

Oriental Medicine

Acupuncture: a new method to treat tic disorders in children

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Competing interests

The authors declare no conflicts of interest.

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Abbreviations

YGTS, Yale Global Tic Severity Scale.

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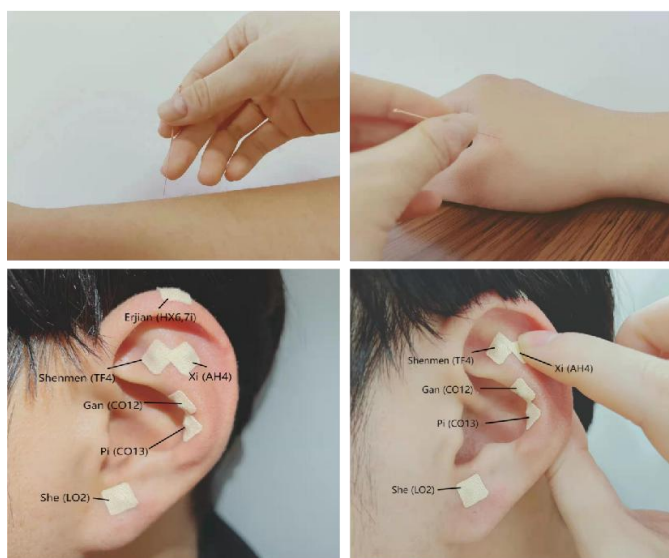
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Abstract

Tic disorder is a common pediatric neurological disorder that severely affects children's quality of life. But in fact, there is still a lack of a very effective treatment for tic disorder. Acupuncture as a flexible treatment time, treatment cycle control, easy to operate treatment method, widely used in the field of neurological disorder, widely praised by clinicians and patients. At the same time, tic disorder belongs to the category of chronic inflammatory convulsion in traditional Chinese medicine, and acupuncture has a good effect of relieving spasticity and fewer adverse reactions, which makes acupuncture have a good application prospect. Now, more and more studies about acupuncture treatment of tic disorder in children have been published. The main methods of treating tic disorder are acupuncture, electroacupuncture, scalp acupuncture and ear acupuncture. The efficacy of acupuncture alone or in combination with other drugs such as tiapride hydrochloride and haloperidol has been shown to be good. The safety of acupuncture is also commendable, and clinical trials showing that the combination of acupuncture and medication can reduce the incidence and severity of adverse drug reactions. According to the existing studies, acupuncture can promote the development and repair of the nervous system, regulate the secretion of neurotransmitters, and reduce the occurrence of local discomfort, which may be the main mechanism of acupuncture treatment of tic disorders.

Keywords: tic disorder; pediatrics; mechanism research; alternative therapy; research progress



Highlights

This review discusses the mechanism of acupuncture treatment of children with tic disorder and compare the advantages and disadvantages of various acupuncture methods.

Medical History of Objective

Acupuncture is a time-honored and common clinical treatment increasingly used to treat pediatric diseases, especially chronic neurological diseases such as tic disorder. The first traditional Chinese medical text to mention the use of acupuncture to treat neurological disorders, especially mental disorders and convulsions, was the *Inner Canon of Yellow Emperor* (unknown author, written from 26 B.C.E. to 6 B.C.E.). However, no details were provided on which acupoints to choose. According to the *A-B Classic of Acupuncture and Moxibustion*, written in 282 C.E. by Mi Huangfu, acupuncture was first used in the treatment of neurological disorders in children, including limb twitching, epilepsy, infantile convulsion and other diseases; the therapeutic effects of acupoints including Xinhui (GV22), Tianzhu (BL10), Benshen (GB13) and Qianding (GV21) on the above diseases were suggested. In 1601, Ji-Zhou Yang discussed in detail acupuncture methods in treating infantile convulsion and other neurological disorders in the *Compendium of Acupuncture and Moxibustion* written in 1961 by Ji-Zhou Yang, and put forward the therapeutic effects of Wangu (SI4), Yanggu (SI5), and Kunlun (BL60). The concepts of tic disorder and Tourette syndrome were introduced into China in the 1980s. Importantly, acupuncture was first reported in a study by Wu et al. in the 1990s with good efficacy for the treatment of Tourette syndrome.

Background

Tic disorder is a neurodevelopmental disorder characterized by involuntary, purposeless, sudden, repetitive movements or sounds, firstly described by the French neurologist, Gilles de la Tourette, as a “Maladie des tics” in 1885 [1, 2]. According to the *Diagnostic And Statistical Manual Of Mental Disorders* (5th ed) of the American Psychiatric Association [3], tic disorders can further be divided into provisional tic disorder, chronic motor tic disorder, chronic vocal tic disorder, and Tourette syndrome according to the duration, symptoms, and severity of tics. In recent years, the increase in emphasis on children’s neurodevelopment and mental health has been paralleled by an increase in the number of tic disorder cases diagnosed. The prevalence of tic disorder is approximately 0.3%–1% globally, with a male incidence rate 3–4 times higher than in females [4]. The number of published studies on tic disorder has substantially increased over the years, accompanied by increased awareness of the influence of tic disorder on children [5]. As children with tic disorder often exhibit a series of involuntary abnormal behaviors, which makes them susceptible to unfair treatment, their psychological health is affected. The influence of tic disorder and its comorbidities on children’s social and psychological factors cannot be ignored. Another concern is that the diagnosis of chronic tic disorder typically requires tic symptoms to last more than a year, and more and more children are now being diagnosed with provisional tic disorder, especially during the coronavirus disease 2019 epidemic. This phenomenon may be related to the panic caused by the coronavirus disease 2019 and the epidemic prevention policies such as home quarantine [6, 7]. Tics typically reach their most severe level at 10–12 years of age, then gradually decline in severity throughout adolescence, and most symptoms disappear in adulthood. Some scholars even believe that tic disorder or provisional tic disorder with mild symptoms may be in remission spontaneously within a few months [8–11], but in fact, most provisional tic disorders cannot be completely relieved within a year and may even worsen or recur within a few years [11]. Therefore, no

consensus has been reached on the optimal treatment approach.

To the best of our knowledge, there is currently no proven and unified treatment plan for the above conditions. Practice guideline recommendations published by the American Academy of Neurology [12], European clinical guidelines [13], and Chinese clinical guidelines [2] point out that drugs such as clonidine, risperidone, tiapride, and haloperidol, cognitive behavioral therapy, and deep brain stimulation are the main treatment methods. However, due to adverse drug reactions and the need for good patient compliance, younger children are not suitable for these treatments [2].

Acupuncture is a time-honored and common clinical treatment increasingly used to treat pediatric diseases, especially chronic neurological diseases such as tic disorder. The first traditional Chinese medical text to mention the use of acupuncture to treat neurological disorders, especially mental disorders and convulsions, was the *Inner Canon of Yellow Emperor* (unknown author, written from 26 B.C.E. to 6 B.C.E.). However, no details were provided on which acupoints to choose. According to the *A-B Classic of Acupuncture and Moxibustion*, written in 282 C.E. by Mi Huangfu, acupuncture was first used in the treatment of neurological disorders in children, including limb twitching, epilepsy, infantile convulsion and other diseases; the therapeutic effects of acupoints including Xinhui (GV22), Tianzhu (BL10), Benshen (GB13) and Qianding (GV21) on the above diseases were suggested. In 1601, Ji-Zhou Yang discussed in detail acupuncture methods in treating infantile convulsion and other neurological disorders in the *Compendium of Acupuncture and Moxibustion* written in 1961 by Ji-Zhou Yang, and put forward the therapeutic effects of Wangu (SI4), Yanggu (SI5), and Kunlun (BL60). The concepts of tic disorder and Tourette syndrome were introduced into China in the 1980s. Importantly, acupuncture was first reported in a study by Wu et al. in the 1990s with good efficacy for the treatment of Tourette syndrome [14]. Nowadays, more and more studies have been published, especially on efficacy and safety. It has certain application value in pediatric neurological disorders owing to fewer adverse reactions, less impact on the nervous system and a more flexible treatment cycle. Therefore, more and more researchers have begun to explore the internal mechanism and treatment plan of acupuncture for tic disorder, and the clinical application of acupuncture has become more widespread. This article aims to discuss the efficacy, mechanism, and specific acupuncture methods in treating tic disorder from the perspectives of human and animal experiments.

The effect of acupuncture on tic disorder

The Yale Global Tic Severity Scale (YGTSS) is one of the most widely used assessment tools for evaluating the severity of tic disorder; a YGTSS score reduction rate is mostly used to evaluate the efficacy of acupuncture treatment for tic disorder, that is, YGTSS score reduction $\geq 30\%$ has been shown to be effective, and vice versa. The specific calculation method is $\text{YGTSS total score reduction rate} = ((\text{pre-treatment scale score} - \text{post-treatment scale score}) / \text{pre-treatment scale score}) \times 100\%$. A study by Lu et al. corroborated that acupuncture could improve YGTSS scores in tic disorder patients more effectively than haloperidol, tiapride, and aripiprazole with fewer adverse reaction reports [15]. Moreover, a study by Kong et al. showed that acupuncture combined with haloperidol could yield better efficacy and fewer adverse reactions than monotherapy with haloperidol, indicating that acupuncture could reduce tics and drug-induced adverse reactions [16]. Meanwhile, an increasing body of evidence suggests that the YGTSS scores of patients in the acupuncture treatment group are not significantly increased during a follow-up period of 6 weeks to 6 months, which indicates that acupuncture has a longer-lasting therapeutic effect on tic disorder [16–18]. In the study by Xu et al., no statistical difference in the effective rate was observed between the acupuncture and tiapride hydrochloride groups [19]. However, after 6 weeks of follow-up, it was found that the acupuncture group had a lower recurrence rate (3.3% versus 45.2%) than the drug group. This finding indicates that acupuncture still plays a positive role in the occurrence and

development of chronic tic disorder. The above studies provide compelling evidence that acupuncture can play a major or auxiliary role in treating tic disorder compared with drug monotherapy.

Mechanisms of acupuncture treatment for tic disorder

Tic disorder animal models currently include the neurotransmitter disorder model, immune disorder model, and gene mutation model [20]. One of the more commonly used tic disorder animal models is the imino- β , β -dipropionitrile model, which can induce dopamine receptor hypersensitivity in rats to cause symptoms such as tics [21]. Zhang and Fang et al. found that levels of dopamine and norepinephrine in the striatum and plasma of rats injected with iminodipropionitrile were significantly increased through animal experiments [22, 23]. Interestingly, Fang et al. further found that both acupuncture and drugs could reduce the concentrations of dopamine and norepinephrine in rats, and there was no statistical difference between the two, indicating that acupuncture could regulate the level of neurotransmitters [23]. Meanwhile, clinical studies by Zhang and Kong et al. showed that acupuncture could reduce plasma dopamine and 5-hydroxytryptamine levels in the human body [16, 22]. Dai et al. found that acupuncture could increase the systemic levels of γ -aminobutyric acid, an inhibitory neurotransmitter; low concentrations of γ -aminobutyric acid have been associated with the occurrence of tics [24]. The above studies suggest that acupuncture can alleviate tics by regulating the levels of neurotransmitters such as dopamine, norepinephrine, 5-hydroxytryptamine, and γ -aminobutyric acid. Furthermore, this effect of acupuncture may be bidirectional since some studies found that tic disorder patients with low dopamine, norepinephrine, or 5-hydroxytryptamine levels experienced a similar therapeutic effect with acupuncture [25–28].

In recent years, the occurrence of tic symptoms caused by premonitory urges has gradually aroused the interest of researchers. Premonitory urge refers to certain kinds of discomfort that occur and accumulate before the onset of tics until tics appear. Tic symptoms are thought to relieve the discomfort, which means that premonitory urge may be the key to tics in tic disorder patients [1, 29]. It has been established that acupuncture is a good treatment method for relieving local discomfort [30, 31]. It can reduce or prevent the occurrence of tics by eliminating gradually accumulated discomfort, which may also be one of the potential mechanisms of acupuncture in treating tic disorder. However, as the pathogenesis of tic disorder is still unclear, with few studies on the mechanism of acupuncture therapy in the treatment of tic disorder, warranting the need for more studies to explore other potential mechanisms.

Common methods of acupuncture treatment for tic disorder

Traditional Chinese medicine acupuncture

Acupuncture in traditional Chinese medicine involves the insertion of needles at specific acupoints, which can adjust the neuroendocrine balance of the whole body by generating a needle sensation. Before acupuncture, each acupuncture point is often disinfected to prevent infection [32]. It is also the most widely used method currently. Commonly used acupoints include Baihui (GV20), Sishencong (EX-HN1), Shenmen (HT7), Neiguan (PC6), Fengchi (GB20), and Zusanli (ST36). In a study by Wu et al., 98 children with tic disorder were randomly divided into acupuncture and tiapride hydrochloride groups [33]. The acupuncture points were Fengchi (GB20), Taichong (LR3), Zhongwan (CV12), Zusanli (ST36), Baihui (GV20), Sanyinjiao (SP6), Neiguan (PC6) and Shenmen (HT7); the results showed that the total effective rate of the acupuncture group was significantly higher than the tiapride hydrochloride group (89.80% versus 73.47%). Zhang et al. randomly divided 70 children with tic disorder into acupuncture and haloperidol combination group and haloperidol group. Acupuncture points were Baihui (GV20), Sishencong (EX-HN1), Yintang (GV29), and Shenting (GV24), Shuigou (GV26), Zusanli (ST36), Sanyinjiao (SP6), Taichong (LR3), Neiguan (PC6), and Shenmen (HT7); the results showed that the combined acupuncture

and haloperidol group can significantly reduce the number of children YGTSS scores, and can reduce the levels of serum dopamine and 5-hydroxytryptamine in children with tic disorder (Figure 1 and Figure 2) [22].

Electroacupuncture

Electroacupuncture is an extension of acupuncture based on traditional acupuncture to perform light electrical stimulation to strengthen the acupuncture and analgesic effect and eliminate abnormal sensations, especially to regulate the central system monoamine transmitters and protect dopaminergic neurons to achieve the therapeutic effect. In a study by Li et al., 64 children with tic disorder were divided into a drug group (oral inosine tablets and vitamin B6) and an electroacupuncture group and acupuncture points Hegu (LI4), Taichong (LR3), Baihui (GV20), Yintang (GV29), and Fengchi (GB20) were used. The results showed that the efficacy rate of the electroacupuncture group was significantly higher than the drug group (96.88% versus 87.50%) [34].

Scalp acupuncture

Scalp acupuncture is a new type of acupuncture method based on human anatomy and the projection of the cerebral cortex on the scalp that involves selecting acupuncture positions that are effective in treating neurological diseases, especially brain diseases. In recent years, it has been found that scalp acupuncture yields a better therapeutic effect in improving tic disorder. Kong et al. randomly divided 60 children with tic disorder into scalp acupuncture, haloperidol and combined acupuncture and haloperidol groups [16]. The results showed that the YGTSS scores of the three groups were significantly improved after treatment, with no statistical difference in the efficacy of the scalp acupuncture group and the drug group. Interestingly, the efficacy of the combined acupuncture and drug group was significantly better than the other two groups, suggesting that scalp acupuncture has similar clinical effects as drugs in improving the symptoms of tic disorder, and the combination of acupuncture and drugs can maximize the efficacy.



Figure 1 Traditional Chinese medicine acupuncture (acupuncture points: Waiguan (SJ5))

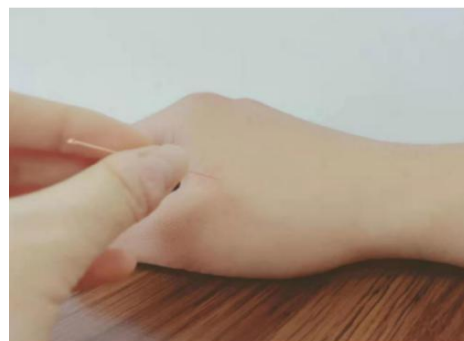


Figure 2 Traditional Chinese medicine acupuncture (acupuncture points: Hegu (LI4))

Auricular acupuncture

Little is currently known on the mechanism of action of auricular acupuncture. It has been established that its therapeutic effect involves stimulating the corresponding area of the ear to play an auxiliary treatment effect. Given that its stimulation is lighter than other acupuncture methods, it is mostly an auxiliary treatment method. In a study by Guan et al., 60 children with tic disorder were divided into a tiapride hydrochloride group and an auricular acupuncture combined with a tiapride hydrochloride group. The

results showed that the combination group yielded significantly better results than the tiapride hydrochloride group in terms of total effective rate (81.25% versus 71.43%), improvement of YGTSS scores, and reduction of recurrence rate [35]. The location of Erjian (HX6,7i), Shenmen (TF4), Xi (AH4), Gan (CO12), Pi (CO13) and She (LO2) are shown in Figure 3 and Figure 4.

A comparison of the advantages and disadvantages of the four acupuncture methods is shown in Table 1.

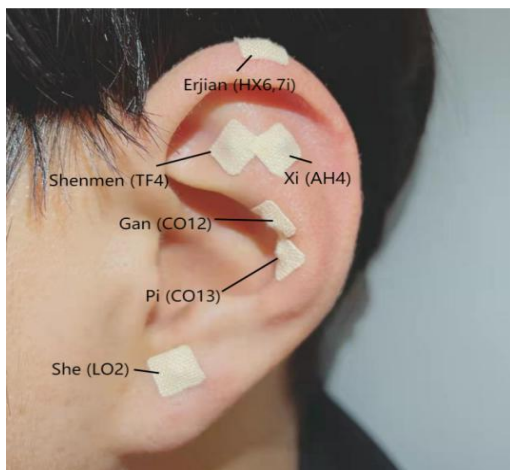


Figure 3 Auricular acupuncture. The acupuncture points include Erjian (HX6,7i), Shenmen (TF4), Xi (AH4), Gan (CO12), Pi (CO13) and She (LO2).

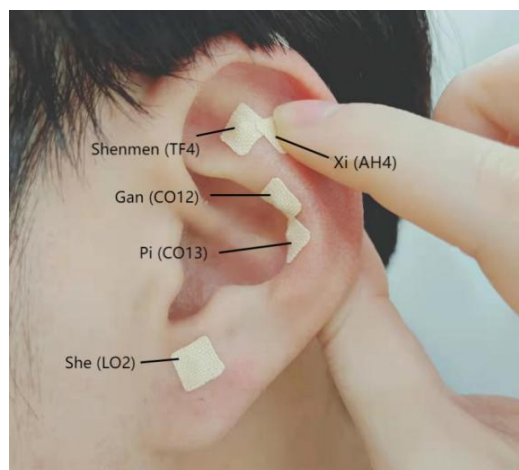


Figure 4 The pressing of auricular acupuncture needs the patient to take the initiative. This figure shows the method of Xi (AH4) pressing. Pressing auricular acupuncture is helpful to improve the curative effect.

Table 1 The comparison of advantages and disadvantages of four acupuncture methods

Methods of acupuncture	Brief introduction	Advantage	Disadvantage
Traditional Chinese medicine acupuncture	Traditional Chinese medicine acupuncture refers to the insertion of needles specially used for acupuncture into specific acupoints with specific manipulations to play a therapeutic role.	(1) There is a complete theoretical support, and the national standard of acupoint location has been issued. (2) The stimulation is small, the trauma is small, and the safety is relatively good.	The patient remains relatively still while being treated, which makes it difficult for the child to cooperate.
Electroacupuncture	On the basis of traditional Chinese medicine acupuncture, electroacupuncture is used to guide a safe-sized current through the needle to the human body through a special device to enhance local stimulation.	(1) On the basis of traditional Chinese medicine acupuncture, there are national norms for reference. (2) Local stimulation is stronger.	Because of the different sensitivity of each person to electrical stimulation, the control of electric current is an important issue, especially for children who have difficulty in expressing their feelings accurately.
Scalp acupuncture	Scalp acupuncture is to insert needle into scalp to stimulate different parts of cerebral cortex. It is based on the fact that different parts of the scalp are projections of different parts of the cerebral cortex.	(1) The skull has the protection, therefore carries on the scalp acupuncture the security to be worthy of trust. (2) The treatment for neurological disorder is very effective.	No relevant national regulations have been issued.
Auricular acupuncture	Auricular acupuncture is to fix the seed of <i>Saponaria vaccaria</i> on the ear by tape and stimulate it continuously by pressing frequently.	(1) The stimulation is on the ear skin and is acceptable to most children. (2) The method of acupuncture is simple and children can cooperate with it. (3) It will hold for two or three days.	Need children and their families to actively press ear acupuncture, otherwise the efficacy will decline.

Safety of acupuncture

As a minimally invasive surgical treatment, acupuncture has almost no obvious adverse reactions, especially with scalp needles, because they have skull protection and are often safer. However, some patients still experience complications such as bleeding, subcutaneous hematoma, fainting during acupuncture treatment, etc. These responses can be managed if managed in time. Indeed, this raises the requirements for the operator, who needs to be familiar with the human anatomy, proficient in acupuncture, and able to respond to emergencies. Meanwhile, the state of the patient should also be considered. For young patients with poor coordination, physical weakness, high mental stress, and severe coagulation disorders, acupuncture treatment should be avoided.

Summary and prospect

The pathogenesis of tic disorder involves intricate and unclear biological processes, including genetic susceptibility [2], neurotransmitter imbalance, immune dysfunction, perinatal factors, social and family environmental factors, other factors [36–38]. Among them, neurotransmitter imbalance especially increased dopamine secretion and/or dopamine receptor hypersensitivity, is reportedly an important mechanism for the occurrence of tic disorder. This is also the first line of treatment for tic disorder. The important reason for the medication is dopamine receptor blockers such as tiapride and sulpiride [2]. At the same time, there are immune dysfunctions, especially group A *Streptococcus* infection and *Mycoplasma pneumoniae* infection, which have been increasingly reported to be correlated with the occurrence and development of tic disorder [37, 39]. Emotional stress factors are also an increasingly important pathogenic factor and aggravating cause. Indeed, with aging, academic pressure and family pressure are increasing, leading to an increase in the incidence of tic disorder in school-age children. Besides, incomprehension and reminders from parents and teachers can aggravate tic symptoms [1].

Acupuncture is an effective method for treating tic disorder with better curative and fewer side effects, widely used in clinical practice. It has a wide range of indications, including provisional tic disorder, chronic tic disorder, or Tourette syndrome. Good therapeutic effects have been reported for these diseases, with few reports of adverse reactions and low recurrence rates. Existing studies have shown that acupuncture can significantly reduce the serum levels of dopamine, 5-hydroxytryptamine, and norepinephrine and increase γ -aminobutyric acid. Acupuncture is also indicated for relieving abnormal feelings in the body. Relieving aura impulse may also be one of the therapeutic mechanisms of acupuncture. However, acupuncture is inclined to adjust the entire human body and restore the balance between the body's neurotransmitter level and nervous system function.

Notwithstanding that an increasing number of studies have been published on the treatment of tic disorder with acupuncture in recent years, no blank control group was set up. Accordingly, the influence of the self-improvement of tic disorder cannot be ruled out. However, it is difficult to conduct a study where tic patients are treated with placebo due to moral ethics. It is only feasible to compare the efficacy among currently available modern medical therapies. At the same time, since acupuncture has individual characteristics, it can treat patients with different symptoms and body constitutions. Large samples and multi-center clinical research are still needed to identify the most optimal acupuncture program and validate the efficacy. Most studies on the mechanism of the therapeutic effect of acupuncture on tic disorder have been limited to exploring the influence of acupuncture on neurotransmitter levels. Importantly, the influence of acupuncture on the nervous system and immune system has not been explored, representing a major research gap.

Overall, the currently published clinical studies have demonstrated the positive effects of acupuncture in the treatment of tic disorder to a certain extent. Its efficacy has been proven irrespective of its use in monotherapy or combination, indicating that acupuncture is a kind of

active clinical promotion, especially. Importantly, acupuncture can treat children with tic disorders with poor compliance or response to drugs. For children with an early diagnosis of tic disorder presenting with mild symptoms, acupuncture therapy can also alleviate their discomfort, relieve the anxiety of the child and parents. Acupuncture is easy to operate and highly flexible in terms of treatment time, making it widely applicable in clinical practice. Further studies on the therapeutic mechanism of acupuncture should be carried out and combined with currently known knowledge on tic disorder to substantiate the efficacy of acupuncture.

Conclusion

Acupuncture is an effective treatment for tic disorders in children. For patients with mild symptoms of tic disorder, monotherapy with acupuncture can be performed. Acupuncture in combination with drug therapy is indicated in severe chronic tic disorder and Tourette syndrome to maximize treatment efficacy. However, the mechanism and therapeutic norms of acupuncture remain unexplored, warranting further studies.

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