Perspective

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The Value of Traditional Medicine Should not be Underestimated—Traditional Chinese Medicine in Treatment of Autoimmune Diseases

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Abstract

Autoimmune diseases of the nervous system (ADNS) are characterized by the formation of a pronounced neurologic deficit and often lead to disability. The attention of doctors and researchers is increasingly attracted by complementary medicine as adjuvant or preventive therapy for various diseases, including autoimmune diseases. Traditional Chinese medicine (TCM) is a combination of treatment methods that include acupuncture, herbal medicine, dietetics, physical exercises, and other methods that are often used in conjunction with recognized approaches of official medical science. The article describes the application of TCM techniques in autoimmune diseases of the nervous system, and demonstrates clinical experience in the use of acupuncture, herbal medicine, diets and physical exercises. Traditional and complementary medicine is an important and often underestimated healthcare resource, especially in the prevention and treatment of autoimmune diseases of the nervous system.

Keywords: Autoimmune diseases; Traditional Chinese medicine; Nervous diseases

1 Introduction

Autoimmune diseases (AD) refer to diseases with complex etiopathogenesis. The manifestation is influenced by external causes such as previous infectious diseases, inflammatory, genetic and endocrine factors. Depending on the immune response and the mechanism of its implementation, AD can be organ-specific [i.e. multiple sclerosis, severe myasthenia gravis (MG)] or organ-non-specific (systemic). According to traditional Chinese medicine (TCM), any disease is considered as the result of energy imbalance. The body is a unified holistic energy system, and the basis of health is *Zhen Qi* (真气 genuine qi), which is the general internal energy that controls all processes in the body. When it is insufficient and/or disharmonious, there is a loss of control over vital functions. The Chinese philosophy's assumptions about cosmogenesis, which are yin (阴) and yang (阳), and the five elements (*Wu Xing* 五行), are the basis of Chinese medicine. According to *Huang Di Nei Jing* (《黄帝内经》*The Yellow Emperor's Inner Classic*), yin and yang are considered as two opposite positions that are in opposition to and complementary to each other. A disease is an energy imbalance, and healing is the process of rebalancing, which is achieved through the methods of Chinese medicine. One of them is acupuncture and moxibustion (*Zhen Jiu* 针灸), which has been used since ancient times and has a stimulating, regulating and coordinating effect on the nervous system. Dietetics is based on achieving a yin-yang balance, and not only do the taste qualities matter, but the color of food, and the five tastes correspond to the five primary elements of the *Wu Xing* system (Water, Fire, Wood, Metal and Earth) also matter.

Autoimmune diseases of the nervous system (ADNS) include more than thirty nosological forms. The most studied are multiple sclerosis (MS), acute demyelinating inflammatory polyneuropathy (ADIP) or Guillain-Barré syndrome (GBS) and myasthenia gravis, which are characterized by the formation of a pronounced neurologic deficit and often lead to disability. The pathogenesis of these conditions is based on autoimmune reactions, which in MS are associated with inflammatory demyelination with genetic predisposition under the influence of environmental factors. Pro-inflammatory cytokine production leads to the activation of autoimmune inflammatory processes and damage of nerve structures with subsequent degeneration. The chain of pathological cascade is represented as follows: changes in the

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immune system, inflammation, demyelination and neurodegeneration, which is the basis of MS pathogenesis. In the heterogeneous mechanisms of the pathogenesis of GBS, the autoimmune process is also leading, but in the implementation of pathological disorders, as in MS, provoking factors are important. These include the presence of Epstein-Barr viruses, hepatitis E, cytomegalovirus, mycoplasma bacteria and Campylobacter jejuni, to the structures of which antibodies are produced, and the process of immune-mediated demyelination (myelinopathy), or axonal nerve damage (axonopathy), often developing dysautonomia, and it often ends in sluggish tetraparesis. Autoantibodies to neuromuscular synapse structures, namely to postsynaptic cholinergic receptors, as well as antibodies to thymus gland tissues play the main roles in the pathogenesis of myasthenia characterized by pathological muscle fatigue.[1,2]

Recently, the attention of researchers has been drawn to the use of complementary and alternative medicine (CAM) as an adjuvant or prophylactic therapy for various diseases and, in particular, for ADNS. The WHO global report on traditional and complementary medicine notes that already 98 members have developed a national CAM policy, which will determine its proper integration into the healthcare system, and the recommendations adopted will lead to the development of higher-quality clinical guidelines that will be of great assistance in its application.[3–7] One of the components of CAM is TCM. The basis of TCM is derived from the Chinese philosophy's assumptions about cosmogenesis, which is yin and yang, and *Wu Xing* (五行 the five elements). The Western approach to the treatment of AD is to suppress immunity, which is allowed by TCM in severe critical conditions (myasthenic crisis, exacerbation of MS), and subsequently Chinese doctors continue treatment to restore the energy potential of the body.

2 Evidence-based medicine in TCM

A certain log of CAM is associated with insufficient involvement of evidence-based medicine in reasoning of its effectiveness and safety. The criteria standards of evidence-based medicine include randomized controlled (prospective) trials with double or triple-blind control, which are referred to as the so-called Class I trials. It is believed that the materials of these trials and the meta-analysis conducted on their basis should determine the reliability of the information. If the interventions mentioned above are justified in terms of safety and a possible favorable effect on the health of the population for pharmacoepidemiology, their application in traditional and complementary medicine is difficult, and sometimes impossible.[8] In our previous work we proposed to distinguish three types of body response to acupuncture treatment, that is immediate, rapid and delayed.[9] Liu et al.[10] in their work demonstrated an immediate rapid effect when applying acupuncture to patients with migraine. It has also been noted that transcutaneous auricular stimulation of the vagus nerve has an immediate modulating effect on the brain structures.[11] A delayed response in treatment of temporomandibular joint dysfunction was noted by Kang et al.[12]

3 Application of TCM for ADNS

3.1 Dietetics and nutriology

Many researchers note the positive role of a low-calorie diet based on the principles of the Mediterranean diet on the course of ADNS. It has been noted that the use of vegetables, fruit, legumes, and seafood, especially in combination with prebiotics and probiotics, helps to reduce inflammation, restore or maintain the composition of the intestinal microflora, which closely interacts with the immune system.[13-15]

Bahr et al.[16] used a ketogenic diet limiting carbohydrate intake to 20-40g per day and intermittent fasting on a representative sample of patients with relapsing-remitting MS. The clinical study indicated a modulating effect of the diet on immunity and reduction of disease severity.

In a systematic review of the Medline, PubMed and Scopus bibliographic databases, Bagur et al.[17] using a sufficient amount of material, established a relationship between macro- and micro-nutrient intake, vitamin D content and MS incidence. It was found that patients who consumed certain plant products along with amino acids (carnitine and melatonin) or coenzyme Q10 and vitamin D, had high concentrations in the blood serum, which significantly reduced the risk of MS, disease recurrence and the appearance of new foci of demyelination, improving cerebral function and walking. A decrease in vitamin D concentration was observed during the disease recurrence. The data obtained indicates that circulating serum vitamin D concentrations can be considered as a biomarker of MS. Some studies indicate a negative correlation between serum vitamin B12 concentrations and the degree of neurological deficit. It has been noted that vitamin B12 plays a fundamental role in central nervous system function, especially in mediating the conversion of homocysteine to methionine, which is essential for DNA and RNA synthesis. Vitamin B12 deficiency can lead to elevated homocysteine concentrations.

In the work of Rinaldi et al.[18] , the clinical effectiveness of the use of probiotics is noted, which stimulates natural immunity, as well as suppresses the activity of pathogenic microflora that may contribute to the development of immune-mediated diseases. Probiotics are non-pathogenic microorganisms that can interact with the intestinal microbiota and attenuate the immune response in autoimmune diseases, particularly MS and MG, and should be used as adjuvant therapy.

The largest number of studies on CAM are devoted to the application of acupuncture, which is used in almost all autoimmune diseases of the nervous system (ADNS).

Generally, the effectiveness of acupuncture in treatment of MS is assessed using the Expanded Disability Status Scale (EDSS), which identifies the degree of neurological damage to eight functional systems as follows: cranial nerves, motor, sensory and coordination systems, pelvic organ function, cognitive sphere, and mobility.[19] For example, Criado et al. note in their work that about 85% of MS patients specify gait disturbance as the major limitation in everyday life. When applying acupuncture to 20 people diagnosed with remitting-type MS, a decrease in spasticity, coordination disorders and walking fatigue was noted.[20]

3.2 Acupuncture

The most comprehensive review of the literature on the use of acupuncture for the treatment of MS noted its positive impact on the quality of life of patients, however, the authors note that most studies were conducted without a control group, randomization or blinding, which causes certain difficulty in interpreting the true effectiveness of the method. This necessitates further studies with a more rigorous design and analysis to evaluate the effectiveness of acupuncture in MS.[21]

A randomized controlled trial conducted by Danish scientists investigated the effect of serum cytokine levels on the health status and quality of life of MS patients. The patients were divided into three groups, one of which used traditional acupuncture, the other randomized acupuncture, and the third (control group) did not use acupuncture. Patients in the first two groups each received six acupuncture treatments over a four-week period. The authors were unable to demonstrate a significant difference in the level of cytokines and quality of life among the patients between the groups.[22]

A study of randomized controlled trials on the use of acupuncture for GBS in medical and biological databases such as PubMed, Embase, the Cochrane Library, CINAHL Complete, the National Digital Science Library, the China National Knowledge Infrastructure (CNKI) and the Wanfang Database (万方数据库) showed high effectiveness and safety of acupuncture as additional therapy.[23] Also of some scientific interest are the results of a generalized quantitative analysis of the data obtained in the study of the effect of acupuncture on MG.[24] In the study of Crestati et al. a positive result is noted when treating the ocular form of MG with anticholinergic medicines, corticosteroids, and immunosuppressants in combination with auricular acupuncture,[24] as well as cauterization together with Chinese phytotherapy medications for MG.[25]

Electroacupuncture in combination with medicine therapy in MG patients made it possible to achieve a clinical effect against the background of a halving of the dose of pyridostigmine and prednisolone compared to the control group, as well as a significant decrease in the level of interleukin-4 (IL-4).[26,27] Finsterer notes the need to clarify the effect of acupuncture on medication dose reduction in MG patients.[28] If the result is positive, public funding of acupuncture can be considered as an additional method in the treatment of patients with myasthenia gravis.

In MS, apitherapy to biologically active points is suggested, which helps to reduce the number of active demyelination foci according to MRI data and disability scores according to the extended EDSS scale.[29] However, Lee et al. noted that treatment with bee venom was widely used even in Oriental medicine, but evidence of effectiveness is limited.[30] Although most complications during apitherapy were local or systemic allergic reactions, the authors report a case of progressive quadriplegia 10 days after multiple sessions of bee venom treatment.

3.3 Phytotherapy

Phytotherapy is one of the oldest methods of treatment, well-proven in the treatment of many diseases. In reviewing herbal remedies used in traditional Persian medicine for the treatment of MS, the authors studied the main Persian pharmacopeias of the 9th-18th centuries. Out of 157 selected remedies, 118 medicinal plants were authenticated whose antioxidant activity, immunomodulatory and anti-inflammatory properties in the treatment of MS are well known.[31] When evaluating the effect of lemon verbena (Lippia Citriodora) extract on pro-inflammatory serum biomarkers in patients with various clinical subtypes of MS, a significant decrease in C-reactive protein concentration was found after 28 days of taking the extract.[32]

Turmeric long (Curcuma longa) is used in folk medicine as an effective anti-inflammatory agent. Polymerized nano-curcumin was administered daily intraperitoneally to rats with experimental autoimmune encephalomyelitis. The study of the lumbar spinal cord sections confirmed a significant decrease in the number of demyelination foci, inflammation, and destruction of the blood-brain barrier. There was also an adjusted balance of pro-inflammatory and anti-inflammatory gene expression, reduced oxidative stress, improved remyelination, and increased progenitor cell markers after treatment.[33]

Mojaverrostami et al.[34] also note improved remyelination and suppression of inflammation in the central nervous system (CNS) in MS patients when using medicinal plants, which opens up new horizons for therapy. The sedative and antidepressant effects of phytotherapy, along with improvements in sleep quality, decreases in muscle rigidity, neuropathic pain, and the degree of pelvic organ dysfunction have drawn attention.[35] A positive therapeutic effect was also noted with the use of plant polyphenols, which include chrysin extracted from the plant Passiflora caerulea. Chrysin has antioxidant,

anti-inflammatory and neuroprotective effects. The data showed that chrysin modulates redox processes and inflammation in MS and GBS; however, additional studies are needed.[36]

Huperzia selago from the Lycopodiaceae family, being an acetylcholinesterase inhibitor, has been used in Chinese medicine to treat many diseases for more than 1,000 years. Lycopodium alkaloids are effective in diseases associated with impairments of the neuromuscular system and are used in the treatment of MG.[37,38] Phytotherapy occupies an important place in TCM. In the 16th century, *Ben Cao Gang Mu* (《本草纲目》 *The Grand Compendium of Materia Medica*) summarized the centuries-old experience in the art of herbal medicine. Since then, Chinese phytotherapy has not undergone significant changes. A complex collection of astragalus root, codonopsis, ural licorice, angelica and wild ginger, known as *Bu Zhong Yi Qi Wan* (补中益气丸 Center-supplementing and Qi-boosting Pills), have proven themselves in the treatment of ophthalmoplegia.[39]

Berberine is widely used in traditional Chinese medicine. Recent studies have demonstrated clinical improvement in experimental autoimmune neuritis in rats, accompanied by suppression of lymphocyte proliferation (particularly for $CD4^+$ T cells), Th1 (TNF-α) and Th2 (IL-10) cytokines, and a decrease in anti-P0 peptide 180-199 IgG1 and IgG2a, i.e. suppression of both cellular and humoral immunity. The authors suggest that the alkaloid berberine can be used to treat autoimmune diseases of the peripheral nervous system, such as GBS.[40]

There are separate publications in the literature demonstrating a good therapeutic effect of cannabinoids for pain management and hypertonicity in MS.[41,42] However, there is no clear evidence of the effectiveness of such therapy.[43]

3.4 Exercise therapy, yoga, *Qi Gong* and Tai chi

An analysis of various data on the positive effects of physical therapy, yoga and breathing exercises when studying a systematic review of publications of relevant original studies, showed their effectiveness in depressive disorders, cognitive and motor function impairment in MS patients.[44,45]

One of the effective methods of CAM is physical therapy. It has been noted that resistance training can be an effective method to improve walking and functional capacity in individuals with physical activity limitation in MS.[46,47] Respiratory muscle training at home is effective and can not only provide short-term results, but also reduce fatigue in patients with mild to moderate MG.[48–51]

Some authors specifically single out yoga classes, which are considered to be an effective auxiliary tool for patients with various neurological disorders, which reduces the duration of hospitalization and also improves the patients' ability to work.[51–54]

In many publications, a particularly significant effect is noted in the use of *Qi Gong* (气功) and Tai chi (太极), which is a system of breathing and motor exercises with a psychophysiological orientation. The results of a detailed meta-analysis convincingly proved the effectiveness of these TCM methods, which reduce fatigue and increase motor activity in patients with MS and MG. The feasibility of regular use of exercises as part of the rehabilitation program for these patients has been substantiated.[55–59]

Methods of TCM are generally shown in the following table (Table 1).

4 Conclusion

The search for treatment methods for ADNS, including those used in TCM, is due to the limited therapy options for these severe diseases. Only in GBS a spontaneous regression of pathological symptoms is possible, the other diseases mentioned require long-term, lifelong therapy. As a type of professional activity, the activity of a specialist in traditional (complementary) medicine is an extremely demanded, safe and effective area of medical activity with qualified application. Despite the recognition of complementary medicine in many countries, its practical application still faces certain difficulties. The purpose of the various areas of TCM is to restore health, improve the quality of life, habilitation and rehabilitation after severe diseases, as well as social integration, and not just the treatment of diseases. Traditional and complementary medicine is an important and often underestimated healthcare resource with many applications, especially in the prevention and treatment of ADNS. It is TCM that meets the requirements of a personalized and predictive approach to the treatment of diseases in general. Despite the widespread use of the principles of evidence-based medicine, most research in TCM is random and descriptive in nature. To date, there are no clear evaluation criteria on which research in the field of CAM in the treatment of ADNS could be based. The search for the effectiveness of various TCM methods and the planned scientific research in relation to a particular nosology should be based on clear methodological developments and the principles of evidence-based medicine.

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Ethical approval

This article does not contain any studies with human or animal subjects performed by the authors.

Author contributions

Yurii O Novikov participated in data collection, literature analysis, text writing, structuring, discussion and

Table 1 Application of TCM for ADNS (source from: the authors)

Methods	Authors (Country)	Design of study	Number of patients	Duration of treatment	Effects	Reference number
Acupuncture	Huybregts et al. (Belgium)	Case control study	99 patients with multiple sclerosis	4-6 weeks	Acupuncture has a positive effect, greater than placebo on the course or symptoms of the disease.	7
	Novikov et al. (Russia, France)	Series of cases	26 patients with gonarthrosis	2-4 weeks	Despite the heterogeneous data undergoing statistical processing, it can be concluded that the method used is effective.	9
	Liu et al. (China)	Randomized controlled trial	40 patients with migraine	6-24 weeks	Acupuncture can relieve the symptoms of migraine, improve dysfunction of cerebellum and activate brain regions involved in modulation of pain and emotion. The cumulative therapeutic effect of acupuncture is more extensive and significant than its immediate effect.	10
	Kang et al. (Korea)	Randomized, single-blind, assessor-blind controlled trial	42 patients with temporomandibular joint disorders	3 weeks	Results suggest that point-selective effects among adjacent, distal or a combination of acupoints are hardly associated with pain intensity or palpation index in participants with TMDs.	12
	Criado et al. (Portugal)	Case-control	20 patients with multiple sclerosis	2-4 weeks	Protocol provides evidence that acupuncture treatment can be an attractive option for patients with multiple sclerosis, with gait impairment.	20
	Karpatkin et al. (USA)	Meta-analysis of 15 articles	110 patients with multiple sclerosis	5 weeks	Many of the studies are case reports and other studies have no randomization and little use of control.	21
	Lynning et al. (Denmark)	Single-blind, randomized controlled trial	66 patients with multiple sclerosis	4 weeks	In this study, the authors were unable to demonstrate that 4-week acupuncture treatment had a measurable effect on plasma levels of seven selected cytokines in people with multiple sclerosis.	22
	Wang et al. (China)	Randomized controlled trial	60 patients with myasthenia gravis	2-4 weeks	Electroacupuncture warming therapy combined with Western medicine has a significant therapeutic effect on myasthenia gravis. One of the mechanisms possibly is to restrain specific immune reaction by regulating the level of IL-4.	27
	Lee et al. (Korea)	Clinical case	1 patient with Guillain-Barré syndrome	10 days	The treatment of a 68-year-old woman who developed progressive quadriplegia 10 days after receiving multiple honeybee venom sting acupuncture treatments.	30
	Stoll et al. (USA)	Cohort study	111 patients with multiple sclerosis	2-6 weeks	37 (64.9%) patients, who used acupuncture and massage, reported 5 disability points or less.	44
	Arji et al. (Iran)	Meta-analysis of 31 articles	168 patients with multiple sclerosis	4-6 weeks	Acupuncture is vastly used in the management of mental functions of MS patients.	45
Herbal	Li et al. (China)	Case control study	135 patients with myasthenia gravis	3-12 months	*Bu Zhong Yi Qi Tang* (补中益气汤 Center-supplementing and Qi-boosting Decoction) is a safe and effective traditional Chinese medicine for the treatment of myasthenia gravis.	39
	Li et al. (China)	Laboratory animal research	Female Lewis rats, 6-8 weeks old, weighing 155-180g	5-17 days	Berberine administrated intragastrically with BBR at doses of 20 and 130 mg/kg/day from day 5 to 17 p.i., respectively. This research also provides new insights into natural compounds extracted from traditional Chinese herbs to be therapeutic in autoimmune diseases.	40
Qi Gong and Tai chi	Buttolph et al. (USA)	Randomized controlled trial	20 patients with multiple sclerosis	10 weeks	Pooled pre- and post-*Qi Gong* comparisons showed trends in improvement in global mental health, fatigue and depression.	59

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Conflicts of interest

The authors declare no financial or other conflicts of interest.

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