Neuropsychiatric Disease and Treatment

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STUDY PROTOCOL

Acupuncture and Tuina Combined with Educational Rehabilitation for Children with Autism Spectrum Disorder: Study Protocol for a Single-Center, Three-Arm, Pragmatic Randomized Controlled Trial

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Background: The prevalence of autism spectrum disorder (ASD) is increasing globally. While educational rehabilitation is the standard of care, Traditional Chinese Medicine (TCM) techniques like acupuncture and tuina are widely used in China as adjunctive therapies, but high-quality evidence from rigorous clinical trials remains limited. The objective of this study is to evaluate the efficacy of acupuncture and tuina, combined with educational rehabilitation, for ASD, and to compare the effects of different TCM intervention methods.

Methods: A single-center, three-arm, pragmatic randomized controlled trial. A total of 120 children aged 2–12 with ASD will be randomized (1:1:1) to: (A) acupuncture + tuina + rehabilitation; (B) acupuncture + rehabilitation; or (C) rehabilitation alone. The intervention duration is 12 weeks with a 4-week follow-up. The primary outcome is the change in the Autism Treatment Evaluation Checklist (ATEC) total score from baseline to week 12. Secondary outcomes include core symptoms (CARS-2, ABC), comorbidities (sleep via CSHQ; constipation via BSFS/SBMs), and neurophysiological measures (EEG). The primary analysis will test the superiority of Groups A and B over Group C, and the non-inferiority of Group B to Group A using a repeated-measures mixed model.

Conclusion: This trial is designed to generate high-quality evidence regarding the efficacy of TCM techniques as adjunctive therapy for ASD. The findings will inform clinical practice and guide the formulation of integrative intervention strategies for ASD.

Trial Registration: This study was registered in the International Traditional Medicine Clinical Trial Registry (ITMCTR) with registration number ITMCTR2025002393.

Keywords: acupuncture, tuina, autism spectrum disorder, ASD, randomized controlled trial, study protocol

Introduction

Autism spectrum disorder (ASD) is a severe neurodevelopmental condition characterized primarily by persistent deficits in social interaction and communication, accompanied by restricted and repetitive patterns of behavior.[1,2] The global prevalence of ASD has increased substantially in recent decades, representing a significant public health challenge.[3] According to reports from the US Centers for Disease Control and Prevention (CDC), the prevalence increased from 1 in 150 in 2000 to 1 in 44 in 2018.[4] The prevalence of ASD in China from 2017 to 2023 was 7/1000, showing an upward trend compared to that before 2017 (26.50/10,000).[5] Symptoms of ASD typically emerge in early childhood, with high heterogeneity in clinical presentations and frequent comorbidities.[6] Approximately 40% of children with ASD present

https://doi.org/10.2147/NDT.S587139
Received: 22 December 2025
Accepted: 14 April 2026
Published: 21 April 2026

with intellectual disability, while up to 80% experience chronic sleep disturbances. In addition, 46–84% suffer from gastrointestinal dysfunction, such as persistent constipation.[7] These comorbidities not only impair daily functioning and social interaction but also contribute to inattention, hyperactivity, aggressive behaviors, and self-injury.[8,9] As a result, long-term prognosis remains generally poor, imposing substantial emotional and economic burdens on families, health-care systems, and society at large, underscoring the urgent need for safe and effective non-pharmacological adjunctive interventions.

At present, no pharmacological therapy specifically targets the core symptoms of ASD. Existing medications mainly aim to alleviate associated emotional and behavioral problems (eg, irritability, aggression) and attention-deficit/hyperactivity disorder.[10,11] Thus, behavioral and educational interventions—represented by applied behavior analysis (ABA) and the Treatment and Education of Autistic and Related Communication-handicapped Children (TEACCH) program—remain the most widely recognized therapeutic approaches.[12,13] This therapeutic gap has prompted the exploration of non-pharmacological adjunctive therapies.

In this context, TCM offers a distinct therapeutic approach. Acupuncture, a core TCM therapy, involves inserting fine needles into specific acupoints (eg, Baihui [GV20] and Zusanli [ST36]) to regulate bodily functions. In children, it is typically applied with milder stimulation and shorter retention time to enhance tolerability. Tuina is a manual therapy using techniques such as pushing and kneading to modulate physiological function, and pediatric tuina is characterized by gentle, non-invasive manipulation. Both therapies are widely used in children with ASD and have shown potential benefits in improving core symptoms, although high-quality evidence remains limited. Building on these methods, TCM theory provides a holistic framework for understanding and guiding their clinical application. In TCM theory, the clinical presentation of ASD closely corresponds to ancient descriptions such as “infantile stupor” “delayed speech” “five delays” and “spirit loss”.[14,15] Pathogenesis is primarily attributed to congenital deficiencies and spleen weakness, leading to insufficiency of the “Sea of Marrow” and lack of nourishment for the spirit.[16] The disease location is considered to lie in the brain and spirit, with patterns predominantly characterized by deficiency of the five Zang organs.[17,18] Guided by a holistic philosophy and syndrome differentiation, TCM techniques—particularly acupuncture and tuina—are widely applied in the auxiliary treatment of ASD, with the potential to alleviate core symptoms while improving common comorbidities such as sleep disorders.[19–21]

In recent years, emerging evidence has suggested that therapeutic potential for TCM techniques in ASD management. Studies have reported that scalp acupuncture may improve cognition, self-care, and sensory function in children with ASD.[22] Animal experiments have also shown that transcutaneous electrical acupoint stimulation (TEAS) can improve social and cognitive performance in ASD model rats.[23] Studies have also indicated that acupuncture may exert beneficial effects on core symptoms, such as social functioning.[24,25] However, a recent scoping review highlights that although acupuncture may offer therapeutic benefits, the available clinical evidence is limited in quality and strength.[26] Consequently, current clinical data are insufficient to justify the widespread adoption of acupuncture or tuina as standard treatment for ASD, which also hinders the internationalization of TCM. High-quality clinical trials, conducted in accordance with evidence-based medicine, are therefore urgently needed to determine the efficacy and safety of TCM techniques on both core symptoms and common comorbidities of ASD.

To address this evidence gap, we designed a single-center, three-arm, pragmatic randomized controlled trial. The study aims to generate high-level clinical evidence by comparing acupuncture plus tuina and acupuncture against educational rehabilitation alone. The primary objective is to determine whether 12-week acupuncture and acupuncture plus tuina improve core ASD symptoms—measured by the Autism Treatment Evaluation Checklist (ATEC)—to a greater extent than educational rehabilitation alone. Secondary objectives include demonstrating the non-inferiority of acupuncture alone compared with acupuncture plus tuina, and assessing the effects of both interventions on frequent comorbidities such as sleep disturbances (CSHQ) and chronic constipation (BSFS/SBMs). By conducting this rigorously designed trial, we aim to provide robust, high-level scientific evidence to support the international promotion of TCM, especially for formulating ASD intervention strategies in Belt and Road Initiative (BRI) countries, ultimately offering a safe and effective non-pharmacological adjunctive therapeutic option to children with ASD worldwide.

Study Objectives and Hypotheses

Objective

This pragmatic trial aims to evaluate the effectiveness of acupuncture (with or without tuina) as an adjunct to educational rehabilitation in children with ASD. Specifically, the study will assess whether acupuncture-based interventions improve core symptoms compared with rehabilitation alone, and whether acupuncture alone is non-inferior to the combined acupuncture and tuina approach.

Research Questions

This study addresses two specific questions:

(1) Do acupuncture-based interventions (with or without tuina) lead to greater improvement in core ASD symptoms compared with educational rehabilitation alone?

(2) Is acupuncture alone non-inferior to acupuncture combined with tuina in improving clinical outcomes?

Hypothesis

We hypothesize that acupuncture-based interventions will provide additional clinical benefits compared with rehabilitation alone, and that acupuncture alone will demonstrate comparable effectiveness to the combined intervention.

Research Methodology

Study Design

This study protocol is reported in accordance with established clinical trial reporting guidelines.[27] It will adopt a single-center, three-arm, pragmatic randomized controlled trial (practical RCT) design. Participants will be randomized in a 1:1:1 ratio into three groups, with a 12-week intervention phase and a 4-week follow-up. The study protocol (Version 3.2, dated 15-OCT-2025) was approved by the Medical Ethics Committee of the Xi'an TCM Hospital of Encephalopathy Affiliated to Shaanxi University of Chinese Medicine (Approval No. XNLL-2025-K-006). The trial will be conducted in accordance with the Declaration of Helsinki. Written informed consent will be obtained from the legal guardians of all participants prior to enrollment. The trial is expected to be conducted from Dec, 2025 to May 2026. A flow chart of the study is shown in Figure 1.

Patient and Public Involvement

The trial will be conducted in a clinical rehabilitation setting. Participants are children diagnosed with ASD, who meet predefined inclusion and exclusion criteria. All principal investigators and research personnel have completed training on human subject protection and the Good Clinical Practice (GCP) requirements. The study protocol, informed consent form, and all participant recruitment materials were reviewed and approved by the Institutional Medical Ethics Committee. Written informed consent must be voluntarily signed by the legal guardians of all participating children after full explanation of the study purpose, procedures, potential benefits, and risks. No identifiable personal information will be disclosed in the publication of study results to ensure maximum privacy protection.

Inclusion and Exclusion Criteria

Diagnostic Criteria

ASD diagnosis follows the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) published by the American Psychiatric Association (2013).[28] Participants must meet all four DSM-5 criteria, including persistent deficits in social communication and interaction; restricted and repetitive patterns of behavior, interests, or activities; symptom onset in early childhood; and clinically significant impairment. Diagnosis is confirmed by a senior clinician specializing in ASD.

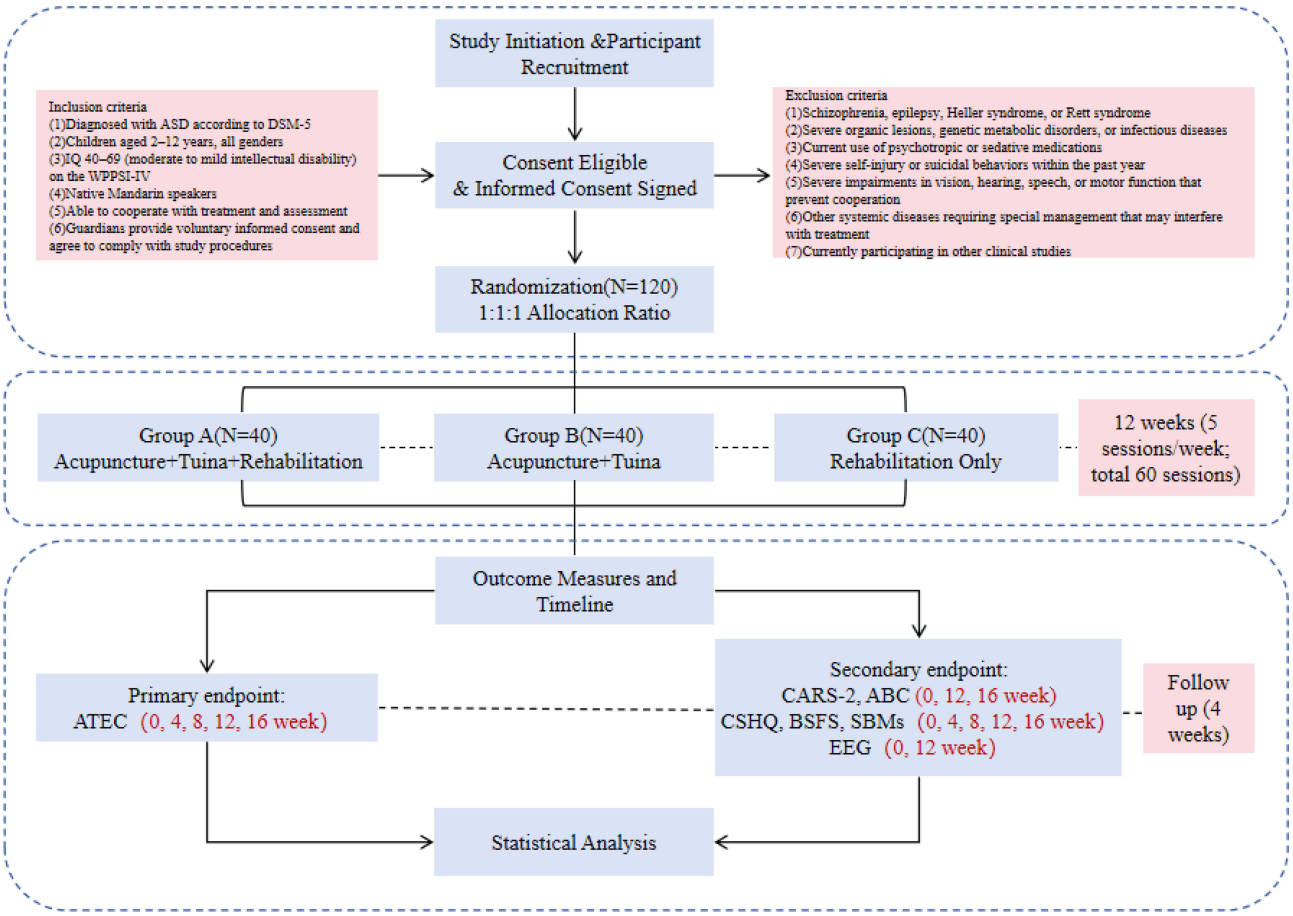

Figure 1 Research Study Flow Chart.

Inclusion Criteria

(1) Diagnosed with ASD according to DSM-5.
(2) Children aged 2–12 years, both genders.
(3) IQ 40–69 (moderate to mild intellectual disability) on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV).
(4) Native Mandarin speakers.
(5) Able to cooperate with treatment and assessment.
(6) Guardians provide voluntary informed consent and agree to comply with study procedures.

Exclusion Criteria

(1) Schizophrenia, epilepsy, Heller syndrome, or Rett syndrome.
(2) Severe organic lesions, genetic metabolic disorders, or infectious diseases.
(3) Current use of psychotropic or sedative medications.
(4) Severe self-injury or suicidal behaviors within the past year.
(5) Severe impairments in vision, hearing, speech, or motor function that prevent cooperation.
(6) Other systemic diseases requiring special management that may interfere with treatment.
(7) Currently participating in other clinical studies.

Sample Size and Recruitment

Sample Size

Based on a previous retrospective review of patient data, the mean difference in the improvement of the Autism Treatment Evaluation Checklist (ATEC) score between the Group A and Group C was 3.88 points. Based on this observed difference, with a one-sided α of 0.05 and 80% power, the sample size was calculated. The variances for Groups A and C were estimated to be 34.6921 and 41.8609, respectively, while the variance for Group B was conservatively set at 38.1924. Applying the formula for comparing means between two independent groups, the initial calculated sample size was 34 participants per group, which was inflated to 40 per group to account for an anticipated 15% dropout rate, ensuring that the final effective sample size maintains adequate statistical power.

Recruitment

Eligible participants will be recruited from the outpatient and inpatient services of the ASD specialty clinic at Xi'an TCM Hospital of Encephalopathy Affiliated to Shaanxi University of Chinese Medicine.

Randomization and Blinding

Randomization

The randomization sequence will be generated by an independent statistician using validated software (eg, SAS or R) with a stratified block randomization method. Participants will be stratified by age (2–6 years vs. 7–12 years) to ensure balanced age distribution across groups. Within each stratum, a block randomization (block size = 6) will be applied. The sequence will be imported into an Interactive Web/Voice Response System (IWRS/RTSM) to ensure allocation concealment. Following informed consent and eligibility confirmation, the clinical research coordinator (CRC) will obtain the group allocation via the system.

Blinding

Due to the nature of acupuncture and tuina, blinding of participants and practitioners will not be feasible. However, to minimize detection bias, all primary and secondary outcome assessors, including the personnel scoring the ATEC, CARS-2, ABC, CSHQ, BSFS, and SBMs, and the independent EEG analysis staff, will be strictly blinded to the treatment group assignment. The data manager and statistician will also remain blind until the final data analysis is complete.

Intervention and Control Groups

All participants will receive standardized educational rehabilitation training (baseline intervention) and are randomly assigned to one of three groups for 12 weeks (5 sessions per week, total 60 sessions). Treatment scheduling may be extended when necessary but must be completed within 14 weeks. TCM interventions will take place from 08:00–12:00 and educational rehabilitation from 14:00–18:00. The grouping information is shown in Table 1.

Table 1 The Grouping Information

Group (1:1:1)	TCM Techniques	Educational Rehabilitation
A: Acupuncture + Tuina + Rehabilitation	Acupuncture + Tuina	✓
B: Acupuncture + Rehabilitation	Acupuncture	✓
C: Rehabilitation Only	None	✓

Note: ✓ indicates the intervention is applied.

Intervention Protocol

Acupuncture Intervention (Groups A and B)

Acupuncture treatment will utilize disposable, sterile filiform needles (0.30×25mm or 0.30×40mm). The skin at the acupoints will be disinfected with 75% alcohol prior to needling. The acupoints are divided into main points and auxiliary points:

Main Acupoints: Baihui (GV20), Sishencong (EX-HN1), Shenting (GV24), Benshen (GB13, bilateral), Naohu (GV17), Naokong (BL19, bilateral), Zusanli (ST36, bilateral), and Sanyinjiao (SP6, bilateral).

Auxiliary Acupoints (for Comorbidities): Shenmen (HT7, bilateral), Neiguan (PC6, bilateral), and Anmian (EX-HN14, bilateral) for sleep disorders; Zhigou (SJ6, bilateral) and Tianshu (ST25, bilateral) for constipation.

Needling Technique: Head points will be inserted using the transverse insertion technique, penetrating 1–1.5 cun into the subaponeurotic layer. Needles at Baihui, Shenting, and Benshen will be directed postero-inferiorly; needles at Naohu and Naokong will be directed inferiorly. The "Chouqi" technique will be applied as a standardized mild stimulation method, consisting of gentle lifting-thrusting and rotating manipulation to elicit a subtle de qi sensation, which is considered appropriate and tolerable for pediatric patients. Strong stimulation is deliberately avoided to enhance compliance and safety in children with ASD. The technique is not an entirely novel invention, but a standardized adaptation of traditional manual needling techniques (lifting-thrusting and rotation) refined through long-term clinical practice in pediatric acupuncture. It is primarily designed to achieve a gentle regulatory effect on the central nervous system, potentially enhancing brain–body interaction and neuroplasticity.

Tuina Intervention (Group A)

Tuina treatment will be performed by qualified TCM physicians, lasting 20 minutes per session. The treatment will be divided into head/face, back, and hand areas. Key techniques include: pushing (Tui), kneading (Rou), and pinching (Nie).

Head and Face: The practitioner will use techniques such as Tui Tianmen (pushing the forehead), Tui Kangong (pushing the eyebrows), and kneading at points like Shenting and Benshen. This manipulation aims to regulate the mind (Tiao Shen).

Back: The Nieji will be applied along the spine from the coccyx (Guiwei) to the base of the neck (Dazhui), performed 5–10 times.

Hands: Techniques focus on stimulating the five-finger meridians (Spleen, Heart, Liver, Kidney). The tonifying (Bu) manipulation for the Spleen and Kidney meridians will be strictly defined as circular pushing (rotational movement) on the palmar surface, performed in a clockwise direction with moderate and consistent force. Straight pushing along the radial edge will not be used in this trial to ensure procedural standardization.

The manipulation should be gentle yet firm, brisk, and consistent, always ensuring the child is calm and receptive during the 20-minute session.

Educational Rehabilitation Training (Groups A, B, and C)

All groups will receive standardized Educational Rehabilitation Training, which serves as the fundamental standard of care and comparison base for the study. The program is developed in accordance with international guidelines for the treatment of ASD. This training focuses on enhancing social interaction, communication, cognition, and behavior, incorporating four main methods:

Applied Behavior Analysis (ABA): Utilizes structured, one-on-one teaching to break down tasks into small components, reinforced by positive reinforcement (eg, food, praise) and fading prompts.

Naturalistic Developmental Behavioral Interventions (NDBI): Focuses on joint attention and imitation skills within the child's natural environment, employing strategies such as modeling, prompting, and differential reinforcement.

Treatment and Education of Autistic and related Communication-handicapped Children (TEACCH): Capitalizes on the visual learning strengths of children with ASD by using a highly structured environment, visual schedules, and clear visual cues for teaching tasks and routines.

Picture Exchange Communication System (PECS): A functional communication system consisting of six phases, teaching non-verbal children to use pictures to initiate requests, discriminate images, and eventually form sentences using sentence strips.

Intervention Adherence and Fidelity

Participant Adherence

The Clinical Research Coordinator (CRC) will track attendance for all sessions. The percentage of completed sessions out of the total 60 planned sessions will be calculated for each participant and reported as a measure of adherence. Participants achieving less than 80% attendance will be flagged for sensitivity analysis in the statistical plan.

Intervention Fidelity

To ensure standardization and consistency of the interventions: 1) Acupuncture and tuina: All licensed TCM practitioners must undergo centralized training and pass a standardized operating procedure (SOP) examination before treating participants. Periodic (monthly) on-site monitoring by an independent investigator will be conducted to verify adherence to the specified points, manipulation techniques, and duration. 2) Educational Rehabilitation: All rehabilitation therapists will use a standardized curriculum, and fidelity checklists will be used by supervisors to assess treatment delivery consistency.

Outcome Measures and Timeline

The trial endpoints are as follows:

Primary Endpoint

Autism Treatment Evaluation Checklist (ATEC) Total Score: The ATEC is a standardized, parent-reported scale widely applied to evaluate symptom severity and functional improvement in children with ASD. It comprises four subdomains—speech/language/communication, sociability, sensory/cognitive awareness, and health/behavior—reflecting the overall clinical improvement.[29] In this study, the change in ATEC total score from baseline to Week 12 is defined as the primary endpoint. This measure will be used to determine the superiority or non-inferiority of the combined Traditional Chinese Medicine intervention (acupuncture/tuina) compared with the control condition.

Secondary Endpoint

(1) Childhood Autism Rating Scale, Second Edition (CARS-2) Score: The CARS-2 is a clinician-rated tool based on structured observation and interviews, used to determine ASD severity across 15 dimensions such as social interaction, emotional response, body use, and verbal communication. It provides an objective and standardized assessment of core autism symptoms.[30] Changes in the CARS-2 score during the intervention period will serve to further evaluate the clinical benefits of the treatment.

(2) Autism Behavior Checklist (ABC) Score: The ABC is completed by parents or teachers and assesses five domains of abnormal behaviors commonly observed in ASD, including sensory responses, social withdrawal, communication challenges, and stereotyped body use. It complements the evaluation of functional and behavioral outcomes beyond core symptoms.[31] A reduction in ABC score will be interpreted as improvement in atypical behaviors and daily functioning.

(3) Children's Sleep Habits Questionnaire (CSHQ-CH-R) Score: The CSHQ is a parent-reported instrument designed to identify sleep disturbances in children across multiple dimensions, such as sleep onset delay, night waking, and sleep-disordered breathing.[32] Given the high prevalence of sleep problems in ASD, this questionnaire allows assessment of the intervention's potential regulatory effects on sleep and autonomic function. Lower scores indicate improvement in sleep quality and nighttime behaviors.

(4) Bristol Stool Form Scale (BSFS) and Spontaneous Bowel Movements (SBMs): The BSFS provides a visual classification of stool consistency ranging from severe constipation to diarrhea,[33] while SBMs track the frequency of bowel movements without the use of laxatives. These indicators allow objective evaluation of bowel health in ASD children. Improvement in stool form and increased regularity of bowel movements will be considered evidence of gastrointestinal functional benefit from the intervention.

Table 2 Assessment Schedule

Timepoint	Baseline (−7 to 0 d)	Week 4	Week 8	Week 12	Week 16
ATEC, CSHQ, BSFS, SBMs	✓	✓	✓	✓	✓
CARS-2, ABC	✓			✓	✓
EEG	✓			✓	

Note: ✓indicates that the assessment will be conducted at the corresponding time point.

(5) Electroencephalogram (EEG) Results: EEG offers quantitative neurophysiological information by recording cortical electrical activity and brain network connectivity.[34] As a mechanistic secondary endpoint, EEG will be used to examine whether acupuncture/tuina induces measurable neuroplastic changes. Alterations in spectral power or functional connectivity will serve as biological correlates of treatment effects.

The outcomes evaluation timeline is shown in Table 2.

Adverse Events

All adverse medical events occurring after intervention will be recorded. Serious adverse events (SAEs) include death, life-threatening events, permanent disability or functional loss, hospitalization, or prolonged hospitalization.

Adverse events potentially attributable to TCM techniques include needling syncope, needle retention, needle breakage, hematoma after needle withdrawal, and soft-tissue injury from tuina.

All AEs will be documented in the case report form (CRF). Non-serious AEs will be followed for 7 days after trial completion; SAEs will be followed for 30 days. Interventions will be discontinued if SAEs occur (eg, persistent high fever), but subsequent study procedures will continue per protocol.

Data Collection, Management, and Statistical Methods

Data collection and quality control.

All data will be reviewed by clinical monitors within 1 week of each visit and entered into the electronic CRF.

On-site monitoring and auditing will be conducted regularly to ensure accuracy and authenticity of research data.

A four-level quality management system (project–hospital–study–third-party) will be implemented.

Data Management and Quality Control

Data collection and management will be conducted using an Electronic Data Capture (EDC) system to ensure data quality, integrity, and security. All clinical data are initially recorded on paper Case Report Forms (CRFs) and subsequently entered into the online database by investigators or CRCs.

Data management will follow the Good Clinical Practice (GCP) guidelines. The system will automatically perform logical consistency checks, supplemented by double data entry and manual verification to ensure accuracy. Data managers generate queries based on discrepancies, which are resolved by investigators. All modifications, queries, and resolutions are documented through a complete audit trail. After completion of data entry and validation, database lock is performed jointly by the data manager, principal investigator, and statistician. Once locked, the database will not be modified and will be used for the final statistical analysis.

Statistical Analysis

Efficacy analyses will primarily be based on the Full Analysis Set (FAS), which includes all randomized participants with at least one post-baseline assessment, analyzed according to the intention-to-treat principle. The Per-Protocol Set (PPS) will serve as sensitivity analyses. The Safety Set (SS) will include all participants who received at least one intervention session.

Primary Outcome Analysis

The primary outcome is the change in the Autism Treatment Evaluation Checklist (ATEC) total score from baseline to Week 12. A repeated-measures mixed-effects model (MMRM) will be used as the primary analysis model. The model will include fixed effects for treatment group, time (baseline, weeks 4, 8, 12), the group-by-time interaction, age stratum (2–6 vs. 7–12 years), and the baseline ATEC score as a covariate, with a random intercept for subjects.

The primary analysis will test two hypotheses:

Superiority: That the reduction in ATEC scores (indicating improvement) is greater in both Group A and Group B compared to Group C. Superiority will be assessed using one-sided tests at a significance level of $\alpha = 0.025$.

Non-inferiority: That the reduction in ATEC scores in Group B is not inferior to that in Group A. The non-inferiority margin is set at 1.94 points on the ATEC scale. This margin (M) is derived as half of the assumed mean difference (3.88) between an active intervention group and the control group from our preliminary data, a conventional and clinically justifiable approach. Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval for the difference in mean change (Group B – Group A) is greater than −1.94.

To control the overall type I error rate for these multiple comparisons, a hierarchical testing procedure will be applied: first testing A vs. C superiority, then B vs. C superiority, and finally A vs. B non-inferiority, proceeding only if the preceding test is significant.

Secondary Outcomes Analysis

Continuous secondary outcomes (CARS-2, ABC, CSHQ) will be analyzed using linear mixed models similar to the primary analysis. The Bristol Stool Form Scale (BSFS) will be analyzed using an ordinal logistic mixed model. Between-group differences at specific timepoints will be estimated with appropriate confidence intervals. EEG data (eg, spectral power, functional connectivity) will be compared across groups at Week 12 using ANOVA or the Kruskal–Wallis test, based on data distribution.

Safety Analysis

The incidence of adverse events (AEs) and serious adverse events (SAEs) will be summarized by group using descriptive statistics. Differences in AE incidence rates will be compared using Chi-square or Fisher's exact tests.

Handling of Missing Data

The primary analysis using MMRM provides a valid approach under the missing-at-random assumption. Sensitivity analyses, including multiple imputation and a complete-case analysis, will be conducted to assess the robustness of the primary results concerning missing data.

Discussion

The rapidly increasing global prevalence of ASD poses a major public health challenge, creating an urgent need for safe, effective, and scalable adjunctive interventions.[35] While education therapies are the mainstream treatment, high-quality evidence supporting non-pharmacological adjunctive therapies for core ASD symptoms remains scarce. Existing clinical studies on TCM techniques such as acupuncture are constrained by the limited number and low quality of available evidence, with a lack of standardized protocols and high-quality randomized controlled trials to support their efficacy.[36] Consequently, the current evidence is insufficient to recommend these TCM techniques as standard therapies. Therefore, we designed this single-center, three-arm, pragmatic randomized controlled trial (pRCT) to generate high-quality, clinically applicable evidence and to establish a robust methodological foundation for future research and clinical translation.

Several features of our trial design enhance its scientific rigor and translational value. The three-arm design, with standardized educational rehabilitation as the foundation for all groups, allows for a direct evaluation of the additive benefit of TCM techniques over standard care alone. Furthermore, centralized randomization, allocation concealment,

and rigorously standardized operating procedures (SOPs) strengthen internal validity and ensure the study can serve as a protocol template for future large-scale trials.

Complementing this rigorous design, the statistical framework is designed to address two clinically relevant questions. The superiority analysis (Group A/B vs. Group C) tests whether TCM interventions provide a measurable added benefit to core symptoms. The non-inferiority analysis (Group B vs. Group A) addresses a pragmatic question of implementation: if Group B (acupuncture alone) is not inferior to Group A (acupuncture + tuina), it is designed not merely to assess efficacy, but to evaluate the "value" of the combined regimen from a medical economics and pragmatic perspective. If acupuncture alone (Group B) is demonstrated to be non-inferior to the combined acupuncture and tuina intervention (Group A), it would suggest that the incremental clinical benefit of adding tuina does not justify the additional time, cost, and potential burden of compliance on children, the additional benefit of tuina may not outweigh the increased time and treatment burden. This would support the adoption of a simpler and more cost-effective intervention strategy, particularly in resource-limited settings, and may facilitate the broader international application of TCM. In addition, although the combined duration of acupuncture (30 min) and tuina (20 min) may appear relatively long for children with ASD, several measures have been implemented to ensure feasibility and compliance. Specifically, interventions are delivered in a child-friendly environment with caregiver involvement when necessary, using pediatric-adapted gentle techniques to minimize discomfort, and allowing flexible session adjustments according to the child's tolerance. Based on our prior clinical experience, this combined intervention duration has demonstrated good tolerability and adherence, supporting its feasibility in real-world settings. Furthermore, the inclusion of neurophysiological measures like EEG may help elucidate the biological correlates of TCM's purported mechanism of "regulating the mind," offering new avenues for integrative medicine research.

In summary, this pragmatic single-center RCT aims to generate high-quality evidence that is urgently needed with real-world relevance for adjunctive ASD treatments. More importantly, it represents a pivotal launch study for the international dissemination of TCM techniques, particularly among BRI countries. By establishing a quantifiable, standardized, and operationally transferrable therapeutic protocol, the study will lay the groundwork for future large-scale multicenter RCTs with high generalizability and strong evidential strength. Ultimately, the successful implementation of this research has the potential to accelerate the clinical translation of safe and effective non-pharmacological therapies, offering new therapeutic opportunities for children with ASD worldwide and meaningful relief for their families.

Limitations

This study has several limitations. First, as a single-center trial, the generalizability of our findings may be limited to similar clinical settings; however, this design allows for rigorous control and standardization of the complex interventions, providing essential foundational data for future multicenter studies. Second, the nature of acupuncture and tuina interventions makes blinding of participants and practitioners infeasible, which may introduce performance bias. We have mitigated this risk by implementing strict blinding of outcome assessors and statisticians. Third, despite standardized protocols, some variation in technique application across practitioners is possible, though centralized training and monitoring aim to minimize this. Finally, the 4-week follow-up period may be insufficient to evaluate the long-term sustainability of the effects, warranting future studies with extended follow-up. Another limitation is the lack of a sham-control or time-matched control group. As a pragmatic RCT, our aim is to evaluate the "add-on" effect of TCM techniques in a real-world clinical setting rather than to isolate the specific efficacy of needle insertion (blinded efficacy). The additional time and therapeutic attention in the TCM groups (Groups A and B) compared to the rehabilitation-only group (Group C) may introduce a non-specific care effect. However, this design reflects real-world clinical practice in China where TCM is prescribed as an adjunctive module. We will interpret the results with caution in light of this potential attention bias.

Ethics Approval

The study protocol (Version 3.2, dated 15-OCT-2025) was approved by the Medical Ethics Committee of the Xi'an TCM Hospital of Encephalopathy Affiliated to Shaanxi University of Chinese Medicine (Approval No. XNLL-2025-K-006).

Acknowledgments

Song HJ and Zhao NX share corresponding authorship. The authors thank all participants for their valuable support and cooperation throughout the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Funding

The study was supported by National Key R&D Program of China (2024YFC3507304) and the Project of Shaanxi Administration of Traditional Chinese Medicine (2025-CXRC-28).

Disclosure

The authors declare that they have no conflicts of interest related to this work.

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