Physical Exercise and the Brain

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Thesis for the degree of Research Master of Cognitive Neuropsychology and Master of Clinical Neuropsychology

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PRELUDE

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Dear Reader,

This is my thesis for the degrees of Master of Clinical Neuropsychology and the Research Master Cognitive Neuropsychology. This paper is the product of my internship at the department of Clinical Neuropsychology at the VU University. Supervised by Professor Oosterlaan and Professor Scherder, I have met with the wondrous world of practicing science. My thesis, in a special form, elaborates on the relation between physical exercise and the brain.

Being one of the areas of focus in investigations at the department, it is not surprising that I have been made familiar with the topic of physical activity in neuroscience. In order to provide myself with a comprehensive understanding of the very interesting literature on this topic, I have written a review of meta-analyses on the effect of physical exercise interventions on neurocognitive and psychological functioning in humans. To provide myself with the opportunity of understanding the biological mechanisms by which physical exercise may improve brain function, I have additionally reviewed the core evidence on the neurobiological consequences of physical activity. It is amazing that a simple intervention as physical exercise can alter the animal as well as the human brain at many levels. The earlier mentioned review of meta-analyses and the additional review on the neurobiology of physical exercise constitute part A of my thesis.

After performing the literature study into the effects of physical exercise, I had of course become very interested in investigating this effect by myself. Therefore I have set up my own project investigating the effect of physical activity on the academic performance of primary school children: Where else should the effects of physical exercise on the brain's structure, neurocognitive functioning and psychological functioning of children better be reflected than in their academic performance? I have contacted many primary schools to request their participation and collect data on the academic performance and the level of physical activity of primary school children. An article on this experimental study into the relations between physical activity, sedentary behaviour and academic performance constitutes part B of my thesis.

Together part A and B constitute my thesis for the degrees of Research Master Cognitive Neuropsychology and the Master Clinical Neuropsychology, which I hereby present to you.

With many thanks to Professor Oosterlaan and Professor Scherder for their professional and intellectual support during the past eight months.

With special thanks to my parents for all their support in every form one can think of.

Sincerely,

Marsh Königs

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PART A

Effects of Physical Exercise on Brain Structure and Function: a Review.

Abstract

Background

Animal research has convincingly shown that physical exercise improves brain structure and function, but the effectiveness of physical exercise interventions in humans is still subject to debate.

Aims

Reviewing the meta-analytic evidence from randomised controlled trials (RCT) on the efficiency of physical exercise interventions for neurocognitive function and psychological health in humans. Additionally the core evidence on the neurobiological effects of physical exercise in animals as well as humans was reviewed.

Results

Meta-analyses have repeatedly shown that physical exercise has small to moderate positive effects on neurocognition and symptoms of depression and anxiety. However, RCT's in this field have systematically failed to employ true randomisation of group assignment, apply blinding procedures and perform intention-to-treat analysis, questioning the reliability of the results. Angiogenesis, cerebral blood flow, brain derived neurogrowth factor, synaptogenesis, neurogenesis and reductions of the stress response are possible mediators of the effect of exercise on brain function.

Conclusions

Physical exercise is a promising intervention to improve neurocognitive function and psychological health. There is need of high-quality RCT's investigating physical exercise interventions.

Effects of Physical Exercise on Brain Structure and Function a Review.

The modern society is adapting to a sedentary lifestyle (Levine, 2010). This global trend is a major threat for public health (WHO, 2001). Lower levels of physical activity have been associated with an increased incidence of cardiovascular risk factors such as hypertension, obesity and diabetes (Laaksonen et al., 2002). Cardiovascular pathology already is the world leading cause of death and its costs for the European Union have been estimated at € 179 billion euro in 2003. (Leal, Luengo-Fernández, Gray, Petersen, & Rayner, 2006; Organisation, 2011; WHO, 2011). However, the consequences of a sedentary lifestyle may not be restricted to cardiovascular pathology: Lower levels of physical activity have been related to lower levels of neurocognitive performance and psychological health (Lojovich, 2010).

Researchers have now collected a convincing body of evidence showing that physical exercise improves neurocognitive performance in animals (Hillman, Erickson, & Kramer, 2008). Likewise there is an increasing amount of evidence showing that exercise promotes human brain structure and function (Lista & Sorrentino, 2010). Physical exercise has even been proposed as a potential valuable and cost-efficient behavioural intervention for conditions that affect neurocognitive function (Cotman & Berchtold, 2002; Lojovich, 2010; Nithianantharajah & Hannan, 2006; Ploughman, 2008). Therefore, physical exercise has received increasing attention in the field of neuroscience and there is now a considerable amount of studies available on the relation between physical exercise and brain function.

One of the first meta-analyses concerning the relation between physical exercise and was performed by Etnier et al. (1997). These authors have aggregated all available evidence, including cross-sectional studies, longitudinal investigations and randomised controlled trials (RCT's). Overall the authors have found a modest positive relationship between physical exercise and neurocognitive function (g = 0.29). Since this result is based on cross-sectional as well as quasi- and true-experimental studies, it is not clear whether this relationship reflects a causal effect of physical exercise or a pre-existing relation between physical activity and neurocognitive function. In line with the latter idea, Etnier et al. have found that as experimental rigor increased, the effect-size of the observed relationship decreased. This finding indicates that the strength of the relation between physical exercise and neurocognitive function diminished when the likelihood of causality increased, indeed suggesting that hidden variables such as IQ, diet and lifestyle contribute to the relation between physical exercise and neurocognitive function (Hillman et al., 2008).

Randomized controlled trials are a suited method to assess the causal component of the effect of exercise on neurocognition (Begg et al., 1996). According to this methodology, subjects are randomly assigned to one of two groups: an experimental group receiving an intervention of interest and a control group preferably receiving a placebo treatment. If the experimental group has a significantly larger pre-post intervention difference on the outcome measure compared to the control group, this effect is attributed to the experimental intervention. RCT's are regarded as being the most robust methodology for investigations into the causal effect of interventions in clinical research (Begg et al., 1996).

There is available a considerable amount of RCT's that have investigated the effectiveness of physical exercise interventions on functional aspects of the brain (Smith et al., 2010). Moreover, multiple systematic reviews have now statistically aggregated the evidence from RCT's, providing excellent evidence on the causal effect of exercise on brain function (Evans, 2003). Surprisingly there is still no consensus on the effectiveness of physical exercise in the field of neuroscience. Therefore, the primary aim of this study was to review the best evidence available on the efficiency of physical exercise interventions on two major functional aspects of the brain: neurocognitive function and psychological health. However, the quality of the RCT design can give rise to important limitations concerning the reliability of the results. Therefore it is important to assess the quality of the RCT's that have been performed before their results are interpreted.

There are multiple important aspects of RCT studies that determines their quality (Begg et al., 1996). First is the randomisation method for the assignment of participants to the experimental or control condition. True randomisation reduces the chances of research bias by participant selection (e.g. assigning participants that are not expected to benefit from the intervention in the control group). Second, is the type of control-treatment. The use of non-intervention groups as control condition disables the investigator to discriminate specific effects caused by the intervention from nonspecific effects that may be caused by placebo effects or social interaction. Third, the blinding of participants and assessors is important to prevent nonspecific effects influencing the results as well. Failure to blind participants may contribute to a placebo effect, whereas non-blinded outcome assessment may increase research bias. Last of the most important indicators of study quality in RCT's is the application of the intention-to-treat (ITT) analysis. This procedure accounts for the problem of bias due to the selective drop-out of participants. In RCT's one risks possibility that the participants that do not experience improvement in response to the treatment, drop out of the study due to decreased motivation. If so, the trial ends with the proportion of the participants in which the intervention was (at least subjectively) more effective. Analysing the results for only these participants may overestimate the effect of the intervention, because the results for the selective drop-outs have been left out. ITT-analysis accounts for this problem by adding the (premature) post-intervention measurement of outcome for the drop-outs into the analysis, preventing the study outcome for inflation due to selective drop-out. For studies that have not applied ITT-analysis, it is thus important that the proportion of participants that was lost to post-intervention measurement (attrition rate) is very low. Otherwise the intervention effect can be alternatively explained by selective drop-out of participants.

The current study will first review the meta-analytic results from RCT's concerning the efficiency of physical exercise on neurocognitive function in humans. Second, meta-analytic results from RCT's into the effectiveness of physical exercise on psychological health in humans, more specifically the symptoms of clinical depression and anxiety, will be reviewed. As an additional aim, the core evidence on the neurobiological effects of physical exercise in animals as well as humans will be reviewed. According to the author's best knowledge, the present study is the first to review of the body of systematic evidence on the relations between physical exercise, neurocognitive performance and psychological health.

Pubmed and Google Scholar were searched using the (MeSH-)terms ‘physical exercise’, ‘physical activity’, ‘cognition’, ‘psychological health’, ‘meta-analysis’ and equivalents. In order to provide an up to date review of the evidence, only meta-analyses published during the past two decades were included for review. There were identified seven meta-analyses that report on RCT’s into the effect of physical exercise on neurocognitive performance in humans and six investigating the effects of physical exercise on clinical depression or anxiety. For every study that was included for review the characteristics, methods, main outcome and conclusions are presented in Table 1 (neurocognitive function) and Table 2 (psychological health).

Physical exercise and neurocognitive function

Many studies have identified a positive effect of physical exercise on neurocognitive function in animals (Hillman et al., 2008). However, the studies that have investigated the effect of physical exercise on human neurocognition retrieved equivocal results. As a consequence most narrative reviews that have dealt with the relevant literature were deemed inconclusive. Meta-analyses have been performed in order to provide statistical aggregates of the available evidence from RCT’s. The results of these studies will be described to provide an overview of the literature on the effect of physical exercise on neurocognitive performance in humans.

Meta-analytic effects of physical exercise on neurocognitive function

The first meta-analysis concerning the effect of physical exercise on neurocognitive function has been performed by Etnier et al. (1997). The RCT’s that have been included comprised a total of 420 healthy as well as clinical individuals within the ages 6-90. It has not been reported what type of control groups were used in the included RCT’s, whether participants and assessors were blinded, what attrition rates were observed or whether ITT-analysis was performed. Among these RCT’s (n = 17) there has been found a modest but significant positive effect on a composite measure of neurocognitive function (Hedge’s g = 0.15).

Colcombe and Kramer (2003) have investigated RCT's that used an aerobic exercise intervention in samples of predominantly healthy elderly (age > 55 years). RCT's applying interventions that were unsupervised or did not involve an aerobic component were excluded, leaving 18 studies of which seven were earlier included by Etnier et al. (1997). The authors have not reported on the nature of the control treatment, blinding procedure, application of ITT-analysis and the attrition rates in the included RCT's. The analysis has revealed a positive effect of exercise on a composite of neurocognitive function that just escaped the threshold for a moderate effect. Within the neurocognitive domain, physical exercise has been found to have a large positive effect on executive function and moderate positive effects on visuospatial function and processing speed. The improvements in neurocognitive function in the intervention groups were all reliably larger compared to the control groups.

These meta-analytic results based on findings from RCT's provide further support for a causal effect of physical exercise on neurocognitive performance. Although partly overlapping in the studies that were included, Colcombe and Kramer have retrieved considerably larger effect sizes compared to Etnier et al. (1997). One explanation is that the Colcombe and Kramer have applied more conservative exclusion criteria compared to Etnier et al. in an attempt to increase the overall methodological quality of the sample. Another explanation refers to differences in the overall age of the included samples between studies. Given that Kramer and Colcombe found larger effects in samples of exclusively elderly than Etnier et al. have found in samples of children, adults and elderly, the effects of exercise may be larger for elderly compared to adults and/or children.

The sole meta-analysis that has concerned exclusively children was performed by Sibley and Etnier (2003). Specifications on the methodology of RCT have not been provided. Additionally it could not be determined what proportion of studies has been included in earlier meta-analyses. The authors have found a small positive effect (g = 0.29).

Heyn et al. (2004) have investigated the efficiency of '*any exercise program or form of rehabilitation strategy, physical activity, fitness or recreational therapy*' (p. 2) for cognitively impaired elderly using exclusively RCT's. Among the 22 included studies, predominantly non-intervention groups were applied as control condition (no numbers specified). Furthermore, six studies applied a blinding procedure and five studies accounted for selective drop-out of participants (no attrition rates reported). Overall studies there has been found a moderate positive effect on a general measure of neurocognitive function (Mini-Mental Status Examination). This indicates that physical exercise can be a successful intervention for clinical groups and moreover, that exercise has the potential of reversing neurocognitive decline during pathological aging.

Angevaren et al. (2008) have investigated RCT's on the effect of any physical exercise intervention on cardiovascular fitness. Control groups consisted of no-intervention groups (n = 5), a strength or balance program (n = 4) or social activities (n = 2). Of the 11 included studies, six have *not* been included in earlier meta-analyses by Etnier et al. (1997), Colcombe and Kramer (2003) or Heyn et al. (2004). One of the included studies has reported an adequate randomisation method, six provided attrition values, none blinded the participants, one blinded the assessors and only three have reported that ITT-analysis was performed (mean attrition 9.6% in the intervention groups). Angevaren et al. have found that eight out of eleven studies show that physical exercise improves cardiovascular fitness. Furthermore it has been shown that exercise interventions had a large positive effect on motor function, moderate positive effects on auditory attention and delayed memory function and a small positive effect on processing speed and visual attention. As compared to controls, the physical exercise group performed better on tests for auditory attention and motor function. Nevertheless, the authors have reported that the majority of the comparisons with control groups concerning various neurocognitive functions retrieved no significant differences. Therefore the findings by Angevaren et al. support a causal effect of physical exercise on neurocognitive function on one hand, but indicate that physical exercise may selectively promote certain neurocognitive functions on the other hand.

Smith et al. (2010) have performed the most recent meta-analysis into the effect of physical exercise on neurocognitive function. RCT's applying interventions with a duration of at least 1 month, involving aerobic exercise in non-demented adults (>18 years), were included only if an adequate randomisation method was performed. The included studies typically used waiting list participants as controls (not further specified). Furthermore, 45% of the studies applied blinded assessment and 24% performed ITT-analysis (mean attrition = 12%). Sixteen out of the 29 studies that were included has been included in at least one of the previous described meta-analyses as well. The authors have found modest but significant positive effects of exercise on measures for attention and neurocognitive speed, executive function and memory function. Surprisingly it has not been described in this study whether the effect sizes were calculated on basis of differences in neurocognitive gains or differences in post-intervention performance between groups. If the former and more reliable method has been employed it is remarkable that the comparisons between group gains are not reported, which questions the reliability of the results.

Moderators of the effect of exercise

The results from meta-analyses have shown that the effects of physical exercise on neurocognitive function are not straightforward. The studies that were described have identified age, exercise intensity and exercise type and health status as moderators of the effectiveness of physical exercise interventions for neurocognitive function. First, moderate exercise duration has been identified as a more efficient intervention than mild and vigorous exercise (Colcombe & Kramer, 2003). Second, aerobic exercise has been found a more effective intervention than flexibility and/or balance training (Angevaren et al., 2008). Interestingly the effects of aerobic exercise and strength training have been found comparable (Angevaren et al., 2008), whereas a combination of the two yielded stronger effects than aerobic exercise alone (Angevaren et al., 2008; Colcombe & Kramer, 2003; Smith et al., 2010). Fourth, aerobic exercise seems to be a more efficient intervention for children and elderly, since considerably larger effects have been observed in these children and elderly compared to adults (Angevaren et al., 2008; Heyn et al., 2004; Sibley & Etnier, 2003; Smith et al., 2010). Last, physical exercise has been found to be an effective intervention in both healthy and clinical populations (Etnier et al., 1997; Heyn et al., 2004; Sibley & Etnier, 2003).

Summary and discussion of the meta-analytic evidence

The effect of physical exercise on neurocognitive performance. Taken together, seven out of seven meta-analyses have retrieved a significant positive relationship between physical exercise and neurocognitive performance. Meta-analytic results from RCT's have repeatedly supported the hypothesis stating that physical exercise interventions improve neurocognitive functioning relative to controls. It has been shown that physical exercise has a small to moderate positive effect on neurocognitive performance in both healthy and clinical individuals, children, adults and elderly. Altogether these findings provide a convincing evidence-based ground in favour of a beneficial effect of physical exercise on neurocognitive functioning. Moreover these findings contribute to the worrying thoughts on the global trend towards a sedentary society: There is accumulating evidence suggesting that, besides cardiovascular health, physical inactivity has a negative influence on neurocognitive function.

Limitations. Although there is meta-analytic ground for a positive effect of exercise on neurocognitive performance, the available literature has several limitations. First, the majority of the observed effect sizes that have been determined are small, suggesting that physical activity has only a minor beneficial effect on neurocognitive functioning. This finding can alternatively be explained by the widespread use of a composite measure for neurocognitive functioning in systematic reviews. These composite measures reflect the average effect of exercise on a range of neurocognitive functions, each assessed by a range of neurocognitive tests. Considering that physical activity might have selective effects within the neurocognitive domain (Tomporowski, Davis, Miller, & Naglieri, 2008), the composite measure reflects an underestimation of the effect on functions that are sensitive to exercise and an overestimation of the effect on functions that are not. In line with this idea, the effect size of exercise interventions vary within the neurocognitive domain (Angevaren et al., 2008; Etnier et al., 1997; Sibley & Etnier, 2003) and is larger for the studies that assessed a single measure of neurocognitive function (Heyn et al., 2004).

Second, the RCT's that have been included in the described meta-analyses systematically suffer from serious methodological shortcomings. The majority of the studies have not performed (or reported) adequate randomisation strategies, increasing the chance of participant selection during group assignment. The majority of the studies have not compared the intervention group with a placebo treatment but with no-intervention groups. Therefore these studies have failed to account for nonspecific effects (e.g. placebo and social interaction). At the same time the majority of the studies have not blinded the participants, which may have contributed to a placebo effect. Furthermore, the majority of the studies have not blinded outcome assessment, failing to account for researcher's bias towards a positive effect. Last, the majority of the studies did not employ ITT-analysis, failing to account for the effects of selective drop-out in the intervention group. Surprisingly, attrition rates were not always reported in both RCT's and meta-analyses, interfering with judgement of the necessity of performing ITT-analysis.

Conclusions. A considerable body of meta-analytic evidence from RCT's shows that physical exercise interventions modestly improve neurocognitive function. Many moderators of exercise interventions have been identified, challenging researchers to further investigate the effects of subject characteristics, intervention characteristics and carefully considering the neurocognitive function that will be assessed.

Physical exercise and psychological health

Psychological health has been identified as an important mediator of Quality of Life (Deslandes et al., 2009; Martinsen, 2008). Interestingly mood disorders have been shown to negatively impact physical activity (Conn, 2010). It has been proposed that increasing the level of physical activity may in turn reverse the symptoms of mood disorders (Ahn & Fedewa, 2011). Given that depression and anxiety have been identified as important threats of psychological health (World Health Organisation [WHO], 2001), this review of meta-analyses was restricted to the meta-analyses that aggregated RCT's concerning the effect of physical exercise on symptoms of clinical depression and anxiety.

Meta-analytic effects of physical exercise on psychological health

Among children, there have been performed two meta-analyses on basis of results from RCT studies. Ahn and Fedewa (2011) investigated the effect of any type of physical exercise on psychological health in both healthy and clinical children between the ages 3-18 years. There was no information provided on randomisation methods, blinding procedures, the application of ITT-analysis and attrition rates. It has been shown that physical exercise has moderate reducing effects on both the symptoms of depression and anxiety compared to controls (Table 2). It has been found that the effect was larger for interventions of higher intensity. Importantly, the authors reported a slight publication bias, questioning the validity of the presented findings.

Larun et al. (2006) have investigated both healthy and clinical samples of children and adolescents between the ages of 11-19 years. The interventions of the included studies involved vigorous exercise for a minimum duration of four weeks. The control groups included waiting list participants, non-intervention groups, low intensity exercise or psychosocial groups. Among the 14 included studies, randomisation methods have been reported to be *adequate* for one study, *unclear* for 11 studies, and *inadequate* for two studies. No information has been provided on blinding procedures, ITT-analysis and attrition rates. Larun et al. have been found that physical exercise moderately reduced symptoms of depression. There was observed a reduction in symptoms of anxiety as well, although this effect did not reach the threshold for a statistical significant effect.

Wipfli, Rethorst and Landers (2008) have investigated samples of children, adults and elderly with and without clinical mood disorders. There has not been provided information on the randomisation procedures of the included studies. No-intervention groups served as control condition. The included studies had an average attrition rate of 7.1%. It has not been reported whether the studies employed ITT-analysis. The authors have shown that physical exercise has a small reducing effect on symptoms of anxiety in children. Compared to other interventions for depression (eg. cognitive therapy, group therapy, stretching, relaxation, stress management, pharmacotherapy and music therapy), physical exercise proved to be a more effective treatment for anxiety.

Lawlor and Hopker (2001) have assessed the effect of exercise on depressive symptoms of clinical depressed adults (> 18 years). Studies that compared varying physical exercise interventions with no-treatment controls, placebo intervention or established treatments for depression were included. The authors have reported that physical exercise was found to have a large reducing effect on depressive symptoms compared to controls. The authors have refrained from firm inference on basis of their results because of the poor methodological quality of the included studies. In line with previous research, RCT's investigating the effect of physical exercise generally have failed to describe the randomisation method, blind assessment of the outcome measure or perform ITT-analysis.

Sathopoulou et al. (2006) have investigated the effect of physical exercise interventions on the level of depressive symptoms. Control groups were no-intervention groups (*n* = 3) waiting list participants (*n* = 2) or received placebo treatment (*n* = 6). Attrition rates in the intervention groups ranged from very low (0%) to very high (62%, mean = 19.9%). No information has been provided on the randomisation methods of the included studies, the blinding procedures or on whether ITT-analysis was performed. The authors have found a very large reducing effect of physical exercise on the level of depressive symptoms. Consequently it has been concluded that physical exercise can be a powerful intervention to relieve depressive symptoms.

Mead et al. (2009) have compared the effect of exercise interventions to no-intervention groups (*n* = 6), waiting list participants (n = 7) and placebo treatment (*n* = 14) among clinically depressed adults (> 18 years). Of the 27 included studies, randomisation methods have been judged *adequate* for eight studies, *inadequate* for eleven studies and *unclear* for eight studies. Six studies blinded assessment of outcome and eight studies applied ITT-analysis. No information on attrition rates has been reported in the majority of the studies. It has been found that physical exercise caused a large reduction in the symptoms of depression. The authors have criticised the majority of the studies suffers for poor methodological quality with respect to the randomisation method, blinding procedures and ITT-analysis. When restricting the analysis to methodologically sound RCT's (*n* = 3), the observed effect has been found reduced to a moderate size and was not statistically significant (g = -0.42). Therefore the authors have concluded that physical exercise seems to improve mood, although there is a need for more large and methodologically robust RCT's to prove this.

Conclusion and discussion

A large body of evidence indicates that physical exercise strongly to moderately reduces the symptoms of depression and anxiety. Given that psychological health is positively related to neurocognitive performance (Kolb & Wishaw, 2008), improvements in psychological health may mediate the effect of physical exercise on neurocognitive function or vice versa, or both.

However, the evidence supporting the former statement suffers systematically from poor methodological quality. RCT's are regarded as a robust method to investigate a causal relationship in clinical practice, but as earlier described concerning the evidence on neurocognitive function, investigators have failed to account for several shortcomings of this method. The randomisation method for group assignment was not reported in the majority of the studies. Control groups often included no-intervention groups or waiting list participants while a placebo intervention is clearly preferable in order to account for the placebo effect. At the same time participants and assessors of outcome were often not blinded. The majority of the studies did not apply ITT-analysis in order to account for selective drop-out, while attrition rates were also not provided in most studies.

Taken together, meta-analytic evidence shows that physical exercise has anti-depressant and anxiolytic effects. However, the evidence suffers from serious methodological limitations, questioning the reliability of the results. Therefore the provided evidence should be interpreted as suggestive for the positive effects of physical exercise on psychological health. More adequately performed RCT's investigating large samples should be performed in order to confirm the efficiency of physical exercise interventions on psychological health. Please refer to *future directions* for a comprehensive proposal for guidelines regarding future studies into the effect of physical exercise on functional aspects of the brain.

Neurobiology of physical exercise

Animal research has identified the physiological, chemical and structural changes that occur in the brain in response to physical exercise. There is now a considerable amount of evidence suggesting that physical exercise influences the cardiovascular system, neurotransmitter system, brain derived neurogrowth factor (BDNF) and the stress-response in ways that are associated with improved neurocognitive function (Hillman et al., 2008). It will be described why and how these mechanisms are thought to mediate the effect of exercise on neurocognitive function.

The cardiovascular system.

One way by which physical exercise has been proposed to improve brain function is by adaptations of the cardiovascular system (Lojovich, 2010). Angiogenesis and cerebral blood flow (CBF) have been identified as possible mediators of the effect of physical exercise on neurocognitive function by promoting brain perfusion. Brain perfusion indicates the level of oxygen supply and withdrawal of metabolites in the brain (Underwood, 2004). Increasing the efficiency of oxygen delivery has been associated with improvements in neurocognitive functioning in humans: Erythropoetin, a stimulating agent of red blood cell formation, improves neurocognitive function in humans (Ajmani et al., 2000). Thus, increasing the number of red blood cells that are responsible for oxygen transport promotes a more efficient oxygen supply, resulting in enhanced brain function. Therefore, brain perfusion has been identified as a mediator of the effect of physical exercise on the brain. Angiogenesis and cerebral blood flow are two important mechanisms that have been thought to influence brain perfusion in response to physical exercise.

Angiogenesis. Angiogenesis is the process of new blood vessel formation or extension which improves the perfusion capacity of target tissues (Underwood, 2004). Evidence from animal models has shown a clear relationship between physical activity and angiogenesis in the brain. For example, RCT's into the effects of aerobic exercise have shown improvements in the vasculature of the motor cortex and striatum of rodents and primates (Ding, Vaynman, Akhavan, Ying, & Gomez-Pinilla, 2006; Rhyu et al., 2010; Swain et al., 2003). The promoting effect of exercise on angiogenesis is not restricted to areas that are involved in motor function, but has been found in the mice' hippocampus as well (Clark, Brzezinska, Puchalski, Krone, & Rhodes, 2009). Moreover it has been shown that exercise-induced angiogenesis in the dentate gyrus and striatum improves the rat's performance on a spatial memory test (Van der Borght et al., 2009).

Up until now there is very little literature available on the effect of exercise on angiogenesis in the human brain. There is evidence showing that physical exercise increases mRNA levels of vascular endothelial growth factor, a promoting agent of angiogenesis, in human skeletal muscle (Gustafsson, Puntschart, Kaijser, Jansson, & Sundberg, 1999; Leung, Cachianes, Kuang, Goeddel, & Ferrara, 1989). This provides indirect evidence for the idea that physical exercise promotes angiogenesis in humans, although it is not known whether this applies to the brain as it does to skeletal muscle.

Cerebral blood flow. CBF is a quantitative measure of blood circulation in the brain. There is a growing body of evidence that has shown a positive relationship between physical exercise and CBF in humans (Querido & Sheel, 2007). For example, it has been shown that moderate exercise increases the blood flow in the middle cerebral, common carotid, internal carotid and vertebral arteries with up to 39%. (Hellström, Fischer-Colbrie, Wahlgren, & Jogestrand, 1996; Sato & Sadamoto, 2010). These arteries are known to provide blood supply to large parts of the frontal, temporal and parietal lobes, which are strongly related to neurocognitive function (Kolb & Wishaw, 2008). This finding indicates that physical exercise promotes cerebral perfusion in brain areas that are very important for neurocognitive function.

The neurotransmitter system

The neurotransmitters system has been identified as a potential mediator of the effect of physical exercise on neurocognitive function (Lista & Sorrentino, 2010; Lojovich, 2010). The neurotransmitters *serotonin*, *noradrenalin*, *dopamine* and *acetylcholine* play important roles in brain processes such as the circadian rhythm, motor behaviour, mood, arousal, feelings of reward, learning, memory and attention (Kolb & Wishaw, 2008). The importance of the neurotransmitter system is illustrated by the consequences of dysfunction of the system: drastic changes in mood, behaviour and neurocognition. Symptoms of clinical depression, anxiety and schizophrenia have been allocated to decreased levels of *serotonin* and *noradrenaline* (Purves et al., 2004). Consequential stimulation of *serotonin* receptors has in turn been found to relieve these psychiatric symptoms (Purves et al., 2004). Furthermore, higher levels of cortical *serotonin* have been associated with increased synthesis of BDNF, neurogenesis in the hippocampus and improvements in neurocognitive functioning of clinically depressed humans (Kolb & Wishaw, 2008; Taragano, Lyketsos, Mangone, Allegri, & Comesaña-Diaz, 1997). Aberrant levels of *dopamine* in the striatum have been found to be a main causal factor in Parkinson’s Disease. Promoting the levels of *dopamine* by administering levodopa (a *dopamine* precursor) or stimulating the subthalamic nucleus relieves the symptoms of Parkinson’s Disease (Fahn et al., 2004; Kumar et al., 1998). Likewise, dysfunction of *acetylcholine* has been found to be associated with the severity of Alzheimer’s disease (Kolb & Wishaw, 2008), while promoting the synaptic level of *acetylcholine* reduces the symptoms (Gauthier, 1999). Taken together, it is clear that the neurotransmitter system plays a vital role in our everyday brain function.

Animal research has provided abundant evidence showing that physical exercise promotes the function of the neurotransmitter system. Physical exercise has been found to increase the levels of *serotonin* and its metabolites in the rat’s brain stem, hypothalamus, hippocampus and striatum (Blomstrand, Perrett, Parry-Billings, & Newsholme, 1989). Moreover exercised rats have been found with elevated levels of *noradrenalin* in the blood plasma and striatum (Blomstrand et al., 1989; Dishman et al., 1997). Physical exercise has been found to reduce the release of *noradrenalin* in response to stress, blunting the stress response which has been found to have detrimental effects on structural and functional aspects of the brain (Soares, Naffah-Mazzacoratti, & Cavalheiro, 1994). *Dopamine* levels in the brainstem, hypothalamus and striatum of rodents have been shown to respond positively to exercise as well (Blomstrand et al., 1989; Sutoo & Akiyama, 1996). Physical exercise has even been shown to postpone the onset and decrease the incidence of Parkinson’s disease in rodents (Poulton & Muir, 2005). Exercise has furthermore been found to increase *dopamine* receptor density in the striatum, thereby reversing the age-related decrease in neurocognitive functioning in rats (MacRae, Spirduso, Walters, Farrar, & Wilcox, 1987). Last, physical exercise has been found to increase *acetylcholine* levels and receptors in the hippocampus of the rat, which may explain the protective effect of exercise for developing dementias such as Alzheimer's disease (Fordyce, Starnes, & Farrar, 1991; Heyn et al., 2004).

There has been performed comparatively little research into the effect of physical exercise on the human neurotransmitter system. Nevertheless, there is evidence indicating that the overwhelming amount of results from animal studies translate to the human neurotransmitter system. For example, it has been shown that the levels of *serotonin* metabolites in human cerebrospinal fluid are elevated in response to physical exercise (Post & Goodwin, 1973). Likewise physically trained men have been found with higher blood *serotonin* levels than their matched untrained controls (Soares et al., 1994). In line with previous findings it has been shown physical exercise increases human plasma levels of *noradrenaline* as well.

Taken together, the human neurotransmitter system is involved in a variety of human brain functions, including neurocognitive function. Research has provided abundant evidence for the beneficial effects of physical exercise on the rodents' neurotransmitter system and there is some evidence indicating that these findings translate into humans.

Neurotrophic factors

One neurotrophic factor that is thought to play a very important mediating role in the effects of physical exercise on neurocognitive function is BDNF. This protein is involved in neurotransmitter regulation (Bolton, Pittman, & Lo, 2000) and the differentiation, extension and survival of neurons throughout the brain (Lu & Gottschalk, 2000). Consequently there is abundant evidence showing that BDNF plays a vital role in the development and function of the brain. Administration of BDNF for example increases spine density and dendritic growth and neurogenesis in the hippocampus, thalamus, striatum, septum and hypothalamus (Pencea, Bingaman, Wiegand, & Luskin, 2001; Tyler &

Pozzo-Miller, 2001). Furthermore, it has been shown that direct injection of BDNF in the rat hippocampus increases long-term potentiation (LTP). LTP is the process of upregulation of post-synaptic receptors that is very important for learning and memory, indicating the importance of BDNF for neurocognitive function (Cooke & Bliss, 2006; Tyler & Pozzo-Miller, 2001). In line with this idea, it has been shown that higher levels of plasma BDNF have been positively related to global neurocognitive function, information acquisition and memory recall in elderly women (Komulainen et al., 2008). There has even been found a mutation in the BDNF gene that causes learning impairments in humans (Hariri et al., 2003), indicating that BDNF is a crucial factor for successful neurocognitive functioning.

Physical exercise has been found to enhance the level of BDNF. There have been found elevated mRNA levels of BNDF in the rodent hippocampus, motor cortex, cerebellum and striatum (Neeper, Gómez-Pinilla, Choi, & Cotman, 1995). Interestingly the increase in transcription was largest in the hippocampus, which is mainly involved in neurocognitive function rather than motor behaviour. Moreover exercise has been shown to increase LTP in the dentate gyrus of the rat hippocampus, accompanied by an improvement in spatial memory (van Praag, Christie, Sejnowski, & Gage, 1999). BDNF is regarded as an important mediator of exercise-induced plasticity, since it has been shown that the exercise-induced improvements in spatial learning and memory recall were prevented by the selective blocking of BDNF receptors in the hippocampus (Vaynman, Ying, & Gomez-Pinilla, 2004). Importantly, Ferris et al. (2007) have replicated findings from animal studies in humans by showing that physical exercise increases the plasma levels of BDNF in humans, paralleled by improvements in performance on a measure of executive function.

These findings illustrate the importance of BDNF for neural development, neural structure, neuroplasticity and neurocognitive functioning in animals and humans. Physical exercise increases BDNF levels in animals as well as humans. Most importantly, blockage of BDNF cell-signalling has been shown to counteract the beneficial effects of physical exercise on neurocognitive function, strongly suggesting that BDNF plays an important mediating role in the relation between exercise and neurocognition.

Neurostructure

In line with the effects of physical exercise on BDNF, there have been observed multiple neurostructural changes in response to physical exercise. Neurogenesis, which is the process of new cell formation, has been found restricted to few areas in the brain such as the hippocampus and olfactory bulb (Purves et al., 2004). The importance of neurogenesis has been illustrated by showing that hippocampal neurogenesis predicts spatial memory performance in the aging rat, strongly suggesting that neurogenesis contributes to neurocognitive function (Drapeau et al., 2003).

Physical exercise has been shown to induce neurogenesis in the rodent hippocampus (Brown et al., 2003; van Praag, Kempermann, & Gage, 1999). Importantly is has been shown that the neurons that are formed in response to physical exercise can integrate into a neural network to become functional (Lledo, Alonso, & Grubb, 2006). In line with this idea, it has been shown that exercise- induced neurogenesis in the rat hippocampus is accompanied with improvements in spatial memory performance (van Praag, Christie, et al., 1999). Furthermore, animal studies have shown that physical exercise improves neural connectivity by extending dendrites, increasing the complexity of dendritic connections and the density of dendritic spines (Eadie, Redila, & Christie, 2005).

Investigations into humans have shown that higher cardiovascular fitness is associated with lower age-related declines in tissue density of the frontal, parietal and temporal cortices (Colcombe et al., 2003). This finding suggests that physical exercise reduces the neuronal loss in the normal human aging process. Likewise, it has been found that physically active elderly humans show larger volumes of the hippocampus (Erickson et al., 2009), which is possibly caused by exercise-induced neurogenesis in the human hippocampus (Pereira et al., 2007). In line with the idea that physical exercise induces neurogenesis, it has been found that preadolescent children with higher cardiovascular fitness show larger volumes of the basal ganglia and hippocampus (Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock, Erickson, Prakash, VanPatter, et al., 2010). Most importantly, larger volumes of the basal ganglia and hippocampus in these children were associated with better performance on tasks for attentional functioning and memory respectively.

Taken together, physical exercise promotes neuroplasticity at the level of the synapse, dendrites and cell formation in animals as well as humans. Possibly these structural changes are the result of increased levels of BDNF, but more importantly they have been directly related to human neurocognitive functions such as learning, memory and attention.

The stress response

The stress response is, from an evolutionary approach, an adaptive reaction to physical danger. The stress response has been found to provide the energy for a fight or flight response by increasing the activity of the HPA-axis and sympathetic nervous system (SNS), leading to the release of glucose and lipids into the bloodstream (Kastello & Sothmann, 1999). Nowadays, humans are less likely to be confronted with physical danger than with emotional, social and professional stress. Psychological stressors differ from physical stressors on two important aspects (Kastello & Sothmann, 1999). First, psychological stressors do often not require an energy demanding response. As a consequence the energy supply that is recruited by the stress response remains largely unused and is restored in the body. Second, the time domain of a psychological stressor is not clearly confined. Therefore, the stress response is likely to be elongated, creating a prolonged hyperenergetic state of metabolism (Kastello & Sothmann, 1999).

Psychological stress has been found to promote prolonged hyperactivity of the HPA-axis and SNS. These prolonged stress responses have been associated with detrimental effects on human health: increased prevalence of obesity, insulin resistance, hypertension, vascular damage and chronic disease (McEwen, 1998; Tsatsoulis & Fountoulakis, 2006). Furthermore the stress response has been shown to negatively influence the levels of noradrenalin, dopamine, serotonin (Grippo & Johnson, 2009) the level of BDNF, the cell count in the hippocampus (Sapolsky, 2000), neurocognitive functioning (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997) and mood (McEwen, 2003).

When summarised in this way, the similarity of the mechanisms on which both physical exercise and the stress response seem to act is striking. This suggests that physical exercise and the human stress system have interacting effects on shared biological mechanisms that are important for human brain function. In line with this idea, physical exercise has been found to counteract the effects of stress on the HPA-axis and the SNS (Tsatsoulis & Fountoulakis, 2006). The rostral ventrolateral medulla (RVLM) may play an important role in the mechanism by which physical exercise and the stress response interact. The RVLM has been found to be the key region in regulating sympathetic activity through which physical exercise reduces the activity of the human SNS (Mueller, 2010). Moreover, higher cardiovascular fitness has been found to blunt the human stress response to psychological stressors, indicating that exercise reduces the vulnerability to environmental stress (Dishman et al., 1998; Soares et al., 1999).

These findings show that psychological stress has a detrimental effect on the structure and function of the human brain. Interestingly psychological stress and physical exercise seem to interact on shared biological mechanisms that are important for neurocognitive function and psychological health. Reducing the excitability of the stress system to psychological stressors, thereby relieving the burden of the stress response on the structure and function of the brain, might be another way in which physical exercise improves neurocognitive function and psychological health.

Final conclusions and future directions

This review described the literature on the efficiency of physical exercise interventions in improving two major functional aspects of the brain at the functional level, showing that there is considerable evidence supporting that physical exercise promotes neurocognitive function and psychological health in healthy individuals as well as clinical groups. As a secondary aim, the neurobiological consequences of physical exercise have been reviewed. Exercise induced improvements in the neurotransmitter system, the level of BDNF, synaptic plasticity, dendritic growth and neurogenesis can explain how physical exercise can improve neurocognitive function. Importantly, exercise-induced plasticity is not restricted to the areas that are involved in motor function, but applies to areas highly involved in higher order neurocognitive function. Furthermore, the blunting effect of physical exercise on the excitability of the human stress system provides a compelling explanation for the anxiolytic and antidepressant effects of physical exercise. Likely, the quality of neurocognitive function and psychological health bear a reciprocal relationship in their response to physical exercise (Ahn & Fedewa, 2011).

The literature on the relation between physical exercise and the brain highlights the importance of the global trend towards a more sedentary lifestyle. Sedentary behaviour does not merely affect cardiovascular pathology, but is likely to interfere with neurocognitive function and psychological health as well. Reduced levels of physical activity in childhood may interfere with neural and academic development, whereas sedentary elderly face higher rates of neurocognitive decline and developing dementia. These findings underline the importance to participate in physical activity, especially in the modern society that is characterised by chair living (Levine, 2010).

The promising effects in current literature have identified physical exercise as a potential valuable clinical intervention. Physical exercise has already been shown to be an effective intervention for pathological aging and may be a suited intervention for other clinical populations as well. Traumatic brain injury (TBI) patients for example suffer from widespread neural dysfunction including both diffuse and focal neuropathology, impaired neurovasculature, deficits in neurocognitive function and reduced psychological health (Lojovich, 2010). The positive effects of physical exercise on angiogenesis, synaptogenesis and neurogenesis promote regeneration of the widespread TBI pathology at multiple levels in the brain. Given the available evidence it is striking that TBI patients suffer from severe levels of chronic reduced cardiovascular fitness. Besides from interfering with neural regeneration, this inactivity moreover makes patients more prone to the effects of psychological stressors that accompany the rehabilitation from their injuries. In line with this idea it has been found that TBI patients suffer from a hyperactive SNS (Su, Kuo, Kuo, Lai, & Chen, 2005). However, there is very little literature available on the effectiveness of physical exercise as an intervention for TBI patients (Xiong, Mahmood, & Chopp, 2009). This once more illuminates the need for high quality research into the effects of physical exercise on the human brain.

The literature on the effects of physical exercise interventions is promising. RCT's widely acknowledged as a robust tool to investigate the causal component of relationship in clinical practice, have repeatedly shown that physical exercise interventions improve neurocognitive function and psychological health. However, the current body of evidence suffers from serious methodological limitations. Therefore, researchers should be committed to improve the quality of RCT's in future research into the effect of physical exercise.

There are multiple issues that should be addressed in future investigations. First, researchers should aim at reaching consensus on a physical exercise intervention that is best suited to improve brain function. There is enormous heterogeneity in the interventions that have been assessed by recent meta-analyses (aerobic exercise vs. non-aerobic exercise, individual vs. group training, strength vs. flexibility vs. cardiovascular training, etc.). This heterogeneity interferes with the comparability of results between studies, which may have contributed to the equivocal results. The consensus on physical exercise interventions should extend to the trial duration and frequency. Up until now, multiple meta-analyses have applied one month as the minimum duration of physical exercise as an inclusion criterion for their studies. Intervention intensity should preferably be standardised on basis of physiological measures (eg. heart pulse frequency) to control for protocol adherence and improve the comparability of results between studies. The intervention should moreover be executed by trained personnel.

Second, the effect of physical exercise on neurocognitive function should not be measured using an overall composite measure of neurocognitive function. There is evidence suggesting that physical exercise has a selective effect within the neurocognitive domain (eg. executive function), meaning that a composite measure will overestimate the negative results and underestimate positive results of clinical interventions.

Third, researchers should address some important methodological issues that accompany the application of RCT's. The randomisation of group assignment should be adequately executed and reported. It is important that researchers in clinical practice control for the placebo effect by giving control groups a placebo-treatment (eg. flexibility training) instead of using no intervention-groups or waiting-list participants. Furthermore, researchers should aim at performing double blind experiments. In order to do so the assessors of outcome measures should be blinded and the participants should preferably not be informed with the alternative hypothesis of the study. Participants could be informed that two treatments will be compared, instead of that the physical exercise intervention will be compared to a control condition. Of course, such a strategy is subject to ethical considerations and should only be deployed if approved by a certified medical ethical commission. Additionally, researchers performing RCT studies should apply ITT-analysis in order to account for the selective drop-out of participants. Not applying ITT-analysis increases the chances of inflating the derived effect size for the intervention, overestimating its efficiency in the general population. Furthermore there should be taken care of accurate reporting of the study procedures, since many of the currently available studies have failed to report randomisation procedures, attrition rates and baseline comparisons between groups. Incompleteness of such procedures interferes with estimation of the study quality and therefore questions the reliability of the results.

Last, it is important that the future investigation will investigate the long-term effects of physical exercise using secondary follow-ups. This will improve our knowledge on whether physical exercise has permanent or transient effects on brain function and whether exercise treatments should be chronic or not.

It is clear that the field of clinical neuroscience is in need of high quality RCT's in order to justify firm conclusions on the effect of physical exercise interventions. Up until so far, physical exercise should be regarded as a promising intervention for the improvement of human brain structure and function.

Table 1

Authors	Year	Independent variable	Sample	Study design	Date range	Significant findings	Conclusions
Etnier et al.	1997	Mixed Exercise	Children, Adult, Elderly	RCT Study *n* = 17 Subject *n* = 420	n/a	Neurocognitive Composite, *g* = 0.15	Physical exercise has a small positive effect on cognition. Exercise paradigm, subject sample, cognitive measure and study quality are moderators. Effect sizes decreased with increasing experimental rigor.
SColcombe & Kramer	2003	Mixed Exercise	Elderly	RCT Study *n* = 18 Subject *n* = n/a	up to 2001	Neurocognitive Composite, *g* = 0.16 Visuospatial Processing, *g* = 0.43 Executive Function, *g* = 0.68 Processing Speed, *g* = 0.27 Cognitive Control, *g* = 0.42	Physical exercise improves neuro-cognitve function. Age, trial duration,exercise duration and training type are significant moderators.
Sibley & Etnier	2003	Mixed Exercise	Children	RCT Study *n* = 9 Subject *n* = n/a	up to 2002	Neurocognitive Composite, *g* = 0.29	Physical exercise is positively related to cognitive function. Age, publication status and neuropsychological measure are significant moderators.
Heyn et al.	2004	Mixed Exercise	Mildly Impaired Elderly	RCT Study *n* = 22 Subject *n* = 423	1970-2003	Neurocognitive Composite, *g* = 0.57	Physical exercise improves neurocognitive function.
Angevaren et al.	2008	Aerobic Exercise	Nondemented Elderly	RCT Study *n* = 8 Subject *n* = n/a	up to 2008	Motor Function, *g* = 1.17 Auditory Attention, *g* = 0.52 Memory, *g* = 0.50 Processing Speed, *g* = 0.26 Visual Attention, *g* = 0.26	Evidence for a beneficial effect of aerobic exercise on neurocognitive function, although the majority of measures retrieved no significant results.
Smith et al.	2010	Mixed Exercise	Adults, Elderly	RCT Study *n* = 29 Subject *n* = 2,049	1966-2010	Attention & Processing Speed, *g* = 0.12 Executive Function, *g* = 0.12 Memory, *g* = 0.13	Aerobic exercise is associated with modest improvements in neurocognition. Rigorous RCT’s with large sample sizes appropriate controls and longer follow-ups are needed.

Overview of the studies that investigated the effect of physical exercise on human neurocognitive function

Note. g = Hedge’s g. HR = Hazard ratio. N/a = not available. RCT = Randomised controlled trial.

Table 2
Overview of the studies that have investigated the effect of physical exercise on human psychological health.

Authors	Year	Independent variable	Sample	Study Design	Date range	Effect size	Conclusions
Larun et al.	2006	Mixed exercise	Children & adolescents	RCT Study *n* = 11 Subject *n* = 1,199	up to 2005	Symptoms of Depression, *g* = -0.66	There is evidence indicating that physical exercise has a small reducing effect on symptoms of depression and anxiety, although no conclusions can be drawn due to the heterogeneity within the study sample.
Ahn & Fedewa	2010	Mixed exercise	Clinical & non-clinical children	RCT Study *n* = 16 Subject *n* = 907	1960-2010	Symptoms of Depression, -0.41 Symptoms of Anxiety, *g* = -0.35	Physical exercise is effective for the reduction of symptoms of depression and anxiety.
Wipfli et al.	2008	Mixed exercise	Clinical & non-clinical children, adults & elderly	RCT Study *n* = 43 Subject *n* = 3,566	up to 2006	Symptoms of Anxiety, *g* = -0.48	There is Grade I level A status evidence for using exercise as a treatment for anxiety.
Lawlor & Hopker	2001	Mixed exercise	Depressed adults	RCT Study *n* = 14 Subject *n* =n/a	1966-1999	Symptoms of Depression, *d* = -1.1	Determination of the effectiveness of exercise in reducing symptoms of depression is hampered by a lack of good quality research.
Stathopoulou et al.	2006	Mixed exercise	Depressed adults and elderly	RCT Study *n* = 11 Subject *n* = 513	1966-2005	Symptoms of Depression, *d* = -1.42	Exercise can be a powerful intervention for clinical depression.
Mead et al.	2010	Mixed exercise	Depressed adults	RCT Study *n* = 23 Subject *n* = 907	up to 2007	Symptoms of Depression, *g*= -0.82	Physical exercise seems to reduce symptoms of depression, although when only methodological robust RCT's are analysed the effect is only moderate and not statistically significant.

Note. d = Cohen's d. RCT = Randomised controlled trial.

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PART B

The Relation between Physical Activity and Academic Performance in Primary School Children

Abstract

Background

Given a global trend towards an increasing sedentary society, it is important to investigate the relation between physical (in)activity and academic development.

Hypothesis

Higher levels of academic performance are associated with higher levels of physical activity and lower levels of sedentary behaviour. Mathematics is the academic ability most sensitive to the level of physical activity.

Methods

Multivariate Analysis of Variance was used to determine differences between children with high versus low performance on national tests for academic performance on standardised parental reports of physical activity and sedentary behaviour.

Results

Children (n = 64) with higher levels of spelling performance had higher levels of physical activity $F(1, 58) = 5.59$, $p < .05$, $\eta_p^2 = 0.10$. There was a trend indicating that children with higher performance for mathematics were more physically active, $F(1, 58) = 3.56$, $p = .07$, $\eta_p^2 = 0.06$. Relations with physical activity seemed larger for spelling skills and mathematics than for reading comprehension and technical reading (no significant effects).

Conclusion

The results support a positive relationship between physical activity and academic development.

Physical Activity and Academic Performance in Primary School Children

Physical activity has been widely acknowledged to improve cardiovascular fitness, reduce metabolic risk factors and lower the chances of cardiovascular disease (Kastello & Sothmann, 1999). Nevertheless there has been identified a global trend towards a more sedentary lifestyle in children (World Health Organisation [WHO], 2011). To date, only 17.1% of the US high school students meet the recommendations for physical activity (Center for Disease Control and Prevention, 2010). As a consequence children of the modern society face higher risks of obesity, cardiovascular disease, diabetes, musculoskeletal disorders and various types of cancer (WHO, 2011). However, the effects of an increasingly sedentary society may be not restricted to these well known consequences of inactivity.

A considerable body of evidence from animal research has now shown that physical exercise improves neurocognitive performance (Hillman, Erickson, & Kramer, 2008). Likewise, there has been found a still growing amount of evidence indicating that physical activity improves the human brain's structure and function (for review see Königs, 2011). Physical activity has been found to improve the brain's vasculature and increase cerebral blood flow. Additionally, there have been found beneficial effects on the levels of serotonin, dopamine and noradrenaline. Furthermore, physical activity has been found to increase the level of brain derived neurogrowth factor. Accordingly, activity has been found to induce synaptic plasticity (e.g. long term potentiation), promote dendritic growth, synaptogenesis and neurogenesis in the hippocampus. There is evidence suggesting that these biological changes translate into functional improvement: Systematic reviews of randomised controlled trials (RCT) have repeatedly shown that physical exercise trials improve neurocognitive function (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Colcombe et al., 2003; Heyn, Abreu, & Ottenbacher, 2004; Sibley & Etnier, 2003). Likewise, systematic reviews of RCT studies suggest that physical exercise improves psychological health by reducing the levels of depression and anxiety (Ahn & Fedewa, 2011; Stathopoulou, 2010 Powers, 2006) .

Therefore, children's adaptation to a more sedentary lifestyle may additionally affect the development of their brain structure and function. Since academic development is thought to be highly dependent on brain function (Barber, 2005; Fuchs et al., 2006), it is plausible to hypothesise that lower levels of physical activity may have a detrimental impact on the academic development of children.

In literature, large scale cross-sectional investigations have shown that cardiovascular fitness is indeed positively related to academic performance. In a study from Dwyer et al. (2001), 7,961 Australian primary school children between the ages of 7 – 15 have been investigated, showing that prospective measurements of cardiovascular fitness, muscle power and physical activity show small but significant positive correlations with academic performance. Unfortunately, there was applied a rather subjective measure of academic (the school's principal estimation of academic performance on a 5 point scale), questioning its validity and reliability.

Chomitz et al. (2005) have investigated the relation between cardiovascular fitness and performance on a standardised annual test of academic performance with adequate validity and reliability, the Massachusetts Comprehensive Assessment System (Massachussetts Department of Education, 1999). Cardiovascular fitness has been measured using the widely used Fitnessgramm tests (Cooper Research Institute, 1999) discriminating cardiovascular endurance, abdominal strength, flexibility, upper body strength and agility. The authors have shown that the odds of passing the mathematics test (n = 1,103) and English test (n = 744) increased significantly as the number passed physical activity tests increased. More specifically, for every test of fitness that has been additionally passed, the odds of passing the mathematics tests increased by 38% and the odds of passing the English test increased with 24%. The analyses in this study were corrected for gender, ethnicity, weight and socio-economic status, indicating that these demographic factors did not contribute to the relations that were observed.

Although these findings by Dwyer et al. and Chomitz et al. are in line with the hypothesis that physical activity improves academic performance, inference on causality is not justified based on the cross-sectional nature of the investigations. In contrast, RCT's are widely acknowledged as a powerful method to investigate the causality of a given relationship in clinical practice (Begg et al., 1996). Unfortunately, only a very small number of RCT's have investigated the effect of physical activity on academic performance (Coe, Pivarnik, Womack, Reeves, & Malina, 2006; Ismail, 1967; Reed et al., 2010).

Ismail (1967) has investigated the effect of a physical exercise intervention in 142 children between the ages 10-12 years. The children have been randomly assigned to the control or experimental group and matched on IQ, gender and health status. The experimental group has received a daily physical activity program intervention for one academic year, whereas the control group received the school's standard curriculum of physical education. It has been found that the experimental group showed small but significant improvements in the performance on the Stanford Achievement Test (SAT). Moreover it was found that benefits of the intervention were independent of pre-intervention level of academic performance.

Coe, Pivarnik, Womack, Reeves, & Malina (2006) have found contrasting results. In their study, 214 children were randomly assigned to a moderate to vigorous physical education program (experimental group) or to arts or computer programs (control group) for the duration of five-and-a-half months. It has been found that the performance on the Terra Nova Standardized Test of Academic Achievement did not improve in the experimental group. The children that had reported levels of physical activity exceeding the Healthy People 2010 guidelines (Coe, et al., 2006) did show higher academic performance compared to their less active counterparts. Therefore the authors have proposed that the effect of activity on academic performance could be subject to a threshold level of activity intensity.

The most recent RCT has been performed by Reed et al. (2010), investigating the effect of a four-month physical activity intervention on the Standard Progressive Matrices test of fluid intelligence and the Palmetto Achievement Challenge Tests of academic achievement. Third grade primary school children (*n* = 150) were randomly assigned to a three times per week half-hour physical activity program (experimental group) or the standard school curriculum (control group). Teachers had received training for execution of the intervention in advance as well as during the study. The authors have found that the experimental group showed significantly higher performance on the tests for social sciences: 82% of the experimental group performed proficient/advanced compared to 61% in the control group. The same trend was observed on tests for mathematics, reading skills and science, although these effects only approached significance. Furthermore, it was found that the experimental group had significantly higher post-intervention fluid intelligence performance compared to the control group (small effect size).

Taken together two out of three RCT's have retrieved positive effects of a physical exercise intervention. It is not clear why Coe et al. have found negative results whereas Ismail and Reed et al. have retrieved positive results from exercise interventions, since all three studies employed very diverging interventions and assessed outcome using different measures of academic performance. Possibly the intervention that was applied in the study of Coe et al. was not effective in initiating the biological mechanisms that are thought to improve neurocognitive function. This cannot be attributed to the duration of the intervention, since the duration of the intervention by Coe et al. has been reported to be longer than that from the study by Reed et al.. The intensity of the study interventions were not standardised (on for example heart rate), therefore it is not possible to judge whether the intensity of the intervention can account for the contrasting results. An alternative explanation might be that the Terra Nova Standardized Test of Academic Achievement used by Coe et al. is not sensitive to the (probably small) effects of physical exercise.

However further research is clearly needed, the majority of the RCT's suggest that physical activity improves academic performance. Therefore, it is interesting to study the relation of physical activity within the academic domain. Since it has been proposed that physical activity has a selective influence on executive function within the neurocognitive domain (Tomporowski, Davis, Miller, & Naglieri, 2008), it is interesting to investigate whether this selective effect of physical activity translates to the academic domain. If executive functions benefit more from physical activity than other neurocognitive functions, the academic abilities that are more dependent on executive functioning should bear stronger relationships with physical activity compared to other academic abilities. Unfortunately there is very little evidence available on the differential effect of physical activity within the academic domain.

The studies that have investigated the relations between physical activity and multiple academic abilities were constrained to the analysis of mathematics and reading skills (Grissom, 2005; Stevens, To, Stevenson, & Lochbaum, 2008). These studies have found no differences in the associations between physical activity and mathematics or reading skills. Contrasting these results, it has been found that cardiovascular fitness bears a stronger relationship with mathematical skills than with language skills (Chomitz et al., 2009). Additionally, gross motor function has been shown to be positively associated with mathematical skills but not with spelling or reading skills (Westendorp, Hartman, Houwen, Smith, & Visscher, 2011). These findings are in line with the hypothesis that physical activity has differential effects within the academic domain, showing stronger associations with mathematics compared to other academic abilities. However, there is no direct evidence available supporting this statement, nor is there a theory available that explains why mathematical abilities may benefit more from physical exercise than do other academic abilities.

Working memory, problem solving, processing speed and long-term memory have been identified as the cognitive processes that underlie mathematical skills (Fuchs et al., 2006). Additionally it has been proposed that poor inhibition and working memory explain difficulties in mathematical skills, because they interfere with set shifting and evaluation of new strategies that are necessary to solve mathematical problems (Bull & Scerif, 2001). Parallel to these findings, it has been shown that mental mathematical computing activates a left fronto-parietal network that maintains and processes a multi-digit representation in visuospatial working memory (Zago et al., 2001). These findings strongly suggest that the mathematical skills of primary school children are highly dependent on executive functions as working memory and problem solving. This idea has been confirmed by findings showing that working memory was specifically predictive of mathematical performance compared to other academic abilities in primary school children (Bull, Espy, & Wiebe, 2008). This strongly suggests that differences in the quality of the working memory may determine differences in mathematical skills compared to other academic abilities. The selective beneficial effect of physical activity on executive functions, in particular working memory, as proposed by Tomporowski et al. (2008) may therefore explain the trend towards a specific effect of physical activity on mathematical performance.

The goal of contemporary study was to determine the relationships between the performance on national tests for mathematical skills, spelling, reading comprehension and technical reading and the level of physical activity and sedentary behaviour. Given the available literature it was expected that: (1) children that retain higher levels of academic performance show higher levels of physical activity; (2) children that retain higher levels of academic performance show lower levels of sedentary behaviour; and (3) mathematical skills are more sensitive to the effects of physical activity and sedentary behaviour compared to other academic abilities.

This study is the first to assess the role of physical activity and sedentary behaviour on a range of academic abilities. Data from a national test for academic performance provide a unique opportunity to investigate the academic performance of primary school children across academic ability, grade and school. The results of this study contribute to our knowledge about the relation between physical activity and academic performance, and provide insight in the effect of our increasingly sedentary society for the academic development of our children.

Method

The study participants were recruited through Dutch primary schools from the areas of Noord-Holland and Flevoland. A total of 54 primary schools from Almere, Putten, Harderwijk, Nijkerk and Ermelo were randomly selected from the online telephone book. This sample of one large city (Almere) and multiple small sized cities was chosen to represent the Dutch population of primary school children. The school principals were contacted by telephone and informed about the study. If interested, the principals were sent an information letter with an official request to participate in the study. A total of 4 schools from Harderwijk (*n* = 1), Putten (*n* = 2) and Almere (*n* = 1) agreed to participate. The participating schools were all public school (*n* = 4). The participating schools distributed information letters and informed consent forms among a total of 710 pupils from the grades 1 to 6.

Participants

Children were included in the study if there was a parental report on physical activity and if data on academic performance were available. Parental informed consent was provided for 94 participants (participation rate = 13.0 %). Children that were older than 11 years and had not provided informed consent were excluded from the study (*n* = 2) according to the Dutch law for Medical Research and Human experimentation (Ministery of Healthcare, 2002). A total of 64 children between the ages 5 and 12 was included in the study (response rate = 9.0 %).

Measures

Physical activity. The child's level of physical activity and sedentary behaviour was measured using an adapted version of the parent questionnaire for Sports and Exercise (Research in Applied Natural Science [TNO], 2003). This measure was selected because it allows to assess the level of physical activity as well as the level of sedentary behaviour. The questionnaire measures the frequency and duration of: (1) Physical Activity using subscales for Active Transportation, Physical Education, Sports and Outdoor Play and (2) Sedentary Behaviour using subscales for TV viewing and Video Gaming (or computer use).

The original questionnaire was designed to assess the level of physical activity during the past week. The questionnaire that was used in this study was adapted to measure the level of physical activity during a usual week. There were two reasons for this adaptation: (1) the level of physical activity in 'a usual week' reflects the level that is applicable most of the time whereas 'the past week' might not be representative for 'a usual week', (2) 'the past week' may not be comparable across subjects since the time of questionnaire administration differed across parents (due to holidays for example).

Furthermore there was applied a scoring system to the questionnaire items in order to derive quantitative measures of physical activity and sedentary behaviour. The frequency items of each scale were coded from 0 to 7 (e.g. never or less than once a week = 0, once a week = 1, etc.) and the duration items were coded from 1 to 5 for the duration items (eg. 1 = less than 10 minutes per occasion, 2 = 10 to 20 minutes per occasion, etc.). The subscale scores were derived by multiplication of the score for its frequency item with the score for its duration item. The sum of the Physical Activity subscales (Active Transportation, Physical Education, Sports and Outdoor Play) defined the Physical Activity Scale score. The sum of the Sedentary Behaviour subscales (TV Watching and Video Gaming) defined the Sedentary Behaviour Scale score.

Academic performance. Academic performance was measured by the participant's performance on tests from the Dutch National Pupil Monitoring System (NPMS; Van Delden, 1994). This system is used throughout 80% of all Dutch primary schools in order to keep track of pupil's self- and peer-referenced academic development throughout their education (Vlug, 1997). Tests from the Dutch National Pupil Monitoring System are administered during three testing times (begin, halfway end) throughout each academic year.

The NPMS comprises tests measuring abilities such as general language skills, listening, spelling, writing skills, vocabulary, decoding, reading comprehension and arithmetic skills according to the item-response model (Vlug, 1997). The item-response model states that the probability that a given student completes a certain item correctly is defined by the student's ability and by item characteristics such as difficulty (Rasch, 1960; Staphorsius & Krom, 1998).

Four scores can be derived from the NPMS tests: (1) the raw test score reflecting the total correct answers on a test, (2) the ability score reflecting academic progress, (3) the norm score reflecting performance relative to the national norm in five classes (A = 75th percentile or higher, B = 50th to 75th percentile, C = 35th to 50th percentile, D = 10th to 35th percentile and E = 1st to 10th percentile) and (4) the learning progress score reflecting the performance relative to the didactic age. The raw test score is not suitable to compare academic performance across tests, due to the variation in length and difficulty across tests of the NPMS (De Jong, 2010). Likewise, the ability scores are not comparable across grades and the learning progress scores are not applied in the latest versions of the NPMS. Therefore, the norm scores were selected as dependent variable for all tests from the NPMS.

The following tests were selected in order to evaluate academic performance: The Mathematics Test, The Spelling Test, The Reading Comprehension Test and The Three Minute Test. The Mathematics Test measures arithmetic skills comprising addition, subtraction, multiplication and division (Janssen & Kraemer, 2002). The Spelling Test measures written spelling skills of words that increase in difficulty (Van der Bosch, Gillyns, Krom, & Moelands, 1997). The Reading Comprehension Test measures the ability to extract meaning from multiple written texts using multiple choice questions (Staphorsius & Krom, 1998). The Three Minutes Test measures technical reading of three different word sheets of increasing difficulty in one minute per sheet (Verhoeven, 1995). Sheets 1 and 2 contain simple monosyllabic words whereas sheet 3 contains complex disyllabic words. Three Minute Test performance is measured by the amount correctly read words diminished with the incorrectly read words for all sheets. In case the total score was not available, performance on the sheet with the highest degree of difficulty (sheet 3) was used to predict the performance of the total Three Minute Test.

Crohnbach's alpha values for the NPMS tests that were used in this study exceed .88 (Janssen & Kraemer, 2002; Staphorsius & Krom, 1998; Van der Bosch, et al., 1997; Verhoeven, 1995). These tests have been evaluated by the Dutch Committee on Tests and Test Affairs and are considered to have adequate test validity, reliability and norms (COTAN, 1998, 2002, 2004, 2010).

Moderator variables. Participant age, gender, body length and body weight were collected by parental report. Body length and body weight were used to compute the body-mass index by dividing body weight (in kilograms) by squared body height (in centimetres) (Andres, Elahi, Tobin, Muller, & Brant, 1985). Since body composition develops through childhood (Poskitt, 2000), raw BMI values are not comparable across age. Therefore BMI z-scores were computed. Because BMI norms providing mean and SD according to age were not available for Dutch children, norms for Swedish Children were used as reference value (Karlberg, Luo, & Albertsson-Wikland, 2001). However Sweden and The Netherlands are both European countries, the Swedish population of primary school children may not be entirely comparable to the Dutch', making the application of Swedish norms to Dutch children less appropriate. However, BMI z-scores were exclusively used to study inter-individual differences across age within the study population, not to investigate deviations of BMI from the norm. If Dutch children would in general have higher BMI values compared to Swedish children, this would be reflected in an underestimation of the z-score but not in the comparison of z-scores within Dutch children, justifying our approach to use the Swedish norms in our study. Last, self-report on parental education was collected according to the seven point scale of Verhage (1984): no full primary school education = 1, full primary school education = 2, middle school education = 3, high school education = 5, full education in applied sciences = 6, full education in university = 7. For an extended list of educations and their classifications please refer to Verhage (1984).

Procedure

Data on physical exercise, sedentary behaviour and moderator variables was collected by providing parents with an individual link to the online version of the adapted Sports and Exercise questionnaire. Academic performance data was collected for all participants at the relevant primary school from digital files.

Statistical analysis.

All statistical analyses were performed using Statistical Package for the Social Sciences 17.0 software for Windows Statistical Package for the Social Sciences (SPSS Inc., 2008).

The mean age, gender ratio, BMI z-score and level of parental education was computed in order to provide insight in the demographical characteristics of the pupil sample that was investigated.

The Sports and Exercise questionnaire was designed to measure the constructs Physical Activity and Sedentary Behaviour. It was investigated to what extent the factor structure of the questionnaire resembles the hypothesised two-factor structure by confirmatory factor analysis (CFA). The rationale for this two-factor model is that the time spent in transportation to and from school, physical education, sports and outdoor play all contribute to the total level of physical activity and not to the level of sedentary behaviour, whereas, the time spent watching TV and video gaming contribute to the total level of sedentary behaviour, but not to the level of physical activity. Therefore it is expected that the subscales Active Transportation, Physical Education, Sports and Outdoor Play will load on the component Physical Activity, whereas the subscales TV Watching and Video Gaming will load on a different factor component called Sedentary Behaviour. Four techniques were applied in order to investigate the appropriateness of performing factor analysis on the available behavioural data. First, the ratio of the number of included subscales to the number of participants was computed, which should be at least 1:10 according to Costello & Osborne (2005). Second, the Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy statistic was computed in order to investigate partial correlations among variables. According to Kaiser, values exceeding 0.5 justify performing factor analysis (1960). Third, Communalities after Extraction were computed to investigate the proportion of the subscales' variance that was common. According to Costello and Osborne, values exceeding 0.4 justify the inclusion of subscales into factor analysis (2005). Fourth, Bartlett's Test of Sphericity was computed to test the hypothesis that the subscales are uncorrelated, which should be rejected for appropriate factor analysis (Tobias & Carlson, 1969). If the data met the previous requirements, factor analysis was performed according to the Prinicipal Component Analysis (Pearson, 1901). Model fit was assessed by judgement of Eigenvalues and the total variance explained by the two-factor model. Components with Eigenvalues exceeding the value of 1 were considered to contribute to the explained variance in the model (Kaiser, 1960). Since Physical Activity and Sedentary Behaviour were expected to be inversely correlated, oblique rotation was performed in order to investigate whether the factors could be alternatively composed by the subscales that were entered in the analysis (Costello & Osborne, 2005).

Cronbach's alpha was computed for the Physical Activity as well as the Sedentary Behaviour Scales in order to assess their internal reliability. Additionally there were performed Shapiro-Wilk test of normality. Non-normally distributed data were transformed by proportion estimation using van der Waerden's formula (Lehmann, 1975).

Since the 5-level norm scores for academic functioning (A-E) showed high skewness, the norm scores were transformed into two levels: low performance and high performance. The aim was to create a 50-50% distribution of the sample size over the two academic performance groups. In doing this, the scores E, D, C and B corresponded to the low performance group (≤75th percentile) and class A corresponded to the high performance group (>75th percentile) for mathematics and technical reading skills. For spelling and reading comprehension skills, level E, D and C corresponded to the low performance group (≥50th percentile) and class B and A corresponded to the high performance group (> 50th percentile). Independent sample t-tests were performed between groups to investigate group comparability in terms of mean age, gender ratio, BMI z-score and parental education.

Exploratory analyses were performed in order to investigate the Pearson Product-Moment correlations between the level of physical activity, the level of sedentary behaviour and BMI percentiles.

In order to determine whether (1) high performing children have higher levels of physical activity and (2) show less sedentary behaviour than their low performing counterparts, we performed four separate Multivariate Analyses of Variance (MANOVA) on the physical activity and the sedentary behaviour scales. For every MANOVA the F_{Max} statistic reflecting the ratio of the largest to the smallest cell variance was computed to test homogeneity of variance across groups. F_{Max} statistics below 10 were considered to reflect acceptable homogeneity of variance according to Tabacknick and Fidell (2001). Academic performance group for mathematics, spelling, reading comprehension or technical reading tests served as fixed factors in the four separate MANOVA's. For all analysis, the normalised scales for Physical Activity and Sedentary Behaviour served as dependent variables. The demographic variables that showed significant differences between academic performance groups were entered in the analysis as covariates. A significant univariate main effect of the academic ability was considered to indicate that the low and high performing groups differ in their mean level of the dependent variable, holding constant possible confounders that were entered as covariates. For the independent variables that showed a significant multivariate effect, there were performed univariate analyses for the physical activity and sedentary behaviour scales separately. Effect sizes were assessed by computing the partial eta squared (η_p^2) translating the values 0.01, 0.06 and 0.14 into small, moderate and large effects respectively (Cohen, 1988).

In order to investigate differences in the strength of the relationships that were found, effect sizes for the effect of academic group on Physical Activity and Sedentary Behaviour were compared using independent t-tests. Prior to significance testing, raw B's were standardised by dividing them by their standard deviation.

All statistical testing was two-sided and α was set at .05.

Results

Sample characteristics

The mean age of the sample was 8.75 years (SD = 1.71, range 5 – 12), 45% was male, mean BMI z-score was 0.31 (indicating that this sample of Dutch children on average had a 0.31 SD higher BMI value compared to Swedish children, SD = 1.77, range -2.77 – 6.03) and the mean level of parental education was 5.56 (SD = 0.89, range 1 – 7). The questionnaire was completed by the participant's biological mother in 95% of the cases.

Physical Activity and Sedentary Behaviour

Regarding CFA, there was found an acceptable subscale to participant ratio (1:11). The KMO Measure of Sampling Adequacy statistic approached the threshold set by Kaiser (0.44). Communalities after Extraction exceeded the 0.4 threshold for all variables (range: 0.47-0.79), except for the Physical Education subscale (0.14). Bartlett's Test of Sphericity was significant, ($\chi^2(15, n = 64) = 39.17, p < .001$). Factor analysis was executed, although the results should be interpreted with prudence since the KMO statistic did only approach the threshold for sampling adequacy. Despite its low value for Communality after Extraction, it was decided to not exclude the subscale Physical Education prop to CFA because on theoretical basis the level of engaging in physical education contributes to the level of physical activity.

CFA revealed that the hypothesised two-factor model explained 51% of the total variance (Table 3). The subscales TV Watching and Video Gaming both loaded on the principal component (Sedentary Behaviour). Surprisingly, Active Transportation loaded on Sedentary Behaviour as well. The subscales Outdoor Play, Sports, Physical Education and Active Transportation loaded on the second factor (Physical Activity). Interestingly, Sports loaded negatively on Physical Activity. Oblique rotation did not influence the distribution of factor loadings.

The results from CFA indicate that the hypothesised structure of the questionnaire matches the actual structure to a large extent, indicating that adapting the structure would not improve the reliability of the measure. Surprisingly however Sports loaded negatively on Physical Activity, indicating that children that engage more in Sports engage less in other forms of physical activity. Furthermore, active Transportation loaded higher on Sedentary Behaviour than on Physical Activity. It was decided to not adapt the structure of the questionnaire because Active Transportation loaded on Physical Activity as well and this structure is better supported by theoretical grounds (the time spent in active transportation to and from school contributes to the level of physical activity and not to the level of sedentary behaviour). Therefore, the original structure of the questionnaire was maintained for all further analyses.

Cronbach's alpha was 0.46 for the Physical Activity Scale and 0.67 for the Sedentary Behaviour Scale. The Shapiro-Wilk test of normality approached significance for the Physical Activity as well as the Sedentary Behaviour Scale ($W(64) = 0.97$, $p = .11$ and $W(64) = 0.97$, $p = .09$ respectively). After performing a van der Waerden transformation, the Shapiro-Wilk test did not longer approach significance for both the Physical Activity Scale and for the Sedentary Behaviour

Scale (W(64) = 0.99, p = .99 and W(64) = 0.99, p = .85 respectively). The transformed dependent variables were consequently assumed to be normally distributed.

The mean scores for the frequency and duration items of each subscale are displayed in Figure 1. Physical Activity was not significantly associated with both Sedentary Behaviour (r(64) = 0.01, p = .94) and BMI (r(64) = -0.14, p = .26). Likewise, Sedentary Behaviour was not significantly related to BMI (r(64) = -0.14, p = 0.29).

Academic performance groups

In order to assess group comparability mean age, gender ratio, BMI z-score and parental education were compared between the academic performance groups. There was found a significant higher mean BMI in the low performance group compared to the high performance group for mathematics (Table 1). Likewise, the low performance group for reading comprehension had significant lower age and compared to the high performance group. All other comparisons of moderator variables between groups retrieved no significant results. In further analyses between the academic performance groups for mathematics, BMI was added as covariate. Likewise, age was added as a covariate in further analyses between the performance groups for reading comprehension.

Physical activity, sedentary behaviour and academic performance

The sample sizes of the comparison groups for academic performance were acceptable, within a ratio of 2 to 1. For both the Physical Activity and Sedentary Behaviour, tests of homogeneity of variance retrieved F_{Max} statistics that were within acceptable limits for all analyses (< 7.90). Table 2 presents the means and standard deviations for Physical Activity and Sedentary Behaviour in all academic performance groups, showing that all high performance groups had higher mean Physical Activity compared to the low performance groups.

Mathematics. A two factor (mathematics, BMI) MANOVA on the level of physical activity and sedentary behaviour revealed a trend towards a moderate multivariate main effect for mathematics group, F(2, 58) = 2.38, p = .10, η_p^2 = 0.08. There was found no significant multivariate effect of covariate BMI, $F(2, 58) = 0.84$, $p = .44$, $\eta_p^2 = 0.03$). There was no interaction effect between mathematics groups and BMI, $F(1, 58) = 1.52$, $p = .23$, $\eta_p^2 = 0.05$. An exploratory univariate analysis for the effect of mathematics group revealed that children with higher mathematics performance had higher levels of Physical Activity, although this moderate effect just escaped the threshold for significance, $F(1, 58) = 3.56$, $p = .07$, $\eta_p^2 = 0.06$. There was no significant difference in the level of Sedentary Behaviour between groups, $F(1, 58) = 1.00$, $p = .32$, $\eta_p^2 = 0.02$.

Spelling. There was found a significant medium sized multivariate effect of spelling group, $F(2, 56) = 3.64$, $p < .05$, $\eta_p^2 = 0.12$. Univariate analysis revealed that children with higher spelling performance had higher levels of Physical Activity (medium effect size), $F(1, 58) = 5.59$, $p < .05$, $\eta_p^2 = 0.10$. Differences in spelling performance were not associated with significant differences the level of Sedentary Behaviour, $F(1, 58) = 0.67$, $p = .42$, $\eta_p^2 = 0.01$.

Reading comprehension. There was found no significant multivariate main effect of reading comprehension group, $F(2, 39) = 0.67$, $p = .52$, $\eta_p^2 = 0.03$. In contrast, covariate age did show a large multivariate effect $F(2, 39) = 5.05$, $p < .05$, $\eta_p^2 = 0.21$. There was found no interaction effect between reading comprehension group age, $F(2, 39) = 0.66$, $p = .52$, $\eta_p^2 = 0.03$. Univariate analysis revealed that covariate age had no significant effect on the level of Physical Activity, $F(1, 39) = 1.24$, $p = .27$, $\eta_p^2 = 0.03$. In contrast, it was found that older children had higher levels of Sedentary Behaviour (large effect size), $F(1, 39) = 8.85$, $p < .01$, $\eta_p^2 = 0.18$.

Technical reading. There was found no significant multivariate main effect for technical reading group, $F(2, 50) = 1.58$, $p = .22$, $\eta_p^2 = 0.06$.

Standardised efect sizes reflecting the difference in normalised dependent variables between the low and high performance groups are presented in Figure 2. The effect size for the level of Physical Activity was found largest for spelling skills, however none of the comparisons between effect sizes of academic abilities retrieved a significant difference ($t < 1.43$, $p > .15$). Concerning the level of Sedentary Behaviour, there was found a trend towards a larger effect of mathematics group compared to technical reading ($t(114) = 1.93$, $p = .06$) and a larger effect of reading comprehension group compared to technical reading ($t(95) = 1.80$, $p = .08$). Other comparisons of effect sizes for Sedentary Behaviour retrieved no significant differences ($t < 1.19$, $p > .20$).

Discussion

This study showed that children's performance on widely used national tests for spelling were predictive of their level of physical activity. Children that show higher levels of spelling skills have higher levels of physical activity (medium effect size). Likewise, there was identified a strong trend indicating that children with higher levels of mathematical skills showed higher levels of physical activity (medium effect size). Performance on measures for reading comprehension and technical reading showed no significant influence on the level of physical activity. Performance for none of the academic abilities was predictive of the level of sedentary behaviour. This indicates that, in contrast to the level of physical activity, the amount of screen time is not associated with academic performance in primary school children.

The findings are in line with the hypothesis stating that academic performance is related to the level of physical activity, although this did not account for all academic abilities. Analyses were corrected for between-group differences in age, gender, BMI and parental education, which have been reported to be important mediators of the effect between physical activity and academic performance. Therefore these findings are in line with the hypothesis stating that physical activity improves academic performance, although the cross-sectional nature of current study does not justify inference on causality of this relationship. There was found no evidence indicating that the academic groups differed in the level of sedentary behaviour, which is not in line with the hypothesis stating that sedentary behaviour has a negative impact on academic performance. Contrasting the expectation that physical activity and mathematical skills would bear the strongest relationship within the academic domain, there were found no significant differences among effect sizes for academic abilities. However, there was identified a trend suggesting that the level of physical activity showed the strongest relationship with spelling skills, followed by mathematical skills.

Given the literature describing the positive effect of physical activity on neural structure and neurocognitive function, it is not very surprising that the level of physical activity is related to academic performance. As previously described, physical activity has been found to improve brain perfusion by promoting its vasculature and blood flow, improve function of the neurotransmitter system, increase the release of neurotrophins that promote neural development, increase connectivity by synaptogenesis, increase efficiency of synaptic transmission by promoting long-term potentiation (a process that is essential to memory function) and increase brain volumes in areas that are important for neurocognitive function such as the hippocampus (for a review see Königs, 2011). This overwhelming amount of neurobiological evidence from research into animals and humans does not translate into equally clear improvements in neurocognitive function, although meta-analytic evidence from RCT's suggests that physical exercise interventions can improve neurocognitive function (Smith et al., 2010). Likewise, meta-analytic evidence from RCT's suggest moderate to large anxiolytic and anti-depressant effects of physical activity, which could in turn have a relieving effect on neurocognitive function as well (Ahn & Fedewa, 2011). Taken together, it is indeed not a surprising finding that the improvements in neurocognitive functioning seem to be reflected in children´s academic functioning.

One interesting finding of this study is that within the academic domain, the relationships between the level of physical activity, spelling skills and mathematical skills show the largest effect sizes. Although no significant differences among effect sizes were identified, these findings suggest that spelling and mathematical skills may be more sensitive to the effects of physical exercise compared to other academic abilities. If so, physical exercise may have specific effects on the neurocognitive functions that underlie both spelling and mathematical skills rather than reading comprehension and technical reading. From a theoretical point of view, working memory is a plausible candidate to explain the neurocognitive mechanism mediating the relationship between physical activity and academic performance.

The concept of working memory as proposed by Baddeley and Hitch is composed of the central executive, phonological loop and the visuo-spatial sketchpad (1974). The central executive controls the flow of information into working memory, the retrieval of information from memory and coordinates parallel information processing. The central executive is complemented by two additional specialised short-term memory subsystems. The phonological loop retains verbal material concerning their phonological characteristics, whereas the visuo-spatial sketchpad holds visual and spatial information. Both subsystems serve to make specialised information accessible to processes that are executed in the central executive. Although it has been found that the central executive underlies both the acquisition of language and arithmetic skills (Bull, Johnson, & Roy, 1999; Swanson, 1994), the acquisition of language is more dependent on the phonological loop, mediating the long-term consolidation of new linguistics material (Cheung, 1996; Gathercole, Tiffany, Briscoe, Thorn, & team, 2005). Consequently, dysfunction of the phonological loop results in severe developmental language disorders (Bishop, North, & Donlan, 1996). In contrast, arithmetic skills are more dependent on the visual and spatial representations mediated by the visuo-spatial sketchpad (Dark & Benbow, 1990). Consequently linguistic skills like spelling, as well as arithmetic skills like mathematics, are (although mediated by differential specialised subsystems) dependent of working memory function. Regarding the earlier described hypothesis concerning a selective effect of physical activity on executive functions, in particular working memory, the shared dependence of linguistic skills and arithmetic skills on working memory function can explain the results from this study suggesting that spelling and arithmetic skills seem to bear stronger relationships to physical activity compared to reading comprehension and technical reading. Although the working memory hypothesis provides a compelling explanation for the results that were found, there is need for further research in order to provide an empirical basis for this theory.

Limitations

In this study the level of physical activity, the level of sedentary behaviour and BMI were found to be unrelated. However this finding is counter-intuitive, is has been previously reported in literature (Biddle, Gorely, & Stensel, 2004). Apparently physical activity and sedentary behaviour may not be mutually exclusive. Nevertheless, this statement is questioned by the low internal reliability of the Physical Activity Scale in this study (Crohnbach's alpha = 0.46). This lack of consistency reflects that either (1) physical activity is a highly heterogeneous construct, meaning that the level of, for example, active transportation to and from school is not related to the level of physical activity in sports or (2) that the questionnaire that was used did not reliably measure the construct Physical Activity. One factor that supports the latter explanation is the coding procedure that was applied to the questionnaire. While the response options of the duration items for Active Transportation and Outdoor Play do not represent equal absolute values of the absolute time participating in physical activity, they received identical codes. For example, a score of 3 on the duration item for Active Transportation reflects 30 to 60 minutes of physical activity compared to 2 to 3 hours for the Sports subscale. Consequently 30 to 60 minutes of physical activity in Active Transportation contributes to the Physical Activity Scale to the same extent as 2 to 3 hours of Physical Education, Sports or Outdoor Play, therefore underestimating the actual contribution of the latter subscales to the level of physical activity. This cannot be corrected for since it is impossible to weight the answer option 'more than 60 minutes per occasion' relative to the answer option 'more than 3 hours per occasion'. Nevertheless, this is an important shortcoming of this measure that is likely to have had a negative impact on the reliability of the measures.

CFA revealed that the two factor model explains a relatively small portion of the variance, which might have had a negative impact on the internal reliability of the questionnaire. However, it was found that the structure of the questionnaire predominantly matched the hypothesised structure. Therefore, adaption of the questionnaire structure could not be adapted to increase its reliability.

Taken together the Sports and Exercise Questionnaire is not suited as a quantitative measure of the level of physical activity in primary school children. The use of parental reports on physical activity could moreover be criticised for its subjectivity. In order to provide a more objective measure of physical activity, future research should be conducted using actigraphy (Reilly et al., 2008).

In contrast to the level of physical activity, the level of academic performance was assessed using a reliable and widely used national test for academic performance in The Netherlands. The norm scores that were applied were furthermore corrected for age, grade and assessment time (begin, middle or end of the academic year). The 5-levelled norm scores were transformed into two levels, providing a rather insensitive measure to detect inter-individual differences in academic performance (low versus high academic performance). This method was applied because the sample was not evenly distributed along the 5-levelled scale of the original norm scores. In order to derive a more equal distribution of participants across the academic performance groups, the norm scale was transformed into two levels, creating groups of more equal sample size. As a consequence the performance groups did not reflect identical comparisons of performance: the low and high performance groups for mathematical skills and reading comprehension represented the 1st to 75th and 75th to 100th percentile respectively, whereas the spelling and technical reading groups represented the 1st to 50th and 50th to 100th percentile. This means that it is possible that the results from comparisons between the academic groups for mathematics and reading comprehension may not apply to the primary school children population in general, but exclusively to the comparison between ‘very high performing children’ (>75th percentile) and ‘not very high performing children’ (≤ 75th percentile).

Last, the participation rate in this study was very low (13%), indicating that the study sample may not be representative of the general population of Dutch primary school children. Unfortunately, the data lack additional demographic data on for example ethnicity and SES that are necessary to investigate the representativeness of the study sample. Consequently, it could not be determined whether this study sample was indeed not representative of the general population. Nevertheless, one should be prudent in generalising the study findings to the population of Dutch primary school children.

Conclusions & future directions

The results show that children retaining higher levels of physical activity had higher performance on national tests for spelling. There was identified a strong trend indicating that children with higher levels of mathematical skills had higher levels of physical activity. Most interestingly there was found evidence suggesting that among academic abilities, spelling and mathematical skills bear stronger relationships with physical activity compared to reading comprehension and technical reading. Assuming the causal effect of physical activity this suggests that exercise has a selective effect on academic function. From a theoretical point of view, the selective effect of physical activity on executive functions (in particular on working memory) can explain that physical activity seems to bear stronger relationships with mathematical and spelling skills compared to other academic abilities. The results are limited by a lack of reliability in the measure of physical activity and sedentary behaviour; the Sports and Exercise Questionnaire. Therefore, future investigations should apply more objective measures such as actigraphy to investigate the physical activity. Furthermore, the representativeness of the study sample is questionable due to the small participation rate among the parents and children that have been invited to participate.

If validated in future investigations, the findings from this study have important clinical implications, highlighting the importance of physical activity in our sedentary society. The consequences of physical inactivity are not restricted to cardiovascular pathology, but likely affect the neurocognitive and academic development of our children as well. Additionally preliminary findings from this study suggest that low levels of physical activity may especially be associated with difficulties in spelling and mathematics skills. Future research should be aimed at providing statistical confirmation for the selective effect of physical activity within the academic domain and investigating the neurocognitive mechanisms through which physical activity promotes academic performance. When the working memory hypothesis is indeed valuable to explain the effect of exercise on academic performance, physical exercise may provide a simple yet efficient intervention to improve academic performance, in particular for spelling and mathematical skills in children that suffer from physical inactivity.

Figure 1

Summary of the responses for the frequency and duration items of each subscale

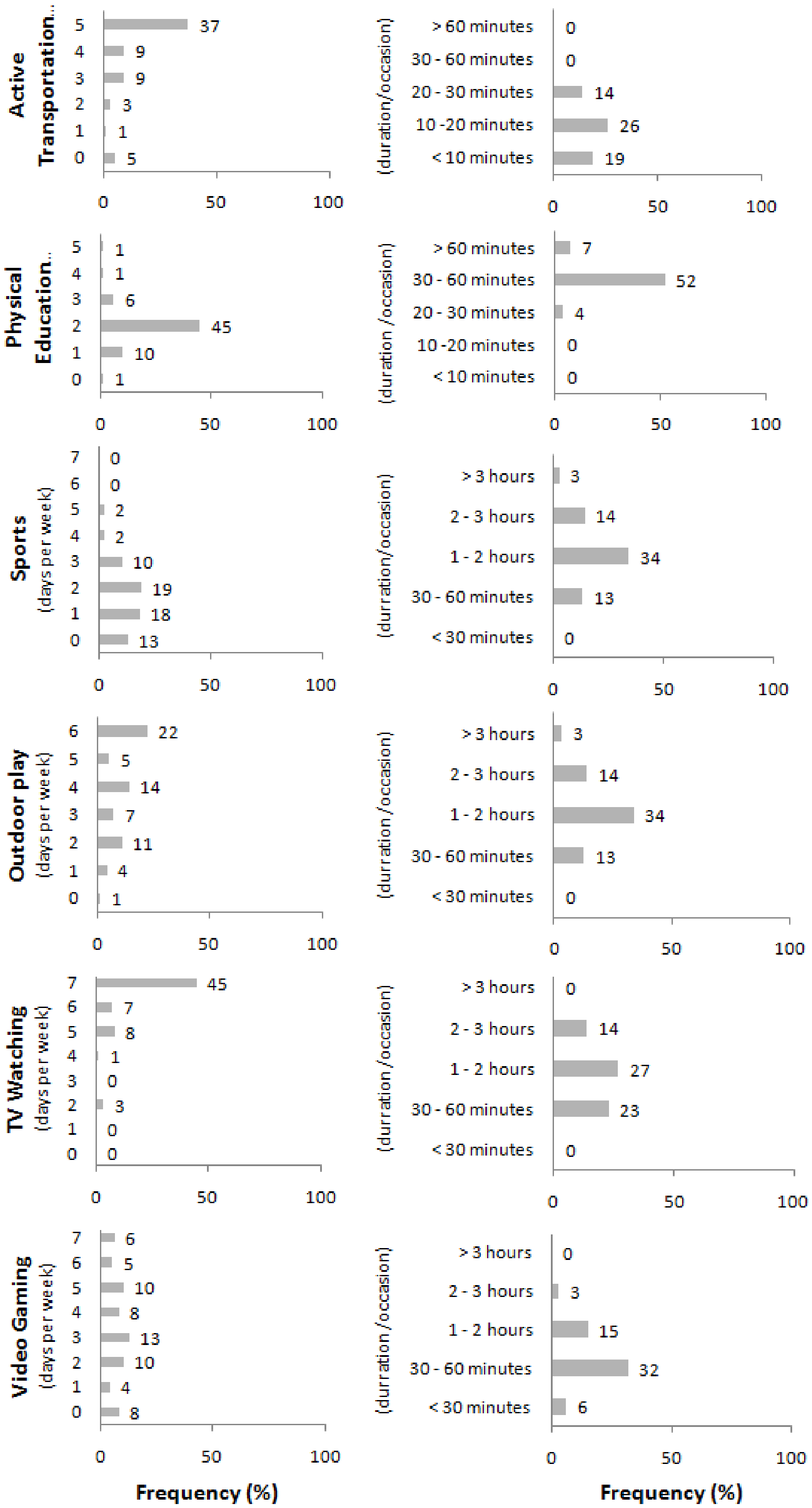


Table 1

Comparison of age, gender ratio, BMI and parental education between the low versus high performance groups for academic abilities.

		Mathematics				Spelling				Reading comprehension				Technical reading			
		Age	Gender	BMI	Education	Age	Gender	BMI	Education	Age	Gender	BMI	Education	Age	Gender	BMI	Education
Low	M	9.13	1.67	0.38	5.67	8.86	1.46	-0.02	5.44	9.42	1.54	0.18	5.48	8.52	1.52	0.17	5.55
	SD	1.68	0.48	0.93	0.48	1.69	0.51	1.05	0.85	1.45	0.51	1.03	1.05	1.75	0.51	1.06	0.95
	n	24	24	24	23	28	28	28	27	26	26	26	25	21	21	21	20
High	M	8.49	1.72	-0.21	5.72	8.81	1.55	0.06	5.58	8.44	1.39	-0.33	5.50	8.59	1.56	-0.12	5.53
	SD	1.72	0.50	0.90	0.79	1.74	0.51	0.92	0.96	1.50	0.50	0.90	0.79	1.72	0.50	0.89	0.92
	n	39	39	39	39	31	31	31	31	18	18	18	18	32	32	32	32
	df	61	61	61	60	57	57	57	56	42	42	42	41	51	51	51	50
	t	1.45	1.80	2.48*	-0.76	0.11	-0.64	-0.32	-0.57	2.17*	0.97	1.69	-0.07	1.10	-0.14	-0.27	-0.07

Note. Gender = Gender ratio. Education = Parental education.

*p <. 05

Table 2

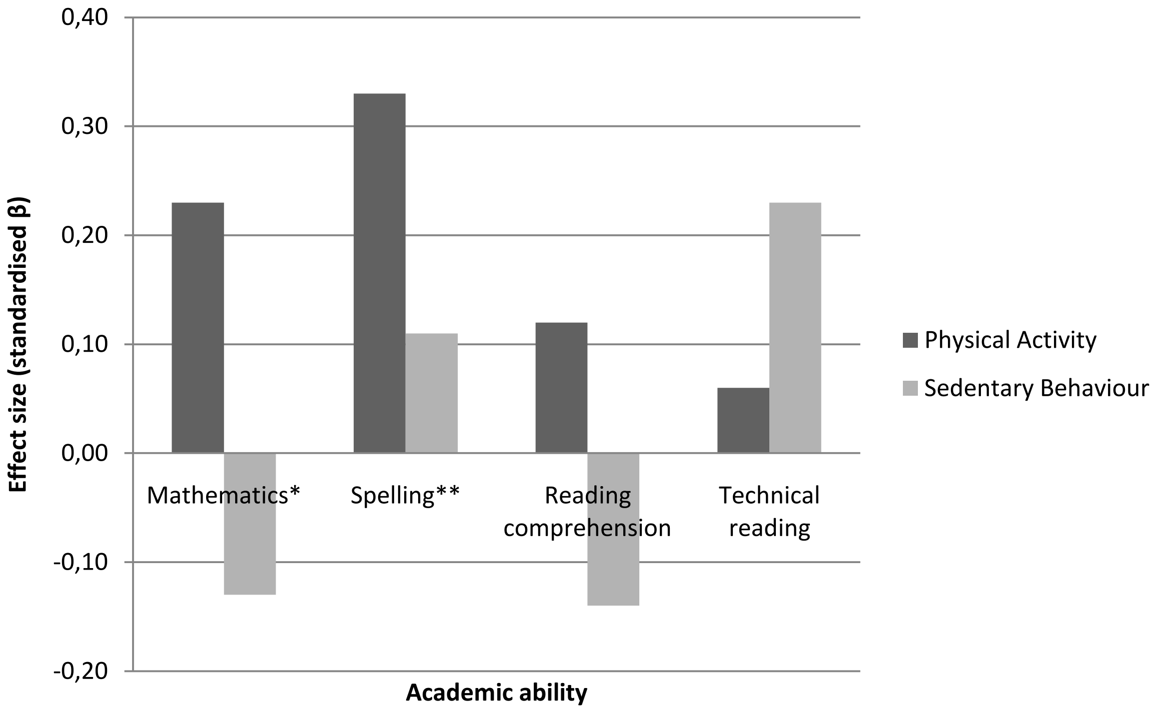
Mean levels of physical activity and sedentary behaviour for the academic performance groups

		Mathematics		Spelling		R. Comprehension		Technical reading	
		Low	*High*	*Low*	*High*	*Low*	*High*	*Low*	*High*
	n	24	39	28	31	26	18	21	51
Physical activity	M (SD)	32.46 (7.67)	38.64 (10.85)	32.61 (7.53)	40.10 (11.40)	36.77 (9.28)	37.33 (11.14)	35.00 (6.40)	37.44 (11.78)
Sedentary behaviour	M (SD)	27.96 (10.48)	25.92 (10.92)	26.04 (7.84)	28.84 (12.42)	29.23 (11.41)	26.78 (9.61)	23.62 (8.02)	29.13 (12.55)

Note. Math = Mathematics. M = Mean. R. Comprehension = Reading comprehension. SD= Standard deviation.

Figure 2

The effect of academic performance group on the level of physical activity and sedentary behaviour.



Note. The effect sizes are represented by standardised B's for the effect of academic performance groups (from low performance to high performance) on the dependent variables.

**p* < .10. ***p* < .05.

Table 3

Results of a confirmatory factor analysis of the Sports and Exercise Questionnaire

	Eigenvalue	Variance Explained (%)	Factor loadings*
Sedentary Behaviour	1.70	28.30	Videogaming (0.83)
			TV Watching (0.75)
			Active Transport (0.55)
Physical Activity	1.42	23.58	Outdoor Play (0.83)
			Sports (-0.57)
			Physical Education (0.51)
			Active Transportation (0.31)
Cumulative		51.87	

*Factor loading were displayed if they exceeded the thresholds of > 0.30 and < -0.30 (Kaiser, 1960).

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