

# Pediatric Tuina in children with autism spectrum disorder: A study protocol for a randomized controlled trial

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## Method Article

**Keywords:** Autism spectrum disorder, Pediatric Tuina, Randomised controlled trial

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# Abstract

## Background

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterised by repetitive stereotypical behaviour and communication disorders. Currently, it lacks a specific clinical treatment method. Pediatric Tuina is a recent therapy in traditional Chinese medicine; however, there have been studies on the treatment of children with ASD by Tuina. Nonetheless, it remains uncommon given the lack of large-scale evidence-based medical studies. This study aims to compare the efficacy of Tuina and conventional treatment in children with ASD.

## Methods

Eligible children will be randomly divided into the pediatric Tuina plus conventional treatment group or conventional treatment group based on a random table at a ratio of 1:1. Effectiveness will be evaluated using a scale; moreover, the primary outcome will be the Childhood Autism Rating Scale. The secondary outcome will be the Autism Treatment Evaluation Checklist. All participants will be assessed on the scale by a third party not involved in the study. Baseline values of the participants will be determined at the registration time. Outcomes will be evaluated after the 30th treatment session. The follow-up period will last for 6 post-treatment months.

## Discussion

This study will evaluate the effectiveness and safety of Tuina in ASD treatment, which could provide reliable evidence-based findings to improve clinical treatment.

## Trial registration:

Chinese Clinical Trial Registry (ChiCTR), ChiCTR2000040452. Registered on 28 November 2020

## Background

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterised by typical repetitive behaviours and communication difficulties [1]. It has a childhood-onset; moreover, patients with ASD have lifelong difficulties with social interaction, communication, and sensory perception [2]. The aetiology of ASD involves complex and polygenic interactions, as well as possible environmental factors [3]. ASD is a serious public health problem worldwide, with its high morbidity and disability rates garnering increasing attention. Based on epidemiological studies, the ASD incidence rate is > 1–2% [4].

However, there remain no specific agents for ASD treatment, which include behavioural interventions, including early parent-mediated interventions [5–8]; naturalistic behavioural developmental interventions; behavioural and social treatments for school-age children, adolescents, and adults [9–12]; and even medical clowns intervention [13]. These clinical interventions can significantly improve the social adaptability of children with ASD.

Clinical treatment of ASD using evidence-based pharmacology is limited to treating co-occurring behaviour caused by mental illness rather than ASD itself. Risperidone [14–17] and aripiprazole [14, 18, 19] have been approved by the Food and Drug Administration to improve irritability or restlessness in children and adolescents with ASD. However, both drugs can cause adverse effects, including sedation and weight gain after long-term use, which increases the risk of subsequent health problems [19].

To alleviate ASD clinical symptoms and to save medical costs, there are studies on ASD developing traditional therapies with numerous advantages.

Tuina is an important external treatment that plays a crucial role in improving stunting, [20] relaxing physical and mental functions [21], and others. Currently, some Tuina manipulations have been applied as interventions for children with ASD [22, 23], with a certain degree of efficacy [24]. Qigong Tuina, which is a specific Tuina intervention in children with ASD [25, 26], has been shown to improve the symptoms of children with ASD.

Pediatric Tuina is a traditional Chinese medicine (TCM) therapy that acts on specific acupoints on the hands, back, and arms [27], including Wujing acupoints for different fingers. These acupoints target the spleen, liver, heart, lung, and kidney based on the meridian and collateral theory. The order is located on the thread surface of the five fingers in children (the spleen acupoint is located on the thumb). Stimulating different acupoints with particular manipulations results in varying curative effects.

However, there remains no strong evidence regarding the single-use of pediatric Tuina intervention for ASD treatment [28]. Therefore, this study aims to evaluate the efficacy of pediatric Tuina as an additional treatment for children with ASD aged 2–6 years by comparing it with conventional treatment in a standardised clinical research design. This evidence-based clinical trial could facilitate and promote the application of pediatric Tuina for ASD.

## **Methods/design**

### **Study design**

This will be a randomised controlled trial. To meet ethical requirements and the particularity of ASD, this study will not apply a blind design. The trial will be conducted at Hunan University of Chinese Medicine, China, from November 2020 to December 2021. Eligible children will be randomly divided into the pediatric Tuina plus conventional treatment group or conventional treatment group based on a computer-generated random table at a ratio of 1:1. Efficacy will be assessed using the Childhood Autism Rating

Scale (CARS) and Autism Treatment Evaluation Checklist (ATEC). Before study commencement, all participants will be assessed using a scale by a third party not involved in the study. The baseline level of the participants will be determined at the enrolment time; further, the participants will be evaluated again after the 30<sup>th</sup> treatment, with a follow-up period of 6 postoperative months. **Figure 1** shows a flowchart of the study.

## **Participants**

This study will recruit 400 children with ASD from autism organisations certified by the Hunan Disabled Persons' Federation, including Xingxueyuan Education Development Center, Tianxin District, Changsha City.

## **Eligibility criteria**

### ***Inclusion criteria***

1. Children who meet the diagnostic criteria of ASD in the diagnostic and statistical manual of mental disorders (DSM-5)
2. Age: 2–6 years old
3. CARS score  $\geq$  30 points
4. The guardian of the children is aware of the intervention, can cooperate well, and can complete the entire treatment cycle
5. Having not participated in other clinical observations and other intervention methods within the previous 30 days
6. Children with non-critical illnesses and coagulopathy
7. Children without acute or chronic infectious diseases.

### ***Exclusion criteria***

1. Children who do not meet the ASD diagnostic criteria in DSM-5
2. CARS score  $<$  30 points
3. Children who refuse to undergo the intervention massage method and cannot normally complete the intervention cycle
4. Children with mental illness that affect the clinical findings

### ***Elimination criteria***

1. Children who have not completed 30 intervention sessions following the research protocol
2. Children who receive other interventions that affect the study results

### ***Shedding criteria***

1. Children whose cooperation degree during the Tuina intervention was extremely low and could not cooperate
2. Children with serious adverse reactions given their poor health during the Tuina intervention

## **Interventions**

### ***Control group***

Based on the training of the autism organisation, the control group will strictly follow the schedule of five applied behaviour analysis training sessions, five key skill training sessions, five music group training sessions, five oral muscle training sessions, and five sensory training sessions per week. All the teachers will have a background in special education.

### ***Tuina group***

The Tuina group will receive pediatric Tuina, with a total of 30 Tuina sessions, five times a week for 6 weeks, and a follow-up period (the 12<sup>th</sup> week after the end of treatment). From the perspective of humanistic care, to make the child feel safe, the child will be held by the parents or relatives during the session and placed in a sitting position. Tuina doctors will perform face-to-face treatments. When performing acupoint Tuina on the back, the child will lie on his parents or relatives in a prone position.

To standardise the Tuina manipulation, all Tuina doctors will be certified Chinese medicine physicians and will have undergone 3 months of training in Tuina techniques. The acupoint prescriptions are mainly based on the TCM theory of the relationship between *Du Meridian* and *Brain*. After assembling clinical evidence and soliciting the opinions of experienced Tuina experts, we have summarized the following acupoints and manipulation times of Tuina. **Table 1** presents the detailed information.

## **Outcome assessment**

The results will be evaluated by a third party who has no interest in this study. This study will be conducted at the Mental Health Center of the Second Xiangya Hospital of Central South University, Hunan Province, China.

### ***Primary outcomes***

The main efficacy score will be based on the CARS, which covers interpersonal relationships, imitation, and other 15 aspects, with a total score of 60 points. Participants with a score < 30, 30–35, and ≥ 36 are considered as non-autistic, moderately autistic, and severely autistic, respectively. Compared with baseline, the curative effect will be considered as significant, effective, and invalid by a total score reduction of > 10 points, 5–10 points (including 10 points), and < 5 points, respectively [29].

### ***Secondary outcomes***

The secondary outcome indicators will be mainly evaluated using the ATEC, including four aspects: (1) speech/language/communication, (2) sociability, (3) sensory/cognitive awareness, and (4) health/physical/behaviour [30]. The main purpose of this study is to clarify the improvement in children with ASD after Tuina therapy from different perspectives.

### ***Safety assessment***

Although pediatric Tuina is a green treatment without side effects, it could have some adverse events (AEs) during the treatment process due to improper operation of the doctor. Skin damage is the most common AE during massage. To prevent AE occurrence, this study will perform strict monitoring. Once such a situation occurs, the researchers will record the time and severity of the AE and promptly deal with it.

### **Participant timeline**

We have designed the schedule for the recruitment, intervention, evaluation, and follow-up of the participants, as shown in *Figure 2*.

### **Sample size estimation**

This research is funded by the Hunan Provincial Department of Science and Technology. This research seeks to help more children with ASD; therefore, we set a fixed number of children and did not consider the minimum sample size. However, given the rigour of scientific research and design, a previous study [31] reported that the overall effective rate of Pediatric Tuina for children with ASD is 81.82%. Regarding the calculation of the sample size, considering a significance level of 0.05, power of 0.80, and maximum dropout rate of 10%, the final study will include 400 children with ASD (200 in each group).

### **Data collection and management**

All parents of children with ASD participating in the project will sign the informed consent form and complete the case report form. Finally, a data file will be established, which will be kept and collected by a dedicated person from the Data Committee of the First Affiliated Hospital of the Hunan University of Chinese Medicine. Inspectors will regularly check the informed consent form, research protocol, and evaluation scale to ensure the quality of clinical research. Regarding the authenticity of this study, all involved researchers will be blinded from the data. When the research plan changes, the researcher should promptly submit the new plan, indicate the date, and report to the committee.

Based on the data disclosure requirements of the *CHICTR*, this study will upload data to the Baidu Cloud Disk or the website of the Acupuncture and Tuina College of Hunan University of Chinese Medicine (zjtn.hnucm.edu.cn) within 6 months after study completion, which will be publicly available. The premise is that the main research results will be published. All outsiders should sign an agreement before accessing the research results.

## Statistical analyses

All data will be analysed using SPSS (version 21.0; IBM Corp., Armonk, NY, USA); further, all analyses will be conducted using a two-sided test. Normally and non-normally distributed measurement data will be analysed using the t-test and rank-sum test, respectively. The significance level will be set at 5% [32]. Statistical significance will be set at  $P < 0.05$ .

## Ethics

To protect the legitimate rights and interests of all our project participants, we will apply for a clinical research ethics review. This study has been approved by the Ethics Committee of the First Affiliated Hospital of Hunan University of Chinese Medicine (HN-LL-KY-2020-020-01).

## Discussion

ASD development is irreversible, with some symptoms persisting throughout life. Given that improving the quality of life of children with ASD is the common pursuit of all medicines, we should actively explore traditional and non-traditional medicines to identify the most suitable treatment for ASD.

TCM contains profound wisdom regarding Chinese philosophy and medical knowledge. Consistent with modern medicine, TCM considers the brain to control emotions, consciousness, and thinking. However, in this theory, the brain is not just an organ; rather, it has several other functions. The cause of autism is associated with the brain, which is a common understanding in academic circles. Specific acupoints can improve brain function and promote nerve development. *Du Meridian* is a special meridian. It is closely associated with the physical location and function of the brain [33]. A large part of the Du Meridian is located on the midline of the back and front of the head; further, it is directly connected to the brain and gathers the Yang qi of the whole body. Du Meridian is an important way for the output of Jing qi [34] as a bridge between the brain and other meridians for communicating qi and blood [35]. Therefore, the normal operation of the function of the Du Meridian can improve the role of the brain; further, children with ASD have problems with obstruction. Under these conditions, external stimulation can be performed through the Tuina. The formulation of this study protocol will be conducted under the guidance of Du Meridian.

The acupoints and treatment plan for Tuina will be based on the TCM. There are several fixed routines in Chinese pediatric Tuina, including starting from the head first, which is known as Kaiqiao, for unblocking the body. There are four fixed acupuncture points: Tianmen, Kangong, Taiyang (Temple), and Wangu (GB12). The number of operations for each acupuncture point is 24, which corresponds to the Chinese 24 solar terms. The Du meridian is also distributed on the head, with the four representative ones including Yamen (GV15), Fengfu (GV16), Baihui (GV20), and Shuigou (GV26). Therefore, they were chosen as the main Tuina parts. The back, from the thoracic spine to the sacral spine, is the main circulation part of the Du meridian and main stimulation point. Three methods are used for stimulation: pressing-kneading, pinching, and grasping with the finger. The last step is Grasping Jianjing (GB21), also known as Guanqiao, which relaxes the body.

However, the efficacy of Tuina in ASD treatment requires further investigation. This clinical randomised controlled trial will compare the effects of Tuina combined with behavioural and single education interventions on the rehabilitation effect of children with ASD. The CARS will be used to evaluate efficacy. Although our goal is to improve the core ASD symptoms in children, there may be other gains in further clinical research, including intestinal symptoms. This research plan could yield a strong evidence-based basis for the treatment of children with ASD by massage, which could allow more people to benefit from this treatment.

## **Study Limitations**

First, this study will not diagnose children with ASD using the Autism Diagnostic Interview-Revised or Autism Diagnostic Observation Scale due to copyright restrictions; instead, the DSM-IV will be used for the diagnosis of ASD.

Regarding evaluation, there are no objective biomarkers for evaluating the ASD treatment efficacy. This study will perform a scale assessment to evaluate the efficacy of the ASD treatment, which yields certain subjective errors.

Additionally, it is impossible to blindly perform Tuina therapy. Furthermore, the standardisation of massage techniques and stimulation amount varies from person to person. There will inevitably be some differences in specific operations. To reduce such errors, all participating Tuina therapists have undergone rigorous training and have professional qualifications to ensure standard treatment.

Finally, given the ethical requirements, it is impossible to prohibit all children from stopping other education or behavioural interventions. Therefore, a single Tuina intervention trial cannot be used for clinical observation.

## **Trial Status**

Currently, this clinical trial is still recruiting patients, which started in November 2020 and will end in September 2021. The trial was registered in the Chinese Clinical Trial Registry on 28 November 2020 (registration number: ChiCTR2000040452).

## **List Of Abbreviations**

AE, adverse event; ASD, autism spectrum disorder; ATEC, Autism Treatment Evaluation Checklist; CARS, Childhood Autism Rating Scale; DSM-5, diagnostic and statistical manual of mental disorders; TCM, traditional Chinese medicine

## **Declarations**

**Ethics approval and consent to participate**

Ethics approval was requested from and granted by the Ethics Committee of the First Affiliated Hospital of Hunan University of Chinese Medicine (HN-LL-KY-2020-020-01).

### **Consent for publication**

All authors read and approved the final manuscript.

### **Availability of data and materials**

The results of this trial will be presented in peer-reviewed journals.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

XF planned the study protocol and drafted then revised the manuscript.

JY participated in designing the trial and helped to prepare the manuscript.

WL was the study coordinator.

TL was responsible for generating and distributing the random numbers.

QRJ participated in collecting clinical data.

YXZ recruited and screened eligible participants in the outpatient department.

WW carried out the Tuina interventions of patients.

JSL managed the study.

All authors read and approved the final manuscript.

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### Authors' information

All authors come from School of Acupuncture-Moxibustion and Tuina, Hunan University of Chinese Medicine, engaged in Tuina teaching and scientific research.

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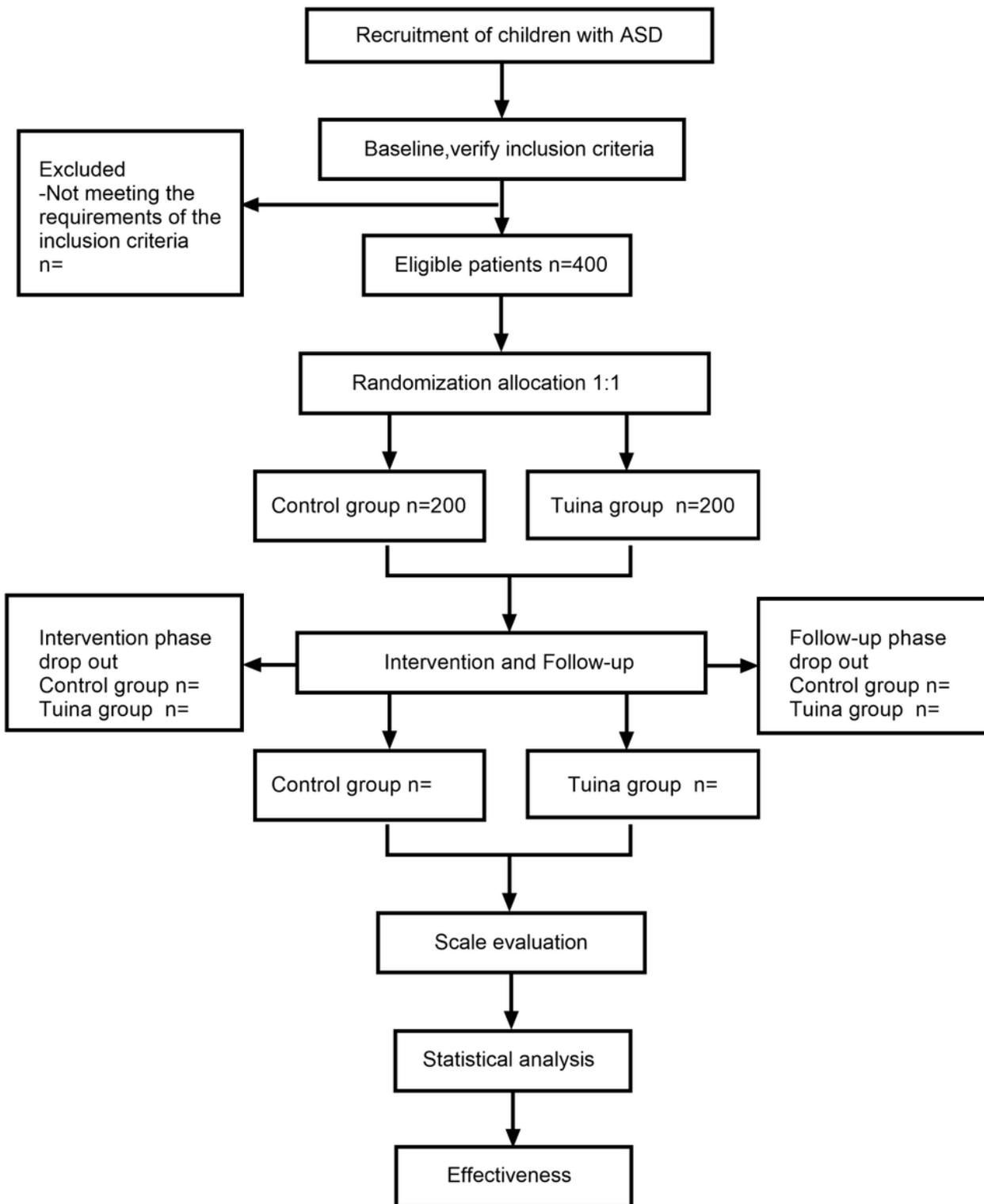
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## Tables

Please see the supplementary files section to view the table.

## Figures



**Figure 1**

Flowchart of the study. A total of 400 participants will be randomized to the two groups. The interventions will last for 25 min and will be conducted two times per week for 6 weeks. After treatment, 6month follow-up. The main efficacy score will be based on the CARS,the secondary outcome indicators will be mainly evaluated using the ATEC.

STUDY PERIOD	Enrollment	Allocation	Post-allocation		Follow-up	
TIMEPOINT (weeks)	-1	0	3	6	9	12
<b>ENROLLMENT</b>						
Eligibility screen	×					
Informed consent	×					
Medical history	×					
Randomization		×				
Allocation		×				
<b>INTERVENTION</b>						
Tuina and education intervention			↔			
Education intervention			↔			
<b>ASSESSMENTS</b>						
CARS	×	×		×		×
ATEC		×		×		×
Adverse events		↔				

**Figure 2**

Study schedule for recruitment, interventions, outcome measurements.

## Supplementary Files

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