



Transcranial Focused Ultrasound Stimulation of the Primary Somatosensory Cortex Evokes Hand Tactile Perception: The Effect of Sonication Duration^{△,*}

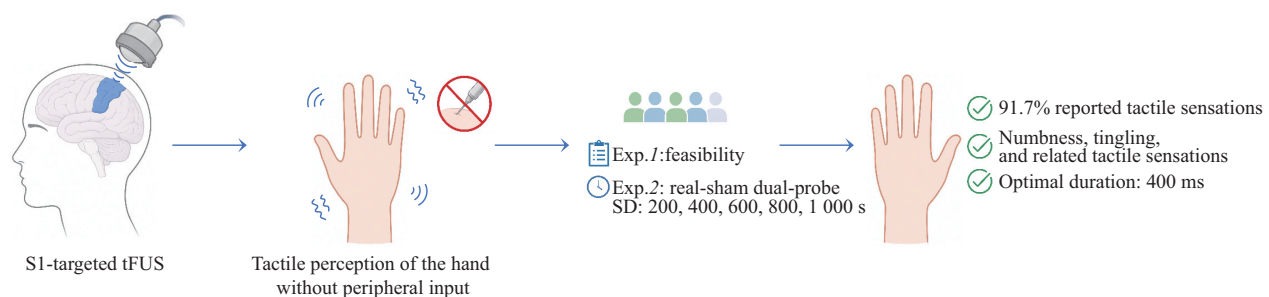
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Graphical abstract



Abstract Objective Transcranial focused ultrasound (tFUS) has emerged as a promising noninvasive neuromodulation technique capable of modulating neural activity with high spatial specificity. However, whether tFUS stimulation of the primary somatosensory cortex (S1) can reliably evoke conscious tactile perception without external peripheral sensory input remains unclear. Therefore, this study examined the feasibility of inducing hand-related tactile perception through targeted S1 stimulation and further investigated how sonication duration (SD), a key temporal parameter, influences the consistency of this perceptual response. The findings may provide empirical evidence for optimizing tFUS parameters in human somatosensory modulation. **Methods** Forty-eight healthy adults participated in the study and were assigned to two experiments. Experiment 1 included 24 participants and was designed to preliminarily examine whether S1-targeted tFUS could evoke hand-related tactile sensations. This experiment comprised two sub-experiments, Experiment 1a and Experiment 1b, with 12 participants in each. Specifically, Experiment 1a used a randomized active stimulation protocol targeting the bilateral S1 to assess the initial feasibility of inducing contralateral tactile perception, whereas Experiment 1b employed an alternating hemispheric design incorporating both active and sham stimulation to verify the specificity of the tFUS-induced sensations. Experiment 2 enrolled another 24 participants and used a real-sham dual-probe design to control for spatial tactile cues that might arise from probe-scalp contact. Five SD levels, including 200, 400, 600, 800, and 1 000 ms, were systematically tested to evaluate how stimulation duration influenced the behavioral response. The primary behavioral outcome was the perceptual consistency rate, quantified according to the accuracy of contralateral tactile localization. **Results** In Experiment 1, 91.7% of participants reported reliable hand-related tactile sensations during active tFUS stimulation, including numbness, tingling,

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or similar sensory experiences. Contralateral localization accuracy under active stimulation was significantly higher than the 0.50 chance level ($P < 0.05$). In contrast, localization performance under sham stimulation did not differ from chance, suggesting that the observed tactile responses were mainly induced by active S1-targeted tFUS stimulation rather than nonspecific stimulation cues. In Experiment 2, perceptual consistency rates significantly exceeded the chance level under the 400 and 1 000 ms SD conditions ($P < 0.05$), whereas no significant effect was observed at 200, 600, or 800 ms. Pairwise comparisons further showed that the 400 and 1 000 ms conditions produced significantly higher perceptual consistency rates than the 200 ms condition ($P < 0.05$). **Conclusion** tFUS stimulation of S1 can elicit distinct hand-related tactile sensations without peripheral sensory input, demonstrating the feasibility of using targeted cortical ultrasound stimulation to induce conscious somatosensory perception. The reliability of this perceptual effect was modulated by sonication duration, indicating that temporal stimulation parameters play an important role in shaping both the occurrence and consistency of behavioral responses. Among the tested conditions, 400 ms appeared to provide a favorable temporal window for generating stable tactile perception, whereas excessively short stimulation may be insufficient to produce consistent responses. These findings highlight the sensitivity of somatosensory networks to ultrasonic modulation and provide useful parameter guidance for the application of tFUS in noninvasive sensory enhancement and cortical functional mapping.

Key words transcranial focused ultrasound (tFUS), sonication duration, tactile perception, primary somatosensory cortex, neuromodulation

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In recent years, focused ultrasound (FUS) neuromodulation has gained increasing attention as a noninvasive tool for both basic neuroscience and treatment of neurological and psychiatric disorders. Its advantages include high spatial resolution and the unique capability to target deep brain structures. Compared with conventional noninvasive brain stimulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), FUS enables precise spatial targeting and effectively modulates neuronal activity through the mechanical interactions of acoustic waves^[1]. Since the first clinical case report using low intensity transcranial FUS (tFUS), its application has expanded to conditions including chronic pain, neurodegenerative disorders, post-stroke cognitive impairment, major depression, and schizophrenia, with studies demonstrating a favorable safety profile and broad therapeutic potential^[2-6]. Concurrently, tFUS is being explored for sensory modulation and cognitive enhancement; for example, stimulation of the primary somatosensory cortex (S1) has been shown to modulate tactile perception and neural activity patterns, potentially improving perceptual sensitivity^[7-8].

The efficacy of tFUS is highly dependent on the precise configuration of multiple stimulation parameters, which collectively govern the spatial distribution of ultrasound energy, the depth of penetration, and the biological outcomes of neuromodulation^[9]. Among these, frequency is a fundamental determinant of spatial resolution and tissue penetration. Low frequency ultrasound (200–800 kHz) provides deeper tissue penetration with less attenuation, making it suitable for targeting

subcortical structures such as the hippocampus, thalamus, and substantia nigra^[10], though at the expense of spatial precision. In contrast, high frequency ultrasound (1–15 MHz) enables superior spatial focusing due to its shorter wavelength, which is advantageous for modulating superficial cortical regions with fine structural organization^[11-12], but suffers from limited penetration and higher skull attenuation. Therefore, frequency selection necessitates a trade-off between penetration depth and spatial specificity.

Acoustic intensity directly influences the energy delivered to the target. While higher intensities can overcome skull attenuation and strengthen modulation of deep regions, excessive levels raise the risk of thermal effects or microvascular injury. Safety guidelines, such as those from the US Food and Drug Administration (FDA) and the international transcranial ultrasound safety and standards taskforce (ITRUSST), recommend that the spatial-peak temporal average intensity (ISPTA) remain below 94 mW/cm², and the spatial-peak pulse average intensity (ISPPA) not exceed 190 W/cm²^[12-14].

Temporal parameters, including pulse duration (PD), pulse repetition frequency (PRF), and duty cycle (DC), jointly determine the temporal characteristics of sonication and the total energy delivered per unit time. Shorter PDs tend to induce transient neuronal excitation, while longer PDs can sustain either excitatory or inhibitory effects^[15]. Higher PRFs increase the instantaneous pulse density, potentiating excitation yet risking neural fatigue or tissue stress; lower PRFs are generally used for inhibitory or chronic modulation. Similarly, a higher DC favors excitation, whereas a lower DC tends to

promote suppression^[16]. Beyond these, the mechanical index (MI) is a crucial safety metric for assessing the risk of nonthermal effects such as cavitation or mechanical perturbation. MI is recommended below 1.9 to prevent adverse bioeffects, including microhemorrhage or cellular damage^[17].

Recently, sonication duration (SD)—the total exposure time per stimulation—has emerged as a key factor influencing the excitatory or inhibitory nature of tFUS-induced neural modulation. Increasing evidence suggests that SD not only determines the cumulative energy delivered during each session but also directly affects the strength and persistence of the neuromodulatory effect^[18]. In animals, shorter SDs preferentially elicit excitation, whereas longer SDs shift the balance to suppression^[19]. In humans, prolonging SD increases motor-evoked potentials (MEPs) success in a dose-dependent manner^[20]. Therefore, goal-directed selection of SD is essential for circuit- and behavior-specific tFUS interventions.

The assessment of tFUS effects has largely relied on electrophysiological and neuroimaging techniques such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). However, these techniques are limited by high cost, complexity, and time consumption. Unlike TMS, which produces observable behavioral or electromyographic outputs, tFUS currently lacks standardized behavioral indices for reliable feedback, constraining its mechanistic investigation and clinical translation^[21–22]. Systematically mapping how stimulation parameters—particularly SD—influence both the neural and behavioral responses to tFUS is therefore critical for translating this technique into sensory rehabilitation and neurotherapeutic protocols. Here, we targeted human S1 to examine whether tFUS elicits conscious tactile sensations in the absence of peripheral stimulation, and to further explore how SD modulates perceptual consistency rate. By elucidating the parameter-effect relationship, we aim to provide guidance on SD optimization and accelerate the clinical application of tFUS for sensory rehabilitation and enhancement.

1 Methods

1.1 Target localization

We employed a probabilistic mapping method that transforms arbitrary cortical targets from montreal neurological institute (MNI) space to the continuous proportional coordinates (CPC) standard scalp space, referred to as the MNI2CPC approach^[23]. Using this approach, the S1 cortical targets defined in

MNI coordinates were projected onto their corresponding locations in the CPC standard scalp space (Figure 1a). Specifically, MNI coordinates (60, −31, 52) and (−60, −31, 52) were mapped to CPC coordinates (0.576, 0.287) and (0.569, 0.711)^[8] respectively. These resulting CPC coordinates represent the standardized scalp positions that correspond to the target cortical regions (Figure 1b)^[22].

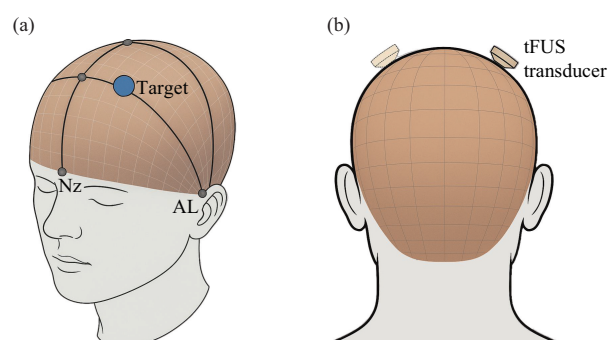


Fig. 1 Target localization and dual-probe setup

(a) Target localization in the continuous proportional coordinates (CPC) system. The blue circle illustrates the projection of one of the primary somatosensory cortex (S1) targets onto the scalp. (b) Illustration of the real-sham dual-probe design used in Experiment 2. Two transducers were placed symmetrically to eliminate spatial tactile cues. The dashed outline represents the location of the sham (phantom) probe, while the solid one indicates the real transcranial focused ultrasound (tFUS) transducer. Nz: nasion; AL: left preauricular point.

1.2 Participants

A total of 48 healthy participants were recruited for this study, including 12 participants in Experiment 1a, 12 in Experiment 1b, and 24 in Experiment 2. Each participant took part in only one experiment. Among all participants, 22 were female, and the ages ranged from 18 to 35 (average 22). The study was approved by The Second Hospital of Anhui Medical University (approval number: YX2025-222) and all participants provided written informed consent prior to participation. None of the participants had a history of psychiatric disorders, brain injury, or invasive brain treatment.

1.3 Experimental design

All experiments were conducted in a quiet, soundproof laboratory. The experiments employed a pulsed FUS stimulation protocol, with ultrasound output controlled by an external trigger signal, as shown in Figure 2. The pulse width of a single ultrasound pulse was 0.2 ms, with a pulse repetition period of 1 ms, corresponding to a PRF of 1 kHz. The tFUS stimulation targets were the left and right S1, with MNI coordinates of (−60, −31, 52) and

(60, -31, 52), respectively. In Experiment 1a, each participant received a total of 4 tFUS stimulation trials, with the stimulation order randomized. Stimulation was applied to the left and right S1 regions, respectively, to preliminarily assess the feasibility of tFUS-induced contralateral hand tactile perception. In Experiment 1b, tFUS was applied alternately to the left and right hemispheres. Each side of S1 underwent 10 active stimulation trials, with 10 corresponding sham stimulation trials. After each trial, participants were asked to report the location and type of tactile sensation perceived in their hands. In the data analysis, the perceptual consistency rate was calculated based solely on the accuracy of tactile localization. A response was considered correct only when the tactile location reported by the participant was on the contralateral hand of the stimulated hemisphere. The tactile sensations reported by participants (*e.g.*, numbness, tingling) were recorded and summarized solely as qualitative indicators of subjective experience and were not included in the statistical analysis of the perceptual consistency rate.

To eliminate potential spatial cues caused by the physical contact of the transducer with the scalp, Experiment 2 adopted a real-sham dual-probe design. Two transducers were symmetrically placed on both sides of the line connecting the nasion and the inion. The real probe delivered ultrasonic stimulation, whereas the sham probe emitted no ultrasound signal and served solely as a tactile-matched control. The sham probe consisted of a circular base and a thin membrane, designed to closely resemble the real probe in both shape and tactile feel, ensuring consistent somatosensory input across conditions.

Left and right side stimulations were presented in a predefined counterbalanced order. Each participant received a total of 100 stimulations, with 10 trials for each SD on both the left and right sides. Within unilateral stimulation blocks, SDs were presented according to a predefined sequence, either increasing from 200 ms to 1 000 ms or decreasing from 1 000 ms to 200 ms, in order to minimize potential order effects. Participants were seated comfortably with their hands resting naturally on their thighs and were instructed to remain still and attend to possible hand sensations. Each trial began with the delivery of a specific SD, followed by a 6 s inter-stimulus interval (ISI), after which the same stimulation was repeated. At 8 s post-stimulation, a 0.3 s auditory cue was presented, and at 8.3 s, participants reported their tactile perception. Each trial lasted 15 s. Participants completed a total of 100 trials, with a 10 min break midway through the session. To ensure participants

safety and comfort, the experimenter actively inquired about scalp sensations both during the midpoint and at the end of the experimental session. If any adverse reactions or discomfort occurred, the experimenters would take appropriate measures to pause or terminate the experiments.

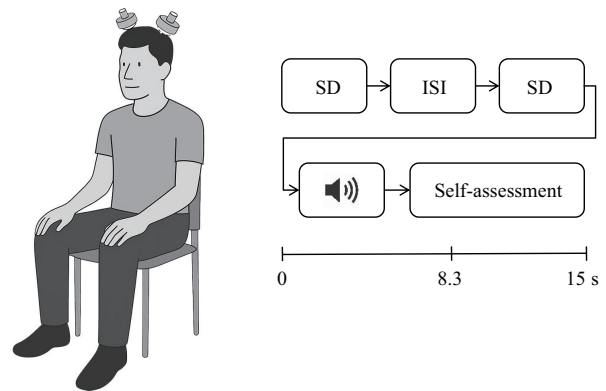


Fig. 2 Experimental trial structure for Experiment 2

1.4 Ultrasound setup

A single-channel ultrasound stimulator (GCBT-1-A001; Zhongke Lvgu Inc., China) was used in this study. The FUS was generated by a transducer (model CO. 5MD-1R50-048) operating at a frequency of 500 kHz, with an element diameter of 70.00 mm and a focal length of 44.58 mm. An appropriate amount of acoustic coupling gel was applied between the transducer cap and the participant's scalp to ensure proper acoustic coupling. The specific ultrasound parameters used in Experiment 2 are illustrated in Figure 3. The ISPPA was 6.63 W/cm², the MI was 1.2, and the DC was 50%, producing a peak rarefactional pressure of 0.892 MPa. The pulse duration (PD) was set to 10 ms, and the SD included five conditions: 200, 400, 600, 800 and 1 000 ms. The ISI was 6 s. All ultrasound waveforms complied with FDA safety standards, and temperature measurements confirmed that heating remained within safe limits, ensuring no risk of skin or skull damage.

1.5 Data processing

The number of correct responses under each condition was recorded, and the proportion of correct responses was calculated as the perceptual consistency rate. To examine the effect of SD, a one-way repeated-measures analysis of variance (ANOVA) was performed to evaluate the overall effect of different SD conditions on perceptual consistency rate. Relevant statistical assumptions were checked prior to the analysis, and appropriate corrections were applied when necessary. Post hoc

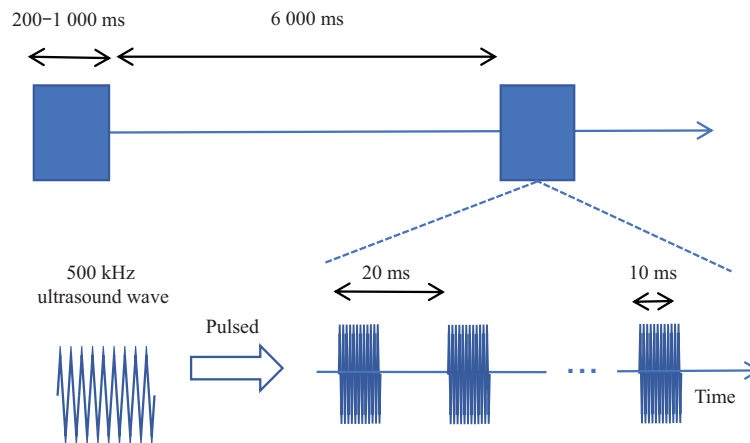


Fig. 3 Schematic of the ultrasound stimulation protocol

comparisons were conducted using Bonferroni correction; in the present study, these comparisons were mainly performed between each SD condition and the 200 ms condition. In addition, one-sample *t*-tests were conducted to determine whether performance under each condition was above chance level. Because the tactile localization task employed a two-alternative forced-choice paradigm (left hand vs. right hand), the theoretical probability of a correct response under random guessing was 50%; therefore, the chance level was defined as 0.5. All statistical analyses were conducted using SPSS software (version 22.0; IBM Corp., USA).

2 Results

2.1 Experiment 1

In Experiment 1, participants reported reliable tactile sensations induced by tFUS stimulation. 91.7% (22/24) of participants reported perceiving tactile sensations, with numbness and slight muscle twitching being the most commonly reported experiences. The consistency of tactile localization varied across participants and stimulation conditions, and the localization consistency rates for individual participants are summarized in Table 1.

In experiment 1b, as shown in Figure 4, one-sample *t*-tests were conducted to compare response accuracy under each stimulation condition against chance level (0.5). Under the active stimulation condition, the mean accuracy (0.613 ± 0.039) was significantly higher than chance, $t(11) = 2.362$, $P = 0.038$. In contrast, accuracy under the sham stimulation condition (0.433 ± 0.034) did not differ significantly from chance level, $t(11) = -1.97$, $P = 0.074$. Taken together, these findings suggest that

Table 1 Types of sensations reported during stimulation ($n=24$)

Types of sensations	Frequency ($n/24$ (%))
Numbness	18/24 (66.70)
Twitching	12/24 (50)
Heat sensation	6/24 (25)
Pressure sensation	10/24 (41.60)
Soreness	4/24 (16.60)
Tingling	12/24 (50)
Ratio of subjects reported	22/24 (91.6)

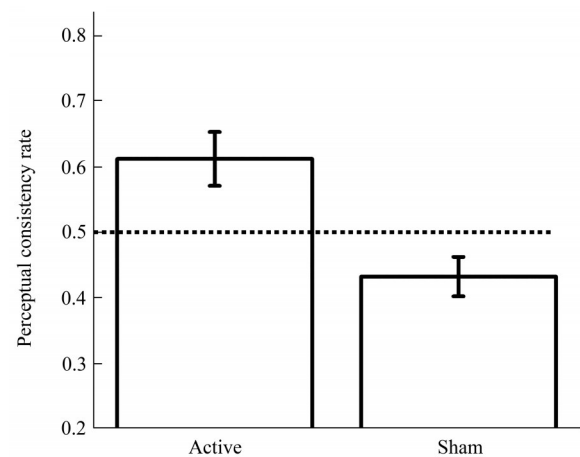


Fig. 4 Perceptual consistency rate under different tFUS stimulation conditions

tFUS can induce tactile sensations that are reliably perceived by participants. Moreover, under the active stimulation condition, participants were able to identify the stimulation location at a level significantly above chance, whereas no such effect

was observed under the sham condition, indicating that this perception was unlikely to be due to random guessing or a simple response bias.

2.2 Experiment 2

2.2.1 Analysis of variance for the effect of SD

ANOVA revealed a significant main effect of SD on the perceptual consistency rate, $F(4, 92)=4.756$, $P=0.002$. Bonferroni-corrected post hoc pairwise comparisons showed that the perceptual consistency rates under the 400 ms and 1 000 ms conditions were significantly higher than that under the 200 ms condition ($P<0.05$), whereas no other pairwise comparisons reached statistical significance (Figure 5). Although the 1 000 ms condition showed a slightly higher mean perceptual consistency rate, the 400 ms condition already produced performance significantly above chance and significantly higher than the 200 ms condition, while not differing significantly from the longer SD conditions. These results suggest that 400 ms may represent a relatively efficient stimulation duration for inducing consistent tactile perception among the tested SD levels.

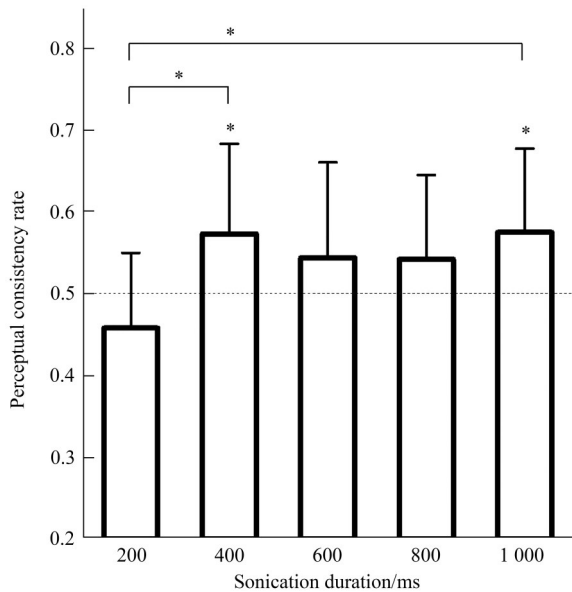


Fig. 5 Behavioral task perceptual consistency rate across different sonication duration (SD) conditions

Bars marked with * indicate performance significantly above chance level (0.5) ($P<0.05$), whereas * indicates significant Bonferroni-corrected pairwise comparisons between conditions ($P<0.05$).

2.2.2 One-sample *t*-tests compared with chance level

One-sample *t*-tests were performed to compare the five SD levels against the chance level (0.5), followed by the false discovery rate (FDR) correction for multiple comparisons. As shown in Table 2 and

Figure 5, the results showed that perceptual consistency rate was significantly above chance under the 400 ms ($P<0.05$), and 1 000 ms ($P<0.05$) conditions. Although participants' perceptual consistency rate under the 600 ms ($P=0.057$) and 800 ms ($P=0.069$) conditions exceeded 0.5, the differences did not reach statistical significance.

Table 2 Effect of ultrasound sonication duration on behavioral response perceptual consistency rate

Duration/ms	Rate (mean±SD)	P-value (Bonf.)
200	0.458±0.092	–
400	0.573±0.110	0.003*
600	0.545±0.116	0.057
800	0.542±0.103	0.069
1 000	0.576±0.102	0.002*

Pairwise comparisons are Bonferroni-corrected relative to the 200 ms condition ($n=24$).

Overall, the influence of SD on task performance exhibited a duration-dependent pattern. While both the 400 and 1 000 ms conditions produced perceptual consistency rate significantly above chance, the 600 and 800 ms conditions showed nonsignificant trends above chance, suggesting a potential nonlinear relationship between SD and behavioral performance.

3 Discussion

This study aimed to investigate the neuromodulatory effects of tFUS on the human S1, with a particular focus on how SD influences the behavioral output of tactile perception. The results showed that, within a safe intensity range, tFUS targeting S1 could directly induce conscious tactile sensations with somatotopic localization specificity in the absence of peripheral sensory input. In addition, tactile localization accuracy did not increase linearly and indefinitely with increasing SD, but instead exhibited a complex non-monotonic pattern: performance reached its peak at 400 ms, suggesting an optimal perceptual window, whereas longer durations (600–800 ms) showed a plateau-like effect with only marginal significance. These findings provide further insight into the spatiotemporal integration and adaptive mechanisms through which neural networks respond to ultrasonic mechanical stimulation.

The successful induction of tactile perception observed in the present study is broadly consistent with previous research on noninvasive brain stimulation and sensory neuromodulation. Early

studies showed that brief excitation of the somatosensory cortex can evoke subjective sensory experiences and may occasionally co-activate motor-related circuits. For example, previous studies using TMS, found that stimulation of S1 within specific temporal windows could significantly alter or suppress the detection of peripheral tactile signals^[23-24]. Later, Blankenburg *et al.*^[25], combining noninvasive stimulation with fMRI, further demonstrated that such stimulation could directly engage dynamic cortical networks and evoke genuine tactile experiences even in the absence of peripheral mechanical input.

In the field of ultrasonic neuromodulation, the performance improvement observed in the present study under the optimal sonication duration further supports and extends previous findings. Liu *et al.*^[26] reported that tFUS could enhance neuronal excitability in S1 and significantly improve tactile discrimination performance. Similarly, Kim *et al.*^[5] showed that tFUS targeting S1 and its thalamic pathways could not only induce sensory percepts but also strengthen short-term functional connectivity within the sensorimotor network. Taken together, these findings suggest that tFUS is capable of inducing short-term cortical plasticity and network reorganization, thereby providing a macroscopic neurophysiological basis for the tactile percepts observed in the present study.

Beyond large-scale changes in brain networks, recent electrophysiological and molecular studies have provided more direct insights into the mechanisms underlying tFUS neuromodulation. At the molecular level, the mechanical force generated by ultrasound acts on neuronal cell membranes and activates mechanosensitive ion channels. Previous studies suggest that transient receptor potential canonical 6 (TRPC6) may be an important channel involved in detecting ultrasonic mechanical stimulation in the mammalian brain. Mild ultrasound-induced deformation of the cell membrane may first trigger the opening of TRPC6, leading to an initial depolarization of the neuron^[27]. This depolarization may then further activate voltage-gated sodium channels and calcium channels, promote Ca^{2+} influx, and ultimately trigger action potential generation.

At the cellular and local circuit levels, this process may also show a certain degree of selectivity. Studies have found that ultrasound more readily drives regular spiking units in the S1 region, which are thought to mainly correspond to excitatory pyramidal neurons. Once these local neurons are activated, their excitatory activity may rapidly

propagate through the cortico-thalamo-cortical circuit, further amplifying sensory signals and thereby facilitating tactile perception^[28].

In addition, computational biophysical evidence based on extended Hodgkin Huxley models suggests that tFUS may not function simply as a direct activator of neurons during sensory induction, but rather as a subthreshold co-modulator. In other words, the stimulation provided by tFUS alone may not always be sufficient to generate a stable percept, but it may interact with ongoing endogenous neural activity and together promote percept formation^[29]. In the present study, participants were instructed to actively attend to local tactile sensations, and this attentional state may have placed S1 and related sensory networks in a more excitable condition. Under such circumstances, the mechanical energy delivered by tFUS may have been more likely to summate with endogenous subthreshold neural activity, thereby helping local cortical activity cross the perceptual threshold and giving rise to conscious tactile experience.

One important finding of the present study is that the relationship between SD and behavioral performance was not simply linear, but may instead reflect dynamic neuromodulatory processes unfolding across multiple timescales. When SD was 200 ms, the perceptual consistency rate did not differ significantly from chance level, suggesting that such a brief stimulation period may have been insufficient to generate a neuromodulatory effect to support reliable percept formation in the target region. From a mechanistic perspective, short-duration ultrasound may already activate mechanosensitive ion channels such as TRPC6^[27] and Piezo-type mechanosensitive ion channel component 1 (Piezo1)^[30] and induce a certain degree of Ca^{2+} influx; however, this ionic accumulation may remain at a subthreshold level. Such subthreshold calcium accumulation may be insufficient to recruit enough excitatory neurons or to trigger ion-channel amplification leading to stable population firing^[31], and therefore may fail to elicit a tactile percept that can be reported consistently.

When SD increased to 400 ms, the perceptual consistency rate rose significantly ($P=0.003$), suggesting that this duration may represent a more favorable temporal window for the generation of stable conscious tactile perception. One possible explanation is that, within this time range, ultrasound-induced mechanosensitive channel activation, Ca^{2+} accumulation^[31], and synchronous activity among local excitatory neurons reach a more effective level of integration, thereby facilitating the transition of

local cortical activity across the perceptual threshold^[28].

Interestingly, when SD was further extended to 600 and 800 ms, the perceptual consistency rate did not continue to increase, but instead remained at approximately 0.54, showing only a trend above chance level. This pattern suggests that the behavioral effect of tFUS may enter a plateau phase within this duration range. One possible interpretation is that, as SD increases, the net excitatory gain of the local circuit may no longer rise in a linear manner. Existing electrophysiological evidence suggests that tFUS may exert cell-type-selective effects on neuronal populations and may differentially modulate excitatory and inhibitory components within local circuits^[32]. In parallel, sustained mechanical stimulation may also lead to adaptation or partial desensitization of mechanosensitive ion channels, which together may constrain further improvement in behavioral performance^[27, 30].

When SD reached 1 000 ms, the perceptual consistency rate again became significantly higher than chance level ($P=0.002$), suggesting that longer duration stimulation may still support percept formation. However, whether this effect reflects enhanced local excitation or the engagement of slower network level processes remains unclear. Previous human studies have shown that tFUS can induce changes in functional connectivity and neurochemical states that outlast the stimulation period, raising the possibility that longer sonication durations may recruit broader integrative processes^[33-34]. Accordingly, the re-emergence of a significant effect at 1 000 ms may reflect the contribution of slower local dynamics or distributed network mechanisms. Nevertheless, this interpretation remains speculative and will require further validation through concurrent electrophysiological and neuroimaging investigations.

Although the present study provides relatively robust empirical support for optimizing tFUS stimulation parameters and offers preliminary insights into its potential mechanisms, several important methodological limitations should be acknowledged. First, the effects of tFUS were not further validated under specific task states. Although the present study adopted relatively simplified and controlled experimental conditions to prioritize testing the basic feasibility of inducing tactile perception in the S1 using tFUS, it did not incorporate specific task paradigms to evaluate whether these effects would remain stable and consistent across different behavioral states. Therefore, the current findings

mainly reflect tFUS induced effects under low task-demand conditions, and their applicability and reliability in more specific task contexts remain to be established. Future studies should incorporate more targeted task designs to systematically examine how task demands, attentional allocation, and behavioral goals may modulate tFUS effects, thereby strengthening the interpretability and external validity of the findings. Second, the examination of tFUS stimulation parameters remained relatively limited, and the potential combined effects or interactions among different parameters were not systematically assessed. Although the present study identified relatively optimal stimulation parameters, this conclusion was based primarily on comparisons among a limited number of parameter combinations within a predefined range, rather than on a systematic exploration of the multidimensional parameter space. As such, key parameters such as acoustic intensity, duty cycle, pulse repetition frequency, and stimulation duration were not examined in terms of their possible synergistic effects on S1 responses. Given that the neuromodulatory effects of tFUS are unlikely to be determined by any single parameter in isolation, but rather by the coupling among multiple parameters, the current definition of optimal parameters should be regarded as provisional. Third, responses to tFUS stimulation varied to some extent across participants. However, because the primary focus of the present study was on overall group-level effects, the potential sources of this variability were not systematically examined. Given the current sample size and the limited availability of individual level characteristic data, we were unable to further assess the possible influence of factors such as sex, age, or cortical structure. Future studies should adopt more systematic factorial designs or parameter-scanning approaches to more comprehensively elucidate the joint effects of different parameter combinations on S1 activity and related cortico-thalamo-cortical network responses. Finally, the generalizability of the present findings remains to be established. The optimal stimulation parameters identified in this study were derived from a group of healthy young adults. Given that older adults and stroke patients may exhibit alterations in neuroplasticity, cortical excitability, and network organization, it remains unclear whether the same parameter settings can be directly generalized to these populations. Further validation through larger scale and more targeted clinical studies is therefore warranted.

4 Conclusion

This study demonstrates that low-intensity tFUS targeting the human S1 can induce conscious tactile sensations with a degree of somatotopic specificity in the absence of peripheral sensory input. The results further show that SD plays an important nonlinear modulatory role in this process. Among the tested conditions, 400 ms yielded the best behavioral performance, suggesting that this duration may provide a more favorable temporal window for the spatiotemporal integration of local neural activity and the generation of stable tactile perception. In contrast, further prolongation of stimulation to 600–800 ms did not lead to a linear improvement in perceptual performance, but instead showed a plateau-like pattern, which may be related to dynamic changes in local excitatory-inhibitory balance and adaptive processes during sustained stimulation. Overall, these findings advance our understanding of the neural mechanisms underlying tFUS-induced somatosensory perception and provide useful guidance for parameter optimization in future applications such as sensory neurorehabilitation and noninvasive brain-computer interfaces.

Date Availability The datasets used and/or analyzed during the present study are not publicly available due to ethical restrictions and participant privacy considerations, but are available from the corresponding author on reasonable request.

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初级体感觉皮层进行经颅聚焦超声刺激可诱发 手部触觉感知：超声持续时间的影响^{△,*}

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摘要 **目的** 经颅聚焦超声 (transcranial focused ultrasound, tFUS) 作为一种具有前景的无创神经调控技术, 能够以高空间特异性调节神经活动。然而, 在缺乏外部周围感觉输入的情况下, tFUS对初级体感觉皮层 (primary somatosensory cortex, S1) 的刺激能否可靠地诱发有意识的触觉感知, 目前尚不明确。本研究旨在探讨通过靶向S1刺激诱发手部相关触觉感知的可行性, 并进一步探究作为关键时间参数的超声持续时间 (sonication duration, SD) 如何影响该知觉反应的一致性。本研究结果有望为优化人类体感觉调控中的tFUS参数提供实证依据。**方法** 48名健康成年人参与了本研究, 并被分配到两个实验中。实验1包括24名参与者, 初步考察S1的tFUS刺激能否诱发与手相关的触觉。该实验包含两个子实验, 即实验1a和实验1b, 各招募12名受试者, 其中, 实验1a采用针对双侧S1的随机化有效刺激方案, 评估诱发对侧触觉感知的基本可行性, 而实验1b则采用交替半球设计, 结合真刺激和假刺激, 验证tFUS诱发感觉的特异性。实验2招募了另外24名参与者, 并采用真假刺激双探头设计, 控制可能源于探头与头皮接触的空间触觉线索。系统测试了5个SD条件, 包括200、400、600、800和1 000 ms, 评估刺激持续时间如何影响行为反应。主要行为结果指标为感知一致率, 该指标根据对侧触觉定位的准确性进行量化。**结果** 在实验1中, 91.7%的受试者在真实tFUS刺激期间报告了可靠的手部相关触觉感觉, 包括麻木、刺痛或类似的触觉体验。真实刺激下的对侧定位准确率显著高于0.50的偶然水平 ($P<0.05$)。相比之下, 假刺激下的表现与偶然水平无异, 这表明, 所观察到的触觉反应主要由针对S1的真实tFUS刺激诱发, 而非来源于非特异性刺激线索。在实验2中, 400和1 000 ms条件下的感知一致率显著高于偶然水平 ($P<0.05$), 而在200、600和800 ms条件下未达到显著水平。进一步的两两比较显示, 400和1 000 ms条件下的感知一致率显著高于200 ms条件 ($P<0.05$)。**结论** 对S1进行tFUS刺激可在没有外周感觉输入的情况下引发明显的手部相关触觉, 这表明利用靶向皮层超声刺激诱导有意识的体觉感知是可行的。这种感知效应的可靠性受SD的影响, 该参数对行为反应的产生及其一致性具有重要的调控作用。在测试的各种条件下, 400 ms可能提供了产生稳定触觉感知的一个理想时间窗口, 而刺激时间过短可能不足以产生一致的反应。这些发现凸显了体觉网络对超声调制的敏感性, 并为tFUS在无创感觉增强和皮层功能映射中的应用提供了有价值的参数指导。

关键词 经颅聚焦超声 (tFUS), 超声持续时间, 触觉感知, 初级体感觉皮层, 神经调控

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