

Network Meta-Analysis of Physical Activity Interventions On Cognitive Functions In Children With Autism Spectrum Disorder: A Protocol of Randomized Controlled Trials

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Protocol

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Abstract

Background: Autism spectrum disorder (ASD) symptoms are usually observed by the age of 2 years. However, the mechanism of ASD is still encompassed in a black box and no identified cure exists. Based on accumulating evidence, intensive early treatment such as physical activity or exercise can make a significant difference in the cognitive control and development in children with ASD. This study aims to update the knowledge on extant literature and explore the efficacy of physical activity intervention strategies (PAIS) on cognitive functions in children with ASD.

Methods: A systematic review and network meta-analysis will be conducted following the preferred reporting items for systematic review and meta-analysis protocols for Network Meta-Analyses (PRISMA-NMA). Nine bibliographic databases (APA PsycInfo, Cochrane Central Register of Controlled Trials, Dimensions, ERIC, MEDLINE Complete, PubMed, Scopus, SPORTDiscus, Web of Science) will be systematically searched to screen eligible articles based on a series of inclusion and exclusion criteria. A study will be considered for inclusion if the study: (a) is not classified as a systematic review with or without meta-analysis; (b) is published from inception to date; (c) includes children aged 0-12 years with ASD; (d) quantitatively measures cognitive outcomes; (e) treatment includes at least one PAIS. The internal validity and quality of evidence will be evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. Statistical analyses will be produced in RStudio 3.6 with the BUGSnet package and Comprehensive Meta-Analysis 3.3.

Discussion: This study will provide an updated review of the extant literature by using an appropriate network meta-analytic model and address the questions regarding efficacy of PAIS that significantly impact cognitive functions in children with ASD with implications for future decision making.

Systematic review registration: PROSPERO CRD42021279054.

1. Background

Autism Spectrum Disorder (ASD) is a lifelong developmental disability. Individuals with ASD commonly present symptoms of insufficient social interaction and communication, and repeated and restricted behavior patterns that have a negative impact on daily functions. The lack of adapting, planning, and organizing skills has a negative influence on personal, physical, mental, academic, vocational, and social domains. The onset of ASD typically presents during the age of 1-2 years, while some symptoms may be observed during the first year after birth [1]. Some categories of ASD have been specified such as Asperger syndrome, childhood disintegrative disorder, and pervasive developmental disorder [2]. World Health Organization (WHO) indicated that children with ASD exhibit deficits in cognitive functions, characterized by social impairment, abnormalities, and repetitive stereotypic behavior [3,4]. Approximately 17% of children were diagnosed with a range of complex neurodevelopmental disabilities between 3-17 years old; 1 in 54 children was diagnosed with ASD [5,6]. The diagnosis rate in children has continuously increased, moving from 1.1% to 2.5% in the past decades [7,8]. While the prevalence of diagnoses is increasing, many evidence-based interventions are still in developmental stages. Specifically, the effectiveness of physical activity interventions in children with ASD are not yet fully understood.

Childhood is a critical period of neurodevelopment, especially for children's memory, attention, creativity, motor skill, and executive functions [9]. ASD is a complex neurodevelopmental disorder and the prognostic of ASD is impacted by environmental, genetic, and physiological factors [1]. Several neurotransmitters including Brain Derived Neurotrophic Factors (BDNF) which contribute to brain development demonstrate correlations with ASD and other neurodevelopmental impairments [10]. The connectivity of the frontal cortex and prefrontal cortex with other parts of the brain was found to be related to ASD behavioral symptoms [11–13]. Atypical development of the ability to recognize and attribute mental states were found with high risk in the autism population [14]. Language and joint attention for social functioning and cognitive control behaviors have been shown to be linked to changes in early maturation of the brain [9,14–16]. The imbalanced process of integrating information such as contextual or sensory perception might be related to ASD symptoms [17].

Cognitive function is manifested as the ability to process thoughts, such as learning and solving problems [18]. Cognitive function has been categorized into executive function (EF) and non-executive function(non-EF). EF presents an individual's adapting skills and ability to conduct goal-oriented meaningful actions [19]. Non-EF has also been identified, including complex attention, learning and memory, visual function, language, and social aspects [1]. Solomon et al. [20] indicted EF hypothesis was an influential cognitive theory of ASD which "proposes that deficits in planning, inhibitory control, attentional set shifting and working memory are central to the disorder" (p. 239). Social and communication skills are part of the characteristic of cognitive function, which individuals with ASD usually lack, and are also impacted by the age and development window [21]. For the population of children, cognitive function is developing along with the human brain [22]. As an example of pro-neurogenic modulators, exercises increase the level of BDNF, Endocannabinoids, and microbiota diversity, which leads to hippocampal neurogenesis and brings long-term changes in cognitive function [23,24]. Various interventions have been studied for children with ASD, such as music therapy, which showed evidence of improving social interaction in preschool children with ASD [14]. Physical activity also is an effective approach to improve cardiovascular fitness and cognitive function in children and adolescents [25].

Evidence shows training positively impacts adult cognitive function and its offspring, which is encouraging for investigations on physical activity's effect on youth [26]. In the current study, we expect to employ statistical methodology to explore the effectiveness of different types of physical activity interventions strategies (PAIS) on cognitive function in children. We believe this study is a promising starting point to guide future health-related practice in the youth population. Closely related to the release of dopamine in the human body, physical activities have also been proved to be emotionally supportive for children, such as by lowering levels of anxiety or depression [27]. Promising evidence has been accumulating of physical activity leading to improvements in cognition, including both academic and behavioral performances in children with ASD [3,28–31]. Liang and colleagues [32] reported chronic exercise interventions are beneficial on overall EFs, especially cognitive flexibility and inhibitory control in children and adolescents with ASD. Several pieces of research indicated a significant increase in social engagement after children with ASD participated in physical activities, especially when group activities were provided [33–35]. Physical activity also proved beneficial to reduce stereotypic behaviors within the population of children with ASD [36].

In prior research, various types of PAIS were investigated individually or through narrow groups. In the current study, a full range of PAIS will be examined. PAIS have included aerobic exercise, mindfulness practices, school physical education programs, and Montessori methods [32,37]. Fang and colleagues [38] concluded favorable results on exergaming interventions on cognitive functions but synthesis results from a follow up meta-analysis are lacking. Horseback riding was found to be beneficial to children with ASD in cognitive functioning, social interaction, and sensory processing improvement [33,35]. Some other physical activities, such as yoga and dance, were also introduced as intervention for children with ASD with positive outcomes in behavioral functioning [39]. Medical/clinical conditions of participants, as well as the session frequencies and lengths of the interventions need more research to be conducted. Hence, there are urgent needs for researchers to explicitly examine what type of PAIS is the most effective to benefit children with ASD.

Systematic review and pairwise meta-analysis are unable to compare treatment effects across interventions and indirect effects. Therefore, the network meta-analysis (NMA) is proposed as a novel analysis technique in the field of physical activity and health promotion to fill the gap and satisfy the urgent need [40]. To the best of our knowledge, the current study will be the first NMA applied to systematically review and analyze the efficacy of PAIS on cognitive functions in children with ASD. Therefore, our expectation is to explore PAIS based on selected direct/indirect head-to-head trials to suggest important considerations for decision making in the field of pediatric health promotion.

2. Mini Review

In order to gain a comprehensive overview on the existing literature as well as justify the necessity of conducting a network meta-analysis on PAIS for children and adolescents with ASD, we conducted a mini review based on the systematic reviews and meta-analyses in the current literature. PubMed, APA PsycInfo, SPORTDiscus, Web of Science, Cochrane Central Register of Controlled Trials, Education Resources Information Center (ERIC), SocINDEX, MEDLINE Complete, and Dimensions were applied for the literature search. The keywords used for the literature search involved four domains: intervention mode, cognitive performance, population, and autism. Combinations of the keywords regarding each domain were “physical activity OR PA OR exercise OR sport*” AND “cognitive function OR cognition OR executive function OR inhibitory control OR memory OR communication OR stereotyp* behavior*” AND “children OR kid* OR teenager OR students” AND “autism spectrum disorder OR ASD”. Eligible studies should meet the following criteria: (1) systematic review or meta-analysis written in English and published between 2001 and 2021; (2) children or adolescents with ASD included; (3) PAIS reviewed; and (4) effects of PAIS on cognitive functions examined.

2.1. Literature Search

Two authors (LL and AW) independently conducted the search and screening process. The initial search resulted in 424 studies. After the removal of 362 repetitive and irrelevant items, 62 items were left for the next phase of screening. There were 31 articles excluded based on abstract examination, leading to 31 articles for full-text review. The final step of screening removed 12 articles due to the following reasons: no cognitive outcome measured ($n = 10$), and populations other than children or adolescents ($n = 2$). Therefore, a total of

19 systematic reviews with or without meta-analysis met the inclusion criteria. The process of study selection was presented in Figure 1.

2.2. Characteristics of the Included Studies

The median publication year of these studies was 2019 (Range: 2008 – 2021), which implies a rapid increase in the number of published review papers on the relevant topic in recent years. The number of studies included in each of the reviews ranged from seven to 41. A variety of types of the included review papers was identified such as systematic review ($n = 9$), meta-analysis ($n = 7$), and systematic review with meta-analysis ($n = 3$). In addition to the individuals with ASD, the included review studies also examined subjects with cognitive impairment due to one of the following reasons: attention deficit hyperactivity disorder (ADHD), cerebral palsy (CP), developmental delay (DD), developmental coordination disorder (DCD), and Down syndrome (DS). The common symptoms observed in individuals with these disorders are difficulties in attention, task performance, and social interaction [1]. Most studies focused on children and adolescents [14,32,34,41–51], while Fang et al. [38], Fragala-Pinkham et al. [52], Healy et al. [53], Lang et al. [54], Ruggeri et al. [55], and Sowa and Meulenbroek [56] conducted studies which involved both children and adult participants. Experimental groups were compared with the counterparts in active behavioral control, waiting list control, or standard care groups. Study characteristics were illustrated in Table 1.

The PAIS applied in the intervention arms typically consisted of two or three 30- to 60-minute sessions per week over 8-16 weeks. Three studies declared only included randomized controlled trials (RCTs) [14,47,50] and others partially included quasi-experimental designs with controlled trials [32,41–44,48,49,51,53–56], cohort [34], pre- and post-tests, and case-control studies [38,45,52], and descriptive [46]. One study lacked a clear definition of the age range of children and a discussion of risk of bias in the studies [41]. The interventions applied to the included studies were conducted through various types of physical activities. Physical exercise and motor skill related interventions, such as aerobic exercise, resistance training, and aquatic activities, were mostly adopted in the clinical practice [32,34,41–56]. In addition, two studies investigated effects of exergaming/technology interventions for individuals with ASD [38,43].

The included studies investigated effects of physical activity intervention on cognitive functions, with small to moderate effect sizes on improved global EF [32,50]. Specifically, the included reviews reported enhanced performance in working memory, attention, task switching, and inhibitory control [34,50]. The evidence also indicated beneficial effects of social functioning and communication skills, which can be attributed to the group-based activity during the interventions [42,44]. Learning and memory outcomes due to PAIS were not fully explored within selected studies. The other limitation of current systematic review and meta-analysis studies was the combination of children and adolescent groups. However, age was recognized as a significant confounder in ASD research. Although common clinical treatments including educational, family, speech, and occupational therapy showed favorable effects, widely supportive evidence showed that physical activity was beneficial for children's lifelong cognitive and motor development. Therefore, it is necessary to explicit the PAIS treatment effects on children's cognitive outcomes from a perspective of physical activity and health promotion. Results are encouraging that various types of evidence showed PAIS were effective to enhance cognitive function in children with ASD; the foundation for the future in-depth data analysis has been established.

2.3. The Present NMA Protocol

An insight into directions of future research was provided based on the preliminary findings of the mini review. Previous outcomes suggested that varying types of PAIS were favored in improving cognitive functions and motor performance, reducing frequency of the symptoms, and enhancing social and communication skill development in children with ASD and other cognitive impairments. The quality of evidence is concerning due to the limited number of meta-analyses on RCTs [53]; we expected to simply include true experimental designs (e.g., RCTs) which might ensure robust synthesis results and increase power to detect effects of interventions [51,57]. The age groups were heterogeneous in nature, whereas we expected to focus on children particularly and explore the efficacy of PAIS on their cognitive performances. However, the limitation of the pairwise meta-analysis procedure was only appropriate for discerning outcome effects “between a selected intervention strategy and a selected comparison or control condition” [40] (p. 511). Considering pairwise meta-analyses were only able to compare multiple outcomes from a single treatment, NMA would make comparing multiple PAIS on multiple outcomes achievable [58]. Concomitantly, there is a need to conduct a NMA to obtain a more accurate estimation of the efficacy of PAIS in the population. We are aiming to provide an updated review of the extant literature in the field of physical activity and health promotion using an appropriate network meta-analytic model. Therefore, the following protocol was developed upon the findings and limitations identified in the mini review.

3. Methods

This review protocol has been registered in the PROSPERO international prospective register of systematic reviews; the registration number is: CRD42021279054. The NMA will comply with the Preferred Reporting Items for Systematic Review and Meta Analyses for Network Meta-Analysis (PRISMA-NMA) statement [59,60]. A component-based Bayesian framework NMA will be conducted following the procedures below [61].

3.1. Search Strategy

Nine bibliography databases will be searched: APA PsycInfo, Cochrane Central Register of Controlled Trials, Dimensions, ERIC, MEDLINE Complete, PubMed, Scopus, SPORTDiscus, and Web of Science. In general, the search will be limited RCTs published in English ranged from inception to date. Keywords combinations and MeSH terms applied in the search are displayed in Table 2.

3.2. Inclusion and Exclusion Criteria

The following explicated the PICOS components regarding population, intervention, comparator, outcomes, and study design.

3.2.1. Population. Children aged between 0-12 years old with a diagnosis of ASD (Asperger's syndrome, autism, or unspecified developmental disorder) with varying severity (mild, moderate, severe) will be accepted. Study will include at least one diagnosis criteria regarding Diagnostic and statistical Manual of Mental Disorder [1], International Statistical Classification of Diseases and Related Health Problems (ICD), or

Autism Diagnostic Observation Schedule (ADOS). In addition, demographic information including subject's age, gender, and sample size should be reported.

3.2.2. Intervention. Any sort intended to increase cognitive functions in subjects with ASD using physical activity or exercise interventions. Physical activity exhibited in school-based physical education, exergaming, mindfulness practice (e.g., yoga, martial arts, Tai Chi, etc.), aerobic exercise and sports, and any types of therapeutic physical activity interventions will be included.

3.2.3. Comparison. A number of comparators will be eligible for inclusion in the network of evidence in terms of active behavioral control group, waiting list control, and standard care.

3.2.4. Outcome Measures. Mean difference in cognitive functions measurements between the beginning of the intervention and follow up test. Study obtained at least one validated outcome measurement of cognitive functions. Study features included the measurement tool with either objective or self-reported patterns.

3.2.5. Design. RCTs had outcome measures conducted in the pre- (baseline) and post-intervention; the study included more than one session of intervention.

3.2.6. Exclusion Criteria. Studies will be excluded with participants who were older than 12 years or unable to conduct psychomotor movements; RCT was not used; intervention lasting less than 8 weeks; manuscript was not written in English.

3.3. Study Selection and Data Extraction

Recording and managing related literature will be accomplished with Mendeley software (Mendeley Ltd, London, UK). Two authors will independently screen the titles and abstracts of the searched peer-review studies which will be based on the pre-established criteria for inclusion. A third reviewer will be involved to initiate a full-text evaluation if any conflicted selections occur. The PRISMA flowchart illustrates the process of search and screening (Figure 2).

Study characteristics including author information, publication year, mean age in sample, diagnostic criteria for ASD, study period, intervention arms, and study design will be summarized using Microsoft Excel (Microsoft Excel, Redmond, Washington: Microsoft Corporation, 2010). Specifically, we will conduct a thematic organization approach to categorize intervention arms within all relevant RCTs into six pre-defined categories: 1) school physical education programs; 2) exergaming, 3) aerobic exercise and sports, 4) mindfulness practice; 5) computerized and non-computer games combination; 6) therapeutic physical activity interventions [32,37]. The project administrator will serve as the coordinator, dealing with potential disagreements or unclearly defined PAIS categories. Internal discussions and consultation with an experienced researcher in physical activity and health promotion are considered two solutions for disagreements and uncertainties. The inter-rater agreement rate Cohen's k between reviewers for the eligibility criteria of the study will be reported [62]. To note, grouped/ungrouped or supervised/unsupervised intervention arms will be separated as one effect size per treatment [51]. Quantified outcomes [mean of intervention arms and comparators, SDs, 95% confidence interval (CI)s] will be extracted from the aforementioned categories including measurement results regarding cognitive functions (e.g., global EFs,

working memory, thinking flexibility, inhibitory control, attention, or memory outcomes). The NMA will compare intervention effects of the pre-defined intervention categories on participants' cognitive performances. Raw data (e.g., sample sizes, t , F , or p values) will be extracted to help estimate the effect size if the means and SDs were not reported [51]. When necessary, the corresponding authors of selected studies will be contacted to obtain unpublished and missing data to allow for effect size estimates.

3.4. Assessment of Risk of Bias

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) will be used to assess the quality of selected studies in the NMA and pairwise meta-analysis [63–65]. Two authors will independently assess bias due to randomization, deviations from intervention, missing data, outcome measurement, and selection of reported results in selected RCTs. Each item is classified as high, some concerns, low or unclear/no information upon risk of bias and results of the grading of evidence quality will then be generated as a table (RoB 2.0; [66]). Homogeneity will be assessed by summarizing selected study characteristics in a general table and observing whether the treatments and participant characteristics are suitable and comparable across all studies [40,58]. Consistency of indicating direct and indirect evidence should essentially agree with each other and should not result in discrepancies [40]. The R package developed by van Valkenhoef and colleagues [67] will be employed to evaluate the inconsistency between indirect and direct comparisons via the node-splitting method. We evaluated consistency with a node-splitting technique that compares the direct and indirect estimates for each comparison. Transitivity will be qualitatively examined to ensure direct trials do not differ with respect to the distribution of effect modifiers which all treatments are jointly randomizable [68].

3.5. Statistical Analysis

The primary outcome for this study will be changes in cognitive functions. However, unlike physiological and biochemical indexes, cognitive performances were measured through pre-established validated psychometric instruments (illustrated in Table 1). Guiding through the approach applied by Désaméricq and colleagues [69], the effect size will be calculated for each extracted result and these effect sizes will be then combined into three cognitive scores, as listed in the Supplementary. An omnibus composite unit free score of cognitive outcomes will be created by averaging all subordinate domain effect sizes within a study, per intervention arm. Study included multiple treatments or outcomes will provide the corresponding amount of effect sizes per study. Extracted data such as sample size, treatment and control means and SDs for between group designs; pre- and post-intervention mean and SDs for within group designs, will be converted to correlated summary results, standardized mean differences (SMDs) for NMA to explore the efficacy of PAIS upon cognitive performances [70]. The effect sizes will be computed using SMD with 95% CIs between groups [32,71]. Hedges' g in a random model will be used in consideration of potential variances across the selected studies if the study number is fewer than 20 [32,51,72]. Effect sizes will be classified as small, moderate, or high respectively, regarding to the cutoff values of 0.2, 0.5, and 0.8 [32,73]. The calculations will be computed through between-case SMD estimator, the web-application scdhlm [74]. Heterogeneity was evaluated through the means of Q test and I^2 values regarding the statistical heterogeneity in 25% as low, 50% as medium, and 75% as high [32,75,76]. Sensitivity analyses will be conducted to determine if any study separately influenced

the overall results [77]. To minimize the impact of heterogeneous outcomes or extreme values, we will apply the threshold of Z score 3.29 for screening out outliers in mean effect scores [46,53,78]. The level of significance will be set at .05 in this study. The NMA will be performed upon RStudio (version 3.6; [79]) with the BUGSnet package (Version 1.1.0; [80]).

3.6. Moderation Analysis

Moderation analysis will be conducted to examine the variability among potential sources owing to heterogeneous PAIS settings. Moderators such as participant age, exercise intensity, and intervention setting (e.g., group versus individual) will be examined via robust variance estimation [51]. Our expectation is providing another perspective of synthesis results to explicit the higher order outcomes from NMA. Moderation analysis will be performed on Comprehensive Meta-Analysis (version 3.3; Biostat, Englewood, NJ, USA).

3.7. Ethics and Dissemination

The ethical approval process is exempted because this study will be based on findings of previous studies. This review protocol has been registered in the PROSPERO international prospective register of systematic reviews with aims regarding promoting transparency and minimizing the risk of bias [81]. Future results will be submitted to a peer-reviewed journal of the relative field for consideration of publication.

4. Discussion

We expect to compare the effects of different PAIS on cognitive outcomes (overall and by domain), over a period of treatment (at least 8 weeks). We will perform an NMA; we will select all randomized controlled trials of considering PAIS as a treatment(s) on cognitive outcomes in children with ASD. This study is going to bridge the gap and provide a novel perspective and robust evidence for clinicians and practitioners for future decision making in children with ASD. Forecasted results will include study characteristics, qualitative appraisal on cognitive tasks and intervention technologies, and quality of selected studies; demonstration visual synthesis results such as network diagram(s) and associated geometry will be generated and evaluated, respectively. Expected results will be able to rank the efficacy of multiple PAIS (e.g., aerobic exercise, mindlessness practices, school-based physical education programs, exergaming, etc.) with effect size differences demonstrated between multiple treatments. In addition to network plots, results will be also illustrated in tables of network characteristics, data plots, league tables and league heat plots, SUCRA plots, and rankograms. In-depth discussion will be generated. In general, results may reveal the rank efficacy of PAIS, in combination or single treatment, on promoting cognitive functions and further social and communication skills in children with ASD.

In addition, confronting with the COVID-19 pandemic, social restriction and isolation were carried out with increasing sedentary behavior and physical inactivity which increased risks of cardiovascular disease and mental wellness crisis in children [82–84]. Especially, there are more concerns regarding children with ASD [85,86]. We will include an in-depth discussion about feasible interventions along with safety suggestions for programming during the global pandemic. Promoting effective PAIS to reduce the impact on children with

disabilities, such as children with ASD, should be considered as urgent needs nowadays as well as in the post-pandemic era. To the best of our knowledge, this will be the first systematic review and NMA protocol to shed light on the efficacy of PAIS on cognitive performances in children with ASD. Our study is giving advantages in combining large existing evidence under similar scheme to make indirect comparisons among different forms of PAIS feasible. Therefore, completing this protocol will provide comprehensive and robust outcomes to further explore the multifaceted nature of PAIS in empirical studies. Concomitantly, we have confidence that this study may provide valuable insights and key recommendations for parents, clinicians, and policymakers to make well-informed decisions to improve the cognition development in children with ASD population in the future.

Abbreviations

ASD: Autism spectrum disorder

BDNF: Brain Derived Neurotrophic Factors

EF: Executive Function

GRADE: Grading of Recommendations Assessment Development and Evaluation

NMA: Network Meta-Analysis

PAIS: Physical Activity Intervention Strategies

PRISMA-NMA: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols for Network Meta-Analyses

PROSPERO: Prospective Register of Systematic Reviews

RCT: Randomized Controlled Trail

WHO: World Health Organization

Declarations

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Consent for publication: Not applicable.

Availability of data and materials: Not applicable.

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Tables

Table 1. Characteristics of Studies Included in Mini Review.

Study	Evidence Type (N ^a)	Population term used	Intervention term used (Intervention arm)	Outcome measures ^b	Selected effect size /Main outcomes
Aleksandrovic et al. [41]	SR (13)	Children (younger than 18 years; with ASD)	Aquatic activities (Armbruster or Halliwick methods or the Constant time delay procedure to learn swimming skills; social and floor warm up activities)	MS (ABC-2, WOTA, HAAR, YMCA checklist, Aquatic Skills Assessment)	Aquatic skills were effectively improved.
Bremer et al. [34]	SR (13)	Children and youth (≤ 16 years; at least one participant with a diagnosis of ASD or PDD)	Physical exercise intervention (Jogging, swimming, yoga/dance, horseback riding, martial arts)	CF + SF (GARS-2, SRS, Sensory profile, ABC-C, ABC, VABS-2, Frequency of child specific behaviors, BOSS, SSBS-2, BASC-2)	Improvements in stereotyped behaviors, social behavior cognition and attention.
Cameron et al. [42]	SR (17)	Children (3–6 years) with autism, CP, Down syndrome, DCD, DD, FASD	Fundamental motor skill group intervention by primary researcher	MS (PDSM-2: GMQ)	Results were inconclusive to support motor-based interventions in this age group due to variability in intervention types.
Case and Yun [43]	MA (18)	Preschool (3–5 years) and school-age children (6–17 years) with ASD	FMS (direct instruction activities), PA (whole-body movement and coordination activities), technology (e.g., video games), EAT (e.g., horseback riding) based interventions	MS (PDMS, PDMS-2, TGMD, TGMD-2, TGMD-3 BOT-2, M-ABC, M-ABC-2)	Overall effect size on gross motor outcomes ($\delta = 0.99, p < .001$); FMS ($g = .68, p < .001$), PA ($g = 1.20, p = .003$), Technology ($g = 1.42, p = .206$), EAT ($g = 1.20, p = .005$).
Chan et al. [44]	MA (12)	Children and adolescents (< 18 years; with ASD)	Individual, combined or group-based physical activity (e.g., Karate, horseback riding, aquatic, mind-	SF (GARS-2, SRS, VABS, ATEC, SSIS)	Communication (SMC = .27, 95% CI [.06, .48]), Social functioning (SMC = .39, 95% CI [.15, .63]).

			body, football, outdoor adventure, or active recreation)		
Fang et al. [38]	SR (10)	Children and young adults (age ranging 5-21 years; with ASD)	Exergaming (e.g., platforms/games included DDR, cybercycling, FroggyBobby, Xbox Kinect, Nintendo Wii, Makoto Arena)	CF + MS (Physical outcomes (e.g., BMI, jump distance), cognitive outcomes (e.g., BRIEF))	Favored results of exergaming interventions on participants' physical and cognitive functions.
Ferreira et al. [45]	SR (8) + MA (8)	Children and youngsters (< 16 years; with ASD)	Aerobic exercise, Kata techniques training, ball exercise	CF (GARS-2, SSB, stereotypic behavior observations)	Physical activity was effective in reducing stereotypic behavior (SMD = 1.11, $p = .009$).
Fragala-Pinkham et al. [52]	SR (8)	Children and young adults (7-26 years; with ASD, Down syndrome, or UID)	Lower extremity cycling (e.g., learning to ride a two-wheeled bicycle, stationary cycling, CO-OP approach)	CF+MS (e.g., cycling time and distance, cycling skill checklist, KT, KTFist, TOLT, PPT-C)	Weak evidence and heterogeneous results on MS and CF in children and young adults with intellectual disabilities between cycling and control groups.
Healy et al. [53]	MA (29)	Youth (2-22 years; with ASD)	Recreational activities in APE, PE, multiple, medical, and other settings (e.g., yoga, kata program, aquatic skill program, dance, mind-body exercise, combined)	CF + MS (Psychometric tools or scales were not specifically discussed)	Overall positive moderate effect exhibited ($g = .62, p < .001$); cognitive ($g = .28, 95\% \text{ CI } [-1.19, 1.74]$), psychomotor ($g = 1.21, 95\% \text{ CI } [.41, 1.66]$).
Howells et al. [46]	SR (11) + MA (7)	Children (5-12.9 years; with ASD)	Individual and group physical activity (e.g., included a range of blocking, punching, sticking, and kicking techniques; climbing rope ladder or rope elevator; horse riding; groups sport games)	SF + COM (SRS, VABS, SRS, BASC-T, SISS, GARS-2)	Non-significant effect for communication ($g = .13, 95\% \text{ CI } [-.12, .38]$) and a significant improvement in overall social functioning ($g = .45, 95\% \text{ CI } [0.19, 0.72]$).

Huang et al. [47]	MA (12)	Children and adolescents (3-18 years; with ASD)	Physical activity interventions (e.g., Kata techniques, therapeutic horseback, outdoor activity, karate, aquatic sport, trampoline, table tennis, Tai Chi, exergaming)	CF + MS +SF + COM (GARS-2, BOT-2, SRS, PPVT-4, SALT, ATEC, ABC, MABC-2, CBS, WCST)	Significant positive effects on social interaction (SMD = -.58, 95% CI [-.87, -.29]), communication (SMD = -.29, 95% CI [-.55, -.04]), stereotyped behavior (SMD = -.13, 95% CI [-.46, .20]), motor skills (SMD = 1.02, 95% CI [.33, 1.71]).
Lang et al. [54]	SR (18)	Children, adolescents, and adults (3-41 years; with ASD)	Physical activity (e.g., walk, jog, playing catch with a ball, ride stationary bike, swim, weight training, etc.)	CF + PF (Psychometric tools or scales were not specifically discussed)	Exercise decreased stereotypy, aggression, off-task behavior, and elopement.
Liang et al. [32]	SR (14) + MA (7)	Children (5-17 years; with ASD)	Physical activity or exercise on EFs (exergaming, jogging, table tennis, progressive muscle relaxation, martial arts, basketball, etc.)	CF (BRIEF, Stroop, CTT, HKLLT, DSFBT, FPT, TOLT, GNG, CBTT, Hearts and Flowers test, attention sustained test)	Positive effect on global EFs ($g = .34$, 95% CI [.08, .60]), CF ($g = .31$, 95% CI [.05, .57]), IC ($g = .49$, 95% CI [.19, .80]), WM ($g = .21$, 95% CI [-.09, .51]).
Petrus et al. [48]	SR (7)	Children (4-15 years; with ASD)	Physical activity or exercise (e.g., aquatic, jogging, ball playing, aerobic exercise)	CF + MS (Stereotypical behaviors and MS were observational measured in frequency, duration, or counts)	Exercise might reduce stereotypic behaviors in the short-term.
Ruggeri et al. [55]	SR (41)	Children and adolescents (3-19 years; with ASD)	Motor and physical activity (e.g., soccer, exergaming, throwing, aquatic, fitness or strength, horse riding, hippotherapy, stationary biking, gymnastic,	MS + ML (e.g., VABS-2, BOT, BOT-2, MABC-2, PDMS-2, TGMD-2, TGMD-3, m-PEDI, ASC, YMCA-checklist,	Motor skill and learning, body structure and function outcomes were improved with various physical activity interventions.

			indoor climbing programs, etc.)	HAAR, SCS, GAS)	
Semple [49]	SR (8)	Youth (3-18 years; with ASD)	Yoga, mindfulness-based, Qi Gong, meditation	CF + MS + SF + COM (Psychometric tools or scales were not specifically discussed)	Improvements in prosocial behaviors; social cognition, communication, motivation, motor control via yoga and mindfulness-based interventions.
Sowa and Meulenbroek [56]	MA (16)	Children, adolescents, and adults (4-41.3 years; with ASD)	Individual and group physical activity interventions (e.g., jogging, therapeutic horseback rides, bike riding, walking, stationary cycling, aquatic exercising, swimming, etc.)	MS + SF + COM (Psychometric tools or scales were not specifically discussed)	Individual programs exhibited positive effects on motor skills ($r = -.32, p = .004$) and social interactions ($r = -.62, p < .001$) compared to group programs.
Zhang et al. [50]	MA (11)	Children (n.a. ^c ; with ADHA and/or ASD)	Chronic physical activity intervention (e.g., rhythm, integrated physical activity; modified aerobic games; exergaming; taekwondo, etc.)	CF + MS (BOT-2, WCST, TGMD-2, Stroop test, Flanker task, Coris block tapping test, etc.)	Large significant improvement in overall EF, inhibitory control, cognitive flexibility, gross motor skills (SMD range from .85 to 1.30); no significant improvements in working memory and fine motor skills.
Teh et al. [51]	MA (22)	Children (n.a. ^c ; with ASD)	Physical exercise interventions (Jogging, cycling, exergaming, ball exercise, therapeutic horse riding, martial arts)	CF (GARS-2, ATEC, ABC, BASC-2, observational measures or time intervals on targeted behaviors, etc.)	Large overall ES ($g = 1.16$) on reducing stereotyped motor behaviors across participants, treatment, and levels from a multi-level modeling MA.

Notes: ^a *N*: number of studies; ^b only ASD relative interventions and outcomes were summarized regarding the established inclusion criteria of this study's protocol. ^c Criteria of age was not mentioned in search strategy; 95% CI: 95% confidence interval; ABC: Aberrant Behavior Checklist; ABC-2: Assessment Battery for Children Second Edition; ABC-C: Aberrant Behavior Checklist – Community; ADHD: Attention deficit

hyperactivity disorder; APE: adapted physical education; ASC: Aquatic Skills Checklist; ASD, autism spectrum disorder; ATEC: autism treatment evaluation checklist; BASC-2: Behavioral Assessment System for Children – 2nd ed.; BASC-T: Behavior Assessment System for Children-Teachers; BMI: body mass index; BOSS: Behavioral Observation of Students in Schools; BOT = Bruininks-Oseretsky test; BRIEF: Behavior Rating Inventory of Executive Function; CARS = Child Autism Rating Scale; CBS = Clancy Behavior Scale; CBTT: Corsi block-tapping task; CF: cognitive flexibility; CF: cognitive functions or performance; CIMT: constraint-induced movement therapy; COM: communication; CP: cerebral palsy; CTT: color trails test; DCD: developmental coordination disorder; DD: developmental delay; DDR: dance dance revolution; DSFBT: digit span forward and backward test; EAT: equestrian assisted training; EF: executive function; EFs = executive functions; ES: effect size; FMS: Fundamental motor skills; FPT: Five-Point Test; *g*: Hedges's *g* effect size; GARS-2: Gilliam Autism Rating Scale – 2nd ed.; GAS: Goal Attainment Scaling; GMQ: gross motor quotient; GNG: go-no-go task; HAAR: Humphries Assessment of Aquatic Readiness checklist; HAAR: Humphries Assessment of Aquatic Readiness; HKLLT: Hong Kong List Learning Test; IC: inhibitory control; KT: Knock-tap-fist; KTFist: Knock-tap-fist; MA: meta-analysis; MABC-2 = Movement Assessment Battery for Children-Second Edition; ML: motor learning; m-PEDI: mobility scale of the Pediatric Evaluation of Disability Inventory; MS: motor skills or performance; n.a.: not applicable; PA: physical activity; PDD: pervasive developmental disorder; PDMS-2: Peabody Developmental Motor Scales (2nd edition); PE: physical education; PF: physical fitness; PPT-C: Perdue Pegboard Test-Combined Unilateral, Bilateral, Assembly; PPVT-4 = Peabody Picture Vocabulary Test, 4th Ed; SALT = Systematic Analysis of Language Transcripts; SCS: Swimming Classification Scale; SF: Social functioning; SF: Social functioning; SMC: standardized mean change; SMD: standardized mean difference; SR: systematic review; SRS: Social Responsiveness Scale; SSBS-2: School Social Behavior Scales, (2nd edition); SSIS: social skills improvement system rating; TGMD = Test of Gross Motor Development-3 physical activity; TOLT: Tower of London Test; UID: unspecified intellectual disability; VABS-2: Vineland Adaptive Behavior Scales – Interview Edition, Survey Form; WCST Wisconsin Card Sorting Test; WCST= Wisconsin Card Sorting Test; WM: working memory; WOTA: Water Orientation Test Alyn; YMCA: Young Men's Christian Association;

Table 2. Flowchart of Search Strategy.

Concept	Keywords
I. Outcome: Cognitive Functions	"Cognitive function*" or "cognitive outcomes" or executive function* or "neurocognitive tasks" or questionnaires or inventory or task* or restricted repertoire or autism spectrum disorder [MeSH Terms] or children behavior disorder [MeSH Terms] or autistic disorder [MeSH Terms] or stereotypic movement [MeSH Terms] or motor skills disorder [MeSH Terms] or cognition [MeSH Terms] or communication disorder [MeSH Terms] or learning disabilities [MeSH Terms] or DSM-V [MeSH Terms]
II. Participants: Children & Adolescents	Children or adolescent* or young people or school-aged or teen or young adult* or youth or kids or teenager* Exclude (NOT): smoking or drinking or criminal* or injury or injuries or accident* or trauma or adult* or older adult* or elderly or seniors or geriatric*
III. Exposure: Comparator	Control* or "control group" or subject* or "human subjects" or human-related or waiting list
IV. Exposure: Exercise Types	"Physical activity" or intervention* or exercise* or fitness or "physical exercise" or sport* or psychomotor or motor activity or recreational sport* or school-based or computerized training or hybrid or games or aerobic or "martial arts" or Tai Chi or "mindfulness practice" or classroom curricula or Montessori methods or "resistance training"
V. Design	Experimental* or clinical trial or randomized control trial* or RCT or non-randomized comparison or NRS Exclude (NOT): observational studies or cross-sectional or case control or cohort or systematic review or meta-analysis or report or protocol or qualitative or mixed method

Bibliographic databases: PubMed, SPORTDiscus, APA PsycInfo, MEDLINE Complete, ERIC, Scopus, Web of Science, Cochrane Central Register of Controlled Trials, and Dimensions; We used "OR" to separate keywords within each concept and "AND" to separate each concept; MeSH terms were used for PubMed search only; Google Scholar was used for cross validation for search results from multiple bibliographic databases.

Figures

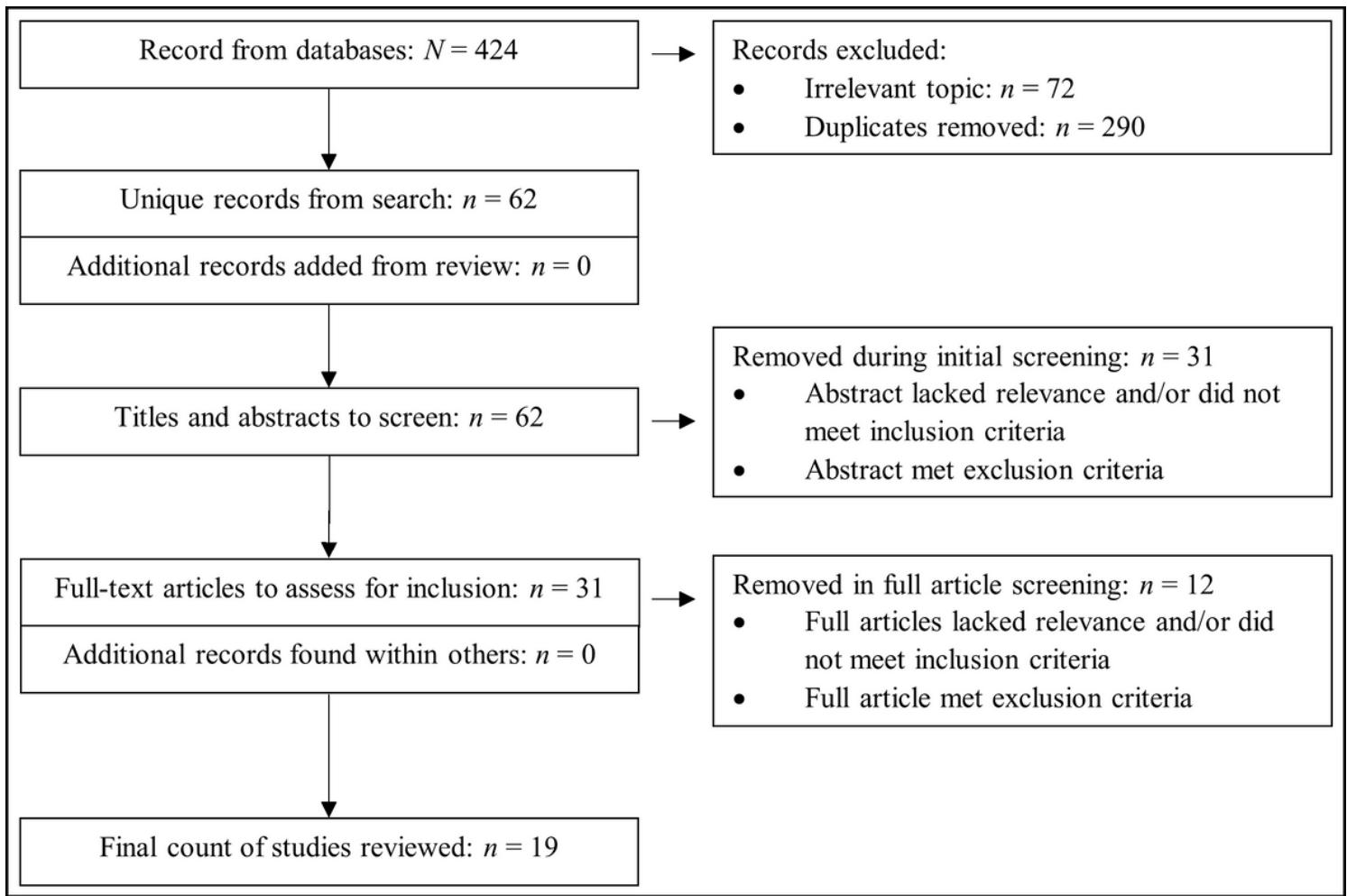


Figure 1

Flowchart of Searching and Screening in Mini Review.

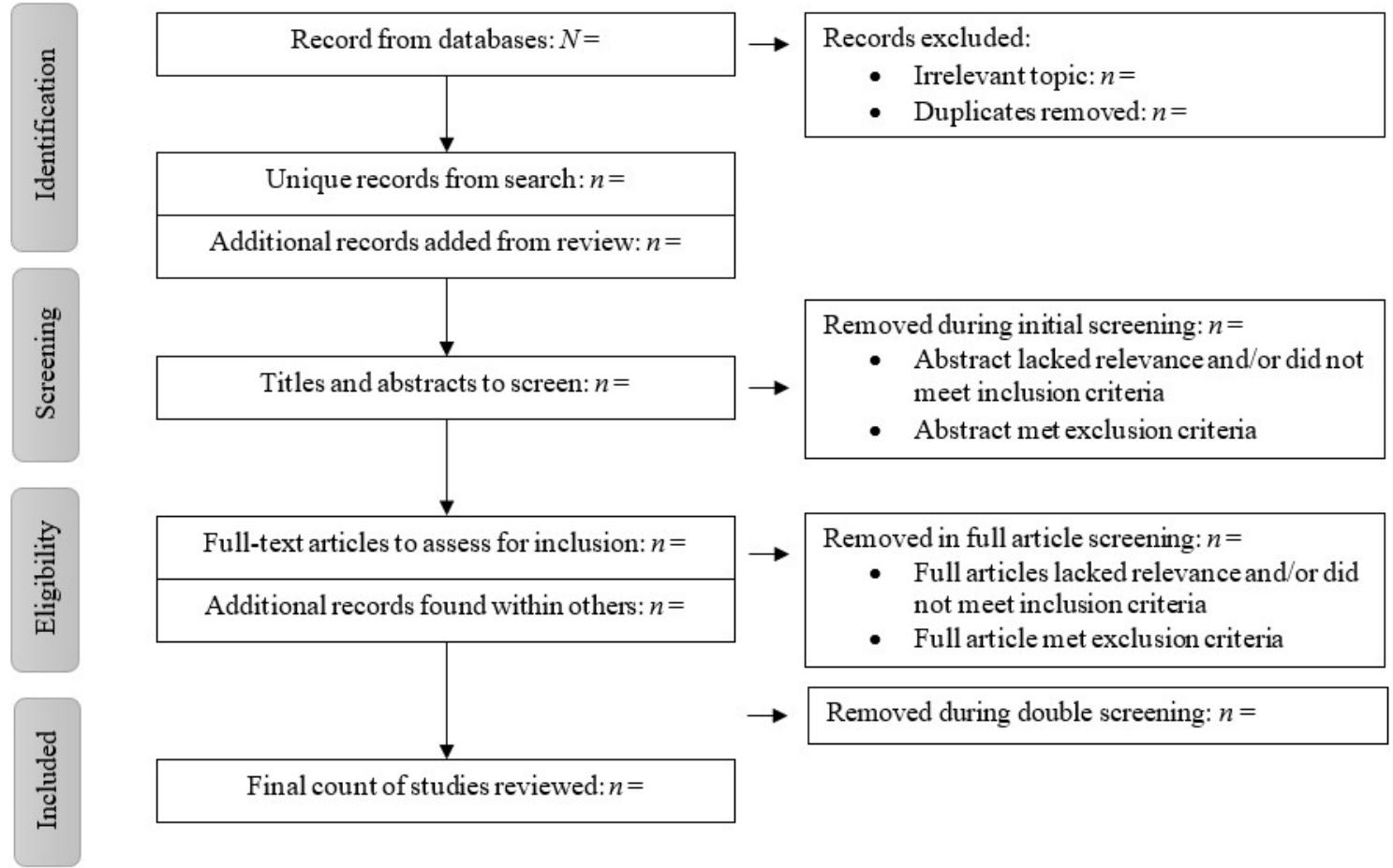


Figure 2

PRISMA Flowchart of Searching and Screening.

Supplementary Files

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- [Supplementary.docx](#)