Research Approaches and Prospects on the Therapeutic Mechanism of Medicine-Engineering Integrated Traditional Chinese Medicine Manipulation for Spinal Degenerative Diseases: Postprint

Authors: Wang Xu, Wei Xu, Zhu Liguo, Feng Tianxiao, Wang Zhipeng, Shi Bin, Wei Xu, Zhu Liguo

Date: 2023-05-29T00:00:00+00:00

Abstract

Spinal degenerative diseases are currently among the most common conditions in orthopedic clinical practice and represent a major advantageous disease category in traditional Chinese medicine (TCM) orthopedics. TCM manipulation constitutes a frequently employed therapeutic modality in TCM orthopedics for such conditions; however, research on the therapeutic mechanisms of TCM manipulation remains inadequately profound at present, thereby impeding the modernization process and international promotion of manipulation research. The medicine-engineering combination represents a novel research approach that has emerged in recent years from the integration of relevant scientific and technological advances with the modernization demands of TCM, which facilitates the modernization of research on the therapeutic mechanisms of TCM manipulation and promotes its internationalization. This article will examine the current application status of modern engineering technologies—including mechanical engineering technology, software engineering technology, neural engineering technology, and artificial intelligence technology—in TCM manipulation research, and will review recent modernization studies on the therapeutic mechanisms of TCM manipulation under the "medicine-engineering combination" research paradigm, thereby providing references for subsequent investigations into the therapeutic mechanisms of manipulation in treating spinal degenerative diseases.

Full Text

Preamble

Research Ideas on the Efficacy Mechanism and Prospects of Traditional Chinese Manipulative Therapy for Spinal Degenerative Dis-

eases Through Medicine-Engineering Integration

WANG Xu[1], WEI Xu[1,2], *ZHU Liguo*[1,2], FENG Tianxiao[1,3], WANG Zhipeng[4], SHI Bin[5]

[1]Wangjing Hospital, China Academy of Chinese Medical Sciences, Beijing 100102, China
[2]Beijing Key Laboratory of TCM Bone Setting, Beijing 100102, China
[3]Beijing University of Chinese Medicine, Beijing 100029, China
[4]Beihang University, Beijing 100083, China
[5]Shandong University of Traditional Chinese Medicine, Jinan 250062, China

*Corresponding authors: WEI Xu, Researcher; E-mail: weixu.007@163.com
ZHU Liguo, Chief Physician; E-mail: zhlg95@aliyun.com

Abstract

Spinal degenerative diseases represent one of the most common clinical conditions in orthopedic traumatology and constitute a major therapeutic focus of traditional Chinese orthopedics. Traditional Chinese manipulative therapy serves as a primary treatment modality for these conditions within Chinese medicine. However, current research on the efficacy mechanisms of traditional Chinese manipulative therapy remains insufficiently deep, hindering the modernization and internationalization of manipulative therapy research. The medicine-engineering integration research paradigm, emerging from the convergence of scientific and technological advances with the modernization demands of traditional Chinese medicine, offers a novel approach to modernizing research on manipulative therapy mechanisms and promoting its global dissemination. This review examines the application status of modern engineering technologies—including mechanical engineering, software engineering, neural engineering, and artificial intelligence—in traditional Chinese manipulative therapy research. We systematically organize recent modernization studies on manipulative therapy efficacy mechanisms under the "medicine-engineering integration" model to provide reference frameworks for future mechanistic investigations of manipulative therapy in treating spinal degenerative diseases.

Keywords: Spinal diseases; Musculoskeletal manipulations; Chinese manipulative therapy; Spinal degenerative disease; Medicine-engineering integration; Modernization of traditional Chinese medicine; Review

1 Literature Search Strategy

This study systematically searched relevant literature published between January 1, 2017, and February 1, 2023 across major Chinese databases (CNKI, CBM, Wanfang, VIP) and English databases (PubMed, Web of Science, Embase), supplemented with select seminal early publications and key articles defining the discipline. Chinese search terms included Chinese manipulative therapy, Tuina, medicine-engineering integration, robot, central nervous system, biomechanics, and artificial intelligence. English search terms included "Traditional Chinese Medical Manipulation," "Manipulation," "Spinal Manipulation," "Massage," "Manual Therapy," "Mobilization," "Medical engineering," "Robot," "Neuroengineering," "Software," "Neural Engineering," and "Artificial intelligence."

Using PubMed as an example, our search strategy was: ("Traditional Chinese Medical Manipulation"[Title/Abstract] OR "Manipulation"[Title/Abstract] OR "Spinal Manipulation"[Title/Abstract] OR "Massage"[Title/Abstract] OR "Manual Therapy"[Title/Abstract] OR "Mobilization"[Title/Abstract]) AND ("Medical engineering"[Title/Abstract] OR "Robot"[Title/Abstract] OR "Neuroengineering"[Title/Abstract] OR "Software"[Title/Abstract] OR "Neural Engineering"[Title/Abstract] OR "Artificial intelligence"[Title/Abstract]).

Following retrieval, literature screening was conducted based on inclusion and exclusion criteria. Inclusion criteria were: (1) Studies using manual therapy or manual therapy simulation devices as interventions, investigating mechanisms of manipulative therapy for spinal degenerative diseases (including cervical spondylosis, lumbar disc herniation, spondylolisthesis, spinal stenosis, etc.); (2) Studies with reliable arguments and evidence closely related to the topic. Exclusion criteria were: (1) Studies with low relevance to the topic; (2) Studies with poor logical rigor or low credibility. A total of 54 relevant articles were ultimately included.

2 Applications of Mechanical Engineering Technology

Mechanical engineering technology has been widely applied in medical research, particularly evident in traditional Chinese manipulative therapy studies. Numerous researchers have explored the clinical application of relevant technical devices. For instance, to address the fatigue and efficacy decline resulting from prolonged manipulative operations by Tuina practitioners, several investigators have developed and explored massage robotic arms and robots [11-13]. To standardize the teaching inheritance of traditional Chinese manipulative techniques, teaching robots and accompanying assessment systems have been developed, using mechanical curves and parameters collected by robots to evaluate the reliability of trainees' rotational-thrust manipulation operations, successfully achieving standardization and digitization of rotational-thrust technique teaching and assessment [14-15].

Furthermore, the application of relevant technical devices in mechanistic studies of manipulative therapy efficacy has become a recent research hotspot, primarily for simulating manual interventions in animal experiments. The greatest advantage of animal-based manipulative research is the ability to obtain post-intervention tissue specimens to investigate the effects of manipulation on the cervical tissue microenvironment and central nervous system. However, a major bottleneck in this research approach is how to reasonably simulate manual operations on experimental animal models [16]. Developing manipulative simulation robots, robotic arms, or force-measuring gloves based on analysis of the mechanical characteristics of traditional Chinese manipulative operations and the histological features of animal cervical tissues can ensure intervention consistency while maximizing the simulation of manipulative operational characteristics, representing a solution to current bottlenecks in mechanistic studies of traditional Chinese manipulative therapy (animal experiments).

Lin et al. [17] used a Grip system wireless tactile force-measuring finger cot to perform quantitative point-pressure stimulation on rat acupoints to simulate the point-pressing and pressing techniques in Tuina. Combined with a rat sciatica model, they verified through a series of animal experiments the correlation between P2X3 protein and pain signal transmission and peripheral sensitization enhancement in chronic compressed dorsal root ganglion models. They further demonstrated that point-pressing and pressing techniques simulated by this device could reverse the elevated P2X3 protein levels and decreased Piezo1 protein levels in dorsal root ganglia caused by neuropathic pain, providing evidence for the peripheral analgesic effects of Tuina in treating nerve root compression [17-19]. The same team conducted in-depth studies on the mechanisms of Tuina in treating nerve root compression diseases, confirming central and peripheral analgesic mechanisms through multiple dimensions including inhibition of spinal astrocyte proliferation and alleviation of peripheral soft tissue inflammatory microenvironment infiltration [20-21].

Harvard University's Seo et al. [22] developed a manipulative simulation device centered on electromagnetic actuators and force sensor components for studying skeletal muscle injury. The device fixed mouse position through a silicone port on the lower arm, unified mechanical stimulation through force sensors, and could be equipped with high-frequency ultrasound sensors for real-time imaging of mouse back muscles to analyze immediate effects on muscle tissue. Using this robot as an intervention, the team verified that cyclic compressive loading within a specific force range significantly promoted mouse skeletal muscle repair, suggesting the potential regulatory effects of manipulative therapy on muscle repair function.

Zhou et al. [23] developed a Tuina manipulative simulation instrument containing a power system and index control system, capable of performing five traditional Tuina techniques (pointing, vibrating, patting, kneading, and plucking) on experimental animal models. Based on this device, they conducted a series of animal experiments to deeply analyze the mechanisms of these Chinese manipulative techniques in alleviating sciatica [24-25] and reducing fever [26-27].

All these studies achieved simulation of traditional Chinese Tuina interventions in animal experiments through manipulative simulation devices, enabling in-depth exploration of intervention mechanisms and mining of potential effects at the molecular level. However, current devices primarily focus on simulating relaxation techniques, while effective simulation methods for thrusting/impulse techniques—more commonly used in orthopedic clinical practice—remain lacking. How to simulate thrusting techniques and deeply explore their effect mechanisms remains a current bottleneck in manipulative intervention research.

---

3 Applications of Software Engineering Technology

Beyond device-based implementation, the mechanical effects of Tuina can also be achieved through deconstruction using biomechanical analysis equipment and software reproduction. Advances in biomechanical software technology have enabled digital analysis of traditional Chinese manipulative techniques, solving the bottleneck problem of simulating thrusting techniques that are difficult to replicate through instruments. This approach also facilitates digital and visual analysis of manipulative effects and mechanical characteristics, becoming one of the primary methods for studying the biomechanical effect mechanisms of manipulative therapy in recent years.

Three-dimensional finite element analysis technology discretizes a continuous object into a model composed of finite units, replacing the original object. Based on the geometric and material properties of the original object and its force conditions, different unit types are employed, with units connected by nodes. Using energy principles and displacement method approaches, numerical methods expressed through matrix algebra [28] constitute the main approach in biomechanical research, offering advantages of lower cost and risk compared to in vivo studies. Representative mechanical analysis software includes MIMICS (Materialise, Belgium), Geomagic Studio (Geomagic, USA), and Solidworks and Abaqus (Dassault Systemes, France). These software programs create three-dimensional models from density differences in imaging data through "Mask" functions and multi-layer connections, enabling digitalization of anatomical structures by assigning material properties such as Young's Modulus, Elastic Modulus, and Poisson's ratio, and simulating manipulative effects through mechanical loading.

For example, Xue et al. [29] constructed a full cervical segment finite element model including the spinal cord and applied cervical rotational manipulation mechanical data to verify that Feng Tianyou's cervical rotational reduction technique [30] posed low risk of spinal cord injury, clarifying the mechanical characteristics of this technique's action on various cervical components. Subsequent studies using this method further confirmed that using cervical rotational manipulation on patients with ossification of the posterior longitudinal ligament carries certain spinal cord injury risks [31]. Cao et al. [32] constructed a C3-C7 segment finite element model to verify the biomechanical effects of three-dimensional balanced manipulation in treating cervical spondylotic radiculopathy, confirming its efficacy and safety. Numerous similar studies [33-35] have used this method to clarify the biomechanical effects of different types of thrusting techniques.

However, this method has technical limitations: most studies assign material properties for cervical tissue structures based on literature reports, where relevant indicators are primarily derived from cadaveric specimens. Significant differences exist between living tissues and cadaveric specimens in muscle, fascia, and other structural components, which may affect simulation accuracy to some extent.

Virtual reality interactive technology [36] is an advanced human-computer interaction technology that comprehensively applies various technologies to create realistic artificial simulation environments and effectively simulate human perceptual system behaviors in natural environments. Combined with motion capture systems, three-dimensional image reconstruction systems, and dynamic simulation systems, this technology can dynamically restore the movement trajectories of various structures during manipulative operations. Liu et al. [37] used virtual reality interactive technology to dynamically restore the morphological and area changes of cervical intervertebral foramina during rotational-thrust manipulation, demonstrating that increasing lower cervical intervertebral foramen area may help release adhesions around the foramen and relieve nerve root irritation symptoms, and proved that 150 N is the most appropriate pulling force for rotational-thrust manipulation. This technology's main advantage lies in achieving dynamic restoration of relevant anatomical structures during manipulative operations, showing significant application potential.

Muscle tension cloud mapping technology combines multi-point muscle tension testing, soft tissue tension testing systems, and MATLAB engineering software to comprehensively evaluate differences in neck and back muscle tension distribution before and after manipulative therapy. Compared with traditional single-point muscle tension testing [38], this method more comprehensively and intuitively reflects the effects of manipulation on neck and back muscle tension. Liang [39] and Wang [40] used this method to evaluate overall changes in neck and back muscle tension in cervical spondylotic radiculopathy patients before and after cervical rehabilitation exercises and rotational-thrust manipulation, confirming that these interventions can reduce muscle tension and balance tension between affected and healthy sides.

These studies represent applications of software engineering technologies in traditional Chinese manipulative therapy mechanistic research. Relevant software is widely used in analyzing biomechanical effects, morphological impacts on anatomical structures, and effects on cervical soft tissue tension, showing considerable promise. However, the models constructed by digital simulation technology are inherently complex digital constructs. Assigning different material properties, boundary conditions, mesh densities, and numerical solutions can significantly alter mechanical index outputs [41], and increased data complexity inevitably reduces simulation fidelity. Overcoming current software limitations and enhancing digital model simulation accuracy remain major challenges for researchers.

---

4 Applications of Neural Engineering and Neuroimaging Technologies

Neural engineering is an emerging 21st-century discipline that employs neuroscience and engineering methods to understand, repair, replace, enhance, or exploit nervous system characteristics, and design solutions for neural constraints and dysfunctions [42]. Exploring nervous system function constitutes an important component of this discipline. With continuous in-depth research in recent years, many devices for neural function research have emerged, enabling non-invasive exploration of central nervous system function and providing new approaches for investigating neural signal transmission processes of external interventions and exploring mechanisms of non-pharmacological therapies such as acupuncture and manipulation.

Functional magnetic resonance imaging (fMRI) is a brain function imaging technique that describes deoxyhemoglobin concentration changes induced by task-based or spontaneous regulation of neural metabolism [43]. It offers broad practicality (can be performed on clinically common 1.5T MRI scanners), non-invasiveness (no radioactive isotopes or drugs required), and good spatial resolution, making it a primary tool in neuroimaging research. Didehdar et al. [44] found that after spinal manipulation therapy (SMT), chronic nonspecific low back pain patients showed significant differences in N-acetylaspartate levels in the thalamus, insula, and dorsolateral prefrontal cortex, and choline levels in the thalamus, insula, and somatosensory cortex compared with sham manipulation groups. This suggests that spinal manipulation achieves pain relief by altering brain metabolite production in regions such as the thalamus and insula to inhibit pain signal generation.

Yang et al. [45] observed fMRI imaging before and after spinal manipulation therapy in patients with chronic low back pain, finding significant changes in regional homogeneity (Reho) in bilateral precuneus and right middle frontal gyrus, indicating that manipulative therapy can significantly improve altered brain neural functional activity in low back pain patients. The Reho value in the left precuneus could predict the immediate analgesic effect and evaluate manipulative analgesic efficacy. Moser et al. [46] found that rotating patients' heads to maximum angle during manipulation significantly increased functional connectivity in the posterior brain and cerebellum. Many domestic studies [47-49] have also used this technology to verify central nervous system responses to traditional Chinese manipulative effects. The widespread application of this technology connects physical therapy with brain science, establishing another pathway for elucidating manipulative therapy mechanisms. With advances in brain science and neural engineering, the central effects of manipulation are expected to be further clarified.

Additionally, electroencephalography (EEG) serves as another tool for exploring manipulative therapy mechanisms for spinal degenerative diseases, with the advantage of continuous measurement during manipulative procedures for recording continuous central effects. Navid et al. [50] used 61-channel EEG to record brain electrical changes in subclinical pain volunteers before and after spinal manipulation, finding that chiropractic treatment may alter central processing of pain and unpleasant sensations. Gevers-Montoro et al. [51] applied capsaicin stimulation to healthy volunteers' backs and used EEG to record pain thresholds and brain electrical changes before and after spinal manipulation. They found that volunteers developed clear hyperalgesia after capsaicin application, which disappeared after spinal manipulation, capturing frontal high-gamma oscillations and suggesting that segmental spinal manipulation can prevent secondary hyperalgesia. A similar study [52] used laser heat stimulation for pain induction and EEG for pain signal capture, preliminarily exploring the potential correlation between decreased pain sensitization and inhibition of Aδ and C fibers.

Currently, such research primarily focuses on exploring the central analgesic mechanisms of spinal manipulation, with limited application in traditional Chinese manipulative therapy effect mechanisms, though showing certain potential.

The application of neural engineering and neuroimaging technologies provides a powerful supplement to research methods for investigating the efficacy mechanisms of traditional Chinese manipulative therapy for spinal degenerative diseases. Combined with advances in brain science, exploring the efficacy mechanisms of manipulative therapy from a central perspective will become a key future research direction.

---

5 Potential Applications of Artificial Intelligence Technology

Artificial intelligence technology is a new technical science that studies and develops theories, methods, technologies, and application systems for simulating, extending, and expanding human intelligence [53]. The rapid development of AI technologies in image recognition, deep learning, neural networks, and robot development has greatly promoted multidisciplinary integration. Currently, many manipulative therapy-related studies have achieved breakthroughs through AI technologies, primarily in intelligent manipulative simulation device development and algorithm-enhanced robotic treatment plan selection.

Yang et al. [54] used an AI robotic arm (Dobot Magician) to learn and simulate the one-finger Zen technique, comparing pressure perception functions of this technique on rabbit and human soft tissues, providing methodological reference for "equivalent dose-equivalent effect" simulation of manipulative techniques in experimental animal models. Some studies employed biomechanical exploration robots [55-57] to detect and intelligently restore the mechanical effect variation process of lumbar thenar pushing techniques on fresh pig cadaver

L3/L4 segments, analyzing stress changes in lumbar muscles and spinal cord. This research method also has potential for application in cervical manipulative studies.

In fact, manipulative robots based on AI technology, genetic algorithms, and other technical means continue to emerge [58-61]. Compared with the mechanical gloves and manipulative simulation instruments mentioned earlier, intelligent manipulative simulation robots can autonomously complete intervention processes and directly generate outcome indicators or images, greatly promoting basic research and mechanistic studies of manipulative therapy. However, current AI robots primarily focus on relatively safe relaxation techniques, while the development of thrusting/impulse manipulation robots still faces numerous ethical and clinical issues.

Furthermore, computer algorithms enhanced by AI offer advantages in imaging index screening, potential pathway identification, and target prediction, also holding value for exploring manipulative therapy mechanisms: techniques such as radiomics [62] and Repeated Incremental Pruning to Produce Error Reduction (RIPPER) [63]. However, these technologies have seen limited application in manipulative therapy research and have not yet formed widely recognized research systems.

---

6 Summary and Outlook

Spinal degenerative diseases represent an advantageous therapeutic domain for traditional Chinese medicine. As a representative non-pharmacological therapy of TCM, traditional Chinese orthopedic manipulation was listed among the first batch of national intangible cultural heritage in 2006 (No. IX-6) and has developed a unique theoretical system and characteristic diagnostic and treatment protocols through long-term practice. However, under the current trend of standardization, modernization, and internationalization in medical research, how to further elucidate the effect mechanisms of traditional Chinese manipulative therapy for spinal degenerative diseases through more scientific research methods combined with modern instruments has become a primary challenge for practitioners.

Previous manipulative research has primarily focused on clinical efficacy and mechanical characteristic analysis, leading to explorations in standardized manipulation operations and digital teaching inheritance models. However, insufficient attention has been paid to deep interpretation of manipulative scientific connotations from multidisciplinary perspectives and modern analysis of effect mechanisms, resulting in a situation where traditional Chinese manipulative therapy enjoys wide clinical application but faces difficulties in achieving international recognition [64]. With the increasing popularity of the "medicine-engineering integration" research model, modern science and technology provide contemporary manipulative practitioners with numerous novel research methods and ideas. Standardized manipulative intervention simulation, digital and visual analysis of manipulative effects, and dynamic restoration and analysis of manipulative operation processes have all become possible. Correctly selecting research methods and technologies to promote the modernization and internationalization of traditional Chinese manipulative therapy research constitutes a primary work objective for manipulative practitioners during the 14th Five-Year Plan period.

Based on current research status, our team believes that on the foundation of clinical efficacy and biomechanical studies of target manipulative techniques, implementing basic research on manipulative effect mechanisms through reliable, quality-controlled manipulative simulation devices, deeply exploring the neuro-humoral-immune effect mechanisms of manipulative therapy for spinal degenerative diseases, and elucidating central effect mechanisms through relevant neural engineering and neuroimaging technologies will enrich the scientific connotation of traditional Chinese manipulative therapy from multiple dimensions. This will be the main research direction for the next stage of manipulative effect mechanism studies.

References

[1] IMAGAMA S, ANDO K, KOBAYASHI K, et al. Multivariate analysis of factors related to the absence of musculoskeletal degenerative disease in middle-aged and older people[J]. Geriatr Gerontol Int, 2019, 19(11): 1141-1146. DOI: 10.1111/ggi.13786.

[2] SAFIRI S, KOLAHI A A, HOY D, et al. Global, regional, and national burden of neck pain in the general population, 1990-2017: systematic analysis of the Global Burden of Disease Study 2017[J]. BMJ, 2020, 368: m791. DOI: 10.1136/bmj.m791.

[3] SHENG C, CHEN M J, WU X H, et al. Global, regional and national burden of low back pain 1990-2019: a systematic analysis of the Global Burden of Disease study 2019[J]. J Orthop Transl, 2022, 32: 49-58. DOI: 10.1016/j.jot.2021.07.005.

[4] KIM J, RYU H, KIM T H. Early reoperation rates and its risk factors after instrumented spinal fusion surgery for degenerative spinal disease: a nationwide cohort study of 65,355 patients[J]. J Clin Med, 2022, 11(12): 3338. DOI: 10.3390/jcm11123338.

[5] THOOMES E, THOOMES-DE GRAAF M, CLELAND J, et al. Timing of evidence-based non-surgical interventions as part of multimodal treatment guidelines for the management of cervical radiculopathy: a Delphi study protocol[J]. BMJ Open, 2021, 11(3): e043021. DOI: 10.1136/bmjopen-2020-043021.

[6] ZHU L G, WEI X, WANG S Q. Does cervical spine manipulation reduce

pain in people with degenerative cervical radiculopathy? A systematic review of the evidence, and a meta-analysis[J]. Clin Rehabil, 2016, 30(2): 145-155. DOI: 10.1177/0269215515570382.

[7] WEI X, WANG S Q, LI J X, et al. Complementary and alternative medicine for the management of cervical radiculopathy: an overview of systematic reviews[J]. Evid Based Complement Alternat Med, 2015, 2015: 793649. DOI: 10.1155/2015/793649.

[8] BLANPIED P R, GROSS A R, ELLIOTT J M, et al. Neck pain: revision 2017[J]. J Orthop Sports Phys Ther, 2017, 47(7): A1-83. DOI: 10.2519/jospt.2017.0302.

[9] CARREON L Y, ANDERSON P A, TRAYNELIS V C, et al. Cost-effectiveness of single-level anterior cervical discectomy and fusion five years after surgery[J]. Spine (Phila Pa 1976), 2013, 38(6): 471-475. DOI: 10.1097/brs.0b013e318273aee2.

[10] WANG Y T, TIAN J. Striving to draw a blueprint for the development of "medicine-engineering integration" in China[J]. Chinese Journal of Emergency Medicine, 2014, 23(1): 6-7. DOI: 10.3760/cma.j.issn.1671-0282.2014.01.003.

[11] YANG Z W, FENG G B. Research on safe traditional Chinese medicine massage robot arm system[J]. China Plant Engineering, 2021(24): 29-30. DOI: 10.3969/j.issn.1671-0711.2021.24.018.

[12] CHEN L L. Design and compliance control research of cervical rehabilitation massage robot[D]. Harbin: Harbin Engineering University.

[13] ZHANG M L, SHI Z X, LUO Y F, et al. Structural design and analysis of the end-effector for traditional Chinese medicine Tuina robot[J]. Journal of Mechanical Transmission, 2020, 44(6): 73-77, 83. DOI: 10.16578/j.issn.1004.2539.2020.06.013.

[14] HUO L Y, FU B F, FENG T X, et al. Self-controlled study of cervical rotatory-thrust manipulation teaching robot for standardized training of rotatory-thrust manipulation[J]. Journal of Traditional Chinese Orthopedics and Traumatology, 2021, 29(5): 6-11. DOI: 10.3969/j.issn.2095-4174.2019.11.016.

[15] FENG M S, ZHU L G, WANG S Q, et al. Stability study of cervical rotatory-thrust manipulation teaching robot[J]. China Journal of Orthopaedics and Traumatology, 2017, 30(3): 241-246. DOI: 10.3969/j.issn.1003-0034.2017.03.011.

[16] WEI X, WANG X, SUN K, et al. Research status and prospects of traditional Chinese manipulative therapy for cervical spondylosis[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(10): 4781-4784. DOI: 10.3969/j.issn.2095-4344.0579.

[17] LIN Z G, JIANG S C, CHENG Y B, et al. Experimental study on the effect of Tuina on P2X3 receptors in DRG neurons of rats with lumbar disc

herniation[J]. Chinese Archives of Traditional Chinese Medicine, 2017, 35(10): 2475-2479. DOI: 10.13193/j.issn.1673-7717.2017.10.002.

[18] LIN Z G, CHEN S J, CHEN L C, et al. Analgesic effect of Tuina kneading technique on neuropathic pain rats and its influence on substance P in serum, dorsal root ganglion, and spinal dorsal horn[J]. Chinese Archives of Traditional Chinese Medicine, 2019, 37(4): 877-880. DOI: 10.13193/j.issn.1673-7717.2019.04.024.

[19] WU Z W, SONG P F, ZHU Q G, et al. Effect of Tuina on astrocytes in spinal dorsal horn of rats with chronic constriction injury model of sciatic nerve[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2022, 37(6): 3462-3466. DOI: 10.3969/j.issn.1007-3205.2018.09.026.

[20] YAO C J, REN J, HUANG R X, et al. Transcriptome profiling of microRNAs reveals potential mechanisms of manual therapy alleviating neuropathic pain through microRNA-547-3p-mediated Map4k4/NF- b signaling pathway[J]. J Neuroinflammation, 2022, 19(1): 211. DOI: 10.1186/s12974-022-02568-x.

[21] YAO C J, GUO G X, HUANG R X, et al. Manual therapy regulates oxidative stress in aging rat lumbar intervertebral discs through the SIRT1/FOXO1 pathway[J]. Aging (Albany NY), 2022, 14(5): 2400-2417. DOI: 10.18632/aging.203949.

[22] SEO B R, PAYNE C J, MCNAMARA S L, et al. Skeletal muscle regeneration with robotic actuation-mediated clearance of neutrophils[J]. Sci Transl Med, 2021, 13(614): eabe8868. DOI: 10.1126/scitranslmed.abe8868.

[23] ZHOU Y, ZHANG Y M, ZHANG X Y, et al. Safety of five Tuina manipulations in rats with deep vein thrombosis[J]. Evid Based Complement Alternat Med, 2021, 2021: 6897124. DOI: 10.1155/2021/6897124.

[24] LÜ T T, YANG C, YU T Y, et al. Effect of three techniques and three acupoints on ultrastructure of descending pathway in rats with sciatic nerve injury[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2019, 34(11): 5212-5216.

[25] LÜ T T, SHAO S, YU T Y, et al. Analysis of the effect of Tuina on gene expression at sciatic nerve injury site in rats based on RNA sequencing technology[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(5): 2589-2592.

[26] ZHANG Y Q, LIU Z F, YU T Y, et al. Effect of six Tuina techniques for reducing fever on COX-2/PGE2/EP3 signaling pathway in hypothalamus of young rabbits with lipopolysaccharide-induced fever[J]. Journal of Beijing University of Chinese Medicine, 2022, 45(11): 1160-1167. DOI: 10.3969/j.issn.1006-2157.2022.11.009.

[27] LIU Z F, ZHANG Y Q, YU T Y, et al. Metabolomics study on the effect of six pediatric Tuina techniques for reducing fever on hypothalamus of young rabbits with lipopolysaccharide-induced fever[J]. China Journal of Traditional Chi-

nese Medicine and Pharmacy, 2022, 37(5): 2645-2650. DOI: 10.3969/j.issn.1674-1749.2022.02.005.

[28] WELCH-PHILLIPS A, GIBBONS D, AHERN D, et al. What is finite element analysis?[J]. Clin Spine Surg, 2020, 33: 323-324. DOI: 10.1097/BSD.0000000000001050.

[29] XUE F, CHEN Z J, YANG H, et al. Effects of cervical rotatory manipulation on the cervical spinal cord: a finite element study[J]. J Orthop Surg Res, 2021, 16(1): 737. DOI: 10.1186/s13018-021-02885-6.

[30] FENG T Y. Clinical study on treatment of soft tissue injury with integrated traditional Chinese and western medicine[M]. Beijing: China Science and Technology Press, 2002.

[31] XUE F, DENG H, CHEN Z J, et al. Effects of cervical rotatory manipulation on the cervical spinal cord complex with ossification of the posterior longitudinal ligament in the vertebral canal: a finite element study[J]. Front Bioeng Biotechnol, 2023, 11: 1095587. DOI: 10.3389/fbioe.2023.1095587.

[32] CAO S N, CHEN Y Z, ZHANG F, et al. Clinical efficacy and safety of "three-dimensional balanced manipulation" in the treatment of cervical spondylotic radiculopathy by finite element analysis[J]. Biomed Res Int, 2021, 2021: 5563296. DOI: 10.1155/2021/5563296.

[33] GUO X, ZHOU J M, TIAN Y Y, et al. Biomechanical effect of different plate-to-disc distance on surgical and adjacent segment in anterior cervical discectomy and fusion - a finite element analysis[J]. BMC Musculoskelet Disord, 2021, 22(1): 340. DOI: 10.1186/s12891-021-04218-4.

[34] ZHOU J M, GUO X, KANG L, et al. Biomechanical effect of C5/C6 intervertebral reconstructive height on adjacent segments in anterior cervical discectomy and fusion - a finite element analysis[J]. Orthop Surg, 2021, 13(4): 1408-1416. DOI: 10.1111/os.13010.

[35] HUANG X C, YE L Q, WU Z X, et al. Biomechanical effects of lateral bending position on performing cervical spinal manipulation for cervical disc herniation: a three-dimensional finite element analysis[J]. Evid Based Complement Alternat Med, 2018, 2018: 2798396. DOI: 10.1155/2018/2798396.

[36] MU L, PEI Y, LI Y, et al. Research and application progress of virtual reality and augmented reality technology in medical imaging teaching[J]. Chinese Journal of Medical Education Research and Practice, 2021, 20(9): 947-950. DOI: 10.3760/cma.j.cn116021-202105016-00678.

[37] LIU G W, FENG M S, ZHU L G, et al. Dynamic analysis of cervical intervertebral foramen structural changes during rotatory-thrust manipulation based on virtual reality technology[J]. Chinese Journal of Tissue Engineering Research, 2023, 27(9): 1346-1351. DOI: 10.12016/j.issn.2096-7991.2023.09.012.

[38] CHEN W J, CHEN Z H, WU J T, et al. Evaluation of performance imbalance of bilateral neck and shoulder muscles in patients with cervical spondylotic radiculopathy using a novel muscle quantitative assessment device[J]. Chinese Journal of Tissue Engineering Research, 2022, 26(3): 430-434.

[39] LIANG L. Study on the intervention effect and mechanism of cervical rehabilitation exercises on cervical spondylotic radiculopathy[D]. Beijing: China Academy of Chinese Medical Sciences.

[40] WANG X. Mechanism study of rotatory-thrust manipulation for cervical spondylotic radiculopathy based on soft tissue tension and finite element technology[D]. Beijing: China Academy of Chinese Medical Sciences.

[41] LAGRAVÈRE M. Finite element analysis: is it justifiable?[J]. Am J Orthod Dentofacial Orthop, 2021, 159(3): 255-256. DOI: 10.1016/j.ajodo.2020.10.017.

[42] EREIFEJ E S, SHELL C E, SCHOFIELD J S, et al. Neural engineering: the process, applications, and its role in the future of medicine[J]. J Neural Eng, 2019, 16(6): 063002. DOI: 10.1088/1741-2552/ab4869.

[43] GLOVER G H. Overview of functional magnetic resonance imaging[J]. Neurosurg Clin N Am, 2011, 22(2): 133-139, vii. DOI: 10.1016/j.nec.2010.11.001.

[44] DIDEHDAR D, KAMALI F, YOOSEFINEJAD A K, et al. The effect of spinal manipulation on brain neurometabolites in chronic nonspecific low back pain patients: a randomized clinical trial[J]. Ir J Med Sci, 2020, 189(2): 543-550. DOI: 10.1007/s11845-019-02140-2.

[45] YANG Y C, ZENG K, WANG W, et al. The changes of brain function after spinal manipulation therapy in patients with chronic low back pain: a rest BOLD fMRI study[J]. Neuropsychiatr Dis Treat, 2022, 18: 187-199. DOI: 10.2147/NDT.S339762.

[46] MOSER N, MIOR S, NOSEWORTHY M, et al. Effect of cervical manipulation on vertebral artery and cerebral haemodynamics in patients with chronic neck pain: a crossover randomised controlled trial[J]. BMJ Open, 2019, 9(5): e025219. DOI: 10.1136/bmjopen-2018-025219.

[47] GUO G X, ZHU Q G, XU S D, et al. Exploring the brain mechanism of analgesia by traditional Chinese Tuina based on brain functional magnetic resonance imaging technology[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(12): 6268-6271. DOI: 10.3969/j.issn.1001-6910.2019.01.28.

[48] YANG Y C, TAN W L, WANG W, et al. Study on changes in default mode network functional connectivity before and after Tuina treatment for chronic low back pain[J]. Chinese Journal of Medical Computer Imaging, 2020, 26(2): 101-108. DOI: 10.3969/j.issn.1006-5741.2020.02.001.

[49] GUO R S, HUANG F, HUANG C Y, et al. Study on the effect of Lingnan Lin's bone-setting manipulation on amplitude of low-frequency fluctuation in resting-state functional magnetic resonance imaging in patients with occipital

neuralgia[J]. Journal of Guangzhou University of Chinese Medicine, 2021, 38(1): 109-115. DOI: 10.13359/j.cnki.gzxbtcm.2021.01.021.

[50] NAVID M S, LELIC D, NIAZI I K, et al. The effects of chiropractic spinal manipulation on central processing of tonic pain - a pilot study using standardized low-resolution brain electromagnetic tomography (sLORETA)[J]. Sci Rep, 2019, 9: 6925. DOI: 10.1038/s41598-019-42984-3.

[51] GEVERS-MONTORO C, PROVENCHER B, NORTHON S, et al. Chiropractic spinal manipulation prevents secondary hyperalgesia induced by topical capsaicin in healthy individuals[J]. Front Pain Res (Lausanne), 2021, 2: 702429. DOI: 10.3389/fpain.2021.702429.

[52] PROVENCHER B, NORTHON S, GEVERS MONTORO C, et al. Effects of chiropractic spinal manipulation on laser-evoked pain and brain activity[J]. J Physiol Sci, 2021, 71(1): 20. DOI: 10.1186/s12576-021-00804-2.

[53] LOEB G E. Developing intelligent robots that grasp affordance[J]. Front Neurorobot, 2022, 16: 951293. DOI: 10.3389/frobt.2022.951293.

[54] YANG L, WANG J H, GAO Y C, et al. Exploring the relationship between pressure parameters of one-finger Zen pushing technique in humans and rabbits based on artificial intelligence robotic arm[J]. Journal of Guangzhou University of Chinese Medicine, 2021, 38(10): 2231-2235. DOI: 10.13359/j.cnki.gzxbtcm.2021.10.031.

[55] FUNABASHI M, NOUGAROU F, DESCARREAUX M, et al. Does the application site of spinal manipulative therapy alter spinal tissues loading?[J]. Spine J, 2018, 18(6): 1041-1052. DOI: 10.1016/j.spinee.2018.01.008.

[56] FUNABASHI M, NOUGAROU F, DESCARREAUX M, et al. Spinal tissue loading created by different methods of spinal manipulative therapy application[J]. Spine (Phila Pa 1976), 2018, 43(18): 1290-1296. DOI: 10.1097/BRS.0000000000002096.

[57] FUNABASHI M, KAWCHUK G N, VETTE A H, et al. Tissue loading created during spinal manipulation in comparison to loading created by passive spinal movements[J]. Sci Rep, 2016, 6: 38107. DOI: 10.1038/srep38107.

[58] DESCARREAUX M, NOUGAROU F, DUGAS C. Standardization of spinal manipulation therapy in humans: development of a novel device designed to measure dose-response[J]. J Manipulative Physiol Ther, 2013, 36(2): 69-77. DOI: 10.1016/j.jmpt.2012.12.007.

[59] ALAVANDAR S, SUNDARAM K, NIGAM M. Genetic-algorithm based robot massage[J]. Journal of Theoretical and Applied Information Technology, 2007, 3(4): 102-109.

[60] WANG W D, ZHANG L, LI J Z, et al. The force control and path planning of electromagnetic induction-based massage robot[J]. Technol Health Care, 2017, 25(S1): 275-285. DOI: 10.3233/THC-171331.

[61] LI C X, FAHMY A, LI S X, et al. An enhanced robot massage system in smart homes using force sensing and a dynamic movement primitive[J]. Front Neurorobot, 2020, 14: 30. DOI: 10.3389/fnbot.2020.00030.

[62] ZHUANG M H. Exploring the construction and application of radiomics model for cervical instability based on the concept of "balance between muscle and bone"[D]. Beijing: China Academy of Chinese Medical Sciences.

[63] LUO X Z, LI K S, ZHANG B, et al. Exploring factors influencing the meridian conduction effect of Zusanli (ST36) with the aid of artificial intelligence technology[J]. Chinese Acupuncture & Moxibustion, 2018, 38(10): 1105-1108. DOI: 10.13703/j.0255-2930.2018.10.019.

[64] WEI X, HAN T, SUN K, et al. Advantages, key issues, and research strategies of traditional Chinese medicine in prevention and treatment of bone and joint degenerative diseases[J]. Chinese General Practice, 2021, 24(35): 4421-4426. DOI: 10.12114/j.issn.1007-9572.2021.01.032.

Author Contributions: WANG Xu was responsible for conceptualization, literature collection, and manuscript drafting; FENG Tianxiao contributed to manuscript revision; WEI Xu and ZHU Liguo were responsible for quality control, review, and overall supervision; WANG Zhipeng and SHI Bin provided technical support.

Conflict of Interest Statement: The authors declare no conflicts of interest.

Received: February 14, 2023; **Revised:** May 5, 2023

Edited by: Cui Sha

Note: Figure translations are in progress. See original paper for figures.