Research Square

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10-Hz tACS Over The Prefrontal Cortex Improves Phonemic Fluency

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Abstract

Verbal fluency is an important indicator of human verbal ability. Methods to improve fluency is an interesting issue necessitating investigation. To do this, the current study required participants to randomly receive transcranial alternating current stimulation (tACS) at 10 Hz, 40 Hz (control frequency), and sham stimulation over the prefrontal cortex before a phonemic fluency task. It was found that 10-Hz tACS significantly improved phonemic fluency relative to sham stimulation. This result demonstrates the modulatory effect of 10-Hz tACS on language ability.

1. Introduction

Verbal fluency is a cognitive function that facilitates the retrieval of knowledge in memory. It describes the efficiency of individuals' vocabulary production, and it is an important indicator of human verbal ability. Phonemic fluency mainly related to letters is one important indicator of verbal fluency (Shao et al., 2014). Generally, a verbal fluency task requires subjects to say words according to certain rules in limited time. Importantly, a phonemic fluency task is variable and depends on the language. In the English version, subjects are often asked to start with a specific letter, such as the letters 'f', 'h', etc., to generate words (Z. Cattaneo et al., 2011). In the Chinese version, on the other hand, some studies require subjects to output as many words as possible starting with a certain radical (C. H. Y. G. X. X. X. Y. C. L. B. Xuejun1, 2014) or an initial consonant(Y. H. X. □Zhou S. □Liu Y. □Bai Xuejun1, 2014) within a fixed time.

Increasing evidence supports that the left frontal lobe plays a crucial role in phonemic fluency. A positron emission tomography study found that phonemic fluency elicited more activation in the left frontal lobe than other areas(Mummery et al., 1998). Similarly, phonemic fluency has been shown to activate the left inferior frontal gyrus in functional magnetic resonance studies (Weiss et al., 2003). Brain injury studies provide direct evidence that phonemic fluency performance decreased when the left frontal lobe was impaired (Robinson et al., 2012). In addition, many tDCS studies have shown that anodal stimulation targeting the left frontal lobe increased the number of produced words, while cathodal stimulation decreased the number of words (Iyer et al., 2005; Vannorsdall et al., 2012; Zaira Cattaneo et al., 2016). A study on repetitive transcranial magnetic stimulation (rTMS) also showed that the use of hf (high frequency)-TMS in the left frontal lobe improved patients' verbal fluency (Trebbastoni et al., 2013)

Altogether, these findings suggest that phonemic fluency is sensitive and specific to the left frontal lobe. Recently, transcranial alternating current stimulation (tACS) offered a new promising method to improve phonemic fluency (Lara et al., 2018□ Marchesotti et al., 2020; Zaehle et al., 2010). tACS applies periodic alternating weak currents to specific brain regions, delivering alternating currents of specific frequencies between electrodes in a bidirectional manner (Lara et al., 2018; Helfrich et al., 2014).Previous studies have shown tACS improves language function. For example, one study found that 10-Hz tACS acting on the left prefrontal cortex significantly accelerated language responses in healthy individuals (Moliadze et al., 2019); whereas, Katharina and Rufener(2016) observed that 40-Hz tACS reduced the ability of phonological categorisation in young adults but enhanced such ability in the elderly (Rufener et al., 2016). In addition, it has been shown on the bilateral prefrontal cortex that tACS regulates creative thinking in the language domain(Grabner et al., 2018). However, the effect of tACS on phonemic fluency remains unknown.

To this end, the current study selected 10-Hz, 40-Hz, and sham stimulation over the left frontal lobe to investigate the influence of different frequencies of tACS on verbal fluency. Since 10-Hz and 40-Hz tACS will alter different cortical excitatory activities, we predict that these two frequencies will produce different effects on on phonemic fluency.

2. Materials And Methods

2.1. Participants

In the study, 18 healthy, Chinese native speakers (9 female, 9 male) aged 18–25 years (*M* = 20.11, *SD* = 3.36) participated in the study. To calculate our sample size, we used g*Power with the following settings: effect size = 0.25, a level = 0.05, power = 0.9, and correlation among repeated measures = 0.7. The minimum sample size was found to be 16, which we increased to 18 to fully counterbalance the order of stimulation conditions across participants. All participants were right-handed according to the Edinburgh Handedness Inventory. None of them took any medication, had a history of neurological diseases, had metallic head implants, or had stuttering problems. To avoid practice effects, the same subjects did not participate in both the phonemic fluency materials and the formal experiment.

2.2. Phonemic Fluency Materials

Phonemic fluency tests are widely used in language research (Soleman et al., 2013; Miller, 1984) so the present study also employed the task and did a phonemic fluency materials to balance the difficulty of the experimental material across stimulation sessions. There were 24 subjects (12 males, 12 females) with an average age of 24 years who did not participate in the formal experiment but completed the phonemic fluency materials.

In the study of Chinese verbal fluency, it is controversial whether to use a ‘Chinese character’ or a ‘consonant’ as a measure of phonemic fluency, or to follow the phonetic alphabet in which the initial letter is used as a measure of phonemic fluency. Due to distinguished orthographical and phonological rules between ideographic and alphabetic writing, it is appropriate to design a specific Chinese task (X.J, 2014; CHI et al., 2014). The ‘consonant’ task has been used to examine phonemic fluency in Chinese phonemic fluency (C. H. Y. G. X. X. X. Y. C. L. B. Xuejun1, 2014). Therefore, the present study required participants to produce as many words as possible starting with a specific consonant in one minute. Based on the number of words in the lexicon, we selected the consonants ‘j’, ‘d’, ‘x’, ‘y’, ‘sh’, ‘zh’, ‘b’, and ‘m’ as the initial phonemes. The exceptions were proper nouns, such as names of people and places, or words that were repeated.

According to the phonemic fluency materials, we excluded the consonant ‘b’, which produced the largest number of words, and the consonant ‘m’, which produced the least number words. The remaining consonants of ‘y’, ‘j’, and ‘sh’ were divided into difficulty-balanced group A, and the consonants ‘d’, ‘x’, and ‘zh’ were divided into difficulty-balanced group B. Each fluency task included one Group A consonant and one Group B consonant, counterbalancing the difficulty of stimulation sessions.

2.3. Control Tasks

To reveal whether the effect of tACS on phonemic fluency depended on changed attention or the subjects’ expectations, each subject had to implement a control task after the phonemic fluency task. In the control task, a gaze point or an arrow appeared in the middle of the screen, and the arrow randomly directed to the left or right. Subjects had to determine the direction of the arrow by pressing a key as quickly as possible. The reaction time and accuracy were then recorded. There were 200 trials in total, with an interval of 800 ms.

2.4. tACS Protocol

The present study used Neuroelectrics'starstim8 to apply tACS through two circular rubber electrodes (5×5 cm^2) soaked by saline. Based on the 10–20 EEG system, the prefrontal cortex (left BA44/45) was localised to the intersection of T3-Fz and F7-Cz; this localisation method has been used in previous tDCS studies (Ruggiero et al., 2017). We finally placed the tACS electrodes at F3. Based on previous phonology studies, we chose tACS frequencies of 10 Hz and 40 Hz (Moliadze et al., 2019; Rufener et al., 2016). The impedance was kept below 10 kΩ. The current would rise and fall in the initial 15 s and the last 15 s. The constant stimulation time was 20 min. In the sham stimulation, the current rose for 15 s, followed by 30 s of electrical stimulation (10 Hz or 40 Hz), and then fell for 15 s. Prior to the experiment, all subjects underwent a tACS threshold measurement to determine the individual threshold. For this purpose, we used a tACS of 1.0 mA and gradually increased or decreased the stimulation by 0.1 mA. Subjects were asked to keep their eyes open and were asked about any visual or sensory changes. To ensure that the participants did not feel the stimulation but were stimulated throughout the experiment， the stimulation intensity for the formal experiment was kept at 0.1 mA below the lower limit of skin sensation. This approach allowed for adequate stimulation based on individual physiological parameters and also ensured that subjects were unable to distinguish between the three stimulations. The order of the three tACS stimulations was counterbalanced across all subjects.

2.5. Experimental Procedure

The specific experimental procedure is presented in Figure 1.In a normally lit and quiet room, the subject sat in front of a computer screen. Before the experiment, each subject would practice for 2-3 min using consonants that would not appear in the experiment until they were familiarised with the task. Subjects were then asked to watch a cartoon and were given tACS stimulation at the same time. Note, to reduce the variability between subjects with the same visual experience, all subjects watched the same cartoon in all three stimulation sessions. After 20 min of tACS stimulation, participants completed two separate phonemic fluency tasks. The output words would be recorded via a recording device.

Since a 20-min tACS aftereffect can last from 30 to 60 min (Lara et al., 2018), whereas our formal experiment and control tasks lasted only 2-3 min, it was ensured that the subjects throughout the formal experimental and control tasks had a similar tACS effect. Therefore, at the end of each stimulation session, participants performed a control task. The matches of three sets of stimulation (10-Hz tACS, 40-Hz tACS, and sham tACS) and the phonemic fluency task were counterbalanced across participants. E match has an interval of seven days. For example, subject A received a 10-Hz tACS stimulation on day 1 and completed a phonemic fluency task. Seven days later, subject A received sham tACS stimulation and completed a second phonemic fluency task. After another seven days, a 40-Hz tACS stimulation was administered, followed by a final phonemic fluency task. The stimulation used in the three phonemic fluency tasks was different and counterbalanced across participants. In addition, to avoid a practice effect, the order of stimulation frequencies was also counterbalanced across participants.The specific program diagram is presented in Figure 2.

3. Results

The indices of the phonemic fluency task included 1)the number of produced words excluding incorrect, repeated words, and nonsense words and 2) the reaction time when the subject reaches the fifth word. (Lanting et al., 2009)

Statistical analysis was performed using SPSS 16.0 software. The number of produced words and the time when reaching the fifth word were submitted to a two-way repeated-measures ANOVA crossing stimulation session (10 Hz, sham stimulation, 40 Hz).

3.1. Phonemic Fluency Materials

We analysed the number of words produced in the phonemic fluency materials. After excluding errors and repetitions, Figure 3 shows the words produced by the subjects in the phonemic fluency materials for each consonant condition. Based on the average vocabulary produced, we tentatively classified the consonants ‘x’,‘d’,‘zh’, and ‘b’, which difficulty-balanced to the A group. The consonants ‘j’, ‘y’, ‘sh’, and ‘m’, which difficulty-balanced, were divided into the B group. The results of the ANOVA for the A group were $F(1,23) = 9.902$ $p = 0.001$, $n^2 = 0.29$, which is a significant difference in difficulty. After removing the consonant ‘b’, we did not find a significant main effect of difficulty, $F(1,23) = 0.150$, $p =0.861$, $n^2 = 0.76$, indicating no difference in difficulty in the produced words using these consonants. Therefore, we removed the consonant ‘b’ and divided the consonants ‘x’, ‘d’, and ‘zh’ into one group. As for the B group, the main effect of the difficulty reached significance, $F(1,23) = 4.243$ $p = 0.008$, $n^2 = 0.83$. After removing the consonant ‘m’, the main effect of difficulty was not significant, $F(1,23) = 0.297$, $p = 0.744$, $n^2 =0.13$. Therefore, we removed the consonant ‘m’ and divided the consonants ‘j’, ‘y’, and ‘sh’ into one group.The specific phonemic fluency materials data is presented in table 1,and the specific phonemic fluency materials results is presented in figure 3.

Table 1 Number of words generated in the pre-experiment

Consonant	j	d	x	y	sh	zh	b	m
Mean numbers	12.5	14.5	14.7	11.9	12.2	14.2	18.08	10.3
SD	4.31	3.9	3.99	3.01	4.48	3.32	3.46	2.18

3.2. Phonemic Fluency Task

We analysed the average number of words produced. After excluding errors and repetitive words, Tale 2 shows the mean number of words produced by the subjects in the phonemic fluency task in 10-Hz tACS, sham stimulation, and 40-Hz tACS, respectively. The interaction between the task and stimulation was analysed and showed a significant main effect of stimulation, $F(2,34) = 5.636$, $p = 0.008$, $n^2 = 0.16$,such that 10-Hz tACS significantly increased the amount of vocabulary produced by the subjects in the phonemic fluency task compared to the sham stimulation (Figure 4). The main effect of task was not significant, $F(2,34) = 0.949$, $p = 0.344$, $n^2 = 0.86$. The stimulation-task interaction was not significant, $F(2,34) = 0.432$, $p = 0.653$, $n^2 =0.32$. The result was $F(2,34) = 3.807$, $p = 0.032$, $n^2 = 0.183$.The number of words produced by phonemic fluency is presented in table 2,and the mean number of words for each consonant produced in the phonemic fluency is presented in figure 4.

Table 2 Number of words produced by phonemic fluency

Stimulation	10Hz	Sham	40Hz
Mean numbers	15.25	13.02	14.36
SD	5.38	4.17	5.42

3.3. The Reaction Times Required to Reach The Fifth Word

We analysed the reaction times required to reach the fifth word. After excluding errors and repetitive words. A repeated-measures ANOVA obtained a significant main effect of stimulation session, $F(2,34) = 3.985$, $p = 0.039$, $n^2 = 0.15$. As shown in Figure 5, compared to the sham stimulation and 40-Hz, 10-Hz tACS significantly increased time until the subjects reached the fifth word. The interaction between the task and stimulation session was not significant, $F(2,34) = 0.766$, $p = 0.473$, $n^2 = 0.07$.

3.4. Control Experiment

The reaction time and correct rates of the subjects in the control experiment are shown in Figure 6. A repeated-measures ANOVA was conducted for the response times in the control experiment for the three stimulation conditions (10-Hz tACS, sham stimulation, and 40-Hz tACS). The results were $F(2,34) = 0.131$, $p = 0.878$, $n^2 = 0.72$. All three stimulations did not significantly speed up or slow down the reaction time. In the same way, the accuracy in the control experiment for the three stimulation conditions did not differ $F(2,34) = 1.482$, $P = 0.243$, $n^2=0.63$.

These findings indicate that the effect of tACS on phonemic fluency was not dependent on the effect of tACS on the subjects' attention and was not influenced by the subjects' expectations.

4. Discussion

In the present study, we respectively induced 10-Hz tACS, 40-Hz tACS, and sham stimulation over the prefrontal cortex to investigate the effect of tACS on phonemic fluency. Compared to the sham stimulation, 10-Hz tACS significantly increased the amount of vocabulary produced by the subjects in the phonemic fluency task. Also, the response time to reach the fifth word in the phonemic fluency task was significantly shorter with 10-Hz tACS compared to the sham stimulation and 40-Hz tACS. This suggests that 10-Hz tACS improved subjects' response time in the phonemic fluency task.

It is noteworthy that the improvement in phonemic fluency with 10-Hz tACS complements previous studies on tACS in relation to language. According to previous studies, 10Hz-tACS over the prefrontal cortex significantly facilitated speech response speed in healthy individuals (Moliadze et al., 2019). In that study, it was reported that 10-Hz tACS significantly increased theta power during voice decision-making. This may indicate that the improvement in phonemic fluency may be associated with increased theta power. In a study about tACS and fluid intelligence, it was found that the tACS aftereffect of fluid intelligence was associated with changes in theta and alpha bands, which may have functional cross-frequency modulation (Pahor & Jaušovec, 2014); furthermore, theta tACS improved subjects' performance on fluid intelligence tests (Brickman et al., 2005).Previous studies have confirmed that theta is associated with the processing of linguistic features (Rufener et al., 2016). We believe that this may explain why 10-Hz tACS improves phonemic fluency in healthy individuals. Several studies have suggested that verbal fluency is supported by fluid intelligence, meaning that an individual's fluid intelligence affects their verbal fluency. For example, in a large-scale study of frontal lobe patients, researchers interpreted the manifestation of impaired verbal fluency as resulting from a deficit in flow intelligence, which is thought to reflect current abstract thinking and reasoning abilities (Roca et al., 2010).

Previous studies have found effects of tACS on working memory and visuomotor perception as well as other factors. For example, in one study it was shown that tACS applied to the frontal regions significantly improved subjects' working memory capacity (Hoy et al., 2015). Likewise, in a study on tACS and motor function and motor cortical excitability, tACS was shown to have a particularly pronounced effect on motor variability (Wach et al., 2013). Thus, the current behavioural aftereffects may also be due to the effects of tACS on working memory or other factors. However, our control task showed that subjects' reactivity and attention were not affected by different tACS frequencies (either true or false stimuli) or by different tasks. Therefore, the possibility that the improvement of phonemic fluency by tACS may be indirectly due to the improvement of other cognitive functions can be excluded.

In the 40-Hz tACS stimulus, we did not find any stimulus effect on performance, either on the amount of words produced or on the time to reach the fifth word. This result contrasts with our experimental hypothesis based on the study by Katharina (Rufener et al., 2016) who found that 40-Hz tACS reduced phonemic categorisation ability in young people and improved phonemic categorisation ability in older people. Although phonemic categorisation ability is relevant to language ability, it is primarily related to perceptual learning and the auditory system, whereas 40-Hz tACS impairs perceptual learning by interfering with relevant neurotransmitters in the auditory system. However, phonemic fluency and phonological categorisation ability depend on different mechanisms, so 40-Hz tACS had no effect in our study. In the current study, only a few studies have used the aftereffects of tACS to study language, so the aftereffects of tACS on language remain to be discussed.

5. Conclusions

In summary, our results found for the first time that 10-Hz tACS over the prefrontal cortex significantly improved phonemic fluency in healthy individuals, including the number of words generated as well as response speed. Our data confirm the modulatory role of tACS for language ability and its potential role in neurological rehabilitation, and further point to the frequency specificity of tACS. In future studies on tACS and phonemic fluency, the differences brought by different languages, the clinical application of tACS in conditions such as aphasia, and the application to the improvement of phonemic fluency in healthy individuals should be emphasised.

Declarations

Author Contributions: Conceptualization, Y.S. and Q.H.; methodology, Q.H. and Y.S.; software, Q.H.; validation, Q.H.,L.H, and Y.S.; formal analysis, Y.S.; investigation, Q.H.; data curation,Q.H.; writing—original draft preparation, Y.S. and Q.H..; writing—review and editing, Y.S., L.H, and Q.L.; visualization, Q.H. and Y.S.; supervision, Q.L.; funding acquisition, Q.L. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Institute of Brain and Psychological Sciences, Sichuan Normal University (the approval number: SICNUIRB200608).

Informed Consent Statement: Informed consent was obtained from all participants involved in the study.

Data Availability Statement: Data are available on request due to restrictions (for example, privacy or ethical). The data presented in this study are available on request from the corresponding authors.

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Conflicts of Interest: The authors declare no conflicts of interest.

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Figures

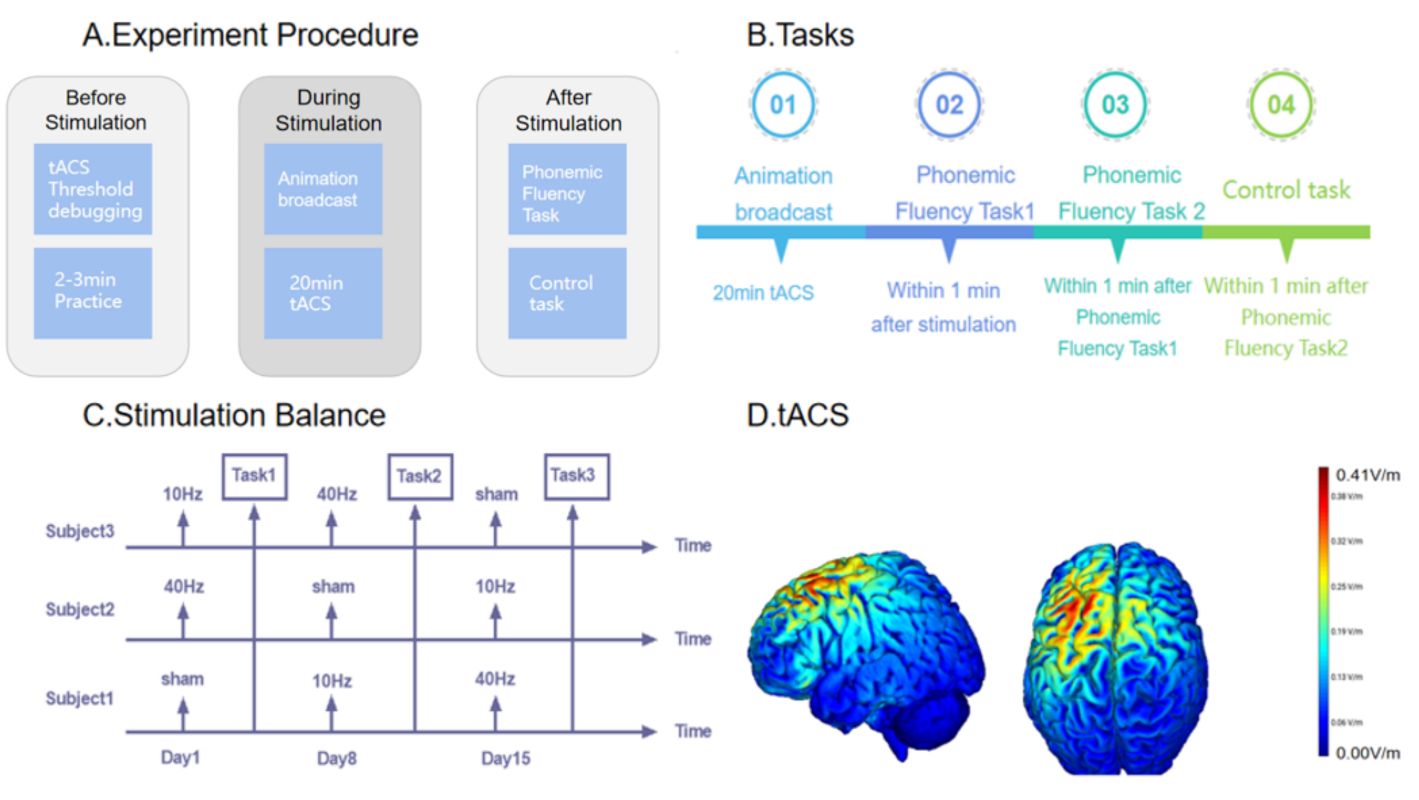

Figure 1

Experimental Design (A) Overview of the experimental design. At the beginning of each session, we completed a tACS threshold debugging, then participants performed a short training of the task. After 20 min of tACS, subjects performed two phonemic fluency tasks and one control task (B) Tasks. After 20 min of tACS, subjects performed the first phonemic fluency task within 1 min of stimulation, then they had another phonemic fluency task within 1 min, ending with a control task within 2 min .(C) The order of stimulations. Prior to each phonemic fluency task, subjects received one stimulation. (D) The tACS applied to the left frontal cortex.

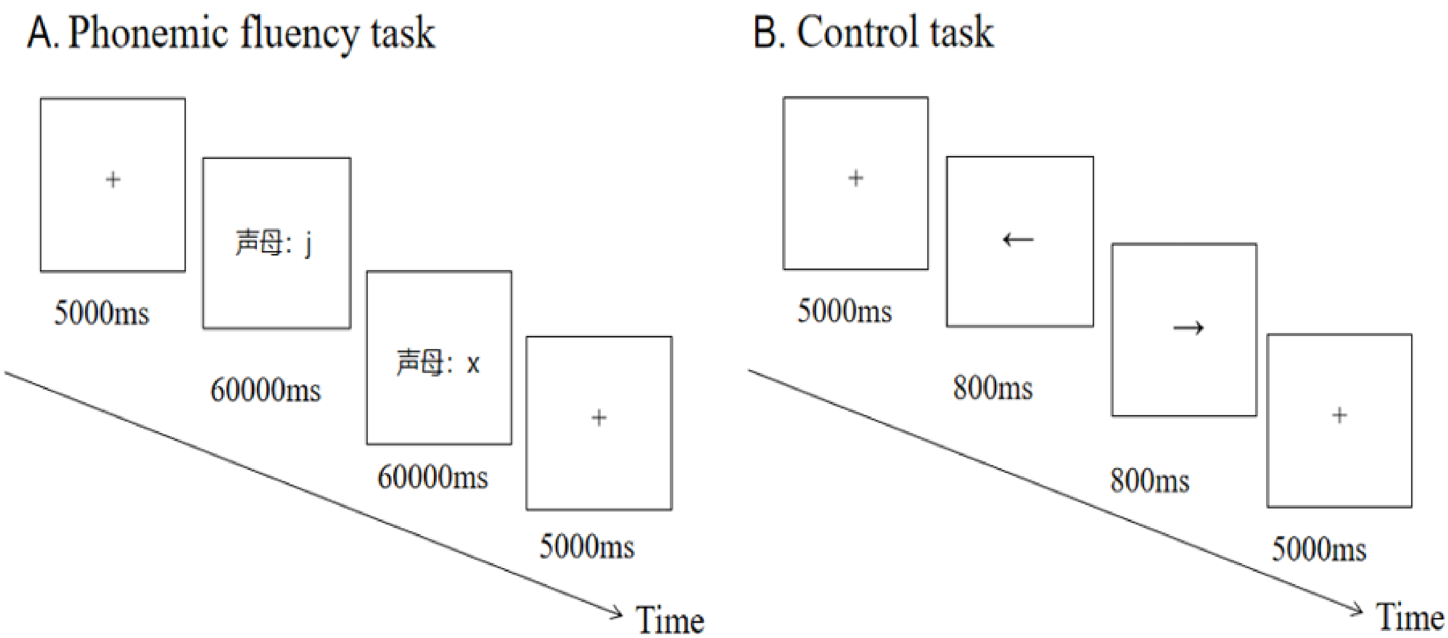

Figure 2

Tasks procedure diagram. （A）Phonemic fluency task. In the phonemic fluency task, a fixation appeared in the middle of the screen for 5,000 ms, and a consonant appeared for 60,000 ms, the words produced by the subjects were recorded via a recording device. （B）Control task. In the control task, a fixation appeared in the middle of the screen for 5,000 ms, and an arrow would randomly direct the left or right for 800 ms. Subjects had to determine the direction of the arrow by pressing buttons.

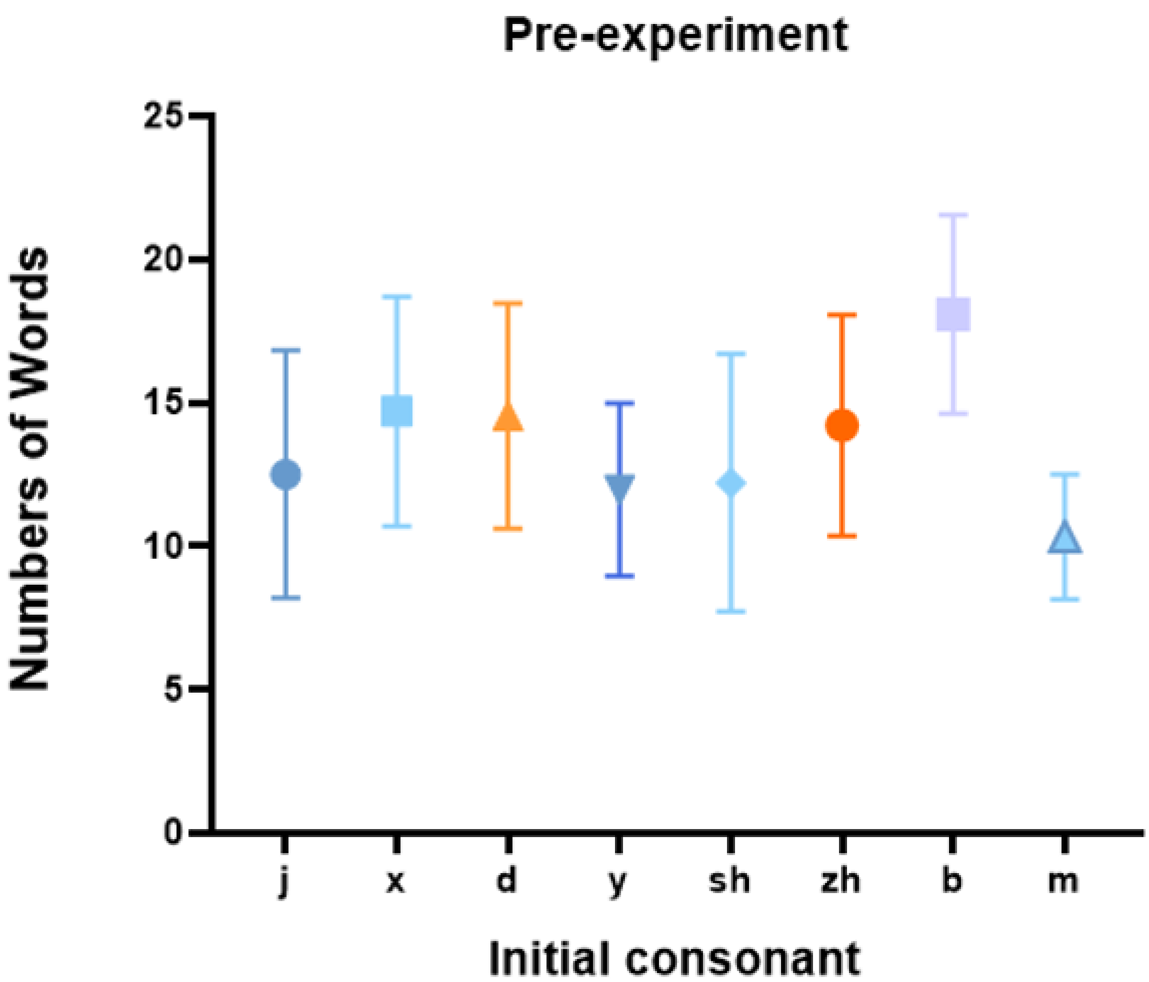

Figure 3

Phonemic fluency material results. The mean number of words for each consonant in the pilot experiment.

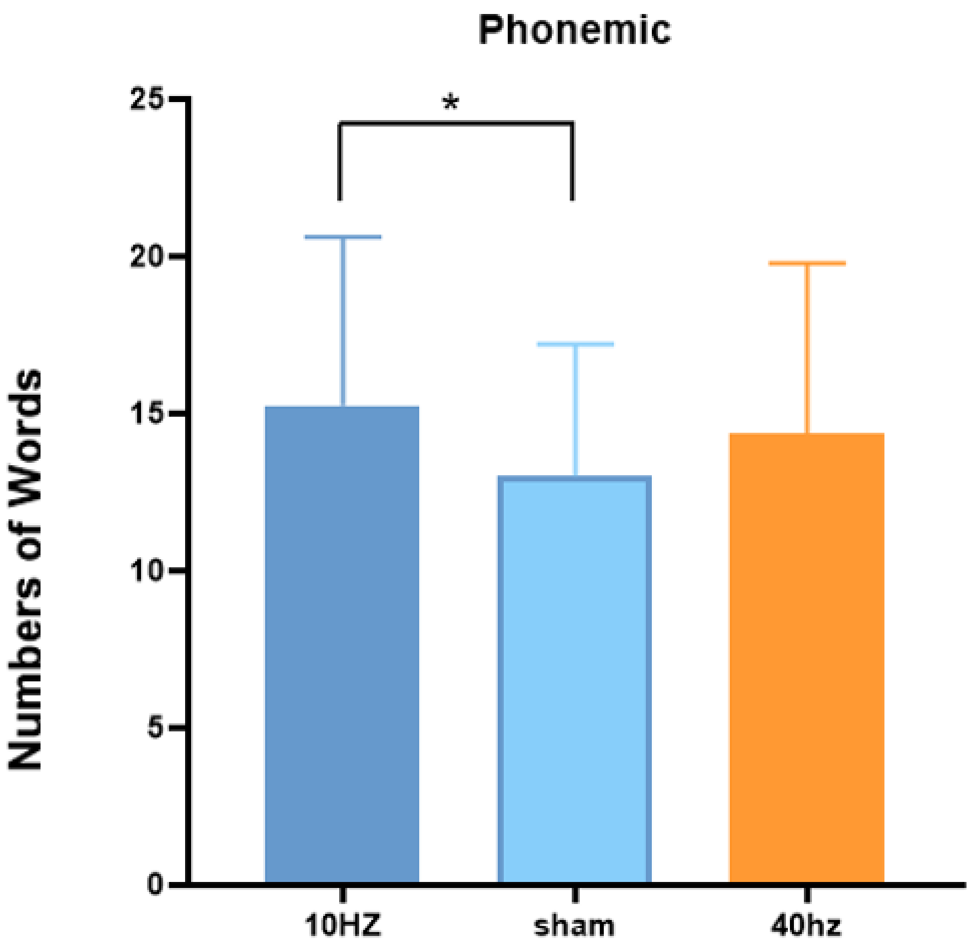

Figure 4

Phonemic fluency task results graph. The mean number of words for each consonant produced in the phonemic fluency task.

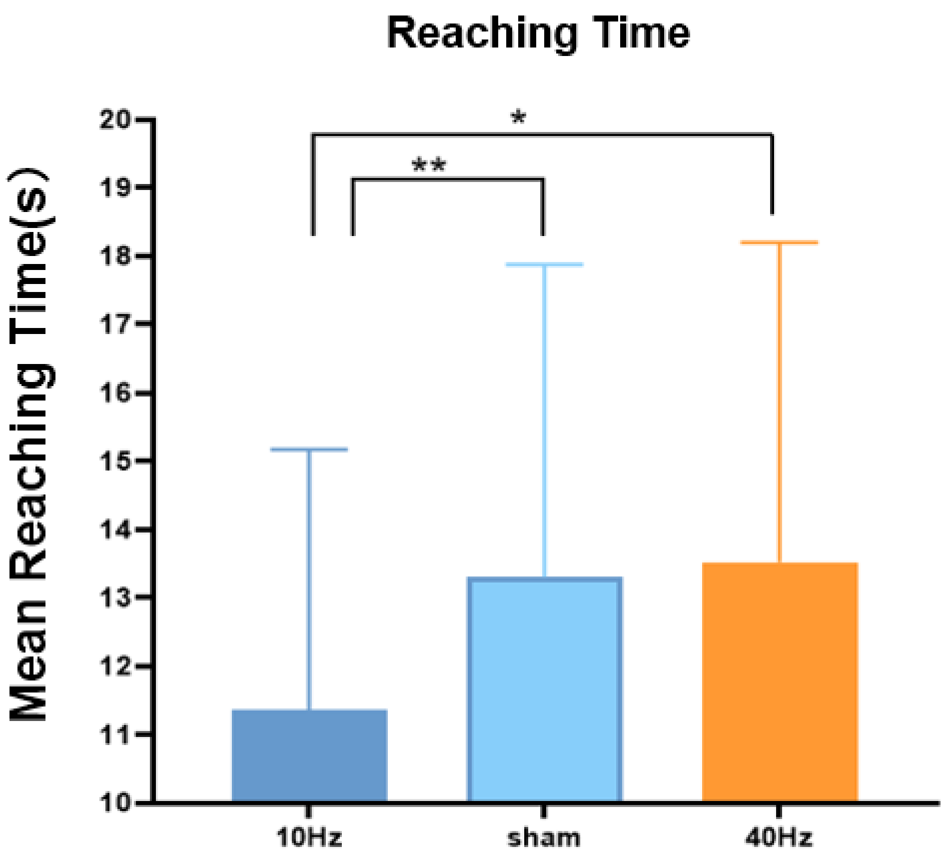

Figure 5

The time required for subjects to reach the fifth word. Mean reaching time (average for one consonant) in the phonemic fluency task in the experiment.

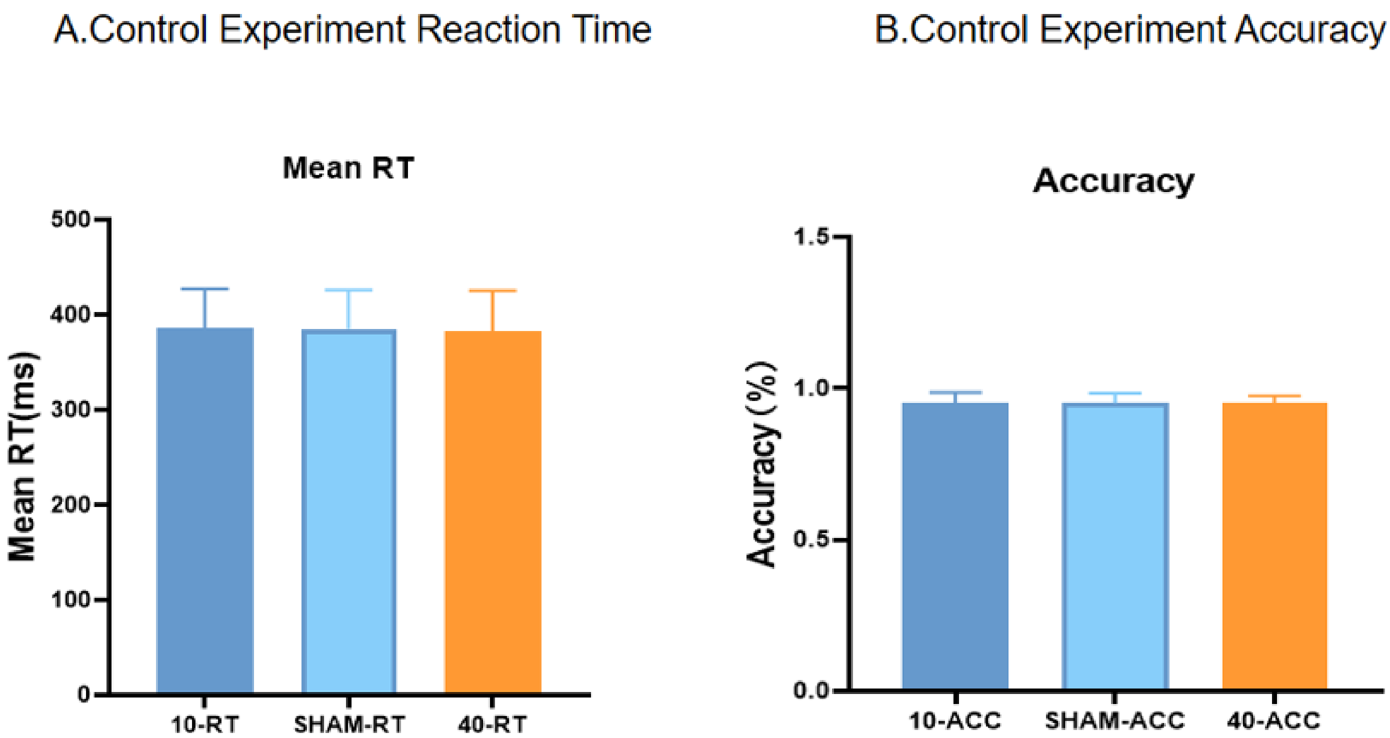

Figure 6

Control experiment results. (A）Control experiment reaction time. (B）Control experiment accuracy.