Degenerative Neurological and Neuromuscular Disease

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ORIGINAL RESEARCH

Study on the Effects of Acupuncture with the "Yizhi Tiaoshen" Acupoint Formula on Blood Oxygen Metabolism and Neural Function in Key Brain Regions of AD Rats

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Purpose: Exploring the effects of acupuncture at the "Yizhi Tiaoshen" acupoint on blood oxygen metabolism and neurological function changes in the brain regions of AD model rats.

Methods: The AD model was replicated by intraperitoneal injection of D-galactose combined with bilateral hippocampal CA1 injection of Okadaic acid (OA). Thirty rats with successfully replicated model were selected through Morris water maze experiment and randomly divided into model group, donepezil hydrochloride group, and acupuncture group, with 10 rats in each group. After treatment, fNIRs were used to detect changes in Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of rats in each group, in order to evaluate the neurological function changes in key brain areas.

Results: The escape latency of the donepezil hydrochloride group and the acupuncture group was shortened, the number of crossings through the original platform increased, and the duration of stay in the quadrant where the original platform was located was prolonged. Based on fNIRs detection, the main differential channels of blood oxygen metabolism in AD rats were identified as 2–2 and 8–7, corresponding to the prefrontal and parietal lobes, respectively. The concentrations of Oxy Hb and Total Hb were significantly increased in both treatment groups, while the concentration of Deoxy Hb was significantly decreased.

Conclusion: Acupuncture with the "Yizhi Tiaoshen" acupoint formula and donepezil hydrochloride can improve the learning and memory function of AD rats, and its mechanism may be related to improving blood oxygen metabolism in the prefrontal and parietal regions and protecting neuronal function.

Keywords: Alzheimer's disease, "Yizhi Tiaoshen" acupoint, acupuncture, functional near-infrared spectroscopy technique, brain function

Introduction

Alzheimer's disease (AD) is a degenerative disease of the central nervous system that is more common in the elderly, characterized by decreased memory and progressive neurocognitive impairment. Its course is long, progressive, and irreversible.[1–3] The 2019 International Alzheimer's Association report indicated that there will be 152 million dementia patients by 2050.[4] At present, the treatment of AD still relies mainly on medication, but medication can only partially improve patients' symptoms, delay the progression of the disease, and cannot reverse or cure AD.[5,6]

Acupuncture has the characteristics of high safety, good compliance, and significant therapeutic effects.[7] Numerous studies have shown that the mechanism of acupuncture intervention in AD is closely related to regulating the expression of related proteins,[8] inhibiting central inflammatory response,[9] resisting oxidative stress damage,[10] regulating brain energy metabolism,[11] improving neuronal synaptic plasticity,[12] regulating autophagy activity levels,[13] and inhibiting neuronal apoptosis.[14] Acupuncture can effectively delay the occurrence and development of Alzheimer's disease by

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reducing the production of Aβ and inhibiting the excessive phosphorylation of Tau protein.[15] The progression of AD is closely related to the sustained inflammatory state of the central nervous system. Acupuncture can inhibit the hippocampal inflammatory response in AD mice and reduce the expression of IL-1β and NLRP3 inflammasome-related proteins.[16] Research has shown that electroacupuncture can effectively improve damage to hippocampal neurons, inhibit abnormal elevation of NOX2 levels in the hippocampus of AD rats, and enhance antioxidant capacity.[17] Electroacupuncture has shown good therapeutic effects in improving cognitive ability and brain glucose metabolism in AD mice. By improving cognitive ability in AD mice, it effectively regulates metabolic disorders in brain regions and is significantly correlated with the activation of BAT thermogenesis.[18] Research has shown that acupuncture can improve synaptic plasticity by inhibiting abnormal activation of the RhoA/ROCK pathway, thereby achieving the goal of treating Alzheimer's disease.[12] In addition, electroacupuncture can activate AMPK/mTOR mediated autophagy, partially improving cognitive impairment in APP/PS1 transgenic mice, enhancing the clearance rate of Aβ, and thereby reducing neuronal apoptosis.[13] Another study has confirmed that acupuncture can significantly improve cognitive dysfunction in AD mouse models, while reducing the generation of Aβ in mouse hippocampal tissue, alleviating neuronal apoptosis and damage, and inhibiting the activation of NLRP1 inflammasome in mice.[19] In summary, acupuncture has the characteristics of multi-level, multi pathway, and multi-target effects, which can effectively delay the occurrence and development of AD and improve the cognitive function of the body.Based on this, our research group has summarized the "Yizhi Tiaoshen" acupoint formula based on previous clinical observations (with "Xuanzhong", "Sanyinjiao", "Baihui", "Sishencong", "Shenmen", and "Neiguan" as the main acupoints).

The precise positioning of acupoints in experimental animals is a key factor in acupuncture treatment of diseases, but there are still differences in anatomy and physiological functions between humans and mice. For example, some acupuncture sites may be located next to specific muscles or acupoints in the human body, while there may not be corresponding anatomical landmarks on the surface of mice and rats. To solve this problem, it is necessary to reposition the acupuncture site based on the anatomical structure of rats and mice, which usually involves using knowledge of anatomy and physiology to find the most similar position for human acupuncture. If the acupuncture site is located on a major meridian, it is necessary to find the corresponding meridian or nerve distribution area on the rat body for acupuncture.[20] In addition, electrophysiological techniques are used to verify the effectiveness of acupuncture points and observe the physiological response changes in rats and mice after acupuncture, in order to ensure the scientific and adaptive nature of the selected points.[21] Modern theoretical techniques such as radiotracer staining, neuroscience localization, infrared radiation, good navigation and high acoustic conductivity, comparison of ion concentration and collagen content, and thermal signals can also be used to assist in localization.[22]

In recent years, numerous studies have explored the cortical structure and functional damage caused by AD from the perspective of brain functional imaging, such as functional magnetic resonance imaging technology. However, this technology focuses on functional connections between brain regions, and there is relatively little research on changes in cortical function.[23–25] This study used fNIRs technology, based on the neurovascular coupling mechanism, to observe the regulatory effect of the "Yizhi Tiaoshen" acupoint formula on the concentration of Oxy Hb, Deoxy Hb, and Total Hb in specific brain regions of AD model rats from the perspective of blood oxygen response, providing a basis for the study of the brain function mechanism of acupuncture intervention in AD.[26]

Materials and Methods

Experimental Animals

Sixty healthy 6-8-week-old male SD rats with a body weight of 180–220g were provided at the Research and Experimental Center of Gansu University of Traditional Chinese Medicine [SPF level, license number: SCXK (Gan) 2020–0001], and were fed in separate cages by the Research and Experimental Center of Gansu University of Traditional Chinese Medicine. 5 rats per cage, feeding and drinking regularly. Ethical approval number: 2021–187. The disposal of animals throughout the entire experimental process complies with the Guiding Opinions on Treating Experimental Animals issued by the Ministry of Science and Technology in 2006.[27]

Main Instruments and Reagents

Huacheng disposable sterile acupuncture and moxibustion needle (0.18 mm × 13 mm, Beijing Keyuanda Medical Supplies Factory); FNIRs collection and analysis system (NIRX, USA); WMT-200 Morris Water Maze Video Tracking System (Chengdu Taimeng Software Technology Co., Ltd).; Rat Stereofixator (NIRStar 15.0, NIRX, USA); 68025 digital brain stereotactic locator, 78001 miniature handheld skull drill (Shenzhen Ruiwode Life Technology Co., Ltd).; Okada acid (J23GS 155528, Shanghai Yuanye Biotechnology Co., Ltd).; Dimethyl sulfoxide (DMSO, 1121 E 0328, Aimijie Technology Co., Ltd).; D-galactose (B 21893, Shanghai Yuanye Biotechnology Co., Ltd).; Donepezil tablets (Weicai (China) Pharmaceutical Co., Ltd., National Pharmaceutical Approval Letter H 20050978, 5 mg); Gentamicin sulfate (2005060121, Shandong Lukang Chenxin Pharmaceutical Co., Ltd).

Establishment of AD Model in Rats

After adaptive feeding for 7 days, SD rats (n = 60) were randomly selected into a blank group and a sham operation group, with 10 rats in each group. The remaining 40 rats were used to replicate the AD rat model using D-galactose combined with Okada acid method.[28–30] Inject D-galactose solution into the abdominal cavity for 4 consecutive weeks (D-galactose dissolved in 0.9% sodium chloride injection at a concentration of 40 $mg \cdot mL^{-1}$), 0.12 g·kg-1·d^{-1}. On the fourth weekend, fast and water for 24 hours, and successfully anesthetize rats by intraperitoneal injection of 5% chloral hydrate (0.7 mL/kg). After that, prepare the head and fix it on the brain stereotaxic device while lying down. After disinfection with iodine, a incision approximately 1.5 cm long was made along the sagittal suture of the rat skull to fully expose the anterior fontanelle. According to the "Stereoscopic Localization Atlas of the Rat Brain",[31] locate the bilateral hippocampal CA1 area (3.0 mm behind the anterior fontanelle, 1.8 mm beside the midline of the brain, and 3.0 mm deep), use a miniature handheld skull drill to break through the skull, and use a micro syringe to slowly inject vertically, with 2 injections on each side μ L Okada acid, injected 4 times in total μ L (Okada acid is dissolved in 10% DMSO at a concentration of 50 $ng \cdot \mu L^{-1}$), injection speed of 1 $\mu L \cdot min^{-1}$, keep the needle for 5 minutes after injection, then slowly remove the needle and perform scalp suturing. For three consecutive days after surgery, intraperitoneal injection of gentamicin sulfate (0.6 $U \cdot kg^{-1}$) was given to prevent infection. In the fake surgery group, an equal amount of 0.9% sodium chloride injection was injected intraperitoneally, and an equal amount of 10% DMSO was injected into the CA1 area of the hippocampus on both sides. On the 10th day after modeling, according to literature.[32,33] Morris water maze experiment (MWM) was used to evaluate the model. Rats were subjected to Morris water maze experiment 4 times a day for 5 consecutive days, and the average of the 4 escape latency periods was taken. Based on the escape latency of rats on the 5th day, the average escape latency of the model rats is calculated as A, and the average escape latency of the fake surgery group rats is calculated as B, where the A-B value is greater than A × 20%.

Grouping and Intervention Methods

Randomly select SD rats (n=60) and divide them into a blank group and a sham operation group (n=10). Thirty rats with successfully replicated models are randomly divided into a model group, a donepezil hydrochloride group, and an acupuncture group (n=10). If the rats die, they will be supplemented according to the principle of randomization. Intervene on the second day after the model evaluation is completed.

Blank group, sham operation group, and model group: The acupuncture group was given the same fixation without any other intervention. To ensure the comparability of the experiment and prevent any impact caused by the surgery itself or the fixation process.

The donepezil hydrochloride group was treated with 0.125 mg/mL donepezil hydrochloride solution (0.45 mg/kg) by gavage, once a day for 7 days as one course of treatment, for a total of 4 courses of treatment. The drug concentration was calculated according to the animal dose conversion table.[34] Provide direct evidence of drug efficacy.

Acupuncture group: the acupoints were positioned according to the acupoint positioning method of rats in the *Common Acupoint Names and Positioning of Experimental Animals Part 2: Rats*[35] formulated by the China acupuncture and moxibustion Association. By calculating the ratio of human body to rat bones, the bone size of rats is estimated to select acupoints. The specific steps for selecting acupoints are to first determine the location of "Baihui", with "Four Divine Congs" located 2 mm away from "Baihui". Routine disinfection of acupoints: 0.18 mm × 13 mm disposable

acupuncture and moxibustion needles were used for acupuncture. Baihui: "located in the center of the parietal bone, using the flat needling method. Four Divine Cong": piercing in the direction of "Baihui", "with a needle depth of about 4–5 mm. Neiguan": located between the radial and ulnar sutures on the inner side of the forelimbs, approximately 3 mm away from the wrist joint; Shenmen: "the edge of the ulna with transverse stripes on the inner wrist of the forelimb; Hanging Bell": "10mm above the tip of the outer ankle of the hind limb; San Yin Jiao": 10mm straight up from the tip of the inner ankle of the hind limb; The above four acupoints are all treated with direct needling, with a needle insertion depth of about 2–3 mm, and are supplemented by twisting and turning. All acupoints were left with needles for 10 minutes, once a day, for 6 days of treatment, 1 day of rest, and 7 days as one course of treatment, for a total of 4 courses of treatment. The setting of this group helps to verify the effectiveness of acupuncture.

Morris Water Maze Test Detection in Each Group of Rats

On the second day after the intervention, conduct positioning navigation and space exploration experiments. Place a video recorder directly above the water maze to record the swimming trajectory of rats, and the Morris water maze video tracking system will complete the data collection and processing.

Positioning navigation experiment: Rats were subjected to a 60 second platform free water maze activity 1 day before the experiment to adapt to the water maze environment. The platform is fixed in the second quadrant, and the rats are placed in four quadrants in a clockwise order facing the pool wall. The time it takes for the rats to find the platform within 2 minutes is recorded. If the rat fails to discover or climb onto the platform within 2 minutes, guide the rat to the platform and stay for 30 seconds before proceeding to the next experiment. Train 4 times a day for 5 consecutive days, and take the average of the 4 tests.

Space exploration experiment: On the 6th day, the platform was removed and rats were placed facing the pool wall in the opposite quadrant of the original platform. The number of times the rats crossed the position of the original platform within 2 minutes and the time they stayed in the quadrant of the original platform were recorded.

Detection of Oxy Hb, Deoxy Hb, and Total Hb Concentrations in the Cerebral Cortex of Rats in Each Group

States. Each rat was collected for 180 seconds, and statistically significant channels were selected. Corresponding cortical blood flow diagrams were constructed based on the absolute values of Oxy Hb, Deoxy Hb, and Total Hb concentrations in the relevant channels. Refer to the rat brain stereotactic map[31] and compare it with the analysis software Matlab plane map to determine the relevant brain regions.

Statistical Analysis

Expressed as mean ± standard deviation ($\overline{X} \pm S$), using SPSS 26 0 statistical software for analysis. If the square difference is uniform, single factor analysis of variance is used for comparing the sample means between multiple groups, and LSD test is used for further pairwise comparison between groups. $P < 0.05$ indicates statistically significant differences. FNIRs were subjected to principal component analysis and partial least squares clustering analysis using SIMCA 14.1 software.

Results

Comparison of Morris Water Maze Experiments in Different Groups of Rats

There was no statistically significant difference in the escape latency between the blank group and the fake surgery group on the 5th day ($P > 0.05$); Compared with the fake surgery group, the escape latency of the model group was prolonged ($P < 0.05$); Compared with the model group, the escape latency of the donepezil hydrochloride group and the acupuncture group was shortened ($P < 0.05$); There was no statistically significant difference in the escape latency between the donepezil hydrochloride group and the acupuncture group ($P > 0.05$). There was no statistically significant difference in the number of times the blank group crossed the original platform and the duration of stay in the quadrant where the original platform was located compared to the fake surgery group ($P > 0.05$); Compared with the fake surgery

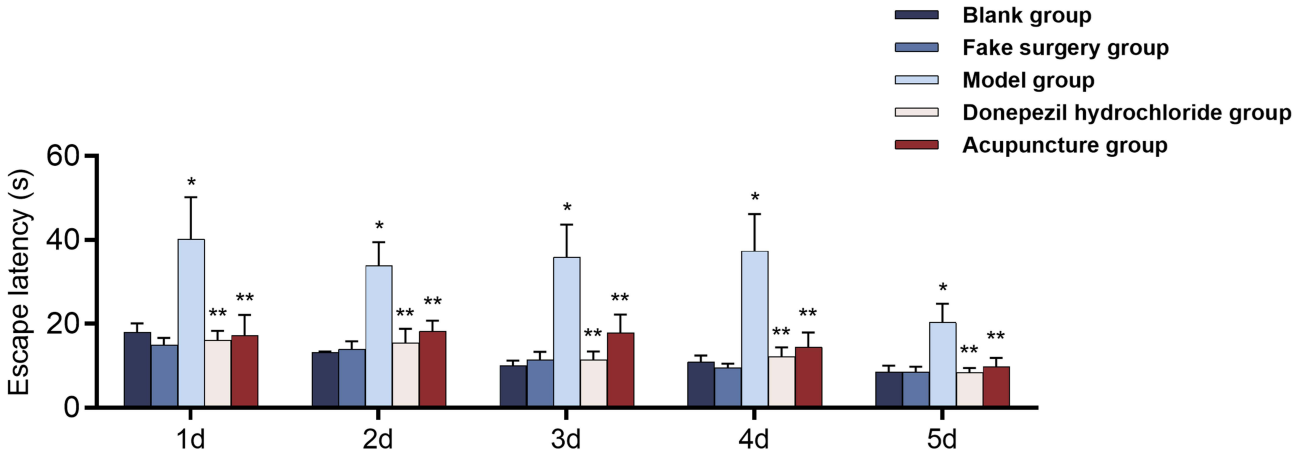

Figure 1 Comparison of escape latency periods among different groups of rats.
Notes: Compared with the fake surgery group, *P < 0.05; Compared with the model group, **P < 0.05.

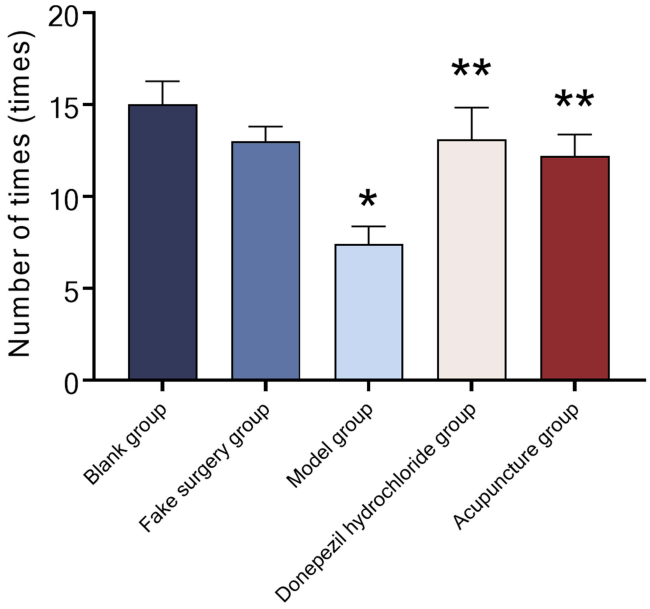

Figure 2 Comparison of the number of times each group of rats crosses the original platform.
Notes: Compared with the fake surgery group, *P < 0.05; Compared with the model group, **P < 0.05.

group, the model group had a decrease in the number of times it crossed the original platform and a shorter stay time in the quadrant where the original platform was located (P < 0.05); Compared with the model group, the donepezil hydrochloride group and acupuncture group had an increase in the number of times they crossed the original platform and a longer residence time in the quadrant where the original platform was located (P < 0.05); There was no statistically significant difference between the acupuncture group and the donepezil hydrochloride group (P > 0.05) (Figures 1–3).

Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the Cerebral Cortex of Rats in Each Group

Principal component analysis and partial least squares clustering analysis were completed using SIMCA 14.1 software to select differential channels 2–2 and 8–7. There was no statistically significant difference in the concentrations of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex between the blank group and the fake surgery group (P > 0.05); Compared with the fake surgery group, the concentrations of Oxy Hb and Total Hb in the model group were significantly reduced,

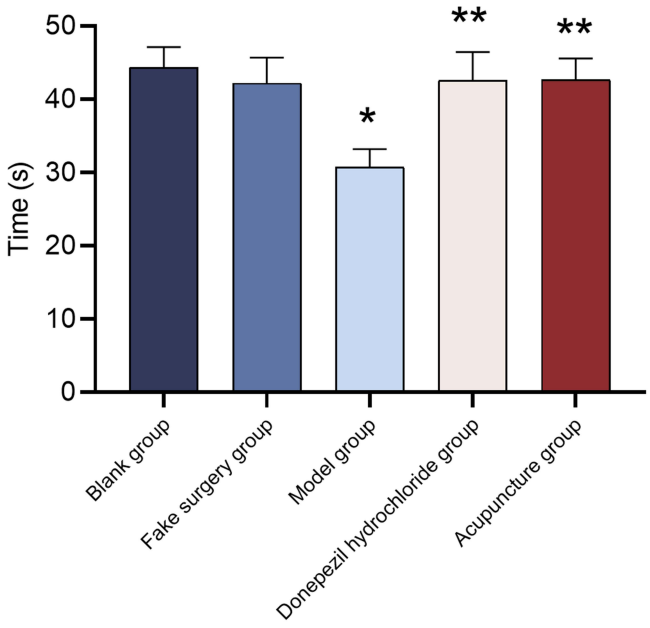

Figure 3 Comparison of dwell time in the quadrant where the original platform of each group of rats is located.
Notes: Compared with the fake surgery group, *P < 0.05; Compared with the model group, **P < 0.05.

while the concentrations of Deoxy Hb were significantly increased (P < 0.05); Compared with the model group, the concentrations of Oxy Hb and Total Hb in the donepezil hydrochloride group and acupuncture group were significantly increased, while the concentrations of Deoxy Hb were significantly reduced (P < 0.05); There was no statistically significant difference in the concentration changes of Oxy Hb, Deoxy Hb, and Total Hb between the acupuncture group and the donepezil hydrochloride group (P > 0.05) (Figures 4 and 5).

Oxy Hb Concentration Blood Flow Chart of Rats in Each Group

Select each group of rats under stimulation for the 150s, and use Oxy Hb as the standard to draw a schematic diagram of cerebral cortex blood flow from top to bottom. Each image represents the cortical blood oxygen concentration of the group, and the changes in cortical blood oxygen concentration are determined by the specific color of the bottom ruler: the closer to dark red, the higher the concentration of Oxy Hb, indicating relatively active cortical activity in that area; The closer it approaches dark blue, the lower the concentration of Oxy Hb, indicating that the activity of the cerebral cortex in that area is relatively inhibited (Figure 6).

Discussion

AD belongs to the categories of dementia, dementia, and forgetfulness in traditional Chinese medicine. Traditional Chinese medicine believes that it is caused by deficiency of the spleen and kidney, as well as deficiency of the medullary sea. The disease is located in the brain and is related to dysfunction of the heart, liver, spleen, and kidney. Due to the lack of energy and blood, the marrow sea is filled with nourishment and deficiency, unable to nourish and nourish the brain orifices, resulting in abnormal function of the brain orifices, leading to the loss of spiritual consciousness.[36] Based on this, our research group has summarized the acupuncture methods for the "Yizhi Tiaoshen" acupoint formula, selecting "Xuanzhong", "Sanyinjiao", "Baihui", "Sishencong", "Shenmen", and "Neiguan" to fill the essence and enhance intelligence, nourish the heart and regulate the mind. Among them, "Hanging Bell" is the essence of the Eight Meeting Points, which can nourish the brain and marrow; "San Yin Jiao" strengthens the spleen, nourishes qi, and nourishes the liver and kidneys; "Baihui" connects the Du meridian and regulates the brain and mind; "Si Shen Cong" is a key acupoint for the treatment of Alzheimer's disease, which is beneficial to the brain and intelligence; "Shenmen" and "Neiguan" calm the mind and nourish the mind. The combination of various acupoints plays the role of enhancing

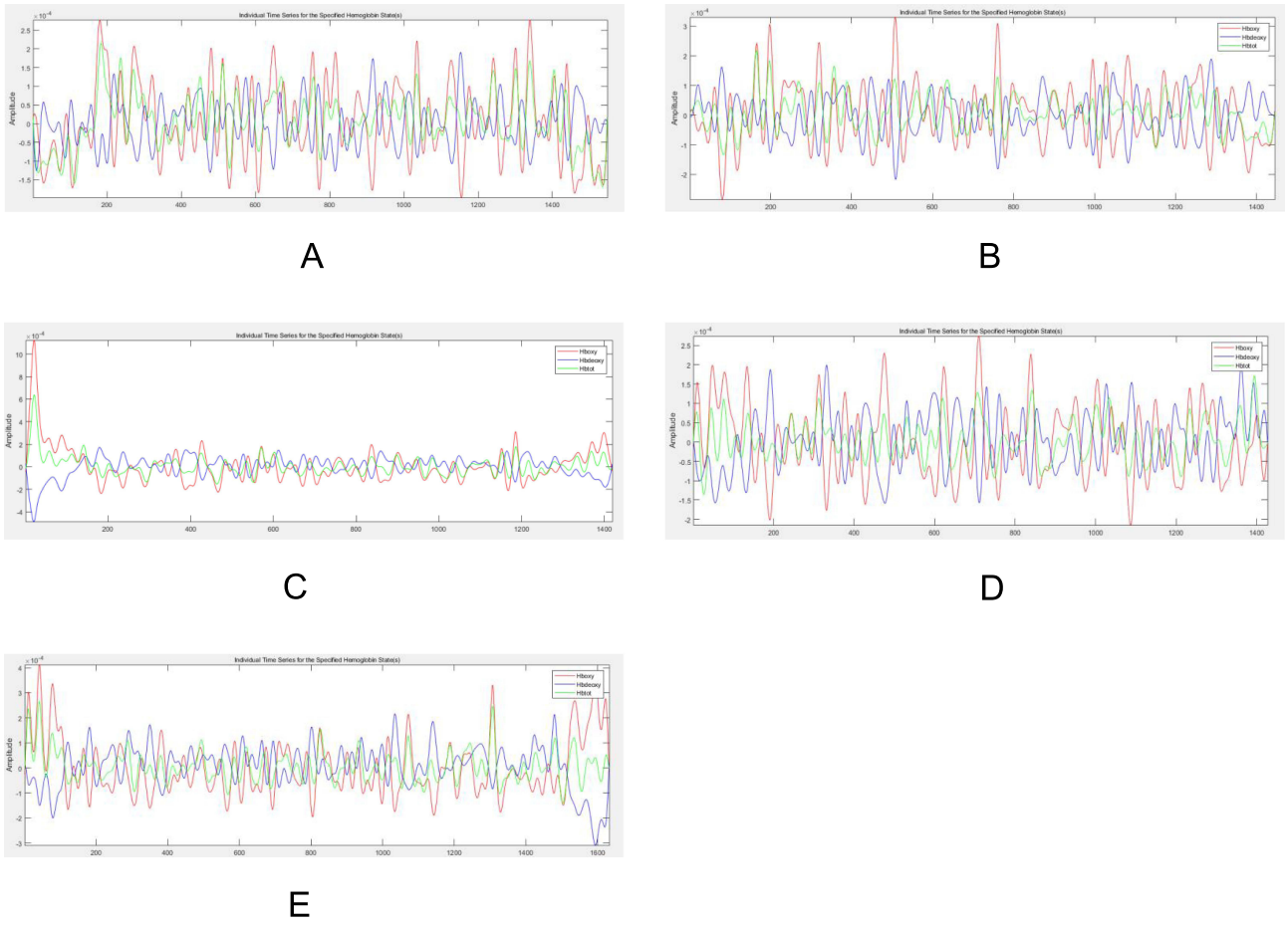

Figure 4 Concentrations of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of rats in each group from 2–2 channels.
Notes: (**A**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of the blank group 2–2 channels. (**B**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of the sham surgery group at channel 2–2. (**C**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of model group 2–2 channels. (**D**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channel 2–2 in the donepezil hydrochloride group. (**E**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channel 2–2 in the acupuncture group.

intelligence and regulating the mind. And our project team used resting state functional magnetic resonance imaging *(rs* fMRI) technology in clinical practice to analyze the effect of acupuncture at the "Yizhi Tiaoshen" acupoint on the functional connectivity between the hippocampus and the whole brain in AD patients. It was found that acupuncture at the "Yizhi Tiaoshen" acupoint can improve the cognitive function of AD patients, and the main brain functional mechanism is to strengthen the functional connectivity between the left hippocampus and the default network (inferior temporal gyrus, middle temporal gyrus, superior frontal gyrus, rectus abdominis muscle), as well as between the left hippocampus and the sensory (central posterior gyrus) and visual (cortex around the fissure and superior occipital gyrus) innervated brain areas.[37] Experimental studies have shown that acupuncture at the "Yizhi Tiaoshen" acupoint can improve learning and memory function in AD model rats, reduce neuronal damage, and its mechanism may be related to downregulating hippocampal GSK-3β expression, upregulating PP2A expression, and thereby inhibiting tau protein phosphorylation.[38]

Acupuncture shows many potential mechanisms in delaying the pathological process of AD, which further proves the good efficacy and unique advantages of acupuncture and moxibustion in treating AD. Acupuncture can promote an increase in cerebral blood flow, improve the oxygen and nutrient supply to nerve cells, and play an important role in alleviating nerve cell damage caused by poor blood circulation.[39] Research has shown that electroacupuncture can enhance the activity of antioxidant enzymes in the brain, reduce oxidative stress, protect nerve cells from free radical damage, and is crucial for preventing neurodegenerative damage in Alzheimer's disease.[17] The anti-inflammatory

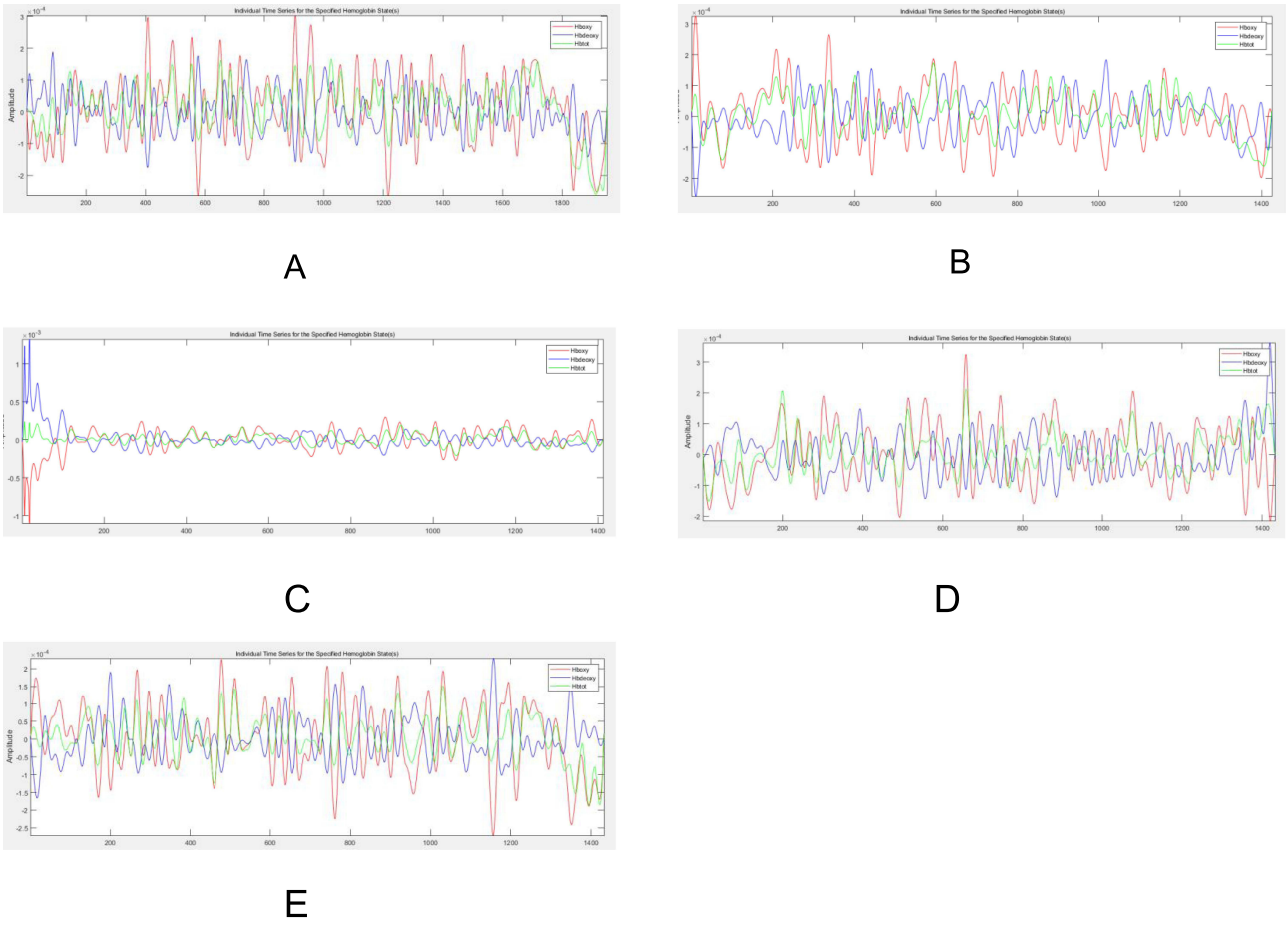

Figure 5 Concentrations of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of rats in each group from 8–7 channels.
Notes: (**A**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channels 8–7 in the blank group. (**B**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channels 8–7 in the sham surgery group. (**C**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channels 8–7 in the model group. (**D**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channels 8–7 in the donepezil hydrochloride group. (**E**) Concentration of Oxy Hb, Deoxy Hb, and Total Hb in the cerebral cortex of channels 8–7 in the acupuncture group.

mechanism of acupuncture and moxibustion is also an important aspect of its influence on AD pathology. The development of AD is closely related to chronic inflammation in the brain. Acupuncture and moxibustion can significantly reduce the expression of inflammatory factors such as TNF-α and IL-1β by regulating immune response, thereby reducing inflammatory response.[40] BDNF plays a key role in maintaining the survival of nerve cells and promoting the formation of neural connections. Its expression is usually reduced in AD rats, which is related to neurodegenerative damage and loss of cognitive function. Acupuncture can promote the expression of BDNF, thereby helping to repair damaged neural networks, enhance neural plasticity, and improve cognitive function in rats.[41] In addition, through BOLD-fMRI and other brain imaging technologies, it is found that acupuncture and moxibustion can activate specific brain regions related to cognition and memory, such as hippocampus and prefrontal cortex, which indicates that acupuncture and moxibustion may fight against the pathological changes of AD by directly acting on key regions of the brain.[42] In summary, acupuncture provides a multidimensional intervention strategy for the treatment of Alzheimer's disease through its complex biological mechanisms, including improving blood circulation, regulating immune responses, enhancing neuroprotective effects, increasing the expression of nerve growth factors, and activating key brain regions.

The Morris water maze experiment is a statistical method that evaluates the spatial memory ability of animals by measuring the number of times they cross the platform's position and the duration of their stay in the target quadrant within a specified time frame. The Morris water maze experiment in this study found that the escape latency of the

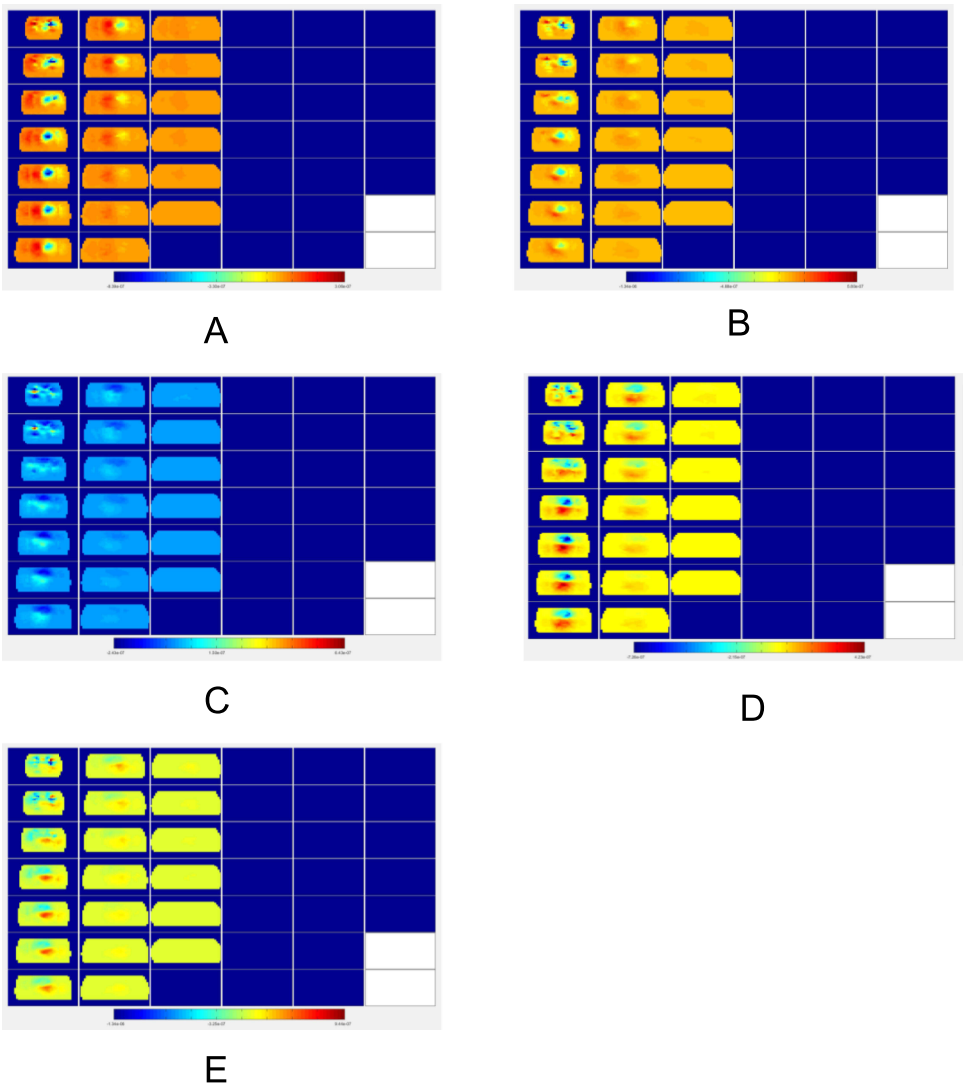

Figure 6 Blood flow maps of cerebral cortex in each group of rats.
Notes: (**A**) Cerebral cortex blood flow map of blank group. (**B**) Cerebral cortex blood flow map of sham surgery group. (**C**) Cerebral cortex blood flow map of the model group. (**D**) Cerebral cortex blood flow map in the donepezil hydrochloride group. (**E**) Cerebral cortex blood flow map of acupuncture group.

acupuncture group and the donepezil hydrochloride group was shortened, the number of times they crossed the original platform increased, and the residence time in the quadrant where the original platform was located was prolonged, confirming that both acupuncture and donepezil can improve and protect neuronal activity damage to varying degrees.

FNIRs technology is based on the neurovascular coupling mechanism, which real-time and dynamically reflects the local blood oxygen metabolism and neuronal activity in the brain area from the perspective of blood oxygen response, providing technical support for the establishment and evaluation of the correspondence between cortical functional activity and brain tissue anatomical location.[43–45] This experiment selected the frontal and parietal lobes as the key brain regions for brain activation changes in AD rats. The frontal lobe participates in the encoding and processing of situational memory, while the parietal lobe plays an important role in cognitive functions such as visual space, working memory, and situational memory. Xu and Xia used fNIRS technology to train the functional connections between the frontal and parietal lobes of subjects, the study showed that only three 15 minute training sessions could effectively increase the functional connections between the frontal and parietal lobes, and significantly improve memory and cognitive abilities.[46,47] Hou used fNIRS technology to regulate the cortical area of hippocampal connectivity (left parietal lobe) in subjects, increasing tasks related to hippocampal activation and improving associative memory.[48] The above studies

collectively indicate that fNIRS technology regulates functional connections between the cerebral cortex, indirectly affecting deep regions to improve related cognitive functions. Activation of the cerebral cortex can cause changes in local oxygen metabolism rate and local cerebral hemodynamics, which can help to understand the interrelationships between active brain regions and various brain regions.[49] At the same time, the fNIRs detection results of this experiment showed that the blood oxygen levels in the prefrontal and parietal lobes of AD rats were abnormal, mainly manifested by a decrease in Oxy Hb concentration, indicating that the activity of neurons in the two brain regions was inhibited, energy metabolism of nerve cells was reduced, and local oxygen consumption was reduced. After intervention, the Oxy Hb concentration significantly increased. This indicates that acupuncture at the "Yizhi Tiaoshen" acupoint can regulate the blood oxygen metabolism and neuronal function in the prefrontal and parietal lobes of AD rats, Further improving cognitive functions such as learning and memory may be the effective brain function mechanism of acupuncture intervention in AD.

In summary, acupuncture intervention can regulate the abnormal activation characteristics of key brain regions in AD rats, indicating that acupuncture may help regulate neuronal activity in the brain of AD rats, thereby slowing down pathological processes. Secondly, acupuncture promotes functional remodeling in key brain regions, suggesting that acupuncture may improve cognitive function in AD rats by promoting changes in neural plasticity and synaptic connections. Clarified the regulatory mechanism of acupuncture on AD brain function, providing a basis for acupuncture intervention in AD. Due to the complexity of brain structures, higher accuracy is still needed for the localization of AD brain regions. Therefore, future research should focus on constructing and analyzing brain networks and functional connections, using fNIRS technology to explore how acupuncture affects brain network integration and information transmission in AD patients. In addition, this study focuses on the functional changes of AD related brain regions and the regulatory effect of acupuncture on responsive brain region functions, but there is limited in-depth exploration of morphological changes in brain regions. Therefore, future research can use neuroanatomical and histological techniques to investigate the regulatory effects of acupuncture on the cellular structure and microstructure of key brain regions in AD, in order to more comprehensively elucidate the mechanism of acupuncture intervention in AD.

Ethics Approval

Experimental Animal Ethics Committee of Gansu University of Traditional Chinese Medicine (2021-187).

Consent for Publication

All authors have given final approval of the version and agreed with the publication of this study here.

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

The authors declare that they have no conflicts of interest for this work.

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