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Transcranial alternating current stimulation enhances speech comprehension in chronic post-stroke aphasia patients: A single-blind sham-controlled study

Aphasia is one of the most devastating complications following stroke [1]. Speech and language therapy (SLT) [2] is recommended for post-stroke aphasia (PSA), but the benefits remain limited. Several recent studies have examined the potential efficacy of combining SLT with various forms of non-invasive brain stimulation (NIBS), including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). While tDCS is accepted by clinicians and patients due to low cost and documented safety, it has not proven effective for improving speech comprehension [3]. Neuronal oscillations in language-related cortical regions are regarded as essential for efficient speech processing and comprehension [4], and transcranial alternating current stimulation (tACS) has been shown to modulate neuronal oscillation [5] and improve speech processing in healthy subjects [6,7]. One of these studies reported that tACS at theta frequency (4–8 Hz) but not delta frequency enhanced discrimination of speech from noise in healthy participants [6]. However, the efficacy of adjunct tACS with SLT on language function among PSA patients has not been examined.

The primary aim of this single-blind sham-controlled study was to investigate the clinical efficacy of 6-Hz tACS as adjunct treatment for chronic PSA. The supplementary motor area (SMA) was chosen as the target region due to its importance for both speech production [8] and comprehension [9]. We predicted that tACS over SMA would enhance the efficacy of SLT in chronic post-stroke aphasia, especially for improving speech comprehension.

Participants with chronic PSA were recruited from the First Affiliated Hospital of Anhui Medical University. The inclusion criteria were (a) first stroke in the left hemisphere, (b) PSA persisting for ≥6 months after stroke, (c) naturally right-handed, (d) aphasia confirmed using the Aphasia Battery of Chinese (ABC) [10], and (e) native speaker of Manderin. Exclusion criteria were (a) history of brain surgery, (b) cerebral tumor or abscess, (c) seizures during the previous 12 months, (d) severe dysarthria, and (e) neglect, severe vision impairment, or hearing loss. The study was approved by the Ethics Committee of Anhui Medical University and was conducted in accordance with the Declaration of Helsinki. All participants and guardians provided written informed consent.

Twenty-five participants (M_{age} = 59 years) were randomized to receive 30 minutes of SLT simultaneously with active tACS (n = 14, 11 males) or sham tACS (n = 11, 10 males) followed by 1.5 h of SLT alone once daily for fourteen consecutive days (Fig. 1A). After this 2-week intervention, all participants believed that they had received the active tACS. Stimulation was delivered using a tACS device (Soterix Medical, Inc., New York, USA) via 5 electrodes in a 4 × 1 ring configuration. The central electrode was placed at FCz and delivered an alternating current below 2 mA, while the four return electrodes were placed at C1, C2, F1, and F2, and delivered one-fourth of the central electrode current as estimated by a 64-channel EEG system. In the active condition, 6-Hz tACS was delivered for the entire 30-min intervention period and 30-s ramp-up and ramp-down phases. For the sham condition, 6-Hz tACS was delivered only during ramp-up and ramp-down phases.

Language functions were assessed using the ABC before the intervention (baseline) and again one day after the last treatment session. The multidimensional ABC consists of four subtests assessing spontaneous speech, auditory verbal comprehension, repetition, and naming. Based on subtest performance, an aphasia quotient (AQ) is calculated as an index of overall language impairment.

There were no significant differences in sex ratio, age, educational status, time of PSA onset, and ABC scores (Supplementary Table 1) between sham and active tACS groups at baseline. Repeated measures ANOVA revealed significant group (sham vs. active) × time (pre-vs. post-treatment) interaction effects on AQ ($F = 15.56$, $p = 0.001$ Bonferroni corrected) and auditory verbal comprehension ($F = 24.15$, $p < 0.001$ Bonferroni corrected), but not on spontaneous speech ($F = 6.76$, $p = 0.016$), repetition ($F = 2.60$, $p = 0.12$), or naming ($F = 0.02$, $p = 0.89$) (Supplementary Table 2). Post hoc tests revealed that active tACS combined with SLT improved overall language performance (AQ, $t = 6.80$, $p < 0.001$), auditory verbal comprehension ($t = 7.10$, $p < 0.001$), spontaneous speech ($t = 3.66$, $p = 0.003$), repetition ($z = -2.76$, $p = 0.006$), and naming ($z = -2.94$, $p = 0.003$) compared to baseline, while only AQ ($t = 3.63$, $p = 0.005$) and naming ($z = -2.65$, $p = 0.008$) were improved in the sham tACS plus SLT group (Fig. 1B and C). The improvement ratios (relative to baseline) of AQ and auditory verbal comprehension were also significantly greater in the active tACS plus SLT group than the sham tACS plus SLT group (AQ ratio: $z = -2.85$, $p = 0.004$; auditory verbal comprehension: $z = -3.12$, $p = 0.002$) (Fig. 1B, D and Supplementary Table 3).

This single-blind sham-controlled study suggests that tACS over the SMA can strengthen the efficacy of SLT for chronic post-stroke aphasia patients. Consistent with previous studies, SLT alone (combined with sham tACS) mainly improved naming performance, while the addition of active tACS also significantly improved speech comprehension, a faculty usually resistant to conventional

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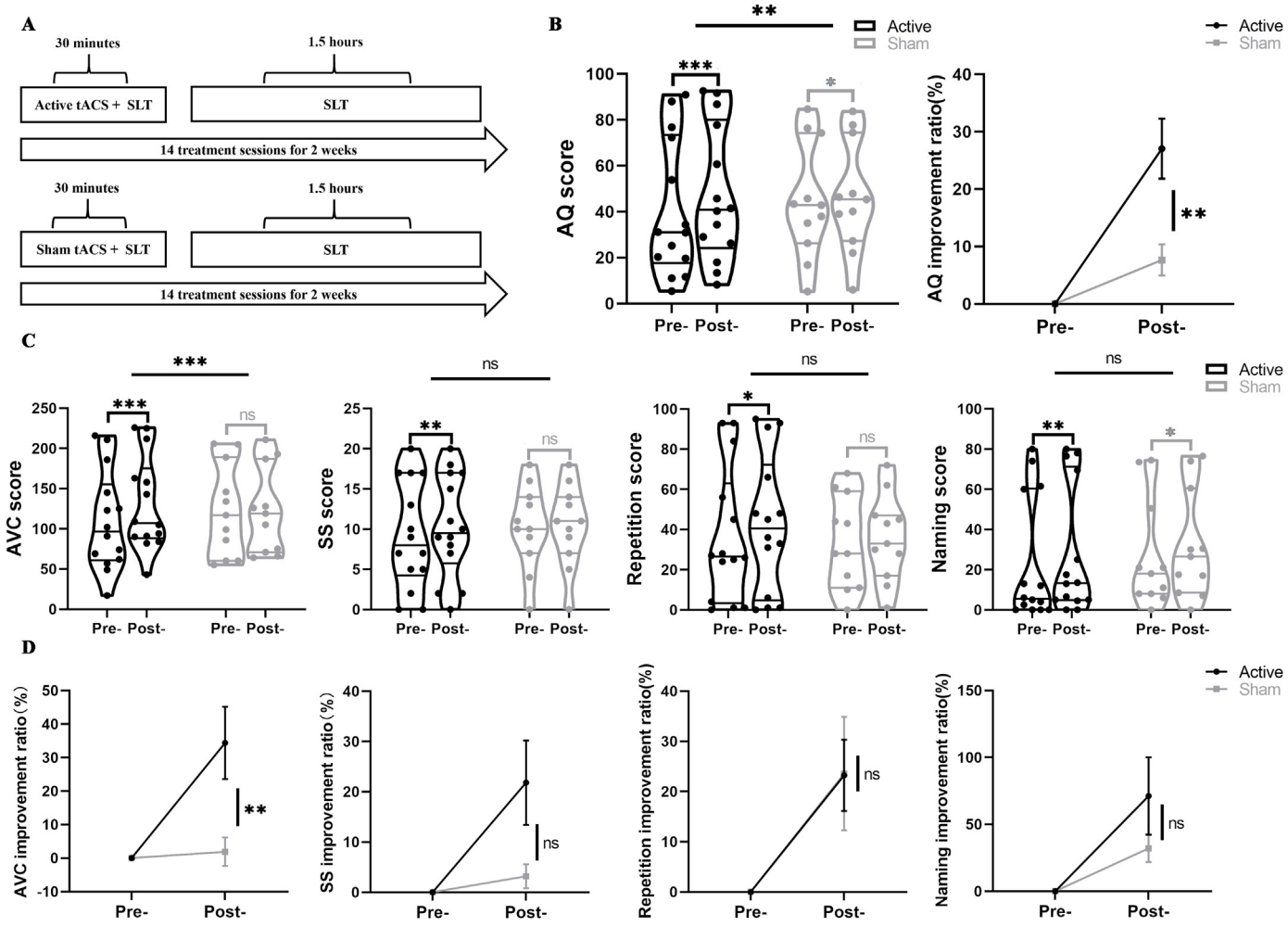

Fig. 1. Study timeline and effects of transcranial alternating current stimulation (tACS) on chronic post-stroke aphasia. (A) Participants received 30 minutes of speech and language therapy (SLT) simultaneously with active or sham tACS, followed by 1.5 hours of SLT alone. (B) Changes in overall performance (AQ) on the Aphasia Battery of Chinese (ABC) following sham or active tACS plus SLT (Post-) compared to baseline (Pre-). Improved AQ was found in both the active group (tACS combined with SLT, dark lines, $p < 0.001$) and sham group (sham tACS combined with SLT, gray lines, $p < 0.01$), but the magnitude of improvement (improvement ratio) was greater in the active group (right panel). (C, D) Treatment effects on ABC subtests. Both groups demonstrated similar improvements in ABC subtests except for auditory verbal comprehension, which was significantly improved only by active tACS plus SLT. Improvement ratio of ABC scores = (post-treatment assessment − pre-treatment assessment)/pre-treatment assessment × 100%. Data presented as mean (symbol) with standard error of the mean (error bar). Abbreviation: SS, spontaneous speech. AVC, auditory verbal comprehension. AQ, aphasia quotient. Pre-, pre-treatment assessment. Post-, post-treatment assessment. *$p < 0.01$, **$p < 0.005$, ***$p < 0.001$, Bonferroni corrected.

treatments such as SLT. This improvement in speech comprehension may in turn lead to improvements in other language domains over time. Moreover, these effects were maintained for at least one month in about 72% of follow-up participants (Supplementary Table 4 and Fig. 1).

This brief follow-up period is a major limitation that must be addressed in future studies. In addition, some effects may be underestimated due to the small sample size and patient heterogeneity. Further, the lack of blinding for assessment may have introduced bias. Nonetheless, these results provide the first evidence for the utility of tACS to improve impaired speech comprehension in chronic PSA patients when paired with SLT.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.12.001.

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Xiaohui Xie
Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei, 230032, China

The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China

Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, 230032, China

Collaborative Innovation Center of Neuropsychiatric Disorders and Mental Health, Anhui Province, 230032, China

Panpan Hu
Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei, 230032, China

The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China

Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, 230032, China

Collaborative Innovation Center of Neuropsychiatric Disorders and Mental Health, Anhui Province, 230032, China

Yanghua Tian
Department of Psychology and Sleep Medicine, The Second Affiliated Hospital of Anhui Medical University, Hefei, 230601, China

Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei, 230088, China

The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China

Kai Wang*
Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei, 230032, China

The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China

Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, 230032, China

Collaborative Innovation Center of Neuropsychiatric Disorders and Mental Health, Anhui Province, 230032, China

Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei, 230088, China

Tongjian Bai**
Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei, 230032, China

The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China

Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, 230032, China

Collaborative Innovation Center of Neuropsychiatric Disorders and Mental Health, Anhui Province, 230032, China

Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei, 230088, China

* Corresponding author. Department of Neurology, The First Affiliated Hospital of Anhui Medical University, No.81 Meishan Road, Shushan District, Hefei, 230032, China.

** Corresponding author. Department of Neurology, The First Affiliated Hospital of Anhui Medical University, No.81 Meishan Road, Shushan District, Hefei, 230032, China.
E-mail address: wangkai1964@126.com (K. Wang).
E-mail address: baiyunong1990@163.com (T. Bai).

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