

REVIEW ARTICLE

Acupuncture in the Treatment of Amyotrophic Lateral Sclerosis: A Research Progress in Clinical Trials

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ABSTRACT

Background • Acupuncture, a complementary and alternative medicine (CAM) modality, shows promise as an integrative therapy for Amyotrophic Lateral Sclerosis (ALS) due to the chronic nature of the disease and its persistent symptoms. Many patients turn to CAM for ALS treatment.

Objective • This review assesses acupuncture's efficacy in treating Amyotrophic Lateral Sclerosis.

Methods • We searched China National Knowledge Network (CNKI) and PubMed databases for Chinese and English articles, including clinical trials, case studies, cohorts, and randomized controlled trials. The search, performed on March 31, 2023, encompassed literature published up to that date. Keywords used in titles and

abstracts were (acupuncture) OR (electro-acupuncture) AND (Amyotrophic Lateral Sclerosis).

Results • Among the 45 articles studied, 34 were included in this research. Acupuncture's benefits primarily lie in neuro-immune system regulation, enhanced quality of life, reduced fatigue, disease progression delay, and fewer relapses.

Conclusions • Recent clinical trials highlight the potential of traditional Chinese acupuncture in improving Amyotrophic Lateral Sclerosis symptoms (e.g., fatigue, neural functional deficits) and curtailing relapses. Consequently, acupuncture holds promise as an integrative therapy for ALS patients. (*Altern Ther Health Med.* 2023;29(7):114-118).

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INTRODUCTION

Amyotrophic lateral sclerosis (ALS) represents a progressive neurodegenerative condition characterized by the gradual loss of motor neurons in the spinal cord, cerebral cortex, cortical spine, and brainstem. Statistically, the incidence of ALS is reported as 1.75 (1.55-1.96) per 100 000 individuals.¹ While 5%–10% of cases are hereditary and familial, most (90%-95%) are sporadic. Unfortunately, effective therapy remains elusive, resulting in high mortality, and patients typically die due to the disease within 3–5 years from symptom onset.²

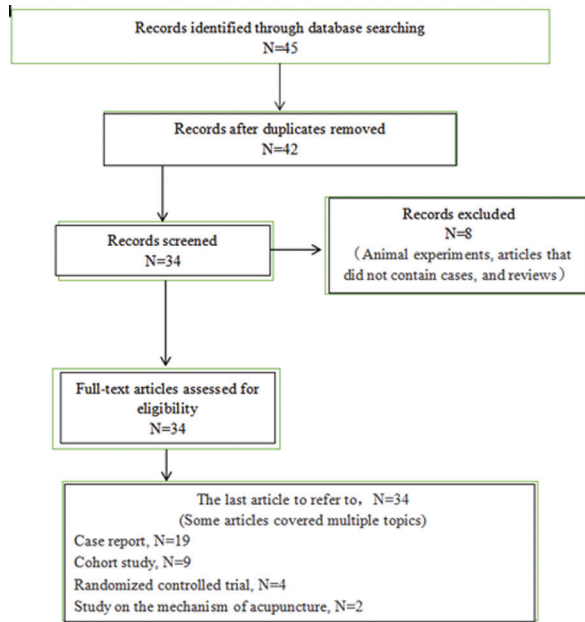
Although the interaction of endogenous and exogenous factors is believed to contribute to ALS development, the fundamental cause of the disease remains undiscovered,³ primarily due to its heterogeneous nature.⁴ The complexity of

addressing ALS can be linked to two primary components. The first involves diverse theories regarding pathogenesis mechanisms, encompassing genetic factors (such as variants of the *SOD1*, *C9orf72*, and *TARDBP* genes which account for most cases⁵), environmental or developmental influences, and issues related to RNA/protein management, excitotoxicity, or oxidative stress.^{6,7}

The second component is that clarifying the authenticity of the various proposed treatments presents a considerable challenge. Based on initial statistics, approximately 20 therapeutic approaches are currently employed in clinical practice. It ranges from synthetic small molecule drug therapy, which has dominated the field for an extended period, to emerging options like stem cell therapy and traditional Chinese medicine. Notably, the oral drug Riluzole, the sole approved disease-modifying treatment for ALS, extends patients' lives by only 2-3 months.⁸ However, it comes with a high cost and potential adverse reactions like nausea and fatigue.

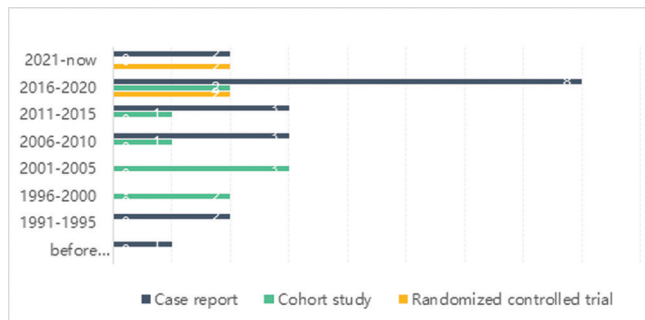
Hence, there is an urgent need to address these challenges and allocate additional resources to ALS research.⁹ It includes identifying novel therapeutic targets¹⁰ and exploring more available therapies. A comprehensive and significant analysis is imperative for therapeutic measures yielding unsatisfactory results. The ALS Functional Rating Scale-Revised (ALS-FRS(R)) currently serves as the gold-standard measure of

Figure 1. Flow Chart



Note: Flow chart illustrating the selection process and inclusion criteria for studies included in the review on the effectiveness of acupuncture in Amyotrophic Lateral Sclerosis (ALS) treatment. The flowchart outlines the screening, evaluation, and final inclusion of studies based on predefined criteria.

Figure 2. Trend analysis of Amyotrophic Lateral Sclerosis (ALS) clinical research publications both within China and abroad



Note: The figure presents a chronological overview of the number of publications related to ALS clinical research, highlighting the comparative trends between domestic and international contributions.

disease progression.¹¹ Other methods, such as the weakness scale, a valuable indicator for measuring numerous issues, also offer valuable insights.

This review is intended to assess the effectiveness of acupuncture in improving symptoms associated with amyotrophic lateral sclerosis. This paper aims to enhance diagnostic and treatment strategies for clinical research on amyotrophic lateral sclerosis while providing practical insights for conducting randomized controlled clinical trials.

METHODS

Study Design

The study design involved a comprehensive review of clinical trials to determine the effectiveness of acupuncture in ALS treatment. A thorough search was conducted on the

China National Knowledge Network (CNKI) and PubMed databases. The search encompassed Chinese and English articles that involved clinical trials, comprising case studies, cohorts, and randomized controlled trials. The search was performed until March 31, 2023, including articles published from the earliest literature to the specified date.

Search Strategy

The search strategy included utilizing keywords in titles and abstracts, with a focus on (acupuncture) OR (electroacupuncture) AND (Amyotrophic lateral sclerosis). The specific query employed was: (“acupuncture” [MeSH Terms] OR “acupuncture” [All Fields] OR (“electroacupuncture” [MeSH Terms] OR “electroacupuncture” [All Fields])) AND (“Amyotrophic lateral sclerosis” [MeSH Terms] OR “Amyotrophic lateral sclerosis” [All Fields]).

Study Selection

A total of 45 articles underwent evaluation, with 42 deemed relevant for inclusion in the present research, see Figure 1. Among these, 34 papers centered on acupuncture’s treatment of amyotrophic lateral sclerosis. Three papers were identified as duplicates and subsequently excluded. Moreover, eight articles about animal experiments or reviews were also omitted from the study. Among the 34 included papers, 9 were cohort studies, 19 were case reports, and only 4 were randomized controlled clinical trials. The remaining 2 papers were focused on animal mechanism explorations within the context of ALS, and due to their non-clinical nature, they were excluded from consideration.

Data Extraction and Analysis

A systematic process of data extraction and analysis was undertaken. Important information from the included papers was thoroughly extracted and organized. It included key details such as study design, intervention methods, outcomes, and relevant statistical data. The extracted data were then subjected to a comprehensive analysis involving a synthesis of findings, patterns, and trends across the various studies.

RESULTS

Prevalence of Acupuncture Usage among ALS Patients

The author conducted a comprehensive analysis of clinical trials involving acupuncture in amyotrophic lateral sclerosis treatment from the CNKI and PubMed databases across various years, as represented in Figure 2 and Figure 3. Since 2016, acupuncture and moxibustion, emblematic components of traditional Chinese medicine, have witnessed rapid growth in clinical research studies.

The rise in relevant research suggests promising results, specifically evident in assessing clinical efficacy within small sample sizes. Among the diverse clinical trials, the majority, constituting 59%, comprise case-by-case reports. Following this, cohort studies contribute the second-largest proportion at 28%. Notably, clinical randomized controlled trials investigating acupuncture as an ALS treatment emerged only

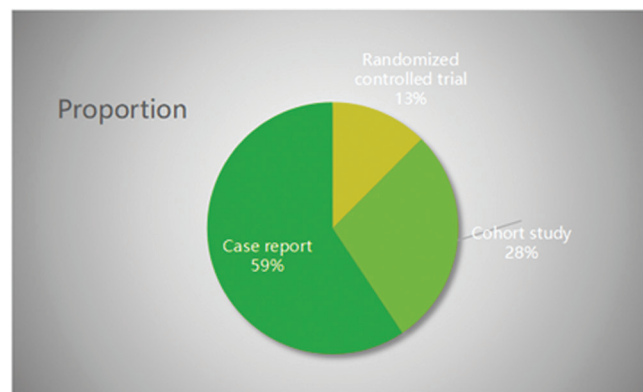
from 2016 onwards, with only four studies published to date representing a modest 13% share, refer to Figure 3.

Acupuncture therapy has garnered recommendations for its safety, minimal side effects, and high patient acceptability, notably excelling in treating neurodegenerative disorders. The studies within China and international scholars have directed their attention towards acupuncture's potential in ALS treatment, predicting a promising avenue for further research.

Summary of Clinical Randomized Controlled Trials

A comprehensive analysis covering 1980 to 2023 reveals consistent statistically significant disparities in main outcome indicators between clinical randomized controlled trials and their respective control groups. This evidence highlights the efficacy of acupuncture interventions. Remarkably, four distinct clinical randomized controlled trials have supported

Figure 3. The proportion of research papers in three different types of clinical trials



Note: The figure presents the relative proportions of research papers within case reports, cohort studies, and randomized controlled trials, shedding light on the distribution of research emphasis across these categories.

Table 1. Summary of Clinical Randomized Controlled Trials (RCT) in Acupuncture Treatment of Amyotrophic Lateral Sclerosis (1980-present)

References	Participants	Acupoints	Intervention	Outcome Measures	Results
Fangfang Cai et al. (2023)	60 (The control group was given oral administration of Western medicine Riluzole tablets 50 mg, and the treatment group was given acupuncture combined with rehabilitation exercise based on the control group)	Jiayu (LI15), Quchi (LI11), Yangxi(LI5), Hegu (LI4), Jiaji(EX-B2), Zusanli(ST36), Xiashi (GB43), Sanyinjiao(SP6), Yangling Spring (GB34), Weizhong (BL40)	Two weeks was a course of treatment, and both groups received one course of treatment.	The score of the Modified Norris and Appel Scale was used as the main reference index, TCM syndrome score before and after treatment	A response rate of the treatment group after treatment 83, 33% better than the control group 53. 33%, the difference was statistically significant
Feng Wu et al. (2021)	60 (The control group received oral riluzole tablets in 30 cases, and the observation group received lightning moxibustion in addition to the control group)	Fei Shu (double) (BL13), Pi Shu (double) (BL20), Wei Shu (double) (BL21)	Moxibustion was applied once every other day for a total of 3 months	ALS Functional Rating Scale-Revised (ALSFRS-R) and ALS Assessment Questionnaire (ALSAQ)-40 were estimated, pulmonary ventilation function indicators such as forced vital capacity (FVC) caused expiratory volume in 1 second (FEV1)	ALSFRS-R and ALSAQ-40 in the observation group were significantly higher than those before treatment ($P < .05$) and were considerably higher than those in the control group.
Xiangjie Xu et al. (2019)	40 cases (experimental group and control group 20 cases). The experimental group was treated with acupuncture based on the control group	1. Prone Position: Baihui (GV20), Fengchi (GB20), Dazhui (GV14), Jianjing (GB21), Feishu (BL13), Xinshu (BL15), Ganshu (BL18), Pishu (BL20), Shenshu (BL23), Yaoyangguan (GV3), Yongquan (KI1). 2. Supine position: Shenting (GV24), Tiantu (CV22), Danzhong (CV17), Yunmen (LU2), Quze (PC3), Juque (CV14), Zhongwan (CV12), Xiawan (CV10), Qihai (BL24), He Ding (EX LE2), Yanglingquan (GB34), Taichong (LR3)	The patients were observed for 60 minutes twice a week for 3 months	After treatment, patients' clinical symptoms such as numbness, cold and limb pain disappeared or disappeared, and TCM syndrome scores were reduced by more than 90%	The therapeutic effect of acupuncture is significant, which can significantly relieve clinical symptoms and improve the quality of life of patients
Bin Meng et al (2017)	28 (Control group 13 cases, oral administration of western drug riluzole tablets; Treatment Group 15 In this case, the oral administration of the Western medicine Riluzole tablets was based on the "Tongdu Wenyang" acupuncture treatment)	Yaoshu (GV2), Yao Yang Guan (GV3), Mingmen (GV4), Jizhong (GV6), Zhongshu (GV7), Jinsuo (GV8), Zhiyang (GV9), Lingtai (GV10), Shendao (GV11), Dazhui (GV14), Baihui (GV20), Shenting (GV24)	Once a day, 2 months as a course of treatment, a total of 3 courses of treatment	TCM syndrome score of potence disease and Appel function scale score	The total effective rate of the treatment group and the control group were 86.7% and 69.2%, respectively. The curative effect of the treatment group was significantly better than that of the control group in improving the TCM syndromes of Potence disease.

Table 2. Summary of Clinical Cohort Study in Acupuncture Treatment of Amyotrophic Lateral Sclerosis (1980-Present)

References	Participants	Acupoints	Intervention	Outcome Measures	Results
Baicheng Qian et al. (2020)	30	Dazhui(GV14), Shenque (CV8), Zusanli (ST36)	All the patients were treated with Qi Antler granules orally and Taiyishen acupuncture.	TCM syndrome score, ALSFRS-R score and Barthel index after 3 months of treatment	Qizhong granules combined with Taiyishen acupuncture can significantly improve the clinical symptoms and neurological function defects of patients with spleen and kidney Yang deficiency in motor neurone disease-amyotrophic lateral sclerosis.
Yan Wei et al (2018)	17	Bilateral C5 ~ T1 Jiaji points, lumbar bilateral L1-S1 Jiaji points (EX-B2)	Once a day, 6 days as a course of treatment, 1-day rest between courses, a total of 4 courses	ALSFRS-R and manual muscle testing	There were 2 cases with obvious effect, 3 cases with improvement and 12 cases with no effect, and the scores of the ALSFRS-R evaluation scale and MMT examination after treatment were better than those before treatment.
Sangmi Lee et al (2013)	18	Acupuncture points SP3, LU9, HT8, and LU10	Each patient received acupuncture treatment twice a day for 5 days	The EtCO ₂ , SpO ₂ , RR, K-ALSFRS-R scores and pulse rate were measured	Sa-am acupuncture appears to have a greater effect on inspiration rather than on expiration
Huaiming Zhou et al. (2006)	20	Fengfu point (GV16), Huatuo Jiaji (EX-B2) point	Once a day, 3 months for a course of treatment	Improvement in muscular atrophy	Effective rate 85%

Table 2. (continued)

References	Participants	Acupoints	Intervention	Outcome Measures	Results
Daguo Zhang et al. (2004)	8	Back group: Huatuo Jiaji points(EX-B2), Ganshu (BL18), Shenshu (BL23), Pishu (BL20); Four limbs group: Sanyinjiao point (SP6), Taixi (K13), Zusanli (ST36), Xuehai (SP10), Yanglingquan (GB34), etc.	Once a day, 10 times as a course of treatment, treatment time for 2 months	Improvement in muscular atrophy	Total effective rate 75%
Xiuguo Zhang et al. (2002)	10	Baihui (GV20), Fengchi (GB20), Pishu (BL20), Weishu (BL21), waist 1-5 Jiaji (EX-B2), Hegu (LI4), Quchi (LI11), Fenglong (ST40), Zusanli (ST36)	Leave the needle for 30 minutes, two weeks for a course of treatment	Improvement in muscular atrophy	Total effective rate 70%
Zuoling Xiong et al (2002)	6	Jiayu (LI15), Quchi (LI11), Shiousanli (ST40), Hegu (LI4), Liangqiu (ST34), Zusanli (ST36) and Jiexi (ST41)	Once every other day, the acupuncture was awakened for 20 minutes	Improvement in muscular atrophy	Satisfactory effect
Yongde Cheng et al. (1999)	46	The main points are Fengfu (GV16), Dazhui (GV14) and Jiaji (EX-B2)	One to 3 months, daily or alternate-day treatment	Improvement in muscular atrophy	Total effective rate 89.13%
Shiju Li et al. (1998)	10	Quchi (LI11), Hegu (LI4), Biguan(ST31), Liangqiu (ST34), Zusanli (ST36), Ganshu (BL18), Shenshu (BL23), Xuanzhong (GB39), Yanglingquan (GB34)	For 5 consecutive days, after 2 days, the next course of treatment was performed	Improvement in muscular atrophy	Total effective rate 70%

Table 3. A Summary of The Clinical Mechanism of Acupuncture Treatment in Amyotrophic Lateral Sclerosis

References	Participants	Acupoints	Intervention	Outcome Measures	Results
Ling Li et al. (2019)	In the same family, patients with the disease (4 cases) and the normal group (5 cases)	Bilateral of Jianyu (LI15), Quchi (LI11), Hegu (LI4), Futu (LI18), Zusanli (ST36), Jiexi (ST41)	Acupuncture was performed once a day for 30 min, once every 10 min, twice during the retention period, 10 times as a course of treatment, and 2d rest after one course of treatment to continue the next course of treatment, a total of 3 courses of acupuncture.	Experiments on relative and absolute quantitative techniques of isotope labelling	The effect mechanism of Yangming meridian acupuncture on FALS patients may be through the regulation of NAD (P) hydrogenase, affecting mitochondrial function, inhibiting cell apoptosis, and playing a therapeutic role.
Ling Li et al. (2020)	The diseased group (n = 4) and the normal group (n = 5) in the same family	Bilateral of Jianyu (LI15), Quchi (LI11), Hegu (LI4), Futu (LI18), Zusanli (ST36), Jiexi (ST41)	Acupuncture was performed once a day for 30min, once every 10min, twice during the retention period, 10 times as a course of treatment, and 2d rest after one course of treatment to continue the next course of treatment, a total of 3 courses of acupuncture	Analysis of panquinone cytochrome C reductase core protein 2 by functional annotation of biological processes	The effect mechanism of acupuncture at the Yangming meridian point on patients with familial amyotrophic lateral sclerosis (FALS) may be that the regulation of panquinone cytochrome C reductase core protein 2 promotes the repair of mitochondrial function.

acupuncture’s potential to influence disease progression across various dimensions, including speech, swallowing, and articulation, as presented in Table 1. These findings explain acupuncture’s multifaceted impact on disease development, providing valuable insights for potential therapeutic avenues.

Summary of Cohort Studies

A significant concentration of cohort study articles addressing acupuncture’s efficacy in ALS treatment was observed predominantly within the timeframe of 1998 to 2020, as presented in Table 2. Notably, the acupuncture points centered on the Du vein, the four meridians of the Foot Sun bladder Meridian in the back, and the Huatuo Jiaji and neck and waist Jiaji points. Across all nine studies examined, evident curative effects were consistently reported.

Exploring Clinical Mechanisms

The investigation into the clinical mechanisms underlying acupuncture’s efficacy in treating ALS has seen relatively recent contributions. Particularly, both clinical studies emerged around 2020; refer to Table 3. These studies unveiled intriguing findings, indicating that the therapeutic mechanism of acupuncture at the Yangming meridian point in individuals with familial ALS might involve the regulation of NAD (P) transhydrogenase. This regulation could impact mitochondrial function, hinder cell apoptosis, and ultimately grant therapeutic benefits.

DISCUSSION

ALS is a progressive neurodegenerative disorder characterized by the degeneration of motor neurons in the brain and spinal cord, leading to muscle weakness, paralysis,

and eventually respiratory failure.¹¹⁻¹² Acupuncture’s potential therapeutic role in ALS lies in its exploration as a complementary intervention that could address symptom mitigation, disease progression, and possible mechanisms of action, contributing to a comprehensive treatment approach.¹²⁻¹³

Summary of Evidence

Out of the 34 articles in this review, four studies presented data on the prevalence of clinical randomized controlled trials in acupuncture’s application for amyotrophic lateral sclerosis treatment. Particularly, starting from 2016, among the 16 clinical trials focused on acupuncture’s efficacy in ALS treatment, a substantial 62.5% of cases were attributed to case reports. Meanwhile, only four trials were classified as randomized controlled trials, highlighting their relatively modest presence.

ALS falls within the “impotence syndrome” category in traditional Chinese medicine, characterized by impaired limb motor function. Acupuncture, a cost-effective and eco-friendly therapy, operates on the neuroendocrine-immune network system, regulating immune function. This approach holds the potential to notably enhance neurological deficits in ALS patients, stimulate nerve myelin sheath regeneration and repair, and ameliorate limb mobility and sensory issues in post-sequelae stages. As a result, patients’ daily living capabilities and quality of life can be improved.¹² Acupuncture treatment primarily focuses on hand-foot Yangming meridian points, Dumai points, Huatuo Jiaji points, and bladder meridian points. Numerous studies further demonstrated acupuncture’s efficacy in addressing this condition.¹³

Based on randomized controlled trials, acupuncture emerges as a potent complementary alternative therapy, showcasing notable therapeutic effects. This data emphasizes

the necessity for high-quality studies to establish acupuncture's effectiveness and mitigate placebo effects correctly. The studied literature has focused on strengthening Yangming for impotence treatment. Considering that the primary muscles of the spleen, liver's fascia, and kidney's essence contribute to vitality, treating amyotrophic lateral sclerosis necessitates regulating the spleen and stomach, nourishing the liver and kidney, and fortifying tendons and strength. Integrating acupuncture and moxibustion with traditional Chinese medicine decoctions further enhances clinical efficacy.

The mechanism underlying acupuncture's impact on demyelination may involve electroacupuncture's potential to hinder neuronal cell apoptosis and inhibit skeletal muscle atrophy by sustaining high muscle volume.¹⁴ Elevated levels of reactive oxygen species (ROS) can trigger the activation of mitochondrial permeability transition pores, facilitating the release of pro-apoptotic proteins like cytochrome C into the cytoplasm, ultimately promoting cell apoptosis.¹⁵ Consequently, the elevation in complex III expression and activity, coupled with SIRT3 activation, leads to ROS clearance and mitochondrial function restoration, encouraging nerve cell protection.

Limitations and Future Implications

The study acknowledges a few limitations; firstly, the clinical trials regarding acupuncture's role in ALS treatment predominantly consist of small-sample randomized controlled trials and individual case studies, which may introduce selection biases. Secondly, acupuncture point selection often lacks syndrome differentiation and tailored treatment, leading to a lack of standardization in acupoint prescriptions and acupuncture techniques. Thirdly, some clinical trials exhibit inadequate design rigor, and there is a lack of standardized efficacy evaluation criteria. Furthermore, the current ALS studies notably lack comprehensive long-term follow-up investigations. The forthcoming ALS study by our research team (currently under submission) aims to address this limitation by extending follow-up periods to over half a year. It seeks to compensate for the current lack of prolonged research in the ALS field.

Future studies should focus on refining experimental protocols, exploring deeper into acupuncture mechanisms, conducting large-scale and high-quality randomized controlled trials, combining Traditional Chinese Medicine's syndrome differentiation approach with acupoint selection, quantifying acupuncture intensity and techniques, standardizing efficacy evaluation criteria, and implementing comprehensive long-term follow-ups to establish a robust evidence-based foundation for acupuncture's potential in treating nervous system autoimmune diseases.

CONCLUSION

In this comprehensive review, the potential of acupuncture as a complementary therapeutic approach for ALS has been thoroughly explored. Significant insights have emerged through careful analysis of clinical trials, cohort

studies, and mechanism investigations. Acupuncture showcases promising efficacy in alleviating ALS symptoms, promoting neurological function, and potentially influencing disease progression. However, the diversity of study designs, limited standardization of acupuncture techniques, and the predominance of small-sample sizes present challenges. Addressing these limitations through rigorous, large-scale, randomized controlled trials, harmonizing Traditional Chinese Medicine principles, and implementing long-term follow-ups will provide a more robust evidence base. Acupuncture's potential to enhance the lives of ALS patients is underscored, making it a valuable avenue for further research and potential integrative therapy in ALS management.

CONFLICTS OF INTEREST

There are no conflicts of interest.

AUTHOR CONTRIBUTIONS

Tianqi Wang and Xvdong Yang contributed equally to this work.

ACKNOWLEDGEMENTS

I would like to thank the Beijing Aiweiou Charity Foundation, the Beijing Billion Future Charity Foundation, the Beijing Liu Minru Institute of Women's Chinese Medicine, and the Gradually ALS Mutual Assistance Home for their fund support.

FINANCIAL SUPPORT AND SPONSORSHIP

Funding Project Name: 2022 Research and Cultivation Fund of Capital Medical University—An exploration of the "enteric-muscle" axis mechanism of acupuncture intervention in amyotrophic lateral sclerosis (PYZ22034).

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