The effectiveness of physical activity and nutrition interventions for children and adolescents with cerebral palsy to improve physical health and cognitive outcomes: A systematic review

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Abstract

Purpose: Using systematic review methodology, we set out to describe the evidence for physical activity (PA) and nutrition interventions for children and adolescents with cerebral palsy (CP) as compared to no intervention or any other type of intervention or exposure, that reports physical health, and cognitive outcomes.

Method: Quantitative, primary studies that explored the effectiveness of these interventions, replicable in school and home contexts, in comparison to any other or no intervention or exposure in children and adolescents between the ages of 6-18 years old with a diagnosis of CP were included (PROSPERO CRD42022322143). Risk of Bias was assessed by JBI and QualSyst.

Results: A total of 16 international heterogeneous studies (13 PA and 3 nutrition) with interventions ranging from a single exposure to 8 months, with quality 58-89 % and effectiveness D= 0.03 -0.97 were included. Outcome measures were varied.

Conclusion: The review brings together a number of high-quality studies on PA and nutrition interventions, and promising findings of impact on cardiovascular, musculoskeletal, and cognitive outcomes. Evidence supports implementation of these interventions in community contexts. Future research would benefit from agreement on the use of core outcome measures for meta-synthesis.

Introduction

Lifestyle factors including low activity levels and poor diet in childhood are related to the development of morbidity, such as cardiovascular metabolic conditions, and subsequent ill health in adulthood (11, 21).

One in 400 children and young people in the UK are affected by cerebral palsy (CP) (25, 31). The NHS reported the cost to the economy at an estimated £4 billion per year in 2009 (14). Whilst in 2018, Australia reported a $5 billion per year based on 35,000 people ($145,000 AUD/person/year) (10). Children with CP are classified according to their mobility and overall functioning. These factors are closely linked to their ability to participate in work and social activities (24).

Children and young people with CP are now living longer but have low physical activity (PA), poorer nutrition (4, 33) and are more likely to have co-morbidity and conditions typically affecting major organ systems such as musculoskeletal, neuromuscular, metabolic, cardiovascular and cardiorespiratory systems both as primary pathology and secondary to lifestyle factors than their peers (2). Children and adolescents with CP face physical challenges with PA due to these altered biologies that compromise cardiorespiratory fitness and muscle strength as well as movement impairments and mobility limitations (32). In addition, the lack of support networks to facilitate active lifestyles leads to more sedentary behaviours. Promoting PA in children and adolescents with CP is important to help reduce the risk of chronic diseases and maintain functional independence, mental health, and overall well-being.

Interventions such as PA and diet have been shown to improve physical and cognitive functioning in young people (23). However, their impact on physical and cognitive health and wellbeing in children and young people with CP is less well described.

This systematic review describes the evidence for PA and nutrition interventions as compared to no or any intervention or exposure to physical and cognitive health outcomes in children and young people with CP. In this review, PA will refer to activities that target cardiovascular, cardiorespiratory, neuromuscular, metabolic, musculoskeletal or cognitive health from acute exposures to structured exercise programs.

Objectives

This review will examine the evidence for PA (inclusive of exercise programs) and nutrition interventions in children and young people with CP that focus on outcomes related to the physical health of the major organ systems, including the musculoskeletal, neuromuscular, metabolic, cardiorespiratory, cardiovascular, and cognitive systems.

Methods

This review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to ensure procedural fidelity (28). The protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO CRD42022322143).

Eligibility criteria

The search focused on quantitative studies, primary study designs, randomised control trials (RCT), prospective trials, cross-sectional, case-control and quasi-experimental studies. Qualitative studies, reviews, single-case studies, protocol papers, and animal and in-vitro studies were excluded.

Study participants included children and adolescents between the ages of 6-18 years old with a diagnosis of CP, inclusive of all Gross Motor Function Classification (GMFCS) Levels I-V or unspecified. Studies that included children under six years old and adults over 19 years old were excluded. If studies used mixed participants (e.g., those with CP and those with similar conditions (i.e. neurodisability) they were included if over 80% of the sample had CP. Comparator groups considered were young people without CP (i.e., typically developing group matched for age and gender) and/or non-exposed comparator group receiving standard care or treatment as usual.

Only interventional studies were included, they had to have PA components (including acute exposures or exercise programs) and/or dietary components with outcomes that benefit physiological health (e.g. musculoskeletal, neuromuscular, metabolic, cardiorespiratory, cardiovascular, and cognitive systems). PA was taken from the WHO definition as any bodily movement produced by skeletal muscles that requires energy expenditure and exercise as a subset of PA as planned, structured, repetitive and intentional movement aimed at improving or maintaining physical fitness (27).

Interventions that trialled drugs or medication were excluded.

Studies were included if they used methodologies that could be replicated in the home and/or in a school setting and considered both group and individual interventions.

Studies were excluded if the interventions primarily focused on treatment therapies that solely targeted single/upper/lower limb abnormalities, spasticity, gait and movement abnormalities as standard care. They were excluded if they could only be replicated in schools or the home (not both), involved equine and aquatic interventions, and publications whose full text was unavailable. Non-English texts were considered but excluded due to the risk of translation tools producing errors that could potentially lead to incorrect interpretations and study conclusions. Studies were excluded if they scored less than 55% when assessed for risk of bias using the QualSyst Tool (19).

Information Sources and Search Strategy

Prior to the search guidance was sought from a librarian, expert data specialist, who helped formulate a search strategy and proposed a selection of relevant sources. A systematic search of the electronic databases CINAHL, MEDLINE and PubMed (National Library of Medicine) was conducted for original articles.

To enable a broader sweep of the literature searches for all three databases used a combination of the terms “cerebral palsy”, “physical activity”, “exercise”, “child”, “adolescent” and “nutrition” (Supplementary A) without any restrictions on publication date. An initial search took place in January 2022 and the last update took place in July 2023.

Selection process

Two reviewers (JC and TM) independently screened the titles and abstracts of the articles based on the inclusion and exclusion criteria. Covidence was used to ensure reviewers were blinded and as an article management system for the review process (15). Full text screening further identified eligible studies. At each stage, any conflicts were discussed between JC and MT until a final consensus was made. Any disagreements between JC and MT were resolved by a third reviewer (SC or LN).

Extraction process

The lead reviewer (JC) independently extracted data from the remaining articles and the researchers overseeing the systematic review (SC and LN) confirmed the extraction. Each researcher was assigned articles relevant to their field of expertise, one in diet/nutrition (SC) and the other in PA (LN). Any disagreements were discussed between JC, SC and LN until a consensus was met. Data were extracted and managed using Covidence and downloaded to an Excel document (Microsoft, 2019).

Data items

Extracted data included the author with year, participant demographics, GMFCS level, intervention type, outcomes, and outcome classification according to organ systems, setting, methods, duration, dose, frequency, outcome measures and results

Study risk of bias assessment

The lead reviewer independently examined each study and appraised it for quality using Joanna Briggs Institute's (JBI) critical appraisal tools (16). Two JBI checklists were manually uploaded to Covidence, one for RCTs (3) and the other for quasi-experimental studies (35). Once appraised, the studies were assigned to the supervisory reviewers via Covidence, and any disagreements were discussed until a consensus was met. A scoring system was introduced for each question outcome using the QualSyst Tool (19) to give percentage weighting to each study. The authors of the QualSyst Tool created a scoring system to assess the quality of various study designs and to establish a minimum quality standard for the included studies. They used a cut-off point of 55% to exclude papers. Researchers JC, SC, LN, and HD agreed that the quantitative aspect of the scoring system helped in excluding studies and as a tool for categorising studies as low, medium, or high quality.

Synthesis methods

Results were grouped separately into PA and nutrition and further divided according to compatible outcomes on the major organ systems, and grouped accordingly e.g., supplements for dietary results and aerobic/strength exercise for PA on cardiovascular or metabolic systems. Heterogeneity was discussed between two researchers by the variability of the intervention type used in both the PA and dietary studies. Results were presented in data extraction tables, one for PA and one for diet/nutrition. Due to the small numbers and the heterogeneity of the studies found in the initial screening, a narrative synthesis was conducted following the SWiM (Synthesis without meta-analysis) guidelines (5). Measures of effect, confidence intervals, effect sizes, clinical significance, and clinical change were used to assess the effectiveness of the interventions.

Results

Study selection

The initial screening of all databases (CINAHL, MEDLINE and PubMed) resulted in 5870 studies, of which 2827 were duplicates, leaving 3043 studies for title and abstract screening. We excluded 3011 of these for not meeting the inclusion criteria. Thirty-two studies remained for full-text screening, 16 of which were excluded (two non-English text; two wrong comparators; one abstract only; one an algorithm assessment of exergame; one follow-up study (no intervention); one limited PA; one no full text available; one non-scientific analysis; one single-subject research design; one under age range; one CP participant; 29% with CP, results reported as collective neurodisability; one low quality). The final 16 studies meeting inclusion criteria underwent extraction and were included in the narrative synthesis (Figure 1).

Figure 1: PRISMA flow chart

Study characteristics

There was a total of 16 studies, 13 were PA based (6-9, 12, 20, 22, 26, 29, 30, 32, 36, 37) and three were nutrition based (17, 18, 34). Results are summarised in Table 1.

The 13 PA studies included in this review were from a range of countries across Europe, Australasia and America. The PA interventions included 11 aerobic exercise studies (9, 12, 20, 22, 26, 29, 30, 32, 36-38), three of which combined aerobic and strength/weight-bearing exercises (9, 36, 37), one compared aerobic to anaerobic exercise (38) and one compared aerobic to strength exercise(30). Two studies solely used strength training (6, 7).

The PA studies took place in various settings including rehabilitation/physiotherapy centres (3 studies) (6, 22, 37), community fitness facilities (1 study) (9), homes (3 studies) (7, 20, 30) schools (2 studies)(12, 38), combined home and rehab centre (1 study) (37). The location was unclear for three studies (29, 32, 36).

Three studies were nutrition based (17, 18, 34), one from Greece, one from Finland and one from the UK. These included two RCTs (65 participants)(18, 34) and one quasi-experimental study (15 participants) (17). The studies (n=3), used supplements including Vitamin D supplementation (2 studies) (17, 18) and leucine (1 study) (34) to examine effects on the skeletal and muscular systems. The length of the nutrition studies ranged from four (17) to ten weeks (18, 34). One nutrition study provided a single high-dose supplement at the start of the study (17) and the other two studies used a daily supplement (18, 34). The studies were conducted in rehabilitation centres (1 study) (17), schools (one study) (18) and home (1 study)(34).

The studies examined outcomes across 11 major organ systems. Six studies focused on cardiovascular outcomes (20, 22, 26, 29, 32, 36), one on cardiovascular and skeletal (9), two on cardiovascular and muscular (37, 38), two on muscular outcomes (30), one on cognitive outcomes (22) and four on skeletal outcomes (6, 7, 17, 18).

Participant Characteristics

Twelve out of 13 PA studies reported sex (6, 7, 9, 12, 20, 22, 26, 29, 30, 36-38), with a total of 164 males and 139 females across the studies~~.~~ Three studies did not use a control group (9, 12, 20). Two studies used typically developing children as controls (22, 26) (10 males, 9 females). Six of the PA studies used control groups who had CP and were matched for age and sex but did not carry out the training programs (6, 7, 26, 36-38). Two studies contained groups that compared different types of exercise Eleven PA studies reported the GMFCS levels of their participants (Level I = 166, Level II =59, Level III= 26). Two studies did not report GMFCS (9, 32). The sample sizes in the PA studies ranged from 8 – 68 (mean: 24.1 ± 16.7).

The three nutrition studies reported sex (17, 18, 34), 45 were males and 35 were females. One study did not have a control group (17). The participants' ages ranged from 2 to 25 years, with a mean of 15.6 ± 5.0 years in the intervention groups and 18.3 ± 2.8 years in the control groups. One study reported a median age of 12.9 years in the intervention group and 13.5 years in the control group (18). All participants had a CP diagnosis and the studies reported GMFCS levels, which ranged from Levels II to V (Level II = 8, Level III = 21, Level IV = 25, Level V = 26).

Quality and Risk of Bias

Nine RCTs and eight Quasi-Experimental studies were reviewed (Supplementary B). One RCT by Cleary (8) was excluded for scoring below the <55% cut point set by QualSyst (19). Six RCTs were in the medium range (Chad (6) :62%; Chen (7):58% ; Kilpen-Loisa (18):69%; Schranz (30) :62%; Theis

(34):62%; Unnithan (36):65%). Two scored in the higher range (Verschuren (38): 73%; Van Wely (37) :77%). Two Quasi-Experimental studies scored medium (Darrah (9) and Knights (20) :67%). The six remaining scored higher (Karagiannis (17):72%; Gorter (12):78%; Maltais (22), Nsenga Leunkeu (26), Robert (29) and Shinohara (32):89%) suggesting higher quality studies with less risk of bias.

Results from individual studies

Physical Activity interventions

There were two strength interventions included in the analysis (6, 7) (Table 1). Chad et al. (6) evaluated an eight-month strength training program and found significant improvements in bone mineral content (BMC) and volumetric bone mineral density (vBMD). The intervention group had an 11.5% change in total proximal femur BMC, compared to a 3.5% change in the control group (p=0.08). Both femoral neck BMC and vBMD saw larger changes in the intervention group, 9.6% and 5.6% respectively compared to the control group (-5.8% and -6.3%, p=0.03 and p=0.02). There was a significant difference for both BMC and vBMD (p=<0.06 and p=0.03, respectively) at baseline to post-intervention for each group. Similarly, Chen et al. (7) evaluated a 12-week home-based virtual cycling training strength training program and found significant improvements in knee muscle strength with a significant, large effect between intervention groups and controls (knee extensor, p=0.023, $\eta 2$ =0.157; knee flexor p=0.002, $\eta 2$ =0.321). Similarly, post-study there was an increase in Distal femur aBMD (areal bone mineral density) for the intervention group and a decrease in the controls with a significant with a large effect (p=0.022, $\eta 2$=0.160) between groups.

Three combined aerobic and strength training programs were also evaluated (9, 36, 37) (Table 1). Darrah et al. (9) evaluated a 10-week fitness program combining aerobic, strength and stretching exercises. The program found significant increases in mean strength from T3 (87.0kg ± 38.5) to T4 (119.3kg ± 37.6). Flexibility improved from T1 (74.0cm ± 32.5) to T3 (85.9cm ± 35.5), but there were no changes in energy efficiency or heart rate (HR). Unnithan et al. (36) evaluated the effect of a 12 week combined aerobic and strength program, the training group had significant improvements in both submaximal V’O2 and peak oxygen uptake (%VO2peak) compared to controls (p=<0.05). Effect sizes for peak V'O2 was 0.55 (medium) and 0.25 (low-medium) for change in submaximal V'O2. Significant interactions for relative peak V'O2, absolute peak V'O2, and V'E (p=<0.05), indicated the training group achieved higher peak values than controls. Additionally, the duration of V'O2 tests in the training group increased from 338.6s ± 16.9 to 415.7s ± 131.3.

Van Wely et al. (37) found increases in moderate-to-vigorous PA after a six-month stimulation program (Table 1). Parent-reported time in moderate-to-vigorous intensity increased (between-group change ratio, 2.2, 95% CI 1.1 to 4.4). At four months there was a positive trend for the one-minute walk test as reflective of cardiovascular fitness, (mean between-group difference 5m, 95% CI 0 to 9). No other changes in PA or secondary outcomes were seen.

One intervention compared strength training to aerobic training (Table 1). Shranz et al. (30) found that 8-weeks of progressive resistance training (PRT) versus high-intensity circuit training (HICT) improved total isometric strength in both groups (5.04 N/kg, 19.6%, p=0.02) but the HICT group had greater improvements in specific muscle groups (p=0.004 maximum muscle power) and anaerobic power (p=0.001 muscle power sprint test). Follow-up showed significant decreases for the HICT group in mean muscle power (p=0.05) and total isometric strength (p=0.03). The PRT group showed no changes supporting the need to maintain training.

One intervention combined aerobic and anaerobic training (Table 1). Verschuren et al. (38) evaluated the effects of an eight-month combined aerobic and anaerobic training program. Results showed significant improvements in the training group: aerobic capacity (+38%, p<0.001), anaerobic capacity (+25%, p=0.004), agility (+15%, p<0.001), and muscle strength of the lower extremities (+20% left side, +23% right side, p<0.001). However, at the 4-month follow up the training group displayed a decrease in aerobic capacity (-8.4%), anaerobic capacity (-8.5%), agility (-4.3%), muscle strength (left side, -4.4%; right side, -8.3%).

There were six aerobic exercise interventions included in the analysis (12, 20, 22, 26, 29, 32) (Table 1). Gorter et al. (12) investigated the effects of a nine-week functional training program on aerobic fitness and walking. Aerobic capacity improved, with lower HR at 6 minutes ($p=0.02$) and longer time on the treadmill ($p<0.001$) at the end of the program compared to baseline. Walking performance also improved, with increased distance in the 6-minute run test ($p=0.03$) and decreased time in the timed up-and-down stairs test ($p=0.00$) at the end of the program. Knights et al. (20) evaluated the effects of a six-week exergame cycling program on cardiovascular fitness (Table 1). Participants spent an average of 202 ±95 mins per week playing the game and 79 ±48 mins (39%) above their target HR. Cardiovascular fitness, measured by the GMFCS level III-specific shuttle run test (SRT-III, $p=0.04$), with large effect size ($d=0.88$) and mean detectable change of 1.7 ±1.9 levels.

Nsenga Leunkeu et al. (26) investigated the effectiveness of an eight-week walking program on cardiorespiratory adaptation (Table 1). Positive test-retest correlations were found between the two six-minute walk tests (6MWT) assessments for VO2peak ($r=0.90$, $p<0.001$, ICC=0.85); peak minute ventilation (VE peak) ($r=0.88$, $p<0.001$, ICC=0.83); peak HR ($r=0.86$, $P<0.001$, ICC=0.82) and distance walked ($r=0.87$, $p=0.007$, ICC=0.80). Mean scores for the 6MWT were similar to those of the cycle-ergometer data. Post-intervention saw significant improvements in the 6MWT for VO2peak, VE peak, and peak HR ($p<0.05$). VO2peak correlated positively with 6MWT walking distance ($r=0.948$, $p=0.001$) and the cycle ergometer VO2peak ($r=0.625$, $p<0.05$). The intervention group, improved V'O2peak ($p=0.046$), VE peak ($p=0.033$), peak HR ($p=0.02$) and walking distance ($p=0.001$); no changes were seen in the control group.

Shinohara et al. (32) assessed VO2 at the anaerobic threshold (AT) after 6-20 weeks of aerobic exercise (Table 1). The leg exercise group trained for 16.7 ± 4.7 weeks on average, compared to 12.7 ± 6.3 weeks for the arm group. VO2 at the AT increased in the leg group but not the arm group. This improvement in the leg group was observed 1-3 months after exercise.

Robert et al. (29) evaluated exercise intensity during active video games (Table 1). There was a significant ($p=0.001$) large main effect (0.97) for the percentage of time spent at an intensity >40% of heart rate reserve (HRR) for >50% of the time for the jogging game and >30% of the time during the bicycling game. The bicycling game was significantly more physically demanding than the snowboarding game and the jogging game elicited greater lower limb articulation than the bicycling game ($p<0.05$).

Maltais et al. (22) assessed the effects of acute aerobic exercise on cognition (Table 1) using population specific Shuttle Run tests. The CP group correctly identified a large number of pictures with an overall response of 96.8 ± 0.65 %. Both groups showed small-to-medium reductions in response accuracy after exercise with a small effect size in the TD group, d=0.42 and a medium effect in the CP group, d=0.50. The CP group significantly improved reaction time ($p<0.002$) with a large effect (d=0.87) and the TD group had a non-significant improvement with a medium effect (d=0.59). Similarly, the CP group had a significant ($p<0.04$) but medium negative effect (d=0.77) for interference effect and the TD group had a small (d=0.03), non-significant effect.

Nutrition interventions

There were three nutrition interventions included in the analysis (17, 18, 34) (Table 1).
Karagiannis and colleagues (17) evaluated a single administered high-dose of vitamin D (100,000 IU) over four weeks, and 25-hydroxy vitamin D (25(OH)D) levels significantly increased from baseline 54.1 ± 45.8 nmol/L (21.7 ± 18.3 ng/mL) to 110.3 ± 60.1 nmol/L (44.1 ± 24.1 ng/mL), $p<0.0001$. Additionally, parathyroid hormone levels (PTH) decreased from 2.85 ± 0.75 pmol/L (26.9 ± 7.1 pg/mL) to 2.36 ± 0.71 pmol/L (22.3 ± 6.7 pg/mL), $p<0.005$). There was no change in serum calcium and all other markers remained within normal ranges. Similarly, Kilpinen-Loisa et al. (18) evaluated vitamin D3, 1000 IU administered orally five days a week over 10-weeks and saw a significant increase in median serum 25(OH)D concentrations (46 to 56nmol/L, p=0.012). The control group saw a decrease (43nmol/L to 37nmol/L, p=0.038). All participants in the treatment group had serum 25(OH)D concentrations >38nmol/L, with 19% reaching >80nmol/L. Conversely, 35% in the control group had levels <38nmol/L,

with none reaching >80nmol/L. There were no notable changes in P-Ca, S-PINP, or S-ICTP during the trial.

Theis et al. (34) found that a daily leucine supplementation of 192 mg/kg (~9-15g/day) body mass over 10 weeks increased muscle strength, volume, and C-reactive protein (CRP) ($p<0.001$) compared to a control group ($p>0.05$). Significant interaction effects were seen for muscle strength, volume, and CRP ($p=0.019$, $p<0.001$, and $p=0.045$, respectively). Post intervention, muscle soreness and stress levels were significantly lower in the leucine group ($p<0.01$), and ratings of mood and general wellbeing were significantly higher ($p<0.05$). A daily questionnaire rated participants' fatigue, sleep quality, muscle soreness, stress, and mood on a 5-point scale. Wellbeing was determined by summing scores. Median ratings in week 1 and 10 were compared between groups.

Discussion

We found a number of high-quality studies on PA and nutrition interventions, and promising findings of impact on cardiovascular, musculoskeletal, and cognitive outcomes. All interventions that induced changes in health measures also showed detraining on withdrawal highlighting the need to integrate PA and dietary interventions over the longer term. The positive effects of both PA and nutritional interventions on muscular functioning support the potential for combining PA and nutrition interventions in future trials.

The overall findings from the non-controlled studies suggest that both the PA and nutrition interventions were effective at increasing musculoskeletal, cognitive, and cardiovascular measures. However, whilst the findings are positive the lack of randomisation and control groups and smaller sample sizes in these studies support the need for well-designed RCTs. Nevertheless, there were six RCTs which all reported improvements in parameters, including one RCT (36) that assessed cardiovascular health using a strength and aerobic program. The primary outcomes from a submaximal exercise intensity test showed an increase in cardiovascular fitness through changes in aerobic capacity in the training group with higher VO2 and VE peak values at week 12 and an increase in the duration of the peak VO2 tests.

An additional two RCTs explored the impact of aerobic and strength interventions on cardiovascular and muscular health outcomes. Interestingly Van Wely et al's study (37) failed to demonstrate effectiveness, specifically, there was no improvement in increasing PA or fitness levels. In comparison, Verschuren et al. (38) showed potential for improvements in both cardiovascular and musculoskeletal health. However, it is important to mention the differences between the PA programs and outcome measures used in each study. Verschuren's (38) assessment of aerobic and anaerobic capacity and muscle strength used methods that could be argued more valid and reliable direct measures of CV and MSK health (shuttle run test, muscle power sprint test (W), 30 sec rep max. Whereas Van Wely (37) indirectly measured CV health by means of stride rate (n/day; mins/day), parent reported PA levels, sports participation (%) and a 1 min walk test (m). One RCT assessed strength vs aerobic exercise on muscular outcomes (6). Progressive resistance training (PRT) was compared to high intensity circuit training (HICT). Both groups experienced functional improvements, but HICT was found to be more effective. Surprisingly, and importantly the HICT group spent less time training compared to the PRT, yet still resulted in significant gains. The remaining two RCTs assessed the impact of strength training on skeletal outcomes. Chad et al.(6) focused on weight bearing activity of the upper, and lower extremities and truncal areas to improve functionality whilst Chen et al. (7) used a home-based virtual cycling program. Both studies reported increases in femoral BMD and BMC compared to controls, however, there was a vast difference in training methodology and duration, 8 months compared to 12 weeks suggesting that even small doses may benefit this group. Further studies and investigation of implementation are warranted.

Notably all intervention outcomes reduced after training stopped, highlighting the need to maintain exercise over the longer term. Two nutrition RCTs similarly showed potential for improvement, Kilpinen Loisa et al. (18) administered a single high dose vitamin D supplement which was effective in increasing serum vitamin D and calcium levels in children and young people with CP, with optimum levels being critical for bone health and metabolism. Theis et al.(34) supplemented with the amino acid Leucine, interestingly this alone resulted in an increase in muscle strength and volume and a reduction of systemic inflammation. Considering the potential effects shown in this study, it may be beneficial to assess the effects of leucine in combination with PA or targeted exercises in this group. This particular study saw a high rate of compliance and it highlights the feasibility and safety of introducing dietary supplementation in this group. Similarly, Hemayattalab et al.(13) carried out a combined PA and diet intervention in children with intellectual disability. They assessed the effects of PA and calcium on bone mineral density with supplementation of a calcium rich cow's milk with added vitamin D. Over 6 months the training group that supplemented with calcium saw a 14% increase in femoral neck BMD compared to a 10% increase in the training group who did not supplement. This highlights the potential that combined interventions are feasible in those with neurodisabilities and combined method studies may indeed increase effectiveness. However, a study carried out in 18-30-year-old healthy males, although not directly comparable found the combination of a leucine supplement with resistance training did not increase muscle mass or strength (1). The study also used ultrasound to determine muscle mass and strength, but measured mass of the lower extremities compared to the upper extremities measured by Theis et al. (34). Importantly, Aguiar et al. (1) supplemented with 3g of leucine daily, compared to the 9-15g daily dose used in Theis et al's study.

Limitations

The main limitation of this review was the heterogeneity of the studies, and therefore there was a lack of consistency concerning intervention methods and the outcome measures chosen, making it difficult to conclude. The PA studies only used participants with GMFCS Levels I-III, dismissing Levels IV-V. Further work needs to be done on those with more severe disability. The use of core outcome sets and the template for intervention description and replication (TIDieR) reporting should be encouraged in clinical trials in this group. Notably, there was a lack of studies for our chosen outcomes, particularly concerning metabolic and cognitive health and more focus on cardiovascular fitness and strength. There was only one study that reported cognitive outcomes and an overall lack of nutrition interventions in this group. Much of the literature surrounding CP and diet focuses on nutritional status and feeding difficulties. Furthermore, there were no combined PA and nutrition interventions in children and young people with CP in the searches, resulting in the need to conduct individual nutrition and PA searches.

Conclusion

To our knowledge and based on the results of this systematic review, no study to date has assessed the effectiveness of PA and nutrition interventions for children and young people with cerebral palsy to improve physical health and cognitive outcomes. The majority of the studies were effective and showed significant results, however, due to the heterogeneity of the methods and outcome measures reported the evidence is lacking to conclude what are the most effective programs and doses to improve physical health. However, it is important to note that many of the studies had promising results and highlighted that both nutrition and PA interventions potentially lead to changes in skeletal, muscular, and cardiovascular systems. Further studies may wish to explore combinations of these interventions to optimise impact. We also noted a trend to detrain quickly on withdrawal of training supporting the need to integrate exercise interventions into everyday life. In addition, this review highlighted the lack of nutrition and dietary studies in this population group, despite the potential for effect. There were no studies exploring the impact of exercise or diet on metabolic functioning. In summary, our review by bringing together all studies shows a potential gap to substantially improve both physical and cognitive functioning with PA and nutrition interventions and a paucity of high-quality research in this group in various settings. This is in stark comparison to extensive research in typically developed and other clinical conditions. Notably, we found no studies describing the impact of interventions on metabolic markers of health despite reported metabolic deficits in people with CP.

Registration and protocol

The systematic review protocol is registered on the PROSPERO database (registration ID: CRD42022322143) under the title: A systematic review of the effectiveness of lifestyle interventions for children and young people with cerebral palsy to improve physical health and cognitive outcomes.

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Table 1: Characteristics of selected studies

Physical Activity Studies

	Study Design	Participants	Type of Activity	Activity	Program Length	Frequency (times per week)	Activity Duration	Setting	Health outcome measured	Health outcome (group)	Effective
Chad, 1999	RCT	n=18 M:5/F:13 Age: 9 ± 2.8 I:9/ 9:C	weight bearing / strength	weight bearing movement	8 months	2 x (1st 2 months) then 3 x (last 6 months)	1 hr	Physio centre	Proximal femur BMC (g) Femoral neck BMC (g) Femoral neck vBMC (g/cm3)	Skeletal	Yes
Chen, 2013	RCT	n=27 M:18/F:9 Age: 8.7 ± 2.2 I:13/C:14	muscle strengthening	home based virtual cycling training	12 weeks	3 x	50 mins	Home	Gross Motor Function Muscle Strength Bone Density	Skeletal	Yes
Darrah, 1999	Single Group Design	n=23 M:8/F:5 Age:14.2 ± 2.3	aerobic and strength	aerobic and weights	10 weeks	3 x	70-90 mins	Community fitness facility	HR for submaximal exercise Energy Expenditure index (EEI) (bpm) Muscle Strength (kg) Flexibility - ROM (cm)	Cardiovascular & Skeletal	Yes

Gorter, 2009	Quasi experimental	n=13 M:8/F:5 Age:9.9 ± 1.2	aerobic	circuit training	9 weeks	2 x	30 mins	School	Maximum aerobic capacity (HR) (Bruce treadmill test) 6-minute-run test (m)(walking distance and walking velocity) Functional mobility (ambulation) (Timed Up and Down Stairs test	Cardiovascular	Yes
Knights, 2016	Case series study	n=8 M:6/F:2 Age:14.3 ± 2.5	aerobic	internet platform exergame cycling programme	6 weeks	3 x (minimum)	30 mins	Home	GMFCS III-specific shuttle run test (SRT-III) 6-minute walk test Wingate arm cranking test Anthropometric measurements	Cardiovascular	No
Maltais, 2016	Quasi experimental	n=17 M:10/F:7 Age:10.2 ± 2.7 CP:8/TD:9	aerobic	shuttle run	1 day	1 day	n/a	Rehab centre	Intense exercise: SRT maximum HR (bpm), number of shuttles completed, the maximal SRT speed (km/h). Cognitive function: Response accuracy (%) (precision), reaction time (ms) (processing speed), interference effect (size)(inhibition)	Cognitive	Yes

Nsenga Leunkeu, 2012	Quasi experimental	n=24 M:12/F:12 Age:14.2 ± 1.9 I:12/C:12	Aerobic	walking	8 weeks	3 x	40 mins	Rehab centre	Peak oxygen consumption (VO2peak) Peak ventilation Peak HR 6MWT distance	Cardiovascular	Yes
Robert, 2013	Cross-sectional	n=20 M:9/F:11 Age:9.3 ± 1.9 CP:10/ TD:10	aerobic	Wii Fit games	1 day	1 day	60 mins	unclear	Exercise intensity (%HRR) (HRR = maximum heart rate - resting heart rate) % time spent at intensity greater >40% of HRR Strength (Nm/kg) (Knee, Hip, Ankle) Active Range of Motion (º) (Knee, Hip, Ankle)	Cardiovascular	Yes
Shranz, 2018	RCT	n=22 M:15/F:7 Age: 12.8 ± 2,6 Strength:11/ Aerobic:11	strength vs aerobic	progressive resistance training or high-intensity circuit training	8 weeks	3 x	40 mins and 28 mins	Home	Total isometric strength (N/kg), MPST mean (PWR) (Muscle power sprint test), MPST max (PWR), TUGT (s) (Timed up and Go test), TST (s) (Timed Stairs test), 6-minute walk test (m), EEI (score) (Energy Expenditure Index), GPS (deg)	Muscular	Yes

Shinohara, 2002	Quasi experimental	n=11 Age 14.4 ± 1.3 Leg group:6/ Arm group:5	aerobic exercise	leg vs arm exercise	6 to 20 weeks	2 x	20 mins	unclear	VO2 at the AT point (ml/kg/min) Frequency of attendance Total period of exercise Self-Assessment of Endurance	Cardiovascular	Yes
Unnithan, 2007	RCT	n=13 M:4/F:9 Age:15.8 ± 1.4 I:7/C:6	aerobic and strength	weights and aerobic intervals	12 weeks	3 x	70 mins	unclear	HR Lactate Submaximal VO2 VO2peak RER, VE, VE/VO2 GMFM	Cardiovascular	Yes
Van Wely, 2014	RCT	n=49 M:28/F:21 Age:9.8 ± 1.7 I:25/C:24	aerobic and strength	muscle strength with weighted vest, anaerobic games (running)	6 months total (4 months PA)	2 x (1st 2 mths) / 1 x (last 2 mths)	1 hour	Home & Rehab centre	Strides (n/day), medium to high stride rate (mins/day), high stride rate (mins/day). Parent reported PA (min/wk), Sports club participation (%), PA norm (%), Inactive (min/wk), 1MWT (m), Functional strength (reps)	Cardiovascular & Muscular	No

Verschuren, 2007	RCT	n=68 M:44/F:24 Age:12.2 ±2.6 I:34/C:34	aerobic and anaerobic	aerobic, anaerobic and strength circuit. Task specific exercise	8 months	2 x	45 mins	School	Aerobic capacity – 10m-shuttle run test Anaerobic capacity - mean power (W) from the Muscle Power Sprint Test, Agility - 10 x 5-m Sprint Test. Muscle strength (lower extremities) 30-sec repetition maximum. BMI	Cardiovascular & Muscular	Yes
Nutrition Studies											
Karagiannis, 2021	Quasi experimental	n=15 M:8/F:7 Age:12.5 ± 8.2 I:15	Vitamin D bolus in fortified Orange Juice	Vitamin D levels	4 weeks	1 high dose	n/a	Rehab centre	25(OH)D PTH (Parathyroid hormone) Calcium (Ca)	Skeletal	Yes
Kilpinen Loisa, 2007	RCT	n=44 M:25/F:19 Age: 13.2 (median) I:21/C:23	High dose Vitamin D	calcium and bone metabolism	10 weeks	5 x	n/a	School	25(OH)D PTH (Parathyroid hormone) Calcium (Ca)	Skeletal	Yes

Theis, 2021	RCT	n=21 M:12/F:9 Age:18.5 ± 2.25 I:10/C:11	Leucine supplement	muscle, metabolism, body comp, inflammation & wellbeing	10 weeks	7 days	n/a	Home	Muscle strength Muscle volume C-reactive protein Wellbeing Fat and carbohydrate oxidation Resting energy expenditure Body composition	Muscular	Yes

Age reported as mean ± SD; RCT = randomised controlled trial, BMC = bone mineral content, vBMC = volumetric bone mineral content, g = gram, g/cm3 = gram per centimetre cubed, HR = heart rate, bpm = beats per minute, EEI = energy expenditure index, kg = kilogram, cm = centimetres, m= metres, GMFCS = gross motor function classification system, CP = cerebral palsy, TD = typically developing, I = intervention, SRT = shuttle run test, km/h = kilometres per hour, ms = milliseconds, VO2 = maximal oxygen consumption, 6MWT = six minute walk test, HRR = heart rate reserve, Nm/kg = newtons per kilogram, º = degrees, PWR = power, s = seconds, AT = anaerobic threshold, ml/kg/min = millilitres per kilogram per minute, RER = respiratory exchange ratio, VE = ventilation, VE/VO2 = ventilatory equivalent for oxygen, GMFM = gross motor function measure, n/day = number per day, min/wk = minutes per week, % = percentage, W = watts, 25(OH)D = 25 hydroxy vitamin D

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