University of Groningen

# Differential effects of long-term aerobic versus cognitively-engaging physical activity on children's visuospatial working memory related brain activation

de Bruijn, A G M; van der Fels, I M J; Renken, R J; Königs, M; Meijer, A; Oosterlaan, J; Kostons, D D N M; Visscher, C; Bosker, R J; Smith, J

*Published in:*
Brain and Cognition

*DOI:*
10.1016/j.bandc.2021.105812

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*
Publisher's PDF, also known as Version of record

*Publication date:*
2021

Link to publication in University of Groningen/UMCG research database

*Citation for published version (APA):*
de Bruijn, A. G. M., van der Fels, I. M. J., Renken, R. J., Königs, M., Meijer, A., Oosterlaan, J., Kostons, D. D. N. M., Visscher, C., Bosker, R. J., Smith, J., & Hartman, E. (2021). Differential effects of long-term aerobic versus cognitively-engaging physical activity on children's visuospatial working memory related brain activation: A cluster RCT. *Brain and Cognition*, *155*, [105812]. https://doi.org/10.1016/j.bandc.2021.105812

**Copyright**
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

**Take-down policy**
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

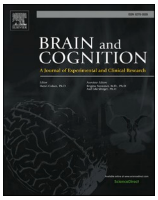
*Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

Brain and Cognition 155 (2021) 105812

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c



# Differential effects of long-term aerobic versus cognitively-engaging physical activity on children's visuospatial working memory related brain activation: A cluster RCT

A.G.M. de Bruijn[a,*], I.M.J. van der Fels[b], R.J. Renken[c], M. Königs[d], A. Meijer[e], J. Oosterlaan[d,e], D.D.N.M. Kostons[a], C. Visscher[b], R.J. Bosker[a], J. Smith[b], E. Hartman[b]

[a] Groningen Institute for Educational Research, University of Groningen, Grote Rozenstraat 3, 9712 TG Groningen, the Netherlands
[b] Center for Human Movement Sciences, University Medical Center Groningen, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, the Netherlands
[c] Neuroimaging Center Groningen, University Medical Center Groningen, University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, the Netherlands
[d] Emma Neuroscience Group, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Postbus 22660, 1100 DD Amsterdam, the Netherlands
[e] Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Van der Boechorststraat 7, 1081 BT Amsterdam, the Netherlands

ARTICLE INFO

*Keywords:*
Exercise
Cognition
Executive functioning
Preadolescents
Functional MRI
Primary education

ABSTRACT

Different types of physical activity are thought to differentially affect children's brain activation, via physiological mechanisms, or by activating similar brain areas during physical and cognitive tasks. Despite many behavioral studies relying on these mechanisms, they have been rarely studied. This study looks at both mechanisms simultaneously, by examining effects of two physical activity interventions (aerobic vs. cognitively-engaging) on children's brain activation. Functional Magnetic Resonance Imaging (fMRI) data of 62 children (48.4% boys, mean age 9.2 years) was analyzed. Children's visuospatial working memory related brain activity patterns were tested using a Spatial Span Task before and after the 14-week interventions consisting of four physical education lessons per week. The control group followed their regular program of two lessons per week. Analyses of activation patterns in SPM 12.0 revealed no activation changes between pretest and posttest ($p >$ .05), and no differences between the three conditions in pretest–posttest changes in brain activation ($p >$ .05). Large inter-individual differences were found, suggesting that not every child benefited from the interventions in the same way. To get more insight into the assumed mechanisms, further research is needed to understand whether, when, for whom, and how physical activity results in changed brain activation patterns.

## 1. Introduction

The positive effects of physical activity on children's cognition and academic achievement are often explained by referring to changes in underlying brain structure and functioning (e.g. Best, 2010; Donnelly et al., 2016; Gunnell et al., 2019; Tomporowski & Pesce, 2019). Recent studies conclude that, in accordance with these mechanisms, physical activity interventions seem to have an effect on children's brain structure and functioning (see Meijer, Königs, Vermeulen, et al., 2020 for a *meta*-analysis; and Valkenborghs et al., 2019 for a review). Interestingly, most studies examining effects of physical activity on children's brains have focused on moderate-to-vigorous physical activity, despite the fact that different types of physical activity are expected to result in different adaptations in the brain because of different underlying mechanisms (Tomporowski & Pesce, 2019). To get more insight into these different mechanisms, in this study we will examine the effects of two different types of physical activity (aerobic and cognitively-engaging) on children's brain activation using functioning magnetic resonance imaging (fMRI).

### 1.1. *Physiological mechanisms*

Most studies examining the effects of physical activity on children's cognition and brain activation have provided evidence for beneficial

---

* Corresponding author at: Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Van der Boechorststraat 7, 1081 BT Amsterdam, the Netherlands.

*E-mail addresses:* a.g.m.de.bruijn@vu.nl (A.G.M. de Bruijn), i.m.j.van.der.fels@umcg.nl (I.M.J. van der Fels), r.j.renken@umcg.nl (R.J. Renken), m.konigs@amsterdamumc.nl (M. Königs), a.meijer@vu.nl (A. Meijer), j.oosterlaan@vu.nl (J. Oosterlaan), d.d.n.m.kostons@rug.nl (D.D.N.M. Kostons), c.visscher@umcg.nl (C. Visscher), r.j.bosker@rug.nl (R.J. Bosker), j.smith@umcg.nl (J. Smith), e.hartman@umcg.nl (E. Hartman).

https://doi.org/10.1016/j.bandc.2021.105812
Received 27 August 2021; Received in revised form 11 October 2021; Accepted 13 October 2021

effects of aerobic physical activity (see García-Hermoso et al., 2021; De Greeff et al., 2018; Donnelly et al., 2016; Valkenborghs et al., 2019). Aerobic physical activity here refers to physical activity at a moderate-to-vigorous intensity level (MVPA), not to be confused with the distinction between aerobic and anaerobic physical activity that is often used in sports medicine. According to physiological mechanisms, aerobic physical activity, after one bout, facilitates cognition via increased cerebral blood flow and an upregulation of neurotransmitters (e.g. dopamine, monoamine, brain-derived neurotrophic factors). More frequent participation in physical activity results in structural and functional brain adaptations due to, amongst others, angiogenesis and neurogenesis in brain areas supporting cognitive performance (Best, 2010).

Only few studies have examined these physiological mechanisms by investigating aerobic physical activity's effects on children's brain functioning (see Meijer, Königs, Vermeulen, et al., 2020; Valkenborghs et al., 2019). All studies focused on brain activation during tasks measuring one specific aspect of cognition, namely inhibition. Inhibition is one of the three core executive functions (together with working memory and task switching; Miyake et al., 2000): the higher-order cognitive functions needed to organize and control goal-directed behavior (Diamond, 2013). Inhibition refers to the ability to withhold prepotent, automatic responses that are considered irrelevant for the task at hand (Diamond, 2013). In one of these studies, Davis et al. (2011) implemented a 13-week daily after-school aerobic physical activity intervention for overweight children. The intervention resulted in increased prefrontal cortex activity and reduced posterior parietal cortex activity during an anti-saccade task. Krafft et al. (2014) examined an 8-month daily after-school aerobic program in overweight children, resulting in decreased activation during an anti-saccade task in regions related to anti-saccade performance (e.g. inferior frontal gyrus and anterior cingulate cortex), and increased activation in regions supporting cognitive control (e.g. superior frontal and medial frontal gyri). Chaddock-Heyman et al. (2013) implemented a 9-month daily after-school aerobic physical activity program, resulting in significant activity decreases in the right anterior prefrontal cortex during Flanker task performance.

Overall, these studies show that aerobic physical activity results in a mix of increases and decreases in brain activity during inhibition tasks. In addition, the observed changes in brain activation were accompanied by improvements in cognitive task performance in all studies. Findings did not result in a clear picture however, as brain activation changes were inconsistent (e.g. significant changes in the anterior cingulate cortex in one study, but not another) or conflicting (e.g. increased prefrontal cortex activity in one study, but decreased activity in another). Part of this inconsistency has to do with the difficulty in interpreting changes in brain activity. When coupled with increased cognitive performance, both increases as well as decreases in activity can represent a positive effect, that is: increases in activity are thought to reflect an increased ability to allocate relevant brain resources, whereas decreases in activity are interpreted as a more efficient use of brain resources (e.g. Voelcker-Rehage et al., 2011; Voelcker-Rehage & Niemann, 2013). These interpretative difficulties and inconsistent results make it difficult to derive definite conclusions on the applicability of the physiological mechanisms. Also, two of the three studies presented above specifically focused on children with overweight, leaving it unknown whether similar results apply to healthy-weight children.

Also, previous studies focused exclusively on inhibition-related brain activity, whereas positive effects of physical activity have also been found for working memory (e.g. De Greeff et al., 2018). Importantly, of the three executive functions, working memory is seen as the strongest predictor of children's academic achievement (Cortés Pascual et al., 2019). To get further insight into the mechanisms underlying the effects of physical activity on children's cognition and academic achievement, it thus seems important to include working memory as outcome measure as well. In this sense, especially the visuospatial aspect of working memory is interesting, because of its strong link to mathematics performance, the academic domain that is most often found to be positively affected by physical activity interventions (e.g. Alvarez-Bueno et al. 2017; Singh et al., 2019).

### 1.2. Cognitive stimulation mechanism

Besides the physiological mechanisms, studies have put forth the cognitive stimulation hypothesis, arguing that cognitively-engaging physical activity is even more beneficial for cognition than aerobic physical activity containing 'simple', repetitive exercises (e.g. Diamond & Ling, 2016; Pesce, 2012; Tomporowski & Pesce, 2019; Vazou et al., 2016). Cognitively-engaging physical activity entails activities requiring a high amount of cognitive effort to understand new information, such as complicated rules; and activities in which complex motor skills are practiced, such as multi-limb coordination (Tomporowski et al., 2015). Examples of this type of activity can be found in team sports, where children have to focus and pay attention to the game, plan a strategy, adhere to game rules, collaborate with their teammates, and so on, while simultaneously executing (complex) motor skills. Cognitively-engaging physical activities require an adaptive ability of the brain to constantly respond to changing demands, thereby supporting neuroplasticity of the brain (De Greeff et al., 2018). Also, these activities are thought to partly activate similar brain areas and networks as those used during cognitive tasks, promoting the development and efficiency of these brain areas and networks, consequently aiding cognitive performance (Pesce, 2012). Promising effects on children's executive functioning and academic achievement have been found for this type of physical activity, with seemingly even stronger effects than for aerobic physical activity (De Bruijn et al., 2020; De Greeff et al., 2018; Egger et al., 2019; García-Hermoso et al., 2021; Mazzoli et al., 2021; Schmidt et al., 2015).

The cognitive stimulation hypothesis is relatively new and, to our knowledge, only one study has examined the effects of cognitively-engaging physical activity on children's brain activity, using functional near-infrared spectroscopy (fNIRS) (Mazzoli et al., 2021). This study specifically focused on effects of classroom breaks: short bouts of physical activity in-between academic lessons that are unrelated to the curricular content. These physical activities cannot directly be equated to the PE classes or physical activity programs that were examined in the previously mentioned RCTs using aerobic physical activity (Chaddock-Heyman et al., 2013; Davis et al. 2011; Krafft et al., 2014) because of their shorter duration (4–5 min). Yet, results of this study can provide some insight into the neural correlates of cognitively-engaging physical activity in children. Results indicated more efficient neural activity (i.e. greater positive change in the proportion of deoxygenated hemoglobin) in the dorsolateral prefrontal cortex of children that followed the cognitively-engaging physical activity classroom breaks compared to the usual practice control group, a result that was not found for children following the simpler physical activity classroom breaks.

In addition, some studies in older adults studied the effects of coordinative physical activity on brain activity (Voelcker-Rehage & Niemann, 2013). Coordinative physical activity shows considerable overlap with cognitively-engaging physical activity, in that both require the involvement of complex motor skills and higher-order cognitive processes (referring to the cognitive skills that guide and control goal-directed behavior, i.e. fluid intelligence, working memory, executive functions; Diamond, 2013). In their review, Voelcker-Rehage et al. (2011) concluded that the acquisition of new skills during coordinative physical activity is related to increased activation in the prefrontal and parietal cortex. With repeated execution of a newly learned skill, frontal lobe activity decreases, and activity becomes more focalized and efficient, presumably reflecting automatization of the newly learned skill. It is unclear how these brain activity changes relate to cognitive performance however.

### 1.3. *Different types of physical activity*

Following the physiological mechanisms and the cognitive-stimulation hypothesis, it is likely that the mechanisms by which physical activity affect cognition and academic performance differs depending on the type of physical activity involved. In line with this assumption, animal studies have revealed that different types of physical activity affect the brain differently (Black et al., 1990). Also in humans, it has been argued that different types of activities differ in underlying brain changes (Voelcker-Rehage & Niemann, 2013). Only one study has directly compared the effects of different types of physical activity on brain activation using fMRI, examining the effects of cardiovascular and coordination training on cognition and brain activation in older adults (Voelcker-Rehage et al., 2011). Both types of physical activity led to improved executive functioning, coupled with decreased activation in the prefrontal areas. In addition, specific effects were found for the different training programs, with decreased activation in the sensorimotor network (i.e. several superior, middle, and medial frontal, superior and middle temporal cortical areas) for the aerobic intervention group; but increased activation in the visual-spatial network (i.e. inferior frontal gyrus, and superior parietal lobule) and subcortical structures that are considered to be important for process automatization (i.e. thalamus and caudate body) in the coordinative intervention group. Based on these results it was concluded that the mechanisms by which physical activity affects cognition depend on the type of activity involved.

A more recent study by Ludyga et al. (2019) could not support these differential effects of different types of physical activity in children however. Using electroencephalography (EEG), they compared effects of two afternoon programs focusing on either aerobic or coordinative physical activity (three session of 45 min per week, during 10 weeks) and a control condition (following a sedentary afterschool program) on the P300 component of event-related potential (ERP). The P300 component is thought to reflect neural activity related to stimulus evaluation speed and allocation of attentional resources. Results did not reveal any difference between the different types of physical activity or the control group, neither on behavioral, nor on neurophysiological indices of inhibitory control. These results were surprising, as they are contradictory to the hypothesized mechanisms, and as they are not in line with previously reported results (see Meijer, Königs, Vermeulen, et al., 2020). Therefore, further research is required to get more insight into the effects of different types of physical activity on children's brain functioning.

### 1.4. *The present study*

To our knowledge, only one study has yet compared effects of different types of physical activity on children's brain functioning, reporting no significant differences between aerobic and coordinative physical activity using EEG (Ludyga et al., 2019). In the present study, we aim to get more insight into these effects, by using fMRI to examine whether children's brain activation during a visuospatial working memory (VSWM) task is differently targeted by distinct types of physical activity. Although EEG and fMRI both give insight into brain activity, fMRI can record activity changes that are not captured by EEG (due to higher spatial resolution and the ability to examine sub-cortical regions; Mulert, 2009). As the strongest evidence base exists for aerobic physical activity, and considering the promising effects of cognitively-engaging physical activity in stimulating children's cognitive and academic development, the focus will be on those two types of physical activity. Different effects on VSWM-related brain activation are expected for the two interventions based on the physiological mechanisms and the cognitive stimulation mechanism (Tomporowski & Pesce, 2019); and based on differential fMRI effects found in older adults (Voelcker-Rehage et al., 2011). Results of this study increase our understanding of how different types of physical activity affect the brain, providing useful information for developing effective physical activity interventions to improve children's cognitive and academic development.

**Table 1**
Baseline characteristics of children included in the analyses, for the total sample and separately for the control group, aerobic intervention group and cognitively-engaging intervention group.

| | Total sample (*n* = 62) | Control group (*n* = 17) | Aerobic intervention group (*n* = 22) | Cognitively-engaging intervention group (*n* = 23) |
|---|---|---|---|---|
| Grade, n grade 3 (%) | 28 (45.2) | 5 (29.4) | 12 (54.5) | 11 (47.8) |
| Gender, n boys (%) | 30 (48.4) | 7 (41.2) | 11 (50.0) | 12 (52.2) |
| Age, in years (SD) | 9.20 (0.61) | 9.37 (0.50) | 9.22 (0.72) | 9.04 (0.57) |
| SES$^{a}$ (SD) | 4.59 (1.12) | 4.59 (0.91) | 4.73 (1.01) | 4.46 (1.37) |
| BMI$^{b}$ n non-overweight (%) | 53 (88.3) | 17 (100) | 19 (90.5) | 17 (73.9) |
| BMI n overweight (%) | 6 (10.0) | – | 2 (9.5) | 4 (17.4) |
| BMI n obese (%) | 1 (1.7) | – | – | 1 (4.3) |
| SR completed tracks (cardiovascular fitness) $^{c}$ | 36.7 (16.8) | 43.1 (17.9) | 38.4 (16.7) | 30.4 (14.6) |

*Note.* $^{a.}$ SES = socioeconomic status; measured with parental questionnaire. Level of parental education ranged from no education (0) to postdoctoral education (7) (Schaart et al., 2008). Mean level of education of both parents was calculated, or, in case only one of the parents' educational level was specified, this was used as measure of SES. $^{b.}$ BMI category was determined based on the international classification values by Cole and Lobstein (2012). BMI data was missing for two participants. $^{c.}$ Number of completed tracks of the 20 m Shuttle Run test (Adam et al., 1988) was taken as an indicator of aerobic fitness.

## 2. Materials and methods

### 2.1. *Design*

This study is part of a large cluster randomized controlled trial at 22 primary schools in the Netherlands (*n* = 891 children) examining the effects of two different types of physical activity interventions on children's physical fitness, motor skills, cognition and academic achievement (RCT; '*Learning by Moving*' (De Bruijn et al., 2020; Meijer, Königs, van der Fels, et al., 2020; van der Fels, Hartman, et al., 2020), for an elaborate description of the project design). At each school a third and a fourth grade class participated, of which one class was randomly assigned to one of the two intervention groups, following four intervention lessons per week. The other class was the control group, following their regular physical education (PE) program of two lessons per week. Parents from participating children could voluntarily sign-up their child for the MRI sub-study. Only children over 8 years without contra-indications for MRI were included. An inclusion protocol was followed to ensure that children were equally sampled over grades, conditions (control, aerobic intervention, cognitively-engaging intervention) and schools, and to ensure that boys and girls were equally represented. If the number of eligible students that signed up exceeded the number of slots that had to be filled, it was randomly decided which child could participate. There were deviations from the inclusion protocol in case the number of children that met the inclusion criteria could not be met. As a consequence, some schools are oversampled in the study, whereas others are underrepresented. The inclusion protocol and deviations from this protocol can be found in Appendix A.

### 2.2. *Participants*

Ninety-two children (47 girls, 51.1%) participated in this study.

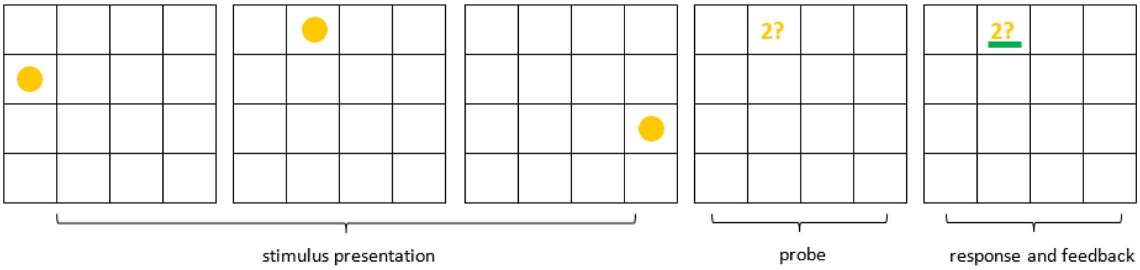


**Fig. 1.** Schematic overview of a low working memory load trial of the spatial span task (18). In this example trial, a sequence of three (low load) yellow (working memory) circles was presented (stimulus presentation). Following, a probe appeared, asking whether the second circle appeared in that specific box of the grid. In this example, 'yes' was the correct answer (the second circle was in the position indicated by the number two). A green bar was presented underneath the probe as feedback, because a correct response was given (response and feedback).

Children were in grade 3 ($N = 46$, 50%) and grade 4 and had mean age of 9.14 years ($sd = 0.63$). Nine children dropped-out at posttest because of logistic problems (e.g. planning of scan time) or personal reasons, leaving 83 children who were scanned at both pretest and posttest. Twenty-one children were excluded from further analyses due to low quality of the data (see image analyses). Excluded children did not significantly differ from included children on relevant background characteristics (cognition, gender, age, BMI, VSWM, intensity of participation, motivation during PE; all $p > .05$), except for study site. Significantly more children were excluded for analyses in Groningen than in Amsterdam ($\chi^2$ (1) = 12.4, $p < .001$). We therefore added study site as covariate in the analysis to control for potential differences. An overview of the included and excluded children in the three groups at each stage of the study can be found in Appendix A.

A post-hoc power analysis was conducted to get an indication of the effect size that could be captured with this deviation from the anticipated sample size of 30 children per group. With the final sample size (comparing the experimental to the control group, $n \approx 20$ per group) and assuming a power of 0.80, an effect size of 0.65 or greater could be detected. When assuming a smaller power of 0.60, still an effect size of 0.50 or greater could be captured. These results show that our sample size, despite the deviations from the anticipated number of participants, was still large enough to capture a meaningful effect.

Descriptive statistics of the final number of included children ($n = 62$) are presented in Table 1. Children in the three groups did not significantly differ on age ($F$ (2, 59) = 1.44, $p = .24$), socioeconomic status (SES; $F$ (2, 59) = 0.32, $p = .73$), gender ($\chi^2$ (2) = 0.51, $p = .78$), grade ($\chi^2$ (2) = 2.55, $p = .28$), BMI classification ($\chi^2$ (4) = 5.48, $p = .24$), or cardiovascular fitness ($F$ (2, 58) = 3.12, $p = .052$). Children's parents or legal guardians provided written informed consent. This study was approved by the ethical board of the Vrije Universiteit Amsterdam (Faculty of Behavioural and Movement Sciences, approval number VCWE-S-15–00197) and is registered in the Netherlands Trial Register (NTR5341).

### *2.3. Materials*

#### *2.3.1. Imaging task*

The Spatial Span task (Van Ewijk et al., 2014; 2015; adapted from Klingberg et al., 2002), an adapted version of the dot matrix task of the Automated Working Memory Assessment (AWMA; Alloway, 2007), was used as a measure of visuospatial working memory. Test-retest reliability ($r = 0.83$) and validity of the test are considered good (Alloway et al., 2006; Alloway et al., 2008). The task has been successfully used in fMRI studies with adolescents (e.g. Van Ewijk et al., 2014; 2015), facilitating interpretation of our results on brain activity patterns. The task was implemented in E-prime (Psychology Software Tools, version 2.0.10.356). In the Spatial Span task, a 4 × 4 grid was presented on a screen behind the MRI scanner that was visible for the participant via a mirror attached to the head coil. In the grid, a sequence of either three (low memory load) or five (high memory load), yellow (working memory) or red (baseline) circles were presented for 500 ms each, with an inter-stimulus interval (empty grid) of 500 ms. Following this sequence, a probe consisting of a number and a question mark was presented in one of the 16 boxes in the grid. In the working memory trials, children were instructed to remember the order in which the circles were presented and, when the probe was shown, had to indicate with a right ('yes') or left ('no') button press whether the probe location matched the location of the stimulus that was indicated by the probe number. Children were instructed to respond within a 2000 ms timeframe. During baseline trials (red circles), three or five circles were shown in a predictable manner in the four corners of the grid and were always followed by a probe with the number 8. Children were instructed to look at the circles, but not to remember their order, and to always press 'no' when the probe appeared. Feedback was provided in both conditions via a green (correct response) or red (incorrect response) colored bar underneath the probe. The task consisted of four blocks each containing 24 trials, with a short break in between blocks, resulting in a total task duration of approximately 16 min. The percentage of correct working memory trials () were used as outcome measures for behavioral performance. A schematic overview of the task is presented in Fig. 1.

#### *2.3.2. Implementation measures*

As a check of intervention fidelity, three implementation measures were taken: number of lessons attended, intensity of the lessons and motivation during the lessons. Children in the aerobic intervention condition were expected to participate at a higher intensity levels compared to their peers in the control or cognitively-engaging intervention condition, as eliciting a high level of MVPA was the main aim of the aerobic intervention program. Attendance rates and motivation were not expected to differ between the three conditions.

The number of lessons attended was recorded only for children in the intervention conditions. The specialist teacher providing the intervention lessons noted when a child was absent during a lesson. Information on the number of lessons is not available for children in the control group, as the regular PE teacher was not asked to keep track of the number of lessons children followed, to lower the burden of study participation for teachers.

Time spent in MVPA during the lessons (in minutes) was used as an indicator of intensity of the lessons. MVPA was measured using accelerometers (ActiGraph GT3x+, Pensacola, FL, USA) which children wore on their right hip. Accelerations were measured in three directions using a frequency of 100 Hz and an epoch length of 1 s (Trost et al., 2011). The cut-off points by Evenson et al. (2008) were used to determine the number of counts per minute. The number of minutes spent at a moderate and a vigorous intensity level was summed to get a measure of time spent in MVPA per lesson, which was averaged over the two lessons.

Motivation was measured using a Dutch translation of the Intrinsic Motivation Inventory (IMI) (Ryan & Deci, 2000), which was slightly adapted to fit the specific PE context of this study. The IMI is a valid, reliable (α = 0.85) and widely-used measure of motivation (McAuley et al., 1989). Individual subscales can be selected and used based on study aims (McAuley et al., 1989). Five subscales of the original questionnaire were selected for this study: interest (3 items), effort (3 items), competence (3 items), pressure/tension (3 items), and value (2 items). The 14 items were scored on a five-point Likert-scale ranging from “strongly disagree” (1) to “strongly agree” (5). Examples of items that were included are: “It was important to me to do well in this PE lesson” and “I think I did pretty well during this PE lesson, compared to other students.”. Reliability analysis showed that the reliability of the initial 14-item scale was insufficient (α = 0.68). Consequently, items belonging to the “pressure/tension” subscale were removed, resulting in an 11-item scale with a good reliability (α = 0.75). The average score on the questionnaires for the two lessons was taken as a measure of students’ motivation during the intervention programs.

### 2.4. Procedure

Two fourteen-week intervention programs, each consisting of four lessons per week (56 lessons in total), were developed by PE teachers and Human Movement Sciences researchers. The intervention length was chosen because of feasibility reasons, as the 14-week intervention period fitted precisely in a primary school year semester (i.e. the intervention was not interrupted by holidays). Support for the 14-week period was provided by a *meta*-analysis in which it was shown that studies using a similar intervention period had reported positive effects on cognition and academic achievement as well (De Greeff et al., 2018). One intervention focused on aerobic physical activity, aiming to improve children’s cardiovascular fitness via exercises that elicited high heart rate levels. Included exercises focused on repetitive and automated skills, for example running, relays, or individualized exercises such as jumping jacks, planks, or squats. The cognitively-engaging intervention focused on challenging children’s cognitive and motor skills by including exercises (e.g. throwing and catching, balancing) and games (e.g. soccer and dodgeball) that required complex movements, and that engaged children’s cognitive skills via difficult or fast-changing rules (Best, 2010). An elaborate description of the intervention programs can be found in previous manuscripts (De Bruijn et al., 2020; Meijer, Königs, van der Fels, et al., 2020; van der Fels, Hartman, et al., 2020).

All intervention lessons had a predetermined duration of 30 min. Lessons were delivered by hired PE teachers who were familiarized with the interventions in a training session and via a detailed manual. Children in the control groups followed their regular PE program, participating in two lessons each week, which were provided by their own teacher. Intensity during and motivation for the PE lessons was measured during two PE lessons chosen based on their representativeness of the intervention (one at the start and one at the end of the intervention). Children participated in the MRI protocol in the two weeks before the start of, and the two weeks after the intervention program. In this same period, behavioral measures were taken of their aerobic fitness, motor skills, cognition, and academic achievement. These measurements were taken at their own school by trained research assistants, during regular PE lessons (physical measures), individually in a quiet room (cognition), and during class time (academic achievement) (see previous publications of the project for more details on the behavioral measures and outcomes: De Bruijn et al., 2020; Meijer, Königs, van der Fels, et al., 2020; van der Fels, Hartman, et al., 2020).

Children were familiarized with the scanner and the task in a half hour session before data acquisition at pretest, using a mock scanner and a laptop. Children responded to the task by using an MRI compatible button-box (Current designs Inc., Philadelphia, USA) which was connected to the computer. Head movements were minimized by inserting small, wedge-formed pillows between the head coil and the child’s head. Children received a small present and a copy of their structural T1-weighted scan after the posttest.

### 2.5. Image acquisition

The imaging protocol was carried out at two different sites (Amsterdam and Groningen) on either a 3 Tesla whole-body unit (Discovery MR750, GE Healthcare, Milwaukee, Wisconsin; Amsterdam) or a 3 Tesla Philips Intera scanner (Philips Medical Systems, Best, the Netherlands; Groningen), using a 32-channel head coil and closely-matched acquisition parameters. Four runs with T2*-weighted functional gradient echo-planar images (EPI) were acquired using the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 35 ms, flip angle (FA) = 80°, field of view (FOV) = 211 mm, slice thickness = 3.0 mm, interslice distance = 0.3 mm, 135 dynamics, and 64 × 64 grid (Amsterdam protocol), or 64 × 60 grid (Groningen protocol), voxel size = 3.3 × 3.3 × 3.3 mm. Two spin echo EPI scans with opposing polarities of the phase-encode blips were acquired (TR = 6000 ms, TE = 60 ms, all other parameters remained the same) which would later be applied to correct for distortions in the functional images caused by the susceptibility distribution of the subject’s head (Andersson & Sotiropoulos, 2016; Smith et al., 2004). Additionally, high resolution, whole-brain T1-weighted sagittal brain images were acquired at the beginning of the scan protocol (TR = 400 ms, TE = min full, FA = 111°, FOV = 250 mm, slice thickness = 3.0 mm, interslice distance = 0.3 mm, and 256 × 192 grid, voxel size = 1 × 1 × 1 mm).

### 2.6. Image analyses

Preprocessing was carried out in FLS feat (FMRI Expert Analysis Tool; FMRIB Analysis group, Oxford, UK). The same preprocessing procedure was followed for the pretest and the posttest data. The first steps were performed separately for all the four experimental blocks. Only those blocks were included that (1) had at least one correct response for each of the four conditions (working memory and control conditions, high and low memory load), and (2) were complete, i.e., the scan was not aborted before the end of the block. In total, 88.7% of the blocks was included in the analyses. Rigid body transformations were used to correct for head motion (MCFLIRT, FSL (Jenkinson et al., 2002)), followed by a correction for the susceptibility distribution of the subjects head (TOPUP tool in FSL (Andersson & Sotiropoulos, 2016; Smith et al., 2004)). The Brain Extraction Tool (BET (Smith, 2002)) was applied to remove non-brain tissue from the functional scans and the T1-weighted structural images. Subsequently, the functional data were spatially smoothed using a 5-mm Full Width Half Maximum (FWHM) Gaussian Kernel. The experimental blocks were combined into a single 4D dataset per subject which could be used for further analyses.

Next, an independent-component analysis (ICA) was conducted using Multivariate Exploratory Linear Optimized Decomposition into Independent Components (Beckmann & Smith, 2005) for each subject’s 4D dataset (both pretest and posttest), in order to remove artifacts from the subject’s data. MELODIC decomposes a 4D dataset into spatial and temporal components, thereby distinguishing activation and artefactual components (Kelly et al., 2010; Thomas et al., 2002). Based on the recommendation to use about one-fourth to one-fifth of the total of time points in the scans (Greicius et al., 2004), and previously widely adopted settings of 20–30 components for ICA (Smith et al., 2009), a fixed number of 30 components was extracted per subject. The spatial components were visually inspected for artefacts, and components with artefacts were removed. The remaining components were used to generate contrast images.

Two contrasts of interest were set-up in Statistical Parameter Mapping (SPM 12.0 v6470, running in MATLAB 2017b) for the pretest, and the posttest data: one contrasting working memory to control (mean working memory), and one contrasting high working memory load to low working memory load (load difference). Only correct trials were included to minimize variability in brain activation between different conditions, because differences in brain activation were expected during incorrect and omission trials as compared to correct trials. This resulted

**Table 2**
Implementation measures for the total sample and separately for the control group, aerobic intervention group, and cognitively-engaging intervention group.

| | Total sample ($n = 62$) | Control group ($n = 17$) | Aerobic intervention group ($n = 22$) | Cognitively-engaging intervention group ($n = 23$) |
|---|---|---|---|---|
| Number of lessons attended | 44.7 (6.6) | – | 46.4 (3.7) | 43.0 (8.3) |
| MVPA, in minutes | 10.69 (2.8) | 10.74 (3.4) | 11.88 (2.7) | 9.56 (1.9) |
| Motivation | 4.25 (0.45) | 4.34 (0.43) | 4.28 (0.37) | 4.16 (0.53) |

in a contrast image representing the activation difference between the conditions for each voxel per subject. See for a detailed description of the image analyses van der Fels, de Bruijn, et al. (2020). The images were rescaled by dividing their intensity scale by its respective standard deviation, to account for differences between the two site in scaling of the contrast images. Both contrast images were co-registered, normalized to an MNI-152 template, and spatially smoothed with an 8-mm FWHM Gaussian Kernel in SPM 12.0.

Consequently, a difference image was constructed by subtracting the pretest contrast image from the posttest contrast image in SPM 12.0, resulting in a contrast image showing changes in brain activation between pretest and posttest for each contrast (i.e. working memory vs. control, and high working memory load vs. low working memory load). Registration was conducted using affine transformations in FLIRT.

### 2.7. Statistical analyses

To check intervention fidelity, attendance rate, time spent in MVPA and motivation were compared in IBM SPSS Statistics 25.0 for the conditions using Analyses of Variance (ANOVA) and post-hoc analyses with Bonferroni correction. An additional ANOVA with Bonferroni-corrected post-hoc analyses was used to examine initial differences in performance on the spatial span task between the three groups. Significance level was set at $p < 0.05$.

First, for both contrasts whole brain activation differences between pretest and posttest across all groups were analyzed in a flexible factorial model in SPM 12.0, by adding the pretest contrast maps and posttest contrast maps for each participant, for both contrasts (i.e. working memory vs. control, and high working memory load vs. low working memory load). The aim of this analysis was to examine whether there were overall differences in brain activation between pretest and posttest. Subsequently, an analysis was conducted to examine interactions between condition and time, that is: whether the three groups (control group vs. aerobic intervention vs. cognitive intervention) showed differences in activity changes between pre- and posttest. For each contrast separately, difference maps representing changes in activation between pretest and posttest were entered in a flexible factorial model. A covariate of interest representing intervention group (aerobic intervention group, cognitively-engaging intervention group, control group) was added to this model, and site was included as covariate of no interest, because differences between scan sites were found. No other covariates were found to be related to task-related brain activity patterns, and therefore only scan site was used as covariate in the models (van der Fels, de Bruijn, et al., 2020). Results that survived the cluster level significance of $p < 0.05$, family wise error (FWE) corrected, initial threshold $p < 0.001$, will be presented.

**Table 3**
Average pretest and posttest scores on the visual span task (percentage working memory trials correct) and corresponding standard deviations for the total sample and separately for the control group, aerobic intervention group, and cognitively-engaging intervention group.

| | Total sample (n = 62) | Control group ($n = 17$) | Aerobic intervention group ($n = 22$) | Cognitively-engaging intervention group ($n = 23$) |
|---|---|---|---|---|
| Pretest | 67.49 (15.3) | 69.24 (13.5) | 66.81 (15.1) | 66.85 (17.1) |
| Posttest | 72.82 (15.7) | 76.47 (15.9) | 73.77 (13.5) | 69.20 (17.4) |
| Difference pretest - posttest | 5.32 (12.28) | 7.23 (14.6) | 6.96 (8.8) | 2.36 (13.2) |
| Min. – max. difference | −29.2 to 35.4 | −16.7 to 35.4 | −8.3 to 25 | −29.9 to 18.8 |

## 3. Results

### 3.1. Implementation measures

First, to get an impression of implementation fidelity of the interventions, the intensity with which children participated in the lessons and their motivation during the lessons were compared for the three conditions, see Table 2. Average time in MVPA significantly differed between conditions ($F$ (2, 58) = 16.37, $p < .001$). Post-hoc analyses revealed that the children in the aerobic intervention group spent significantly more time in MVPA than children in the control group ($p < .001$) and children in the cognitively-engaging intervention group ($p < .001$). The control group and cognitively-engaging intervention group did not significantly differ in the average percentage of time spent in MVPA ($p = .77$). There was no significant difference in number of lessons attended between the two intervention groups ($F$ (1, 43) = 2.93, $p = .09$) nor in motivation between the three conditions ($F$ (2, 59) = 0.72, $p = .49$).

### 3.2. Behavioral results

Mean scores on the Spatial Span task at pretest and posttest for the three groups are presented in Table 3. At pretest, the three groups did not significantly differ in performance on the spatial span task ($F$ (2, 59) = 0.15, $p = .86$). Overall, children performed significantly better at posttest than at pretest ($F$ (1, 59) = 12.32, $p < .001$). There was no significant interaction between condition and time ($F$ (2, 59) = 1.08, $p = .35$), indicating that the improvement between pretest and posttest did not significantly differ between the three groups. When looking more closely at the differences in performance between pretest and posttest (see Table 3), it is noticeable that the difference measure varies from a decrease of 29% in the percentage of trials correct between pretest and posttest to an increase of 35% in the percentage of trials correct between pretest and posttest. There was substantial variance in performance changes within the three groups, despite the fact that there were no significant differences in the performance changes between pretest and posttest between the three conditions. The variance in performance changes was much larger in the control group and cognitively-engaging intervention group compared to the aerobic intervention group.

### 3.3. fMRI results

The mean activation pattern for the working memory contrast, over both scanning sessions and for all groups, is presented in van der Fels, de Bruijn, et al. (2020). VSWM-related brain activation was found in the angular gyrus (right hemisphere), the superior parietal cortex (bilateral), and the thalamus (bilateral); and VSWM-related deactivation was found in the inferior and middle temporal gyri (bilateral). This activation pattern is largely in line with what was found in previous studies, supporting the validity of the task. There was no significant activation associated with load difference (van der Fels, de Bruijn, et al., 2020). Consequently, this contrast was not further examined.

First, mean activation differences between pretest and posttest for all groups together were analyzed to see whether brain activation patterns changed over the fourteen weeks. No significant activation changes in activity were found between pretest and posttest (all $p > .05$).

Second, time-by-group interactions were examined to investigate intervention effects. No significant differences in activation changes were found between the three groups (all $p > .05$), indicating that the interventions did not result in changed brain activation patterns based on comparison of the group mean activation maps.

## 4. Discussion

This study examined the effects of two different types of physical activity, aerobic and cognitively-engaging, on children's brain activation during a visuospatial working memory task. By examining two types of physical activity, we aimed to unravel the mechanisms underlying effects of physical activity on a core aspect of executive functioning, thereby potentially providing explanations for previously reported inconsistent results. However, contradictory to our hypotheses, no significant effects of the interventions on brain activation were found.

### *4.1. Relation to previous findings*

The results of our study are surprising in light of the previously reported effects of aerobic physical activity on brain activation (Chaddock-Heyman et al., 2011; Davis et al., 2011; Krafft et al., 2014). Yet, several differences between previous studies and ours should be noted here in light of the contradictory results. First, previous studies solely focused on one outcome measure, namely inhibition; one of the three core executive functions. We wanted to extend these results by looking at VSWM, an important cognitive function that strongly develops during childhood. Although VSWM is related to inhibition, as both are core aspects of executive functioning (Miyake et al., 2000), they are seen as separate constructs that are differently related to other aspects of children's development, such as academic achievement (De Bruijn et al., 2018). Some studies suggest that effects of physical activity are most pronounced for inhibition (e.g.Barenberg et al., 2011; Xue et al., 2019), possibly explaining why no effects on VSWM were found in our study. Yet, positive effects of physical activity on working memory have been reported in numerous studies as well (see Wassenaar et al., 2020). Results of the study by Alvarez-Bueno et al. (2017) suggest that the type of physical activity can partly explain these inconsistencies, as the largest effect sizes on inhibition were found for qualitatively-enriched physical activity interventions, whereas quantitatively-enhanced interventions resulted in larger effects on working memory. Further research is needed to better understand which cognitive functions are most likely to benefit from physical activity. Second, two of the three previous studies (Davis et al., 2011; Chaddock-Heyman et al., 2011) included only overweight children, who might respond differently to physical activity interventions (Crova et al., 2014). Thirdly, all three studies examined effects of an afternoon physical activity program. Our study focused on effects of a school-based physical activity program, meaning that the extra time spent on PE was at the cost of academic instruction time. Consequently, our results can be positively interpreted as well, as spending time on PE instead of academic content did not seem to go at the expense of children's cognitive or brain development. Lastly, the total dose of physical activity in the previous studies was higher than the dose that children in our study were exposed to. That is, all previous studies implemented daily PE lessons over a period of 13 weeks (Davis et al., 2011) to 9 months (Chaddock-Heyman et al., 2011). As dose–response effects of physical activity have been suggested in previous studies (see Valkenborghs et al., 2019), the dose of PA that children in our study were exposed to might have been too low to bring about positive effects. Positive effects might have shown after a longer intervention period or a higher number of lessons. Yet, other studies conclude that dose is not a moderator in determining intervention effectiveness (Xue et al., 2019). Based on current evidence base, it is difficult to draw conclusions on the optimal duration to derive effects on cognition (Erickson et al., 2019).

Results of our study are in line with the non-significant effects reported in the, to our knowledge, only study in which the effects of different types of physical activity on children's brain functioning have been compared (Ludyga et al., 2019). Together, these studies suggest that physical activity does not necessarily result in improved cognition or changes in brain activity. The discussion points outlined above suggest that there are characteristics of physical activity that might affect the effectivity of the intervention program. This statement is supported by results of the large number of recent *meta*-analyses and reviews which have been inconclusive on the effects of physical activity on cognition (see Wassenaar et al., 2020), showing that if we want to come to results that can inform policy and practice, much work is to be done.

Additionally, the large inter-individual variability in intervention effectiveness that we found within groups suggests that characteristics of individual participants determine whether and which physical activity interventions will be effective. Results of our behavioural studies suggest that intervention effectiveness, amongst others, depends on children's initial achievement level (De Bruijn et al., 2020; van der Fels, Hartman, et al., 2020). Other studies have also suggested that individual characteristics such as weight status (Crova et al., 2014; Vazou et al., 2019) and baseline fitness or changes in fitness (Krafft et al., 2014) influence the effectiveness of physical activity for improving cognition and brain functioning. Nowadays, more and more imaging studies refer of the potential of examining inter-individual differences, treating variance between subjects as data rather than noise (Seghier & Price, 2018). As the design of our study is not well-suited to examine inter-individual differences in intervention responsiveness (i.e. a larger sample size is needed to infer reliable results and fit more complex models; e.g. Dubois & Adolphs, 2016), we recommend that future studies start taking an individualized approach, looking deeper into background characteristics that are related to intervention effectiveness, to get a better idea of what works for whom. In the same vein, a person-centred approach might be valuable, as this type of analysis can reveal whether there are specific 'types' of children who benefit from intervention programs.

It should be noted that some researchers have suggested that physical activity has to result in improvements in cardiovascular fitness in order to bring about beneficial effects on cognition (the cardiovascular fitness hypothesis). Yet, studies have provided little evidence for this idea (see Voss and McMorris, 2016). It is consequently not clear whether cardiovascular fitness is a correlate in the link between physical activity and cognition, or whether it is a direct predictor of cognition and brain health (Voss and McMorris, 2016). Results of a recent study support the latter idea, as it was shown that children's cardiovascular fitness and gross motor skills were related to neurocognitive functioning and white matter microstructure, whereas no evidence was found for a mediating role of white matter microstructure (Meijer, Königs, van der Fels, et al., 2020). We did measure cardiovascular fitness in the present study (see baseline characteristics in Table 1), but did not include it in our analyses, because of the limited evidence base for the cardiovascular fitness hypothesis, and because cardiovascular fitness was not related to children's brain activity patterns underlying VSWM (see van der Fels, de Bruijn, et al., 2020).

### *4.2. Underlying mechanisms*

By comparing the effects of two types of physical activity, the aim was to get a better understanding of how physical activity affects cognition and academic performance. The two physical activity interventions that were implemented were closely related to the mechanisms that are used to explain the positive effects of physical activity on cognition and academic achievement. The aerobic intervention was based on physiological mechanisms, which assume that aerobic physical activity results in changes in brain structure and functioning as a result of physiological changes in the brain, such as an increase in growth factors and neurotransmitters (Best, 2010). The cognitively-engaging intervention followed the cognitive stimulation hypothesis, in which it is argued that cognitively-engaging physical activity and cognitive tasks activate overlapping brain areas, thereby resulting in more efficient use of those areas for both motor skill execution and cognitive performance (e.g. Diamond & Ling, 2016; Pesce, 2012; Tomporowski & Pesce, 2019; Vazou et al., 2019). Neither of the interventions resulted in changes in brain activation, or in improved cognitive functions or academic achievement as previously reported (De Bruijn et al., 2020; Meijer, Königs, van der Fels, et al., 2020). It can be argued that is not surprising that changes in brain activation were not significant, given that we did not find measurable changes in cognition and academic achievement. Yet, it is known that changes in the brain can precede behavioral effects (e.g. Ross & Tremblay, 2009; Tremblay et al., 1998), meaning that the non-existent effects on cognition and academic achievement did not necessarily rule out neuronal effects on brain activation.

Based on our results, it is difficult to draw definite conclusions about the applicability of the two mechanisms. Recent studies have suggested that the amount of cognitive engagement is a determining factor in explaining intervention effectiveness (e.g. Pesce, 2012; Diamond & Ling, 2016; Tomporowski et al., 2015; Tomporowski & Pesce, 2019), an idea that is underlined by results of behavioral studies revealing positive effects of cognitively-engaging physical activity (De Bruijn et al., 2020; De Greeff, Bosker, Oosterlaan, Visscher, & Hartman, 2018; Egger, Benzing, Conzelmann, Schmidt, & Parmenter, 2019; García-Hermoso, Ramírez-Vélez, Lubans, & Izquierdo, 2021; Mazzoli et al., 2021; Schmidt, Jäger, Egger, Roebers, & Conzelmann, 2015). Yet, research on effects of physical activity on the brain has focused on aerobic physical activity, reporting positive effects (Meijer, Königs, Vermeulen, et al., 2020; Valkenborghs et al., 2019).

In explaining these contradictory results, a complication in this line of research is that physical activity interventions are never purely aerobic or purely cognitively-engaging, making it difficult to interpret conclusions of studies examining different types of physical activities (see Hillman et al., 2019; Vazou et al., 2019). That is, aerobic activities always include cognitively-engaging aspects, for example when children cooperate in teams, engage in dancing activities, or execute complex motor activities such as jumping jacks. Also, aerobic physical activity requires following of rules and engagement in socially acceptable behaviors, for which cognitive capacities such as inhibition, attention, flexibility, and working memory are needed. Likewise, cognitively-engaging activities also include aerobic aspects, such as running and jumping. Although theoretically it is interesting to isolate the two in order to outline the underlying mechanisms of the effects, in practice most types of physical activity include both aerobic and cognitively-engaging aspects (Diamond & Ling, 2016; Pesce, 2012; Tomporowski et al., 2015; Vazou et al., 2019). To come up with recommendations for practice, it therefore makes sense to examine physical activity that combines cognitive engagement with aerobic activities.

In a recent *meta*-review, based on a large number of systematic reviews, this combined type of physical activity was also mentioned, concluding that physiological mechanisms (focusing on the quantity: frequency, duration, or intensity of activities) and the cognitive stimulation hypothesis (focusing on the quality – type of activities) should be seen as complementary, rather than being isolated mechanisms (Pesce et al. 2021). Possibly, interventions focusing on only one of the mechanisms result in small changes in brain activity that are difficult to detect, whereas interventions combining the two mechanisms result in more pronounced effects (Ludyga et al., 2018; 2019; also see Tomporowski & Pesce, 2019), thereby explaining the non-significant effects of our interventions focusing on the mechanisms in isolation. In line with this idea, a behavioral study found that this combined type of physical activity had stronger effects on executive functioning than a regular PE program, and a program focusing only on aerobic physical activity (Schmidt et al., 2015). Combining aerobic and cognitively-engaging physical activities thus seems a promising recommendation for future research, as it can be expected that this type of physical activity will have more pronounced effects on brain activation and, consequently, cognitive and academic performance (Mavilidi et al., 2018).

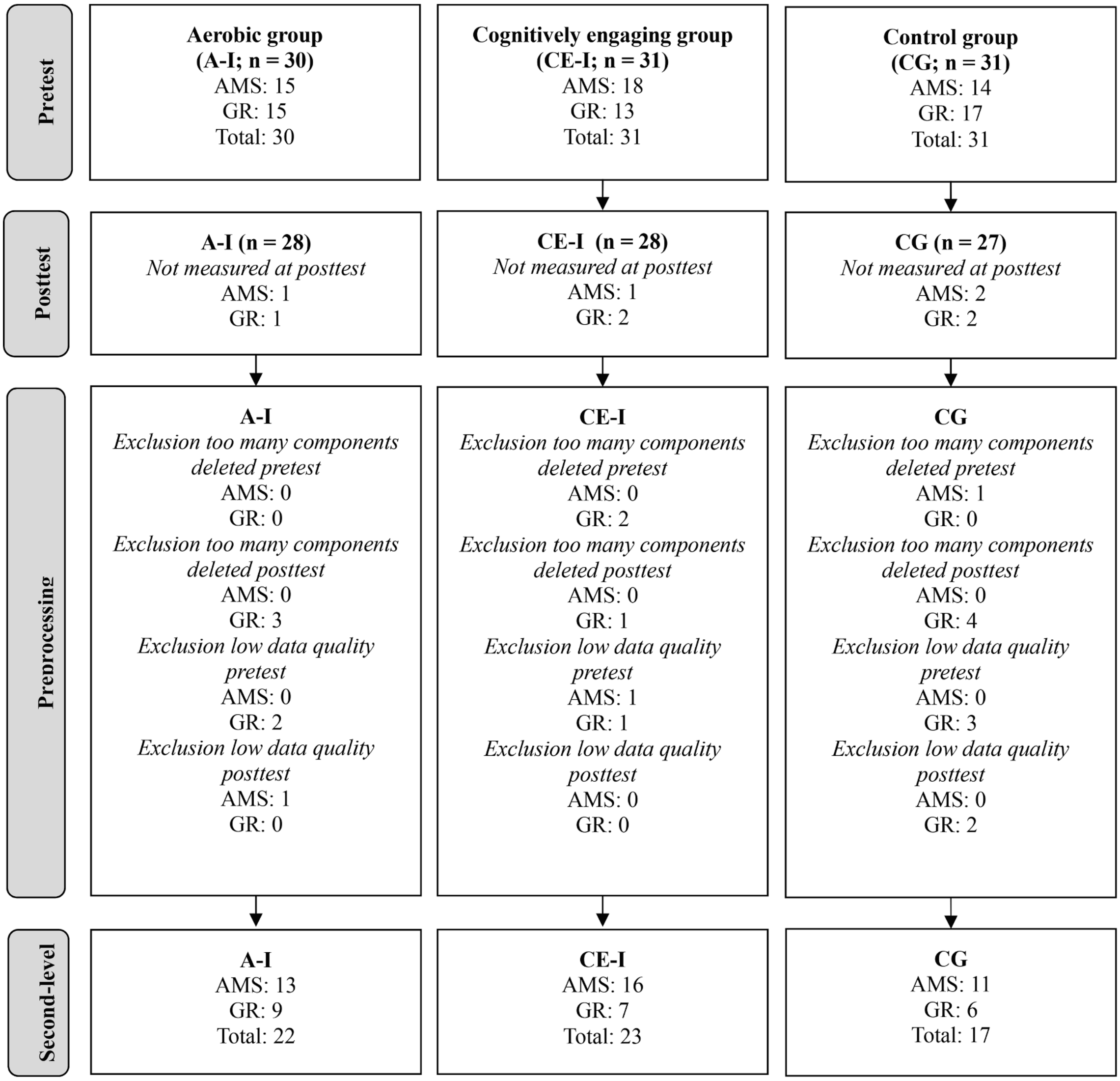
Importantly, when examining effects of physical activity interventions, it is argued to be important to look beyond isolated factors related to the dose and type of physical activity, by also including contextual factors (Pesce et al. 2021). Three main types of contextual mechanisms are thought to influence intervention effectiveness: 1) the emotional and physical load of the context (capacity boosting); 2) the cognitive and social load of the context (capacity building); and 3) the restorative properties (i.e. amount of stress relief) of the context (capacity restoring). In order to examine these contextual influences, studies should not focus on isolated mechanisms in a decontextualized manner, but aspects such as delivery mode, implementation setting, and the expertise of the deliverer (i.e. physical activity teacher) should be included as well (Pesce et al. 2021). Although our interventions were administered in a naturalistic context (i.e. the physical education context), we were not able to draw conclusions on how contextual variables might have influenced or might explain our results. In implementing the interventions, a structured protocol was followed (lessons were administered by instructed specialist teachers, who followed a structured manual), meaning there was no or little variation in contextual variables. As recommended by Pesce et al. (2021) it would be interesting for future studies to include such contextual factors in future studies to get further insight into why and when physical activity is effective in facilitating cognition.

Furthermore, additional mechanisms might be needed to explain the effects of physical activity on cognition and academic performance. Pesce et al. (2021) suggest to take a holistic lens when examining effects of physical activity on cognition, not only by taking into account contextual conditions, but also by examining multiple mechanisms acting at different levels. Besides the physiological and cognitive stimulation mechanisms examined in our study, they for example mention emotional mechanisms, in which it is argued that physical activity affects cognition via enjoyment of the activities involved (Diamond & Ling, 2020; Ekkekakis et al., 2013), and psychosocial mechanisms, in which it is assumed that physical activity affects cognition and academic achievement by increasing social engagement and interaction (see Pesce et al. 2021). Relatedly, other studies have referred to, amongst others, increased self-esteem and higher school engagement (Bailey, 2017; Lubans et al., 2016), or positive effects on behaviors that are related to cognitive and mental outcomes, such as healthier eating patterns and improved sleep quality (Bailey, 2017; Lubans et al., 2016).

### 4.3. Strengths and limitations

This study aimed to reveal the effects of different types of physical activity on children's brain activation during a visuospatial working memory task. Strengths of this study include the representative sample resulting from the structured inclusion protocol, and the comparison of the effects of two types of physical activity interventions.

A first limitation is that the task that was used possibly was not sensitive enough to pick up changes in brain activation patterns, thereby also providing an explanation for why no significant intervention effects were found when using mass univariate analysis. This idea is underlined by the fact that none of the children's background characteristics were related to brain activation during the task (van der Fels, de Bruijn, et al., 2020). Based on previous studies it was expected that factors such as age, SES, or gender would be related to differences in visuospatial working memory related brain activation (Barriga-Paulino et al., 2015;



*Note.* AMS = Amsterdam; GR = Groningen; A-I = aerobic intervention group; CE-I = cognitively-engaging intervention group; CG = control group

**Fig. A1.** Flowchart of the number of included children in the control group, aerobic intervention group and cognitively-engaging intervention group at each stage of the study, in total and separately per study site. Note. AMS = Amsterdam; GR = Groningen; A-I = aerobic intervention group; CE-I = cognitively-engaging intervention group; CG = control group.

Schweinsburg et al., 2005; Thomason et al., 2009; Zilles et al., 2016). None of these relations was found however, and even performance on the task itself (percentage of trials with a correct answer) was not related to brain activation patterns. Still, the task activity pattern that was found largely coincided with results of previous studies using the same task (Van Ewijk et al., 2014; 2015), providing support for the validity of the visuospatial working memory task that we used.

Alternatively, not the task itself, but the way it was implemented in the scan protocol might explain the lack of relations with, and changes in VSWM related brain activation. The active state fMRI scans that were taken were part of a larger MRI protocol lasting one hour, also including diffusion tensor imaging (DTI) and resting state fMRI. The active state fMRI scans used for the present study were taken at the end of the protocol. It proved to be difficult for children to lay still for such a long time, resulting in high movement parameters for the active state fMRI scans. In order to filter out the movement-related brain activation, extensive preprocessing steps had to be taken, and a number of participating children had to be excluded. It can be questioned whether the quality of the resulting data was high enough to reveal changes in brain activity in the three conditions.

Further, in this study we included only one aspect of cognition, namely VSWM, meaning that we cannot derive conclusions on the overall causal relationship between physical activity and cognitive functioning. That is, physical activity might have resulted in changes in brain activity if we would have used different outcome measures, also explaining why positive effects of physical activity on cognition have been found in previous studies, as these exclusively focused on inhibition (Chaddock-Heyman et al., 2013; Davis et al., 2011; Krafft et al., 2014). Future studies could include multiple cognitive outcome measures to get further insight into the cognitive functions and underlying brain mechanisms that are most likely to change as a result of physical activity.

Lastly, we had only limited information on implementation fidelity of the interventions. We tried to get an indication of implementation fidelity by measuring motivation and intensity of participation. Yet, we do not have any measures regarding the amount of cognitive engagement children experienced during the interventions; nor do we have information on the attendance rate of children in the control condition;

or about the type of activities that children in the control condition engaged in. Also, we do not know how the intervention lessons were implemented in the curriculum, i.e. what teachers changed in practice in order to double the amount of PE that their students engaged in. For future studies, we suggest to also include measures of intervention fidelity to understand whether (non-significant) effects may be caused by environmental factors (Pesce et al. 2021; Wassenaar et al., 2020); or whether dose–response effects might exist (i.e. effects only for children who participate at a higher intensity level or who experience high levels of cognitive engagement).

### *4.4. Conclusion*

Neither an aerobic physical activity intervention program, nor a cognitively-engaging physical activity program resulted in significant changes in children's brain activation. Our results suggest that physical activity, at least the type and amount that we used, does not necessarily bring about changes in children's brain activation patterns. Possibly, different types of physical activity are needed to bring about effects, or the same types of physical activity require more time to create noticeable changes in brain activation. Alternatively, additional mechanisms might be needed to explain effects of physical activity on cognition and academic achievement. The large inter-individual differences that we found further suggest that there are individual characteristics that can predict whether, and what type of physical activity will be effective for specific participants. As our study is one of the first to examine the effects of two different types of physical activity intervention on brain activation, more research is needed to understand whether, when, for whom, and how physical activity can result in changes in brain activation, and whether these changes can explain changes in cognition and academic achievement as well.

## Data availability statement

The datasets for this manuscript are not publicly available because of sensitivity of the data and restrictions from the informed consent. Requests to access the datasets should be directed to dr. Esther Hartman, e.hartman@umcg.nl.

## Permission to reproduce material

The authors declare that they do not make use of any previously published material.

### *CRediT authorship contribution statement*

**A.G.M. de Bruijn:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft. **I.M.J. van der Fels: . R.J. Renken:** Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Writing – review & editing. **M. Königs:** Conceptualization, Data curation, Supervision, Methodology, Writing – review & editing. **A. Meijer:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – review & editing. **J. Oosterlaan:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing, Supervision, Writing – review & editing. **D. D.N.M. Kostons:** Conceptualization, Methodology, Supervision, Writing – review & editing. **C. Visscher:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing, Supervision, Writing – review & editing. **R.J. Bosker:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing, Supervision, Writing – review & editing. **J. Smith:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **E. Hartman:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

The authors would like to thank all participating children and their parents/legal guardians, schools, and school directors. This work was supported by a grant from Nationaal Regieorgaan Onderwijsonderzoek (NRO) (grant number: 405-15-410) and Hersenstichting (grant number: GH 2015-3-01). The funding source had no involvement in the study design, data collection and analysis, and writing and submission of the manuscript.

## Appendix A. Inclusion protocol

See Fig. A1

## References

Adam, C., Klissouras, V., Ravazzolo, M., Renson, R., & Tuxworth, W. (1988). *Eurofit: European Test of Physical Fitness.* Council of Europe, Committee for the Development of Sport.

Alloway, T. P. (2007). *Automated Working Memory Assessment.* Pearson Assessment.

Alloway, T. P., Gathercole, S. E., & Pickering, S. J. (2006). Verbal and visuospatial short-term and working memory in children: Are they separable? *Child Development, 77*(6), 1698–1716. https://doi.org/10.1111/cdev.2006.77.issue-610.1111/j.1467-8624.2006.00968.x

Alloway, T. P., Gathercole, S. E., Kirkwood, H., & Elliott, J. (2008). Evaluating the validity of the automated working memory assessment. *Educational Psychology, 28* (7), 725–734. https://doi.org/10.1080/01443410802243828

Alvarez-Bueno, C., Pesce, C., Cavero-Redondo, I., Sanchez-Lopez, M., Martínez-Hortelano, J. A., & Martinez-Vizcaino, V. (2017). The effect of physical activity interventions on children's cognition and metacognition: A systematic review and meta-analysis. *Journal of the American Academy of Child and Adolescent Psychiatry, 56* (9), 729–738. https://doi.org/10.1016/j.jaac.2017.06.012

Andersson, J. L. R., & Sotiropoulos, S. N. (2016). An integrated approach to correction for off resonance effects and subject movement in diffusion MR imaging. *NeuroImage, 125*, 1063–1078. https://doi.org/10.1016/j.neuroimage.2015.10.019

Bailey, R. (2017). Sport, physical activity and educational achievement–towards an explanatory model. *Sport in Society, 20*(7), 768–788. https://doi.org/10.1080/17430437.2016.1207756

Barenberg, J., Berse, T., & Dutke, S. (2011). Executive functions in learning processes: Do they benefit from physical activity? *Educational Research and Reviews, 6*(3), 208–222. https://doi.org/10.1016/j.edurev.2011.04.002

Barriga-Paulino, C. I., Benjumea, M.Á. R., Rodríguez-Martínez, E. I., & González, C. M. G. (2015). Fronto–temporo–occipital activity changes with age during a visual working memory developmental study in children, adolescents and adults. *Neuroscience Letters, 599*, 26–31. https://doi.org/10.1016/j.neulet.2015.05.017

Best, J. R. (2010). Effects of physical activity on children's executive function: Contributions of experimental research on aerobic exercise. *Dev Rev., 30*(4), 331–351. https://doi.org/10.1016/j.dr.2010.08.001

Beckmann, C. F., & Smith, S. M. (2005). Tensorial extensions of independent component analysis for multisubject FMRI analysis. *NeuroImage, 25*(1), 294–311. https://doi.org/10.1016/j.neuroimage.2004.10.043

Black, J. E., Isaacs, K. R., Anderson, B. J., Alcantara, A. A., & Greenough, W. T. (1990). Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar cortex of adult rats. *Proceedings of the National Academy of Sciences of the United States of America, 87*(14), 5568–5572. https://doi.org/10.1073/pnas.87.14.5568

Chaddock-Heyman, L., Pontifex, M. B., Hillman, C. H., & Kramer, A. F. (2011). A review of the relation of aerobic fitness and physical activity to brain structure and function in children. *Journal of the International Neuropsychological Society, 17*(6), 975–985. https://doi.org/10.1017/S1355617711000567

Chaddock-Heyman, L., Erickson, K. I., Voss, M. W., Knecht, A. M., Pontifex, M. B., Castelli, D. M., et al. (2013). The effects of physical activity on functional MRI activation associated with cognitive control in children: A randomized controlled intervention. *Frontiers in Human Neuroscience, 7*. https://doi.org/10.3389/fnhum.2013.00072

Cole, T. J., & Lobstein, T. (2012). Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatric Obesity, 7*(4), 284–294. https://doi.org/10.1111/ijpo.2012.7.issue-410.1111/j.2047-6310.2012.00064.x

Cortés Pascual, A., Moyano Muñoz, N., & Quilez Robres, A. (2019). The relationship between executive functions and academic performance in primary education: Review and meta-analysis. *Frontiers in Psychiatry, 10*, 1582–1600. https://doi.org/10.3389/fpsyg.2019.01582

Crova, C., Struzzolino, I., Marchetti, R., Masci, I., Vannozzi, G., Forte, R., et al. (2014). Cognitively challenging physical activity benefits executive function in overweight children. *Journal of Sports Sciences, 32*(3), 201–211. https://doi.org/10.1080/02640414.2013.828849

Davis, C. L., Tomporowski, P. D., McDowell, J. E., Austin, B. P., Miller, P. H., Yanasak, N. E., et al. (2011). Exercise improves executive function and achievement and alters brain activation in overweight children: A randomized, controlled trial. *Health Psychology, 30*(1), 91–98. https://doi.org/10.1037/a0021766

De Bruijn, A. G. M., Hartman, E., Kostons, D. D. N. M., Visscher, C., & Bosker, R. J. (2018). Exploring the relations among physical fitness, executive functioning, and low academic achievement. *Journal of Experimental Child Psychology, 167*, 204–221. https://doi.org/10.1016/j.jecp.2017.10.010

De Bruijn, A. G. M., Kostons, D. D. N. M., van der Fels, I. M. J., Visscher, C., Oosterlaan, J., Hartman, E., et al. (2020). Effects of aerobic and cognitively-engaging physical activity on academic skills: A cluster RCT. *Journal of Sports Sciences, 38*(15), 1806–1817. https://doi.org/10.1080/02640414.2020.1756680

De Greeff, J. W., Bosker, R. J., Oosterlaan, J., Visscher, C., & Hartman, E. (2018). Effects of physical activity on executive functions, attention and academic performance in preadolescent children: A meta-analysis. *Journal of Science and Medicine in Sport, 21* (5), 501–507. https://doi.org/10.1016/j.jsams.2017.09.595

Diamond, A. (2013). Executive functions. *The Annual Review of Psychology, 64*, 135–168. https://doi.org/10.1146/annurev-psych-113011-143750

Diamond, A., & Ling, D. S. (2016). Conclusions about interventions, programs, and approaches for improving executive functions that appear justified and those that, despite much hype, do not. *Developmental Cognitive Neuroscience, 18*, 34–48. https://doi.org/10.1016/j.dcn.2015.11.005

Diamond, A., & Ling, D. S. (2020). Review of the evidence on, and fundamental questions about, efforts to improve executive functions, including working memory. In J. Novick, M. F. Bunting, M. R. Dougherty, & R. W. Engle (Eds.), *Cognitive and working memory training: Perspectives from psychology, neuroscience, and human development* (pp. 143–431). Oxford University Press.

Donnelly, J. E., Hillman, C. H., Castelli, D., Etnier, J. L., Lee, S., Tomporowski, P., et al. (2016). Physical activity, fitness, cognitive function, and academic achievement in children: a systematic review. *Medicine & Science in Sports & Exercise, 48*(6), 1197–1222. https://doi.org/10.1249/MSS.0000000000000901

Dubois, J., & Adolphs, R. (2016). Building a science of individual differences from fMRI. *Trends in Cognitive Sciences, 20*(6), 425–443. https://doi.org/10.1016/j.tics.2016.03.014

Egger, F., Benzing, V., Conzelmann, A., Schmidt, M., & Parmenter, B. (2019). Boost your brain, while having a break! The effects of long-term cognitively engaging physical activity breaks on children's executive functions and academic achievement. *PLoS ONE, 14*(3), e0212482. https://doi.org/10.1371/journal.pone.0212482

Ekkekakis, P., Hargreaves, E. A., & Parfitt, G. (2013). Envisioning the next fifty years of research on the exercise-affect relationship. *Psychology of Sport and Exercise, 14*(5), 751–758. https://doi.org/10.1016/j.psychsport.2013.04.007

Erickson, K. I., Hillman, C., Stillman, C. M., Ballard, R. M., Bloodgood, B., Conroy, D. E., & Powell, K. E. (2019). Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Psychology of Sport and Exercise, 51*(6), 1242–1251. doi:10.1249%2FMSS.0000000000001936.

Evenson, K. R., Catellier, D. J., Gill, K., Ondrak, K. S., & McMurray, R. G. (2008). Calibration of two objective measures of physical activity for children. *Journal of Sports Sciences, 26*(14), 1557–1565. https://doi.org/10.1080/02640410802334196

García-Hermoso, A., Ramírez-Vélez, R., Lubans, D. R., & Izquierdo, M. (2021). Effects of physical education interventions on cognition and academic performance outcomes in children and adolescents: A systematic review and meta-analysis. preprint *British Journal of Sports Medicine*. https://doi.org/10.1136/bjsports-2021-104112.

Greicius, M. D., Srivastava, G., Reiss, A. L., & Menon, V. (2004). Default-mode network activity distinguishes Alzheimer's disease from healthy aging: Evidence from functional MRI. *Proceedings of the National Academy of Sciences of the United States of America, 101*(13), 4637–4642. https://doi.org/10.1073/pnas.0308627101

Gunnell, K. E., Poitras, V. J., LeBlanc, A., Schibli, K., Barbeau, K., Hedayati, N., et al. (2019). Physical activity and brain structure, brain function, and cognition in children and youth: A systematic review of randomized controlled trials. *Mental Health and Physical Activity, 16*, 105–127. https://doi.org/10.1016/j.mhpa.2018.11.002

Hillman, C. H., McAuley, E., Erickson, K. I., Liu-Ambrose, T., & Kramer, A. F. (2019). On mindful and mindless physical activity and executive function: A response to Diamond and Ling (2016). *Developmental Cognitive Neuroscience, 37*, 1–5. https://doi.org/10.1016/j.dcn.2015.11.005

Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage, 17*(2), 825–841. https://doi.org/10.1006/nimg.2002.1132

Kelly, R. E., Alexopoulos, G. S., Wang, Z., Gunning, F. M., Murphy, C. F., Morimoto, S. S., et al. (2010). Visual inspection of independent components: Defining a procedure for artifact removal from fMRI data. *Journal of Neuroscience Methods, 189*(2), 233–245. https://doi.org/10.1016/j.jneumeth.2010.03.028

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology, 24*(6), 781–791. https://doi.org/10.1076/jcen.24.6.781.8395

Krafft, C. E., Schwarz, N. F., Chi, L., Weinberger, A. L., Schaeffer, D. J., Pierce, J. E., et al. (2014). An 8-month randomized controlled exercise trial alters brain activation during cognitive tasks in overweight children. *Obesity, 22*(1), 232–242. https://doi.org/10.1002/oby.v22.110.1002/oby.20518

Lubans, D., Richards, J., Hillman, C., Faulkner, G., Beauchamp, M., Nilsson, M., & Biddle, S. (2016). Physical activity for cognitive and mental health in youth: a systematic review of mechanisms. *Pediatrics, 138*(3). https://doi.org/10.1542/peds.2016-1642

Ludyga, S., Gerber, M., Herrmann, C., Brand, S., & Pühse, U. (2018). Chronic effects of exercise implemented during school-break time on neurophysiological indices of inhibitory control in adolescents. *Trends in Neuroscience and Education, 10*, 1–7. https://doi.org/10.1016/j.tine.2017.11.001

Ludyga, S., Koutsandréou, F., Reuter, E. M., Voelcker-Rehage, C., & Budde, H. (2019). A randomized controlled trial on the effects of aerobic and coordinative training on neural correlates of inhibitory control in children. *Journal of Clinical Medicine, 8*(2), 184–195. https://doi.org/10.3390/jcm8020184

Mavilidi, M. F., Ruiter, M., Schmidt, M., Okely, A. D., Loyens, S., Chandler, P., et al. (2018). A narrative review of school-based physical activity for enhancing cognition and learning: The importance of relevancy and integration. *Frontiers in Psychology, 9* (2079), 1–17. https://doi.org/10.3389/fpsyg.2018.02079

Mazzoli, E., Salmon, J.o., Teo, W.-P., Pesce, C., He, J., Ben-Soussan, T. D., et al. (2021). Breaking up classroom sitting time with cognitively engaging physical activity: Behavioural and brain responses. *PLoS ONE, 16*(7), e0253733. https://doi.org/10.1371/journal.pone.0253733

McAuley, E., Duncan, T., & Tammen, V. V. (1989). Psychometric properties of the Intrinsic Motivation Inventory in a competitive sport setting: A confirmatory factor analysis. *Research Quarterly for Exercise and Sport, 60*(1), 48–58. https://doi.org/10.1080/02701367.1989.10607413

Meijer, A., Königs, M., van der Fels, I. M., Visscher, C., Bosker, R. J., … Oosterlaan, J. (2020). The effects of aerobic versus cognitively demanding exercise interventions on executive functioning in school-aged children: A cluster-randomized controlled trial. *Journal of Sport and Exercise Psychology, 1*, 1–13. https://doi.org/10.1123/jsep.2020-0034

Meijer, A., Königs, M., Vermeulen, G. T., Visscher, C., Bosker, R. J., Hartman, E., et al. (2020). The effects of physical activity on brain structure and neurophysiological functioning in children: A systematic review and meta-analysis. *Developmental Cognitive Neuroscience, 45*, 100828. https://doi.org/10.1016/j.dcn.2020.100828

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe tasks": A latent variable analysis. *Cognitive Psychology, 41*(1), 49–100. https://doi.org/10.1006/cogp.1999.0734

Mulert, C. (2009). What can fMRI add to the ERP story? In C. Mulert & L. Lemieux (eds): *EEG-fMRI*, pp. 83-95. Springer.

Pesce, C. (2012). Shifting the focus from quantitative to qualitative exercise characteristics in exercise and cognition research. *Journal of Sport and Exercise Psychology, 34*(6), 766–786. https://doi.org/10.1123/jsep.34.6.766

Pesce, C., Vazou, S., Benzing, V., Álvarez-Bueno, C., Anzeneder, S., Mavilidi, M. F., & Schmidt, M. (2021). Effects of chronic physical activity on cognition across the lifespan: a systematic meta-review of randomized controlled trials and realist synthesis of contextualized mechanisms. *International Review of Sport and Exercise Psychology (ahead of print), 3*, 1–39. https://doi.org/10.1080/1750984X.2021.1929404

Ross, B., & Tremblay, K. (2009). Stimulus experience modifies auditory neuromagnetic responses in young and older listeners. *Hearing Research, 248*(1–2), 48–59. https://doi.org/10.1016/j.heares.2008.11.012

Ryan, R. M., & Deci, E. L. (2000). Intrinsic and extrinsic motivations: Classic definitions and new directions. *Contemporary Educational Psychology, 25*(1), 54–67. https://doi.org/10.1006/ceps.1999.1020

Schaart, R., Mies, M. B., & Westerman, S. (2008). *The Dutch standard classification of education, SOI 2006*. Voorburg/Heerlen: Statistics Netherlands.

Schmidt, M., Jäger, K., Egger, F., Roebers, C. M., & Conzelmann, A. (2015). Cognitively engaging chronic physical activity, but not aerobic exercise, affects executive functions in primary school children: A group-randomized controlled trial. *Journal of Sport and Exercise Psychology, 37*(6), 575–591. https://doi.org/10.1123/jsep.2015-0069

Schweinsburg, A. D., Nagel, B. J., & Tapert, S. F. (2005). fMRI reveals alteration of spatial working memory networks across adolescence. *Journal of the International Neuropsychological Society, 11*(5), 631–644. https://doi.org/10.1017/S1355617705050757

Seghier, M. L., & Price, C. J. (2018). Interpreting and utilising intersubject variability in brain function. *Trends in Cognitive Sciences, 22*(6), 517–530. https://doi.org/10.1016/j.tics.2018.03.003

Singh, A. S., Saliasi, E., van den Berg, V., Uijtdewilligen, L., de Groot, R. H. M., Jolles, J., et al. (2019). Effects of physical activity interventions on cognitive and academic performance in children and adolescents: A novel combination of a systematic review and recommendations from an expert panel. *British Journal of Sports Medicine, 53*(10), 640–647. https://doi.org/10.1136/bjsports-2017-098136

Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping, 17* (3), 143–155. https://doi.org/10.1002/hbm.1006

Smith, S. M., Fox, P. T., Miller, K. L., Glahn, D. C., Fox, P. M., Mackay, C. E., et al. (2009). Correspondence of the brain's functional architecture during activation and rest. *Proceedings of the National Academy of Sciences of the United States of America, 106* (31), 13040–13045. https://doi.org/10.1073/pnas.0905267106

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage, 23*, S208–S219. https://doi.org/10.1016/j.neuroimage.2004.07.051

Thomas, C. G., Harshman, R. A., & Menon, R. S. (2002). Noise reduction in BOLD-based fMRI using component analysis. *NeuroImage, 17*(3), 1521–1537. https://doi.org/10.1006/nimg.2002.1200

Thomason, M. E., Race, E., Burrows, B., Whitfield-Gabrieli, S., Glover, G. H., & Gabrieli, J. D. (2009). Development of spatial and verbal working memory capacity in the human brain. *Journal of Cognitive Neuroscience, 21*(2), 316–332. https://doi.org/10.1162/jocn.2008.21028

Tomporowski, P. D., McCullick, B., Pendleton, D. M., & Pesce, C. (2015). Exercise and children's cognition: The role of exercise characteristics and a place for metacognition. *Journal of Sport and Health Science, 4*(1), 47–55. https://doi.org/10.1016/j.jshs.2014.09.003

Tomporowski, P. D., & Pesce, C. (2019). Exercise, sports, and performance arts benefit cognition via a common process. *Psychological Bulletin, 145*(9), 929–951. https://doi.org/10.1037/bul0000200

Tremblay, K., Kraus, N., & McGee, T. (1998). The time course of auditory perceptual learning: Neurophysiological changes during speech-sound training. *NeuroReport, 9* (16), 3557–3560. https://doi.org/10.1097/00001756-199811160-00003

Trost, S. G., Loprinzi, P. D., Moore, R., & Pfeiffer, K. A. (2011). Comparison of accelerometer cut points for predicting activity intensity in youth. *Medicine and Science in Sports and Exercise, 43*(7), 1360–1368. https://doi.org/10.1249/MSS.0b013e318206476e

van der Fels, I. M. J., de Bruijn, A. G. M., Renken, R. J., Königs, M., Meijer, A., Oosterlaan, J., et al. (2020). Relationships between gross motor skills, cardiovascular fitness, and visuospatial working memory-related brain activation in 8-to 10-year-old children. *Cognitive, Affective, & Behavioral Neuroscience, 20*(4), 842–858. https://doi.org/10.3758/s13415-020-00805-5

van der Fels, I. M. J., Hartman, E., Bosker, R. J., de Greeff, J. W., de Bruijn, A. G. M., Meijer, A., et al. (2020). Effects of aerobic exercise and cognitively engaging exercise on cardiorespiratory fitness and motor skills in primary school children: A cluster randomized controlled trial. *Journal of Sports Sciences, 38*(17), 1975–1983. https://doi.org/10.1080/02640414.2020.1765464

van Ewijk, H., Heslenfeld, D. J., Luman, M., Rommelse, N. N., Hartman, C. A., Hoekstra, P., et al. (2014). Visuospatial working memory in ADHD patients, unaffected siblings, and healthy controls. *Journal of Attention Disorders, 18*(4), 369–378. https://doi.org/10.1177/1087054713482582

van Ewijk, H., Weeda, W. D., Heslenfeld, D. J., Luman, M., Hartman, C. A., Hoekstra, P. J., et al. (2015). Neural correlates of visuospatial working memory in attention-deficit/hyperactivity disorder and healthy controls. *Psychiatry Research: Neuroimaging, 233*(2), 233–242.

Vazou, S., Pesce, C., Lakes, K., & Smiley-Oyen, A. (2019). More than one road leads to Rome: A narrative review and meta-analysis of physical activity intervention effects on cognition in youth. *International Journal of Sport and Exercise Psychology, 17*(2), 153–178. https://doi.org/10.1080/1612197X.2016.1223423

Vazou, S., Pesce, C., Lakes, K., & Smiley-Oyen, A. (2016). More than one road leads to Rome: a narrative review and meta-analysis of physical activity intervention effects on cognition in youth. *International Journal of Sport and Exercise Psychology, 1–26*. https://doi.org/10.1080/1612197X.2016.1223423

Valkenborghs, S. R., Noetel, M., Hillman, C. H., Nilsson, M., Smith, J. J., Ortega, F. B., et al. (2019). The impact of physical activity on brain structure and function in youth: A systematic review. *Pediatrics, 144*(4), e20184032. https://doi.org/10.1542/peds.2018-4032

Voelcker-Rehage, C., Godde, B., & Staudinger, U. M. (2011). Cardiovascular and coordinationtraining differentially improve cognitive performance and neural processing in older adults. *Frontiers in Human Neuroscience, 5*(26). https://doi.org/10.3389/fnhum.2011.00026

Voelcker-Rehage, C., & Niemann, C. (2013). Structural and functional brain changes related to different types of physical activity across the life span. *Neuroscience & Biobehavioral Reviews, 37*(9), 2268–2295. https://doi.org/10.1016/j.neubiorev.2013.01.028

Voss, M. W. (2016). The chronic exercise-cognition interaction: fMRI research. In T. McMorris (Ed.), *Exercise-cognition interaction: neuroscience perspectives* (pp. 187–209). Academic Press. https://doi.org/10.1016/C2013-0-18937-4.

Wassenaar, T. M., Williamson, W., Johansen-Berg, H., Dawes, H., Roberts, N., Foster, C., et al. (2020). A critical evaluation of systematic reviews assessing the effect of chronic physical activity on academic achievement, cognition and the brain in children and adolescents: A systematic review. *International Journal of Behavioral Nutrition and Physical Activity, 17*(1), 1–18. https://doi.org/10.1186/s12966-020-00959

Xue, Y., Yang, Y., & Huang, T. (2019). Effects of chronic exercise interventions on executive function among children and adolescents: A systematic review with meta-analysis. *British Journal of Sports Medicine, 53*(22), 1397–1404. https://doi.org/10.1136/bjsports-2018-099825

Zilles, D., Lewandowski, M., Vieker, H., Henseler, I., Diekhof, E., Melcher, T., et al. (2016). Gender differences in verbal and visuospatial working memory performance and networks. *Neuropsychobiology, 73*(1), 52–63. https://doi.org/10.1159/000443174