Effect of Acupuncture Treatment on Cortical Activation in Patients With Tinnitus: A Functional Near-Infrared Spectroscopy Study

Xianghua Yu, Bin Gong, Hao Yang, Zheng Wang, Gaowei Qi, Jie Sun, Yu Fang, and Xiaoli Fan

***Abstract*— Tinnitus is an auditory phantom percept that affects the perception of sound in the patient's ears, and the incidence of prolonged tinnitus is as high as ten to fifteen percent. Acupuncture is a unique treatment method in Chinese medicine, and it has great advantages in the treatment of tinnitus. However, tinnitus is a subjective symptom of patients, and there is currently no objective detection method to reflect the improvement effect of acupuncture on tinnitus. We used functional near-infrared spectroscopy (fNIRS) to explore the effect of acupuncture on the cerebral cortex of tinnitus patients. We collected the scores of the tinnitus disorder inventory (THI), tinnitus evaluation questionnaire (TEQ), hamilton anxiety scale (HAMA), and hamilton depression scale (HAMD) of eighteen subjects before and after acupuncture treatment, and the fNIRS signals of these subjects in sound-evoked activity before and after acupuncture treatment. According to the fNIRS detection results of tinnitus patients, acupuncture increased the concentration of oxygenated hemoglobin in the temporal lobe of tinnitus patients, and affected the activation of the auditory cortex. The study may reflect the neural mechanisms of acupuncture treatment for tinnitus and ultimately help to provide an objective evaluation method for the therapeutic effect of acupuncture treatment for tinnitus.**

***Index Terms*— Functional near-infrared spectroscopy, tinnitus, acupuncture, hemodynamic response, auditory stimulation.**

I. Introduction

TINNITUS is an auditory phantom percept with a tone, hissing, or buzzing sound in the absence of any objective physical sound source [1]. It usually manifests as an abnormal sound perception in the ear or head of the patient, but it is difficult for the outside world to perceive the existence of the sound source [2], [3]. Ten to fifteen percent of people have prolonged tinnitus that requires medical evaluation [4]. Long-term tinnitus can affect people's work, hearing, mood and sleep, and severe tinnitus can cause psychological stress and even disability in patients [5].

Tinnitus is an extremely common clinical symptom due to its complex etiology and its unclear pathogenesis [6]. Therefore, the treatment of tinnitus has always been one of the most cutting-edge research topics in ontology. There is evidence that tinnitus is associated with functional alterations in the central nervous system [7]. Several animal studies have been used to explain the underlying central nervous system mechanisms of tinnitus. Changes in the auditory cortex have been detected in animal models of tinnitus, and putative neural correlates of tinnitus, such as increased neural firing rates and enhanced neural synchrony, have been found [2]. In humans, increased activity in the auditory cortex is thought to be associated with tinnitus neurons [6], [8]. Several studies have shown that tinnitus is associated with an imbalance of excitation and inhibition of neural activity, which is enhanced by spontaneous activity along the auditory pathway [9], [10].

Acupuncture is a unique treatment method of traditional Chinese medicine. It is a practice of treatment based on influencing acupuncture points or acupoints on the body by inserting needles [11]. Acupuncture has great advantages in the treatment of tinnitus due to its characteristics of simple operation, quick effect, low cost, and easy popularization [12]. Clinical studies have found that acupuncture can increase blood and lymphatic circulation in the cochlea, improve the metabolic level of surrounding tissues and cells, increase the excitability of the auditory center of the cerebral cortex, enhance the hearing sensitivity of the affected ear, and improve the corresponding cerebral cortex's perception of sound and analytical power [13]. Clinical practice has shown that acupuncture therapy has a good effect on the treatment of tinnitus [14]. In recent years, the efficacy of acupuncture in the treatment of tinnitus has been recognized by an increasing number of scholars, but its effect is still unclear [15]. Although there have been studies on animal models of tinnitus, tinnitus is a subjective symptom of patients, and there is currently no objective detection method to reflect the improvement effect of acupuncture on tinnitus [16].

Manuscript received 20 June 2022; revised 15 October 2022 and 12 November 2022; accepted 21 December 2022. Date of publication 2 January 2023; date of current version 2 February 2023. This work was supported in part by the Chinese Medicine Research Fund from the Shanghai Municipal Health Commission under Grant 2014LP024A.
(Corresponding authors: Yu Fang; Xiaoli Fan.)

Xianghua Yu, Bin Gong, Hao Yang, and Yu Fang are with the Institute of Intelligent Equipment and Precision Detection, School of Mechanical and Automotive Engineering, Shanghai University of Engineering Science, Shanghai 201620, China (e-mail: y_xianghua@163.com; gong12185216@126.com; yanghao2525@sues.edu.cn; fangyu_hit@126.com).

Zheng Wang, Gaowei Qi, Jie Sun, and Xiaoli Fan are with the Shanghai Songjiang District Central Hospital, Shanghai 201699, China (e-mail: ytwang0220@163.com; 29246529@qq.com; 494467120@qq.com; fxldoctor88@126.com).
Digital Object Identifier 10.1109/TNSRE.2022.3231899

With the rapid development of modern medical technology, different functional imaging techniques have been used in brain regions associated with tinnitus [17]. Commonly used methods include electroencephalogram (EEG), magnetoencephalography (MEG), positron emission computed tomography (PET), and functional magnetic resonance imaging (fMRI). Each of these imaging modalities has limitations, but findings using the above imaging modalities have confirmed that tinnitus brain changes may reflect correlations with tinnitus neural factors described in animal models [18]. An updated optical imaging technique is needed to further investigate some hypotheses related to the human tinnitus brain.

In recent years, functional near-infrared spectroscopy (fNIRS) has become a hot spot in tinnitus research and acupuncture research. fNIRS is a novel noninvasive functional brain imaging method that can detect brain activity by measuring signals related to blood oxygen levels [19]. Both functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) work on the principle of measuring changes in cerebral blood flow in response to neuronal activation through time-dependent fluctuations in hemoglobin species in the brain [20]. FMRI studies have shown that acupuncture can affect the cerebral hemodynamic response and induce hemodynamic changes in the brain network [21], [22], acupuncture as an alternative therapy method may reduce the severity of tinnitus by decreasing the time variability of dynamic functional connectivity in patients with chronic tinnitus [23]. However, the accuracy of fMRI time resolution is not high enough, the cost of instruments is high, the instruments are huge, and they are too sensitive to the movement of the subjects' bodies during the experiment. Compared to fMRI, fNIRS has the advantages of no noise, good portability, low cost, and good temporal resolution and it is more suitable for hearing-related research [24]. The effect of tinnitus on the brain is related to abnormal neural activity. fNIRS is a imaging technology that has the least impact on tinnitus perception and it is very suitable for tinnitus research [25]. As a portable neuroimaging system, fNIRS can be used by patients who are unable to tolerate an magnetic resonance environment [20]. The effect of acupuncture treatment can be identified according to the hemodynamic response measured by fNIRS [26], [27]. Therefore, the use of functional near-infrared spectroscopy to detect the effect of acupuncture on tinnitus is feasible.

The purpose of this study was to investigate the effect of acupuncture treatment on cortical activation in patients with tinnitus and to explore the ability to use fNIRS as a potential indicator to assess the efficacy of acupuncture treatment for tinnitus. To this end, in an experimental design, we compared the activation of cerebral cortex under sound-evoked activity in patients with tinnitus before and after acupuncture treatment, and discussed the effects of acupuncture on symptoms and hemodynamic activity of tinnitus patients.

II. Material and Methods

A. Participants

All participants were from the outpatient department of traditional Chinese medicine and the outpatient department of otolaryngology of Shanghai Songjiang District Central Hospital. Eighteen participants (8 females and 10 males, age 27-67 years, average age 49.38 years, average duration 20.44 months) with bilateral subjective tinnitus participated in the study (Table I). All participants were tested using an audiogram, within the measured frequency range (including 8000 Hz), the average pure-tone threshold was lower than 30 dB HL. The Shanghai Songjiang District Central Hospital approved the study, which was conducted in accordance with the Declaration of Helsinki. The basic measurement principle of fNIRS was explained to each participant before the experiment, and written informed consent was obtained from each participant. Treatment costs were reimbursed for each participant. The exclusion criteria included the following: 1) patients with objective tinnitus; 2) patients with external ear disease or acute inflammatory disease of the middle ear; 3) pregnant or lactating women and women planning to become pregnant; 4) patients with tumors in the brain or other parts; 5) patients with severe cardiovascular and cerebrovascular diseases, malignant liver and kidney diseases and other serious diseases; and 6) patients with uncontrolled acute infection.

TABLE I
Basic Information About Subjects With Tinnitus

Subject	Gender	Age, years	Duration, months	Subject	Gender	Age, years	Duration, months
1	M	56	24	10	F	42	10
2	M	55	21	11	M	67	36
3	F	46	11	12	M	41	15
4	M	42	30	13	M	58	35
5	M	53	19	14	F	46	18
6	M	39	9	15	M	38	20
7	F	57	23	16	F	45	7
8	F	27	12	17	F	57	18
9	F	59	32	18	M	61	28

B. Procedure

Participants received a 20-minute acupuncture session every other day for a total of ten times. A millimeter needle with a diameter of 0.25 mm and a length of 2.5 mm was selected to acupuncture the basic acupoints of tinnitus. The acupoints were located according to the national standard of the People's Republic of China GB-12346-90 meridian and acupoints standard, and the selected acupoints were Ermen (bilateral), Tinggong (bilateral), Tinghui (bilateral) and Yifeng (bilateral). fNIRS measurements were performed before the first acupuncture session, and after the tenth acupuncture session.

Before the treatment and after the treatment, all participants completed the Tinnitus Handicap Inventory (THI), Tinnitus Evaluation Questionnaire (TEQ), Hamilton Anxiety Scale (HAMA), and Hamilton Depression Scale (HAMD). The THI quantifies the severity of tinnitus by assessing the emotional burden and the level of daily disruption caused by the condition [28]. The Chinese version of the THI was

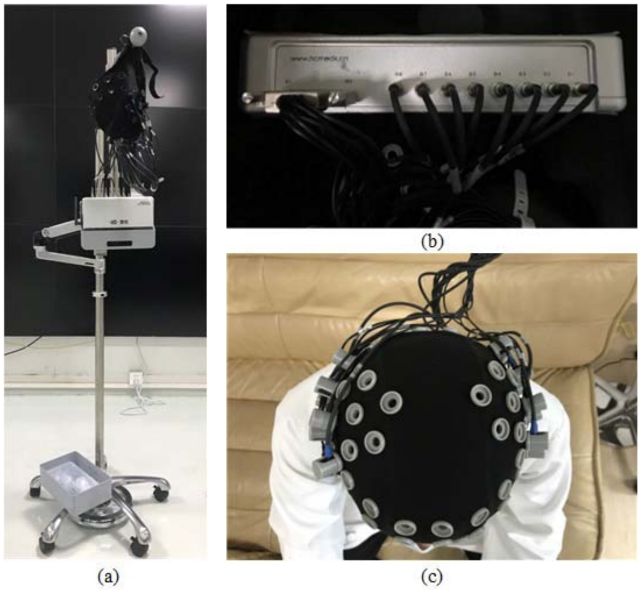

Fig. 1. (a) The functional near-infrared spectroscopy device; (b) Optic cable and probe cable; (c) Experiment photo.

used in this study, which included a total of 25 items [29]. Scores were calculated based on participants' responses, and scores from 0 to 100 were used to quantify the severity of tinnitus. THI divides the degree of tinnitus into 4 grades: slight (0-16 points), light (18-36 points), moderate (38-56 points), and severe and extremely severe (58-100 points). TEQ is a tinnitus assessment tool developed by Chinese clinicians in their long-term tinnitus diagnosis and treatment practice [30]. The TEQ evaluates the severity of tinnitus according to the total score from six aspects, including the environment in which tinnitus occurs and the duration of tinnitus [31]. TEQ divides the degree of tinnitus into 5 grades: grade I (1-6 points), grade II (7-10 points), grade III (11-14 points), grade IV (15-18 points), and grade V (19-21 points). The HAMA is the most widely used scale for assessing anxiety symptoms in clinical and scientific psychiatry [32]. In this study, the Chinese version of the HAMA was used to classify the degree of anxiety into 5 grades: very severe anxiety (total score $\geq$ 29), severe anxiety ($\geq$ 21 points), moderate anxiety ($\geq$ 14 points), mild anxiety ($\geq$ 7 points), and no anxiety symptoms ($<$ 7 points). Higher scores represent more severe anxiety symptoms. HAMD is the most commonly used scale for the clinical assessment of depression [33]. The scale has three versions, including 17 items, 21 items, and 24 items, which can evaluate the severity of the disease and the treatment effect. Seventeen items of the Chinese HAMD were used in this study [34]. The HAMD divided the degree of depression into 4 grades: normal ($<$ 7 points), mild depression (7-17 points), moderate depression (17-24 points), and severe depression ($>$ 24 points).

1) fNIRS imaging: A portable near-infrared brain imaging system (NirSmartII-3000C, Huichuang Medical Co., Ltd, China) operating at two different wavelengths (730 and 850 nm) with a sampling frequency of 10 Hz was used to measure relative changes in absorbed near-infrared light (Fig. 1). The same number of optodes were placed in

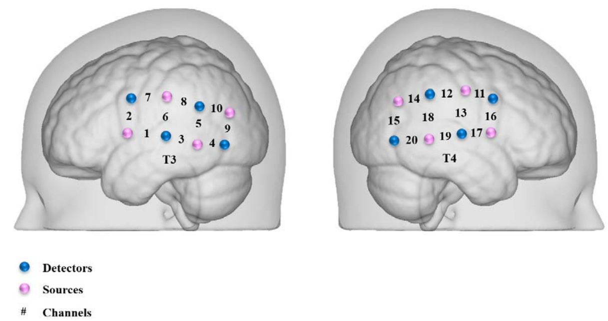

Fig. 2. Configuration of channels (numbers) with identified detectors (pink circles) and sources (blue circles) over the left and right cortical hemispheres. There are 4 detectors and 4 sources resulting in 10 channels per hemisphere. T3 and T4 are the reference points of the International 10-20 System.

TABLE II
AREAS AND PERCENTAGES CORRESPONDING TO THE LEFT AND RIGHT HEMISPHERE CHANNELS

	Left Hemisphere			Right Hemisphere		
Cerebral Cortex	Channel Number	Brodmann Areas	Percent	Channel Number	Brodmann Areas	Percent
TL	1	22	0.566	17	22	0.638
TL	3	21	0.498	19	21	0.509
TL	4	37	0.993	20	37	0.857
TL	5	22	0.424	18	22	0.842
TL	6	22	0.498	13	22	0.399
FL	2	6	0.495	16	6	0.669
OL	9	19	0.532	15	37	0.413
PL	7	43	0.567	11	43	0.527
PL	8	40	0.425	12	1,2	0.526
PL	10	39	0.582	14	39	0.505

* TL (Temporal Lobe) ; FL (Frontal Lobe) ; OL (Occipital Lobe) ; PL (Parietal Lobe).

each hemisphere. Eight detectors and 8 sources form the source-detector pairs, which are fixed on the measurement cup (based on the International 10-20 System) and cover both sides of the brain (Fig. 2). The 10-20 system electrode placement method is the standard electrode placement method stipulated by the International Federation of Clinical Neurophysiology. In this system, the position of the electrodes is mainly based on the skull and does not vary due to differences in individual head circumference or head shape. The distance formed between each pair of sources and detectors is called the light spacing and it is kept at a distance of approximately 30 mm to ensure the best balance between the signal-to-noise ratio and detection sensitivity [35]. The area between each source and detector is defined as a channel, so a set of optodes has a total of 20 channels, covering an area of 4 × 10 cm^2 on each side of the measuring cap. After each participant wore the measuring cap, the positions of T3 (the left temporal) and T4 (the right temporal) were carefully adjusted such that the optode position remained roughly the same. The table below shows the corresponding Brodmann areas of each channel and the percentage of the Brodmann area in the channel (Table II). Each channel may cover multiple brain

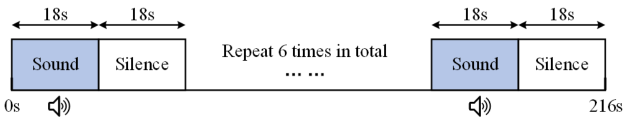

Fig. 3. Schematic diagram of the auditory stimulus paradigm. Participants passively listened to sequentially presented 18-second sound blocks (8000 Hz tone) and 18-second silence blocks before and after the sound blocks. Each block was repeated 6 times. The total time of the experiment was approximately 8.6 minutes.

areas. When the channel covered more than one area, only the Brodmann area with the greatest coincidence with the channel was listed.

2) *Auditory stimulus:* A block-averaged design was used to detect changes in oxygenated hemoglobin (HbO2) concentration elicited by sound-evoked activity. Similar to the previous study, we chose the tone of 8000 Hz as the sound stimulus [36]. The auditory stimuli 8000 Hz tone was created using Audacity (GNU General Public License) and presented via NirSmart (fNIRS data collection software). The sound was played on a headset (Edifier, W800BT) at a 50 dB sound pressure level (SPL; Creative Inspire T12). The auditory stimulation paradigm consists of 6 rounds of sequentially selected 18-second blocks of 8000 Hz, and 18-second blocks of silence from the interval between every two blocks of sound. The auditory stimulus paradigm performed by each participant consisted of 12 blocks: 6 blocks of auditory stimulation and 6 blocks of silence (Fig. 3). The entire auditory stimulation session was performed in a quiet room. Before the collection began, participants were asked to sit still for 5 minutes to calm their blood oxygen level. The total time of the experiment is approximately 8.6 minutes. When the collection began, participants were asked to close their eyes tightly, keep their heads as still as possible, and keep their bodies in a relaxed sitting position and awake.

C. fNIRS Data Analyses

1) *Data processing:* All data was processed using MATLAB-based NirSpark 1.7.5 (Danyang, China) software. Compared with the deoxygenated hemoglobin (HHb) signal, the signal-to-noise ratio of the HbO2 signal is higher [36], [37], and the correlation between the HbO2 model and the hemodynamic response function model is also higher. Therefore, this study only analyzed the HbO2 signal. The light intensity (Int) signal curve is shown in Fig. 4 (a), and the unit of light intensity is mV. Time periods with severe artifacts in the signal were deleted to avoid the interference of invalid data in subsequent calculations. The optical density curve is obtained by correcting artifacts by the cubic spline difference method (Fig. 4 (b)). High-pass filtering of 0.01 Hz was performed on the data to remove the low-frequency drift generated by the instrument, and low-pass filtering was performed on the data at 0.5 Hz to filter out the physiological noise introduced by heartbeat or respiration (Fig. 4 (c)). The light intensity signal was converted into an image of the concentration change of HbO2 according to the modified Beer-Lambert law [38]. For each wavelength, the differential path

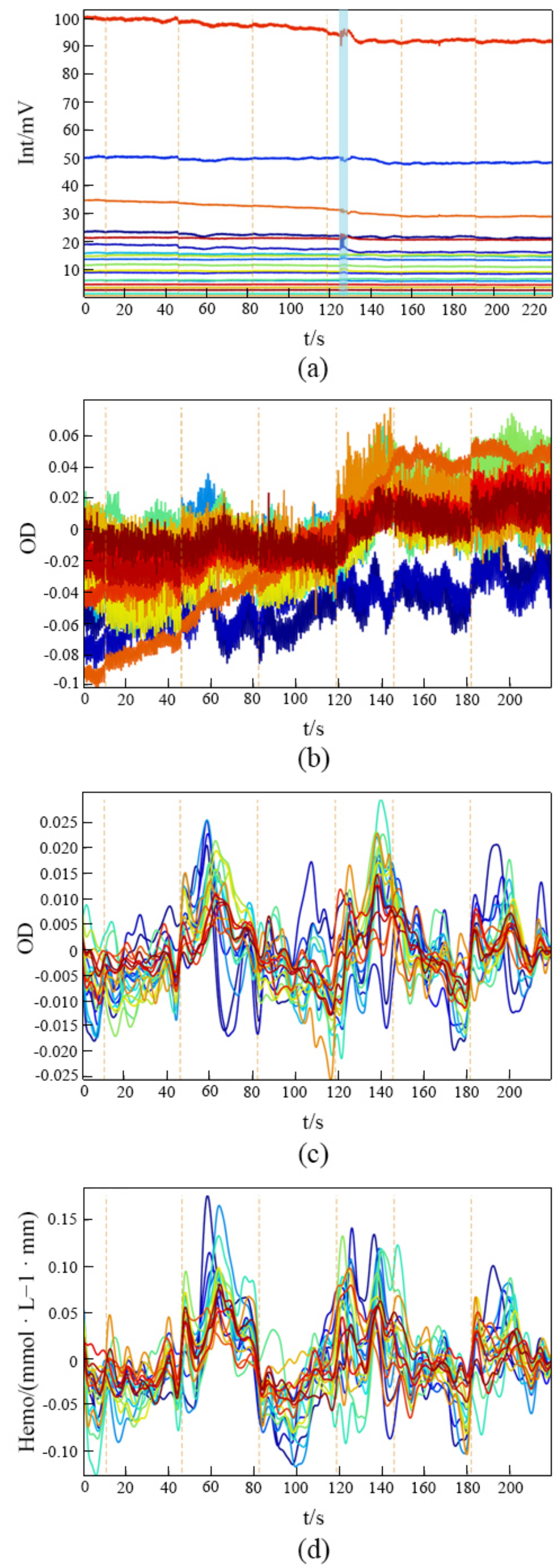

Fig. 4. (a) Eliminate time period; (b) Remove motion artifacts; (c) Filter; (d) Converted to HbO2 concentration.

factor (DPF) was set to 6, and the unit of HbO2 concentration after conversion was mmol/L $*$ mm (Fig. 4 (d)). Based on the labeled signal of each sound stimulus, the average response of each block was obtained by 6 repeated calculations (Fig. 5).

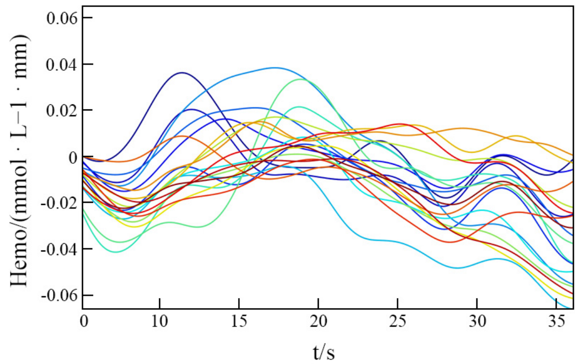

Fig. 5. HbO2 concentration curve after block average.

The hemodynamic response after auditory stimulation takes approximately 4-6 s to reach the maximum level [39], so the onset of block averaging was set to 5 s after the stimulus marker appeared. The 5 s after the sound stimulus appeared was set as the pre-baseline, and the mean of this interval was corrected to zero during data analysis. The average of the first three seconds was subtracted from the average of the overall time of each block to obtain the normalization of the hemodynamic activity of the sound block or silence block. The purpose of this operation is to reduce the influence of the previous block on the hemodynamic activity of this block [40].

The degree of correlation between HbO2 changes and the experimentally designed time-series model was calculated using a generalized linear model (GLM) [41]. GLM can quantify the amplitude of the hemodynamic response and the significance of cortical activation, and we performed a statistical analysis of the HbO2 data based on GLM.

$$Y = Bata * X + e \tag{1}$$

Y is the measured value of the real blood oxygen response curve, X is the design matrix, $Beta$ is the weight and e is the residual. Alternating silence blocks and sound blocks in sound-evoked activity form a design matrix X, which is convoluted with the standard hemodynamic response function (HRF) to obtain the change of blood oxygen response under ideal conditions. This process included fitting a first-order autoregressive process to the model residuals and transforming the original model according to the estimated autoregressive parameter [42]. Then, the beta weights were re-estimated based on the transformed model, and the beta weight reflected the magnitude of the hemodynamic response.

2) *Statistical analyses:* We use Nirspark (based on MATLAB) and SPSS for data processing and statistical analysis. The t-test has been widely used in other fNIRS studies to detect activation or compare conditions against the control. A one-sample t-test can be used to test the difference of means in fNIRS experiments [43]. False discovery rate (FDR) can reduce the errors in performing statistical tests in multiple comparison problems [41]. FDR has been applied to channel-wise analysis of fNIRS data, for making inferences about the activated region. As the FDR approach does not require a spatial smoothing process in the calculation of the p-value, it might be an optimal method for channel-wise statistics of fNIRS [44].

TABLE III
SCALE SCORES OF PARTICIPANTS BEFORE AND AFTER ACUPUNCTURE TREATMENT

	THI		TEQ		HAMA		HAMD	
Subject	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	38	20	8	5	20	18	29	19
2	20	4	7	3	29	22	34	16
3	22	22	8	7	10	7	12	4
4	76	56	15	8	37	20	33	28
5	20	22	7	7	4	2	9	7
6	98	56	20	16	14	17	23	15
7	80	72	14	11	18	18	15	12
8	32	16	8	4	1	0	0	0
9	62	8	22	6	12	0	20	1
10	68	40	12	8	4	3	3	1
11	22	10	8	5	8	6	5	0
12	16	14	8	7	16	12	10	7
13	14	2	6	1	0	2	3	0
14	44	24	14	7	24	16	8	6
15	26	24	8	7	4	1	11	8
16	52	32	11	6	14	7	18	12
17	40	32	9	4	20	8	14	8
18	36	20	10	8	16	8	7	4

A paired sample t-test was used to analyze the changes in HbO2 concentration in the auditory cortex caused by acupuncture treatment. We analyzed the correlation between the change in scale score and the change in HbO2 concentration in the auditory cortex, and selected the Pearson correlation coefficient (r) as the measure of correlation. The value of r is between -1 and 1, the larger the absolute value of r, the stronger the correlation between variables. After statistical analysis of the data using GLM, the activation of each channel before and after treatment was evaluated for the duration of sound stimulation using a single sample t-test in group-level analysis. A one-sample t-test was used to analyze the response of each channel to sound stimuli, reflecting the influence of acupuncture treatment on channel activation. We compared beta weights to 0 and used FDR to correct the p-value, an FDR corrected p-value, $p < 0.05$, was used as a threshold for significance.

III. RESULTS

A. Behavioral Data

All participants completed the THI, TEQ, HAMA, and HAMD before the first treatment and after the last treatment. Tables III show the scale scores of each participant before and after acupuncture treatment. After receiving acupuncture treatment, the number of people whose scores of THI, TEQ, HAMA and HAMD decreased was 12, 12, 9 and 8 respectively. After acupuncture treatment, the mean and standard deviation (SD) of THI decreased from 42.556±24.912 to 26.333±19.063. Similarly, the score of TEQ decreased from 10.833±4.554 to 6.667±3.236, the score of HAMA decreased from 13.944±9.914 to 9.278±7.482, and the score of HAMD decreased from 14.111±10.226 to 8.222±7.643 (Fig. 6).

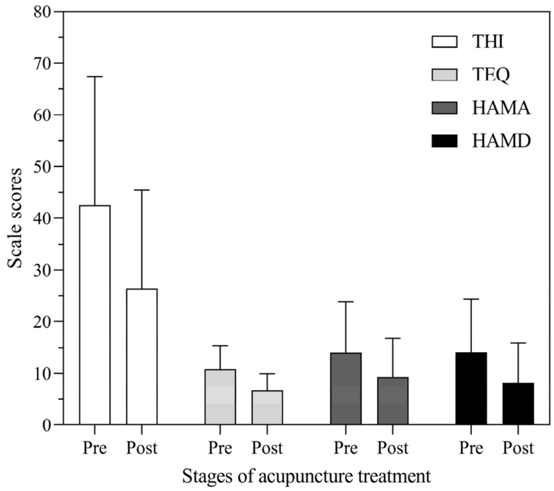

Fig. 6. Group averaged scores on each scale before and after acupuncture treatment.

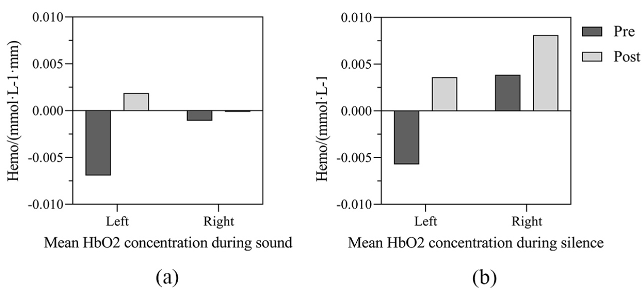

Fig. 7. Comparison of HbO2 concentration in the left temporal lobe and right temporal lobe before and after acupuncture treatment: (a) During the sound period; (b) During the silence period.

B. Changes in Average HbO2 Concentration in the Auditory Cortex

Because the change in auditory cortex may be the basis of affecting tinnitus perception, we analyzed the changes in mean HbO2 concentrations in the auditory cortex (channels in Table II: CH1, CH5, CH6, CH13, CH17, CH18). We calculated the mean HbO2 concentration before and after acupuncture treatment during the sound block (Sound) and the silence block (Silence). We found that acupuncture treatment increased the HbO2 concentration in the auditory cortex during sound and silence (Fig. 7). After acupuncture treatment, the HbO2 concentration of the left and right auditory cortex increased from −0.007 to 0.002 and from −0.001 to −0.0001 respectively during the sound period. During the silence period, the HbO2 concentration of the left and right auditory cortex increased from -0.006 to 0.004, and from 0.004 to 0.008, respectively. The concentration of HbO2 in the silence period was higher than that in the sound period. We made a statistical analysis of the HbO2 concentration in the left and right auditory cortex before and after acupuncture treatment. The results of the paired sample t-test showed that there were significant changes in the left cerebral cortex during the silence period (T=−2.232, p=0.023) (Table IV).

TABLE IV
STATISTICAL ANALYSIS OF HBO2 CONCENTRATION IN THE AUDITORY CORTEX

	Sound		Silence	
	Left	Right	Left	Right
T-value	-6.497	-0.610	-2.232	-0.470
p-value	0.155	0.604	0.023*	0.648

* Corresponds to the value below 0.05.

TABLE V
PEARSON CORRELATION COEFFICIENT BETWEEN SCALE SCORE CHANGE AND HBO2 CHANGE IN THE AUDITORY CORTEX

	Sound		Silence	
	Left	Right	Left	Right
THI	-0.857**	-0.894**	-0.865**	-0.849**
TEQ	-0.726**	-0.828**	-0.799**	-0.816**
HAMA	-0.166	-0.228	-0.193	-0.244
HAMD	-0.146	-0.194	-0.167	-0.234

** Correlation is significant at the 0.01 level (two-tailed).

TABLE VI
ACTIVATION OF EACH CHANNEL BEFORE ACUPUNCTURE

Channel Number	T-value	p-value	Channel Number	T-value	p-value
1	-2.572	0.137	11	-2.547	0.137
2	-2.890	0.135	12	-1.402	0.397
3	-0.536	0.674	13	-1.284	0.397
4	-0.976	0.464	14	-0.907	0.464
5	0.002	0.998	15	-1.272	0.397
6	-1.785	0.280	16	-1.556	0.352
7	-1.218	0.397	17	-2.934	0.135
8	-0.930	0.464	18	-2.115	0.194
9	-0.982	0.464	19	-2.913	0.135
10	-0.287	0.822	20	-2.109	0.194

C. The Relationship Between the Change of Scale Scores and HbO2 Concentration in the Auditory Cortex

We analyzed the relationship between the change in scale score and the change in HbO2 concentration in the auditory cortex caused by acupuncture treatment. Table V shows the correlation between the change in different scale scores and the change in HbO2 concentration in the auditory cortex. The results showed that the changes in the scores of THI and TEQ were significantly correlated with the changes in the concentration of HbO2 in the auditory cortex. The r between the THI and the HbO2 concentration in the auditory cortex were −0.857, −0.894, −0.865 and −0.849, respectively. For the TEQ, r were −0.726, −0.828, −0.799 and −0.816, respectively.

D. Effects of Acupuncture on Channel Activation

We analyzed the effect of acupuncture on the activation of different channels (CH1∼CH20) under sound-evoked activity. The activation maps show the activation of each channel (Fig. 8). Before acupuncture treatment, there was no obvious activated channel (Table VI). After acupuncture treatment, the superior temporal gyrus (CH6, T=−2.907, p=0.045; CH13, T=−4.258, p=0.027) showed significant activation (Table VII).

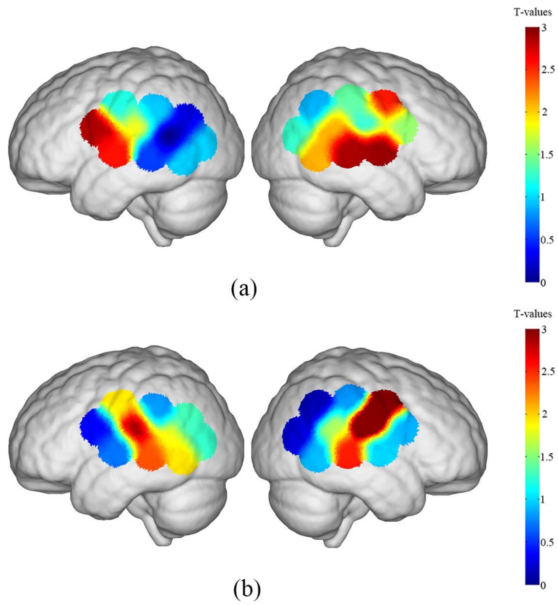

Fig. 8. The rows show auditory stimuli conditions, and the columns show different measurement times (a): Pre-treatment, (b): Post-treatment). For each map, the left and right images show the measured areas of the left and the right hemisphere respectively.

TABLE VII
ACTIVATION OF EACH CHANNEL AFTER ACUPUNCTURE

Channel Number	T-value	p-value	Channel Number	T-value	p-value
1	-0.691	0.592	11	-3.435	0.056
2	-0.367	0.801	12	-0.800	0.551
3	-2.399	0.141	13	-4.258	0.027*
4	-1.950	0.225	14	-0.153	0.881
5	-1.818	0.241	15	-0.240	0.858
6	-2.907	0.045*	16	-0.874	0.551
7	-1.937	0.225	17	-0.975	0.551
8	-0.804	0.551	18	-1.601	0.306
9	-1.273	0.417	19	-2.551	0.135
10	-1.314	0.417	20	-0.914	0.551

* Corresponds to the value below 0.05.

IV. DISCUSSION

In this study, we combined fNIRS with sound stimulation to explore the effect of acupuncture on the cerebral cortex of people with tinnitus. It was assumed that acupuncture would increase the activation of some regions of the human brain, improve the tinnitus symptoms of tinnitus patients, and reduce the anxiety and depression symptoms of patients. After collecting the fNIRS signal, the changes in brain activation and hemodynamic responses in patients with tinnitus were obtained by analysis.

Animal models of noise-induced tinnitus demonstrate increased spontaneous and tone-evoked neural firing rates and enhanced neural synchrony in the auditory cortex [45]. Increased neuronal firing rates and enhanced synchrony have both been touted as putative physiologic correlates of tinnitus [2]. However, the human brain is more complex, so animal models cannot be equated with human models. Using fNIRS to detect the changes in cortical area can reflect the effect of acupuncture treatment on neural plasticity. Brain tissue in the cortical area of the damaged brain can promote neural plasticity through repeated treatment to restore damaged function [46].

Studies have explored the effects of acupuncture on cerebral blood oxygen metabolism in healthy subjects, based on fNIRS. For example, Széles and Litscher [47] performed electroacupuncture on auricular points of 2 healthy people and showed that HbO2 in the brain increased steadily and had certain follow-up effects. Han et al. [48] randomly divided 12 healthy subjects into a Hegu acupuncture group and a blank control group and found that the HbO2 in the Hegu acupuncture group was significantly higher than that in the blank control group, suggesting that acupuncture on the Hegu acupoint could activate the prefrontal cortex. Reference [49] examined the effects of hand acupuncture and laser on HbO2 in 3 subjects and found that acupuncture on acupoints could increase HbO2, but acupuncture on sham acupoints had no similar effect. Litscher and Schikora [50] performed a variety of acupuncture stimulations in 88 healthy people and showed that hand acupuncture and laser acupuncture at specific acupoints could promote an immediate increase in HbO2, and there was a follow-up effect. Our research also shows that acupuncture at acupoints can increase the concentration of HbO2. Our results show that before and after acupuncture treatment, the concentration of HbO2 in the silence period is higher than that in the sound period. According to the neurovascular coupling mechanism, the increase of regional cerebral blood oxygen reflects the activity of neurons. Previous studies have found that auditory cortical activity was increased in tinnitus subjects during silence, whereas this activity was suppressed during broadband noise auditory stimulation [51]. In our study, the concentration of HbO2 in the silence period was higher than that in the sound period, which may also be related to the inhibition of auditory cortical activity by sound stimulation. Similar to other fNIRS studies related to acupuncture, we must admit that the relationship between the changes in acupuncture-induced blood oxygen activity observed in tinnitus and its neuronal correlation remains to be clarified. The changes in blood oxygen activity caused by acupuncture can only provide an indirect hint to the neuronal changes underlying tinnitus.

We observed that after the participants received sound stimulation after acupuncture, in addition to some brain regions related to hearing, the significance of other brain regions also changed. Among the brain regions activated after treatment, CH6 and CH13 are located in Broadmann area 22, which is mainly used for auditory processing and language reception. Our examination of the cerebral cortex of tinnitus participants showed that multiple acupuncture treatments affected tinnitus-related neural plasticity. This change in the human tinnitus brain may reflect the potential plasticity of acupuncture on the auditory central nerve and prove that acupuncture is helpful for the treatment of tinnitus. Tinnitus always has subjective factors, and objective measurement methods will help to increase the clinical persuasiveness of acupuncture therapy. Using fNIRS to measure the changes in hemodynamic response can be used as an objective means of tinnitus rehabilitation.

As a new imaging method, fNIRS is more suitable for the application of tinnitus than other imaging methods because of its advantages of no noise and strong anti-interference ability. However, fNIRS can only measure hemodynamic activity in the superficial regions of the outer cortex and cannot measure activity that occurs in deeper layers of the brain [52]. In this study, although all participants had tinnitus, we did not control for the participants' hearing level and degree of tinnitus. In future research, we need to consider looking for participants whose hearing levels and the degree of tinnitus are as close as possible.

V. Conclusion

fNIRS is an effective method for evaluating auditory cortical activation, and it can be used in auditory-related imaging studies. In this study, fNIRS was used to detect the changes of blood oxygen in the cerebral cortex of patients with tinnitus, which shows that acupuncture can improve the symptoms of tinnitus. In this study, acupuncture reduced the severity of tinnitus in patients with tinnitus and reduced symptoms of anxiety and depression. According to the fNIRS detection results of tinnitus patients, acupuncture increased the concentration of oxygenated hemoglobin in the temporal lobe of tinnitus patients, and affected the activation of the auditory cortex, which may reflect the potential plasticity of acupuncture on the auditory central nervous system. With the continuous development of fNIRS, fNIRS will show obvious advantages in brain imaging, which will contribute to the study of tinnitus neural mechanisms of acupuncture treatment of tinnitus, and may be used as an effective tool to evaluate the effect of acupuncture treatment for tinnitus in the future.

References

[1] S. Vanneste, M. Plazier, E. Van Der Loo, P. V. de Heyning, M. Congedo, and D. De Ridder, "The neural correlates of tinnitus-related distress," *NeuroImage*, vol. 52, no. 2, pp. 470–480, Aug. 2010.

[2] A. J. Noreña and J. J. Eggermont, "Changes in spontaneous neural activity immediately after an acoustic trauma: Implications for neural correlates of tinnitus," *Hearing Res.*, vol. 183, nos. 1–2, pp. 137–153, Sep. 2003.

[3] J. S. Baizer, S. Manohar, N. A. Paolone, N. Weinstock, and R. J. Salvi, "Understanding tinnitus: The dorsal cochlear nucleus, organization and plasticity," *Brain Res.*, vol. 1485, pp. 40–53, Nov. 2012.

[4] A. J. Heller, "Classification and epidemiology of tinnitus," *Otolaryngol. Clinics North Amer.*, vol. 36, no. 2, pp. 239–248, Apr. 2003.

[5] A. Ahmed, M. Aqeel, T. Akhtar, S. Salim, and B. Ahmed, "Moderating role of stress, anxiety, and depression in the relationship between tinnitus and hearing loss among patients," *Pakistan J. Psychol. Res.*, vol. 34, no. 4, pp. 753–772, Jan. 2020.

[6] C. P. Lanting, E. de Kleine, and P. van Dijk, "Neural activity underlying tinnitus generation: Results from PET and fMRI," *Hearing Res.*, vol. 255, nos. 1–2, pp. 1–13, Sep. 2009.

[7] S. B. Minami et al., "Repetitive transcranial magnetic stimulation (rTMS) for treatment of chronic tinnitus," *Auris Nasus Larynx*, vol. 38, no. 3, pp. 301–306, Jun. 2011.

[8] P. Adjamian, M. Sereda, and D. A. Hall, "The mechanisms of tinnitus: Perspectives from human functional neuroimaging," *Hearing Res.*, vol. 253, nos. 1–2, pp. 15–31, Jul. 2009.

[9] J. J. Eggermont and L. E. Roberts, "The neuroscience of tinnitus," *Trends Neurosci.*, vol. 27, no. 11, pp. 676–682, Nov. 2004.

[10] J. J. Eggermont and L. E. Roberts, "The neuroscience of tinnitus: Understanding abnormal and normal auditory perception," *Frontiers Syst. Neurosci.*, vol. 6, p. 53, 2012.

[11] A. J. Vickers et al., "Acupuncture for chronic pain: Individual patient data meta-analysis," *Arch. Internal Med.*, vol. 72, no. 19, pp. 1444–1453, Oct. 2012.

[12] F. Liu, X. Han, Y. Li, and S. Yu, "Acupuncture in the treatment of tinnitus: A systematic review and meta-analysis," *Eur. Arch. Oto-Rhino-Laryngol.*, vol. 273, no. 2, pp. 285–294, Oct. 2014.

[13] P. Zhang and T. Su, "Analysis on the neurological mechanism of acupuncture treatment in Idiopathic tinnitus based on the theory of 'central plasticity,'" *TMR Integrative Med.*, vol. 5, Sep. 2021, Art. no. e21032.

[14] J.-I. Kim, J.-Y. Choi, D.-H. Lee, T.-Y. Choi, M. S. Lee, and E. Ernst, "Acupuncture for the treatment of tinnitus: A systematic review of randomized clinical trials," *BMC Complementary Alternative Med.*, vol. 12, no. 1, p. 97, Dec. 2012.

[15] K. Itoh, S. Saito, S. Sahara, and Y. Naitoh, "Mechanisms of acupuncture and moxibustion on symptoms of neurology," *Rinsho Shinkeigaku*, vol. 52, no. 11, pp. 1294–1296, 2012.

[16] D. J. McFerran, D. Stockdale, R. Holme, C. H. Large, and D. M. Baguley, "Why is there no cure for tinnitus?" *Frontiers Neurosci.*, vol. 13, p. 802, Aug. 2019.

[17] M. Moazami-Goudarzi, L. Michels, N. Weisz, and D. Jeanmonod, "Temporo-insular enhancement of EEG low and high frequencies in patients with chronic tinnitus. QEEG study of chronic tinnitus patients," *BMC Neurosci.*, vol. 11, no. 1, p. 40, Dec. 2010.

[18] P. Adjamian, "The application of electro- and magneto-encephalography in tinnitus research—Methods and interpretations," *Frontiers Neurol.*, vol. 5, p. 228, Nov. 2014.

[19] M. Ferrari and V. Quaresima, "A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application," *NeuroImage*, vol. 63, no. 2, pp. 921–935, Nov. 2012.

[20] J. C. Wagner et al., "Comparison of whole-head functional near-infrared spectroscopy with functional magnetic resonance imaging and potential application in pediatric neurology," *Pediatric Neurol.*, vol. 122, pp. 68–75, Sep. 2021.

[21] K. Takamoto, S. Urakawa, K. Sakai, T. Ono, and H. Nishijo, "Effects of acupuncture needling with specific sensation on cerebral hemodynamics and autonomic nervous activity in humans," in *International Review of Neurobiology*, vol. 111. Toyama, Japan, 2013, pp. 25–48, doi: 10.1016/B978-0-12-411545-3.00002-X.

[22] J. Fang et al., "The limbic-prefrontal network modulated by electroacupuncture at CV4 and CV12," *Evid.-Based Complement Altern. Med.*, vol. 2012, Jan. 2012, Art. no. 515893.

[23] Y. Wei et al., "Acupuncture treatment decreased temporal variability of dynamic functional connectivity in chronic tinnitus," *Frontiers Neurosci.*, vol. 15, Jan. 2022, Art. no. 737993.

[24] J. C. Ye, S. Tak, K. E. Jang, J. Jung, and J. Jang, "NIRS-SPM: Statistical parametric mapping for near-infrared spectroscopy," *NeuroImage*, vol. 44, no. 2, pp. 428–447, Jan. 2009.

[25] C.-M. Lu, Y.-J. Zhang, B. B. Biswal, Y.-F. Zang, D.-L. Peng, and C.-Z. Zhu, "Use of fNIRS to assess resting state functional connectivity," *J. Neurosci. Methods*, vol. 186, no. 2, pp. 242–249, Feb. 2010.

[26] R. F. Rojas, M. Liao, J. Romero, X. Huang, and K.-L. Ou, "Cortical network response to acupuncture and the effect of the Hegu point: An fNIRS study," *Sensors*, vol. 19, no. 2, p. 394, Jan. 2019.

[27] X. Si, S. Xiang, L. Zhang, S. Li, K. Zhang, and D. Ming, "Acupuncture with deqi modulates the hemodynamic response and functional connectivity of the prefrontal-motor cortical network," *Frontiers Neurosci.*, vol. 15, p. 803, Aug. 2021.

[28] F. Zeman et al., "Tinnitus handicap inventory for evaluating treatment effects: Which changes are clinically relevant?" *Otolaryngol., Head Neck Surg.*, vol. 145, no. 2, pp. 282–287, Aug. 2011.

[29] Z. Meng et al., "Reliability and validity of the Chinese (Mandarin) tinnitus handicap inventory," *Clin. Exp. Otorhinolaryngol.*, vol. 5, no. 1, pp. 10–16, Mar. 2012.

[30] Z. Chen, Y. Zheng, Y. Fei, D. Wu, and X. Yang, "Validation of the Mandarin tinnitus evaluation questionnaire: A clinician-administered tool for tinnitus management," *Medicine*, vol. 100, no. 27, Jul. 2021, Art. no. e26490.

[31] P. L. Peng et al., "Study on reliability and validity of the tinnitus evaluation questionnaire," *Chin. J. Otorhinolaryngol. Head Neck Surg.*, vol. 47, no. 9, pp. 716–719, 2012.

[32] S. Ball, L. B. Marangell, S. Lipsius, and J. M. Russell, "Brain-derived neurotrophic factor in generalized anxiety disorder: Results from a duloxetine clinical trial," *Prog. Neuro-Psychopharmacol. Biol. Psychiatry*, vol. 43, pp. 217–221, Jun. 2013.

[33] R. Sharp, "The Hamilton rating scale for depression," *Occup. Med.*, vol. 65, no. 4, p. 340, Jun. 2015.
[34] Y. Cao, W. Li, J. Shen, R. T. Malison, Y. Zhang, and X. Luo, "Health-related quality of life and symptom severity in Chinese patients with major depressive disorder: Quality of life and severity of symptoms," *Asia–Pacific Psychiatry*, vol. 5, no. 4, pp. 276–283, Dec. 2013.
[35] G. E. Strangman, Z. Li, and Q. Zhang, "Depth sensitivity and source-detector separations for near infrared spectroscopy based on the Colin27 brain template," *PLoS ONE*, vol. 8, no. 8, Aug. 2013, Art. no. e66319.
[36] M. Issa, S. Bisconti, I. Kovelman, P. Kileny, and G. J. Basura, "Human auditory and adjacent nonauditory cerebral cortices are hypermetabolic in tinnitus as measured by functional near-infrared spectroscopy (fNIRS)," *Neural Plasticity*, vol. 2016, pp. 1–13, Mar. 2016.
[37] G. Strangman, J. Culver, J. H. Thompson, and D. A. Boas, "A quantitative comparison of simultaneous BOLD fMRI and NIRS recordings during functional brain activation," *NeuroImage*, vol. 17, no. 2, pp. 719–731, Oct. 2002.
[38] T. Yamamoto and T. Kato, "Paradoxical correlation between signal in functional magnetic resonance imaging and deoxygenated haemoglobin content in capillaries: A new theoretical explanation," *Phys. Med. Biol.*, vol. 47, no. 7, pp. 1121–1141, Apr. 2002.
[39] H. Obrig and A. Villringer, "Beyond the visible-imaging the human brain with light," *J. Cerebral Blood Flow Metabolism*, vol. 23, no. 1, pp. 1–18, Jan. 2003.
[40] T. J. Huppert, S. G. Diamond, M. A. Franceschini, and D. A. Boas, "HomER: A review of time-series analysis methods for near-infrared spectroscopy of the brain," *Appl. Opt.*, vol. 48, no. 10, p. D280, Apr. 2009.
[41] S. Tak and J. C. Ye, "Statistical analysis of fNIRS data: A comprehensive review," *Neuroimage*, vol. 85, pp. 72–91, Jan. 2014.
[42] M. M. Plichta, S. Heinzel, A.-C. Ehlis, P. Pauli, and A. J. Fallgatter, "Model-based analysis of rapid event-related functional near-infrared spectroscopy (NIRS) data: A parametric validation study," *NeuroImage*, vol. 35, no. 2, pp. 625–634, Apr. 2007.
[43] K. Matsuo et al., "Hypoactivation of the prefrontal cortex during verbal fluency test in PTSD: A near-infrared spectroscopy study," *Psychiatry Res., Neuroimag.*, vol. 124, no. 1, pp. 1–10, Sep. 2003.
[44] A. K. Singh and I. Dan, "Exploring the false discovery rate in multichannel NIRS," *NeuroImage*, vol. 33, no. 2, pp. 542–549, Nov. 2006.
[45] J. A. Kaltenbach, M. A. Zacharek, J. Zhang, and S. Frederick, "Activity in the dorsal cochlear nucleus of hamsters previously tested for tinnitus following intense tone exposure," *Neurosci. Lett.*, vol. 355, nos. 1–2, pp. 121–125, Jan. 2004.
[46] N. Takeuchi and S.-I. Izumi, "Rehabilitation with poststroke motor recovery: A review with a focus on neural plasticity," *Stroke Res. Treat.*, vol. 2013, Apr. 2013, Art. no. 128641.
[47] J. C. Széles and G. Litscher, "Objectivation of cerebral effects with a new continuous electrical auricular stimulation technique for pain management," *Neurol. Res.*, vol. 26, no. 7, pp. 797–800, Oct. 2004.
[48] Y.-D. Han, B. Yuan, Y.-F. Zhang, X.-F. Wang, W.-Y. Lang, and X.-K. Yan, "Role of fNIRS technology in observing the effect of needling Hegu (LI 4) on the functions of prefrontal cortex in healthy volunteers," *J. Acupuncture Tuina Sci.*, vol. 15, no. 2, pp. 94–98, Apr. 2017.
[49] G. Litscher and L. Wang, "Cerebral near infrared spectroscopy and acupuncture–results of a pilot study," *Biomed. Eng.-Biomed. Technik*, vol. 45, nos. 7–8, pp. 215–218, Jul. 2000.
[50] G. Litscher and D. Schikora, "Near-infrared spectroscopy for objectifying cerebral effects of needle and laser needle acupuncture," *Spectroscopy*, vol. 16, nos. 3–4, pp. 335–342, 2002.
[51] T. Zhai et al., "Tinnitus and auditory cortex; using adapted functional near-infrared-spectroscopy to expand brain imaging in humans," *Laryngoscope Investigative Otolaryngol.*, vol. 6, no. 1, pp. 137–144, Feb. 2021.
[52] A. M. Leaver, L. Renier, M. A. Chevillet, S. Morgan, H. J. Kim, and J. P. Rauschecker, "Dysregulation of limbic and auditory networks in tinnitus," *Neuron*, vol. 69, no. 1, pp. 33–43, Jan. 2011.