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ORIGINAL ARTICLE

Effects of Ball Combination Exercise Combined with cTBS Intervention on Sleep Problems in Children with Autism

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Sleep problems significantly affect the quality of life of autism spectrum disorder (ASD) children. This study aimed to evaluate the effects of a 12-week ball combination exercise, continuous theta burst stimulation (cTBS) stimulation, and combined intervention on sleep problems in children with ASD. Forty-five ASD children were divided into three intervention groups (ball combination exercise($n=12$), cTBS stimulation($n=10$), combined ($n=12$) and a control group ($n=11$). The intervention groups underwent intervention, while the control group maintained daily activities. The effects were assessed using the Children's Sleep Habits Questionnaire (CSHQ) scale. The results revealed that after 12 weeks of intervention, three programs reduced sleep problems in children with ASD. The post-test scores of the cTBS group ($p=0.002$) and the combined group ($p<0.001$) were significantly lower than the baseline scores on the CSHQ scale. The exercise group ($p=0.002$) and the combined group ($p<0.001$) showed significant improvement in sleep anxiety, while there was no statistically significant difference in the effectiveness of the three interventions for sleep-onset delay. The combined group outperformed the single intervention groups in the CSHQ score and sleep anxiety sub-dimensions. The combined intervention group showed slightly superior performance in sleep onset latency, however, there was no significant difference. Three interventions alleviated sleep issues in ASD children, with the combined method proving more effective. This study validates non-pharmacologic and combined approaches for ASD sleep problems. Future research should delve deeper into the mechanisms of these interventions in ASD children's sleep improvement.

Keywords ASD children · Sleep problems · Ball combination exercise · cTBS stimulation · Combined intervention

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Autism spectrum disorder (ASD) is a lifelong neurodevelopmental disorder (Hyman et al., 2020). According to published data, the prevalence of ASD among 8-years-old in the United States has increased to 1 in 36 (Maenner et al., 2021), Similarly, the prevalence among Chinese children aged 6–12 years is as high as 1 in 143 (Zhou et al., 2020). Sleep problems are one of the behavioral symptoms that plague children with ASD, and research indicates that children with ASD are more likely to have sleep problems than typically developing children, with the prevalence of sleep problems in children with ASD ranging from 50 to 80%, compared to 25–40% in typically developing children (Abel et al., 2016; Kamara & Beauchaine, 2019; Richdale, 2007). Sleep problems can be accompanied by delayed sleep, night terrors, and inadequate sleep duration that may disrupt bedtime and circadian rhythms (Fadini et al., 2015; Giannotti et al., 2008; Malow et al., 2006; Price et al., 2013). Moreover, sleep problems can adversely affect memory, attention, mood, and behavior of children with ASD (Mazurek & Petroski, 2015; Veatch et al., 2015) and exacerbate their major clinical symptoms such as social impairment and repetitive stereotyped behaviors (Deliens et al., 2015; Krakowiak et al., 2012). Therefore, how to effectively improve the sleep problems of children with ASD is critical.

Ball Combination Exercise Intervention and Sleep Problems in Children with ASD

As an effective complementary therapy, sports such as martial arts, water sports and ball games have been shown to improve sleep problems in children with ASD (Kanupka et al., 2018; Liang et al., 2024; Mische Lawson & Little, 2017; Tse et al., 2019). Among them, ball games, which have the advantages of being easy to perform, widely acceptable, and inexpensive, have gradually attracted the attention of researchers and have been implemented in the symptomatic relief of children with ASD (Cai et al., 2020; Wang et al., 2020). A growing body of research suggests that soccer improves behavioral symptoms in children with ASD (Lopez-Diaz et al., 2021). Notably, there is variability in the focus of interventions in single ball sports (basketball: upper extremity; soccer: lower extremity) (Demeco et al., 2022; Kinchington et al., 2010). It is difficult to improve the overall coordination and physical fitness of children with ASD in a comprehensive manner, and a combination training program of basketball and soccer may be one of the viable avenues. In addition, studies have shown that diverse sport type interventions have a positive impact on improving behavioral symptoms in children with ASD (Haghighi et al., 2023), suggesting an important application prospect for combined sport intervention programs. However, the effectiveness of basketball and soccer combination sports intervention in improving sleep problems in children with ASD has not yet been demonstrated, and research is needed to confirm the effectiveness of this program.

cTBS Intervention and Sleep Problems in Children with ASD

Transcranial magnetic stimulation (TMS) is another intervention that can effectively improve behavioral symptoms in children with ASD (Hameed et al., 2017; Huang et al., 2018). It is a painless, noninvasive, green treatment method that stimulates the nerves in the brain using magnetic signals that can pass through the skull without attenuation (Wischnewski & Schutter, 2015). It does not require anesthesia and can be easily combined with other treatments. Previous studies indicate that repetitive transcranial magnetic stimulation (rTMS) of the left and right dorsolateral prefrontal cortex (DLPFC) regions in patients with ASD, either at high or low frequencies, can improve their sleep problems (Ezedinma et al., 2022; Gao et al., 2022). However, rTMS interventions usually require longer treatment durations and higher costs, and some children may not tolerate rTMS stimulation. Moreover, continuous theta burst stimulation (cTBS), a specific pattern that stimulates the cortex directly via magnetic and electric pulses, exhibits a more rapid and pronounced effect on neuromodulation compared to other types of TMS methods, making it more suitable for children with ASD (Huang et al., 2005). It can improve behavioral symptoms by inhibiting activity in specific brain regions, which in turn affects synaptic plasticity (Jannati et al., 2020; Romero et al., 2022). It has been shown that cTBS is effective in improving sleep in insomnia patients (Hildebrand et al., 2024). However, few studies have evaluated whether cTBS stimulation improves sleep problems in children with ASD, and its efficacy in practical application remains to be confirmed.

Combined Interventions and Sleep Problems in Children with ASD

Combined intervention strategies have received increasing attention in the field of mental illness rehabilitation in recent years. With the inherent advantages of TMS, researchers have evaluated various combined TMS intervention methods. Dębowska et al. (2023) demonstrated that the combination of TMS and ketamine can have a positive effect on depressed patients. In Alzheimer's disease(AD), TMS combined with cognitive training has been shown to provide low-risk therapeutic benefits for patients with AD (Sabbagh et al., 2020). The integration of rTMS with treadmill training has been shown to enhance ambulatory function in individuals diagnosed with Parkinson's disease (PD) (Mak, 2013). Furthermore, in addition to the combined TMS intervention approach, recent studies have shown that physical activity combined with transcranial direct current stimulation (tDCS) can positively influence balance in patients with PD (Lazzari et al., 2019). Mahmoodifar et al. (2019) demonstrated that a combined intervention of tDCS and physical activity enhances balance in children with ASD. However, there is still a lack of evidence regarding the effects of sports combined with TMS intervention on sleep problems in children with ASD. Whether ball combination exercises combined with cTBS can effectively improve sleep problems in children with ASD requires further research.

Different Intervention Programs and Sleep Problems in Children with ASD

Combined intervention approaches may lead to more beneficial outcomes than single intervention approaches. For example, Duarte et al. (2014) demonstrated that the combination of tDCS with treadmill training improved static balance and functional performance in children with cerebral palsy better than the treadmill training alone. Yang et al. (2020) discovered that rTMS and physical exercise have a synergistic effect on synaptic and network plasticity, surpassing the effect of the intervention alone. Simultaneously, Jin et al. (2017) demonstrated that the use of rTMS in combination with exercise training can improve motor function in the paralyzed upper limb in a manner that is not possible using rTMS or exercise training alone. However, the combined intervention approach has limited application in the field of ASD, providing only some specific perspectives to refer to, and lacks evidence of its applicability to sleep problems. The combination of ball combination exercise and cTBS stimulation, an extrinsic behavioral intervention method, and an intrinsic physiological stimulation intervention technique, respectively, may have potential synergistic effects in improving sleep problems in children with ASD. Therefore, three interventions were used in this study: ball combination exercise, cTBS stimulation, and ball combination exercise combined with cTBS stimulation, to investigate whether the combined intervention can effectively improve sleep problems in children with ASD.

In summary, sleep problems in children with ASD can significantly affect their daily functioning and quality of life. Previous studies have indicated that combined exercise intervention programs exhibit important application prospects in improving behavioral symptoms in children with ASD. However, the efficacy of a ball combination exercise intervention in improving sleep problems in children with ASD remains uncertain. Moreover, although TMS positively influences sleep problems in children with ASD, cTBS efficacy in improving sleep problems in children with ASD remains unknown. Furthermore, researchers have identified a variety of effective combined TMS interventions, and there is still a lack of evidence regarding the effectiveness of ball combination exercises combined with cTBS in alleviating sleep problems in children with ASD. Combined intervention approaches may lead to more beneficial outcomes than single intervention approaches. Therefore, further research is required to determine whether ball combination exercises combined with cTBS may be more effective in improving sleep problems in children with ASD. The primary objectives of this study were as follows:

(1) Investigating the effects of a ball combination exercise intervention on sleep problems in children with ASD.
(2) Investigating the effects of cTBS stimulation on sleep problems in children with ASD.
(3) Investigating the effects of ball combination exercise combined with cTBS on sleep problems in children with ASD.
(4) Comparing the effects of ball combination exercise, cTBS stimulation, and ball combination exercise combined with cTBS on sleep problems in children with ASD.

The purpose of this study were designed to explored the effects of a combined exercise intervention, stimulation of cTBS, and a combination of interventions on sleep problems in children with ASD, and whether the combination of interventions is more effective than a single intervention, thus providing a more effective approach to addressing sleep problems in children with ASD and improving overall quality of life.

Materials and Methods

Participants

This study recruited 89 children diagnosed with ASD according to the DSM-5 criteria from a specialized educational institution using convenience sampling. Children aged 3–12 years were selected, as this age group covers a critical developmental stage for children with ASD and has a high incidence of sleep problems. The specific inclusion criteria were as follows: (1) Han Chinese population, (2) children diagnosed with moderately severe ASD according to the DSM-5, (3) aged 3–12 years old, and (4) all subjects must provide consent of their guardians and must be eligible for TMS and exercise. The exclusion criteria were as follows: (1) a clear history of head trauma with a metallic foreign body in the skull, (2) neurological and psychiatric disorders, including epilepsy and Tourette's syndrome, (3) people with pacemakers, implantable defibrillators, neurostimulators, and other implantable devices in the body, (4) taking drugs that rapidly affect the central nervous system, (5) have taken basketball lessons recently, (6) physical disability that prevents participation in sports interventions, (7) visual and auditory impairments, and (8) have received TMS therapy. They were assigned to ball combination exercise group ($n=16$), cTBS group ($n=15$), combined group ($n=17$), and control group ($n=17$), according to general data (age, gender, admission time, etc.). This allocation method facilitated the establishment of a balanced baseline across groups, thereby enabling a more controlled comparison between them. Several children with ASD did not complete some of the assessments and were therefore not included in the final statistical analysis. The final data included 45 subjects: ball combination exercise group ($n=12$), cTBS group ($n=10$), combined group ($n=12$), and control group ($n=11$) (Fig. 1).

Study Design

This study used a 4*2 mixed experimental design, with the group as the between-subjects factor and the test time point as the within-subjects factor. This quasi-experimental research was conducted in Yangzhou, China, from June to October 2023. The study protocol was registered with the Ethics Committee of Yangzhou University School of Medicine (YXYLL-2023-147) before starting the experiment, and all study procedures complied with the latest version of the declaration of Helsinki. Written informed consent was obtained from the parents of children with ASD.

Ball Combination Exercise Training Program

The ball combination exercises were performed for 45 min five times a week for 12 weeks. There were three main phases, Phase I (one week), comprised 5 classes. The primary objective of this phase was to establish norms for physical education classrooms designed specifically for children with ASD. The aim was to assist children with ASD in adapting to the structured environment of the classroom while also mitigating their sensitivity to intervention equipment. Phase II (nine weeks), comprised 45 lessons. The principal focus during this phase was to enhance the complex motor skill learning of children with ASD through instruction in fundamental movement techniques of basketball and soccer. Additionally, the aim was to foster the generalization ability of children with ASD in acquiring new behaviors, ultimately targeting the improvement of behavioral challenges and brain development disorders. Phase III

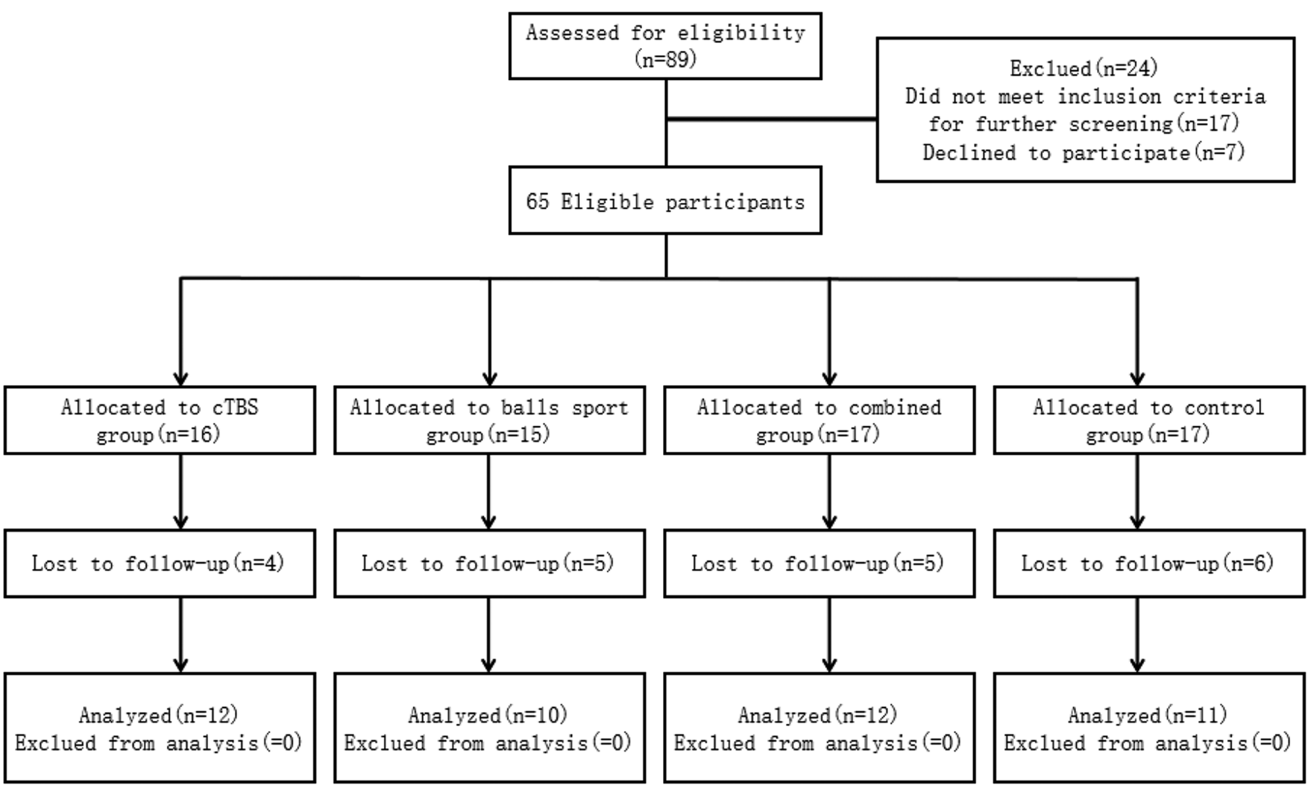

Fig. 1 Flow chart of subjects screening

(two weeks), comprised 10 lessons. The primary objective was to design and implement engaging situational activities to facilitate the flexible application of basic basketball skills by autistic children in various scenarios. The overarching objectives included promoting cooperative awareness, socialization, and the amelioration of behavioral issues and brain development disorders (Table 1).

cTBS Intervention Program

The entire treatment comprises 180 sessions over 12 weeks, with 3 sessions per day from Monday to Friday, each session lasting 40.02 s, and with a 15-minute interval between each 2 sessions. A Rapid2 transcranial magnetic stimulation therapy device (British Magstim Company) was used for treatment. This device uses an "8" shaped coil and operates in the cTBS mode. This mode involves a combination of three burst pulses transmitted at a frequency of 50 HZ every 200 ms (equivalent to 5 HZ). The cTBS mode is uninterrupted and consists of 600 pulses. The intensity, targets, and process of the cTBS intervention are listed in Table 2.

The cTBS intervention program was executed by two professionals by providing individualized stimulation. Given the clinical symptoms manifested by autistic children, cTBS

Table 1 Combined ball exercise intervention process

Practice phase	Training Drills
Phase I	Assemble the team (2 min), warm up (8 min), sports intervention (mini-basketball tactile desensitization, mini-basketball visual desensitization, physical fitness exercises (return running with the ball), sports games (high-five passing games) (33 min), relaxation (2 min).
Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (basic mini-basketball skills learning, such as passing, dribbling, and shooting), physical fitness exercises, sports games (jumping jacks + two-handed dribbling, seeing who can react faster) (33 min), relaxation (2 min).
Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (basic mini-basketball skills learning, such as passing, dribbling, and shooting), physical fitness exercises, sports games (jumping jacks + two-handed dribbling, seeing who can react faster) (33 min), relaxation (2 min).
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Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (basic mini-basketball skills learning, such as passing, dribbling, and shooting), physical fitness exercises, sports games (jumping jacks + two-handed dribbling, seeing who can react faster) (33 min), relaxation (2 min).
Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (basic technical learning of soccer, such as kicking a spot kick, alternating feet on the ball, and dribbling with the inside of the foot), physical fitness exercises, sports games, such as spot dribbling and one-foot dribbling around obstacles,) (33 min), relaxation (2 min).
Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (basic technical learning of soccer, such as kicking a spot kick, alternating feet on the ball, and dribbling with the inside of the foot), physical fitness exercises, sports games, such as spot dribbling and one-foot dribbling around obstacles) (33 min), relaxation (2 min).
Phase II	Assemble the team (2 min), warm up (8 min), sports intervention (integrate 2–9 weeks of mini-basketball and soccer skills learning) (33 min), and relaxation (2 min).
Phase III	Assemble the team (2 min), warm up (8 min), and sports intervention (combine the basic movement techniques of mini-basketball and soccer to design group sports games, such as relay throwing and catching, dribbling relay games, small circle shooting, and large circle jumping games) (33 min), relaxation (2 min).
Phase III	Assemble the team (2 min), warm up (8 min), and sports intervention (combine the basic movement techniques of mini-basketball and soccer to design group sports games, such as relay throwing and catching, dribbling relay games, small circle shooting, and large circle jumping games) (33 min), relaxation (2 min).

stimulation might be challenging to implement. Therefore, the presence of at least one guardian during cTBS is mandatory to ensure the successful completion of the intervention. If the experiment is interrupted, the stimulation will restart once the next child has completed the session. A professional teacher was present in each session to keep track of attendance. Children must inform the teacher at least one day in advance if they need a break. The number of consecutive days off cannot exceed three, and the total number of leave requests cannot surpass seven days to guarantee the continuity of the stimulation.

Combined Intervention Program

Combined intervention five times a week for 12 weeks, the specific intervention parameters of the ball combination exercise intervention and cTBS were consistent with those described in the previous section. To prevent the intensity of the cTBS stimulation treatment and the exercise intervention from overlapping, the cTBS stimulation was scheduled to be implemented from 9:00 to 11:00 a.m. every Monday through Friday; the ball combination exercise intervention was scheduled to be implemented from 4:00 to 5:00 p.m. every Monday through Friday.

Control Group Intervention

In this study, the control group received a series of rehabilitation sessions provided by the agency based on applied behavior analysis (ABA) theory, including early intensive behavioral intervention (EIBI) and discrete trial training (DTT), among others, with each type of intervention session being 45 min long and occurring five times per week.

Behavioral Measurement

Demographic information (age and gender) was collected at the beginning. Age (Wiggs & Stores, 2007), parental stress (Cotton & Richdale, 2006; Tobing & Glenwick, 2002), repetitive stereotyped behaviors (Tsai et al., 2019), executive functioning (Tsai et al., 2019), and the severity of the disease (Mayes & Calhoun, 2009) affect the sleep problems in children with ASD. Therefore, the Childhood Autism Rating Scale (CARS), Parent Stress Index/Short Form (PSI/SF), Repetitive Stereotyped Behavior Scale-Revised

Table 2 cTBS intervention process

Experimental equipment	Rapid2 transcranial magnetic stimulation therapy instrument produced by British company Magstim was selected	Select the “8” type coil
Positioning mode	1. Prepare	The child sits on the treatment chair, keeping the hands completely relaxed, and the skin surface of the test site is cleaned with alcohol to remove grease and reduce interference.
	2. Treatment target positioning	The child wears a positioning cap, and the method used for positioning of M1 and DLPFC targets is based on the standard “5-centimeter rule” of electroencephalography. The intersection of the nasion-inion line and the bilateral preauricular line is defined as Cz. Moving 5 centimeters to the left along the preauricular line from Cz locates the left primary motor cortex (M1) area, and moving 5 centimeters anteriorly from M1 defines the left dorsolateral prefrontal cortex (DLPFC) of the left hemisphere. Target regions: left and right DLPFC.
	3. Visual measurement of resting motor threshold (MT)	The participants placed their palms upward on their knees in a relaxed state, and the opposite cortex’s corresponding M1 area was stimulated by the TMS stimulation coil to adjust the intensity of the motor threshold (MT), which is the minimum percentage of intensity that can cause contraction of finger muscles, known as the resting motor threshold (MT). The stimulation intensity of AMT is approximately 40–50% of RMT, followed by stimulation of the dorsolateral area. .
Treatment programs	cTBS stimulation parameters	Stimulation is conducted at an intensity of 80% of RMT intensity, with an intra-frequency of 50 Hz and an inter-frequency of 5 Hz, delivering 600 pulses per treatment session, completing 3 treatment sessions; with a total duration of 40 s.
Treatment time	The duration of intervention was 12 weeks	The entire treatment comprises 180 sessions over 12 weeks, with 3 sessions per day from Monday to Friday, with a 15-minute interval between each 2 sessions.

(RBS-R), and the revised version of Executive Functioning Inventory (CHEXI) were used to evaluate the corresponding indicators to balance the confounding variables mentioned above in the experimental group. The CSHQ scale was used to evaluate sleep problems.

The CARS scale was used to determine the severity of ASD and consisted of 15 items (14 items to assess autistic behaviors and one item to assess the overall impression of ASD), with each item scored on a scale of 1 to 4 (higher scores indicate more severe impairment). A score above 30 is considered a sign of autism (mild to moderate autism: 30-36.5; severe autism: 37–60) (Lu Jian-ping, 2004; Schopler et al., 1980).

The PSI/SF was designed to measure the degree of parental stress felt by the individual and contains three subscales: parental distress, parent-child interaction disorder, and difficult child. It is applicable to the parents of children aged one month to 12 years. The total number of questions is 36, and the scoring is based on the Likert scale (1 = strongly disagree, 5 = strongly agree), with higher scores indicating severe parenting stress (Luo et al., 2019).

The RBS-R was a valid tool for assessing stereotypic behaviors in children with ASD. It was compiled by Bodfish and others in 1999 and includes six fundamental parts: stereotyped behaviors (six items), self-injurious behaviors (eight items), obsessive-compulsive behaviors (eight items), ritualistic behaviors (six items), fixation behaviors (11 items), and restrictive behaviors (four items), with a total of 43 entries. The scale scoring criteria are as follows: 3 points for severe behavioral problems, 2 points for moderate behavioral problems, 1 point for mild behavioral problems, and 0 points for no behavioral problems. Higher scores represent severe stereotypic behavior problems (Bodfish et al., 2000; Luo et al., 2022).

The revised version of CHEXI consists of 24 items (1 = completely inconsistent, 5 = completely consistent) in three dimensions: regulation, inhibition, and working memory. The total score is 120, with higher scores representing poorer executive functioning (Thorell & Nyberg, 2008; WEI Wei, 2018).

The CSHQ was used to evaluate sleep problems in children with ASD. The CSHQ is a parent-scored questionnaire that assesses the frequency of eight behaviors (bedtime resistance, delayed sleep onset, sleep duration, sleep anxiety, night wakings, sleep anomalies, sleep apnea, and daytime somnolence) that are associated with sleep difficulties in children. A total score of more than 41 indicates a sleep problem (Shui et al., 2021; Tan et al., 2018).

Statistical Analysis

The data were analyzed using SPSS 27.0.1 One-way ANOVA and chi-square tests were used to test for homogeneity of the demographics (age and gender) of the 45 participants, as well as the subjects' scores on the CARS, PSI/SF, RBS-R, and revised version of CHEXI as covariates if there was a significant effect. Repeated measures ANOVA was used to test whether there were significant changes in sleep problems before and after the intervention in the four groups of children with ASD. Moreover, if the time-group interaction effect was significant, simple effect analyses were conducted using the Bonferroni correction method. If there was an improvement in multiple groups for the same dimension, LSD multiple comparisons were used to determine whether there was a significant difference between the effect of the combined intervention and the single intervention. Data were analyzed using descriptive statistics: mean ± standard deviation (M ± SD).

Results

Participant Characteristics

The homogeneity analyses revealed that gender ($\chi^2 = 6.354$, $p = 0.57$), age ($F_{(3,41)} = 1.681$, $p = 0.186$), symptomatic severity ($F_{(3,41)} = 0.446$, $p = 0.722$), parenting stress ($F_{(3,41)} = 2.006$, $p = 0.128$), repetitive stereotypic behavior ($F_{(3,41)} = 1.187$, $p = 0.326$), and executive functioning (working memory $F_{(3,41)} = 0.468$, $p = 0.706$/inhibition $F_{(3,41)} = 0.887$, $p = 0.456$) exhibited no statistically significant difference between groups (Table 3).

Effects of Different Interventions on Sleep Problems in Children with ASD

Repeated-measures ANOVA showed that the time*group interaction effect was not significant on the sub-dimensions of the CSHQ scale, including bedtime resistance ($F_{(3,41)} = 2.535$, $p = 0.070$, partial$\eta^2 = 0.156$), sleep duration ($F_{(3,41)} = 1.446$, $p = 0.243$, partial$\eta^2 = 0.096$), night wakings ($F_{(3,41)} = 2.126$, $p = 0.112$, partial$\eta^2 = 0.135$), parasomnias ($F_{(3,41)} = 0.999$, $p = 0.403$, partial$\eta^2 = 0.068$), sleep-disordered breathing ($F_{(3,41)} = 1.243$, $p = 0.306$, partial$\eta^2 = 0.083$), and daytime sleepiness ($F_{(3,41)} = 1.539$, $p = 0.219$, partial$\eta^2 = 0.101$). However, the time*group interaction effect was significant for the three dimensions of the CSHQ scale, total score ($F_{(3,41)} = 4.618$, $p = 0.007$, partial$\eta^2 = 0.253$), sleep onset delay ($F_{(3,41)} = 2.970$, $p = 0.043$, partial$\eta^2 = 0.179$), and sleep anxiety ($F_{(3,41)} = 11.961$, $p < 0.001$, partial$\eta^2 = 0.467$) (Fig. 2). These results

Table 3 Baseline characteristics of participants (M ± SD)

Measure	cTBS group	Ball sports group	Combined group	Control group	F	P
N	10	12	12	11	-	-
Gender(boys/girls)	8/2	10/2	7/5	11/0	-	0. 57
Age(years)	8.20 ± 1. 40	7. 33 ± 2. 39	7. 83 ± 2. 08	9. 09 ± 1. 58	1. 681	0. 186
CARS[a]	39. 60 ± 6. 64	37. 08 ± 7. 59	37. 08 ± 4. 64	36. 36 ± 8. 05	0. 446	0. 722
PSI/SF[b]	104. 60 ± 15. 39	101. 50 ± 20. 76	118. 33 ± 17. 87	107. 64 ± 16. 07	2. 006	0. 128
RBS-R[c]	35. 20 ± 19. 60	26. 42 ± 10. 32	23. 08 ± 17. 35	27. 55 ± 13. 07	1. 187	0. 326
CHEXI[d] (working memory)	47. 50 ± 7. 69	50. 50 ± 5. 32	49. 25 ± 8. 52	46. 73 ± 11. 17	0. 468	0. 706
CHEXI(inhibition)	37. 60 ± 6. 92	42. 50 ± 5. 40	38. 50 ± 8. 27	41. 18 ± 10. 92	0. 887	0. 456

Note a CARS: Childhood Autism Rating Scale. b PSI/SF: Parenting Stress Scale. c RBS-R: Repetitive Stereotyped Behavior Scale. d CHEXI: Executive Functioning Inventor

indicate that the total score of the CSHQ scale, as well as its sub-dimensions of sleep onset latency and sleep anxiety, exhibited a significant difference between the different interventions in terms of the time versus group interaction effect. Therefore, a post-hoc simple effects analysis was conducted.

Effects of Different Interventions on CSHQ Scale Total Scores in Children with ASD

The total CSHQ scale scores of the four groups were homogeneous in the pre-test scores ($F_{(3,41)} = 1.189$, $p = 0.326$) and borderline significant in the posttest scores ($F_{(3,41)} = 2.794$, $p = 0.052$). Post-hoc simple effects analyses revealed that after 12 weeks of intervention, the control group ($p = 0.996$) exhibited no significant difference in posttest scores compared to baseline. The cTBS group ($p = 0.002$) and the combined group ($p < 0.001$) showed significant decreases in post-test scores compared to baseline, whereas the combined ball sports group ($p = 0.434$) the difference was not statistically significant compared to the baseline assessment, (Fig. 3A). The results indicated that the combined and cTBS groups were effective in reducing the CSHQ scale total score, and the combined ball sports group exhibited no statistically significant difference.

The Effect of Different Interventions on Sleep-onset Delay in Children with ASD

There was no significant difference between the four groups in the pre-test scores for sleep-onset delay ($F_{(3,41)} = 0.491$, $p = 0.689$). However, a significant difference was observed between the four groups in the post-test scores ($F_{(3,41)} = 2.949$, $p = 0.044$). Post-hoc simple effects analyses revealed that, after 12 weeks of intervention, the control group ($p = 0.020$) exhibited a significant difference in post-test scores compared to baseline scores. In contrast, the ball combination exercise ($p = 1.000$), the cTBS ($p = 0.530$), and the combined ($p = 0.090$) groups exhibited no significant differences in post-test scores compared to baseline scores. It is noteworthy that the difference in the control group was due to the higher posttest score than the baseline (Fig. 3B). Therefore, the results indicated that there was no statistically significant difference in the effectiveness of the three interventions for sleep-onset delay on children with ASD.

Effects of Different Interventions on Sleep Anxiety in Children with ASD

There was no significant difference between the four groups in the pre-test scores for sleep anxiety ($F_{(3,41)} = 0.890$, $p = 0.455$). However, a significant difference was observed between the four groups in the post-test scores ($F_{(3,41)} = 10.247$, $p < 0.001$). Further post-hoc simple effects analyses revealed that the control group ($p = 0.024$) exhibited a significant difference in posttest scores compared to baseline scores after 12 weeks of intervention. In contrast, the ball combination exercise ($p = 0.002$) and the combined ($p < 0.001$) groups exhibited significant differences in post-test scores compared to baseline scores. However, the cTBS group ($p = 0.507$) revealed no significant difference in post-test scores compared to the baseline scores. However, it was noteworthy that the difference in the control group was due to a higher posttest score than the baseline (Fig. 3C). These findings indicated that the ball combination exercise and combined groups effectively improved sleep anxiety in children with ASD, whereas, there was no statistically significant difference in the improvement of sleep anxiety in children with ASD in the cTBS group.

Comparison of the Effectiveness of Different Interventions on Sleep Problems in Children with ASD

These results indicated that after 12 weeks of intervention, the CSHQ scale total score and its sub-dimensions, sleep-onset delay and sleep anxiety, improved in multiple groups. Therefore, the differences between the posttest and the

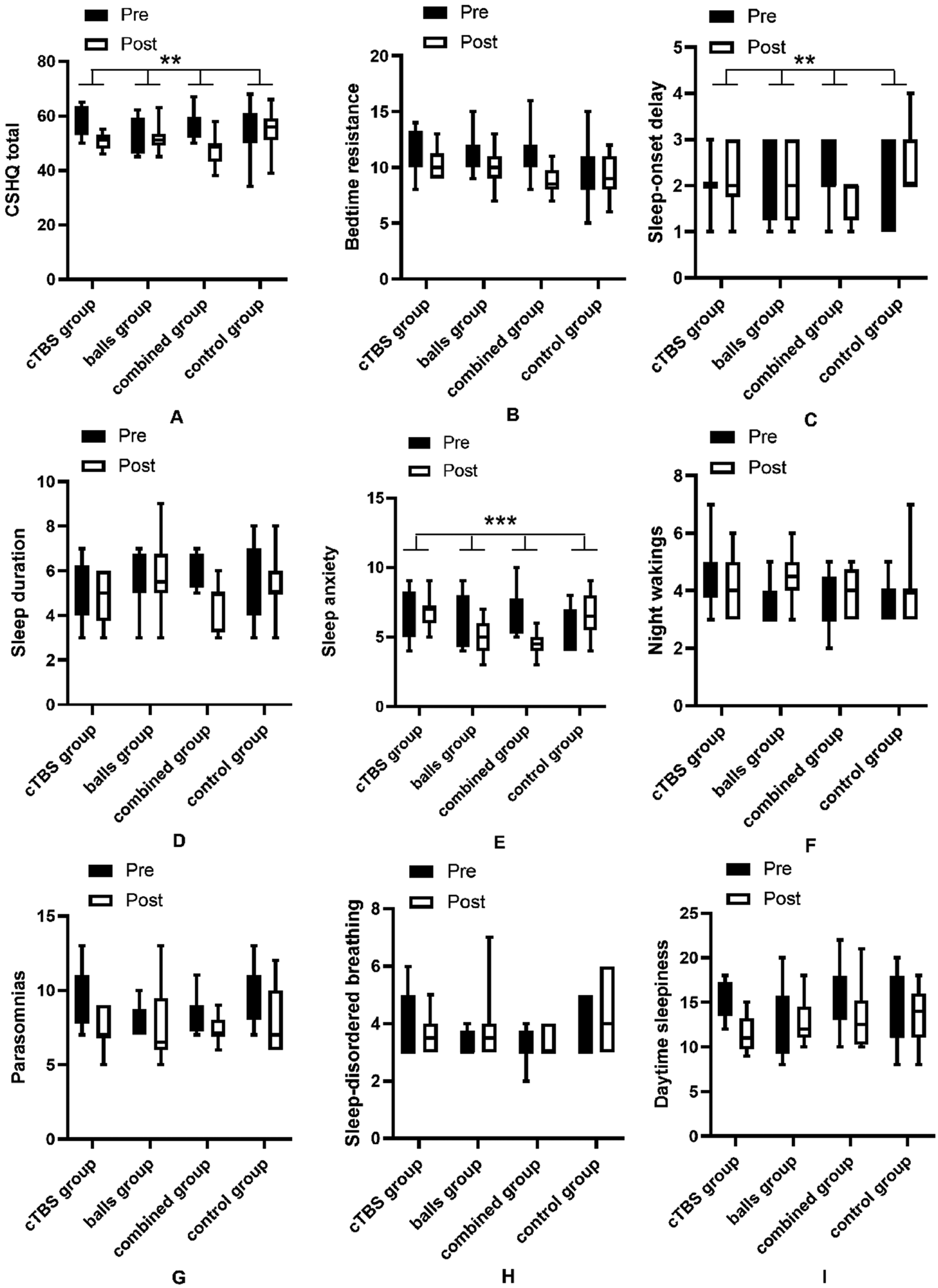

Fig. 2 Time*group interaction effect plots for each dimension of the CHSQ scale. * represent a significant time* group interaction effect, ** indicates $p < 0.05$, *** indicates $p < 0.001$

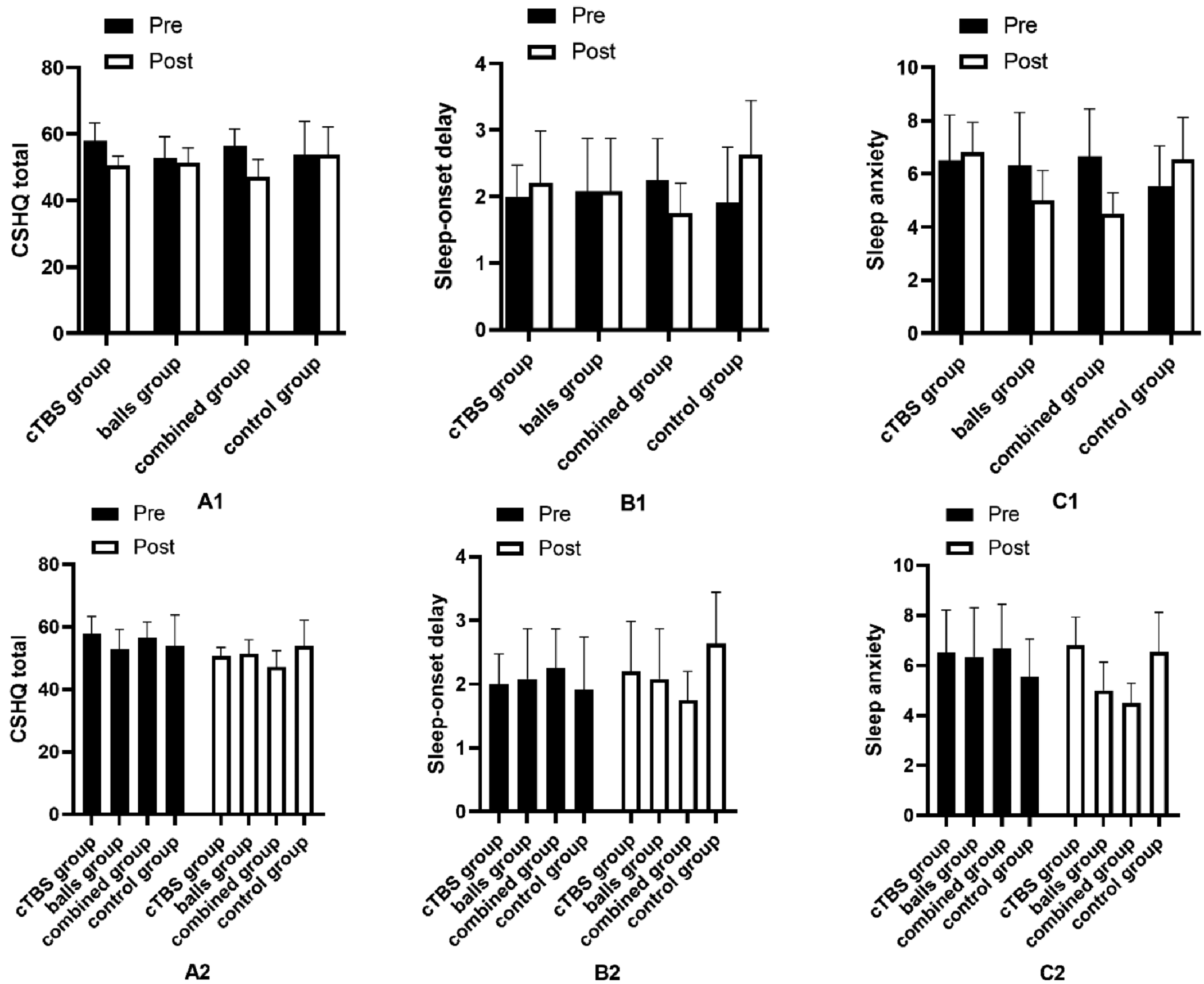

Fig. 3 Pre- and post-intervention results for each group

pre-test were analyzed. The results revealed significant differences in the total CSHQ score ($F_{(3,41)}=4.681, p=0.007$), sleep-onset delay ($F_{(3,41)}=2.970, p=0.043$), and sleep anxiety ($F_{(3,41)}=11.961, p<0.001$). LSD post-hoc comparisons were used to analyze the differences between the effects of the combined intervention and single intervention.

The results of the LSD post-hoc comparative analysis revealed no significant difference in the intervention effect between the combined and cTBS groups in terms of the total CSHQ scale score ($p=0.512$), whereas a significant difference was observed in the intervention effect between the combined and ball combination exercises groups ($p=0.011$). There was no significant difference in the intervention effect on sleep-onset delay between the combined group and both the cTBS ($p=0.109$) and ball combination exercise groups ($p=0.226$). In terms of sleep anxiety, no significant difference was observed between the combined and ball combination exercise groups ($p=0.158$), while there was a significant difference in the cTBS group ($p<0.001$) (Table 4). These results indicate that the combined group exhibited better intervention effects than the single interventions in the CSHQ scale total score and sub-dimension sleep anxiety, while there was a tendency to exhibit better effects than single interventions in sleep-onset latency. However, there was no significant difference.

Discussion

This study aimed to evaluate the effects of a 12-week ball combination exercise, cTBS, and combined intervention on sleep problems in children with ASD and to compare whether the combined intervention was more effective than a single intervention. The results demonstrated that the ball

Table 4 Multiple comparative analysis

Measure	cTBS group	Ball group	Combined group	Conrtol group	F	*P*
CSHQ total	–7. 20 ± 5. 18	–1. 58 ± 8. 59*	–9. 17 ± 5. 17	0. 09 ± 7. 94*	4. 618	0. 007
Sleep-onset delay	0. 02 ± 0. 92	0. 00 ± 0. 85	–0. 50 ± 0. 80	0. 73 ± 1. 35*	2. 970	0. 043
Sleep anxiety	0. 30 ± 1. 25*	–1. 33 ± 1. 92	–2. 17 ± 1. 27	1. 00 ± 1. 00*	11. 961	< 0. 001

Note * indicates comparison with the combined group, $p < 0.05$. All comparisons were made using the LSD multiple comparison method

combination exercise intervention could effectively improve sleep anxiety in children with ASD, cTBS intervention could improve the overall sleep problems in these children, and the combined intervention significantly improved the overall sleep problems and sleep anxiety in children with ASD. There was no statistically significant difference between the three groups of interventions on sleep-onset delay in children with ASD. However, the combined intervention was more effective in improving sleep problems in children with ASD than the single intervention.

First, we investigated the effect of ball combination exercises on sleep problems in children with ASD. The results of this study demonstrated that ball combination exercises can be effective in reducing sleep problems in children with ASD to some extent. This result was consistent with our first hypothesis that ball combination exercises were effective in improving sleep problems in children with ASD. However, this effect is more likely to be reflected in the reduction of sleep anxiety rather than the improvement of overall sleep problems. These results differed from those of similar previous studies. For example, a study by Tse et al. (2019) demonstrated that a 12-week basketball intervention effectively improved sleep efficiency and duration and reduced the number of night awakenings in children with ASD. Few studies have investigated the mechanisms through which ball combination exercises improve sleep anxiety in children with ASD. Sleep anxiety is defined as anxiety and worry that occurs before going to sleep or during nighttime sleep and may manifest as symptoms such as difficulty falling asleep, night waking, and poor sleep quality. Sleep anxiety is closely related to anxiety and is a symptom of anxiety disorders. Therefore, we hypothesized that the mechanism by which ball combination exercise improved sleep anxiety in children with ASD may be similar to that of anxiety disorders. Numerous studies have shown that exercise is effective in reducing anxiety-producing hormones (e.g., cortisol and glucocorticoids) as well as facilitating the body's release of neurotransmitters (e.g., endorphins, dopamine, serotonin, etc.), thereby ameliorating anxiety (Lin & Kuo, 2013; Mahalakshmi et al., 2020). These physiological mechanisms may help reduce sleep anxiety in children with ASD. Additionally, exercise was a way to relieve stress and anxiety (Chi & Wang, 2022), and participating in sports may allow children with ASD to distract themselves, reduce anxiety, and improve self-control. This psychological mechanism could help alleviate sleep anxiety. This study employed a moderate-intensity exercise intervention dosage. Research has indicated that moderate-intensity exercise interventions are more effective in reducing sleep anxiety and improving sleep compared to low-intensity or high-intensity exercises (Kredlow et al., 2015). Therefore, we inferred that moderate-intensity combined ball exercises may also be a reason for reducing sleep problems in children with ASD.

Furthermore, we investigated the effects of cTBS on sleep problems improvement in children with ASD. The results demonstrated that cTBS positively influenced sleep problems in children with ASD. This result was consistent with our second hypothesis, which was that cTBS had a significant effect on the improvement of overall sleep problems in children with ASD. Few studies have evaluated the mechanisms through which cTBS improves sleep problems in children with ASD. However, it has been suggested that sleep problems in children with ASD are related to neurotransmitters, including 5-hydroxytryptamine (5-HT) and gamma-aminobutyric acid (GABA), dopamine, glutamate, and melatonin (Chung et al., 2017; Kang et al., 2019; Li, 2020). Moreover, the DLPFC region plays an important role in sleep regulation. Several studies have shown that stimulation of the right and left dorsolateral prefrontal regions using rTMS increases the production of dopamine, 5-HT, and GABA, leading to reduced sleep problems (Morgan et al., 2012; Mostafavi et al., 2020). The cTBS, as a form of rTMS, can produce similar biological effects and can effectively improve the overall sleep problems in children with ASD by stimulating the left and right DLPFC regions (Gao et al., 2022). Therefore, the current study hypothesized that, based on the mechanism of rTMS to improve sleep problems, cTBS might improve sleep problems in children with ASD by affecting neuronal activity in specific brain regions and regulating the release of neurotransmitters, thereby affecting the neural circuits of sleep regulation. The application of cTBS may influence synaptic plasticity within the brain, thereby modulating the connectivity and functionality of neural networks associated with sleep-related regions. However, further research is required to confirm its specific mechanism of action.

We investigated the effects of combining ball combination exercise with cTBS intervention on sleep problems in children with ASD and assessed whether the combined intervention was more effective than the intervention alone.

The results demonstrated that the combined intervention improved the CSHQ total score and its subdimension of sleep anxiety. This result was consistent with our third hypothesis, that combined intervention can improve sleep problems in children with ASD. Furthermore, we investigated whether the combined intervention was superior to the single intervention, and the results revealed that the combined intervention outperformed the different single interventions in terms of the CSHQ total score and the subdimension sleep anxiety. Moreover, there was a tendency for the combined intervention to be better than the single interventions in terms of delay in falling asleep. However, the difference was not statistically significant. Previous studies have not examined the effect of a combination of interventions on sleep problems. Therefore, we were only able to compare results using similar interventions but measuring different dependent variables. The results of our study were similar to those of previous studies, both demonstrating the superiority of the combined intervention (Byrne et al., 2014; Mahmoodifar & Sotoodeh, 2019). Research on the effects of the combined intervention of ball combination exercises and cTBS on the sleep problems of children with ASD and its superiority to the single intervention is limited, and its precise mechanism of action remains unknown. The current study hypothesized that the combined intervention might effectively improve sleep problems in children with ASD compared to a single intervention. Furthermore, the underlying mechanisms by which these sleep problems are addressed in children with ASD were explored. Firstly, both exercise and cTBS may alleviate mood and anxiety (Li et al., 2022; Mahalakshmi et al., 2020). Since children with ASD frequently experience sleep problems and anxiety, the combined effect of exercise and cTBS may improve their sleep problems by alleviating anxiety and mood problems. Secondly combined interventions may provide a more comprehensive and integrated intervention effect because cTBS and ball combination exercises act on the brain and body's motor system, respectively, thereby improving sleep problems in children with ASD on multiple levels. Thirdly, exercise and cTBS modulate neuroplasticity and neurotransmitter release, which was closely related to sleep. Therefore, combining exercise with cTBS may exhibit a superimposed and synergistic effect on improving sleep problems in children with ASD, which is superior to a single intervention. The mechanisms hypothesized in this study are not well-documented and require further research. However, based on the hypothesized mechanisms described above, it would be meaningful to further explore whether anxiety might be a moderating variable for improving sleep in children with ASD in future studies.

The results of this study demonstrated that there was no significant time*group interaction effect for any of the six subdimensions of the CSHQ scale: bedtime resistance, sleep duration, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness. It was not excluded that these three interventions did not improve the above dimensions, and it is certainly possible that this is due to some of the following limitations: (1) Due to various reasons, including limitations in research resources and difficulties in screening and recruiting participants, we collected data from a small number of subjects. Therefore, the reliability and generalizability of the results may have been affected to some extent. (2) The CSHQ scale used in this study may be highly subjective, thereby introducing some degree of bias into the results. (3) This was not possible due to the specificity of autism and the limitation of research resources, which may affect the results of the study. Therefore, further research is required to investigate the specific mechanisms through which ball exercises, cTBS, as well as combined interventions, improve sleep problems in children with ASD. The sample size should be increased in future studies. A larger sample size could help reduce the impact of individual variability in children with ASD on the results of the study, thereby obtaining more conclusive results. Moreover, the use of more objective measures and rigorous randomization of groups is recommended to increase the objectivity of the results and reduce the influence of potential factors other than the intervention on the results.

Conclusion

Our study aimed to investigate the effects of ball combination exercise, cTBS stimulation, and combined intervention on sleep problems in children with ASD and whether the combined intervention effect was more effective than the single intervention. The results revealed that Ball combination exercise, cTBS, and Combined intervention ameliorated sleep problems in children with ASD to some extent, whereas there was no significant difference in the combined intervention effect. However, it tended to be more effective than a single intervention. Moreover, the results confirmed the feasibility of non-pharmacological treatments and combined interventions in improving sleep problems among children with ASD. Further research is required to investigate the specific mechanisms of ball combination exercise, cTBS, and combined intervention in improving sleep problems in children with ASD.

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Data Availability The data presented in this study are available on request from the corresponding author.

Declarations

Institutional Review Board Statement The study was conducted in Yangzhou, China, from June to October 2023 and was approved by the Ethics and Human Protection Committee of Yangzhou University Hospital. The study protocol was registered with the Ethics Committee of YangzhouUniversity School of Medicine (YXYLL-2023-147) before starting the experiment, and all study procedures complied with the latest version of the Declaration of Helsinki.

Informed Consent Informed consent was obtained from all subjects involved in the study.

Competing Interest All authors declare that they have no conflicts of interest to report regarding the present study.

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