit the study's ability to yield significant results in Bayesian analysis but also introduce confounding variables that could compromise its internal validity and restrict the generalizability of the findings to the broader population of Cantonese-speaking individuals with aphasia.

5. Conclusion

This study provides preliminary evidence supporting the efficacy of tACS combined with speech therapy for enhancing language recovery in post-stroke aphasia. Our findings suggest that IC tACS protocols may offer advantages over GC and SH conditions, particularly for improving aphasia quotient scores and naming abilities. The IC group demonstrated the strongest evidence for post-treatment improvements in key language measures, with Bayesian post-hoc tests supporting these outcomes.

Despite the lack of strong statistical effects due to methodological challenges (e.g., small sample size, participant heterogeneity and time constraints), our results align with emerging research suggesting that personalized neurostimulation approaches may enhance therapeutic outcomes in aphasia rehabilitation. This underscores the need for larger-scale trials to validate and generalize the findings. Therefore, future studies are recommended to recruit larger cohorts, include longer follow-up, and consider similar ot alternative analytical approaches to identify more notable group-level trends and to facilitate a more conclusive analysis.

While definitive conclusions about the superiority of individualized over generalized tACS protocols cannot yet be drawn, this study provides a foundation for future investigations into personalized neuromodulation techniques for aphasia rehabilitation. As our understanding of the neural mechanisms underlying language recovery continues to evolve, so too will our ability to develop more effective, targeted interventions for individuals with post-stroke aphasia.

Acknowledgment

I would like to express my deepest gratitude to my supervisors, Prof. Anthony Pak-Hin KONG and Mr. Chester Yee-Nok Cheung, for their invaluable guidance, support, and expertise throughout this study. This research was inspired by Mr. Cheung’s innovative idea, which was developed under the Aphasia Research and Treatment Lab, led by Prof. Kong. Mr. Cheung’s contributions, particularly to the neuroscience analysis, were crucial to the success of this project. Their mentorship has been instrumental in shaping this work and my growth as a student researcher. I also extend my sincere thanks to the Laidlaw Foundation and the University of Hong Kong for their generous financial support that made this research endeavor possible.

References

Ambrus, G. G., Al-Moyed, H., Chaieb, L., Sarp, L., Antal, A., & Paulus, W. (2012). The fade-in – Short stimulation – Fade out approach to sham tDCS – Reliable at 1 mA for naïve and experienced subjects, but not investigators. Brain Stimulation, 5(4), 499 504. https://doi.org/10.1016/j.brs.2011.12.001

Antal, A., & Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Frontiers in Human Neuroscience*, *7*, 317–317. https://doi.org/10.3389/fnhum.2013.00317

Brady, M., Kelly, H., Godwin, J., Enderby, P., & Campbell, P. (2016). Speech and language therapy for aphasia following stroke. *The Cochrane database of systematic reviews*, 6, CD000425 . https://doi.org/10.1002/14651858.CD000425.pub4.

Bulut, T., & Hagoort, P. (2024). Contributions of the left and right thalami to language: A meta-analytic approach. Brain Structure and Function, 229(9), 2149–2166. https://doi.org/10.1007/s00429-024-02795-3

Cheung, R. W., Cheung, M. C., & Chan, A. S. (2004). Confrontation naming in Chinese patients with left, right or bilateral brain damage. Journal of the International Neuropsychological Society, 10(1), 46–53. https://doi.org/10.1017/S1355617704101069

Cheung, C. Y.N., Kong, A. P.H., & Bakhtiar, M. (2025). Individualized connectomic tACS immediately improves oscillatory network with language facilitation in post-stroke aphasia: A feasibility study of a dysfunctome-based targeting approach. *Frontiers in Computational Neuroscience, 19*, Article 1635497. https://doi.org/10.3389/fncom.2025.1635497

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. Journal of Neuroscience Methods, 134(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Efstratiadou, E., Papathanasiou, I., Holland, R., Archonti, A., & Hilari, K. (2018). A Systematic Review of Semantic Feature Analysis Therapy Studies for Aphasia.. *Journal of speech, language, and hearing research: JSLHR*, 61 5, 1261-1278. https://doi.org/10.1044/2018_JSLHR-L-16-0330.

Flowers, H., Skoretz, S., Silver, F., Rochon, E., Fang, J., Flamand-Roze, C., & Martino, R. (2016). Poststroke aphasia frequency, recovery, and outcomes: A systematic review and meta-analysis. *Archives of physical medicine and rehabilitation*, 97 12, 2188-2201.e8 . https://doi.org/10.1016/j.apmr.2016.03.006.

Fridriksson, J., den Ouden, D.-B., Hillis, A. E., Hickok, G., Rorden, C., Basilakos, A., Yourganov, G., & Bonilha, L. (2018). Anatomy of aphasia revisited. *Brain (London, England: 1878)*, *141*(3), 848–862. https://doi.org/10.1093/brain/awx363

Garnier, J., Soluch, P., Malej, K., Szostakowska, S., Leśniak, M., Iwanski, S., Bielecki, M., Cortes, M., Sarzyńska-Długosz, I., & Nitsche, M. (2022). PO105/#841 High gamma tacs in post-stroke aphasia therapy: E-poster viewing. Neuromodulation: Technology at the Neural Interface, 25(7), S243. https://doi-org.eproxy.lib.hku.hk/10.1016/j.neurom.2022.08.278

Gobbo, M., & Marini, A. (2024). Transcranial alternating current stimulation applied to language recovery in persons with aphasia: a scoping review. *Aphasiology*, *39*(5), 684–709.. https://doi.org/10.1080/02687038.2024.2373135

Gronberg, A., Henriksson, I., & Lindgren, A. (2020). Abstract TP149: Aphasia recovery after ischemic stroke. *Stroke (1970)*, *51*(Suppl_1). https://doi.org/10.1161/str.51.suppl_1.TP149

Grover, S., Fayzullina, R., Bullard, B. M., Levina, V., & Reinhart, R. M. G. (2023). A meta-analysis suggests that tACS improves cognition in healthy, aging, and psychiatric populations. Science Translational Medicine, 15(697), eabo2044–eabo2044. https://doi.org/10.1126/scitranslmed.abo2044

JASP Team (2025). JASP (Version 0.95.1)[Computer software]

Keator, L. M. (2022). Transcranial Alternating Current Stimulation as an Adjuvant for Nonfluent Aphasia Therapy: A Proof-Of-Concept Study (Doctoral dissertation, University of South Carolina).

Kong, A. P. H., & Law, S. P. (2019). Cantonese AphasiaBank: An annotated database of spoken discourse and co-verbal gestures by healthy and language-impaired native Cantonese speakers. *Behavior research methods, 51*, 1131-1144.

Omae, E., Shima, A., Tanaka, K., Yamada, M., Cao, Y., Nakamura, T., Hoshiai, H., Chiba, Y., Irisawa, H., Mizushima, T., Mima, T., & Koganemaru, S. (2024). Case report: An N-of-1 study using amplitude modulated transcranial alternating current stimulation between Broca’s area and the right homotopic area to improve post-stroke aphasia with increased inter-regional synchrony. *Frontiers in Human Neuroscience*, *18*, 1297683-. https://doi.org/10.3389/fnhum.2024.1297683

Perrin, F., Pernier, J., Bertnard, O., Giard, M. H., & Echallier, J. F. (1987). Mapping of scalp potentials by surface spline interpolation. Electroencephalography and Clinical Neurophysiology, 66(1), 75–81. https://doi.org/10.1016/0013-4694(87)90141-6

Porcaro, C., Medaglia, M. T., & Krott, A. (2015). Removing speech artifacts from electroencephalographic recordings during overt picture naming. NeuroImage, 105, 171–180. https://doi.org/10.1016/j.neuroimage.2014.10.049

Quique, Y., Evans, W., & Dickey, M. (2019). Acquisition and Generalization Responses in Aphasia Naming Treatment: A Meta-Analysis of Semantic Feature Analysis Outcomes. *American journal of speech-language pathology*, 28 1S, 230-246. https://doi.org/10.1044/2018_AJSLP-17-0155.

Schönbrodt, F. D., & Wagenmakers, E.-J. (2018). Bayes factor design analysis: Planning for compelling evidence. *Psychonomic Bulletin & Review, 25*(1), 128–142. https://doi.org/10.3758/s13423-017-1230-y

Siqi, L., Yuan, Z., Li, Y., Liu, Y., & Zhang, Y. (2025). Abstract 27: The Brain-behaviour Mechanisms of Impaired Linguistic and Cognitive Function Impairments in Stroke Patients with Aphasia. Stroke (1970), 56(Suppl_1), A27–A27. https://doi.org/10.1161/str.56.suppl_1.27

The MathWorks Inc. (2022). MATLAB version 9.14.0 (R2023a). http://www.mathworks.comWeb

Williams, E. E. R., Sghirripa, S., Rogasch, N. C., Hordacre, B., & Attrill, S. (2024). Non-invasive brain stimulation in the treatment of post-stroke aphasia: a scoping review. *Disability and Rehabilitation, 46*(17), 3802–3826. https://doi.org/10.1080/09638288.2023.2259299

Wilsch, A., Neuling, T., Obleser, J., & Herrmann, C. S. (2018). Transcranial alternating current stimulation with speech envelopes modulates speech comprehension. NeuroImage (Orlando, Fla.), 172, 766–774. https://doi.org/10.1016/j.neuroimage.2018.01.038

Xie, X., Hu, P., Tian, Y., Wang, K., & Bai, T. (2022). Transcranial alternating current stimulation enhances speech comprehension in chronic post-stroke aphasia patients: A single-blind sham-controlled study. *Brain Stimulation, 15*(6), 1538–1540. https://doi-org.eproxy.lib.hku.hk/10.1016/j.brs.2022.12.001

Yang, S., Yi, Y. G., & Chang, M. C. (2024). The effect of transcranial alternating current stimulation on functional recovery in patients with stroke: a narrative review. *Frontiers in Neurology*, *14*, 1327383-. https://doi.org/10.3389/fneur.2023.1327383

Yiu, E. M. (1992). Linguistic assessment of Chinese-speaking aphasics: Development of a Cantonese aphasia battery. *Journal of Neurolinguistics, 7*(4), 379-424

Zoefel, B., Allard, I., Anil, M., & Davis, M. H. (2020). Perception of Rhythmic Speech Is Modulated by Focal Bilateral Transcranial Alternating Current Stimulation. Journal of Cognitive Neuroscience, 32(2), 226–240. https://doi.org/10.1162/jocn_a_01490

Appendix

Appendix 1. Participant screening form. 研究参與者篩查問卷

〈第一部份 – 個人資料〉

出生日期： 性別：

種族： 國籍：

職業： 居住地區：

最高學歷： 接受教育年期：

母語： 其他語言：

請註明任何中風以外的已知病患（如智力障礙、精神心理相關疾病、腦退化症、柏金遜症、糖尿病、心臟病、癌症等）：

〈第二部份 – 中風病歷〉

1. 你是否曾經中風？ •是 •否

2. 你是否只曾中風過一次？ •是 •否

3. 中風類型 •缺血性中風 •出血性中風

4. 中風日期

_________年 _____月 _____日

5. 中風位置

____

6. 中風後哪邊身較受影響？ •左邊 •右邊

7. 中風後語言能力有否受影響？ •有 •沒有

8. 你認為中風後的症狀是否已完全康復？ •是 •否

9. 你認為現時有哪些中風後的症狀仍未康復？

____

〈第三部份 – 接受經顱電刺激 Transcranial Electric Stimulation 安全性問卷〉

1. 你現時有否在頭顱或腦內植入任何金屬（除鈦金屬外）或電子儀器？（例如：人工耳蝸 Cochlear Implant、腦深層電刺激儀 Deep Brain Stimulation、或其他手術後遺留的金屬零件等。）如有，請註明金屬種類及植入位置。

2. 你現時有否在身體其他部位植入任何金屬或電子儀器？（例如：心臟起搏器 Cardiac pacemaker、或其他手術後遺留的金屬零件等。）如有，請註明金屬種類及植入位置。

3. 你曾否進行過任何頭顱、腦部、或脊髓手術？如有，請註明位置。

4. 你曾否受過頭部創傷導致意識受損？

5. 你是否患有任何皮膚相關問題？（例如：皮膚炎、銀屑病、濕疹等。）如有，請註明位置。

6. 你是否患有癲癇症或曾出現過抽搐或痙攣？

7. 你曾否出現過短暫性失去意識或昏厥？

8. 你是否（或有機會）正在懷孕？

9. 你是否正在服食藥物？如有，請註明。

10. 你以往曾否接受過經顱電刺激 Transcranial Electric Stimulation 或經顱磁刺激 Transcranial Magnetic Stimulation？如有，當時有否出現過任何不良反應？請註明。

姓名：

日期：

____

簽署：

____

以上資料將幫助研究員評估參與者參與研究的風險與得益，並不絕對代表參與者是否適合接受經顱電刺激。

〈第四部份 –緊急聯絡人資料〉緊急聯絡人姓名：

____

緊急聯絡人與參與者之關係：

____

緊急聯絡人電話：

____

Appendix 2. Sensations and aversive events questionnaire.
經顱電刺激相關感覺問卷

〈研究員填寫部份〉

- Participant code:
- Date of session:
- Session number:
- Experimental condition:
- Type of electrode:
- Type of stimulation: •DC •AC
- Waveform: •Monophasic •Biphasic
- Stimulating electrodes & intensity:
- Return electrodes & intensity:
- Total intensity: ____________mA
- Frequency: ____________Hz
- Duration:

〈參與者填寫部份〉

在接受電刺激時，你有否感到任何不適？例如：痕癢 刺痛 灼燒感 疲倦 頭痛 噁心 心情低落。

____

這些不適感由何時起出現？

○ 開始時　○ 中段時　○ 尾段時　○ 結束後

這些不適感持續多久？

○ 只在開始時維持　○ 維持到中段　○ 直到結束　○ 在結束後一直維持

這些不適感出現在什麼位置？

____