Baduanjin as a Treatment for Hyperactive-Impulsive Symptoms Of Attention Deficit Hyperactivity Disorder: study protocol for a randomized controlled trial.

Trial registration: NCT04282460 [ClinicalTrials.gov] [registered on 21-02-2020]

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Content

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1 Introduction

1.1 Background and rationale

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders among school-aged children. The prevalence in China is estimated to be 6.26%[1]. ADHD is characterized by age-inappropriate inattention and/or hyperactivity-impulsivity[2]. ADHD marks a significant risk for later development of the oppositional defiant disorder, conduct disorder, and more serious antisocial behavior in adolescence, impairs academic achievement and social function, which may lead to impaired relationships with family and peers, self-esteem, and quality of life[3].

Treatment for ADHD is typically recommended as multimodal approaches, which usually include medication and behavioral interventions as first-line treatment[4]. Stimulant and non-stimulant medications are the most efficacious treatments for inattentive and hyperactive/impulsive symptoms. However, parents' side effects and concerns have limited medication use in many patients[5]. Non-pharmaceutical behavioral interventions mainly consist of parent training in behavior management and behavioral classroom interventions. Behavioral interventions are shown to improve social and behavioral outcomes. Still, it is not as effective as medication in reducing the core symptoms of ADHD. It is usually quite time and labor-consuming and costly, making it challenging to implement in developing countries like China[6,7].

Given these findings, physical exercise is indicated as an alternative approach to the treatment of ADHD. It is proposed by many researchers to be used independently or complementary to medication or behavioral interventions to attenuate the adverse effects of ADHD. Physical exercise improves cognition, fitness, physical function, mood, and behaviors in household and school settings in children with ADHD[8–12]. Several studies also highlighted the efficacy of physical exercise in the reduction of core symptoms of ADHD[8,9,12–16]. Furthermore, physical exercise interventions can yield acute and lasting positive effects on executive function (EF), known as the core neurobiological deficit in ADHD[17]. This neural rehabilitating effect is shown by improvements in processing speed, working memory, planning, and inhibitory control after physical exercise[13,18–21]. The underlying mechanism may be associated with the increased levels of synaptic proteins, glutamate receptors, norepinephrine and dopamine levels, and the availability of brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 generated by physical exercise, all of which can promote neural plasticity leading to the adaptive biological response of brain function[22–26].

Physical exercise, including tai chi chuan and Baduanjin, is also seen as an essential alternative approach in Traditional Chinese Medicine (TCM). In the theory of TCM, the pathogenesis of ADHD is the imbalance of yin-yang and dysfunction of the Zang-fu (viscera) organs[27]. The TCM treatment of ADHD is individualized, mainly composed of Chinese herbal medicine, adjuvant acupuncture, tui na, diet, and physical exercise [28,29]. The Eight-brocade Exercise (Baduanjin) is an ancient Chinese qigong physical exercise that likely originated more than one thousand years ago. Baduanjin exercise comprises 8 sets of gentle, elastic, and integrated mind-body movements; each group targets a specific organ or health need, which can be easily administered to children

and adolescents. Baduanjin has already been proven to improve the physical function of primary school students, including physical coordination, abdominal strength, and flexibility[30]. Researchers have also demonstrated that Baduanjin has a protective effect on cognitive functions such as selective attention in patients with mild cognitive impairment. The result is significantly larger than the brisk walking group[31]. The score of the Schulte grid scale was also considerably improved after 12 weeks of daily practice of Baduanjin in another research, which showed its potential for attention improvement[32].

Given the above backgrounds, investigators will evaluate the effectiveness of Baduanjin exercise compared to routine physical exercise and its underlying mechanism in a randomized controlled trial.

1.2 Objectives

This randomized controlled trial aims to compare the efficacy of Baduanjin exercise to routine physical exercise in ADHD patients with Hyperactive-Impulsive Symptoms after three months of exercise and evaluate whether this effect will last for another three months.

The primary objective is to compare the Hyperactivity/Impulsivity change scores between two groups of The Swanson, Nolan, and Pelham Questionnaire (SNAP-IV) Rating Scale in 3th and 6th months after initiation. The secondary objective of this study is to evaluate the change in Scoring evaluation of the TCM symptoms after 3 months of treatment and 6 months of follow-up. In addition, the mediating effect of executive function measured by the CANTAB test and BRIEF2 scale will be calculated. Furthermore, we will determine whether these effects extend to other ADHD-related problems, including the sensory integration score, the Developmental Test of Visual Perception, and other behavioral problems.

1.3 Trial design

This is a single-center, single-blind, superiority, randomized controlled trial. This study is planned to be conducted from October 2020 to March 2022 at the Children's Hospital of Fudan University. Patients will be recruited at the child psychology clinic and TCM clinic of the Children's Hospital of Fudan University. Each participant who fulfills the eligibility criteria outlined in the protocol is randomly allocated consecutively to either the Baduanjin exercise group or the general physical exercise group with a ratio of 1:1.

2 Methods: Participants, interventions, and outcomes

2.1 Study setting

This trial is being performed in the Children's Hospital of Fudan University, which is a comprehensive tertiary pediatric hospital and one of the national children's medical centers. Patients are enlisted at the clinic of both the Child psychology department and TCM department.

2.2 Eligibility criteria

Patients are considered for inclusion if they meet the criteria as defined below.

2.2.1 Inclusion Criteria

Inclusion criteria: (1) Age between 7 years 0 months to 16 years 11 months. (2) Diagnosed with ADHD at the clinic of the Child psychology department, with Combined Presentation or Predominantly Hyperactive-Impulsive Presentation. (3) Doctor version of SNAP-IV Hyperactivity/Impulsivity score $\geqslant$ 12. (4) Full-Scale Intelligence Quotient $\geqslant$ 80 (Wechsler intelligence scale for children-IV). (5) Resident in Shanghai, Zhejiang province, and Jiangsu province. (6) The parents or caregivers can understand the content of the study, are willing to participate in the follow-up visits, and complete the required information.

2.2.2 Exclusion Criteria

Exclusion criteria: (1) Currently using psychiatric medication other than methylphenidate as the treatment plan at the time of enrollment and planning to use it within the upcoming three months. (2) Comorbid with the epileptic disorder, attack stage of child asthma, or other existing physical illness that makes the routine physical exercise risky to the patient. (3) Comorbid with Tourette syndrome, Autism Spectrum Disorder, Learning disorder, Mood disorder, Psychotic disorder, or under suicidal risk. (4) Attending other regular athletic training under professional guidance during the intervention period. The gym class and after-class sports activities at school are not considered professional-guided athletic training. (5) Receiving regular psychological treatment or attending any other clinical research during the intervention.

2.3 Who will take informed consent?

This trial's information is posted in our clinic's hallway and introduced to all the families. All the families receiving this information are welcome to sign up for the trial by completing a simple electric application form on their mobile phones. We will screen their application to assess their eligibility and call the parent to provide initial study information and answer their questions. After this discussion, the family intent to participate in the study will be scheduled to meet with the research physician to discuss any remaining questions, finish the inclusion evaluation and sign in the informed consent. Written informed consent is obtained from the legal guardian of each participant before they undergo any interventions related to the study. Researchers will also explain the trial details explicitly to participants over eight years old and obtain their signed consent.

2.4 Interventions

2.4.1 Explanation for the choice of comparators

Many cross-sectional studies support a positive relationship between routine physical activity and executive function development, decreased behavioral problems, and impulsivity control in children with ADHD. We assumed that Baduanjin exercise is superior to other routine physical exercises. Therefore, the control group is guided to take any routine physical exercise, including jogging, bike-riding, badminton, table tennis, soccer, basketball, aerobics, and rope skipping for 30 minutes, five days each week, under the supervision of caregivers. The caregivers are trained during inclusion interviews by the physician to understand the idea of aerobic physical exercise and the technique to help their child choose their favorite sports activity and make it a daily routine. Each child participating in this trial is given a Huawei fitness tracker with a heart monitor, which is used to monitor the body information during their daily exercise. Researchers will check the uploaded data of the fitness tracker on a daily basis. The time of exercise is required to exceed 30 minutes each time, and the maximum heart rate during the exercise should be over 120 beats per minute. This is the comparator of choice for the Baduanjin exercise in this study.

2.4.2 Intervention description

The Baduanjin exercise group is asked to use the Baduanjin training system to practice the whole set of Baduanjin at least once a day and at least 5 days each week for 3 months. The Baduanjin training system is a video game designed with motion tracking and motion recognition strategy by the research team, providing a motivating full-body interactive experience for children with ADHD to engage in practice. Caregivers included in the Baduanjin intervention group were equipped with a Kinect sensor bar, connector, and software package on the day of enrolment. The software and electronic equipment installation is guided by researchers on the same day in the

hospital and at their homes later if necessary.

During the study, the children were asked to practice Baduanjin using the given software for at least 30 minutes daily, 5 times each week. They can practice any single brocade or the whole combination of 8 movements using the different game modes in the software. Instructions for movements and the variety of breath are provided in each game mode. The eight movements of Baduanjin are listed as follows:

1. Hold up the hands to regulate the triple burner;
2. Draw a bow like shooting a hawk;
3. Raise one arm to regulate the spleen and stomach;
4. Turn the head back to treat consumptive diseases and injuries;
5. Sway the head and swing the buttocks to expel the heart-fire;
6. Hold the feet by the hands to reinforce the loins and kidneys;
7. Punch with anger;
8. Hold and drop the heels to improve the health of the spine.

During their exercise, the child's motion will be captured and projected onto the screen, and their movement will be scored according to accuracy. The advice on motion adjustment is given immediately, and the feedback of data will be shown on the screen after each round of the game, then uploaded to a management website to be monitored by researchers.

The children in the Baduanjin group were asked to use the fitness tracker and uploaded data the same as the control group. The time of exercise is required to exceed 30 minutes each time, and the maximum heart rate during the exercise should be over 120 beats per minute. Researchers will also check with the data uploaded automatically by the Baduanjin software to ensure the movements are adequately practiced.

2.5 Criteria for discontinuing interventions

Participants can leave the trial at any time for any reason without any consequences if they request to do so. If they decide to leave before the intervention starts, the patient will be replaced by the following new patient. During the intervention, the drop-out is defined as the following: changing the dose of methylphenidate and or receiving another behavioral intervention according to the advice of an independent child psychiatrist, stopping taking exercise for two consecutive weeks without a reasonable cause, and/or the refusion to attend both study visits at 3 months$\pm$4 weeks and 6 months$\pm$4 weeks after allocation. Advises about preventing sports injury are talked about with caregivers at the enrollment. In case of a sports injury or illness for other reasons, the caregivers are asked to contact the primary investigator to discuss whether to pause the exercise or end it. The patient data will be recorded up to the drop-out and included in the analysis.

2.5.1 Strategies to improve adherence to interventions

In this trial, each family has a Wechat discussion group where they can upload their biological data and contact the researcher conveniently. Researchers will check the uploaded data every

morning and give feedback to caregivers in the discussion group. When the data is not uploaded, researchers will remind the caregivers to upload data and make sure that if they have any difficulty in continuing the exercise. Researchers will also check the data uploaded automatically by the Baduanjin software to ensure the movements were adequately practiced. When unqualified exercise data is identified, the researcher will contact the caregiver to modify their exercise status and guide them to meet the requirement of exercise intensity and movement accuracy.

2.5.2 Definition of adherence

Researchers will check the uploaded data every day. If the time of exercise exceeds 30 minutes, and the maximum heart rate during the exercise is over 120 beats per minute, it is recorded as a day that meets the adherence standard. For the participants in the Baduanjin group, the score automatically rated by the Baduanjin software should also exceed 77.5. We require the participants to meet the adherence standard for at least 5 days each week. Participants that finished less than 80% required days are defined as having poor adherence.

2.5.3 Relevant concomitant care permitted or prohibited during the trial

Both groups receive standard care in the clinic during the intervention. Additional sensory integration therapy and child behavioral group or individual therapy are permitted once they complete the 3-months follow-up.

2.5.4 Provisions for post-trial care

The WeChat discussion group will be kept after the trial so that the participants can access the researchers if they have any further questions about ADHD or physical exercise.

2.6 Outcomes

2.6.1 Primary Outcome Measure:

Hyperactivity/Impulsivity score change in SNAP-IV clinician-rated scale. The Swanson, Nolan, and Pelham Questionnaire (SNAP-IV) Rating Scale is a revised version of the Swanson, Nolan, and Pelham (SNAP) Questionnaire that utilizes the DSM-IV criteria for ADHD and oppositional defiant

disorder, rated by caregivers or professionals[33,34]. It comprises three subscales: Inattention, Hyperactivity/Impulsivity, and Oppositional Defiant Disorder. The score of each item is rated with a 4-point Likert scale (0 = not at all, 3 = very much). The Chinese version of the SNAP-IV has good internal consistency (α = 0.95) and test–retest reliability (ICC = 0.68), and its sensitivity and specificity for ADHD diagnosis are 0.87 and 0.79, respectively[35]. We ask the blinded clinician to rate the 9-item-Hyperactivity/Impulsivity subscale to evaluate change in ADHD Hyperactivity/Impulsivity symptoms in children. The Hyperactivity/Impulsivity subscale score is calculated by adding the 9 items; the score will range from 0 to 27. The change of score is calculated by the Hyperactivity/Impulsivity score at 3 months after enrollment (both the Baduanjin exercise group and Routine physical exercise group went through 3 months of intervention at this point) minus the Hyperactivity/Impulsivity score at baseline (enrollment).

2.6.2 Secondary Outcome Measure:

(1) Change of Scoring evaluation of the TCM symptoms. The TCM symptom scale was developed from the guideline system for traditional Chinese medicine's new drug clinical research to evaluate the severity of TCM symptoms in children[36]. This scale includes 23 items; each presents one common TCM symptom. Each symptom is rated 1-4 points according to its severity by a trained researcher with extensive experience in TCM, using observation, auscultation and olfaction, inquiry, pulse feeling, and palpation. The total score is calculated by adding the scores of all 23 items. The change of score is calculated by TCM symptoms score after 3 months of enrollment (both the Baduanjin exercise group and Routine physical exercise group went through 3 months of intervention at this point) minus TCM symptoms score at baseline (enrollment).
(2) SNAP-IV parent scale score change of inattention and Oppositional Defiant Disorder(ODD) subscales are used as outcome measures to evaluate the effect of treatment on inattention and ODD symptoms. Both the parent-rated and clinician-rated scores will be analyzed.
(3) The change of Weiss Functional Impairment Rating Scale (WFIRS) scores. The WFIRS is an ADHD-specific impairment measure that is widely used across the world[37]. The items of this scale describe functional difficulties most likely to represent the patient's treatment target. This instrument has been translated into Chinese and validated in the ADHD population [38]. The scale uses a Likert scale of 0-3, and subscales including family, school, life skills, child's self-concept, social activities, and risky activities are designed to cover different areas of functional impairment.
(4) Behavioral problems of children are evaluated by the parent version of the Achenbach Child Behavior Checklist（CBCL） and self-rated Strengths and Difficulties Questionnaire(SDQ) by the child. The CBCL scale was first published in 1976 and revised in 1983 and 1991[39,40]. It is a scale widely used internationally to assess children's behavior problems, with a three-level Likert score of 0-2 and nine subscales formed according to different ages and genders. Su et al. normalized this scale in China in 1998 and reported satisfactory psychometric characteristics [41]. The SDQ was developed by Goodman. R in 1997 and revised in 2001[42]. It is also scored by a Likert scale of 0 to 2, with 25 items divided into 5 subscales. Both parents and children over the age of 9 can use this questionnaire to report behavior problems. Du et al. have built the norm in China and reported mixed findings concerning the psychometric properties of the Chinese version of SDQ[43]. The change in scores in these rating scales will be compared between the two groups.

(5) Children's executive function is extrapolated by neuropsychological tests and ecological rating scales. The Cambridge neuropsychological test automated battery (CANTAB) is chosen to evaluate the executive function change after physical exercise. The CANTAB is a computer-based validated cognitive assessment system consisting of a battery of neuropsychological tests administered to participants using a touch screen computer[43]. This system provides accurate and sensitive computerized psychological testing. It aims to be culture and language-independent by using non-verbal stimuli in most tests suitable for school-age children and adolescents. The Motor Screening Task, Spatial Working Memory, Stop Signal Task, and Rapid Visual Information Processing are applied in this trial.

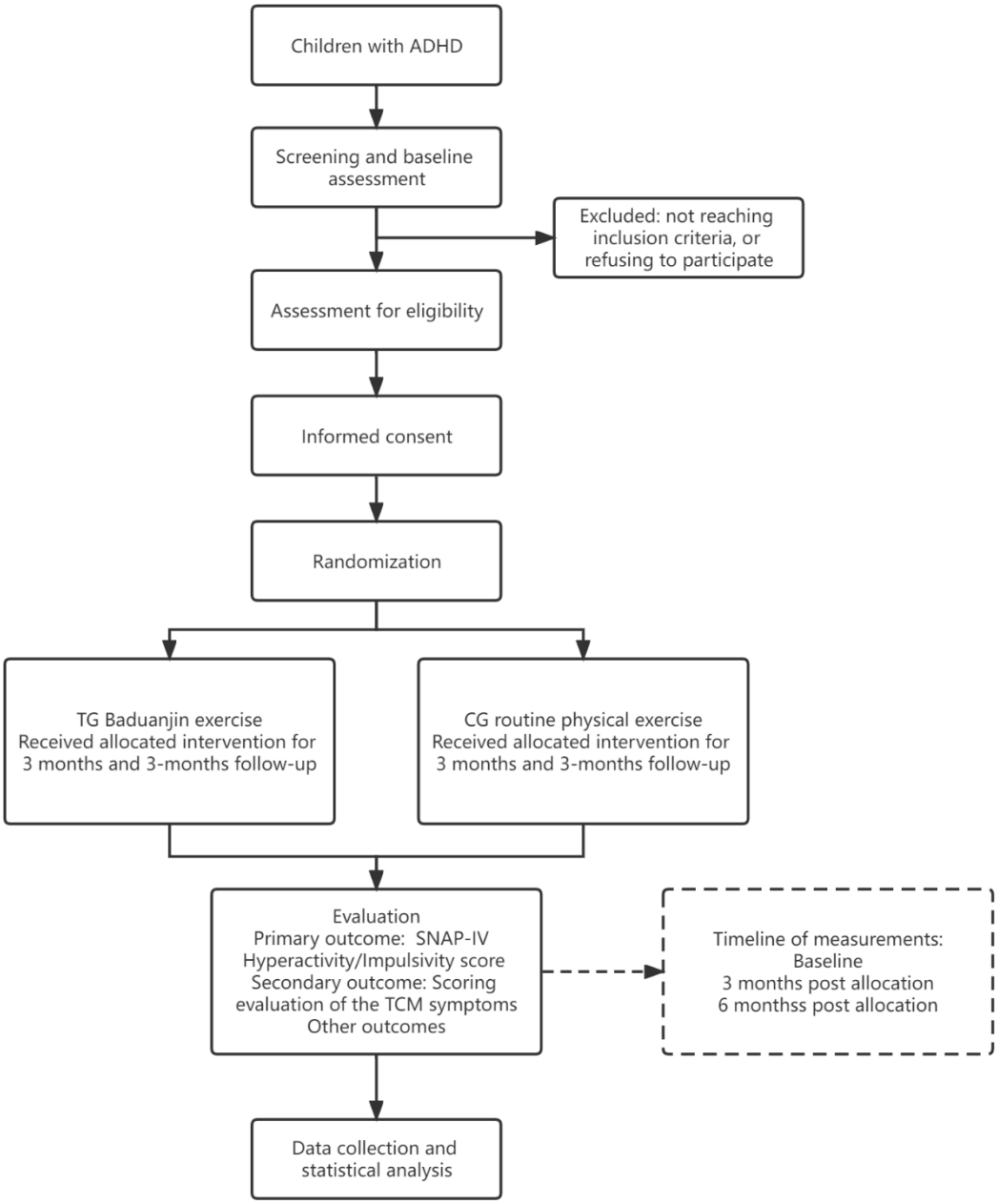
The ecological executive function of participants is assessed by the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF-2). Originally developed by Gerard Gioia, this scale is an assessment of executive function behaviors at home for children and adolescents ages 5–18, mainly used to evaluate ADHD in children and has been shown to be superior to other rating systems as it taps into unique behaviors typically associated with the disorder[43]. This scale has nine different well-validated subscales and three indexes consistent with widely accepted theory: Behavior Regulation, Emotion Regulation, and Cognitive Regulation. This scale is translated into Chinese and has been proven to have convincing reliability and validity[44]. The performance change in CANTAB and BRIEF-2 will be compared between the two groups in this trial.

(6) Visual Perception of children is measured by the Developmental Test of Visual Perception-2nd edition (DTVP-2)[45]. It is a well-researched, norm-referenced measure of visual perception and visual-motor abilities in individuals ages 4 to 12. It has 8 subtests that measure different but interrelated visual-perceptual and visual-motor abilities along with 3 index scores--General Visual Perceptual Index, Motor-Reduced Visual Perception Index, and Visual-Motor Integration Index. The different visual perception performances will be tested before and after intervention and compared between groups.

(7) The sensory integration problems of children with ADHD are evaluated by Child Sensory Integration Checklist, which was first created by Xinxiong Zheng and then retested in Mainland China[46]. This scale is composed of 5 factors, including gross motor and balance, excessive tactile sensitivity and emotional instability, poor proprioception, insufficient learning ability or poor coordination, and particular problems of older children. It is assumed that physical exercise can improve the sensory integration ability of participants. Therefore, the change in the score of each factor will be compared between the two groups.

2.7 Participant timeline

Outcome measures are collected at enrolment, 3 months allocation, and 6 months post allocation. The flow of the trial is presented in Figure 1. A schematic diagram of enrolment, interventions, and assessments is described in Table 1.



TG: treatment group, CG: control group, SNAP-IV: The Swanson, Nolan, and Pelham Questionnaire

Figure 1 Flow diagram showing study design and subject allocation

Table 1 Enrolment, interventions, and assessments

	STUDY PERIOD			
	Enrolment	**Allocation**	**Post-allocation**	**Close-out**
TIMEPOINT**	***-2 Weeks***	**0**	***3 months***	***6 months***
ENROLMENT:				

Eligibility screen	✓			
Informed consent	✓			
Allocation		✓		
INTERVENTIONS:				
Baduanjin practice	✓	✓	✓	✓
routine physical exercise	✓	✓	✓	✓
ASSESSMENTS:				
Primary Outcome: SNAP-IV clinician-rated Hyperactivity/Impulsivity score	✓		✓	✓
Secondary Outcome: Scoring evaluation of the TCM symptoms(researcher rated)	✓		✓	✓
Other outcome measures: SNAP-IV parent/clinician-rated inattention and ODD score	✓		✓	✓
WFIRS (parent completed)	✓		✓	✓
CBCL (parent completed)	✓		✓	✓
SDQ(parent and child completed)	✓		✓	✓
CANTAB(child completed)	✓		✓	✓
BRIEF-2 (parent completed)	✓		✓	✓
DTVP-2(child completed)	✓		✓	✓
Child Sensory Integration Checklist (parent completed)	✓		✓	✓

SNAP-IV: The Swanson, Nolan, and Pelham Questionnaire; TCM: Traditional Chinese Medicine; ODD: Oppositional Defiant Disorder; WFIRS: Weiss Functional Impairment Rating Scale; CBCL: Achenbach Child Behavior Checklist; SDQ: Strengths and Difficulties Questionnaire; CANTAB:

Cambridge neuropsychological test automated battery; BRIEF-2: Behavior Rating Inventory of Executive Function, Second Edition; DTVP-2: Visual Perception of children is measured by the Developmental Test of Visual Perception-2nd edition.

2.8 Sample size

Detailed information is displayed in the SAP.

2.9 Recruitment

Patients will be recruited at the child psychology clinic and TCM clinic of the Children's Hospital of Fudan University. The information of this trial will also be introduced at our 3-hour online ADHD parent training, which is provided to all the families who recently received the diagnosis of ADHD. The advertisement of this trial is also posted both in the hallway of our clinic and on our hospital's WeChat social media platform. Families interested in participating in this trial will fill in the online application form via mobile phone.

2.10 Assignment of interventions: allocation

2.10.1 Sequence generation

Recruited patients will be randomly assigned in a 1:1 ratio to the control group or the experimental group through blocked randomization. The randomization sequence is created by the center using SAS (version 9.4) with a block size of 4. An independent statistician will generate the randomization list. A sequence of subjects' IDs and intervention allocations was generated by creating a random variable and ordering that variable.

2.10.2 Concealment mechanism

The statistician will conceal the allocation sequence and place it sequentially numbered, opaque, sealed, and stapled envelopes. After signing the informed consent from parents, the study investigators will open the envelopes in consecutive orders and randomly assign the subjects to the intervention group or the control group according to the allocation scheme in the envelope.

2.10.3 Implementation

The statistical department of our hospital generates the allocation sequence. The researchers will use the prepared sealed envelopes to allocate the patient to a study arm and finish the enrollment procedures. The study group will be revealed, and intervention will be introduced after allocation to the participants.

2.11 Assignment of interventions: Blinding

2.11.1 Who will be blinded

The standard clinic care will be given by a doctor who knows that the patient is participating in this trial but is unaware of the patient's study group. The primary and secondary outcomes investigator will also be unaware of the patient's grouping. One psychiatrist blind of allocation will talk with the family about their children's ADHD and ODD symptoms and rate it with the SNAP-IV scale. Another Chinese traditional medical doctor blind of grouping will evaluate the severity of traditional Chinese medicine symptoms of children and rate it with TCM symptom scale.

All researchers conducting outcome assessments will be masked in the trial. The trial statistician will also be blinded regarding the treatment code when he develops the statistical analysis plan and writes the statistical programs, which will be validated and completed using dummy randomization codes. The actual allocation will only be provided to the study team after locking the database.

2.11.2 Procedure for unblinding if needed

There is no planned unblinding procedure in this trial since there is no known severe side effect of physical exercise that could lead to an emergency unblinding. The unblinded standard clinic care participants receive during the trial can deal with minor complaints caused by physical exercises, such as muscle soreness and fatigue.

2.12 Data collection and management

2.12.1 Plans for assessment and collection of outcomes

The outcomes will be collected at 3 months and 6 months after allocation. Considering the ongoing COVID-19 quarantine, we allow participants to finish the first outcome evaluation at 3 months$\pm$4 weeks, and for the second outcome evaluation, 6 months$\pm$4 weeks.

The research staff is required to receive a three-hour training session to ensure that they fully understand the protocol and standard procedures for the trial. The blinded physicians for evaluating the primary and secondary outcomes attend a one-hour training on the outcome assessment. All the research questionnaires and tests will be conducted at the Children's Hospital of Fudan University. Data will be collected with a case report form (CRF) and recorded in an ACCESS database. The description of study instruments is provided in the outcome part of this protocol. The demographic information of participants, including birth date, sex, height, weight, routine habit of exercise, and current drug use, are recorded on the CRF. The test record of CANTAB will be downloaded from the Cambridge cognition official website and automatically saved as an excel document. All data collected during the study will be kept in a locked room or protected research server. Back-ups in the study folder on this protected research server will be saved regularly (once per 3 months). Only the study team has access to these documents. To ensure this trial is applied consistently to high quality, the Clinical Trial Unit (CTU) of Children's Hospital of Fudan University will regularly monitor enrolment records, CRFs, informed consent, and data records.

The CRF will be double-entered into the ACCESS database by two investigators independently. The data will then be checked according to the correct range of values to ensure no erroneous entries. All missing data will also be checked and properly coded. Data monitoring and validation will be performed by the CTU of the Children's Hospital of Fudan University periodically. The CTU will preserve the original CRFs and all other study documents until 5 years after the last publication of this trial. The ACCESS database will record any changes to the raw data. For each time point, once all data have been inputted and checked, the database will be locked, and a data download request will be made so that only the authorized person gets access to the data. The data will be downloaded into SAS, R, and STATA formats for statistical analyses.

2.12.2 Plans to promote participant retention and complete follow-up

Before the beginning of the intervention, researchers and caregivers will discuss the best way to implement the exercise at home and strategies to encourage the child's participation. During the intervention, several actions were taken to engage parents and children of both groups in promoting physical exercise at home. Each family was invited to join a Wechat (a Chinese multi-purpose messaging and social media app) discussion group, where they can check their fitness tracker data with researchers daily. Children are given a set of toy coins and a money box on the day of consent signing. They can add one coin into the money box once their data are examined the next morning. Children are given a brochure containing a list of prizes and encouraged to choose gifts with values ranging from 15 to 90 coins. Gifts can be exchanged and sent to their home at any time during the intervention and within 2 months after the intervention. Furthermore, a handwritten, personally signed thank-you card from researchers is sent at the end of the first week of their intervention. Three designed medals—a bronze, a silver, and a golden- are awarded to the children at the end of each month of their intervention sequentially.

2.13 Data management

Detailed information is displayed in the SAP

2.14 Confidentiality

Research data will be saved using a unique study identification code for each participant. The identification code list will only be approached by the research team during the study. It will be documented and safeguarded by the principal investigator according to ethical guidelines after the completion of the study. The data manager from the CTU will have access to the completed anonymous final dataset. No patient identification details will be reported in any published papers.

2.15 Statistical methods

2.15.1 Statistical methods for primary and secondary outcomes

The primary outcome is a continuous variable: Hyperactivity/Impulsivity score change in the SNAP-IV scale. The primary analysis will be based on the intention-to-treat (ITT) population. The generalized linear model (GLM) will be used to test the difference 3 months after allocation between the groups. The estimated means and two-sided 95% confidence intervals (CI) will be derived. All secondary outcomes will be analyzed for a superiority-designed trial and two-sided significance with alpha=5% and standard 95% CIs for the treatment differences in these outcomes between the two treatment groups. Secondary outcome analyses will be based on the ITT population unless specified. SAS (version 9.4) will be used to perform all data analyses and generate the majority of data displays. STATA® (version 16.0) or SPSS, S-Plus, or R may also be used for data analyses and for generating statistical graphs. The other outcome measures will be calculated and presented with the same method of primary and secondary outcomes. Continuous variables will be summarized according to the number of subjects with non-missing data (n), mean, standard deviation (SD), median, minimum, maximum, and range interquartile (IQR). The confidence intervals will be reported on summaries of continuous effectiveness variables. Categorical variables will be summarized according to the absolute frequency and percentage of subjects (%) in each category level. The denominator for the percentages is the number of subjects in the treatment arm with data available unless noted otherwise.

Detailed information is displayed in the SAP.

2.15.2 Plans to give access to the complete protocol, participant-level data, and statistical code

The datasets used and analyzed during this trial can be granted access by the corresponding author and the safety monitoring board(DSMB) of CTU upon reasonable written request.

3 Oversight and monitoring

3.1 Composition of the coordinating center and trial steering committee

This monocenter-designed study is performed and coordinated at the Children's Hospital of Fudan University. Daily support is provided by:
Principle investigator: supervises the trial and takes medical responsibility for the patients.
Data manager: organizes data collection and analysis and safeguards quality and data.
Study physician: trial registration, identifies potential recruits, performs outcome measures, takes informed consent, ensures follow-up according to protocol annual safety reports.
Study therapist: performs outcome measures, coordinates study visits, and daily follow-up of participants.

The study team meets weekly. There is no trial steering committee or stakeholder and public involvement group.

3.2 Composition of the data monitoring committee, its role, and reporting structure

This study will be monitored by a data and DSMB of the CTU of the Children's Hospital of Fudan University. The DSMB is independent of the sponsor and has no competing interests in this study. Consisting of independent clinical experts and statisticians, the DSMB reviews the progress and safety of the trial weekly.

3.3 Adverse event reporting and harms

There is no known severe adverse event caused by routine physical exercise or Baduanjin exercise. Study physicians will take care of the common response to exercise, including sore

muscles and fatigue. Unintended effects of trial interventions discovered by study physicians or therapists will be recorded and reported to the principal investigator within 24 hours.

3.4 Frequency and plans for auditing trial conduct

The process will be independently audited by investigators and the sponsor every three months.

3.5 Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees)

When a substantial modification is made in the case of significant changes to eligibility criteria, outcomes, or analysis that may impact the scientific value of the research or the safety or quality of the intervention, it will be notified to the CTU and the competent authority. Minor revisions of the protocol will be recorded and reported to the CTU. Participants will be informed about the eligibility criteria or intervention changes. Additional consent forms will be signed and filed if needed.

3.6 Dissemination plans

Both positive and negative results of this trial will be fully disclosed in international peer-reviewed journals. Patients who require to receive study outcomes will be provided a layperson summary of the results.

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