

Modulation of Brain Activity in Patients with Acute Non-Specific Low Back Pain by Wentong Guan Therapy: A Functional Near-Infrared Spectroscopy Study

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Background: Wentong Guan Therapy (WTG) integrates techniques from Chinese massage, moxibustion, scraping, and cupping. Its analgesic mechanisms remain unclear. The brain functional network in patients with acute non-specific low back pain (ANSLBP) is impaired, and central nervous system regulation is one of the important mechanisms through which traditional Chinese medicine external therapies alleviate pain and functional impairment in ANSLBP. This study neurophysiologically evaluates WTG's pain modulation effect on the cerebral cortex in acute non-specific low back pain (ANSLBP).

Methods: Twelve ANSLBP patients received a single WTG session. Subjective pain (Visual Analogue Scale, VAS), pressure pain threshold (PPT) using a force-measuring glove, and cortical hemodynamic changes via functional near-infrared spectroscopy (fNIRS) were assessed pre- and post-treatment. False discovery rate (FDR) corrected multiple comparisons.

Results: Post-treatment, VAS scores significantly decreased (4.75 ± 1.29 to 3.58 ± 1.17 , $p < 0.001$) and PPT increased (77.29 ± 39.83 N to 94.58 ± 39.79 N, $p < 0.001$). No significant brain network differences were found ($P_{FDR} > 0.05$). Pre-treatment HbO₂ concentration in channel 17 (DLPFC) was significant ($P_{FDR} = 0.042$), but post-treatment, no channels showed significance. Channel 33 (Somatosensory Association Cortex, SAC) showed a significant HbO₂ change post-treatment ($P_{FDR} = 0.038$). Δ HbO₂ in SAC (CH33) negatively correlated with Δ PPT ($P = 0.045$, $r = -0.587$).

Conclusion: WTG effectively alleviates ANSLBP. The SAC and DLPFC are involved in WTG's neuromodulatory analgesic effects. Reduced Δ HbO₂ in the SAC may be a potential biomarker for WTG's analgesia.

Keywords: Wentong Guan therapy, acute non-specific low back pain, functional near-infrared spectroscopy, neuroactivity, somatosensory association cortex, dorsolateral prefrontal cortex

Introduction

Acute non-specific low back pain (ANSLBP) is one of the most common medical conditions. It is characterized by acute onset of low back pain (LBP), limited mobility, and a disease duration of less than 6 weeks.¹ The lifetime prevalence of ANSLBP in adults reaches up to 40%, leading to significant socioeconomic costs worldwide.^{2,3} Approximately, 20% of patients continue to experience symptoms one year post-onset, and 3% remain unable to work, seriously affecting their quality of life, and physical and mental health.⁴ Therefore, effective treatment during the acute phase is essential to alleviate pain and prevent chronic progression.



International clinical practice guidelines focus on symptomatic treatment for managing ANSLBP, with drug treatment options including non-steroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, or short-term application of weak opioids.⁵ However, systematic reviews have highlighted limitations of drug treatment. For example, one review indicated that acetaminophen is ineffective for acute low back pain, while skeletal muscle relaxants offer short-term analgesia for acute low back pain but have sedative effects. Opioid use carries risks of adverse reactions such as central nervous system suppression and constipation.⁶ Certain exercises, kinesiology taping, and electro-physical agents are frequently used in treatment.⁷ Therefore, non-drug treatments like spinal manipulation, massage, and acupuncture are recommended for the treatment of LBP.⁸

Numerous studies have shown that traditional Chinese medicine (TCM) rehabilitation therapies such as moxibustion,⁹ scraping,¹⁰ cupping,¹¹ and Chinese massage¹² can significantly alleviate pain and improve low back dysfunction in LBP patients. Recent studies indicate that combining multiple therapy techniques is more effective than a single one.^{13–16} Therefore, the combined application of multiple TCM rehabilitation techniques may improve the treatment efficacy.

Wentong Guan Therapy (WTG), a non-drug treatment therapy, has been used for various pain and dysfunction conditions in China.^{17–19} Wentong Guan Therapy is an external TCM technique that integrates TCM principles of Chinese massage, moxibustion, scraping, and cupping, and thus particularly effective for LBP,^{20–22} as shown in Figure 1. It exerts its effects through multiple links. When the moxa stick in WTG is ignited, it releases heat, which raises the temperature inside the cup to form negative pressure. The lower opening of the cup adheres to the muscle surface, enabling the functions of cupping and moving cup. When the opening of the cup is repeatedly scraped on the muscle surface, sha spots appear, realizing the function of gua sha (scraping therapy). By using the protrusions on the cup body and the edge of the cup's lower opening to perform manipulations such as pushing, pressing, pointing, kneading, plucking, and rolling, the function of massage can be achieved.

Recent studies have primarily focused on patient self-reports, physical examinations, and some serological analyses.^{21,23} There is a notable lack of neuroimaging research on the mechanism by which WTG regulates brain activity in patients with ANSLBP.

The pain signals caused by low back pain are transmitted in the brain through two pathways, namely the lateral transmission system and the medial transmission system, which convey pain sensory information and emotional information respectively. With the advancement of modern imaging technology, it has been found that abnormal activities



Figure 1 Wentong Cup.

in brain regions responsible for sensory, emotional, and cognitive functions are closely associated with acute low back pain. This, to a certain extent, confirms the pain modulation effect of the brain center on LBP-related disorders, including ANSLBP.²⁴ Some scholars have proposed the “low back pain cortex” theory, pointing out that the excitability of the sensorimotor cortex is reduced in patients with acute low back pain,^{25,26} and the brain activation areas are mainly located in the prefrontal cortex, insula, cingulate cortex, and other regions.²⁷ This suggests that the brain center plays an important role in ANSLBP.

Functional magnetic resonance imaging (fMRI), a classic neuroimaging evaluation technique, accurately records pain-related brain activity.²⁸ However, fMRI requires limiting head and body movement and involves lengthy detection times making it unsuitable for long-term monitoring of patients with LBP. Recently, functional near-infrared spectroscopy (fNIRS), has emerged as a robust non-invasive functional neuroimaging technology with strong resistance to head movements. Compared to electroencephalogram (EEG) and other techniques, fNIRS offers superior robustness and has been increasingly utilized in brain functioning research.

The fNIRS technology measures changes in brain activity and metabolism by detecting concentrations of oxygenated hemoglobin (HbO₂) and deoxygenated hemoglobin (HbR) in the cerebral cortex.²⁹ This provides a new method for exploring the brain effect mechanisms underlying WTG. Based on our previous clinical observations and literature review, we hypothesize that WTG can alleviate pain symptoms in patients with acute non-specific low back pain ANSLBP by modulating the brain activity of the somatosensory cortex and prefrontal cortex. In this study, we used fNIRS to assess the cerebral hemodynamic responses of patients with ANSLBP before and after WTG treatment. This approach aims to deepen our understanding of the neurophysiological mechanisms of WTG, thus providing a stronger scientific basis for its clinical application.

Materials and Methods

Participants

We recruited twelve patients diagnosed with ANSLBP who visited the Rehabilitation Department of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine from November 11, 2024 to February 25, 2025, based on the following criteria:

Inclusion Criteria

1. Diagnosis of ANSLBP with symptoms persisting for less than six weeks.
2. Age between 18–75 years and right-handed, as determined by Edinburgh Handedness Inventory.
3. Average Visual Analogue Scale (VAS) score ≥ 3 over the past week.
4. No receipt of other related treatments for ANSLBP in the past month.
5. No history of discectomy or other related surgeries.
6. Willingness to accept and comply with the treatment schedule and to sign the informed consent form.

Exclusion Criteria

1. Presence of scoliosis, ankylosing, spondylitis, bone tuberculosis, tumors, severe osteoporosis, and other orthopedic diseases, or history of acute pain from other causes in the past month.
2. History of severe spinal trauma and spinal surgery.
3. Contact allergy or moxa smoke allergy.
4. Skin damage, allergy, infection, or other conditions at the treatment site unsuitable for WTG.
5. Head deformities, scalp damage, inability to wear headgear, or poor fNIRS signals in pre-acquisition.
6. Presence of autoimmune diseases, allergic diseases, acute or chronic infectious diseases, or serious medical or mental diseases such as cardiovascular, hematological, and digestive system diseases.
7. Participation in other clinical research within the past week.

This research protocol was approved by the Ethics Review Committee of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine (No.2024–032-01). The protocol has been registered with the International

Traditional Medicine Clinical Trial Registry and conducted in accordance with the Declaration of Helsinki (ITMCTR2024000666). Written informed consent was obtained from all participants.

Study Procedure

Participants underwent resting-state and task-based fNIRS scans at two time points: baseline and after one treatment session. Patients were also asked to rate their pain intensity using a VAS. Before the task-based scan, the doctor applied pressure on the patient's low back tender points to determine the pressure pain threshold, using this intensity for task-based scan. The test sequence was as follows: resting-state scan, VAS score assessment, pressure pain threshold determination, and task-based scan, as shown in Figure 2.

WTG Treatment

All WTG treatments were administered by a doctor with five years of operating experience in this technique. The patient was instructed to lie prone, and Vaseline was evenly applied to the lower back. The doctor then inserted a moxa stick into the fixing clip at the center of the Wentong Cup and ignited, allowing it to preheat for five minutes. The cup was then placed at an angle against the skin, and the doctor performed scraping along the Du Meridian from bottom to top using a flat push method. This was then followed by scraping from top to bottom along the bilateral bladder meridian until the skin exhibited redness or Sha. Subsequently, the cup was pressed flatly against the skin around Dachangshu (BL25) and Shenshu (BL23), and was rotated and moved in a regular pattern. These were then followed by a press and knead at the acupoints with a dentate of the lower edge of the Wentong cup, as shown in Figure 3. Each treatment session lasted 20 minutes. No adverse events were reported during the WTG treatment study period.

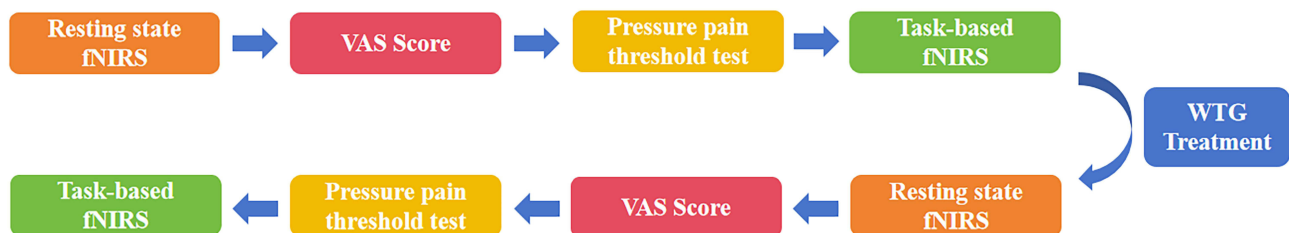


Figure 2 The procedure of the experiment.



Figure 3 Treatment of ANSLBP patient using WTG.

VAS Score and Pressure Pain Threshold Test

After systematic training and examination, an independent doctor conducted the VAS score assessment and pressure pain threshold test. Patients rated their current pain on a scale from 0 (no pain) to 10 (pain severe enough to seriously affect their lives).

The pressure pain threshold test was performed using an intelligent mechanical collection glove (SK-HTA-01, Guangzhou Shuangkong Technology Co., Ltd). Patients were placed in a prone position with the lower back skin exposed and they were instructed to relax. The doctor identified the most obvious palpable response in the distribution area of the erector spinae myofascial trigger point on the affected side of the patient's lumbar region³⁰ and marked the spot. If the patient's pain did not show a lateral tendency, the left lower back was pressed.

The doctor wore the intelligent mechanical collection glove on the right hand, positioning the thumb perpendicular to the patient's skin surface, and applied pressure slowly and at a constant speed, as shown in Figure 4. When the patient's pain perception reached a VAS score of five,^{31,32} the screen value was recorded. The pressure pain threshold test was performed three times, and the average of these results was taken as the final measurement.³³ Measurement locations were consistent before and after treatment.

Functional Near-Infrared Spectroscopy Detection and Data Preprocessing

Device Information

A portable fNIRS device (NirSmart II-3000A, Danyang Huichuang Medical Equipment Co., Ltd.) was used to monitor real-time changes in the cerebral cortex HbO₂ and HbR. The device included 21 light sources and 15 detectors, forming a total of 47 channels. The arrangement of light sources, detectors, and channels are shown in Figure 5. Following the international standard 10/20 electrode placement system, the setup covered the forehead and bilateral sensorimotor areas. The light source probes used wavelengths of 730nm and 850nm, with a sampling rate of 11Hz. To ensure high-precision data collection, the detector and light source were fixed with black headgear. The average distance between each detector and light source was set to 30 mm. The headgear was adjusted to ensure direct contact between the detectors, light sources, and the scalp. Patients were instructed to close their eyes and avoid engaging in any cognitive activities during the measurement.

Resting-State Data Acquisition

Before starting the test, the patient must rest for 5 minutes to adapt to the examination room environment, after which the examination can proceed. Resting-state data should be collected for 8 minutes per session. During the test, patient remains still, avoids cognitive activity, and keeps their eyes closed but must not fall asleep. Resting-state fNIRS measurements were conducted on all patients before and after WTG treatment.



Figure 4 SK-HTA-01 was used to record pain values. (a) Using SK-HTA-01 to press the lower back. (b) The inside of SK-HTA-01 glove. (c) The outside of SK-HTA-01 glove.

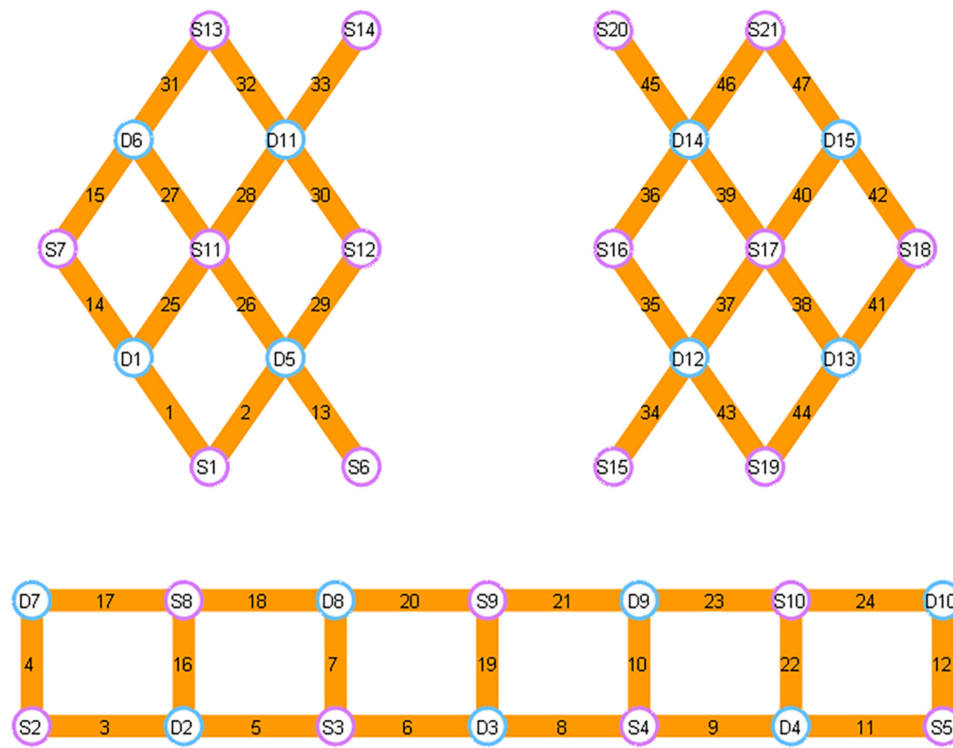


Figure 5 Arrangement of light sources, detectors, and channels.

Task-Based fNIRS Data Acquisition

The procedure is divided into two phases: the preparation period and the task period. During the preparation period, the patient remained quiet for 20 seconds. In the task period, the doctor performed “pressing” or “rest” according to the fNIRS system instructions. During the rest phase, the subject remained quiet and minimized cognitive activity. The doctor applied pressure with the intensity measured in the Pressure Pain Threshold Test. Both the compression and rest phases lasted 20 seconds each and were alternated eight times. All patients underwent a task-based fNIRS assessment before and after treatment. The task paradigm is shown in Figure 6.

Data Processing

Preprocessing

The fNIRS data were preprocessed using the NirSpark software package (v1.8, Danyang Huichuang Medical Equipment Co., Ltd), which has been validated in previous studies.^{34,35} The preprocessing steps included: First, converting raw fNIRS light intensity data into optical density signals. Secondly, detecting and monitoring motion artifacts caused by head movements.³⁶ Thirdly, the optical density signals were filtered with a bandpass filter from 0.01 to 0.1 Hz. Lastly, the

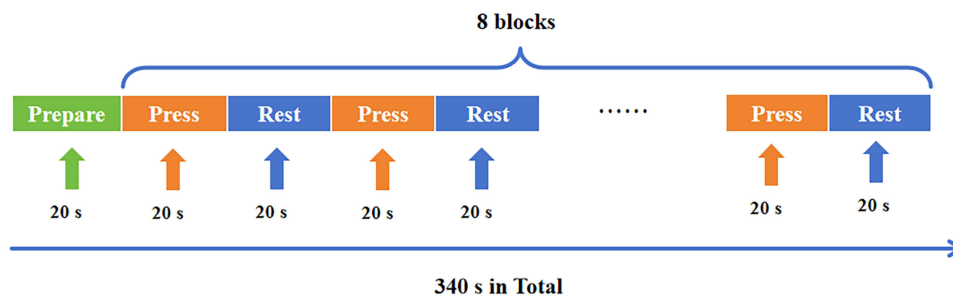


Figure 6 The examination procedure of the task-based fNIRS.

filtered optical density signals were converted into relative concentrations of HbO₂ and HbR using the modified Beer-Lambert law.³⁷ Due to superior signal-to-noise ratio of HbO₂ compared to HbR, only the HbO₂ data were used for subsequent analysis.³⁸ For patients with the compression site on the right side, data were mirror-flipped across the left and right brain area channels to standardize the compression site as being on the left.

Analysis of HbO₂ Concentration Changes

The changes in HbO₂ concentration (ΔHbO_2) during the compression task and the rest phase were quantified using feature value editing. A one-sample *t*-test was used to identify channels exhibiting significant ΔHbO_2 before and after treatment. A two-sample *t*-test was used to compare the ΔHbO_2 before and after treatment.

Brain Network Functional Connectivity Strength Analysis

Region of Interest (ROI) were defined as detailed in Table 1. Pearson correlation analysis was used to calculate the correlation of HbO₂ concentration changes between different channels and ROIs for the resting state. These correlation values were then converted into *z*-scores using the Fisher *r-z* transformation and defined as functional connectivity strength.

Statistical Analysis

Statistical analysis was conducted using SPSS software version 23.0 (IBM SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean \pm standard deviation ($\bar{x} \pm s$). The Shapiro–Wilk test was used to assess the normality of the data distribution. For comparisons before and after treatment, paired *t*-tests were used at $p < 0.05$. Spearman correlation analysis was performed to examine the relationship between HbO₂ concentration and clinical data. Multiple comparisons were corrected using the false discovery rate (FDR) method ($p < 0.05$), thereby adjusting for potential false positives in all results rejecting the null hypothesis.³⁹

Results

Clinical Data

A total of twelve patients with ANSLBP were recruited for the study. The cohort had a mean age of 51.2 ± 15.0 years, ranging from 30 to 72 years, including eight males and four females, all of whom were right-handed. The Body Mass Index (BMI) was 22.97 ± 3.62 kg/m². Table 2 presents detailed information on each patient's stimulation side, BMI, VAS scores, and pressure values before and after treatment.

Treatment with the WTG approach had significant effect on both VAS scores and pressure values. As shown in Figure 7, the mean VAS score post-treatment was 3.58 ± 1.17 (95% Confidence Interval [CI], 2.84 to 4.32), significantly lower than pre-treatment mean VAS score of 4.75 ± 1.29 (95% CI, 3.93 to 5.57), with a *t*-value of 7.000 and $p < 0.001$. The mean difference in VAS scores was 1.17 ± 0.58 (95% CI, 0.80 to 1.53).

The pressure values, determined by the average compression measured by mechanical gloves, also showed significant. As shown in Figure 8, the mean pressure value post-treatment was 94.58 ± 39.79 N (95% CI, 51.99 to 102.60), significantly higher than mean pressure value pre-treatment of 77.29 ± 39.83 N (95% CI, 69.29 to 119.86) with a *t*-value of 4.796 and $p < 0.001$. The mean difference in pressure values was -17.28 ± 12.48 N (95% CI, -25.21 to -9.35).

Table 1 ROI Settings and Channel Correspondence Table

ROI Of Cortical Area	Channels	
	Left	Right
Pre-Motor and Supplementary Motor Cortex (PMC and SMA)	34, 35, 37, 38, 41	13, 14, 25, 26, 29
Frontopolar area (Fp)	8, 9, 10, 21, 23	5, 6, 7, 18, 19, 20
Dorsolateral Prefrontal Cortex (DLPFC)	22, 24	16, 17
Primary Somatosensory Cortex (S1)	39, 40	27, 28
Primary Motor Cortex (M1)	36	30
Somatosensory Association Cortex (SAC)	45, 46	32, 33

Table 2 Demographic Information and Clinical Behavioral Measurement of Participants

ID	Age (Year)	Sex (M/F)	Stimulation Side (L/R)	BMI (kg/m ²)	VAS Score (Before WTG)	VAS Score (After WTG)	Pressure Value (Before WTG) (N)	Pressure Value (After WTG) (N)
1	60	M	R	18.72	6	5	22.53	26.10
2	59	M	L	24.49	3	2	75.43	113.70
3	43	F	R	20.03	4	3	132.20	138.33
4	63	M	L	24.21	5	4	121.17	124.67
5	30	F	L	19.05	6	5	83.47	108.67
6	32	M	R	29.22	4	3	126.27	157.47
7	32	F	R	18.36	4	2	31.27	64.93
8	62	M	R	26.99	4	3	61.70	69.73
9	60	M	R	25.95	5	3	44.23	65.77
10	63	M	R	19.92	3	3	125.00	131.67
11	38	M	L	24.02	7	5	46.17	57.97
12	72	F	R	24.65	6	5	58.07	75.90

Functional Near-Infrared Spectroscopy Data

Reduction in the Strength of Functional Connectivity

The Pearson correlation coefficient, calculated from the HbO₂ concentration data, was transformed using the Fisher *r-z* transformation to define the functional connectivity between channels and ROIs. By analyzing the *z*-scores of each pair of channels in the time series, a 47×47 correlation matrix was generated for each patient. The results showed that the overall functional connection strength between the channels of the patients was 0.28±0.13 pre-treatment and 0.22±0.10 post-treatment, showing a downward trend (Figures 9 and 10). However, these differences did not remain significant after correction for multiple comparisons ($P_{FDR}>0.05$).

At the ROI level, the bilateral Pre-Motor Cortex (PMC), Supplementary Motor Area (SMA), Frontopolar area (Fp), Somatosensory Association Cortex (SAC), and left Dorsolateral Prefrontal Cortex (DLPFC) all exhibited a decrease in the functional connectivity strength of the homologous ROIs. However, the differences did not pass the FDR correction ($P_{FDR}>0.05$), as detailed in [Supplementary Table 1](#). For the functional connectivity between ROIs, most connections demonstrated a downward trend, except for an increasing trend observed in the functional connectivity strength between the right DLPFC and the right PMC and SMA, bilateral M1, right SMA, and between the right Fp and the right M1 region. However, none of these results remained significant after FDR correction ($P_{FDR}>0.05$) as shown in [Figures 11, 12](#), and [Supplementary Table 2](#).

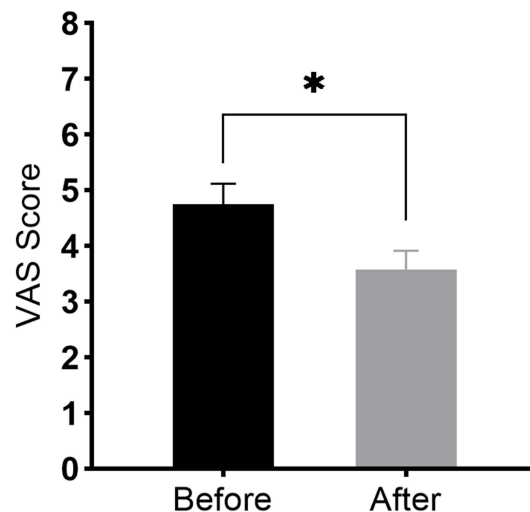


Figure 7 The VAS Score between before and after treatment. * $P<0.001$.

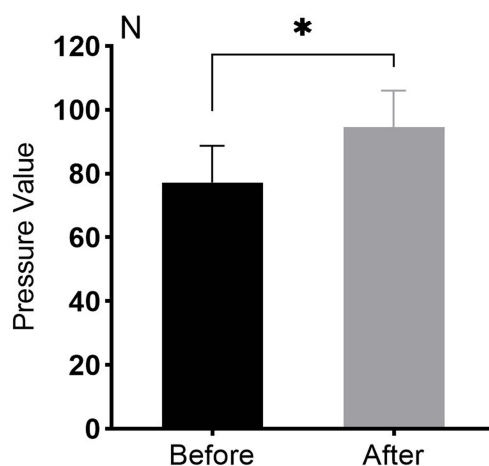


Figure 8 The Pressure Value between before and after treatment.* $P < 0.001$.

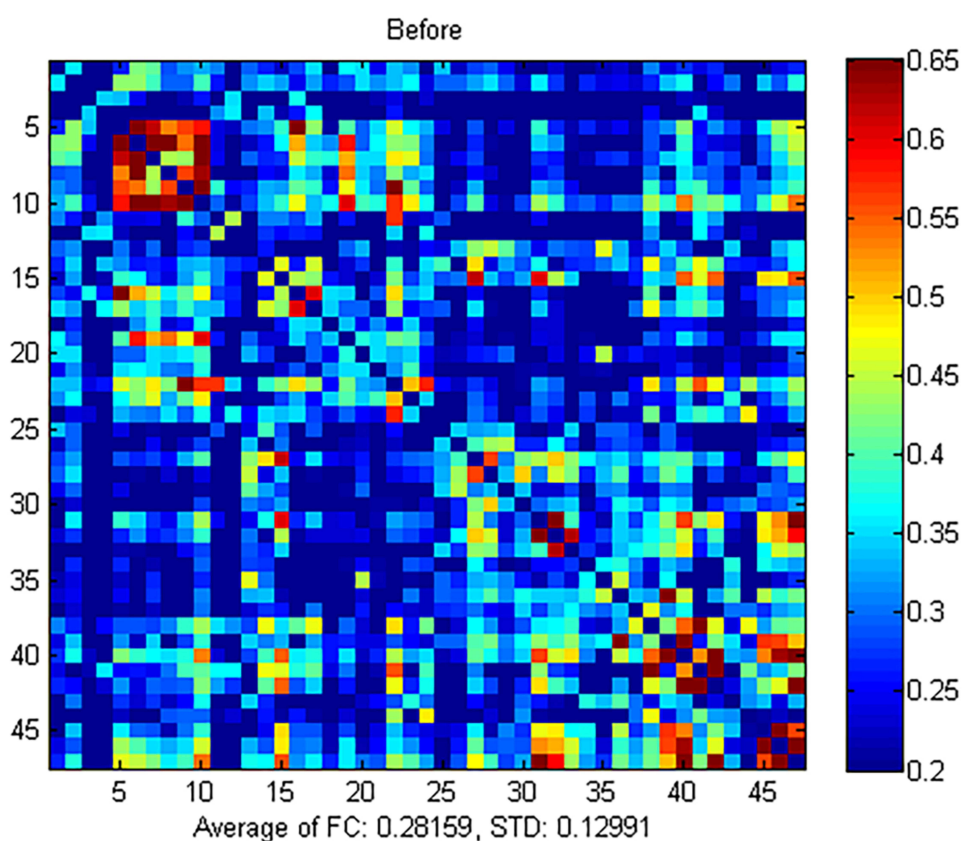


Figure 9 Functional connectivity strength between channels before treatment.

ΔHbO_2 Concentration Reduction

One-sample t -test results showed that the ΔHbO_2 concentration in Channel (CH) 17 was 0.029 ± 0.022 mmol/L*mm before WTG treatment, and the difference was statistically significant ($t=4.505$, $P_{FDR}=0.042$), as shown in Figure 13. However, there was no statistical significant difference in ΔHbO_2 concentration in all channels after treatment ($P_{FDR} > 0.05$), as shown in Figure 14. The ΔHbO_2 concentration in CH33 was 0.011 ± 0.017 mmol/L*mm before treatment, while the concentration after treatment was -0.004 ± 0.022 mmol/L*mm. The results of the paired t -test showed that the difference in ΔHbO_2

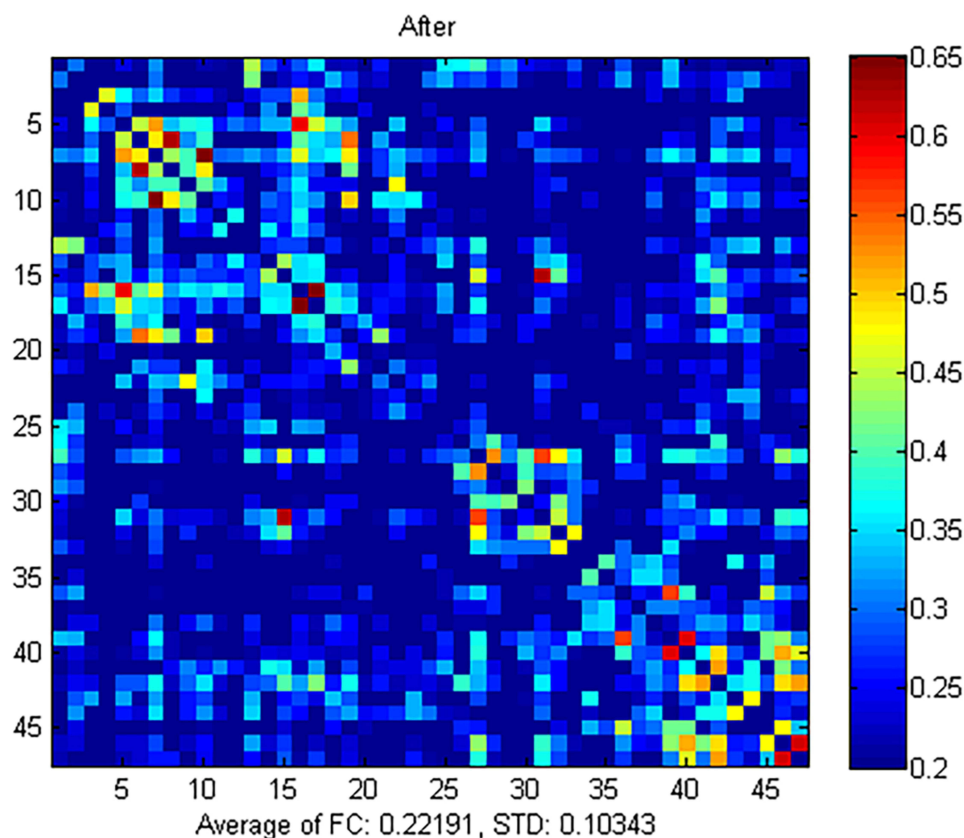


Figure 10 Functional connectivity strength between channels after treatment.

concentration in CH33 before and after treatment was statistically significant ($t=4.571$, $P_{FDR}=0.038$), as shown in Figure 15. The corresponding brain regions and MNI coordinate information of the channels are shown in Table 3.

Correlation Between Clinical Data and ΔHbO_2 Concentration

The WTG was found to reduce the ΔHbO_2 concentration in CH33 during the pressing task and also increase the pressing pain threshold. To quantify these effects, we calculated the ΔHbO_2 concentration for CH33 and the change in pressure pain threshold before and after treatment. To reveal the correlation between the difference in pain threshold and the change in HbO_2 concentration, Spearman correlation analysis was conducted. The results showed that there was a significant negative correlation between the change in ΔHbO_2 concentration and pressure pain threshold ($P=0.045$, $r=-0.587$), as shown in Figure 16.

Discussion

To the best of our knowledge, this study is the first to use fNIRS to investigate the effects of WTG on brain function in ANSLBP patients. We examined the analgesic effect of WTG therapy, changes in ΔHbO_2 concentration, and impacts on functional connectivity in 12 ANSLBP patients using a pre-post treatment design. Data analysis revealed a significant decrease in ΔHbO_2 concentration in SAC (CH33) following WTG treatment. Additionally, the analysis of VAS score and pressure value of the patients showed significant pain relief for these patients. All these changes indicate that WTG has a significant effect on analgesics in ANSLBP patients. Moreover, we also found that the DLPFC (CH17), a brain region that exhibited significantly increased activity in response to pressure before treatment, did not show a significant response after treatment. This suggests that the DLPFC, along with the SAC, may be key brain regions involved in the pain modulation mechanism of WTG therapy in ANSLBP patients.

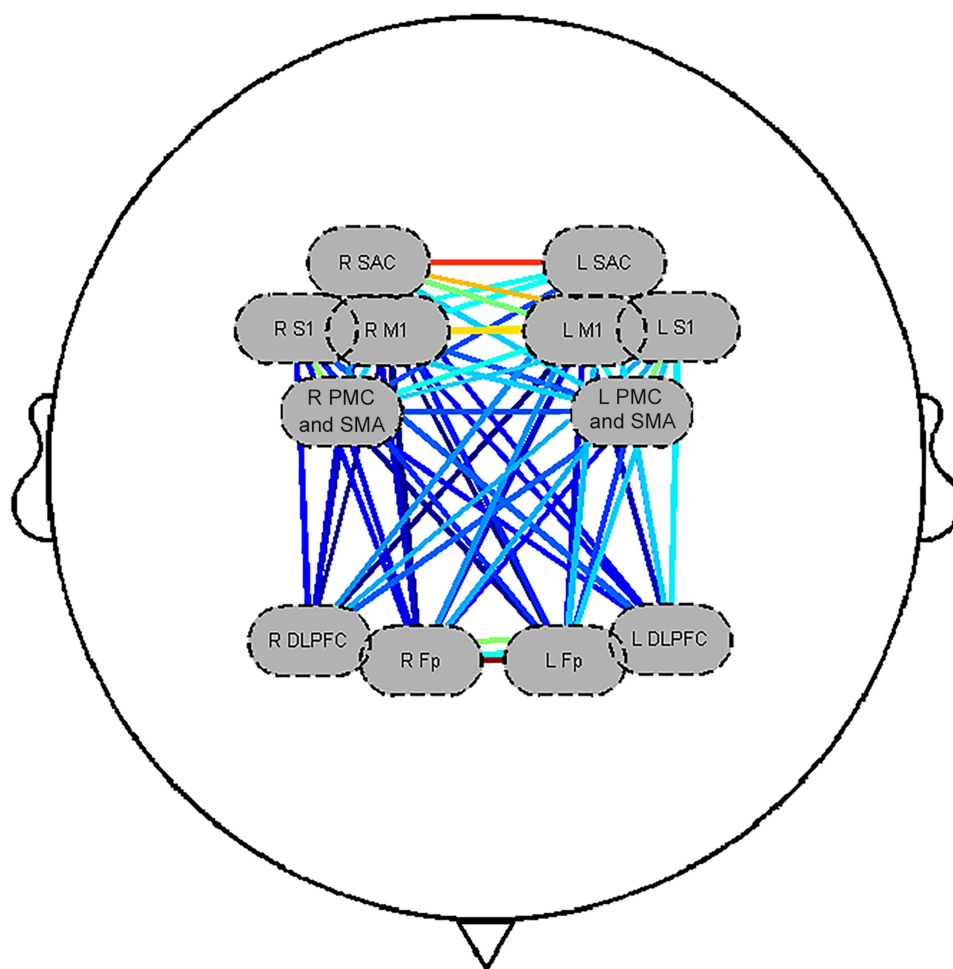


Figure 11 Functional connectivity strength between ROIs before treatment.

Abbreviations: R, Right; L, Left; DLPFC, Dorsolateral prefrontal cortex; SAC, Somatosensory Association Cortex; PMC and SMA, Pre-Motor and Supplementary Motor Cortex; Fp, Frontopolar area; S1, Primary Somatosensory Cortex; M1, Primary Motor Cortex.

Over the years, the American College of Physicians has recommended non-drug therapies such as massage and spinal manipulation for the treatment of ANSLBP.^{40,41} Several systematic reviews have also confirmed the positive effects of massage on pain relief and functional improvement in LBP patients.^{12,42–45} In essence, the brain effect mechanisms of non-drug therapies are gradually being applied. Research has also established that Chinese massage therapy affects brain activity, mainly in the DLPFC, inferior frontal gyrus, posterior cingulate gyrus, and postcentral gyrus of patients with LBP.^{32,46}

Markowski⁴⁷ investigated the effects of cupping therapy on subacute LBP, and the results demonstrated that cupping can reduce muscle tenderness and improve joint range of motion. Also, a systematic review involving 10 randomized controlled trials with a total of 627 patients,⁴⁸ confirmed scrapping therapy significantly reduces pain in LBP patients and continuously improve lumbar function both at the end of treatment and during follow-up. Lee et al⁴⁹ obtained similar findings. Currently, several systematic reviews that have validated the efficacy and safety of moxibustion for LBP.^{9,50,51} Utilizing technologies such as fNIRS, and EEG, researchers have found that moxibustion treatment can significantly increase cerebral cortical blood flow, increase blood oxygen concentration, with widespread EEG responses observed in areas such as the prefrontal lobe, Primary somatosensory cortex (S1), secondary somatosensory cortex, and cingulate cortex.^{52–54} Studies by Lee et al found that acupuncture can reduce the functional connectivity between the medial prefrontal cortex and the posterior cingulate cortex, thereby alleviating low back extension pain.⁵⁵ Kim's research revealed that acupuncture can improve somatosensory processing and relieve low back pain.⁵⁶ Li et al discovered that

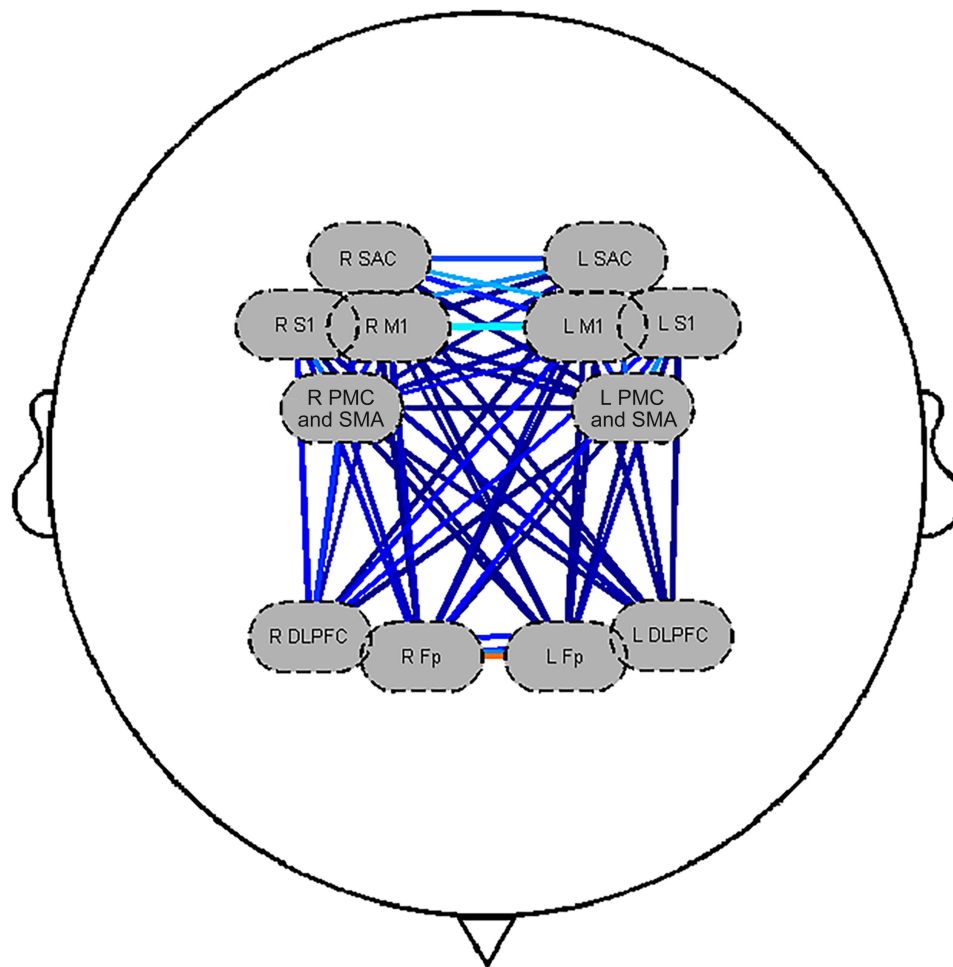


Figure 12 Functional connectivity strength between ROIs after treatment.

Abbreviations: R, Right; L, Left; DLPFC, Dorsolateral prefrontal cortex; SAC, Somatosensory Association Cortex; PMC and SMA, Pre-Motor and Supplementary Motor Cortex; Fp, Frontopolar area; S1, Primary Somatosensory Cortex; M1, Primary Motor Cortex.

the mechanism by which acupuncture relieves sciatica may be related to the reduced activity of the DLPFC and the anterior cingulate cortex, which is similar to the results of this study.⁵⁷

These studies support the effectiveness of complementary and alternative medicine methods including spinal manipulation, massage, acupuncture, and moxibustion in the treatment of LBP.⁴⁰ ANSLBP is the interaction between physical dysfunction and psychological and social factors.⁵⁸ Consequently, the multidisciplinary rehabilitation approach for ANSLBP is increasingly being adopted. Among these therapies being adopted is the WTG which is a combination of treatment with better efficacy than single therapy.^{13–16} In this study, WTG demonstrated significant analgesic effects. Neuroimaging studies have found that low back pain changes the spatiotemporal dynamics of blood oxygen level-dependent (BOLD) signals in response to sustained noxious stimulation, involving sensory, emotional, cognitive, and other functional networks.^{24,59} The mechanisms by which complementary and alternative therapies such as Chinese massage and moxibustion treat LBP have been revealed through neurofunctional imaging, highlighting the adaptation of the central nervous system to regulate and maintain LBP pain processing.^{32,60} However, the mechanisms underlying the efficacy of WTG remain unclear. Existing research is primarily based on patient self-reports, physical examinations, and some serological studies.^{21,23} The regulatory mechanisms of WTG on the brain in ANSLBP patients are yet to be fully understood.

Pain is not solely the result of sensory input directly caused by injury, inflammation, or other pathologies.⁶¹ Instead, it is caused by the activation of cognitive, emotional, and motor networks after injury, and is the output of widely distributed neural networks in the brain.^{62,63} Therefore, pain is an experience related to actual or potential tissue damage, which includes

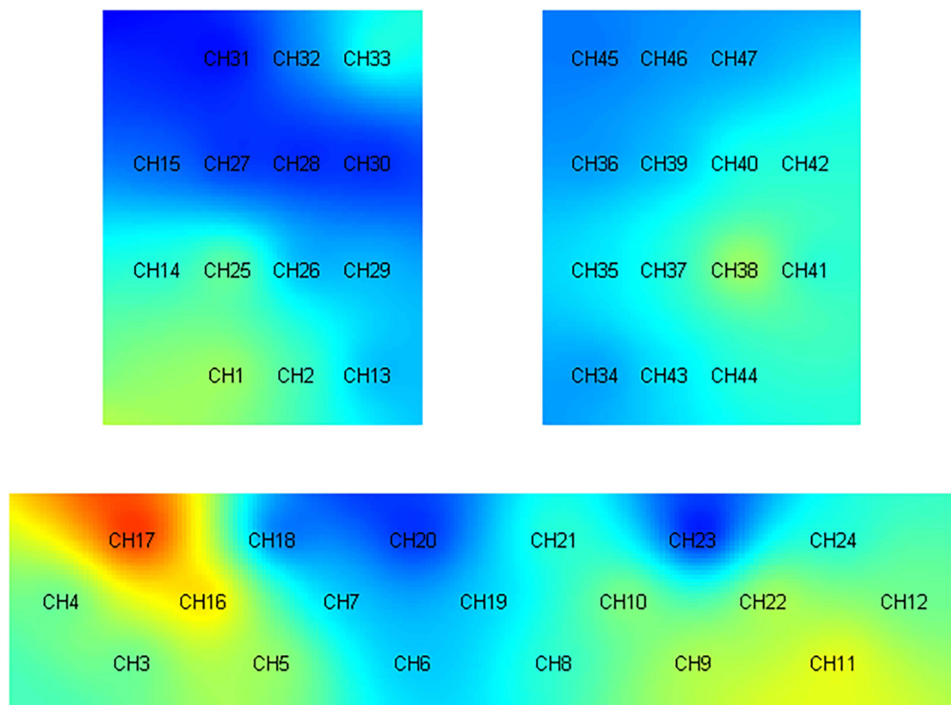


Figure 13 T value diagram of ΔHbO_2 concentration in each channel before treatment.

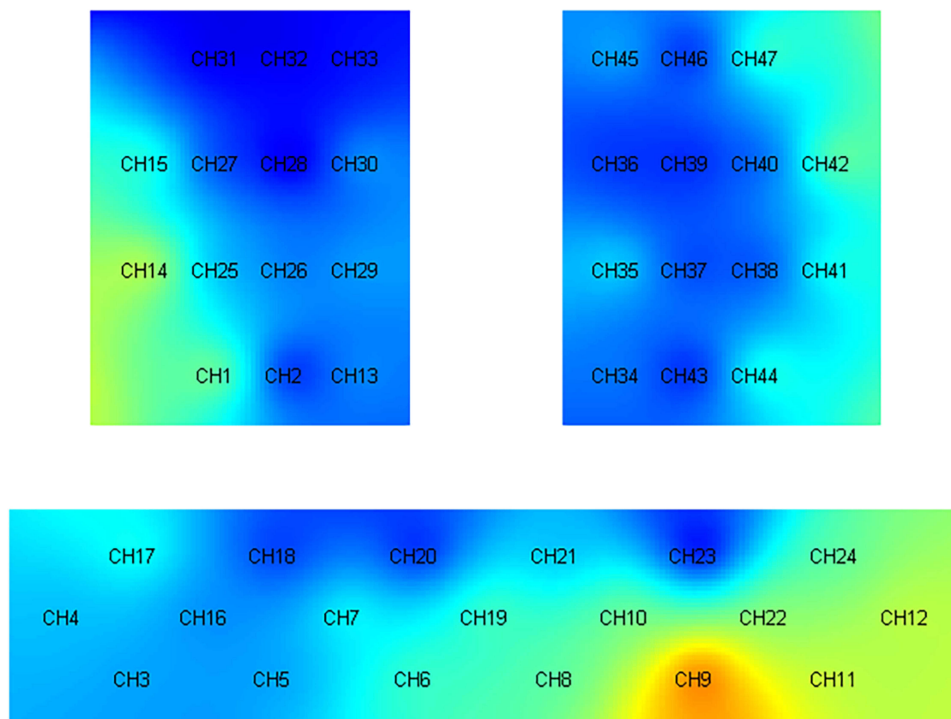


Figure 14 T value diagram of ΔHbO_2 concentration in each channel after treatment.

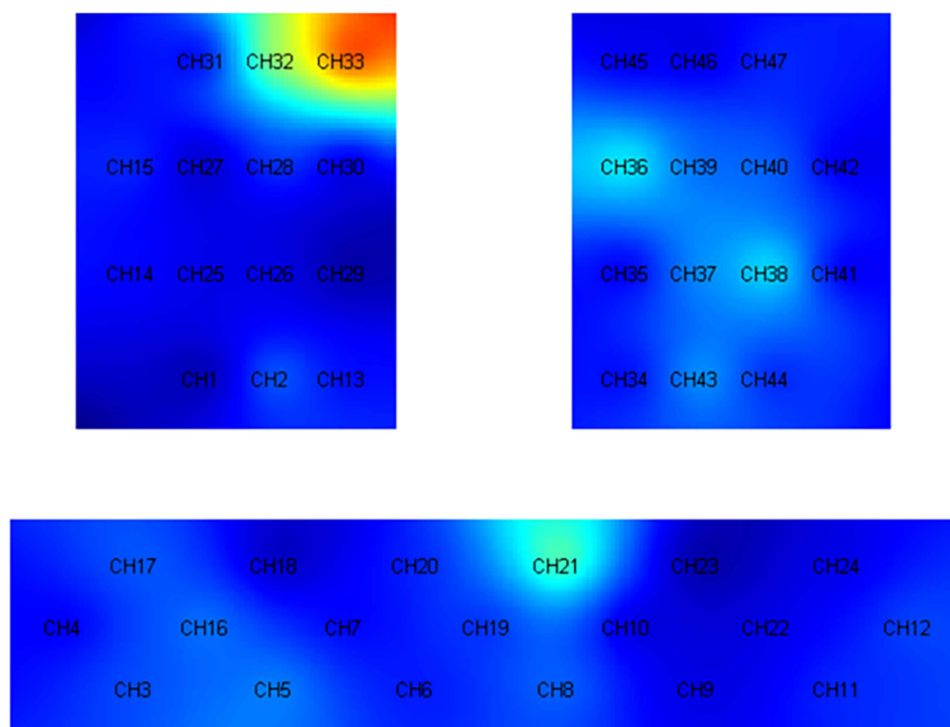


Figure 15 T value diagram of ΔHbO_2 concentration difference in each channel before and after treatment.

multiple components such as sensation, emotion, cognition, and movement.⁶⁴ Our study observed a statistically significant difference in the decrease in ΔHbO_2 concentration in SAC (CH33) during pressure application before and after WTG treatment. This area is generally considered to integrate and interpret somatosensory information from S1 and is involved in the comprehensive processing of somatosensory information, including pain perception.^{65–67} This finding is consistent with Matsuo et al's study⁶⁸ which found that LBP patients showed deactivation in large areas of the bilateral parietal lobes (including the upper part) under pressure stimulation. Previous fMRI studies have shown that BOLD signal inactivation reflects the inhibition of neuronal activity.^{69,70} Given that BOLD signal is related to changes in hemoglobin concentration,⁷¹ the observed reduction in ΔHbO_2 response in this study may indicate potential inhibition of neural activity. A study involving lumbar compressions in healthy volunteers⁷² observed significant changes in HbO_2 concentrations in S1 and SMA. Another study involving LBP patients showed⁷³ that hemodynamic activity in the somatosensory area was significantly reduced when pain was alleviated. These findings suggest that pain relief in ANSLBP patients may be related to the inhibition of neural activity in the somatosensory association cortex. This inhibition could represent the brain mechanism underlying the efficacy of WTG in treating low back pain.

The prefrontal cortex is important in human cognition, emotion, and executive function, and is also plays a significant role in pain processing.^{74–76} Kobayashi's study showed⁷⁷ that pressing stimulation activates the contralateral prefrontal cortex, with stronger activation in LBP patients compared to healthy volunteers. DLPFC is involved in higher-order cognitive functions related to attention, working memory, response inhibition, and information processing.⁷⁸ It plays a key role in the top-down regulation of pain perception and is also an important brain region involved in pain regulation in patients with

Table 3 The Detailed Information on CH17 and CH33

Channel	Light Sources and Detectors	Brodmann Area	Region	MNI Coordinates		
				X	Y	Z
17	S8-D7	BA 46	R-Dorsolateral prefrontal cortex	54.0002	34.2817	23.119
33	S14-D11	BA 5	R-Somatosensory Association Cortex	32.1519	-50.1517	73.0715

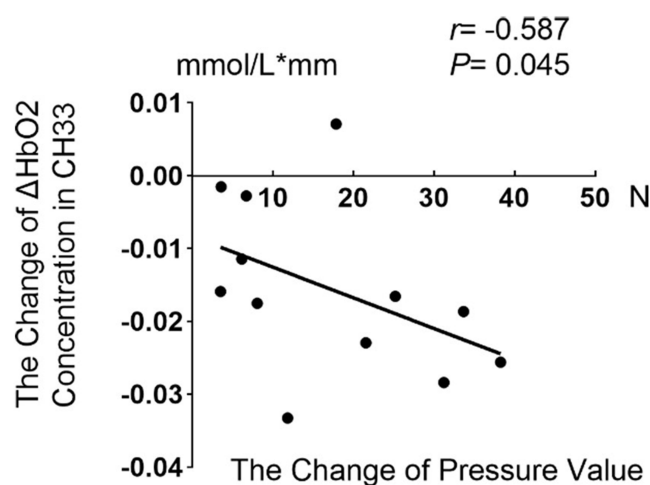


Figure 16 Correlation analysis between ΔHbO_2 Concentration and Pressure Value.

LBP.^{79,80} In this study, significant results in ΔHbO_2 concentration were observed in CH17 (DLPFC) before treatment, whereas post-treatment compression did not elicit a significant response in this region. This suggests that the DLPFC is engaged in responding to pressure pain, requiring increased neural resource recruitment. During the acute phase of pain, the DLPFC utilizes more cognitive resources to manage pain, resulting in a significant response.⁸¹ Previous studies have shown^{82,83} that reduced activation in the DLPFC, orbitofrontal cortex, anterior cingulate cortex, and other regions may be associated with pain relief. In this study, the patients' pain was relieved after treatment, and the ΔHbO_2 concentration of DLPFC caused by pressing decreased compared to that before treatment, which suggest that WTG inhibited the activation of DLPFC and reduced the unpleasant emotional experience caused by pain.⁸⁴ This diminishes the ability of DLPFC to sense pain and produce an analgesic effect. However, the post-treatment ΔHbO_2 concentration changes in the DLPFC did not remain significant after FDR correction, likely due to the small sample size of this study.

Resting-state brain networks differ between LBP patients and healthy volunteers.⁸⁵ One study had shown,⁸⁶ that when the default mode network (DMN) connection is frequent, then a person becomes more sensitive to pain. This study found that before and after WTG, the functional connection strength between channels and ROI demonstrated an overall downward trend, but the results do not apply for multiple comparisons. We suggest that the immediate effect of a single WTG treatment does not cause significant brain network changes. However, cumulative effects can occur after long-term and multiple WTG treatments resulting in significant changes in the brain network.^{32,46} Additionally, SAC and DLPFC may be key brain network nodes in WTG analgesia.

Current pain assessment methods are limited to self-reporting, mainly including VAS scores and McGill Pain Questionnaire (MPQ), which may lead to objective pain assessment.⁸⁷ This study implemented an innovative approach to pain assessment using a mechanical testing glove (SK-HTA-01). The glove objectively measures pain by recording three force values. Averaging these values minimizes measurement error and enhances the reliability of the data. In previous studies, the use of real-time compression as a mechanical stimulus to determine the pain threshold of the subject was reported.^{32,88} Another study⁷⁷ found that under pressure stimulation, the pain threshold of LBP patients was lower than that of healthy subjects, that is, when experiencing the same degree of pain, the pressure used to press on LBP patients is less. Matsuo et al⁶⁸ used a fixed pressure value to stimulate the low back to induce pain. In this study, we employed a similar method to apply pressure as Tan,³² in which fixed pressure value was not used, but used the same pain sensation subjectively felt by the subjects (ie., VAS = 5). However, we believe that the same pressure may produce different subjective pain perceptions in different subjects, especially in subjects with different pain perceptions and genders.^{89,90} This may introduce confounding variables that affect the findings from brain function research.

This study demonstrates that the ΔHbO_2 concentration in CH33 (SAC) during the compression task changes significantly before and after treatment. Therefore, the correlation between the ΔHbO_2 concentration change on CH33 and the pressure pain value was calculated to explore the correlation between pain perception and brain activity. We

found that the Δ HbO₂ concentration was negatively correlated with the pressure change value. As the pressure change value increased, the spontaneous neural activity of SAC in patients decreased significantly. This suggests that clinicians can objectively predict the pain level of ANSLBP patients based on the changes in Δ HbO₂ concentration in this area. As a relatively newer neuroimaging technology, Δ HbO₂ concentration detected by fNIRS offers an important brain biomarker for objective assessment of acute pain and prediction of pain relief. However, such potential biomarkers need to be validated before they can be applied in clinical practice.

Limitation

This study has some potential limitations. Firstly, the longitudinal effect of WTG treatment on brain pain processing over time cannot be studied after only one treatment. Secondly, the sample size of our study was small, and hence complex statistical analyses and subgroup analyses could not be performed. In future, researchers should observe the activity of brain function of ANSLBP patients treated with WTG by expanding the sample size, long-term intervention longitudinal study, and setting up the sham WTG and healthy volunteer groups. In addition, we employed the Pearson correlation coefficient to calculate functional connectivity, which may not reveal the causal relationship between brain area activities. In the future, Granger causality analysis should be adopted to further quantify the strength of effective connectivity between brain regions, as this will be more helpful in revealing the brain mechanism of WTG efficacy.

Conclusion

This study found that WTG can relieve the pain symptoms of ANSLBP patients. Although WTG is a commonly employed TCM for the treatment of pain, the potential mechanism neuromodulatory effect of WTG on the human brain need to be further clarified. In this study, multi-channel fNIRS recordings were performed before and after WTG treatment, and the results showed that WTG decreased Δ HbO₂ concentration in the contralateral SAC during compression. We speculate that the mechanism of the analgesic effect of WTG may be related to the inhibition of neuronal activity in the SAC of the brain. By examining the relationship between pressure changes and Δ HbO₂ concentration, we discovered that a decreased Δ HbO₂ concentration could serve as a potential biomarker for the analgesic effect of WTG. Our research offers objective neuroimaging evidence to elucidate WTG's neuromodulatory impact on the human brain and provides a methodological reference for studying the brain mechanisms underlying the efficacy of Complementary and Alternative Medicine.

Based on the regulatory effects of WTG on pain-related brain regions and the subjective analgesic effects observed in patients with acute non-specific low back pain ANSLBP in this study, it is initially confirmed that WTG has the potential to serve as a non-pharmacological pain intervention method. It can alleviate pain through the “warming and unblocking” effect, providing a more diverse non-pharmacological option for clinical pain management.

Given that this study adopts a single-group design without a sham control group, it has limitations in that confounding factors such as the placebo effect and natural recovery cannot be completely ruled out. Future studies can set up a “sham WTG group”, which simulating only cupping/massage operations without actual warming and unblocking effects, to more accurately distinguish the specific efficacy of WTG from non-specific effects. Meanwhile, a multi-session design can better align with the actual clinical treatment process, which helps observe the persistence of WTG's regulatory effect on brain activity and its long-term analgesic effect, and reduces the potential randomness of results caused by a single intervention.

Abbreviations

ANSLBP, Acute non-specific low back pain; BMI, Body Mass Index; BOLD, blood oxygen level-dependent; CH, Channel; CI, Confidence Interval; DLPFC, Dorsolateral Prefrontal Cortex; DMN, Default mode network; EEG, electroencephalogram; FDR, false discovery rate; fMRI, Functional magnetic resonance imaging; fNIRS, Functional near-infrared spectroscopy; Fp, Frontopolar area; Δ HbO₂, The changes in HbO₂ concentration; HbO₂, oxygenated hemoglobin; HbR, deoxygenated hemoglobin; LBP low back pain; M1, Primary Motor Cortex; MPQ, McGill Pain Questionnaire; NSAIDs, non-steroidal anti-inflammatory drugs; PMC and SMA, Pre-Motor and Supplementary Motor Cortex; ROI, Region of Interest; S1, Primary Somatosensory Cortex; SAC, Somatosensory Association Cortex; TCM, Traditional Chinese medicine; VAS, Visual Analogue Scale; WTG, Wentong Guan Therapy.

Data Sharing Statement

We plan to share de-identified individual participant data, including participants' demographic information, condition-related indicators, treatment parameters, and brain activity data. Data can be obtained by contacting the corresponding author.

Consent Statement

The study participants gave consent to publish.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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