1 General introduction
Relations between gross motor skills and cognitive functions

Gross motor skills
The childhood years are critical years for the development of gross motor skills. Gross motor skills represent abilities that involve large body muscles in posture, orientation and movement of the trunk and limbs and involve abilities such as locomotor skills, balancing and ball skills (Bishop, 2014). Children obtain gross motor skills during childhood through experience and practice, either in unstructured or structured situations, and this forms the foundation for more complex movements and sport-specific skills (Clark & Metcalfe, 2002). Therefore, proficiency in gross motor skills is a strong predictor for a lifelong active lifestyle (Clark & Metcalfe, 2002; Seefeldt, Nadeau, Newell, & Roberts, 1980).

Gross motor skills are not only important for physical development, but also for the development of cognitive functions (e.g. Rigoli, Piek, Kane, & Oosterlaan, 2012a; Roebers & Kauer, 2009; Wassenberg et al., 2005). At a young age, a child is able to move through the environment, interacting with objects or other people, therefore exposed to opportunities to further develop gross motor skills, but also to learn and acquire knowledge (Bornstein, Hahn, & Suwalsky, 2013). Later in life, children play together in structured or unstructured physical activity requiring goal-oriented behavior and cognitive strategies, which supports the development of cognitive functions.

Cognitive functions
Cognitive functions encompass a set of mental processes that contribute to perception, memory, and action, and include, amongst others, executive functions, information processing, and attention. From a neuropsychological view, it is assumed that gross motor skills are particularly related to cognitive functions that require a high amount of cognitive control, e.g. executive functions (Tomporowski, Davis, Miller, & Naglieri, 2008). Executive functions are higher-order cognitive functions important for goal-directed behavior (Banich, 2009). Three core aspects of executive functions can be distinguished: inhibition (response inhibition and interference control), working memory (verbal and visuospatial), and cognitive flexibility (also called shifting; Miyake et al., 2000). These functions play a critical role in the development during childhood and are necessary for success throughout life in general (Best, Miller, & Jones, 2009; Diamond, 2013). Furthermore, executive functions are strongly related to academic achievement as the ability to inhibit automatic behavior and conflicting stimuli, updating of working memory, and shifting between different tasks have shown to be related to reading, mathematics and spelling (Best, Miller, & Naglieri, 2011).

1 Definitions of terms shown in italics can be found in Box 1.
The speed and variability with which information is processed (information processing) and the ability to maintain attention are cognitive functions that are important prerequisites for executive functioning. Information processing develops rapidly during childhood and improvements in information processing have been shown to be related to improvements in executive functions (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Christ, White, Mandernach, & Keys, 2001; Fry & Hale, 1996; Hale, 1990; Span, Ridderinkhof, & van der Molen, Maurits, 2004; Welsh, Pennington, & Groisser, 1991). Furthermore, short-term unavailability of attention, also known as lapses of attention, affects the speed and quality of executive functioning (Unsworth, Redick, Lakey, & Young, 2010). Information processing and attention have also shown to be related to gross motor skills in children, although this is mainly investigated in children with developmental disorders (Klotz, Johnson, Wu, Isaacs, & Gilbert, 2012; Niederer et al., 2011). Children with attention deficit/hyperactivity disorder (ADHD) or developmental coordination disorder (DCD) show both motor and cognitive deficits which are linked to attentional and information processing problems (Dewey, Kaplan, Crawford, & Wilson, 2002; Klimkeit, Sheppard, Lee, & Bradshaw, 2004). Furthermore, information processing and attention have shown to attenuate relations between gross motor skills and executive functions in typically developing children (Luz, Rodrigues, & Cordovil, 2015; Piek et al., 2004; Roebers & Kauer, 2009; Wassenberg et al., 2005), although these have not been investigated together. Therefore, further research is needed to investigate the influence of information processing and lapses of attention together in the relationship between gross motor skills and executive functions in typically developing children.

Neuropsychological pathways

Hypothesized relations between gross motor skills and executive functions can be explained at a brain level. Neuroimaging studies have shown that the prefrontal cortex is not only important for executive functions, but also plays an important role in skilled motor performance (Desmond, Gabrieli, Wagner, Ginier, & Glover, 1997; Diamond, 2000; Dum & Strick, 1991). Functions depending on the prefrontal cortex, such as holding information in mind, inhibiting actions when another behavior is more appropriate, resisting distraction, sequencing, monitoring and planning, are also important for motor performance (Desmond et al., 1997; Diamond, 2000). Furthermore, the prefrontal cortex is connected with brain regions that are more directly involved in motor skills, such as the premotor cortex and the supplementary motor area (Dum & Strick, 1991; Künzle, 1978; Tanji, 1994). Additionally, the cerebellum and basal ganglia, neuroanatomical structures important for the control of movements, have also shown to be involved in executive functions (Desmond et al., 1997; Diamond, 2000; Dum & Strick, 1991; Lou, Henrikson, Bruhn, Børner, & Nielsen, 1989). Therefore, the prefrontal cortex, motor cortices, the cerebellum and the basal ganglia appear to participate in neural circuitries that are important for both motor skills and executive functions and this gives support for an interrelation between the two domains. The proposed underlying functional brain mechanisms have not yet been investigated in children by linking brain activity during executive function tasks to motor skill performance, therefore leaving this theory untested.
Physical activity and cognitive functioning

Physical activity is important for several health-related factors in children, such as gross motor skills and cardiovascular fitness. Unfortunately, children have become less physically active and significant declines in gross motor skills and cardiovascular fitness have been shown since the 1980s (Runhaar et al., 2010; Timmermans et al., 2017; Tomkinson, Lang, & Tremblay, 2017). Therefore, there is a need for physical activity interventions that stimulate gross motor skills and cardiovascular fitness.

Physical activity interventions are not only important to stimulate gross motor skills and cardiovascular fitness, but can also be effective for the development of executive functions. The development of executive functions goes hand in hand with maturation of the brain (Stuss, 1992). Maturation of the brain occurs by progressive and regressive changes and this is partly driven by the child’s experience (O’Hare & Sowell, 2008). Physical activity seems to be such an experience that enhances maturation and could therefore subsequently stimulate the cognitive development (Best, 2010). Physical activity interventions can be distinguished into acute interventions and longitudinal interventions, and into aerobic interventions and cognitively engaging interventions, each relying on different underlying mechanisms.

Acute physical activity interventions

Several meta-analyses and reviews have shown that one single bout of physical activity, e.g. an acute bout, can be beneficial for cognitive functioning in children (Chang, Labban, Gapin, & Etnier, 2012; McMorris & Graydon, 2000; Tomporowski, 2003; Verburgh, Konigs, Scherder, & Oosterlaan, 2014). A recent meta-analysis by de Greeff, Bosker, Oosterlaan, Visscher, and Hartman (2018a) has shown that acute physical activity does not influence cognitive functions in general, but specific domains of cognitive functions are enhanced through acute physical activity in children. This meta-analysis showed that acute physical activity has a small to moderate effect on inhibition (Effect Size [ES] = 0.28, p = 0.042) and attention (ES = 0.43, p = 0.013), whereas there is no significant effect on working memory and cognitive flexibility.

The strongest positive effects of acute physical activity on attention and inhibition have been shown in laboratory settings, where the intensity is controlled and adjusted to the child’s individual level (e.g. Chen, Yan, Yin, Pan, & Chang, 2014; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Niemann et al., 2013; Pontifex, Saliba, Raine, Picchietti, & Hillman, 2013; Tine & Butler, 2012). Positive effects of physical activity on attention and inhibition in ecologically valid learning environments for children, such as physical education, have also been found, but the effects were less pronounced (e.g. Jäger, Schmidt, Conzelmann, & Roebers, 2014). The effects were dependent on the test sequence (Pirrie & Lodewyk, 2012), were only found 90 minutes after the activity and not immediately (Schmidt, Egger, & Conzelmann, 2015a), or were only found after two bouts of activity, whereas not after one bout (Altenburg, Chinapaw, & Singh, 2016).
Some studies have investigated the effects of different types of acute physical activity on inhibition and attention in children. Studies by Jäger, Schmidt, Conzelmann, and Roebers (2015) and Schmidt, Benzing, and Kamer (2016) showed no effect of either aerobic physical activity or cognitively engaging physical activity on inhibition and selective attention respectively. The study by Gallotta et al. (2015) found that cognitively engaging physical activity led to significantly less improvements on selective attention compared to aerobic physical activity. The study by Best (2012) showed that physical activity, independent of the type of activity, did enhance processing speed in an inhibition task. Thus, there is an inconsistency between studies regarding the effects of different types of physical activity, which may be due to difference in duration, types of activity, or outcome variables (de Greeff et al., 2018a). This highlights the importance of further examining the differential effects of acute aerobic and cognitively engaging physical activity in ecologically valid learning environments for children.

**Longitudinal physical activity interventions**

Studies on longitudinal aerobic interventions, varying from 15 weeks to nine months, performed five times per week during physical education or after school interventions have shown to enhance specific aspects of executive functioning. The meta-analysis by de Greeff et al. (2018a) showed that longitudinal physical activity did have a small to moderate effect on working memory (ES = 0.36, p = 0.007), a small effect on cognitive flexibility (ES = 0.18, p = 0.040) and a large effect on attention (ES = 0.90, p < 0.001). Longitudinal physical activity had no significant effect on inhibition. Regarding the type of physical activity, a small to moderate effect was found for effects of aerobic physical activity on cognitive functions (ES = 0.29, p = 0.001) and a moderate to large effect was found for effects of cognitively engaging physical activity on cognitive functions (ES = 0.53, p = 0.008). These results suggest that longitudinal cognitively engaging physical activity is a promising type of physical activity to enhance cognitive functions. However, heterogeneity between the studies that were included in the meta-analysis was high and several factors influence the effectiveness of interventions, such as duration, intensity, frequency and type of intervention. Furthermore, there may be subgroups of children that benefit from physical activity interventions, whereas other subgroups do not (de Greeff et al., 2018a; Vazou, Pesce, Lakes, & Smiley-Oyen, 2016). Therefore, further research is needed to examine the effects of different types of physical activity and take into account individual characteristics of children.

**Mechanisms underlying the effects of physical activity on cognitive functions**

Several mechanisms have been proposed to explain the effects of physical activity on cognitive functions. The physiological mechanism and the cognitive stimulation hypothesis have been used as a framework for this thesis.

**Physiological mechanism**

The physiological mechanism is based on physiological changes in the body as a result of physical activity that subsequently lead to better cognitive functions (Sibley & Etnier, 2003). Acute physical activity is thought to lead to immediate changes in the brain, such as enhanced cerebral
blood flow (Querido & Sheel, 2007), and triggers the upregulation of neurotransmitters that are important for cognitive functions (e.g., dopamine, epinephrine, norepinephrine; Dishman et al., 2006; McAuley, Kramer, & Colcombe, 2004). It is assumed that these neurophysiological changes lead to an increase in the level of arousal, which in turn leads to better cognitive performance. This mechanism has been investigated with brain studies. Hillman et al. (2009) and Pontifex et al. (2013) investigated the effects of 20 minutes of acute aerobic physical activity on a treadmill on brain functioning and cognitive functions in children. The P3 amplitude increased after aerobic physical activity, which is likely to represent the allocation of attention (Polich, 1987), and this was related to better cognitive functions, supporting evidence for the physiological arousal mechanism.

In the long-term, the up-regulation of neurotransmitters is thought to lead to neurogenesis and angiogenesis in brain areas that are important for cognitive functions, which subsequently leads to better cognitive performance (Cotman, Berchtold, & Christie, 2007; Dishman et al., 2006; Holmes, Galea, Mistlberger, & Kempermann, 2004; Van Praag, 2008). There are a few studies that have investigated the effects of longitudinal physical activity on functional and structural changes in the brain in children. Higher white matter integrity in the uncinate fasciculus (Schaeffer et al., 2014) and in the superior longitudinal fasciculus (Krafft et al., 2014), which are white matter pathways between brain areas that are important for executive functions, has been found as a result of physical activity in overweight children. Functional brain studies showed a decrease in brain activation in the inferior frontal gyrus, the anterior cingulate cortex (Krafft et al., 2014), and in the parietal cortex (Davis et al., 2011a) during executive function tasks, whereas an increase in brain activation was shown in the prefrontal cortex (Davis et al., 2011a) after longitudinal aerobic interventions in overweight children. Only one study linked the changes in brain activation to cognitive functioning and found that a decrease in activation in the anterior prefrontal cortex was related to better executive functioning in typically developing children (Chaddock-Heyman et al., 2013). As effects of physical activity on the brain have been mainly studied in overweight children, further research is needed to examine the effects of physical activity on the brain in typically developing children.

Cognitive stimulation hypothesis

Many forms of physical activity are cognitively engaging. For example, team games require cooperation between children, strategic play and anticipation of teammates and opponents and this recruits similar processes as executive function tasks (Best, 2010). Furthermore, the cognitive demands inherent in the coordination of motor tasks lead to the involvement of neural circuitries that are also important for cognitive functions (Diamond, 2000; Serrien, Ivry, & Swinnen, 2007). Therefore, it can be hypothesized that physical activity that is cognitively demanding, either by the demands inherent in games or by the demands inherent in the coordination of complex motor tasks, would lead to larger effects on cognitive functions than aerobic physical activity alone (Schmidt, Jäger, Egger, Roebers, & Conzelmann, 2015b).
The cognitive stimulation hypothesis has been investigated in a study with rats. It was found that physical activity in an engaging context leads to angiogenesis in both the hippocampus and the prefrontal cortex, whereas simple and repetitive physical activity only leads to angiogenesis in the hippocampus (Ekstrand, Hellsten, & Tingström, 2008). Only one study examined the differential effects of aerobic physical activity and cognitively engaging physical activity on the brain in humans, but this was investigated in older adults (Voelcker-Rehage & Niemann, 2013). It was found that both interventions lead to decreased activation in the prefrontal cortex and also to improved executive functioning. Differential effects of different types of physical activity were also shown; the aerobic intervention group showed decreased activation in the sensorimotor network, while the coordination group showed increased activation in the visuospatial network and the thalamus and caudate body (both important subcortical structures for process automatization). These studies showed that different types of physical activity may lead to differential effects on the brain. However, this needs to be further examined in children.

**Objectives and outline of this thesis**

The first aim of this thesis is to investigate relationships between gross motor skills and specific aspects of cognitive functions in children and the proposed brain mechanisms underlying relations between gross motor skills and executive functions. The second aim of this thesis is to explore the differential effects of *acute* aerobic and cognitively engaging physical activity on response inhibition and attention. Third, the effects of *longitudinal* aerobic and cognitively engaging physical activity on cardiovascular fitness, gross motor skills, visuospatial working memory, and underlying brain functioning will be examined.

This thesis is part of a larger project, “Learning by Moving”, which is a cluster randomized controlled trial (RCT) investigating the effects of aerobic physical activity and cognitively engaging physical activity on cardiovascular fitness, gross motor skills, cognitive functions, academic achievement, brain structure, and brain functioning. Participants in this project were 8-10-year-old children (n = 891) from 22 primary schools (grades three and four) in the Netherlands. Two 14-week longitudinal interventions were developed and delivered. The aerobic intervention contained activities performed at a moderate-to-vigorous intensity. The cognitively engaging intervention consisted of team games or exercises that require complex coordination of movements, strategic play, cooperation between children and anticipating the behavior of teammates or opponents. The interventions were implemented four times per week by specialist teachers during regular physical education lessons and during two additional physical education lessons. The control group followed the regular physical education lessons two times per week. Children’s cardiovascular fitness, gross motor skills, cognitive functions, academic achievement, brain structure and brain functioning were measured at baseline and after the interventions. Baseline measures were used for the studies related to the first aim of this thesis (Chapters 3 and 4). Baseline and posttest measures were used for the studies related to the second and third aims of this thesis (Chapters 5 – 7). The effects on executive functions and academic achievement are the main focus of two other theses (executive functions: Meijer, in progress; academic achievement: de Bruijn, 2019).
Chapter 2 contains a systematic review investigating relations between broad domains of motor skills and cognitive functions in 4-16-year-old typically developing children. It examines which specific domains of motor skills and cognitive functions are related and whether these relations change over age categories. The results of this review contribute to the understanding of specific relations between motor skills and cognitive functions in children.

The aim of Chapter 3 is to investigate the relation between gross motor skills and specific aspects of executive functions, namely verbal working memory, visuospatial working memory, response inhibition and interference control. Furthermore, the role of information processing and lapses of attention is examined. Baseline scores of the children in the “Learning by Moving” project (n = 891) on gross motor skills and cognitive functioning are used for this study. The results contribute to the understanding of relations between gross motor skills and specific domains of executive functions in 8-10-year-old children and the role of information processing and lapses of attention in these relations.

Chapter 4 investigates visuospatial working memory-related brain activity with functional Magnetic Resonance Imaging (fMRI). Additionally, it is examined whether brain activity during visuospatial working memory is related to gross motor skills and cardiovascular fitness. A subsample of 92 children from the total sample in the “Learning by Moving” project participated in an MRI protocol in which brain activation during a visuospatial working memory task was measured. This study contributes to insights into the mechanisms underlying the relations of gross motor skills and cardiovascular fitness with visuospatial working memory in 8-10-year-old children.

Chapter 5 studies the effects of an acute aerobic intervention and an acute cognitively engaging intervention on response inhibition and lapses of attention. A subsample of 89 children from the total sample in the “Learning by Moving” project participated in this study. Children in the intervention group followed either an acute aerobic physical education lesson or an acute cognitively engaging physical education lesson. Heart rate was monitored during the intervention lessons with Polar heart rate monitors. Children in the control condition followed a seated academic classroom lesson with their own teacher. This study contributes to insights into the differential effects of acute aerobic and cognitively engaging physical activity, performed in ecologically valid learning environments, on inhibition and attention, two aspects of cognitive functions that have shown to benefit most from acute physical activity.

The aim of Chapter 6 is to study the effects of a longitudinal aerobic and cognitively engaging intervention on gross motor skills and cardiovascular fitness. Furthermore, it is investigated whether effects depend on baseline levels of gross motor skills and cardiovascular fitness and the

2 Chapters 4 and 7 have shared first authorship with A.G.M. de Bruijn and appear therefore also in the thesis by de Bruijn (The brain in motion, 2019). Both authors have equally contributed to these chapters.
dose of moderate-to-vigorous physical activity (MVPA). Children (n = 891) were assigned to the aerobic intervention group, the cognitively engaging intervention group, or the control condition in a Cluster RCT design. Children in the intervention groups (either aerobic or cognitively engaging physical activity) followed four physical education lessons per week for 14 weeks. Children in the control group followed their regular physical education lessons two times per week. The amount of MVPA during the physical education lessons was measured with accelerometers in all study conditions. The results of this study contribute to insights into the differential effects of two types of physical activity on gross motor skills and cardiovascular fitness. The results will also lead to insights into individual characteristics that are important to take into account for the development and delivering of physical activity interventions.

Chapter 7\(^2\) investigates the effects of the longitudinal aerobic and cognitively engaging physical activity interventions on visuospatial working memory-related brain activation with fMRI in children (n = 92). Brain activation before and after the intervention period are compared for three study conditions (the control group, the aerobic intervention group and the cognitively engaging intervention group). Insights into the brain mechanisms underlying the effects of different types of physical activity on cognitive functions will be obtained with this study.

Finally, Chapter 8 presents a summary of the most important results of this thesis and provides a discussion in light of existing knowledge and the theories described in this introduction. Additionally, limitations are discussed and practical implications and suggestions for further research are given.

\(^2\) Chapters 4 and 7 have shared first authorship with A.G.M. de Bruijn and appear therefore also in the thesis by de Bruijn (The brain in motion, 2019). Both authors have equally contributed to these chapters.
Box 1. Definitions

**Acute physical activity.** One single bout of physical activity.

**Aerobic physical activity.** Physical activity to improve cardiovascular fitness.

**Angiogenesis.** The growth of new blood vessels linked to neurogenesis (Best, 2010).

**Attention.** A cognitive state of focused awareness on a selection of available perceptual information (Gerrig & Zimbardo, 2002).

**Cardiovascular fitness.** The ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity (Corbin, Pangrazi, & Franks, 2000).

**Cognitive engagement.** The amount of cognitive effort and allocated attention that is needed for a certain activity, or to master certain skills (Tomporowski, McCullick, & Pesce, 2015a).

**Cognitive flexibility.** The ability to alternate attention between two simultaneous goals (Arbuthnott & Frank, 2000).

**Cognitive functions.** A set of mental processes that contribute to perception, memory, and action which include, amongst others, attention and executive functioning (Donnelly et al., 2016).

**Executive functions.** A subset of inter-related processes that are involved in purposeful, goal-directed behavior, such as inhibition and working memory (Banich, 2009).

**Gross motor skills.** The involvement of large body muscles in balance, limbs and trunk movements (Bishop, 2014).

**Information processing.** The efficiency (speed and variability) with which information is processed (Kail & Salthouse, 1994).

**Inhibition.** The ability to deliberately suppress dominant, automatic, or prepotent responses and conflicting stimuli (Nigg, 2000; Verbruggen & Logan, 2008).

**Interference control.** The ability to cognitively suppress conflicting stimuli (Nigg, 2000).

**Longitudinal physical activity.** Continuous physical activity over several weeks.

**Neurogenesis.** The process of proliferation and development of new neurons (Churchill et al., 2002).

**Physical activity.** All bodily movements produced by skeletal muscles that result in energy expenditure (Ortega, Ruiz, Castillo, & Sjöström, 2008).

**Response inhibition.** The ability to suppress planned actions that are no longer required or appropriate (Verbruggen & Logan, 2008).

**Selective attention.** The ability to complete a task without being distracted by other stimuli that are being presented (Janssen et al., 2014).

**Working memory.** The ability to store and manipulate information in short-term memory, whereby specialized processes exist for verbal and visual information (Baddeley & Hitch, 1994).