

The relations between objectively measured moderate-to-vigorous physical activity, chronic aerobic exercise and cognitive control in children and adolescents

by

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Abstract

Physical inactivity among young people is a public health concern. Markers of physical inactivity, such as low cardio-respiratory fitness (CRF) and obesity are adversely related to higher order cognitive functions, which underpin goal directed behaviour (i.e. cognitive control) and are implicated in academic achievement. Regular aerobic exercise can benefit cognitive control in children. However, it remains unknown whether daily physical activity behaviour is associated with cognitive control. Investigating this is important as targeting increments in daily moderate-to-vigorous physical activity (MVPA) may initially be a more realistic policy goal than developing aerobic exercise interventions. Nominal number of studies assessed this relationship using objective monitoring of physical activity (accelerometry), and yielded mixed results. None of the studies into objectively measured physical activity and cognitive function in young people controlled for CRF, which is posited to mediate the relationship between regular aerobic exercise and cognitive control. Likewise, other important confounders such as intelligence, have yet to be addressed in the literature. Moreover, it is unknown whether this relationship varies with age, as extant studies looked solely at younger adolescents. For example, meta-analytical findings (Fedewa & Ahn, 2011) suggest that children can benefit more cognitively from CRF and chronic aerobic exercise than adolescents as greater effect sizes have been observed for younger compared to older youngsters. Alternatively, chronic aerobic exercise may be specifically needed for cognitive benefits to emerge. However, none of the aerobic exercise interventions included objective assessments of baseline physical activity and few studies assessed the effects of chronic aerobic exercise interventions on multiple indices of cognitive control. This thesis aimed to address the limitations of previous research and to investigate: 1) the associations between objectively measured daily MVPA and cognitive control in older adolescents (study 1), and 2) in preadolescent children (study 2), while controlling for CRF, general intellectual ability and a number of important confounders (e.g. adiposity, attention-deficit hyperactivity disorder); 3) the relationship between daily MVPA and academic achievement (study 2); 4) the effects of chronic aerobic exercise intervention on cognitive control in children, while controlling for objectively measured daily MVPA and time sedentary at baseline (study 3).

Methods: Study 1. A sample of 667 adolescents ($M_{age} = 15.4$, $SD = .17$, 55.5% girls) from the Avon Longitudinal Study of Parents and Children was included in the analyses. MVPA was measured with ActiGraph, GT1M accelerometer. CRF was assessed with sub-maximal cycle ergometer test and expressed as weight adjusted predicted physical work capacity at the heart

rate of 170 beats per minute (PWC-170). Attentional control was measured with Stop Signal task. **Study 2.** A sample of 81 children ($M_{age} = 8.64$ years, $SD = .57$, 45.7 % girls) was included in the analyses. MVPA was objectively measured using the ActiGraph, wGT3X+ accelerometer. CRF was measured using a maximal graded exercise test on a treadmill. Inhibitory control was assessed with a modified Eriksen flanker task, working memory with Operation Span Task; and academic achievement with Kaufman Test of Educational Achievement. **Study 3.** 32 children ($M_{age} = 8.64$, $SD = .58$, 56.2% girls) were randomised into a physical activity intervention (FITKids2) or a waitlist control group. Changes in VO_{2max} were measured using a maximal graded treadmill exercise test and changes in MVPA were objectively monitored for 7 days using the ActiGraph, wGT3X+ accelerometer. Behavioural measures of inhibition (reaction time, and accuracy) and working memory (accuracy) were taken using computerised laboratory tasks (modified Eriksen flanker task and Operation Span Task).

Results: Study 1. MVPA was not significantly related to cognitive processing speed or variability of cognitive performance in hierarchical linear regression models. In simple regression models, CRF was negatively related to mean RT on the simple go condition ($R^2 = 2.6\%$, $F(1, 308) = 8.28$, $p = .004$). **Study 2.** No significant associations were noted between MVPA and either inhibition, working memory, or academic achievement. In contrast, CRF explained 4.7% of variance in accuracy interference ($\Delta R^2 = .047$, $p = .045$; $\beta = -.22$, $t(78) = 2.03$, $p = .045$, $F(2, 78) = 4.95$, $p = .009$). **Study 3.** FITKids2 physical activity intervention had a positive effect on the speed of responding during incongruent condition of flanker task ($F(1, 30) = 4.69$, $p = .038$, $\eta_p^2 = .13$). A significant increase in BMI percentile was observed in the control ($Z = 2.17$, $p = .03$) but not in the intervention group ($p = .53$).

Discussion: Study 1. Our results suggest that aerobic fitness, but not MVPA, was associated with cognitive processing speed under less cognitively demanding task conditions. The results thus indicate a potential global effect of aerobic fitness on cognitive functions in adolescents but this may differ depending on the specific task characteristics. **Study 2.** The results of this study suggest that CRF but not objectively measured MVPA was associated with better interference control in preadolescent children. Given the intermittent nature of children's daily MVPA, it is possible that aerobic exercise, which increases CRF is needed for cognitive benefits to emerge. **Study 3.** FITKids2 after-school physical activity intervention had a positive effect on children's inhibitory control, namely this cognitive function, which is closely related to academic achievement and future job and health outcomes. Thus, the results of this study

convey a positive public health message, where promoting child's engagement in aerobic exercise can engender benefits to their cognitive function.

Conclusions: The findings from this thesis can inform development of physical activity interventions to benefit cognitive functions in young people and contribute to the evidence base to inform future health and educational policies.

Keywords: accelerometry, cardio-respiratory fitness, cognition, young people, ALSPAC, FITKids2, RCT

For Patrick

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Table of Contents

Abstract	i
Acknowledgements	v
Table of Contents	vii
List of Tables	xiii
List of Figures	xiv
List of Abbreviations	xv
Chapter 1 Introduction	1
Chapter 2 Literature Review	7
2.1 Physical activity, aerobic exercise, cardio-respiratory fitness and cognitive control	8
2.1.1 Cognitive control	8
2.1.1.1 The unity and diversity of cognitive control	8
2.1.1.2 Theory behind the measurement of cognitive control in children	10
2.1.1.3 Inhibition: Definition, measurement, importance	11
2.1.1.3.1 Definition	11
2.1.1.3.2 Development	12
2.1.1.3.3 Measurement	13
2.1.1.3.4 Importance	15
2.1.1.4 Working memory: Definition, measurement, importance	16
2.1.1.4.1 Definition	16
2.1.1.4.2 Development	17
2.1.1.4.3 Measurement	18
2.1.1.4.4 Importance	18
2.1.1.5 Task switching involves both inhibitory control and WM	19
2.1.1.6 Laboratory tasks versus cognitive batteries	19
2.1.2 Physical activity, chronic aerobic exercise and cardio-respiratory fitness	21
2.1.2.1 Physical activity: Definitions, measurement, relevance to cognition	21
2.1.2.1.1 Definitions	21
2.1.2.1.2 Measurement: Accelerometry is the method of choice to assess physical activity in young people	22
2.1.2.1.3 Measurement: Advantages of accelerometers over other physical activity measures	23
2.1.2.1.4 Relevance	26
2.1.2.2 Chronic aerobic exercise: Definitions, measurement, relevance	27
2.1.2.2.1 Definitions	27

2.1.2.2.2	Measurement	27
2.1.2.2.3	Relevance	28
2.1.2.3	Cardio-respiratory fitness: Definitions, measurement, relevance	29
2.1.2.3.1	Definition	29
2.1.2.3.2	Measurement: Physiological principles in the measurement of maximal oxygen uptake	30
2.1.2.3.3	Measurement: Maximal exercise tests	31
2.1.2.3.4	Measurement: Sub-maximal exercise tests	31
2.1.2.3.5	Measurement: Change in cardio-respiratory fitness over time	32
2.1.2.3.6	Relevance	33
2.1.3	Critical review of literature on cardio-respiratory fitness, daily MVPA, aerobic exercise and cognitive control in children and adolescents	34
2.1.3.1	Cardio-respiratory fitness and cognitive control in children and adolescents	34
2.1.3.2	Daily MVPA volume and cognitive control in children and adolescents	38
2.1.3.3	The effects of chronic aerobic exercise on cognitive control in children and adolescents	45
2.1.4	Overview of the thesis	50
2.1.5	Thesis aims	50
Chapter 3 Methods		52
3.1	Accelerometry data reduction in the Avon Longitudinal Study of Parents and Children (ALSPAC; study 1)	53
3.2	Accelerometry data reduction in cross-sectional and intervention studies (studies 2 and 3)	55
3.3	Cognitive data reduction in the Avon Longitudinal Study of Parents and Children (study 1)	58
3.4	FITKids2 intervention	60
3.4.1	Purpose	60
3.4.2	FITKids2 background	60
3.4.3	Daily physical activity sessions (120 minutes)	60
3.4.4	Instant activities (approximately 30 minutes)	61
3.4.5	Activities in an Instant	61
3.4.6	Educational component (15 minutes)	61
3.4.7	Intensity of physical activity	62
3.4.8	Staff and staff training	62
Chapter 4 The relationship of moderate-to-vigorous physical activity to cognitive processing in adolescents: Findings from the ALSPAC birth cohort		63

4.1	Study 1 context	64
4.2	Introduction	66
4.3	Methods	68
4.3.1	ALSPAC study population	68
4.3.2	Participants	69
4.3.3	Measures	71
4.3.3.1	Anthropometrics and body composition	71
4.3.3.2	Cognitive task	71
4.3.3.3	Accelerometry	73
4.3.3.4	Cardio-respiratory fitness	73
4.3.4	Statistical Analyses	74
4.4	Results	74
4.4.1	Adherence to accelerometer wear	74
4.4.2	Group differences	75
4.4.3	Sex differences	75
4.4.4	Task performance	75
4.4.5	Associations between daily MVPA, CRF and cognitive processing	76
4.4.6	Cardio-respiratory fitness and cognitive processing speed	78
4.5	Discussion	79
4.5.1	Summary of findings	79
4.5.2	Daily MVPA, attentional control and processing speed	79
4.5.3	Cardio-respiratory fitness and processing speed	81
4.5.4	Strengths and limitations	82
4.6	Conclusion	82
Chapter 5 The associations among daily moderate-to-vigorous physical activity, indices of cognitive control and academic achievement in preadolescent children		89
5.1	Study 2 context	90
5.2	Introduction	92
5.3	Methods	96
5.3.1	Design and participants	96
5.3.2	Measures	97
5.3.2.1	Anthropometric assessment	97
5.3.2.2	Accelerometry	97
5.3.2.3	Cardio-respiratory fitness	98
5.3.2.4	Inhibitory control	99

5.3.2.5	Working memory	100
5.3.2.6	Academic achievement	101
5.3.3	Statistical analyses	102
5.4	Results	102
5.4.1	Descriptive statistics	102
5.4.2	Sex differences	103
5.4.3	Cognitive task performance and academic achievement	103
5.4.4	Moderate-to-vigorous physical activity, cognitive control and academic achievement	104
5.5	Discussion	105
5.5.1	Summary of findings	105
5.5.2	Daily MVPA and cognitive control	105
5.5.3	Daily MVPA and academic achievement	109
5.5.4	Strengths and limitations	110
5.5.5	Future directions	111
Chapter 6 Effects of an after-school physical activity programme on cardio-respiratory fitness and cognitive control: Preliminary findings from the FITKids2 RCT		117
6.1	Study 3 context	118
6.2	Introduction	119
6.3	Methods	121
6.3.1	Study design	121
6.3.2	Participants	122
6.3.3	FITKids2 physical activity intervention	123
6.3.4	Measures	123
6.3.4.1	Anthropometric assessment	123
6.3.4.2	Accelerometry	123
6.3.4.3	Cardio-respiratory fitness	124
6.3.4.4	Inhibitory control	125
6.3.4.5	Working memory	126
6.3.5	Statistical analyses	127
6.4	Results	127
6.4.1	Baseline characteristics	127
6.4.2	Programme evaluation	128
6.4.3	Changes in cognitive performance and treatment effects	129
6.4.4	Attendance, changes in adiposity and task performance	130

6.5	Discussion	130
6.5.1	Summary of findings	130
6.5.2	The effects of the FITKids2 aerobic exercise intervention on measures of cognitive control	130
6.5.3	Evaluation of the FITKids2 intervention: Effects on cardio-respiratory fitness	133
6.5.4	Strengths and limitations	134
6.6	Conclusions	135
6.7	Acknowledgements	136
Chapter 7 General Discussion		146
7.1	Summary of findings	147
7.2	Objectively measured daily MVPA and cognitive control in children and adolescents (studies 1 and 2)	148
7.2.1	Potential role of confounders	151
7.2.1.1	Age	151
7.2.1.2	Sex	152
7.2.1.3	CRF	153
7.2.1.4	Adiposity	154
7.2.2	MVPA: Measurement, patterns and variability	155
7.2.3	Cognitive measures	157
7.2.4	Academic achievement	158
7.3	The effects of aerobic exercise intervention on cognitive control in children (study 3)	160
7.3.1	Evaluation of FITKids2 intervention in relation to other RCTs	161
7.3.2	The effects of chronic aerobic exercise on cognitive control	163
7.3.3	Potential mediating mechanisms	165
7.3.3.1	Physiological mechanisms	166
7.3.3.2	Psycho-social mechanisms	167
7.4	Strengths and limitations	169
7.4.1	Study 1	169
7.4.2	Study 2	170
7.4.3	Study 3	171
7.4.4	Limitations of accelerometry	172
7.5	Future directions	172
7.5.1	Daily MVPA and cognitive function	173
7.5.2	Chronic aerobic exercise interventions	173

7.6 Overall conclusions _____	174
References _____	175
APPENDIX A: Journal publications and conference presentations related to work presented in this thesis _____	222
APPENDIX B: Consent to collect diagnostic interview information in the ALSPAC study research clinics at 15.5 years _____	225
APPENDIX C: Consent to cycle ergometer test in the ALSPAC study research clinics at 15.5 years _____	227
APPENDIX D: Data collection sheet: Cycle ergometer test in the ALSPAC study research clinics at 15.5 years _____	229
APPENDIX E: Accelerometer data collection sheet: ALSPAC Research Clinics at 15.5 years _____	232
APPENDIX F: Stop Signal Task instructions at ALSPAC Research Clinics at 15.5 years _____	235
APPENDIX G: An example of a raw excel file with Stop Signal task data _____	238
APPENDIX H: Parental Consent Form (Studies 2 and 3) _____	240
APPENDIX I: Child Assent Form (Studies 2 and 3) _____	242
APPENDIX J: Health History & Demographics Questionnaire (Studies 2 and 3) _____	244
APPENDIX K: ADHD IV Rating Scale _____	246
APPENDIX L: Tanner Staging Questionnaire (Girl) _____	248
APPENDIX M: Tanner Staging Questionnaire (Boy) _____	250
APPENDIX N: Physical Activity Readiness Questionnaire _____	252
APPENDIX O: VO _{2max} Run Sheet _____	254
APPENDIX P: The Children's OMNI scale of perceived exertion (OMNI Scale) _____	256
APPENDIX Q: Accelerometer Information Sheet _____	258
APPENDIX R: Cognitive Tasks Run Sheet _____	261
APPENDIX S: Flanker Task Instructions _____	263
APPENDIX T: Flanker Stimuli _____	265
APPENDIX U: OSPAN Instructions _____	268
APPENDIX V: OSPAN Stimuli _____	270
APPENDIX W: OSPAN Record Sheet _____	272
APPENDIX X: FITKids2 Physical Activity Programme Registration Form _____	274
APPENDIX Y: FITKids2 - Telephone screening criteria _____	276
APPENDIX Z: FITKids2 – Telephone ADHD Screening Protocol _____	278
APPENDIX AA: FITKids2 Intervention Schedule _____	280
APPENDIX BB: FITKids2 Content: Matching Illinois Learning Standards _____	282
APPENDIX CC: Examples of strategies used by staff to assure intervention fidelity _____	284

List of Tables

Table 2-1. Comparative summary of physical activity methods used in paediatric physical activity research _____	25
Table 2-2. Review of cross-sectional studies on CRF and cognitive control in children and adolescents _____	36
Table 2-3. Review of the studies into the associations of objectively assessed MVPA and cognitive function in children and adolescents _____	40
Table 2-4. Review of the randomised controlled trials on the effects of chronic aerobic exercise interventions on cognitive control on children _____	46
Table 4-1. Descriptive characteristics of 15 years old ALSPAC participants who received stop signals at longer delays (group one) _____	83
Table 4-2. Descriptive characteristics of 15 years old ALSPAC participants who received stop signals at shorter delays (group two) _____	84
Table 4-3. Performance of 15 years old ALSPAC participants on the Stop Signal task ____	85
Table 4-4. Spearman's rank order correlations between the performance of ALSPAC adolescents on Stop Signal task, demographic characteristics, cognitive and anthropometric variables and cardio-respiratory fitness (group one) _____	86
Table 4-5. Spearman's rank order correlations between the performance of ALSPAC adolescents on Stop Signal task, demographic characteristics, cognitive and anthropometric variables and cardio-respiratory fitness (group two) _____	87
Table 4-6. A summary of regression analyses for variables predicting mean RT and response variability on Stop Signal Task (group two) _____	88
Table 5-1. Mean (SD) values for participants' demographic, anthropometric, CRF and physical activity data _____	113
Table 5-2. Performance on flanker task, OSPAN and academic achievement _____	114
Table 5-3. A summary of regression models predicting cognitive and academic performance from moderate-to-vigorous physical activity and cardio-respiratory fitness _____	115
Table 6-1. Baseline characteristics of intervention and control groups _____	138
Table 6-2. Comparisons of pre- and post-test measures of cardiorespiratory fitness between intervention and control group participants _____	139
Table 6-3. Comparisons of pre-test and post-test measures of cognitive control and academic achievement among intervention and control groups _____	140
Table 6-4. Comparisons of intervention and control groups at pre-test and post-test on measures of cognitive control _____	141

List of Figures

Figure 2-1. The unity and diversity of executive functions. _____	10
Figure 2-2. A schematic information processing model representing sequential stages of information processing from the onset of an event to a response. _____	11
Figure 2-3. An example of the modified Eriksen flanker task paradigm. _____	14
Figure 2-4. An example of a Stop Signal paradigm. Each picture represents a separate screen. _____	15
Figure 3-1. A flow diagram of accelerometer data reduction in study 1. _____	54
Figure 3-2. A flow diagram of accelerometer data reduction in study 2 on daily MVPA and cognitive control. _____	56
Figure 3-3. A flow diagram of accelerometer data reduction in study 3 on the effects of FITKids2 intervention on cognitive control. _____	57
Figure 3-4. A flow diagram of Stop Signal data reduction in the Avon Longitudinal Study of Parents and Children (ALSPAC). _____	59
Figure 4-1. Number of participants from the Avon Longitudinal Study of Parents and Children (ALSPAC) excluded from the study on physical activity and attentional control. RT, reaction time; ADHD, Attention Deficit and Hyperactivity Disorder; SEN, Special Educational Needs. _____	71
Figure 6-1. The flow of participants through the randomised controlled trial. _____	137
Figure 6-2. The effect of Intervention by Time interaction on the mean RT to congruent trials on the flanker task ($p = .08$). _____	142
Figure 6-3. The effect of Intervention by Time interaction on the mean RT to incongruent trials on the flanker task ($p = .038$). _____	143
Figure 6-4. The effect of Time by Congruency interaction on the mean RT on the flanker task in the control group ($p = .69$). _____	144
Figure 6-5. The effect of Time by Congruency interaction on the mean RT on the flanker task in the intervention group ($p = .057$). _____	145

List of Abbreviations

ACSM	American College of Sports Medicine
ADHD	Attention Deficit Hyperactivity Disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
ANL	All-or-nothing load score
ANU	All-or-nothing unit score
ATP	Adenosine triphosphate
BDNF	Brain derived neurotrophic factor
BMI	Body Mass Index
CANTAB	Cambridge Neuropsychological Test Automated Battery
CAS	Cognitive Assessment System
CATCH	Coordinated Approach to Child Health trial
CPM	Accelerometer counts per minute
CRF	Cardio-respiratory fitness
DAWBA	Development and Well-Being Assessment
DXA	Dual X-ray Absorptiometry
EYHS	European Youth Heart Study
HELENA	Healthy Lifestyle in Europe and Nutrition in Adolescence
HBSC	Health Behaviour in School-aged Children
HR	Heart Rate
IGF-1	Insulin-like growth factor 1
IQ	Intelligence quotient
MET	Metabolic equivalent
MVPA	Moderate-to-vigorous physical activity
NHANES	National Health And Nutrition Examination Survey
OSPAN	Operation Span Task
PASS	Planning Attention Simultaneous and Successive
PE	Physical education
PCL	Partial-credit load scoring
PCU	Partial-credit unit scoring
PFC	Prefrontal cortex
PWC-170	Physical Working Capacity at the heart rate of 170 beats per minute
RER	Respiratory exchange ratio
RCT	Randomised controlled trial
RT	Reaction time
SAS	Supervisory Activating System
SDRT	Standard deviation of reaction time
SES	Socio-economic status
SSD	Stop signal delay
TEA-Ch	Test of Everyday Attention for Children
TBFM	Total body fat mass
VBA	Visual basics for applications
VO₂	Oxygen uptake

VO₂max	Maximal oxygen uptake
VO₂ peak	Peak oxygen uptake
WASI	Wechsler Abbreviated Scale of Intelligence
WM	Working memory

Chapter 1

Introduction

Physical activity (PA) is paramount to young people's health, growth and development (Barnett et al., 2013; Boreham & McKay, 2011; Ekelund et al., 2012; Fairclough, Boddy, Ridgers, & Stratton, 2012; Hills, King, & Armstrong, 2007; Janssen & LeBlanc, 2010). Despite its well-established physical (Gutin & Owens, 2011; Janssen & LeBlanc, 2010) and psychological (Biddle & Asare, 2011) health benefits, we live in societies that are largely inactive and sedentary (Finucane et al., 2011; Kohl et al., 2012; Swinburn et al., 2011; Wang, McPherson, Marsh, Gortmaker, & Brown, 2011). The adverse consequences of inactive and sedentary lifestyles are already apparent during developmental ages (Janssen & LeBlanc, 2010; Tremblay et al., 2011) and continue into adult years (Biddle, Pearson, Ross, & Braithwaite, 2010; Magnussen et al., 2010; Singh, Mulder, Twisk, Van Mechelen, & Chinapaw, 2008; Telama, 2009). According to the recent survey of self-reported Health Behaviour in School-aged Children (HBSC), only a third of children and adolescents in Western countries are physically active at the level that could benefit their health (i.e. engaging in at least 60 minutes of MVPA daily; Currie et al., 2012). These data converge with objectively assessed physical activity levels in countries such as the UK, Canada and the USA, where only a third of boys and a fifth of 4-16 years old girls meet current physical activity guidelines (Colley et al., 2011; Esliger & Hall, 2009; Troiano et al., 2008). Meanwhile, approximately a third of children and adolescents in the UK, Canada and USA are overweight or obese (Health and Social Care Information Centre, 2014; Ogden, Carroll, Kit, & Flegal, 2014; Roberts, Shields, de Groh, Aziz, & Gilbert, 2012). Age related decrease in physical activity levels (Jago, Anderson, Baranowski, & Watson, 2005; Nader, Bradley, Houts, McRitchie, & O'Brien, 2008) and secular increase in time spent sedentary (Nelson, Neumark-Stzainer, Hannan, Sirard, & Story, 2006) are both related to epidemic levels of childhood obesity (Janssen et al., 2005; Marshall, Biddle, Gorely, Cameron, & Murdey, 2004; Nelson, et al., 2006; Tremblay & Willms, 2000). Therefore, increasing the levels of physical activity in young people is crucial from the perspective of their health as well as a public health target (World Health Organization [WHO], 2013).

The negative health consequences of childhood physical inactivity may extend to cognitive health. However, at present it remains unknown how physical activity behaviour relates to cognitive function in young people. The emerging body of evidence suggests that correlates of physical inactivity, such as low cardio-respiratory fitness (CRF), overweight and obesity, are negatively associated with cognitive and brain function (Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Hillman, Erickson, & Kramer, 2008; Hillman, Kamijo, & Scudder, 2011; Kamijo et al., 2012; Li, Dai, Jackson, &

Zhang, 2008), as well as academic achievement in young people (Hillman et al., 2012; Singh, Uijtdewilligen, Twisk, van Mechelen, & Chinapaw, 2012). In contrast, the associations between physical activity behaviour and cognitive functions have not been established. Evidencing whether such a relationship exists is the first step in evidence gathering to guide future interventions, as outlined within the behavioural epidemiology framework (Sallis, Owen, & Fotheringham, 2000). That is, in order to adequately inform behavioural interventions (e.g. increasing physical activity to benefit cognition in children and adolescents), first observational evidence on the link between physical activity behaviour and cognitive outcome in children needs to be gathered. Existing data are limited to samples of younger adolescents and the lack of control for important confounders (e.g. CRF, intelligence quotient (IQ); Booth, Tomporowski, et al., 2013; Syväoja, Tammelin, Ahonen, Kankaanpää, & Kantomaa, 2014; van der Niet et al., 2014).

Research suggests that higher order cognitive functions, which govern goal-directed behaviour, self-regulation, and are implicated in academic achievement, can specifically benefit from higher CRF (Buck, Hillman, & Castelli, 2008; Buck, Osher, Castelli, & Hillman, 2006; Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Moore et al., 2013; Pontifex et al., 2011; Pontifex, Scudder, Drollette, & Hillman, 2012; Scudder, et al., 2014; Voss et al., 2011) and regular aerobic exercise (Colcombe & Kramer, 2003; Davis et al., 2011; Hillman, et al., 2011; Hillman et al., 2014). These findings are important in view of protracted brain maturation, which renders child and adolescent brain sensitive to modifying factors such as environment and behaviour (Andersen, 2003; Gogtay et al., 2004). Specifically, prefrontal cortex (PFC), namely the brain structure implicated in higher order cognitive functions such as scheduling and goal directed behaviour, termed jointly cognitive control (or executive functions; Braver, Paxton, Locke, & Barch, 2009; Carlson, Zelazo, & Faja, 2013; Diamond, 2013; Miyake et al., 2000), undergo structural (Gogtay, et al., 2004) and functional (Luna, Padmanabhan, & O'Hearn, 2010) changes still into the second decade of life. Consequently, the cognitive processes dependent upon these structures are more sensitive to environmental influences during the process of brain maturation that spans childhood and adolescence (Andersen, 2003; Casey, Galvan, & Hare, 2005; Gogtay, et al., 2004; Luna, et al., 2010; Rosenzweig, 2003; Tomalski & Johnson, 2010). Thus, childhood and adolescence can be the most opportune periods for physical activity interventions, which in turn could benefit cognitive development (Diamond & Lee, 2011).

Cognitive control is particularly important to a child's cognitive development, academic achievement as well as future health and financial well-being. This is because cognitive control is tightly related to child's ability to self-regulate behaviour and emotions (Rueda, Posner, & Rothbart, 2005). This ability in turn predicts a variety of socially salient outcomes, such as future health, wealth and crime (Moffitt et al., 2011). That is, children with greater self-regulatory skills grow up to be healthier (as indicated by a combined health indicator across metabolic, dental, sexual and respiratory health), more socially successful (achieving higher socio-economic status and income) and more financially planful adults (Moffitt, et al., 2011). Likewise, greater self-regulatory skills are negatively related to criminal behaviour. Since the ability to self-regulate is modifiable (Diamond & Lee, 2011; Moffitt, et al., 2011), efforts focused on improving cognitive control, which is implicated in self-regulation, are especially important.

Investigating the benefits of physical activity on young people's cognitive control can help advance physical activity within public health and educational agendas. Cognitive control is of particular importance to academic achievement. Not only is cognitive control moderately to strongly associated with school achievement (Alloway & Alloway, 2010; Best, Miller, & Naglieri, 2011; Blair & Razza, 2007; Borella, Carretti, & Pelegrina, 2010; St Clair-Thompson & Gathercole, 2006), but it can also predict future academic performance (Alloway & Alloway, 2010; Blair & Razza, 2007). This is important, as schools are the most opportune environments to target the majority of children and adolescents during a large proportion of their wakeful hours, which has been recognised by government bodies and national organisations in both the UK and the USA (Department of Health, 2005; US National Physical Activity Plan Coordinating Committee, 2010). Further, children accumulate a large proportion of daily MVPA during school time (Fairclough, Beighle, Erwin, & Ridgers, 2012; Fairclough, Butcher, & Stratton, 2008; Nilsson et al., 2009). For example, primary school children in the UK accumulate between 40-56% of daily MVPA during school hours (Fairclough, Beighle, et al., 2012; Fairclough, et al., 2008). Similarly, children from Northern European countries accumulate more MVPA during school than out of school hours (Nilsson, et al., 2009). However, despite the call by leading organisations (e.g. American Heart Association, Institute of Medicine, National Institute for Health and Care Excellence, Department for Children, Schools and Families, and Department of Health in the UK) for schools to introduce more physical activity across the school day, such as daily high quality physical education (PE) with at least 50% of time dedicated to MVPA, physical activity during recess, as well as before,

during and after school (Institute of Medicine [IOM], 2013; Pate et al., 2006), competing curricular demands lead to the marginalisation of PE and physical activity (e.g. during recess or as active parts of the curriculum). For example, children in both the UK and the USA average approximately 2 hours a week in PE (European Commission, Education, Audiovisual and Culture Executive Agency [EACEA], Eurydice, 2013; The National Institute of Child Health and Human Development [NICHD] Early Child Care Research Network, 2003; Quick, Simon, Thornton, & TNS-BMRB, 2010). It has been estimated that children spend on average only 15 minutes in MVPA during the school day (PE accounts for only 4 of these 15 minutes; Bassett et al., 2013; Delva, O'Malley, & Johnston, 2006; Gauthier, Laurence, Thirkill, & Dorman, 2012; IOM, 2013; Lee, Burgeson, Fulton, & Spain, 2007; Ridgers, Stratton, & Fairclough, 2005; Rush et al., 2012; Tudor-Locke, Lee, Morgan, Beighle, & Pangrazi, 2006). In contrast, significant increments in daily MVPA (up to 57 minutes in MVPA) could be accrued with daily, enhanced quality PE, introducing MVPA into the class curriculum and enhanced recess (Bassett, et al., 2013; IOM, 2013). However, given the increasing pressures on schools to meet academic targets set forth by standardised testing, many are willing to sacrifice time spent in PE in favour of academically focused subjects (Office for Standards in Education [Ofsted], 2013; Scott, 2008). In the USA, since the No Child Left Behind Act (2003), 44 percent of schools reported significantly reducing the time allocated to PE in favour of academic instruction (McMurrer, 2007; Scott, 2008). In the UK, in one quarter of schools young people do not engage in enough MVPA during PE to increase student's CRF (Ofsted, 2013). Therefore, evidencing the link between young people's MVPA and their cognitive control, which is associated with academic achievement, has a potential to help prioritise physical activity (including time allocated to PE, recess and in-class physical activity) not only on public health but also on educational agendas.

MVPA has been most consistently related to multiple health outcomes in youth (Janssen & LeBlanc, 2010; Physical Activity Guidelines Advisory Committee [PAGAC], 2008). Daily engagement in at least 60 minutes of MVPA is the main recommendation of physical activity guidelines for young people (Department of Health, 2011; U.S. Department of Health and Human Services, 2008). Therefore, daily MVPA is of particular interest in the study of physical activity and cognition. However, the assessment of MVPA in young people poses a challenge, as children and adolescents accumulate MVPA in a highly intermittent fashion (Bailey et al., 1995; Baquet, Stratton, Van Praagh, & Berthoin, 2007; Riddoch et al., 2004). Likewise, physical activity in young people vary substantially across a day (Fairclough, Beighle, et al.,

2012; Nilsson, et al., 2009) and from day to day (Collings et al., 2014; Fairclough, Boddy, Mackintosh, Valencia-Peris, & Ramirez-Rico, in press; Mattocks, 2007). Self-reports are inaccurate measures of physical activity in general (Adamo, Prince, Tricco, Connor-Gorber, & Tremblay, 2009; Prince et al., 2008), and in particular in child populations due to problems with recall and conceptualising physical activity constructs (Kohl, Fulton, & Caspersen, 2000). To establish a meaningful relationship between young people's MVPA and cognitive control, objective measurement of MVPA is needed.

Therefore, the purpose of this thesis was to investigate the associations between objectively measured MVPA and cognitive control in previously unstudied populations of children and adolescents, while controlling for CRF and factors relevant to cognitive performance. To provide an applied context for these associations, the relationship between objectively measured MVPA and academic achievement was also considered. The second aim of this thesis was to inspect whether, in contrast to daily MVPA, a chronic aerobic exercise intervention was needed for cognitive benefits to emerge, while controlling for baseline levels of MVPA and time sedentary, which was not previously considered.

Chapter 2

Literature Review

2.1 Physical activity, aerobic exercise, cardio-respiratory fitness and cognitive control

2.1.1 Cognitive control

Cognitive control (also referred to as executive control, central executive or executive functions) is not a unitary concept and encompasses a range of cognitive functions (which are both distinct and inter-related), each with their own theoretical underpinnings and methodology (Diamond, 2013; Etnier, 2012; Miyake & Friedman, 2012; Miyake, et al., 2000; Tomporowski, 2009). This thesis will focus on two particular domains of cognitive control: inhibitory control and working memory (WM), which have been most consistently related to academic achievement (Alloway & Alloway, 2010; Blair & Razza, 2007; Borella, et al., 2010; Espy et al., 2004; Monette, Bigras, & Guay, 2011; St Clair-Thompson & Gathercole, 2006) and also showed consistent associations with CRF (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011). However, these two domains are related through a common cognitive (or attentional) control factor (Miyake & Friedman, 2012). This is important, as such common factor forms the basis for the executive function hypothesis, which posits that chronic aerobic exercise yields specific benefits to the cognitive functions that engage cognitive control (in general; Colcombe & Kramer, 2003; Kramer et al., 1999). Therefore, first a brief outline of the theory behind the unity and diversity of cognitive control will be provided together with a theoretical basis for cognitive measurement, before a more in depth discussion of inhibitory control and WM.

2.1.1.1 The unity and diversity of cognitive control

Cognitive control refers to a set of higher order cognitive processes of inhibitory control (resisting distractions), WM (actively manipulating information in mind) and shifting (multitasking), which subserve goal directed behaviour (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Miller, 2000; Norman & Shallice, 1986). These processes direct and optimise behaviour through selection, scheduling, coordination of mental operations, which underpin perception, memory and action. That is, cognitive control is engaged always when learnt and automatic responses do not adequately meet our current goals and thus new or alternative behaviours must be adopted, such as in novel situations, or when we are faced with conflicting cues or distraction (Diamond, 2013; Munakata, Snyder, & Chatham, 2012). For example, a child engages cognitive control when learning new material at school, when choosing to cross

the road safely instead of following an overly keen peer, or when he or she maintains attention on the school task despite the anticipation of recess. The concept of cognitive control draws upon Baddley's (1996) central executive, which can be defined as a general pool of (information) processing capacity, further developed into Supervisory Attentional System (SAS) by Norman and Shallice (Norman & Shallice, 1986). SAS was proposed as an attentional controller called upon when habitual, routine, and learnt behaviour was inadequate or insufficient to meet current goals. This is important, as the general pool of information processing and attentional controller metaphors emphasise that our attentional resources are limited. Thus, child's ability to flexibly adjust and direct attention to the salient aspects of environment (e.g. the teacher rather than chatting with a classmate) is key to goal directed behaviour such as learning. In this respect, attentional control underpins the unity of cognitive control.

Factor analytic studies of cognitive control in children and adolescents (7 to 17 years old) confirm the unity but also the diversity of cognitive control. Research conducted across different samples (e.g., Dutch and Northern American children and adolescents, aged 7-17 years, adults) suggests a two-factor model with WM and task switching (shifting) and a super-ordinate cognitive control factor (Friedman, Miyake, Robinson, & Hewitt, 2011; Friedman et al., 2008; Huizinga, Dolan, & van der Molen, 2006; van der Sluis, de Jong, & van der Leij, 2007). The super-ordinate factor represents the unity of cognitive control; it explained 99% of variance in inhibition, and approximately half of variance in WM and shifting (43 and 44%, respectively; Friedman, et al., 2008). Consequently, inhibition is most akin to the super-ordinate factor and thus inherent in all other cognitive control domains. The conceptual framework of cognitive control is illustrated in figure 2-1 below. The evidence from neuroimaging studies provides neural underpinnings for the unity of cognitive control with a common fronto-parietal network (which is largely dependent on prefrontal cortex) mediating performance on cognitive control tasks (Braver, et al., 2009; Cole, Yarkoni, Repovš, Anticevic, & Braver, 2012; Derrfuss, Brass, & Yves von Cramon, 2004; Miller, 2000; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). Therefore, when considering evidence on the relationships between physical activity, aerobic exercise and cognitive control, it is important to ascertain whether such relationships exist across cognitive control functions or whether specific associations with some but not other cognitive control constructs could be observed. The former would align with the executive function hypothesis (Colcombe & Kramer, 2003; Kramer, et al., 1999) and point to the importance of the unity aspect of cognitive control.

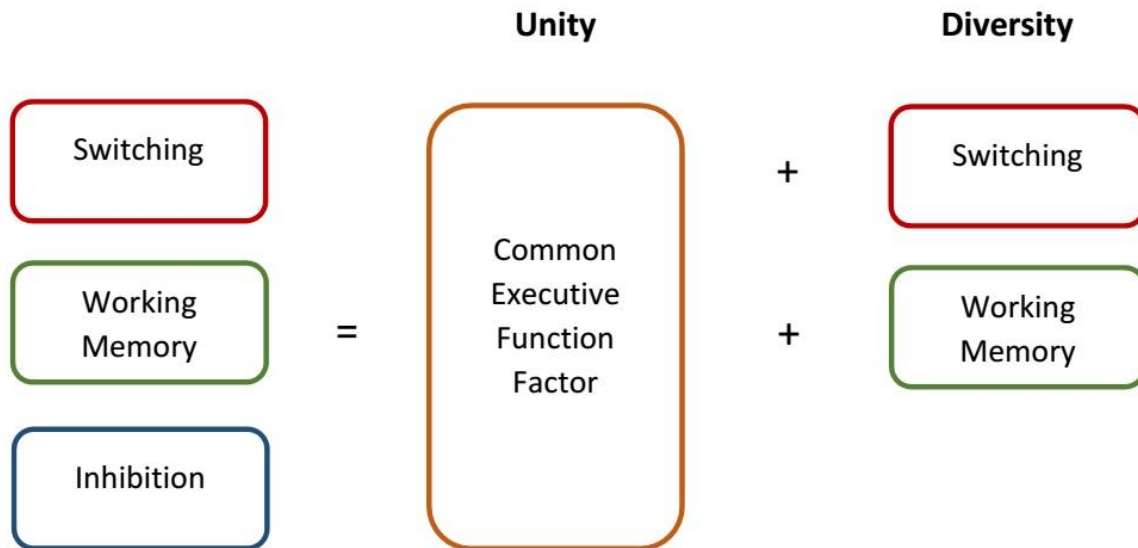


Figure 2-1. The unity and diversity of executive functions.

Adopted from “The nature and organization of individual differences in executive functions: Four general conclusions,” by A. Miyake and N.P. Friedman, 2012, *Current Directions in Psychological Science*, 21(1), p. 11. Copyright [2012] by Association for Psychological Science. Reprinted with permission.

2.1.1.2 Theory behind the measurement of cognitive control in children

The basic measurement of the efficiency of cognitive processes is reaction time. This metric has been adopted based on information processing framework, which explains how the chain of processes of perception, attention, encoding, retrieval and evaluation of the perceived stimuli guide response, and thus overt behaviour. The stimuli first impact the sensory system, then information is selected for further processing, which ultimately provide basis for response selection and response. Thus, cognitive tasks can measure time involved in multiple stages of information processing, from stimulus presentation (termed ‘event’) to participant’s overt response (e.g., pressing the response key or providing verbal response; figure 2-2). Response latency is therefore used as an index of efficiency of cognitive processes (Jones, Hinkley, Okely, & Salmon, 2013). The speed of responding needs to be considered in the context of accuracy, as these two parameters define successful and situation appropriate responses. Many cognitive tests rely specifically on the measures of response latency and accuracy as indicators of information processing efficiency. The following section will review the most common cognitive tasks and measures as applied in research of physical activity and cognition in children and adolescents.

Figure 2-2. A schematic information processing model representing sequential stages of information processing from the onset of an event to a response.
Adopted from *Exercise and cognitive function* (p. 106), by P.D. Tomporowski and M. Audiffren (Eds.), 2009, Chichester: John Wiley & Sons, Ltd.

2.1.1.3 Inhibition: Definition, measurement, importance

2.1.1.3.1 Definition

Inhibition is not a unitary concept. In this thesis the term inhibition will be used to denote conscious and wilful processes (Aron, 2007). Inhibition can be divided into inhibitory control (i.e. cognitive component) and response inhibition (i.e. behavioural component; Aron, 2007; Friedman & Miyake, 2004; Harnishfeger, 1995; Nigg, 2000). Inhibitory control (or cognitive inhibition) refers to the control of attention by selectively attending to salient stimuli (selective attention) and suppressing interference from distracting or competing stimuli, i.e. interference control (Harnishfeger, 1995; Nigg, 2000). Response inhibition (or the inhibition of prepotent response) refers to the suppression of overt behaviours such as physical responses (e.g. withholding a motor response, resisting saccadic movement towards irrelevant location on the screen) or prepotent, learnt, habitual or emotionally salient response in favour of a more appropriate one (Harnishfeger, 1995; Miyake, et al., 2000; Nigg, 2000). Although conceptually distinct, research suggests that both forms of inhibition are closely related (Friedman & Miyake, 2004), and subserved by an overlapping brain network (Luna, et al., 2010). For example, in young adults performance across multiple tasks of response inhibition and interference control is moderately correlated ($r = .67$) and loaded on the same latent factor in the confirmatory factor analyses (factor loading: .68; Friedman & Miyake, 2004; Harnishfeger, 1995; Nigg, 2000). Children also recruit a common set of brain areas within the fronto-parietal brain network during performance on these tasks (Huizinga, et al., 2006; Luna, et al., 2010; Nee, Wager, & Jonides, 2007). Thus, when two aspects of inhibition are considered, participants who do well on one of the aspects (for example interference control) are likely to

also do well on the other aspect of inhibition (behavioural or response inhibition; Friedman & Miyake, 2004).

2.1.1.3.2 Development

Although the first signs of inhibitory control are already apparent in infancy (Diamond & Gilbert, 1989), inhibitory control continues to develop throughout childhood and adolescence (Davidson, Amso, Anderson, & Diamond, 2006; Luna & Sweeney, 2004). During that time, children become more flexible in adapting to changing rules (e.g. overcoming habitual behaviour), self-directed in exerting cognitive control over their behaviour (e.g. putting toys away without prompting, solve problems) and better at proactive control, that is they are better able to monitor and correct their behaviour (Munakata, et al., 2012). The most dynamic development in inhibitory control (after the spurt during preschool) occurs between the ages of 6 and 13 years (Davidson, et al., 2006; Luna, et al., 2010). While increments in performance during childhood are best described by increments in accuracy, as children trade accuracy for speed, gains in speed better characterise performance during adolescence (Davidson, et al., 2006). These improvements continue to accrue throughout adolescence (Fischer, Biscaldi, & Gezeck, 1997; Klein & Foerster, 2001; Luna, Garver, Urban, Lazar, & Sweeney, 2004; Munoz, Broughton, Goldring, & Armstrong, 1998). For example, although substantial gains in performance occur during late childhood (until approximately the age of 10 years; Davidson, et al., 2006), 13 years old adolescents still have lower accuracies and longer latencies of performance than adults across multiple inhibitory tasks (e.g. Stop Signal task; Williams, Ponesse, Schachar, Logan, & Tannock, 1999), Eriksen flanker task, (Konrad et al., 2005; Ridderinkhof & van der Molen, 1997), spatial incompatibility task (Davidson, et al., 2006). The magnitude of developmental gain is reflected in the difference between adult levels of accuracy (typically 80 to 90%) and that of younger (7 years old) children whose performance is near chance (Luna, et al., 2010). These developments enable transition to self- and goal-directed in contrast to impulse driven behaviours (Munakata, et al., 2012). Consonant with the cognitive reserve hypothesis (Chodzko-Zajko & Moore, 1994), stronger associations between physical activity, chronic aerobic exercise and inhibition can be expected in children than adolescents (Fedewa & Ahn, 2011). However, even older adolescents show increments in cognitive performance on more challenging inhibitory tasks (e.g. Stop Signal task; Williams, et al., 1999), suggesting that their cognitive reserve is not yet fully developed.

In summary, improvements in inhibitory task performance in childhood are first evident on measures of accuracy, while faster reaction times can be a better index of performance in adolescence. Children and adolescents also become less prone to interference from distracting stimuli (i.e. those aspects of the task and environment, which are irrelevant to successful performance). Although cognitive control shows rapid development during early childhood, the efficiency and fine tuning of these functions continue to develop into early adulthood.

2.1.1.3.3 Measurement

Inhibitory control has been the most investigated component of cognitive control within paediatric exercise and physical activity literature. The great majority of studies employed modified Eriksen flanker task to assess inhibitory control (Chaddock-Heyman et al., 2013; Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, et al., 2014; Moore, et al., 2013; Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011). The task requires a selective response to a centrally positioned stimulus (e.g. an arrow, a fish as illustrated in figure 3 below) amid an array of congruent (matching the directionality of the central stimulus) or incongruent (pointing in the opposite direction) flankers. A pre-potent response based on the directionality of flankers must be inhibited. Response latency and accuracy to incongruent trials are taken as measures of inhibitory control. In addition, an interference score, which is a decrement in performance between congruent and incongruent trials (termed a “congruency effect”; Gratton, Coles, & Donchin, 1992) provides further information on the efficiency of inhibitory control system to suppress interference from the distracters. The conceptual basis for the interference effect and the main premise behind the Eriksen flanker task (i.e. congruency effect brought about by opposing flankers) has been replicated by many studies across a variety of populations (e.g. Eriksen & Eriksen, 1974; Eriksen & Schultz, 1979; Eriksen, 1995; Mullane, Corkum, Klein, & McLaughlin, 2009; Rueda, et al., 2005; Salthouse, 2010; Stins, Polderman, Boomsma, & Geus, 2007; van Leeuwen, van den Berg, Hoekstra, & Boomsma, 2007). In children and adolescents, the reliabilities of the task range from modest to moderate (.35 to .66) over a three week period (van Leeuwen, et al., 2007).

Paper and pencil tests of inhibitory control can also be used. However, they contain larger error of measurement due to human error (e.g. manual recording of reaction time and accuracy). In addition many paper and pencil tasks of inhibitory control (for example a classic Stroop interference task; (Golden, Freshwater, & Godlen, 2003; Stroop, 1935) or a trail Making Test,

which measures task switching (Reitan, 1958; Reynolds, 2002)) are complex and therefore pose cognitive demands on multiple cognitive processes. Thus performance on these tasks is not purely representative of a single cognitive construct, the phenomenon termed a task impurity problem (Burgess, 1997). Computerised laboratory tasks reduce the task impurity problem as they are simpler and focused on manipulating a single dimension of the task while holding other parameters constant. For example, in Eriksen flanker task the directionality of flankers is manipulated and their effect on reaction time and accuracy is then measured (congruency effect). Once this effect is controlled for, another task manipulation can measure flexibility to reverse response mappings by manipulating task instructions (e.g. press a left response key for right pointing stimulus).

Figure 2-3. An example of the modified Eriksen flanker task paradigm.

Participants are instructed to respond to the directionality of the centrally positioned fish amid congruent (top two pictures) and incongruent (bottom pictures) flankers. In this particular task stimulus exposure was 200 ms with fixed inter-stimulus intervals of 1700 ms. Adapted from “Aerobic fitness is associated with greater efficiency of the network underlying cognitive control in preadolescent children,” by M.W. Voss, L. Chaddock, J.S. Kim, M. Vanpatter, M.B. Pontifex, L.B. Raine, . . . A.F. Kramer, 2011, *Neuroscience*, 199, p. 168.

A task, which has especially good reliability across childhood and adolescence ($r_s = .86$ to $.97$; Williams, et al., 1999) and is also sensitive to age-related cognitive increments throughout adolescence (9-17 years; Williams, et al., 1999) is Stop Signal task (Logan, Cowan, & Davis, 1984). This is one of the most cognitively demanding inhibitory tasks, as it requires inhibiting and overriding an already initiated motor response (upon a visual or auditory cue (a stop signal); Logan, 1994; Logan, et al., 1984). First, participants perform a simple choice reaction time task (for example, press left arrow key for X and right for O). Second, a small proportion of trials with a stop signal is introduced, which necessitate response inhibition. Response inhibition is expressed as stop signal reaction time, which is the estimated latency required to withhold an already initiated response (Logan, 1994; Verbruggen & Logan, 2009). However, response latency to go trials within the stop signal block also provides information on the efficiency of attentional control as an individual needs to balance two mutually exclusive responses under uncertainty created by task manipulation (i.e. presence or absence of a stop signal). This uncertainty of stop signals requires ongoing performance monitoring for accurate responding.

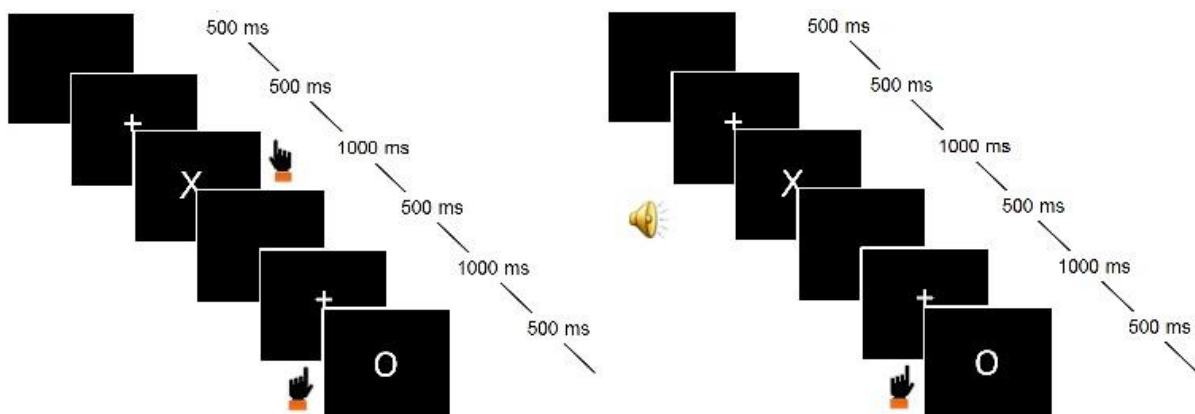


Figure 2-4. An example of a Stop Signal paradigm. Each picture represents a separate screen. First blank screen appears, followed by a fixation point and a stimulus (a letter X or O), which always requires a response under the Go condition (left panel). In the Stop Signal condition (right panel), a response must be inhibited if a cue (e.g. a beep) appears after (or concurrently with) the stimulus. Time markers on the right indicate stimulus and fixation exposure times. Blank screen and fixation exposure times add to inter-stimulus intervals.

2.1.1.3.4 Importance

Inhibition is an especially salient construct. This is because child's ability to inhibit prepotent responses and to suppress distractions are the hallmark of self-regulation (Blair & Razza, 2007; Gewirtz, Stanton-Chapman, & Reeve, 2009; Rueda, et al., 2005; Sarkis, Sarkis, Marshall, &

Archer, 2005; White, McDermott, Degnan, Henderson, & Fox, 2011), which in turn predicts future academic (Blair & Razza, 2007), health, and socio-economic (status and income) outcomes (Moffitt, et al., 2011). Furthermore, inhibition subserves complex cognitive functions such as planning and reasoning (Asato, Sweeney, & Luna, 2006; Baughman & Cooper, 2007; Friedman, et al., 2011; Welsh, Satterlee-Cartmell, & Stine, 1999), which underlie intelligence and are directly related to academic achievement (Kaufman, Reynolds, Liu, Kaufman, & McGrew, 2012; Mayes, Calhoun, Bixler, & Zimmerman, 2009). Last, child's performance on inhibitory tasks is also positively and directly related to academic achievement (Blair & Razza, 2007; Borella, et al., 2010; Espy, et al., 2004; Monette, et al., 2011; St Clair-Thompson & Gathercole, 2006). For example, performance of younger children (5 years) on peg tapping tasks of response inhibition predicted academic performance in mathematics one year later (Blair & Razza, 2007). Likewise, inhibitory control (indexed by a Stroop-like day and night task) at kindergarten predicted academic achievement in math, reading and writing at the end of Grade 1 (Monette, et al., 2011). Proactive interference (i.e. child's ability to suppress irrelevant information from a distracting task) was associated with higher reading comprehension in 10-11 years old children (Borella, et al., 2010). In sum, evidencing the link between physical activity and inhibitory control has direct relevance to academic achievement and therefore a potential to affect educational policy.

2.1.1.4 Working memory: Definition, measurement, importance

2.1.1.4.1 Definition

Working memory (WM) is the ability to actively store and manipulate information in mind in service of goal directed behaviour (Baddeley, 2003; Conway, Kane, & Engle, 2003). Two processes of WM can be distinguished: storage of information in short term memory and executive (attentional) control, which assures active maintenance of current goals in face of distracters, or active retrieval of goal relevant information from long term memory (Baddeley, 2003; Unsworth & Engle, 2007). Short term storage is modality specific and can depend either on phonological storage (i.e. articulatory loop), which permits rehearsal of verbal material to increase WM span, or a visuo-spatial storage (i.e. visuo-spatial sketchpad) to retain and process visual and spatial visual information (Baddeley, 1976). In contrast, central executive is modality neutral and akin to SAS (Norman & Shallice, 1986). For example, remembering a teacher's instruction to perform a task would require storing information in phonological loop but its content can easily be affected by child redirecting attention to external cues, such as a friend's remark (Baddeley, 2003; Conway, et al., 2003; Unsworth & Engle, 2007). In contrast,

the ability to correctly recall the same instruction after responding to a friend's unrelated query would require attentional controller to actively store and then retrieve the item despite distraction. Individual differences in WM arise from the efficiency of attentional control (Baddeley, 2003, 2010; Baddeley, 1976) and the ability to actively maintain and/or retrieve task relevant information from long term memory (despite distractions) to guide behaviour (Conway et al., 2005; Conway, et al., 2003; Unsworth & Engle, 2007).

2.1.1.4.2 Development

The developmental transitions towards self-directed, goal oriented behaviour and proactive control are possible due to child's increasing ability to actively maintain robust and abstract goal representations in WM, which is a key function of cognitive control (Miyake & Friedman, 2012). Changes in WM occur both in capacity (the number of items that can be held, manipulated and updated in WM; Cowan, 2010), as well as accuracy, interference suppression (i.e. inhibition), which enhances maintenance processes in WM, and manipulation of items in WM (Bunge & Wright, 2007; Crone, Wendelken, Donohue, van Leijenhorst, & Bunge, 2006; Davidson, et al., 2006; Klingberg, Forssberg, & Westerberg, 2002). For example, seven year old children are able to correctly recall only half of unattended items compared to adults and older children (1.5 items versus 3 items; Cowan, 2001). A shift in the efficiency of WM occurs around the age of 9 years (Crone, et al., 2006; Davidson, et al., 2006). Younger children (4 to 9 years) show greater decrements in accuracy and increases in response latency with increasing number of items to be manipulated in WM (e.g. 2 to 6) than older peers (≥ 10 years; Davidson, et al., 2006). A fine-tuning of these skills continues throughout adolescence into adulthood. Increases in precision, efficiency of WM manipulation, use of strategies (e.g. verbal rehearsal, chunking, use of associations during maintenance stage), and interference suppression all enhance maintenance of information in WM and consequently accuracy and efficiency of performance (Luna, et al., 2010). Even under low WM loads (e.g. when 3 items need to be retrieved), older adolescents (13 – 17 years) are dramatically ($\sim 10\%$) more accurate than younger peers (8-12 years old), when manipulation of the remembered sequences is required (e.g. reverse ordering of recalled items; Crone, et al., 2006). The increasing efficiency and capacity of WM allows children to transition from reactive (i.e. late correction of mistakes) towards proactive (i.e. planful anticipation and early adjustments of behaviour) forms of control, as goal representations can be maintained over longer delays. In that respect, WM helps advance higher order cognitive skills of planning and reasoning (Kail, 2007; Welsh, et al., 1999).

2.1.1.4.3 Measurement

WM has been relatively understudied in paediatric exercise literature (Verburgh, Königs, Scherder, & Oosterlaan, 2014). Studies, which examined the association between chronic aerobic exercise and WM employed either a modified Sternberg tasks (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014; Kamiyo et al., 2011; Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009; Scudder, et al., 2014) or a complex span task (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014). In Sternberg task participants memorise an array of, for example one, two or five items (letters, numbers, or words; e.g. KRM) and subsequently make judgments, whether a probe item is matching one of the memorised sets (e.g. ?k?). Response latency, which increases with WM load, and accuracy, are taken as measures of WM. It has been argued that performance on this task is more dependent on short term memory capacity and recognition rather than executive control due to low updating requirements (Conway, et al., 2005; Klein, Rauh, & Biscaldi, 2010).

Dual span tasks are considered especially good measures of WM as they have high reliability (coefficient alphas range from .70 to .90 in young adult populations; Conway, et al., 2005) and preclude maintenance of the information in short term memory by rehearsal. This is because participants engage in an alternative task (e.g. solving simple mathematical equation, reading aloud). In contrast to a modified Sternberg task (Sternberg, 1966), complex span tasks require participants to remember stimulus sequences (e.g. nouns, letters or numbers), while also attending to a secondary processing task (e.g. reading, mathematical operations; Conway, et al., 2005). A composite score based on accuracy of (sequential) recall is calculated and can vary between scoring systems, which award partial scores for only partly correctly recalled sequences, and those which require a full sequence to award the points (Conway, et al., 2005). The latter scoring method necessitates greater engagement of cognitive control, and may therefore better differentiate amongst individuals of higher cognitive ability.

2.1.1.4.4 Importance

WM is a key concept in cognitive control and one of the most influential concepts in psychological research in both children and adults, due to its strong relationship to general cognitive abilities (Alloway & Passolunghi, 2011; Conway, et al., 2003) and predictive value in scholastic achievement (Alloway & Alloway, 2010). Specifically, performance on WM tasks (verbal WM comprising backward digit span and verbal span tasks) at the age of 5 years predicted academic performance in mathematics six years later (Alloway & Alloway, 2010).

Likewise, children's performance on digit and word backward span was associated with reading ability in 5-6 years old children (Borella, et al., 2010). Improvements in WM also contribute to the development of higher order cognitive processes of reasoning and abstract thinking, which are instrumental to scholastic performance (Handley, Capon, Beveriddge, Dennis, & Evans, 2004; Kail, 2007; Süß, Oberauer, Wittmann, Wilhelm, & Schulze, 2002). Taken together, these results underscore the importance of WM to child's general intellectual ability and academic performance. Thus, studying the relationships between physical activity and WM is of public health significance as it has consequences for cognitive development and educational attainment.

2.1.1.5 Task switching involves both inhibitory control and WM

A third component of cognitive control is task switching (also termed shifting between mental sets, mental flexibility or attention switching; Diamond, 2013; Miyake, et al., 2000). Shifting is one's ability to change perspectives (both spatially and interpersonally), refine thinking (thinking outside the box), to flexibly adapt to changing circumstance, and to multi-task. It draws upon both WM and inhibition as to switch perspectives one needs to inhibit current perspective and activate an alternative one in WM. Thus, task switching poses the greatest challenge to the cognitive control system and undergoes the most protracted development (Davidson, et al., 2006; Espy, 1997; Zelazo, Frye, & Rapus, 1996; Zelazo & Reznick, 1991). This thesis will focus on inhibition and WM as performance on these tasks has been most consistently associated with CRF and chronic aerobic exercise (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014; Hillman, et al., 2011; Kamijo, et al., 2011; Scudder, et al., 2014), and due to their direct relevance to the applied forms of cognition (i.e., academic achievement; Alloway & Alloway, 2010; Blair & Razza, 2007; Borella, et al., 2010; Espy, et al., 2004; Gathercole, 2004; St Clair-Thompson & Gathercole, 2006).

2.1.1.6 Laboratory tasks versus cognitive batteries

Since very little is known about the relationship of physical activity to cognition in children, an intuitive approach is to test these associations across a wide variety of cognitive functions in order to determine whether physical activity may have a selective or generalised effect on cognition (Etnier, 2012). Researchers using such approaches turn to a set of pre-determined tasks included in specific cognitive batteries (Booth, Tomporowski, et al., 2013; Davis et al., 2007; Davis, et al., 2011; Krafft et al., 2014; Syväoja, et al., 2014). This approach, however, may not allow for testing of specific hypotheses relevant to distinct cognitive constructs (e.g. WM and/or inhibitory control), as test batteries offer limited set of tasks and little or no

flexibility in adjusting task parameters. For example, Test of Everyday Attention for Children (TEA-Ch; Manly, Robertson, Anderson, & Nimmo-Smith, 1998) includes pencil and paper tasks relevant to inhibitory control and task switching but not WM. A measurement error is increased due to human error in taking reaction time and accuracy measures. Another paper and pencil cognitive battery of tests, Cognitive Assessment System (CAS; Naglieri & Das, 1997), comprises four scales (Planning, Attention, Simultaneous and Successive) each measured with a variety of cognitive tasks. However, the tasks included in each scale tap different cognitive constructs. For example, Attention scale from CAS comprises of an interference (Stroop-like) task, a task of selective attention (identifying rare targets amongst distracters), and task switching. Thus, a composite score is not representative of either inhibition or task switching but of a latent construct which includes selective attention, inhibition and task switching. The other three scales (Planning, Simultaneous and Successive) include tasks relevant to intelligence (general intellectual ability), which the battery was specifically designed to measure. For example, Simultaneous subscale tests child's ability to perceive relations among the stimuli, to understand logical and grammatical connections, to perceive objects as a group and to integrate separate items into the whole. Successive subscale requires children to work with material in a specific serial order to reproduce sequences and to understand syntactic relationships. Therefore, CAS does not provide the information on specific constructs of cognitive control, rather it measures higher order and more complex cognitive functions. Last, computerised Cambridge Neuropsychological Test Automated Battery (CANTAB; Luciana, 2003; Luciana & Nelson, 2002) used by Syväoja et al. (2014) to investigate the associations between cognitive functions and objectively measured MVPA, overcomes the problem of human error, however task parameters in this battery are fixed. Even though CANTAB was validated for use in children aged 5 to 12 years (Luciana & Nelson, 2002), the lack of flexibility in adjusting task parameters may lead to decreased sensitivity of the tasks to differentiate performance of healthy adolescents as noted by Syväoja et al. (2014). Last, the high cost of CANTAB (~ £9,000) can be prohibitive.

2.1.2 Physical activity, chronic aerobic exercise and cardio-respiratory fitness

The majority of literature within paediatric exercise and cognition is based on the associations between CRF (a physical state, not a behaviour) and cognition, with emergent evidence from randomised controlled trials (RCTs) on the effects of chronic aerobic exercise on children's cognitive control. The associations between CRF, chronic aerobic exercise and cognition can share some of variance. However, at present it remains unknown whether the volume of daily physical activity, and MVPA in particular, is associated with cognition or whether chronic aerobic exercise is needed for cognitive benefits in children to emerge. Therefore, it is important to define physical activity concepts before reviewing the evidence on the associations between daily physical activity, CRF, chronic aerobic exercise and cognition.

2.1.2.1 Physical activity: Definitions, measurement, relevance to cognition

2.1.2.1.1 Definitions

Physical activity is defined as “any bodily movement produced by skeletal muscles that results in caloric expenditure above resting levels” (Caspersen, Powell, & Christenson, 1985). The dose (or total volume of physical activity) is the product of frequency, intensity and duration (Haskell, 2001; Montoye, 2000). Frequency of physical activity refers to the rate at which physical activity (which can be defined as physical activity bouts or specific physical activities such as for example football or swimming) occur over time (e.g., day, week, month, year; Haskell, 2001; Shephard, 2003); intensity is the effort required to perform physical activity (e.g. light, moderate, vigorous) expressed as energy expenditure in either metabolic equivalents (METs), kilocalories, joules, millilitres of oxygen consumption or speed. Duration is the total time (e.g., minutes, hours) spent in physical activity summarised over pre-defined period of time (e.g., day, week; Shephard, 2003). Physical activity is also characterised by its mode (e.g., walking, running, swimming), and the context of daily life when an individual engages in physical activity (e.g., leisure time, school physical activity, which includes physical education, recess and active transport; Shephard, 2003). This thesis will specifically focus on the volume of MVPA, which is defined by energy expenditure equal to or greater than 3 METs for adolescents, and 4 METs for children (Harrell et al., 2005; Roemmich et al., 2000).

In this thesis, the term daily physical activity or daily MVPA will denote the overall time spent in MVPA accumulated throughout the entire day as objectively measured using accelerometers. Daily MVPA is an estimate of children's habitual engagement in MVPA within the limitation of brief (usually a week long; Corder, Brage, & Ekelund, 2007; Ridgers

& Fairclough, 2011) assessment adopted in objective physical activity monitoring. Therefore, the term daily in place of habitual MVPA will be used, when referring to objectively measured MVPA. Physical inactivity will be defined as not meeting physical activity recommendations (i.e. for children and adolescents, engaging in at least 60 minutes of MVPA daily; Department of Health, 2011; Centers for Disease Control and Prevention [CDC], 1996; Sedentary Behaviour Research Network, 2012; U.S. Department of Health and Human Services, 2008). Last, sedentary behaviour is distinct from physical inactivity as being sedentary does not preclude being physically active. For example, a child may spend a large proportion of the day sedentary but engage in sports for an hour daily, therefore accumulating both a relatively high volume of MVPA and time sedentary. This distinction has only recently been recognised. Thus, sedentary behaviour (or time spent sedentary) is defined as “(...) any waking behaviour characterised by an energy expenditure ≤ 1.5 METs while in a sitting or reclining posture” (Sedentary Behaviour Research Network, 2012, p. 540). In practice, this means that any time a child is sitting or lying down, they are engaging in sedentary behaviour. Sedentary behaviours include TV viewing, computer time, video games, internet browsing, reading and screen time.

2.1.2.1.2 Measurement: Accelerometry is the method of choice to assess physical activity in young people

In order to capture MVPA volume in young people, an objective method, which affords high resolution, is valid, feasible and has low reactivity (i.e. change in physical activity behaviour as the result of the measurement process) is needed. Accelerometers offer the best combination of these qualities, as they are objective, capture temporal patterns of movement (duration, frequency), with a resolution of the raw signal, which can be summarised over second based epochs (Baquet, et al., 2007; Mattocks, 2007). Thus, accelerometers capture the majority of physical activity, which is not possible with recall (i.e. self-reports). Furthermore, accelerometers have low reactivity (limited to 5% during the first day of measurement; Dössegger et al., 2014). The feasibility of accelerometers as tools of physical activity assessment in children is high, with low data loss (15%) and high participant reported acceptability (80%; De Vries et al., 2009).

Accelerometers measure acceleration in one of the three orthogonal axes: vertical, medio-lateral and antero-posterior. Uniaxial devices measure movement in a vertical axis, while triaxial models include three orthogonal axes (vertical, medio-lateral and antero-posterior), which measure acceleration in each of the axes and provide a summary metric across all three

planes (i.e., vector magnitude). Despite this advantage, the use of data from three axes shows negligible improvement in accuracy (no more than 2%) over the uniaxial devices (Vanelst et al., 2012). Therefore, the use of vertical axis alone affords comparable accuracy and greater comparability. Furthermore, the use of a single vertical axis allows for data comparisons with large scale epidemiological studies, which objectively assessed physical activity in young people (e.g. the Avon Longitudinal Study of Parents and Children (ALSPAC; Mattocks et al., 2008), National Health And Nutrition Examination Survey (NHANES; Troiano, et al., 2008), the European Youth Heart Study (EYHS; Riddoch, et al., 2004), and Healthy Lifestyle in Europe and Nutrition in Adolescence (HELENA; Martinez-Gomez et al., 2010)). The ActiGraph accelerometer has been the most validated accelerometer in research with children and adolescents across a wide age spectrum (2-18 years; De Vries, et al., 2009), and used in all aforementioned epidemiological research (ALSPAC, NHANES, EYHS, HELENA). The ActiGraph has shown a good criterion validity across multiple studies using indirect calorimetry as a criterion ($r_s = .66$ to $.85$; Garcia, Langenthal, Angulo-Barroso, & Gross, 2004; Pate, Almeida, McIver, Pfeiffer, & Dowda, 2006; Schmitz et al., 2005; Treuth et al., 2004; Trost, Way, & Okely, 2006), and good reproducibility ($ICC = .54$; Mattocks, 2007).

2.1.2.1.3 Measurement: Advantages of accelerometers over other physical activity measures

The advantages of accelerometry over other methods of physical activity assessment most commonly used in research with paediatric populations are summarised in table 2-1. Accelerometers are superior measures of physical activity in young people compared to self-reports, which are inaccurate (Kohl, et al., 2000; Adamo et al., 2009), show low criterion validity when assessed against accelerometers ($r_s = .09$ to $.53$; Corder, Ekelund, Steele, Wareham, & Brage, 2008), overestimate physical activity by as much as 200% (Adamo et al., 2009; Prince, et al., 2008), and have been found invalid as assessment methods in children younger than 10 years who cannot correctly conceptualise some of the physical activity concepts (Kohl, et al., 2000; Trost, 2000). In confirmation, stronger and more consistent associations of MVPA to multiple health outcomes (e.g., metabolic syndrome, overweight/obesity, CRF) have been observed when MVPA was objectively assessed with accelerometers as compared to self-reports (Dencker & Andersen, 2008; Janssen & LeBlanc, 2010). Consequently, when observing a relationship between the total volume of daily MVPA and cognition (which is a new health outcome in paediatric physical activity epidemiology), accelerometers afford the best measure to capture the total volume of children and adolescents'

daily MVPA, which is largely intermittent (Bailey, et al., 1995; Baquet, et al., 2007) and not easily captured by other methods such as self-report or heart rate monitoring.

In comparison to heart rate monitors, accelerometers provide a direct measure of movement, while the momentary lag of heart rate in relation to changes in movement, and elevation of heart rate even after the movement has ceased, can mask children's sporadic activity (Armstrong, 1998; Trost, 2007). Although, heart rate monitoring affords a better measure of physical activity intensity and therefore indirectly of energy expenditure (Emons, 1992; Eston, Rowlands, & Ingledew, 1998; Livingstone et al., 1992), its accurate assessment requires burdensome calibration of individual's heart rate to the oxygen uptake (Rowlands, 2007; Rowlands, Eston, & Ingledew, 1997; Trost, 2007). Importantly, factors other than physical activity affect the relationship between heart rate and oxygen consumption (thus estimated energy expenditure), which include age, body size, proportion of muscle used, CRF, psychological stress (Armstrong, 1998; Rowlands, 2007; Rowlands, et al., 1997). Therefore, heart rate monitors cannot accurately assess child's daily MVPA volume, which limits their utility when associations between daily MVPA volume and cognition are of interest. In contrast, accelerometry provides both a good estimate of total volume and intensity of MVPA, which is accurate at a group level (e.g., accelerometers show moderate to high validity compared to heart rate telemetry in children aged 7 to 15 years over a 3 day assessment ($r_s = .50 - .74$; Janz, 1994; Rowlands, 2007)).

In sum, accelerometers afford the best compromise between greater accuracy of heart rate monitors to assess energy expenditure and are superior to commonly used self-reports as they measure the total volume, frequency, intensity and duration of movement directly and with high temporal resolution, which helps capture intermittent nature of children and adolescents' physical activity.

Table 2-1. Comparative summary of physical activity methods used in paediatric physical activity research

	Validity	Validity to Assess MVPA	Affordabil ity	Objective	Ease of Administr ation	Easy to Complete/ Complian ce	Measures Patterns, Modes and Dimensio ns of PA	Resolutio n	Non- reactive	Suitable for Ages < 10 years	Feasible in Large Studies
Accelerometers	++	++	+	+++	++	++	++	+++	+++	+++	++
DOB	+++	+++	X	++	++	+++	++	++	+	+++	+
HR	++	+++	++	+++	+	+	++	++	+	+++	+
Pedometers	++	++	+++	+++	++	++	X	+	+	+++	+
Self-reports	+	X	+++	X	+++	+++	++	X	+++	X	+++

Note: X Poor or Inappropriate; + Acceptable, ++ Good, +++ Excellent; PA, physical activity. DOB, direct observation; HR, heart rate; Adapted from: “State of the art reviews: Measurement of physical activity in children and adolescents.” By S. G. Trost, 2007, *American Journal of Lifestyle Medicine*, 1(4), p. 312. Copyright [2007] by SAGE Publications. Reprinted with permission.

2.1.2.1.4 Relevance

MVPA volume has been most consistently associated with multiple health outcomes in children, including CRF, metabolic health, adiposity (Belcher et al., 2010; Dencker & Andersen, 2011; Ekelund, et al., 2012; Holman, Carson, & Janssen, 2011; Mark & Janssen, 2009; Martinez-Gomez, et al., 2010; PAGAC, 2008) and psychological health (e.g. self-esteem, depression, anxiety; Biddle & Asare, 2011). Daily MVPA volume also shows stronger associations with CRF than the overall volume of physical activity as assessed with accelerometers (Dencker & Andersen, 2011), while CRF has been consistently related to cognitive control in preadolescent children (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011). Consequently, this thesis focuses on the total volume of daily MVPA and its relationship to children and adolescents' cognitive control, which is a novel health outcome.

Accelerometry quantifies the intensity of movement of the centre of body mass (as the most common accelerometer placement is on the hip or waist; Trost, 2005). The common metric used across the studies are "movement counts". Counts are a proprietary metric specific to particular accelerometer brand, which precludes direct comparisons of accelerometer outputs across brands (Reilly et al., 2008). Thus, the use of ActiGraph, which is the most common device in paediatric research, facilitates data comparison and interpretation (Cain, Sallis, Conway, Van Dyck, & Calhoun, 2013; Trost, 2007). The total volume of physical activity is then summarised as either daily counts per minute (CPM) or counts per day. Accelerometer counts are converted into intensities using intensity cut points. For ActiGraph accelerometer and time spent in MVPA, intensity cut points for children and adolescents can vary from 400 (Krishnaveni et al., 2009) to 3,600 CPM (Mattocks et al., 2007). The most commonly applied intensity cut point to class MVPA in children and adolescents (used by 32.6% of the 248 recently reviewed studies; Cain, et al., 2013) is age-adjusted cut point developed by Freedson et al. (2005) and first published by Trost et al. (2002). Intensity estimates from accelerometer output are affected by growth, including differences in body size, relative leg length and maximal oxygen uptake (Boreham & McKay, 2011; Stone, Esliger, & Tremblay, 2007). Consequently, age-specific cut points can provide some adjustment for such growth-related individual differences. Compared to indirect calorimetry, age-adjusted cut point has a good classification agreement of 75%, and fair to good classification accuracy for minutes spent in

MVPA (AUC = .76 - .82) during walking and running in 10-18 year olds (Trost, et al., 2006). Linear regression equations are unlikely to over-estimate the time spent in MVPA. To the contrary, out of four evaluated equations (Evenson, Catellier, Gill, Ondrak, & McMurray, 2008; Freedson, et al., 2005; Puyau, Adolph, Vohra, & Butte, 2002; Treuth, et al., 2004; Trost, et al., 2002), three (Evenson, et al., 2008; Freedson, et al., 2005; Treuth, et al., 2004; Trost, et al., 2002) underestimated the time spent in MVPA compared to direct calorimetry (Crouter, Horton, & Bassett, 2013). For example, Freedson's age specific equation (Freedson, et al., 2005; Trost, et al., 2002) underestimated time in MVPA by approximately 18 minutes in 11-15 year olds (Crouter, et al., 2013). In sum, MVPA is of specific interest in the study of cognition in young people and accelerometry provides the best and conservative measure (i.e. which under- rather than over-estimates MVPA volume) to estimate the total volume of daily MVPA.

2.1.2.2 Chronic aerobic exercise: Definitions, measurement, relevance

2.1.2.2.1 Definitions

In contrast to physical activity, which incorporates intermittent physical activity, aerobic exercise refers to planned, structured and repetitive physical activity with an objective to improve or maintain CRF (Caspersen, Pereira, & Curran, 2000). The physiological (and health) responses to aerobic exercise can be either acute (immediate but transient, following a single bout of aerobic exercise) or chronic, namely accumulated over longer period of regular aerobic exercise and stable over time; (Haskell, 2001). This thesis focuses on the cognitive benefits of chronic (as opposed to acute) aerobic exercise. Chronic as opposed to acute effects of aerobic exercise on cognition are durable as they depend on changes to brain metabolism (e.g., increased cerebral blood volume, up-regulation of proteins implicated in neural learning and energy metabolism (i.e. brain derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1); Boecker, Hillman, Scheef, & Strüder, 2012; Cotman, Berchtold, & Christie, 2007; Gomez-Pinilla & Hillman, 2013; Gomez-Pinilla, Vaynman, & Ying, 2008; Hillman, et al., 2008). These changes result in increased structural plasticity in brain regions, which underpin memory and learning (e.g., hippocampus) leading to improved brain function (Boecker, et al., 2012; Buck, et al., 2008; Gomez-Pinilla & Hillman, 2013).

2.1.2.2.2 Measurement

The effects of chronic aerobic exercise on cognition are thought to be mediated by CRF (Chodzko-Zajko & Moore, 1994; Etnier, 2006; Hötting & Röder, 2013). Therefore, in order to

assess the efficacy of chronic aerobic exercise interventions on children's cognition, measures of both CRF as well as duration, frequency and intensity of exercise sessions are needed. This section will consider the measurement of physical activity intensity and adherence to an aerobic exercise programme, while measures of CRF will be discussed in the following section. Heart rate telemetry has high validity in estimating energy expenditure in children as assessed against indirect calorimetry ($r_s = \sim .80$; Eston, et al., 1998) and doubly labelled water (error of estimate $\sim 10\%$ in estimating total energy expenditure; Emons, 1992; Livingstone, et al., 1992) and therefore is the best measure of physical activity intensity during aerobic exercise sessions. Heart rate telemetry has been adopted as the measure of intervention fidelity by extant chronic aerobic exercise interventions focused on children's cognition (Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014). To ensure fidelity, children are given a specific heart rate target to maintain during exercise session, which is equivalent to MVPA (e.g., target heart rate zone equivalent to 55-80% child's maximum heart rate (Hillman, et al., 2014) or 150 bpm (Davis, et al., 2007; Davis, et al., 2011)).

The effects of chronic aerobic exercise on cognition also depend on the frequency and duration of exercise sessions. Daily nine-month after-school aerobic exercise intervention, which included MVPA in excess of physical activity recommendations (~ 70 minutes), benefited children's inhibitory control (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014), WM (Kamijo, et al., 2011) and task switching (Hillman, et al., 2014). Attendance was positively related to task switching, suggestive of a dose-response effect of the intervention volume on cognition (Hillman, et al., 2014). Likewise, a dose-response effect of session duration (40 compared to 20 minutes) on planning was observed following a three-month after-school aerobic exercise intervention in overweight and obese children (Davis, et al., 2007; Davis, et al., 2011). Thus, intervention volume (attendance) and session duration are important indices of the effects of chronic aerobic exercise on cognition. At present it remains unknown if these effects also vary with the baseline levels of child's daily MVPA (and time sedentary), as research using objective measurement of baseline physical activity is lacking. Stronger cognitive response to aerobic exercise could be expected in children who are largely inactive in parallel to dose-response curves for multiple health outcomes (PAGAC, 2008).

2.1.2.2.3 Relevance

Evidencing the causal relationship between chronic aerobic exercise and cognition in children and adolescents has potential to influence public health and educational policy (IOM, 2013).

Causality can only be addressed within an RCT, which simultaneously evaluates the effects of regular aerobic exercise on CRF (a hypothesised mediator; Chodzko-Zajko & Moore, 1994; Etnier, 2006) and cognitive control. Such research is both theoretically and practically relevant. Theoretically, because the mechanisms behind chronic aerobic exercise and cognitive control in children need to be addressed (Etnier, 2006; Hötting & Röder, 2013). Practically, as the causal link between aerobic exercise and cognition provides a strong argument to increase regular MVPA in children in order to benefit their cognitive function. Such knowledge paired with the observational evidence on the associations between daily MVPA and cognitive control in young people would contribute to the evidence base, which in time can help formulate future physical activity recommendations to improve cognitive function in young people.

2.1.2.3 Cardio-respiratory fitness: Definitions, measurement, relevance

2.1.2.3.1 Definition

Cardio-respiratory fitness (CRF; also termed cardiovascular endurance, or cardiovascular fitness), is a health-related component of physical fitness and defines individual's ability to perform large muscle, whole body exercise at moderate to high intensities for extended periods of time (Saltin, 1973). Thus, children and adolescents with high CRF can engage in vigorous exercise for at least moderate durations or light to moderate exercise for more extended periods without undue fatigue. Importantly, CRF indexes the efficacy of the circulatory and respiratory systems to supply oxygen during sustained aerobic exercise (Corbin, 2000) and is expressed as maximal oxygen intake during maximal exercise (Institute of Medicine, 2012). CRF is an important health marker as it indexes the efficiency of cardiovascular and pulmonary systems in supplying oxygenated blood to the working muscle and brain. Although CRF can be modulated by physical activity behaviour, it is also largely (~ 50%) genetically determined (Bouchard et al., 2011). Importantly, CRF is a physical state and thus a health outcome, while physical activity is a modifiable behaviour (Dobbins, Husson, DeCorby, & LaRocca, 2013; Metcalf, Henley, & Wilkin, 2013), which can affect this physical state (Armstrong, Tomkinson, & Ekelund, 2011). However, in children and adolescents CRF is only weakly to moderately related to objectively measured (accelerometry) physical activity ($r_s = .10$ to $.45$; Dencker & Andersen, 2011). Therefore, it is not a good marker of child's regular physical activity.

2.1.2.3.2 Measurement: Physiological principles in the measurement of maximal oxygen uptake

The measurement of CRF relies on the pulmonary oxygen uptake and its kinetics during aerobic exercise (McArdle, 2010). Oxygen uptake rises exponentially during the first two to three minutes of aerobic exercise (a fast component of exercise oxygen consumption), when oxygen levels do not match the energy requirements of working skeletal muscle. During this stage the adenosine triphosphate (ATP, a high energy phosphate, the body's main energy currency) is synthesised anaerobically from muscle glycogen. Oxygen consumption attains a plateau ("a steady state") between the third and the fourth minute of aerobic exercise and remains stable for the duration of aerobic exercise at the same intensity. The attainment of a steady state reflects a balance between the energy requirement of the working muscles and the synthesis of ATP during aerobic metabolism. The exercise oxygen consumption kinetics forms the basis for the measurement of individual's aerobic capacity (also termed maximum oxygen uptake, maximum aerobic power, aerobic capacity or $\text{VO}_{2\text{max}}$). $\text{VO}_{2\text{max}}$ is measured during maximal or sub-maximal exercise tests, which challenge cardio-respiratory system through the planned increments in exercise intensity until volitional exhaustion.

When average values of oxygen consumption achieved at each phase are plotted, a continuous increase in oxygen uptake can be observed until the point of no further increase despite an increase in exercise intensity (McArdle, 2010). This plateau in oxygen uptake reflects individual's maximal aerobic capacity (i.e. $\text{VO}_{2\text{max}}$) and is considered a gold standard measure of CRF (Pescatello & American College of Sports Medicine [ACSM], 2014). $\text{VO}_{2\text{max}}$ is expressed either as an absolute value in litres per minute ($\text{L}\cdot\text{min}^{-1}$) or relative to body weight in millilitres per kilogram body weight per minute ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). In a progressive exercise test to volitional exhaustion the attainment of a plateau in oxygen uptake is the main criterion to establish $\text{VO}_{2\text{max}}$, as exercise above this plateau is assumed to be supported by anaerobic ATP re-synthesis (Pescatello & ACSM, 2014; Armstrong & Fawcner, 2007). However, an absolute VO_2 plateau seldom occurs in children (Armstrong, 2013). Consequently, age-related criterion to define a VO_2 plateau in young people has been adopted. The most commonly used criterion is an increase in VO_2 relative to body mass of no more than $2\text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ for a 5-10% increase in exercise intensity (Armstrong & Fawcner, 2007). An alternative valid measure to VO_2 plateau in children is VO_2 peak (i.e. the highest reading of oxygen consumption during an exercise test to exhaustion; Armstrong, Welsman, & Winsley, 1996; Cooper, Weiler-Ravell,

Whipp, & Wasserman, 1984; Rowland, 1993b; Welsman, Bywater, Farr, Welford, & Armstrong, 2005).

2.1.2.3.3 Measurement: Maximal exercise tests

The direct measurement of VO_2 peak requires maximal aerobic effort. In a laboratory setting a maximal exercise test on a treadmill ergometer is considered a method of choice due to its high reliability ($r \sim .70$) and validity (Armstrong & Fawcner, 2007; Cunningham, van Waterschoot, Paterson, Lefcoe, & Sangal, 1977; Figueroa-Colon et al., 2000; Welsman, et al., 2005). This is because performance on the cycle ergometer is largely limited by anaerobic factors such as fatigue of quadriceps muscles and decreased blood flow to the muscles, which leads to fatigue and exercise termination (Armstrong & Welsman, 1994). In contrast, treadmill ergometer engages large muscle groups and therefore termination of the test (and resulting VO_2 peak value) is limited by aerobic rather than anaerobic capacity (Armstrong & Fawcner, 2007; Armstrong & Welsman, 1994). However, the two VO_2 peak values obtained with cycle and treadmill ergometers are very highly correlated ($r = .90$) and thus VO_2 peak is independent of a maximal exercise protocol. Graded maximal exercise tests at constant speed and progressively increasing grade are commonly used in children and adolescents due to their brevity (approximate test duration of 10-12 minutes) and reliability (intra-individual CV $\sim 7.5\%$ (Figueroa-Colon, et al., 2000); $r = .74$; (Cunningham, et al., 1977)). The results of these tests also show consistent relationship to cognitive control in preadolescent children (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Voss, et al., 2011).

2.1.2.3.4 Measurement: Sub-maximal exercise tests

However, maximal exercise tests are costly as they require specialist equipment and are time consuming, which limits their application in population based research. Field based tests are therefore more appropriate, although they contain an error inherent in the prediction of $\text{VO}_{2\text{max}}$ from sub-maximal effort (Armstrong & Welsman, 2007; Institute of Medicine, 2012). Amongst field based methods used in large scale surveys, heart rate extrapolation tests (treadmill or cycle ergometer) and shuttle runs to volitional fatigue are most frequently used and show consistent associations with several health markers (e.g. adiposity, metabolic risk factors; Boddy, Fairclough, Atkinson, & Stratton, 2012; Institute of Medicine, 2012; Kim et al., 2005; Olds, Tomkinson, Léger, & Cazorla, 2006; Ruiz et al., 2014). Heart rate extrapolation tests are based

on the principle of the linear association between heart rate and increasing intensity of endurance exercise. The tendency for the maximal heart rate and $\text{VO}_{2\text{max}}$ to co-occur at the same intensity of exercise is used as the basis to estimate CRF from graded, sub-maximal exercise tests. For example, the best known and widely used sub-maximal graded exercise test is Physical Working Capacity at the heart rate of 170 (PWC-170) beats per minute (bpm; Wahlund, 1948). The test includes three stages of progressively increasing intensity, while participant's response to these increments is tracked with heart rate recordings. CRF is expressed as the power output at a heart rate of 170 bpm, estimated with a linear regression line from the power outputs and heart rates obtained during each stage of exercise (Bland, Pfeiffer, & Eisenmann, 2012). PWC-170 shows adequate convergent validity relative to $\text{VO}_{2\text{max}}$ (correlation coefficients range from 0.20 to 0.84 with higher variability in values expressed relative to body mass; Bland, et al., 2012; Boreham, 1990; Rowland, 1993a) and high reliability (test-retest correlation coefficients range from 0.89 to 0.98; Watkins & Ewing, 1983; Watson & O'Donovan, 1976). The advantage of the PWC-170 is the brevity of assessment (usually 3 stages of 2-6 minutes) and simplicity of equipment, which include cycle or treadmill ergometer and a heart rate monitor.

In conclusion, when choosing between direct measures of maximal oxygen uptake and its estimates based on sub-maximal exercise tests, feasibility of both methods in the given context and the focus of the research question need to be considered.

2.1.2.3.5 Measurement: Change in cardio-respiratory fitness over time

When measuring change over time in CRF in young people, it is important to account for growth and maturity-related changes. The age-related changes in maximal oxygen uptake are driven by physiological changes in cardio-respiratory system and movement efficiency (Armstrong & Fawcner, 2007; Malina, Bouchard, & Bar-Or, 2004). The age-related increase in absolute maximal oxygen uptake varies by sex, and is greater for boys than girls, who have greater $\text{VO}_{2\text{max}}$ than girls at any given age (Armstrong, McManus, & Welsman, 2008; Malina, et al., 2004). Boys show greater than two-fold increase (164%) in absolute values of $\text{VO}_{2\text{max}}$ between the ages of 8 to 16 years, averaging 11% increase per year (Hallal et al., 2013). In contrast, girls show a smaller increase (70-80%) from 8 to 13 years, and a plateau thereafter (2-12% increase between the ages of 13 and 17 years; Armstrong, et al., 2008; Brage et al., 2004; Hallal, et al., 2013; Kwon, Janz, Burns, & Levy, 2011). Before puberty, girls' $\text{VO}_{2\text{max}}$ is 10% lower than that of boys, but this difference increases to as much as 48% by the age of 17

years (Armstrong, et al., 2008). The age-related changes in $\text{VO}_{2\text{max}}$ are driven by increases in body mass (i.e., predominantly in fat free mass), increases in cardiac output (mainly due to an increase in stroke volume) and movement efficiency (Armstrong, et al., 2008; Malina, et al., 2004). The largest influence is due to increases in body mass, specifically in fat free mass, as evident from consistently strong correlations between maximal oxygen uptake and body size (weight and height), which average $r = .70$ (Armstrong, et al., 2008). Consequently, when maximal oxygen uptake is expressed relative to body mass, age and maturity related differences (but not sex differences as relative $\text{VO}_{2\text{max}}$ values remain on average higher in boys (48-50 $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) than girls (35-45 $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; Armstrong, et al., 2008)) are no longer observed (Armstrong, et al., 2008; Malina, et al., 2004). Therefore, when interpreting inter-individual differences both cross-sectionally and when considering change in $\text{VO}_{2\text{max}}$, relative rather than absolute values are needed.

2.1.2.3.6 Relevance

CRF is particularly relevant to the study of daily MVPA and cognition in young people, due to its consistent associations with cognitive control in children (Buck et al., 2004; Buck, et al., 2008; Buck, et al., 2006; Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011). Nonetheless, these associations are not necessarily indicative of the associations between daily MVPA and cognitive control (i.e., due to its modest associations with objectively measured MVPA in young people (Dencker & Andersen, 2011)) and large genetic component (Bouchard, et al., 2011). It is important to account for CRF in the study of daily MVPA and cognition in children and adolescents, as CRF can either mediate or confound the proposed associations. At present, it is not clear whether the associations between objectively measured MVPA and cognition exist due to equivocal findings (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014; van der Niet, et al., 2014). To the author's knowledge, the possible contribution of CRF to these relationships has not been assessed. Last, CRF is purported to mediate the effects of chronic aerobic exercise on cognitive control (Chodzko-Zajko & Moore, 1994; Etnier, 2006). Therefore, RCTs into the effects of aerobic exercise on cognition in children are specifically designed to increase CRF (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Kamijo, et al., 2011). Consequently, inspecting intervention effects on the change in CRF is integral to ascertaining intervention fidelity.

2.1.3 Critical review of literature on cardio-respiratory fitness, daily MVPA, aerobic exercise and cognitive control in children and adolescents

2.1.3.1 Cardio-respiratory fitness and cognitive control in children and adolescents

The study into the associations between physical activity and cognition in children largely relies on cross-sectional evidence of the relationship between CRF and cognitive control (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011). However, CRF is a poor proxy of physical activity in children and adolescents. Importantly, CRF is not a behaviour but a physical state, which only partly results from physical activity behaviour (Armstrong, et al., 2011; Dencker & Andersen, 2011). The most consistent associations in the literature have been noted between CRF and inhibitory control in preadolescent children (ages 6-11 years; (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011), as reviewed in table 2-2). That is, the performance of higher fit children is more consistent across task conditions, which vary in cognitive control demands suggesting greater flexibility of higher fit children in up-regulating cognitive control (Chaddock, Hillman, et al., 2012; Hillman, et al., 2009; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014). The up-regulation of cognitive control was manipulated either by the presence of incongruent flanking stimuli (i.e. congruency effect; Gratton, et al., 1992) or by reversing response mappings (e.g., responding with a right key to a left pointing stimulus). Specific positive associations between CRF and children's performance on these task conditions, which require the up-regulation of cognitive control were also observed (Moore, et al., 2013; Voss, et al., 2011). For example, Moore et al. (2013) observed that higher fit children were faster than lower fit peers on incompatible task condition, which required reversal of response mappings. Similarly, Voss et al. (2011) found specific effects of higher fitness on accuracy for the task condition, which required suppression of distractions (i.e., due to flankers pointing in the direction opposite to the stimulus). Higher fit children have also smaller performance decrements, when performance on easy and more cognitively demanding task conditions is compared (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Voss, et al., 2011). These effects of CRF vary in magnitude between 3 and 12 %, and are larger for more demanding task conditions (i.e. those, which require the up-regulation of cognitive control). Although only one study inspected the effects of CRF on WM, its results

are consistent with those for inhibitory control (Scudder, et al., 2014). That is, higher CRF was associated with better performance across task conditions, which varied in cognitive demands. For example, higher CRF was associated with greater accuracy and greater ability to discriminate between targets and non-targets on the spatial n-back task (Scudder, et al., 2014). Spatial n-back task requires constant updating of the items in WM in order to compare the position of a displayed object with that of the previous (1-back) or two trials back (2-back). In sum, higher CRF shows consistent, albeit modest associations with inhibitory control and, based on preliminary evidence, with WM in prepubescent children. These associations are both general (i.e. apparent across task conditions which do and do not engage cognitive control) and specific to task conditions, which require engagement of cognitive control.

Table 2-2. Review of cross-sectional studies on CRF and cognitive control in children and adolescents

Author	Year	n (% F)	Mean age (years)	Age range (years)	Country	CRF measure	Cognitive outcome / measure	Covariates	Results
Chaddock et al.	(2010)	55 (54%)	10.0 (± 0.6)	9-10	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70th percentile relative to norms	Inhibitory Control / Flanker task (CONG) MRT; Accuracy; % Interference (MRT)	Age, IQ, SES, ADHD	HF less % interference HF: 5% LF: 11%
Chaddock et al.	(2012)	32 (50%)	9.9 (± 0.55)	9-10	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70th percentile relative to norms	Inhibitory Control / Flanker task (CONG) MRT; Accuracy	Age, IQ, SES, ADHD, Pubertal Stage	HF did not decrease in accuracy towards the end of the task (incongruent trials; $\Delta M = 2.8\%$) LF decreased in accuracy at the end of the task (incongruent trials; $\Delta M = 12.1\%$)
Chaddock et al.	(2012)	32 (53%)	10.0 (± 0.6)	9-10	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70th percentile relative to norms	Inhibitory Control / Flanker task (CONG/COMP) MRT Accuracy	Age, IQ, SES, ADHD, Pubertal Stage	HF higher overall accuracy (across compatibility conditions) HF: 85% ; LF: 76.9% HF shorter MRT at 1 year follow-up HF: 494.3 ms; LF: 617 ms HF became faster LF became slower across compatibility conditions
Hillman et al.	(2005)	24 (49%)	9.6 (± 0.9)	NR	IL, USA	PACER test HF: top 10% LF: bottom 10%	Response Inhibition / Oddball task MRT; Accuracy (targets)	IQ, SES	HF faster than LF HF: 430.7ms LF: 509.1ms
Hillman et al.	(2009)	38 (47%)	9.4 (± 0.95)	8-11	IL, USA	PACER test HF: top 10% LF: bottom 10%	Inhibitory Control / Flanker task (CONG) MRT; Accuracy	Age, IQ, SES, ADHD, BMI	HF higher accuracy on both congruent and incongruent trials HF: 82.1% LF: 75.2%
Moore et al. (2013)	(2013)	93 (42%)	8.8 (± 0.6)	8-10	IL, USA	VO _{2max} indirect calorimetry	Inhibitory Control / Flanker task (CONG/COMP) MRT; Accuracy; SDRT	Age, IQ, SES ADHD, Pubertal Stage	HF and older age predicted shorter MRT on incompatible condition $\Delta R^2_{\text{cong}} = .06$ $\Delta R^2_{\text{incong}} = .14$
Pontifex et al.	(2011)	48 (48%)	10.1 (± 0.6)	NR	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70th percentile	Inhibitory Control / Flanker task (CONG/COMP) MRT; Accuracy	Age, IQ, SES ADHD, Pubertal Stage	HF group had higher accuracy on both compatibility conditions $\Delta M_{\text{comp}} = 5.8$; $\Delta M_{\text{incong}} 12\%$ HF group did not change in accuracy between compatibility conditions: $\Delta M = -0.1\%$ LF group significantly decreased in accuracy from compatible to incompatible condition: $\Delta M = 6.1\%$

Author	Year	n (% F)	Mean age (years)	Age range (years)	Country	CRF measure	Cognitive outcome / measure	Covariates	Results
Pontifex et al.	(2012)	52 (54%)	10.1 (± 0.6)	9-11	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70 th percentile	Inhibitory Control / Flanker task (CONG) MRT; Accuracy	Age, IQ, SES, ADHD, Pubertal Stage	HF group had higher accuracy across congruent and incongruent trials (combined score) HF: 83% LF: 75%
Scudder et al	(2014)	397 (57%)	7.6 (± 0.6)	6-9	IL, USA	PACER # of laps	<u>Inhibitory Control</u> / Flanker task (CONG/COMP) MRT Accuracy <u>Working Memory</u> / n-back task (0, 1 and 2-back): MRT; Accuracy; False alarms; d'	Age, Sex, Grade, SES, Race, BMI, BMI percentile	<u>Inhibitory control</u> HF associated with faster performance across congruency trials and compatibility conditions ΔR^2 s = .009 to .031 Larger effect for incongruent trials HF associated with greater accuracy on compatible condition for both congruent and incongruent trials ΔR^2 = .10 <u>Working memory:</u> HF associated with increased accuracy (targets and non-targets) HF associated with higher discrimination rate between signals and false alarms on more demanding task conditions (1 and 2-back) HF associated with lower false alarm rate on 1-back ΔR^2 s = .010 to .027
Voss et al.	(2011)	36 (53%)	9.85 (± 0.6)	9-10	IL, USA	VO _{2max} indirect calorimetry Low fit < 30th High fit >70th percentile relative to norms	Inhibitory Control / Flanker task (CONG) MRT; Accuracy; Interference Accuracy	Age, Sex, IQ, Pubertal Stage	LF group less accurate on incongruent trials ΔM = 8% LF group greater interference cost on accuracy HF: 2% LH: 5%

Note. F, female; VO_{2max} percentiles relative to norms published by Shvartz et al. (1990); All inhibitory tasks measured with a modified Eriksen flanker task (Eriksen & Eriksen, 1974); CONG, congruency effect; COMP, compatibility condition; MRT, mean reaction time; IQ, intellectual quotient assessed with standardised tests; SES, socio-economic status assessed with trichotomous index based on parental reports of: 1) child's participation in free or reduced price lunch programme at school, 2) the highest level of education obtained by mother and father, and 3) the number of parents who work full time, (Birnbbaum et al., 2002); In Scudder et al. (2014), SES was based on household income; ADHD, Attention Deficit and Hyperactivity Disorder, assessed with parental report on ADHD Rating Scale IV (DuPaul, Power, Anastopoulos, & Reid, 1998); Pubertal stage was assessed by parents with a questionnaire (Taylor et al., 2001) based on criteria described by Tanner (Tanner, 1962); d', ability to discriminate between targets and non-targets d' = (z(adjusted target accuracy) - z(adjusted false alarm rate).; HF, high fit; LF, low fit; n-back task of working memory included 3 conditions: (1) 0-back, required participants to respond with a right thumb when Tab appeared in the target position on the screen; (2) 1-back, participants pressed a right button when a cartoon cow character appeared in the same position as on the previous trial, (3) 2-back, same as 1-back but now comparison between the current position and that two trials back (Scudder, et al., 2014).

CRF is a poor surrogate for physical activity, and changes in CRF are not proportional to changes in children and adolescents' daily physical activity (Kristensen et al., 2010). Importantly, on average children rarely engage in sustained aerobic physical activity, which could lead to increases in CRF (Bailey, et al., 1995; Baquet, et al., 2007; Riddoch, et al., 2004; Troiano, et al., 2008).

Little is known about the associations between daily MVPA and cognitive control in young people. It is important to establish these relationships in order to inform the design of physical activity and/or chronic aerobic exercise interventions, which could benefit cognitive control. Specifically, such research can help answer the question whether interventions targeting changes in CRF (i.e. physical state) are necessary for cognitive benefits to accrue or whether interventions targeting increments in daily MVPA (e.g. over the course of the whole day) would suffice. Since evidence is most consistent for the associations between daily MVPA and multiple health outcomes in children and adolescents (Janssen & LeBlanc, 2010; PAGAC, 2008), the focus on MVPA volume in relation to cognition is warranted.

Modification to daily MVPA could be achieved through small increments throughout the day, which can be incorporated more easily into the daily routine of children than structured aerobic exercise. Such an approach can draw upon school environment to target increases in MVPA across a large part of the day, in the majority of children. For example, Institute of Medicine in the USA advocates small increments in MVPA by introducing daily active recess, daily high quality PE (i.e. with 50% of time is spent in MVPA), incorporating physical activity breaks into lessons, promoting active transport and after-school programmes (IOM, 2013). These increments could add up to 57 minutes spent in MVPA as opposed to current 15 minutes (Bassett, et al., 2013; IOM, 2013).

2.1.3.2 Daily MVPA volume and cognitive control in children and adolescents

The research into the associations between objectively measured daily MVPA and cognition in young people is scant and suffers from important methodological limitations. Table 2-3 presents the review of extant studies, identified through periodic searches of databases including PubMed, Web of Science and Scopus, discussions with colleagues, conference attendance and personal contact with researchers in the field. Objective measurement of daily MVPA is important, as the assessment of both physical activity behaviour (Janz, 2006; Mattocks, 2007) and cognitive control (van der Sluis, et al., 2007) suffer from large measurement errors, which can be reduced with objective monitoring of physical activity and

computerised testing of cognitive control. Second, judging from the effect sizes of the reviewed associations between CRF and cognitive control, the effect of daily MVPA on cognition is likely to be small. Thus, in order to establish any meaningful relationships, objective and sensitive measures of both constructs are needed. The results of the studies reviewed in table 2-3 are equivocal. For example, Booth and colleagues (2013) reported weak but positive associations between the proportion of time spent in daily MVPA, selective attention and task switching in 11 years old boys. For girls there was a marginal association for task switching. In contrast, neither Syväoja et al. (2014), nor van der Niet et al. (2014) found such associations for measures of task switching or inhibitory control, respectively. These discrepancies in findings can be attributed to differences in the definitions of MVPA, statistical power of the studies to detect the effect, and/or differences in characteristics of tasks used to assess cognitive constructs.

Table 2-3. Review of the studies into the associations of objectively assessed MVPA and cognitive function in children and adolescents

Author	Year	n (%F)	Mean age	Age range	Country	MVPA measure	Time spent in MVPA	Cognitive measure	Covariates	Results
Booth et al.	(2013)	4,755 (55.2 %)	11.7 (±0.23)	NR	England	% time in MVPA = (mins of mvpa/ mins of light + mins of moderate + mins of vigorous activity) *100/day ActiGraphActiGraph 7164 Cut point: 3,600 CPM 60 s epochs Non-wear: ≥ 10 min of 0 cpm	M: 8% F: 5%	Selective Attention, Sustained Attention, Task Switching / Paper and pencil TEA-Ch/ Standardised scores based on errors and accuracies adjusted for reaction time; Attentional Vigilance measured with 3 reaction time tasks: Simple, Choice and Vigilance Factors computed: Accuracy and RT	Age Wear time Birth weight Gestation Age of mother at delivery Mother's oily fish intake Maternal smoking during pregnancy BMI Z score Pubertal stage Maternal SES (Education and Occupation)	Boys ¹ % time in MVPA at 11 years predicted better performance on selective attention, and task switching at age 11 years, and higher accuracy on RT tasks at 13 yrs (β s = 0.09 - 0.12) Girls % MVPA at 11 yrs marginally predicted better performance on task switching β = .07, p = .05
Syv��oja et al.	(2014)	224 (56%)	12.2 (±0.6)	NR	Finland	MVPA min/day ActiGraph GT1M/GT3X Cut point: 2,296 CPM Epoch: 10s Non-wear: 30 minutes of 0 CPMs Self-reported MVPA #days in the last week physically active for at least 60 min	58 min/day (sex diff ns) Self-reported MVPA: 5 days/week (sex diff ns)	CANTAB: Visual memory (PRM) Working memory (SSP) Sustained attention (RVP A'), Mental flexibility (IED) 5-choice Reaction Time task (RTI; vigilance/impulsivity)	Gender SES (Parental Education) Special Educational Needs	MVPA was associated with shorter RT on 5-choice RT task
van der Niet	(2014)	80 (55%)	8.9 (±1.0)	8 – 12	The Netherlands	GT3X+ MVPA cut point: > 2240 CPM Epoch: 10 s Non-wear: 20 min of <10 CPM	M: 52 (±14) F: 37 (±14) min/day	Inhibitory Control / Visual Working Memory/Switching/Planning: Stroop Test/VMS/TMT/ToL Interference score/Accuracy/B-A RT/RT (decision, execution)	Gender Age SES Wear time	MVPA was associated with shorter reaction time on the planning task (r = -0.29)

Note. F, female; ¹Results based on fully adjusted models; TEA-Ch, Test of Everyday Attention for Children (Manly, et al., 1998); CANTAB: Cambridge Automated Neuropsychological Test Battery(CANTAB, 2014; Luciana, 2003); Tasks: PRM, Pattern Recognition Memory SSP, Spatial Span; IED, Intra-Extra Dimensional Set Shift; RTI, Reaction Time; RVP, Rapid Visual Information Processing; VMS, Visual Working Memory Span from Wechsler Memory Scale Revised (Wechsler, 1987);TMT, Trail Making Test (B-A; Reitan, 1958; Reynolds, 2002); ToL, Tower of London (Shallice, 1982); SES, socio-economic status.

First, the studies differed in how they defined accelerometer assessed MVPA thresholds. Booth et al. (2013) used the highest intensity cut point for MVPA (3,600 CPM; Cain, et al., 2013; Mattocks, et al., 2007), while both Syväoja et al. (2014) and van der Niet et al. (2014) used lower intensity cut points (~2,200CPM) and thus could have captured some of the light activity as well. However, van der Niet et al. (2014) observed the association between MVPA, based on a lower intensity threshold, and planning, which speaks against the intensity threshold argument. Second, the discrepant findings between the studies could also be attributed to differences in task characteristics. For example, Syväoja et al. (2014) used a computerised task of impulsivity (5-choice reaction time task), while van der Niet et al. (2014) employed a paper and pencil Stroop task. Further, although in both studies (Booth, Tomporowski, et al., 2013; van der Niet, et al., 2014) inhibitory control was measured with a variant of a classic Stroop task (which involves overcoming a prepotent response such as reading or naming), only Booth et al.'s (2013) study was powered enough to detect a small effect. A large sample size likely helped to overcome the problem of large variance attributable to both error and task impurity, which are inherent in the Stroop task (van der Sluis, et al., 2007). That is, a large proportion of variance in performance on this task can be attributed to factors other than inhibitory control, including 61% of variance explained simply by naming (van der Sluis, et al., 2007), which is an automatic process and does not require cognitive control.

Consonant with the executive function hypothesis (Colcombe & Kramer, 2003; Kramer, et al., 1999), it is possible that the associations between daily MVPA and cognition are specific to tasks, which require the up-regulation of cognitive control. In confirmation, van der Niet et al. (2014) noted a modest but significant association between response latency on the task of planning (measured with the Tower of London task; Shallice, 1982) and time spent in daily MVPA. The Tower of London is a cognitively more demanding task than Stroop, as it necessitates the consolidation of both inhibition and WM (Asato, et al., 2006). Therefore, sensitive tasks which up-regulate cognitive control requirements may be necessary to assess the associations between MVPA and cognitive control in children and adolescents.

Importantly, the reviewed studies suffer from several limitations, which preclude meaningful conclusions on the associations between daily MVPA and cognitive control in young people. First, none of the reviewed studies controlled for the confounding effects of CRF and IQ. Based on consistent relationships between CRF and cognitive control in children, at present it remains unclear whether the weak associations between MVPA and cognitive control in studies by

Booth et al. (2013) and van der Niet et al. (2014) could not have been explained by the effects of CRF.

Controlling for IQ is necessary for at least three reasons: first, cognitive control and intellectual capacity are interlinked, as developmental transitions in WM and general processing speed drive intellectual development (Demetriou et al., 2014). Specifically, a synthesis of evidence on these relationships across developmental spectrum (2-87 years) indicates that WM is strongly associated with fluid intelligence (standardised beta coefficients $\sim .70$; Demetriou, et al., 2014). Fluid intelligence reflects child's capacity to think logically, to solve problems in novel situations, which is independent of current knowledge (Cattell, 1987). Furthermore, adolescents' performance on less demanding task conditions, which place relatively little demands on cognitive control are also strongly related to general fluid intelligence ($r = .82$; Demetriou, et al., 2014). Second, meta-analytical findings on the effects of physical fitness (across multiple domains including strength and aerobic capacity) and PE programs on children and adolescents' intellectual capacity and academic achievement (taken as a proxy of cognitive function) indicated strongest effects of fitness and PE interventions on mathematics ($ES = .44$) and IQ ($ES = .39$). Third, child's general intelligence moderated these relationships such that the effect of both physical fitness and PE interventions on the indices of cognition (generally defined as intellectual capacity and academic achievement across multiple domains) were twice as strong for cognitively impaired compared to normally intellectually developing children (Fedewa & Ahn, 2011). These findings are congruent with cognitive reserve hypothesis, which advocates that the effects of CRF are more beneficial to individuals with compromised or limited cognitive reserve (Chodzko-Zajko & Moore, 1994). Children and adolescents have limited cognitive reserve as their cognitive control is still developing (Davidson, et al., 2006; Luna, et al., 2004). Last, child or adolescent's task performance is dependent upon multiple factors, including general intelligence. For example, the speed of performance during relatively simple task conditions (e.g. congruent condition of the flanker or reading condition on the Stroop task) is significantly and strongly related to fluid intelligence ($\beta = .65$ in children and $\sim .82$ in adolescents; Demetriou, et al., 2014). Therefore, individual variability in IQ might have occluded or confounded the reported associations between MVPA and cognitive control in the reviewed studies. Consequently, further evidence while controlling for the effects of these important confounders is needed.

Likewise, previous research assessed the relationship between objectively measured MVPA and cognitive function in a relatively homogeneous group of young adolescents (11-13 years

old; Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014), or collapsed the analyses across childhood and adolescence (8-12 years; van der Niet, et al., 2014). The majority of evidence on chronic aerobic exercise, CRF and cognition in young people pertains to preadolescent children, whose cognitive control functions undergo dynamic development (most substantial developmental gains in cognitive control occur before the age of 10 years; Davidson, et al., 2006; Rueda et al., 2004). Further, age has been identified as a potential moderator of the associations between physical fitness and cognition (albeit measured with academic achievement and tasks tapping intelligence as proxies) with strongest effects ($ES = .36$) observed for primary school children (Fedewa & Ahn, 2011). Positive effects of physical fitness were also noted for older adolescents ($ES = .28$). However, older adolescents are an understudied group in the literature on daily MVPA, aerobic exercise, CRF and cognitive function in general (Verburgh, et al., 2014).

To the author's knowledge, none of the studies on objectively measured physical activity and cognition evaluated these relationships in older adolescents (≥ 15 years). Older adolescents are less physically active than children (Jago, Anderson, Baranowski, & Watson, 2005; Nader, Bradley, Houts, McRitchie, & O'Brien, 2008; Riddoch, et al., 2004; Sallis, 2000). Therefore, in parallel to the dose-response curves of the effects of MVPA on other health outcomes (PAGAC, 2008), greater daily MVPA could be associated with better cognitive control also in this age group. Furthermore, adolescents still improve in the efficiency of cognitive performance, which can be observed on more cognitively demanding tasks such as Stop Signal task (Luna, et al., 2010; Williams, et al., 1999). The efficiency can be indexed by measures of performance variability (Moore, et al., 2013; Tamnes, Fjell, Westlye, Østby, & Walhovd, 2012; West, Murphy, Armilio, Craik, & Stuss, 2002; Williams, Hultsch, Strauss, Hunter, & Tannock, 2005; Wu et al., 2011), which was not considered by previous research into daily MVPA and cognition. Therefore, it is important to assess the relationships between daily MVPA and cognitive control in older adolescents to gain further insights into these associations across developmental spectrum.

None of the reviewed studies used computerised laboratory tasks, which reduce measurement error and minimise task impurity problem. Only one study employed computerised tasks of cognitive control. Syväoja et al. (2014) measured WM, task switching and impulsivity with the CANTAB battery, which included a pre-specified set of task parameters. Pre-defined task parameters may not be ideal for every sample. In confirmation, the authors observed that adolescents in their study attained high scores on multiple CANTAB tasks (Syväoja, et al.,

2014), suggesting that cognitive control may not have been adequately challenged in some adolescents. The CANTAB was originally developed to detect neurocognitive deficits, and may not be sensitive enough to differentiate healthy adolescents based on physical activity levels. Laboratory designed tasks allow flexibility of modulating inter-stimulus interval and stimulus exposure time to properly challenge cognitive control system according to developmental capacity of the studied population. For example, Eriksen flanker task is one of the most well researched experimental paradigms in developmental cognitive literature. It has been successfully applied across samples of different ages (Checa & Rueda, 2011; Ridderinkhof & van der Stelt, 2000; Ridderinkhof, Band, & Logan, 1999; Rueda, et al., 2004; Rueda, et al., 2005; Salthouse, 2010; Stins, van Baal, Polderman, Verhulst, & Boomsma, 2004; Stins, et al., 2007; van Leeuwen, et al., 2007), and proved sensitive to the differences in CRF among children (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, et al., 2009; Moore, et al., 2013; Scudder, et al., 2014; Voss, et al., 2011). Therefore, in order to limit measurement error and increase sensitivity, researchers should strive to use laboratory designed measures of cognitive control, which allow for adjustments in task parameters to suit the population under investigation.

Last, although all studies controlled for SES (low SES has been related to poorer neurocognitive outcomes; Farah et al., 2006; Hackman & Farah, 2009; Hackman, Farah, & Meaney, 2010; Mezzacappa, 2004; Noble, McCandliss, & Farah, 2007), only one study controlled for BMI (Booth, Tomporowski, et al., 2013), and none included information on symptoms related to attention-deficit hyperactivity disorder (ADHD). Past research suggests that relative to normal weight peers, overweight and obese children are disadvantaged on measures of cognitive function (e.g., WM; Kamijo, et al., 2012) and general cognitive ability as measured with block design and digit span from Wechsler Intelligence Scale for Children – Revised (Li, et al., 2008; Wechsler, 1974). Consequently, the associations between cognition and daily MVPA may be stronger in overweight and obese children, who start off with lower cognitive performance. Likewise, stronger associations between daily MVPA and cognitive control may be expected for children with ADHD symptoms, who have specific deficits in inhibitory control and response inhibition (Nigg, 1999; Nigg, 2000, 2001, 2005; Nigg, Blaskey, Huang-Pollock, & Rappley, 2002). Preliminary evidence suggests that 8 to 10 week physical activity interventions benefited cognitive performance in children with ADHD on several measures of inhibition assessed with ecological tasks (Smith et al., 2013), as well as selective and sustained attention (Verret, Guay, Berthiaume, Gardiner, & Béliveau, 2012). In conclusion,

it is important to account for variables, which can either confound (e.g., IQ, BMI, SES, ADHD) or mediate (e.g. CRF) the associations between daily MVPA and cognitive control in young people.

2.1.3.3 The effects of chronic aerobic exercise on cognitive control in children and adolescents

In contrast to the mixed findings from studies on daily MVPA, evidence on a causal relationship between regular aerobic exercise and children's cognitive control is more consistent albeit scant. Table 2-4 reviews available evidence from the RCTs inspecting the effects of daily after-school chronic aerobic exercise interventions and cognitive control in children. Only studies, which focused on the effects of chronic aerobic exercise on cognitive function in children and adolescents were included. One study, which specifically focused on increasing MVPA within school PE was excluded as the increase in MVPA during an hour of bi-weekly PE was deemed insufficient to increase CRF (i.e. children spent only 12 minutes in MVPA per hour of PE twice a week; (Fisher et al., 2011). Thus, this trial was not designed as chronic aerobic exercise intervention.

Table 2-4. Review of the randomised controlled trials on the effects of chronic aerobic exercise interventions on cognitive control on children

Author	Year	n (%F)	Mean age (pre-test) years	Age range (pre-test) years	Country	Inclusion criteria	Intervention name / duration	Attendance	Session frequency and duration	Measure of intervention intensity	Change in CRF assessed? / Intervention effect?	Cognitive measure	Covariates	Results
Chaddock-Heyman et al.	(2013)	INT: 14 (50%) CON: 9 (67%)	8.9 (± 0.7) 8.9 (± 0.4)	8-9	IL, USA	IQ >85/ ADHD < 85 PCTL/PUB STAGE ≤ 2 / NO ADVERSE HEALTH CONDITIONS/ RH/ NO MEDS; ACC > 50%	FITKids 9 months (150 days)	82% (± 13.3)	5 d/ week; 2 hours; 77 minutes in MVPA	HR ¹	Yes / No VO _{2max}	Inhibitory Control / Flanker task (CONG) MRT; Accuracy	IQ, SES, ADHD, Pubertal Stage, BMI	No INT effect on either accuracy or MRT; INT group increased in speed on incongruent trials
Davis et al.	(2007)	94(60%) HD: 32 LD: 33 CON: 29	9.2 (± 0.84)	7-11	GA, USA	OW/OB (≥ 85 th BMI PCTL)/ INACTIVE (< 1h/wk REG PA)/ NO MED COND (except ADHD)	~3 months (15 weeks)	85% (± 11.5)	5d/week; HD: 40 min MVPA LD: 20 min MVPA	HR Daily goal > 150 bpm; MHR = 166 (± 8.2) bpm	Yes / Yes Treadmill time	CAS scales: Planning; Attention; Simultaneous; and Successive; Standard scores	Sex, Race Cohort, Pre-test scores, Self-reported MVPA (last week)	INT effect on Planning only for HD group HD > CON (8% of variance explained) LD < HD (p = .05) LD did not differ from CON
Davis et al.	(2011)	171 (56%) HD: 56 LD: 55 CON: 60	9.3 (± 1.0)	7-11	GA, USA	OW/OB (≥ 85 th BMI PCTL)/INACTIVE (< 1h/wk REG PA)/ NO MED COND (except ADHD)	~3 months (13 $\pm$ 1.6 weeks)	85% (± 13)	5d/week; HD: 40 min MVPA LD: 20 min MVPA	HR Daily goal > 150 bpm; MHR = 166 (± 8) bpm	NR	CAS scales: Planning; Attention; Simultaneous; and Successive; Standard scores	Sex, Race, Cohort, Parental education	Dose-response effect on Planning indicated by linear contrast (graded effect)
Kamijo et al.	(2011)	36 INT: 20 (55%) CON: 16 (50%)	INT: 8.9 (± 0.5) CON: 9.1 (± 0.6)	7-11	IL, USA	NO NEURDISEASE/ PHYS DISABILITY/ NO RMALVISION/ PRE-PUBESC	9 months (150 days)	82.2% (± 8.2)	5d/week; 120 min; ~ 70 min in MVPA	HR	Yes / Yes VO _{2max}	Working Memory / Modified Sternberg task RT and Accuracy	Age, IQ, SES, BMI, ADHD, PUB STAGE	INT effect on overall ACC; Post-hoc: INT effect only for 3 letter condition

Author	Year	n (%F)	Mean age (pre-test) years	Age range (pre-test) years	Country	Inclusion criteria	Intervention name / duration	Attendance	Session frequency and duration	Measure of intervention intensity	Change in CRF assessed? / Intervention effect?	Cognitive measure	Covariates	Results
Krafft et al.	(2014)	22 INT:13 (77%) CON ³ : 9 (56%)	9.5 (±0.6) 9.6 (±0.9)	8-11	GA, USA	OW/OB (≥85th BMI PCTL)/ INACTIVE (< 1h/wk REG PA)/NO MED COND (except ADHD)	~8 months (135±9 days)	68% (±25)	5d/week; 40 min MVPA	HR Daily goal > 150 bpm; MHR = 164 (± 10) bpm	NR	CAS scales: Planning/Attention/Simultaneous/Successive; Standard scores	Age, Sex, Race, Parental Education	No INT effects observed
Hillman et al.	(2014)	221 INT: 109 (49%) CON: 112 (44%)	8.8 (CI: 8.7-8.9) 8.8 (CI: 8.7-8.9)	7-9	IL, USA	NO SEN/NO NEUR DISORDERS/NO PHYS DISABILITY	9 months (150 days)	80.6 (±15.1)	5d/w 70 min MVPA	HR MHR = 137 (±8.3)	Yes / Yes INT > CON (1.5 mL/kg/min d=0.39) VO _{2max}	Inhibitory Control / Flanker task MRT, Accuracy (CONG) Switching MRT, Accuracy (HOMO/HETERO)	Age, Sex, Race, SES, VO _{2max} , IQ, Pubertal Stage	Both groups increased in overall ACC and for each condition on inhibitory control task; but INT group increased more in overall ACC than CON (3.2%, d=.27); this effect was driven by change in less cognitively demanding condition; On switch task both groups increased in accuracy on both conditions, but INT had greater increase on HETERO condition (4.8%; d=.35), indicating greater cognitive flexibility

Note. INT, intervention group; CON, control group; HD, high dose; LD, low dose; IQ, intelligence quotient assessed with standardised tests; ADHD, attention deficit and hyperactivity disorder, assessed with parental report on ADHD Rating Scale IV (DuPaul, et al., 1998); PCTL, percentile; PUB STAGE, pubertal stage assessed by parents with a questionnaire (Taylor, et al., 2001) based on criteria described by Tanner (Tanner, 1962); RH, right handed; MEDS, medications; ACC, accuracy; OW/OB, overweight/obese; PA, physical activity; REG, regular; wk, week; NEUR, neurological; PHYS, physical; PRE-PUBESC, prepubescent; SEN, Special Educational Needs; CAS, Cognitive Assessment System, a standardised battery of computerised tests comprising of (1) Planning scale, which requires strategy generation, use of knowledge and self-regulation; (2) Attention scale measures interference, selective attention and switching; (3) Simultaneous subscale tests ability to perceive relations among the stimuli; (4) Successive subscale tests ability to reproduce sequences and understand relationships (Naglieri & Das, 1997); Modified Sternberg task (Sternberg, 1966) requires memorising 1, 3 and 5 letter sets and recognising whether subsequent probe letter was previously presented within the letter set; Switch task required participants to react to a character shape based on either colour (blue or green) or shape (circle or square); in HOMOGENOUS condition only one rule was present (either colour or shape); under HETEROGENOUS condition, the rule changed and was signalled by character's hands, up for shape and down for colour (Hillman, et al., 2014); HR, heart rate; MVPA, moderate-to-vigorous physical activity; ¹Mean HR values were included if reported; ² Self-reported moderate and vigorous physical activity over the past week assessed with 2 questions from the 2001 Youth Risk Behavior Survey (CDC., 2001), i.e. "at least 30 min that did not make you sweat or breathe hard", and "at least 20 min that made you sweat or breathe hard", respectively;

³Sedentary Attention Control condition, involved instructor led sedentary activities e.g., art and board games, in all other studies the control group was a waitlist or no-exercise control.

In aggregate, the results of these studies suggest that chronic aerobic exercise interventions of at least three and up to nine months duration, which included at least 20 minutes of aerobic exercise, benefited cognitive control. The effects were noted across the domains of cognitive control: inhibition (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014), WM (Kamijo, et al., 2011) and task switching (Hillman, et al., 2014). All available studies focused on preadolescent children. In alignment with findings on CRF and cognition, the effects of chronic aerobic exercise interventions are both general (i.e. evident across task conditions which do and do not engage cognitive control) and specific to those task conditions which up-regulate cognitive control. For example, Hillman et al. (2014) observed an effect of a nine-month after-school physical activity intervention (FITKids), where at least 70 minutes were dedicated to MVPA, on inhibitory control and task switching. In contrast, Davis et al. (2007; 2011) found specific effects of a three-month after-school physical activity intervention, where children engaged in either 20 or 40 minutes of MVPA, on planning, which requires integration of multiple cognitive control functions (inhibitory control and WM). One study reported null findings (Krafft, et al., 2014), but was underpowered and therefore its results should be interpreted with caution.

However, the evidence base is scant as only six studies could be identified, half of which were based on samples of overweight and obese children (Davis, et al., 2007; Davis, et al., 2011; Krafft, et al., 2014). Therefore, their results cannot be easily generalised, as overweight and obese children may have had a stronger response to an aerobic exercise intervention. In addition, two studies were underpowered (Chaddock-Heyman, et al., 2013; Krafft, et al., 2014). Several limitations of these studies need to be noted. First, based on their results it remains unclear whether increments in CRF are necessary for cognitive benefits to emerge. Only four studies analysed and reported the results on the change in CRF (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Hillman, et al., 2014; Kamijo, et al., 2011). Three of these studies reported intervention related increments in CRF (Davis, et al., 2007; Hillman, et al., 2014; Kamijo, et al., 2011) but Chaddock et al. (2013) did not. In addition, a meta-regression, which included a formal test of the dose-response relationship between gains in CRF and its effects on the change in cognitive function in children, yielded null results (Etnier, 2006). Therefore, it is plausible that factors other than CRF could contribute to the observed effects of chronic aerobic exercise on cognitive function (Hötting & Röder, 2013; Tomporowski, Davis, Miller, & Naglieri, 2008). One such factor may be a baseline level of MVPA and sedentary behaviour. Based on the dose-response curves of the effects of MVPA on multiple health outcomes

(PAGAC, 2008), it can be expected that physically inactive children would gain greater cognitive benefits from such interventions. Likewise, highly sedentary children underperform academically (Tremblay, et al., 2011) and could benefit to a greater extent from aerobic exercise. However, none of the RCTs objectively assessed children's baseline levels of MVPA or sedentary behaviour. Davis et al. (2007) attempted to control for physical activity but used self-reports. Physical activity was assessed with two questions from Youth Health Behavior Survey (2001) and expressed as the number of days over the past week that a child participated in MVPA. However, children included in the study by Davis et al. (2007) were relatively young (age range 7-11 years). Self-report was unlikely to provide a valid representation of their physical activity due to the lack of understanding of some physical activity concepts (Kohl, et al., 2000; Trost, 2000). In confirmation, questions from Youth Health Behavior Survey were only validated in youth older than 12 years (Booth, Okely, Chey, & Bauman, 2001). Thus, Davis et al. (2007) could not adequately control for children's baseline levels of MVPA and did not control for time sedentary.

Last, it is important to ascertain whether the effects of chronic aerobic exercise interventions generalise across cognitive control domains, as could be expected based on the unity of cognitive control (Miyake & Friedman, 2012; Miyake, et al., 2000). Only one study inspected the effects of chronic aerobic exercise intervention on multiple indices of cognitive control, namely inhibition and task switching (Hillman, et al., 2014). Interestingly, in relation to inhibitory control these authors observed the effect of the intervention on a task condition, which did not engage inhibitory control. In contrast, a specific effect of the intervention was observed on task switching (heterogeneous condition), which required the up-regulation of cognitive control. Since both inhibitory control and WM are involved in performance on task switching (Davidson, et al., 2006), it is unclear whether these results were due to intervention effects on inhibitory control or WM. This is an interesting question, as WM has been an understudied construct in physical activity and cognition literature in general. Only one study inspected the effects of chronic aerobic exercise intervention on WM in children (Kamijo, et al., 2011), but their results are inconclusive due to the limitations of the task. Specifically, a modified Sternberg task used by Kamijo et al. (2011) has been criticised as a measure of WM, as the task has been argued to place relatively small demands on cognitive control (Conway, et al., 2005; Klein, et al., 2010). That is, successful performance on this task can be due to recognition and rehearsal of the letter sets and therefore may not engage cognitive control. Given that WM is an important predictor of child's academic achievement (Alloway &

Alloway, 2010), inspecting these associations using sensitive measures of WM is valuable from a public health and educational perspective.

2.1.4 Overview of the thesis

This thesis aimed to investigate whether objectively measured daily MVPA was associated with cognitive control or whether chronic aerobic exercise was needed to benefit cognition in young people. First, studies 1 and 2 assessed cross-sectional associations between objectively measured MVPA and cognitive control in two distinct age groups: older adolescents and preadolescent children. Second, study 3 evaluated the effects of a nine-month after-school chronic aerobic exercise intervention (Fitness Improves Thinking 2, FITKids2) specifically designed to improve CRF, on cognitive control in preadolescent children, after controlling for baseline levels of daily MVPA and time sedentary. These studies make a novel contribution to the field because they: 1) inspected the associations between objectively measured daily MVPA and cognitive control in previously not researched populations (studies 1 and 2); 2) were able to answer the question whether the relationship between daily MVPA and cognitive control was independent of CRF and variability in child's intellectual ability and other confounders (studies 1 and 2), which previous studies did not address; 3) used computerised laboratory tasks, which proved sensitive to age (Stop Signal task (Williams, et al., 1999), modified Eriksen flanker task (Checa & Rueda, 2011; Ridderinkhof & van der Stelt, 2000; Ridderinkhof, et al., 1999; Rueda, et al., 2004; Rueda, et al., 2005; Salthouse, 2010; Stins, et al., 2004; Stins, et al., 2007; van Leeuwen, et al., 2007)), and CRF-related inter-individual differences (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, et al., 2009; Moore, et al., 2013; Scudder, et al., 2014; Voss, et al., 2011); 4) addressed previously not considered cognitive indices (response variability, study 1) and an under-explored aspect of cognitive control, WM (studies 2 and 3); 5) placed the associations between daily MVPA and cognitive control in the context of applied forms of cognition (academic achievement; study 2) using standardised tests; 6) investigated the effects of a chronic aerobic exercise intervention on the change in CRF (study 3), and 7) also controlled for the baseline levels of daily MVPA and time sedentary (study 3), which previous studies did not.

2.1.5 Thesis aims

Aim 1a: To evaluate whether objectively measured daily MVPA uniquely contributes to cognitive performance in 15 years old adolescents from a British birth cohort, using measures

of attentional control, cognitive processing speed and variability, while also statistically controlling for CRF, IQ and other important confounders (e.g. objectively measured adiposity, SES, ADHD).

Aim 1b: To evaluate the associations between objectively measured daily MVPA and multiple indices of cognitive control (inhibitory control and WM), applied forms of cognition (academic achievement in reading, mathematics, and spelling) in preadolescents, while statistically controlling for CRF, IQ and other important confounders (BMI, ADHD, SES, pubertal stage).

Aim 2: To evaluate the effects of a nine-month randomised controlled physical activity trial FITKids2 designed to increase CRF, on multiple aspects of cognitive control (inhibitory control and WM) in preadolescent children, while controlling for objectively measured baseline MVPA and time sedentary.

Chapter 3

Methods

3.1 Accelerometry data reduction in the Avon Longitudinal Study of Parents and Children (ALSPAC; study 1)

Pre-collected raw .DAT accelerometer data files were requested and made available by the ALSPAC for the purpose of study 1. ActiGraph accelerometers (GT1M, ActiGraph LLC, Fort Walton Beach, FL, USA) were initialised to start recording at 5 AM on the day following child's visit to the ALSPAC research clinic. Data were collected in 60 seconds epochs. Raw ActiGraph data files were re-processed in 2012 to derive outcome variables using a custom made data reduction software (KineSoft, ver 3.3.67, Loughborough, UK; <http://www.kinesoft.org>). Figure 3-1 presents a data reduction flowchart with the number of files processed and retained for further analyses. Files were first screened for duplicates. Second, files were flagged as spurious, if they were deemed corrupt due to technical faults defined based on a plateau of 3 consecutive counts at the same number at a count of ≥ 10 were excluded (with plateaus occurring most often at 32,767 counts). Flagged .DAT files were subsequently graphed to verify their viability for further analyses. Further, files were scanned for overnight wear. Overall out of 3,006 available files, after exclusion of duplicates ($n = 97$), missing data ($n = 1,024$), spurious files ($n = 20$), files with less than 4 days of wear ($n = 306$), 1,598 files were available for further analyses. The final sample for study 1 included 667 files based on further exclusion criteria specific to study objectives. Data reduction for accelerometer files followed the same procedures across studies 1, 2 and 3.

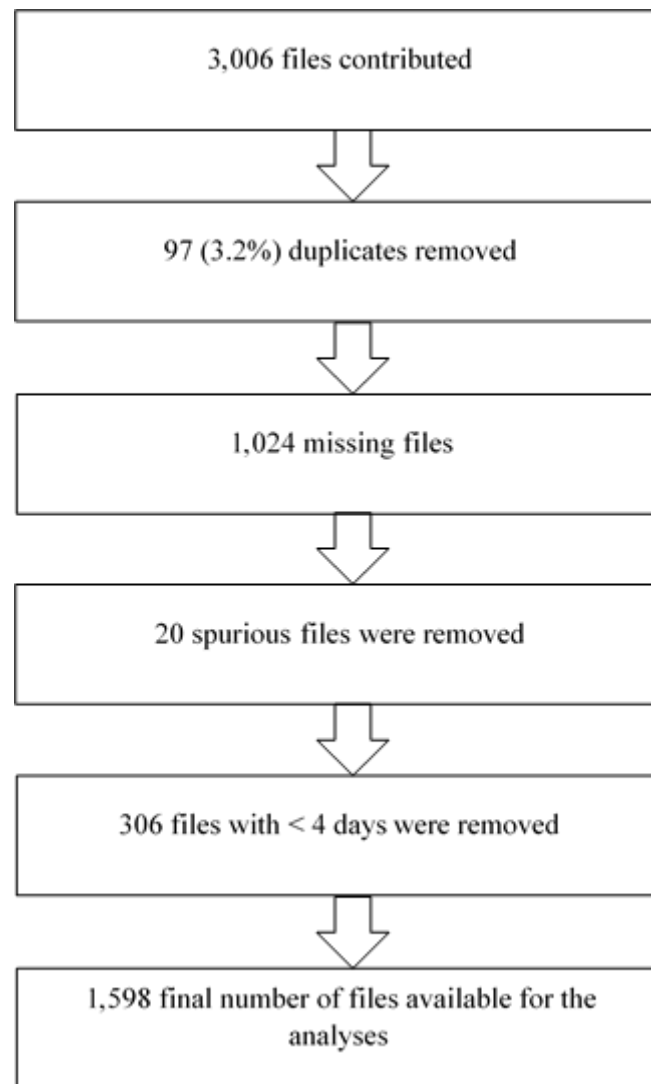


Figure 3-1. A flow diagram of accelerometer data reduction in study 1.¹

¹Final sample was reduced to account for study inclusion criteria.

3.2 Accelerometry data reduction in cross-sectional and intervention studies (studies 2 and 3)

ActiGraph accelerometers (wGT3X+, ActiGraph, Pensacola, FL, USA) were deployed to children in the presence of parents at one of the testing visits to the Neurocognitive Kinesiology Laboratory during summer of 2013 (studies 2 and 3) and 2014 (study 2). Devices were initialised to start recording at midnight on the night following child's visit to the laboratory. The return of the device was scheduled for the following visit to the laboratory or a drop off was arranged with a parent. Raw .gt3x data files were integrated into 15 s epochs using ActiLife software (versions 6.7.1 to 6.10.0 and a firmware version 2.2.1; ActiGraph, Pensacola, FL, USA). Epoched data files were subsequently processed to derive outcome variables using a custom made data reduction software (KineSoft, version 3.3.76, Loughborough, UK; <http://www.kinesoft.org>). Figures 3-2 and 3-3 present data reduction flowcharts with the number of files processed and retained for further analyses in studies 2 and 3, respectively. Files were first screened for duplicates, and spurious files were flagged (the same definition of a spurious file was adopted as in study 1). Duplicates resulted from re-deployment of the device due to either child misplacing the device ($n = 1$, study 2) or non-compliance (study 2: $n = 4$, study 3: $n = 2$). The data files with more valid days of wear were included in the analyses.

In study 2, out of 108 available files, after exclusion of duplicates ($n = 5$) and files with less than 10 hours of wear ($n = 2$), 101 files were available for further analyses. No missing data or spurious files were identified. The final sample for study 2 included 81 files based on further exclusion criteria specific to study objectives.

In study 3, out of 41 available files, after exclusion of duplicates ($n = 2$) and files with less than 10 hours of wear ($n = 2$), 39 files were available for further analyses. No missing data or spurious files were identified. The final sample for study 3 included 32 files based on further exclusion criteria specific to study objectives.

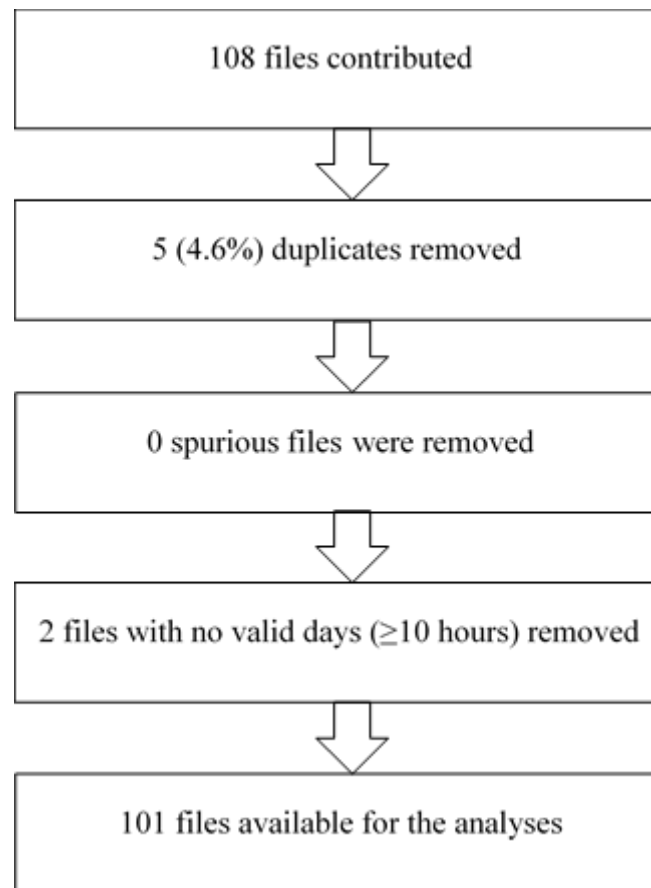


Figure 3-2. A flow diagram of accelerometer data reduction in study 2 on daily MVPA and cognitive control.²

²Final sample was further reduced to account for study inclusion criteria.

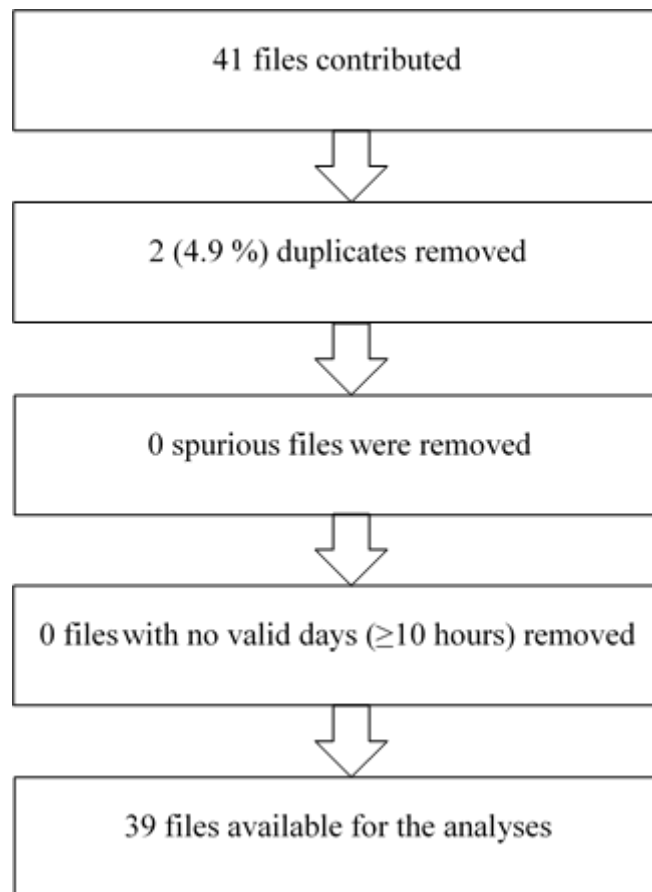


Figure 3-3. A flow diagram of accelerometer data reduction in study 3 on the effects of FITKids2 intervention on cognitive control.³

³Final sample was further reduced to account for study inclusion criteria.

3.3 Cognitive data reduction in the Avon Longitudinal Study of Parents and Children (study 1)

Raw excel cognitive data files were requested from ALSPAC for re-processing to meet the aims of study 1. Stop Signal excel data files included trial by trial accuracy and reaction times for two task conditions: a go condition (30 trials) and stop signal condition (96 trials, including 32 stop signals) for each individual participant. An example of a raw cognitive data file is presented in appendix G. Raw Stop Signal task data for each participant were re-processed in 2013 using a custom written visual basics for applications (VBA) code by the author. Data were screened for computer errors and marked as spurious if they contained responses marked as correct when they were not, or when no reaction time (RT) or no response was recorded. To derive mean RT and standard deviation of the mean RT during go condition and stop signal conditions, reaction times to correct trials were used. RTs < 200 ms were discarded. Further, incomplete data files were discarded. Figure 3-4 presents a cognitive data reduction flow diagram. Out of 5,515 adolescents who visited ALSPAC research clinics at 15.5 years, 5,364 started the Stop Signal task and 5,255 completed the task. After excluding missing ($n = 9$) and spurious files ($n = 7$), 5,239 files were available for the analyses. The final sample for the study was reduced based on the exclusion criteria to meet study objectives.

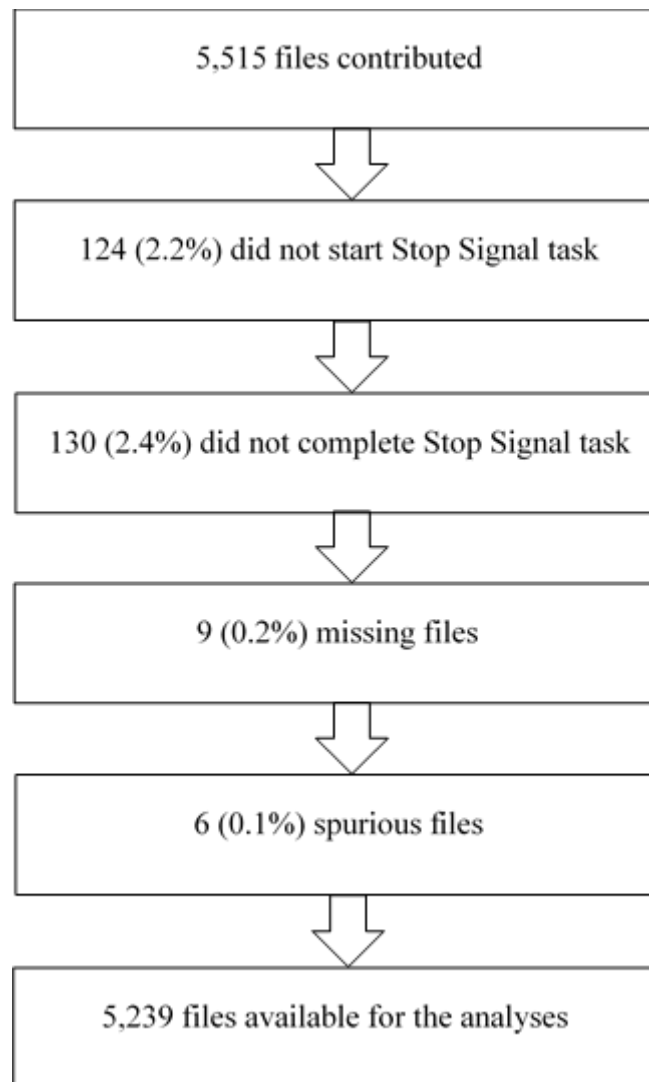


Figure 3-4. A flow diagram of Stop Signal data reduction in the Avon Longitudinal Study of Parents and Children (ALSPAC).⁴

⁴ The final sample size was based on further exclusion criteria relevant to study objectives.

3.4 FITKids2 intervention

3.4.1 Purpose

FITKids2 RCT is the second phase of the FITKids trial (trial identifier NCT01334359) previously described by Hillman et al. (2014). The trial was designed as a nine-month after-school physical activity intervention with the primary goal to increase children's CRF through the engagement in developmentally appropriate and fun physical activities. As such, FITKids2 is a chronic aerobic exercise intervention. A secondary aim of the FITKids2 was to increase motor skills (e.g., dribbling a basketball) and to promote social responsibility (e.g. fair play, cooperation) within a physical activity setting (Hillman, et al., 2014; Khan et al., 2014). FITKids2 includes several methodological modifications to an earlier fully completed FITKids trial (Hillman, et al., 2014). For example, the inclusion of a task specifically measuring WM, new neuroimaging techniques (e.g. magnetic resonance imaging, eye tracking) and inclusion of objective measures of physical activity.

3.4.2 FITKids2 background

FITKids2 was offered daily, after-school for two hours. The sessions were structured to include 70 minutes of MVPA. The trial was based on the Coordinated Approach to Child Health (CATCH) and adopted to meet Illinois Learning Standards for Physical Development and Health (<http://www.isbe.net/ils/pdh/standards.htm>). Examples of Illinois Learning Standards and how FITKids2 was designed to meet them are presented in appendix BB. CATCH was first developed in 1987 and implemented in 9,000 communities across the USA since. CATCH was used as the basis for FITKids2 due to its efficacy in increasing children's physical activity (Luepker, Perry, McKinlay, & et al., 1996), reducing overweight (Coleman, Tiller, Sanchez, & et al., 2005; Hoelscher et al., 2010), and sustainability (Nader, Stone, Lytle, & et al., 1999). The main aim of the FITKids2 to increase children's CRF was achieved through the engagement in 70 minutes of MVPA in the form of integrated fitness activities (e.g. through activity stations focused on development of CRF) and organisational games (e.g. Fitness Scavenger Hunt combined timed search for colours underneath the cones and running; See You Later Alligator included elements of tag with activities such as jumping rope and skipping).

3.4.3 Daily physical activity sessions (120 minutes)

Daily lessons took place at the University of Illinois at Urbana-Champaign premises. Children were offered free transport from the school to the intervention venue. Daily lessons were carefully structured and included instant activities, snack/educational component, and game

play. That is, immediately upon arrival to the centre children were engaged in instant activities or activities with a partner focused on specific health component (e.g. CRF, endurance). A brief educational component focused on specific health-related theme (e.g. cardio-respiratory fitness, exercise, nutrition). Water break and a healthy snack were also included (please see appendix AA for the outline of daily physical activity session). Instant activities were predominantly aerobic in nature or offered opportunities to refine motor skills (e.g. throwing, catching). Children were also encouraged to continue engagement in physical activity on the weekends with their parents and siblings (Hillman, et al., 2014).

3.4.4 Instant activities (approximately 30 minutes)

Educational materials from CATCH-K5 curriculum (Flaghouse, Inc., Hasbrouck Heights, NJ) were utilised to provide age-appropriate physical activities as soon as children arrived on the site (Hillman, et al., 2014). Four to six activity cards were used daily, which focused on aerobic, muscular strength and endurance activities, and development of movement skills such as rhythm or cooperative games. Activities were organised in work stations, where children worked with a partner or within a group. Upon completion, children immediately moved on to the next station. Once children were familiar with how to correctly perform instant activities, further sessions focused on achieving personal goals such as specific number of repetitions and maintaining heart rate within a target heart rate zone. The target heart rate zone was defined as 55-80% of child's maximum heart rate in accordance with ACSM recommendations (Whaley, Brubaker, Otto, & Armstrong, 2006).

3.4.5 Activities in an Instant

Brief activities such as jumping jacks, agilities, specifically designed to increase children's heart rate were used either as a form of an active break or to get children moving following an educational component and a water break (Hillman, et al., 2014).

3.4.6 Educational component (15 minutes)

Educational component included weekly themes focused on CRF, benefits of physical activity and healthy nutrition. A brief educational instruction followed by activity were used to increase children's awareness of health behaviour and nutrition. For example, an instruction would be to "eat five fruits and vegetables a day" and a worksheet would ask a child to identify five fruits and vegetables (Hillman, et al., 2014). A snack and a water break were also included.

3.4.7 Intensity of physical activity

All children wore a E600 Polar heart rate monitors (Polar Electro, Finland, and Accusplit Eagle 170 pedometers, San Jose, CA) during physical activity sessions and were instructed to maintain their heart rate within a target heart rate zone (THZ). Children spent 92.5% of the time either in or above the THZ. A monitor watch with a visual representation of the target heart rate zone helped children learn to self-regulate his/her level of physical activity during the session (Hillman, et al., 2014).

3.4.8 Staff and staff training

The staff of FITKids intervention consisted of physical activity leaders who were certified physical education teachers, and college students majoring in Kinesiology who assisted with the sessions. The staff leaders attended one-day CATCH training session annually, which focused on interactive teaching strategies including the use of instant activities, and how to create cooperative, enjoyable, positive and minimally competitive environment. Staff were also taught how to use effective strategies to manage the group, focus children on the task and keep the pace during physical activity sessions (Hillman, et al., 2014). An example of staff training strategies is included in appendix CC.

Chapter 4

The relationship of moderate-to-vigorous physical activity to cognitive processing in adolescents: Findings from the ALSPAC birth cohort

4.1 Study 1 context

At the conception of this thesis, to the author's knowledge no published data on the relationships between objectively measured MVPA and cognitive function in children and adolescents were available. Establishing such relationship between daily physical activity and a new health outcome (cognitive function) was important from public health perspective and the potential to influence public health and educational policy. This is because higher order cognitive functions (cognitive control) are consistently and moderately associated with academic achievement (Jacob & Parkinson, 2015). To establish whether the link between daily MVPA and cognitive control existed, quality correlational evidence, based on a large sample was needed. A number of influences define child and adolescent's cognitive control outcomes, which include genetic make-up, general intellectual ability, behavioural and neurocognitive characteristics (such as presence of symptoms associated with attention-deficit hyperactivity disorder (ADHD) and history of neurological disease), socio-economic background, and especially relevant to this thesis, aerobic capacity as a well as adiposity. The collection of such varied and sensitive data requires an inter-disciplinary effort as well as substantial time and resource commitment, which likely explains the lack of control for many important confounders (e.g., intelligence quotient, cardio-respiratory fitness, history of neurological symptoms) in emergent research literature (e.g., Syväoja et al., 2014; van Dijk et al., 2014; van der Niet et al., 2014). Nonetheless, such quality evidence is necessary if the field is to move forward, and the relationship between daily MVPA and cognitive control in young people is to be ascertained.

The author identified (July 2012) a unique resource, which could provide such quality evidence to answer this research question in a large sample of British adolescents. The data collected within the Avon Longitudinal Study of Parents and Children (ALSPAC; Boyd et al., 2013; Mahmood et al., 2013) included objectively measured physical activity (accelerometry), the data from a computerised cognitive Stop Signal task. Importantly, the information on multiple important confounders of this relationship was also available, based on standardised and/or validated methods (for example, Wechsler Abbreviated Scale of Intelligence (WASI; Oldfield, 1971), sub-maximal cycle ergometer exercise test, clinical assessment of ADHD, objective measurement of adiposity).

The pre-collected data offered author a resource to work on rather than a finalised, "custom-made" data set. The work presented herein is based on author's re-analyses of the raw cognitive

and accelerometry data, which involved the writing and the design of a custom-made code (visual basic for applications) to pull a set of cognitive variables for more than 5,000 ALSPAC participants. Such data treatment allowed for analytical decisions with respect to the definitions of variables, greater flexibility in the exploratory analyses and quality control. This information was instrumental in gaining a deeper understanding of the cognitive performance of the sample. Likewise, given the lack of consensus on the standard data reduction protocol in accelerometry, the re-analyses of raw accelerometry data using a custom-made software (KineSoft, ver 3.3.67, Loughborough, UK; <http://www.kinesoft.org>) allowed the author to compare physical activity sample characteristics based on different non-wear criteria (e.g. 20 minutes of consecutive zero counts versus 60 minutes of consecutive zero counts allowing for two minute interruptions), and intensity cut-points. Such comparison is essential if informed analytical decisions are to be made and ensured the thorough knowledge of the data. Further input into the data reduction, included the computation of a CRF indicator (PWC-170; following the consultation with experts in the field⁵), maternal education and the integration of information on the history of epilepsy and meningitis across multiple time points.

⁵ The author would like to thank Professor Ashley Cooper and Dr Justin Bland for their assistance with the syntax.

4.2 Introduction

The adverse physical health consequences of physical inactivity in youth are well understood (Gutin & Owens, 2011; Hallal, Victora, Azevedo, & Wells, 2006; Iannotti, Kogan, Janssen, & Boyce, 2009). However, the relations of daily (i.e. accumulated throughout the entire day) physical activity to cognitive functions in youth are less well understood. Thus far, the majority of research has focused on cardio-respiratory fitness (CRF) as a proxy for regular physical activity. The results of these studies indicate that relative to lower fit children, higher fit children modulate attention more efficiently in relation to task demands (Pontifex, et al., 2011); demonstrate greater inhibitory control over prepotent responses (Chaddock, Hillman, et al., 2012); and are less affected by task difficulty and conditional manipulations (Voss, et al., 2011). That is, higher fit children demonstrate greater performance on tasks requiring cognitive control, particularly for tasks that modulate attentional demands. Cognitive control (also known as executive control or executive function) refers to higher order computational processes underlying perception, memory and action, which serve to regulate and optimise goal directed behaviours (Botvinick, et al., 2001; Meyer & Kieras, 1997; Norman & Shallice, 1986). Its core processes include: planning and mental flexibility, working memory and inhibition/interference control (Braver, et al., 2009; Luna, et al., 2004; Miller & Cohen, 2001). Cognitive control functions have been identified as an important target for early intervention (Diamond & Lee, 2011) due to their positive associations with children's academic achievement (Best, et al., 2011; Monette, et al., 2011; St Clair-Thompson & Gathercole, 2006), as well as their ability to predict future health, socio-economic status, and income (Moffitt, et al., 2011). Therefore, research demonstrating the benefit of CRF for cognitive development suggests that higher CRF may prime children and adolescents' chances for life success in a variety of domains. Although these studies have helped elucidate the benefits of CRF on neurocognitive development, a child's CRF is in large part genetically determined (Bouchard, et al., 2011), and only moderately related to objectively measured daily physical activity ($0.15 \leq rs \leq 0.47$ across studies; Dencker & Andersen, 2011). Consequently, the relation of daily physical activity to children's (and adolescents') neurocognitive development remains less clear.

A better understanding of the relation between physical activity and cognitive development can be gained from intervention studies, which test the influence of regular aerobic exercise on children's cognitive function (Chaddock-Heyman, et al., 2013; Davis & Cooper, 2011; Davis, et al., 2007; Hillman, et al., 2014; Kamijo, et al., 2011). While only a few randomised

controlled trials have been conducted, the results are encouraging, demonstrating that involvement in daily aerobic exercise ranging from three to nine months can lead to significant improvements in children's cognitive function. Specifically, improvements on tasks requiring planning (Davis, et al., 2007; Davis, et al., 2011), working memory (Kamijo, et al., 2011), inhibition/interference control (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014) and task switching (Hillman, et al., 2014) have been observed. Thus, similar to cross-sectional analyses of CRF, physical activity interventions of moderate-to-vigorous intensity also appear to benefit cognitive control functions during development. Preliminary evidence further suggests a dose-response relation, with greater exercise durations leading to greater improvements on planning, which requires the integration of working memory and inhibitory control (Davis, et al., 2011).

Intervening across the whole day to increase overall time in moderate-to-vigorous physical activity (MVPA) may initially be a more realistic public health goal than implementing aerobic exercise interventions, which are not easily incorporated into the school day. The need for such an approach has recently been voiced in the United States, where integrating MVPA across the whole school day (including active transport, active breaks, recess and increases in high quality PE) is advocated (IOM, 2013). Its rationale stems from evidence that small increases in objectively measured MVPA during recess, the introduction of active breaks into curriculum, and mandatory PE can add up to 47 minutes of daily MVPA (Bassett, et al., 2013). Thus, bringing the majority of children closer to the recommended daily 60 minutes of MVPA (Department of Health, 2011; U.S. Department of Health and Human Services, 2008). As such, studies assessing the relation between daily accumulation of MVPA and cognition in developing populations are warranted. To the author's knowledge, no studies assessed the relation of daily MVPA, while statistically controlling for CRF (Booth et al., 2013; Syväoja et al., 2014; van der Niet et al., 2014). This is an important limitation as CRF is weakly to moderately associated with daily MVPA in adolescents (Dencker & Andersen, 2011) and has been consistently related to cognitive control in children (e.g., Chaddock et al., 2010; Hillman et al. 2009; Moore et al., 2013; Pontifex et al., 2011, 2012; Scudder et al., 2014). Extant studies into objectively measured MVPA and cognition in young people are sparse (Booth et al., 2013; Syväoja et al., 2014; van der Niet et al., 2014; Van Dijk, De Groot, Van Acker, et al., 2014), report mixed findings and at best weak associations (e.g. $\beta = .07$ to $.12$; Booth et al., 2013). Therefore, it remains unclear in children and adolescents, whether the associations between daily MVPA and cognition exist once inter-individual differences in CRF are statistically controlled for.

Thus far, most studies examining CRF and cognition have used measures of central tendency (i.e., mean reaction time (RT) and accuracy) as indicators of cognitive performance. However, fluctuations in cognitive performance as indexed by the standard deviation of reaction time (SDRT) may provide a useful complementary measure of cognitive stability, as increases in task difficulty have been associated with increased performance variability across the lifespan (Walhovd et al., 2011; West, et al., 2002). Although only two studies have assessed response variability in relation to CRF, the results of both studies suggest that more aerobically fit children not only respond more accurately, but also more consistently during conditions requiring the up-regulation of cognitive control (Moore, et al., 2013; Wu, et al., 2011). To date, there are no studies evaluating response variability as a function of daily MVPA in developing populations. Accordingly, the study also sought to inspect the association between accelerometer assessed daily MVPA and response variability using a task that taps cognitive control.

Attentional control was assessed using a Stop Signal task, which consists of two conditions that vary the degree to which they engage cognitive control (Logan, et al., 1984; Verbruggen & Logan, 2008). Based on previous research demonstrating a positive relation between regular aerobic exercise and cognitive performance during more cognitively demanding conditions, we hypothesised that adolescents who engage in greater daily MVPA would show better performance (expressed as shorter and less variable reaction times) for the stop signal condition, which requires the up-regulation of attention and cognitive control. It was further hypothesised that daily MVPA would be positively related to attentional control, after inter-individual differences in CRF are statistically controlled for.

4.3 Methods

4.3.1 ALSPAC study population

ALSPAC is a prospective birth cohort study of parents and children from the Bristol area of the UK (Boyd et al., 2013). A detailed description of the study together with information on attrition and study compliance is available elsewhere (Mahmood et al., 2013). Briefly, all pregnant women from the former County of Avon in the UK (South West region) whose expected delivery date fell between 1st of April 1991 and 31st of December 1992 were eligible and enrolled in the study. The total ALSPAC sample comprised of 15,458 fetuses, 14,775 were live births and 14,701 were alive at 1 year of age. Data were routinely collected with questionnaires and ten percent of children were also invited to attend research clinics

(“Children in Focus”), where more in depth physical and psychological assessments were performed. The current study is based on a subsample of adolescents attending research clinics at age 15 years. Please note that the study website contains details of all the data that is available through a fully searchable data dictionary (ALSPAC, 2014).

4.3.2 Participants

In total 5,515 adolescents contributed data to the research clinics at 15 years of age (approximately 37.5 % of the core ALSPAC cohort). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Thus, the study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The manuscript does not contain clinical studies or patient data. Figure 4-1 shows the number of participants included in the study. To be included in the analyses participants were required to have a valid accelerometer file (i.e., spurious data files were excluded using similar methods as reported in Sherar et al. (2011)); only files with a minimum of 10 hours of accelerometer wear per day on at least four days of wear were included; $n = 1,908$, 34%) and cognitive data (i.e., RT within three standard deviations of the mean, and overall accuracy greater than 50% on go and stop signal conditions). The sample was further restricted to adolescents with: 1) the full scale intelligence score of at least 85 on the Wechsler Abbreviated Scale of Intelligence (WASI; Oldfield, 1971), 2) valid CRF data (as described below), 3) no clinical diagnosis of Attention Deficit Hyperactivity Disorder (ADHD; based on a diagnostic classification derived from the structured clinical interview Development and Well-Being Assessment (DAWBA); Goodman, Heiervang, Collishaw, & Goodman, 2011; Goodman, Ford, Richards, Gatward, & Meltzer, 2000), 4) no history of epilepsy or meningitis, as reported by parents (expressed as a cumulative score based on questionnaire assessments across 11 time points; questions included were: “Has child ever had epilepsy / meningitis?” and “Has child had epilepsy/meningitis in the last 12 months?”), 5) English as a first language (as reported based on the records from the Department of Education), and 6) no special provisions as indicated by Special Education Needs status. Socio-economic status was estimated based on maternal education at the age of 8 years⁶ yielding four categories: ‘1’ = GCSE D-F/CSE/none, technical qualifications; ‘2’ = O-Level/GSCE A-C; ‘3’ = A-Level/Vocational Qualification; and ‘4’ = university degree (Gutman & Feinstein, 2008). To minimise variance associated with cognitive maturation,

⁶ When data at the age of 8 were not available, maternal education at child’s birth was taken instead ($n = 53$, 8%).

participants' age was restricted to 15 years. Seven participants were excluded due to the lack of anthropometric data (body weight) required to compute weight-adjusted values of CRF. The final sample included in the analyses comprised of 667 participants (12%; figure 4-1). The majority of adolescents ($n = 560$, 83.9%) had normal or corrected to normal vision; 97 participants who reported ever wearing glasses or contact lenses did not use vision correction during testing. Information on vision was not available for 10 participants.

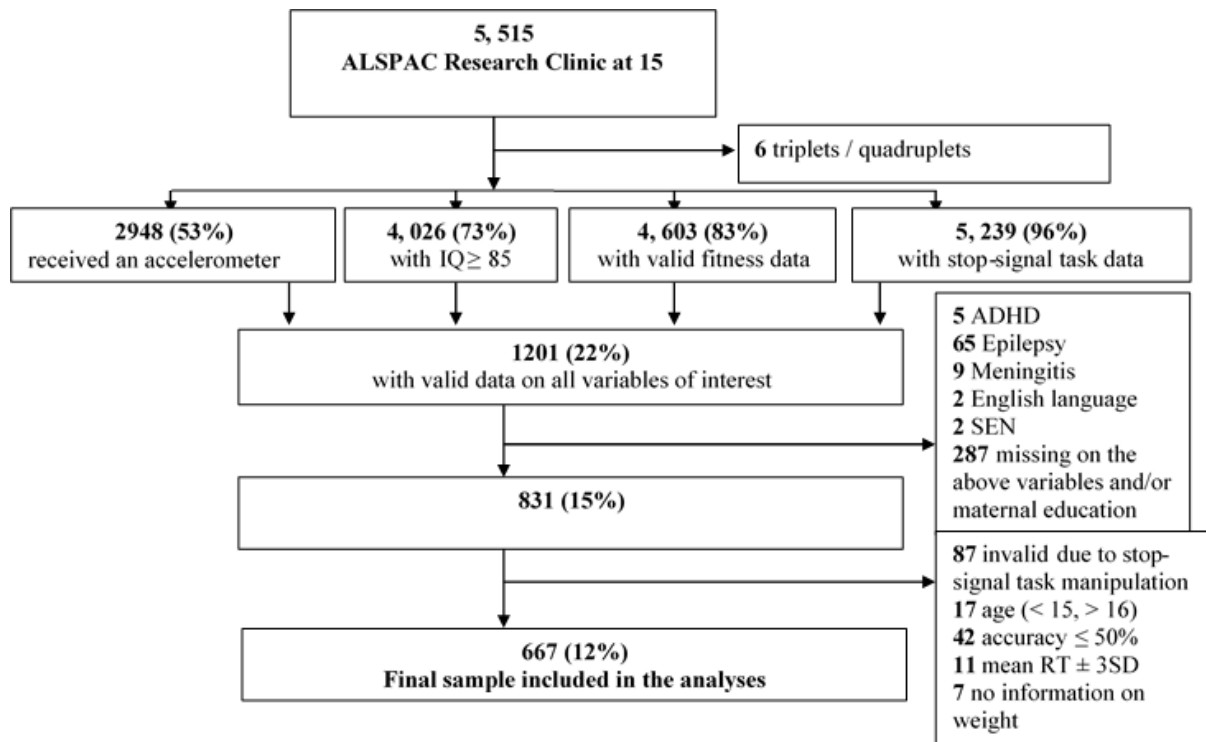


Figure 4-1. Number of participants from the Avon Longitudinal Study of Parents and Children (ALSPAC) excluded from the study on physical activity and attentional control. RT, reaction time; ADHD, Attention Deficit and Hyperactivity Disorder; SEN, Special Educational Needs.

4.3.3 Measures

4.3.3.1 Anthropometrics and body composition

Height was measured to the nearest millimetre using a Harpenden stadiometre (Holtain Ltd., Crosswell, UK) and weight to the nearest 0.1 kg using a calibrated Tanita scale (THF 300GS body fat analyser; Tanita UK Ltd, Yewsley, Middlesex, UK). Total body fat mass was measured using Dual X-ray Absorptiometry (DXA; GE Healthcare, Bedford, UK). Percent total body fat mass (TBFM) was calculated as $100 \times \text{total body fat mass} / \text{body mass}$ (total bone mass + total lean mass + total fat mass; (Ong et al., 2009).

4.3.3.2 Cognitive task

Attention and inhibitory control were measured with a Stop Signal task (Logan, 1994; Logan, et al., 1984). The Stop Signal task consisted of two conditions: a go condition and a stop signal condition. The go condition is a dual choice RT task, which requires a response to a visual stimulus (either a letter X or a letter O) appearing focally on the computer screen. Responses to the stimuli were mapped onto two response boxes marked X and O. Participants responded

with a right index finger to an X and with a left index finger to an O. The stimuli X and O were equiprobable and were presented at random. Participants were presented with 30 trials and instructed to respond as quickly as possible. For the go condition, a fixation point was presented focally for 500 ms, followed by a stimulus (X or O) presented for 1000 ms, followed by a blank screen presented for 500 ms and another fixation point. Thus, the interstimulus interval was equal to 1000 ms. The stop signal condition consisted of 64 go and 32 (33%) randomly interspersed stop signal trials. Participants were instructed to withhold an already initiated response if they heard an auditory cue (a tone) presented at varied delays relative to the go signal. Two (short and long) equiprobable stop signal delays (SSDs) were calculated for each participant. SSDs were expressed as the difference between participant's mean RT on the go condition and either a 150 ms (i.e. long SSD = MRT – 150 ms) and 250 ms (i.e. short SSD = MRT – 250 ms) subtrahend. These parameters were successfully employed in previous research with ALSPAC cohorts (Handley, et al., 2004; Kothari, Solmi, Treasure, & Micali, 2013). The objective of varied SSDs is to bias the probability of inhibition towards chance (Logan, et al., 1984). However, due to high probabilities of inhibition (87.8%) observed under these task conditions, the subtrahends used to calculate SSDs were adjusted, leading to inconsistent task manipulation across participants. First, smaller subtrahends (50 ms and 150 ms to derive long and short SSDs, respectively) were used. This manipulation resulted in even higher probabilities of response inhibition (91.7%). Therefore, the subtrahends were further increased. Subsequently two sets of subtrahends were tested: 1) 250 ms and 350 ms, and 2) 250 ms and 400 ms, for long and short SSDs, respectively. The latter adjustment resulted in the lowest probabilities of response inhibition (83.9%) and was therefore retained for further testing. Only participants who received either the original or the final set of subtrahends (in total 88.7% of those who contributed the data to a computer session) were included in the current analyses. Consequently, a sample split based on a subtrahend set used to calculate long and short SSDs was deemed necessary and analyses were carried out on two groups. In group one, 150 ms was used to calculate longer and 250 ms to calculate shorter SSDs. In group two, 250 and 400 ms subtrahends were used, for longer and shorter SSDs, respectively. Thus, participants in group one received on average longer SSDs, relative to the go signal, than participants in group two. If the resulting delay was negative, go and stop signals were presented concurrently. More than 50% of participants in group two received a stop signal concurrently with a go signal on 50% of stop signal trials, which resulted in quantitatively and qualitatively different task condition than for group one (further justifying the sample split).

Raw data were reprocessed with a custom written visual basics for applications (VBA) code. RTs shorter than 200 ms were discarded. The variables of interest were: mean RT on go and stop signal conditions (go trials) and variability in reaction time (SD of the RT for both go and stop signal conditions).

4.3.3.3 Accelerometry

The details of accelerometer deployment in ALSPAC have been previously described (Mattocks, et al., 2007; Mattocks, et al., 2008). All adolescents attending research clinics at 15 years were asked to wear an ActiGraph GT1M accelerometer (ActiGraph LLC, Pensacola, FL, USA) around their waist, over the right hip for seven consecutive days. Data were recorded as accelerometer counts and averaged across a 60 second interval (epoch) to create counts per minute (CPM). Raw ActiGraph data files were reprocessed in 2012 to derive outcome variables using a custom made data reduction software (KineSoft, ver 3.3.67, Loughborough, UK; <http://www.kinesoft.org>). The procedure followed that described by Sherar et al. (2011). In brief, all duplicates ($n = 97$, 3%) and spurious files (defined as those with a plateau in accelerometer count values, with 3 consecutive counts at the same number at a count ≥ 10 ; $n = 23$, 0.76%) were removed. After exclusion of spurious files and duplicates, and missing files 1,865 data files were available for further analyses. Non-wear time was defined as 60 minutes of consecutive zero counts, allowing for 2 minutes of non-zero interruptions (Troiano, et al., 2008). The main variable of interest was MVPA, defined as $\geq 1,963$ CPM (Freedson, Melanson, & Sirard, 1998). Sedentary time was defined as < 100 CPM, and light physical activity was defined as ≥ 100 and $< 1,963$ CPM.

4.3.3.4 Cardio-respiratory fitness

CRF was measured with a three stage sub-maximal test using an electronically braked cycle ergometer (Lode Rechor P, Groningen, the Netherlands). Workload was increased every three minutes (20, 40 and 60 Watts), when measures of a heart rate (HR) were taken every five seconds using a chest mounted HR monitor (Polar S180). CRF was expressed as predicted physical work capacity at the heart rate of 170 beats per minute (bpm; PWC-170) relative to adolescent's body weight (kg). PWC-170 was estimated with linear regression models based on the mean HR at the last 30 seconds of each stage. The data were included in the analyses if the HR was at least 80 bpm and 150 bpm (which is approximately equivalent to a workload of $> 70\%$ of maximum heart rate) at the end of the first and the last stage, respectively. These criteria were applied to ensure that the physiological response to the workload was achieved (Lawlor, et al., 2008). Weight adjusted PWC-170 based on a three minute protocol has been

shown to have good convergent validity based on the correlations with maximal oxygen consumption ($r = 0.56$, $p \leq .01$; Bland, et al., 2012).

4.3.4 Statistical Analyses

All analyses were conducted using IBM SPSS Statistics software version 20.0.1. An alpha level of .05 was used to define statistical significance. Data were screened for normality and outliers. The differences in demographic, physical activity variables, mean RT and SDRT between the study samples and cases excluded from the analyses were compared using independent-sample t-tests, analyses of covariance (adjusting for accelerometer wear time) and Chi square statistics, where appropriate. Group differences on all variables of interest were also inspected. Further, intra-individual differences in task performance on stop signal relative to go condition were assessed with related samples Wilcoxon signed rank test. The relation between mean RT, SDRT and demographic variables (age, sex, maternal education), CRF, percent total body fat mass, BMI, IQ and ADHD ratings were inspected using Spearman's rank order correlation coefficients. The relations of daily MVPA (controlling for accelerometer wear time), CRF, mean RT and SDRT were explored with partial and bivariate correlations, for MVPA and CRF respectively. Multiple hierarchical regression models were employed to examine the associations between daily minutes spent in MVPA and mean RT and SDRT for the go and stop signal conditions controlling for CRF. Four models were tested: two models for each of the cognitive variables (go mean RT and go SDRT), for each of the samples (group one with on average longer SSDs and group two with on average shorter SSDs). In all models, CRF was controlled for and entered in step one, confounders, which were significantly associated with the outcome in zero-order correlations were entered in step two, and MVPA was entered in step three. In models with SDRT, mean RT was entered in the first step, followed by CRF in step two, remaining confounders were entered in step three, and MVPA in step four. Based on bivariate correlations, the direct relations of CRF to mean go RT and SDRT were also tested with hierarchical regression models; CRF was entered in step one and relevant confounders in step two. All models were assessed for multi-collinearity and distributional normality of error terms. Where appropriate data were log transformed.

4.4 Results

4.4.1 Adherence to accelerometer wear

1,604 (86%) of the participants had four or more valid days of accelerometer data and thus were retained for analyses. Of these, 12, 20, 28 and 40% provided 4, 5, 6 and 7 valid days of

data, respectively. The remaining participants in the current study were significantly younger, had higher IQ, lower CPM, time sedentary, and daily MVPA than those who had fewer than four valid days of wear time.

4.4.2 Group differences

Tables 4-1 and 4-2 present descriptive statistics for group one (i.e., those who received longer SSDs) and group two (i.e. those who received shorter SSDs), respectively. Groups did not differ on demographic or anthropometric characteristics ($p > .25$; table 4-2); however, adolescents included in group one had significantly higher IQ ($\Delta M = 1.97$, $SE = 0.75$, $t(664) = 2.64$, $p = .01$), CRF ($\Delta M = 0.15$, $SE = 0.05$, $t(665) = 3.11$, $p = .002$), time spent in light physical activity ($\Delta M = 12.4$, $SD = 4.57$, $F(1, 664) = 7.42$, $p = .007$; table 4-2), but lower sedentary time ($\Delta M = -13.1$, $SE = 5.53$, $F(1, 664) = 5.59$, $p = .018$). No further group differences were noted ($ps > .26$).

4.4.3 Sex differences

No sex differences were noted for age, IQ or socio-economic status in group one or two ($ps > .07$; tables 4-1 and 4-2). Boys in group one were significantly taller ($\Delta M = 9.95$, $SE = 0.68$, $t(355) = 14.6$, $p < .001$), heavier ($\Delta M = 5.14$, $SE = 1.09$, $t(355) = 4.73$, $p < .001$) and more aerobically fit ($\Delta M = 0.82$, $SE = 0.05$, $t(318) = 16.1$, $p < .001$) than girls in group one. In each group, girls had significantly higher BMI (group one: $\Delta M = 0.72$, $SE = 0.32$, $t(355) = 2.23$, $p = .026$; group two: $\Delta M = 1.18$, $SE = 0.36$, $t(308) = 3.32$, $p = .001$) and percent total body fat mass (group one: $\Delta M = 13.2$, $SE = 0.84$, $t(354) = 15.8$, $p < .001$; group two: $\Delta M = 14.6$, $SE = 0.88$, $t(308) = 16.6$, $p < .001$) than boys. In group one, no sex differences in accelerometer wear time were noted ($p = .32$); however, boys in group one accrued more CPM ($\Delta M = 90.3$, $SE = 18.2$, $t(300) = 4.86$, $p < .001$), daily MVPA ($\Delta M = 15.2$ min, $SE = 3.04$, $F(1, 354) = 25.1$, $p < .001$) and less sedentary time ($\Delta M = -26.2$ min, $SE = 7.87$, $F(1, 354) = 11.1$, $p = .001$) than girls. Similar sex differences were noted in group two (CPM: $\Delta M = 98.7$, $SE = 16.8$, $t(236) = 5.6$, $p < .001$; accelerometer wear time: $p = .75$; MVPA: $\Delta M = 16.5$ min, $SE = 2.93$, $F(1, 307) = 31.8$, $p < .001$; light physical activity: $\Delta M = 15.4$ min, $SE = 6.36$, $F(1, 307) = 5.91$, $p = .016$; sedentary time: $\Delta M = -32.0$ min, $SE = 7.44$, $F(1, 307) = 18.5$, $p < .001$; table 4-2).

4.4.4 Task performance

No differences in cognitive performance were noted between adolescents whose data on vision were either missing or who reported ever wearing glasses or contact lenses but did not do so

during testing ($p > .05$). All task performance data are summarised in table 4-3. The inspection of accuracy scores on stop signal trials revealed mean accuracies of 88.8% ($Mdn = 90.6\%$) and 83.8% ($Mdn = 87.5\%$) in groups one and two, respectively. These values are significantly higher than a chance level performance and above the usual cut off used to ascertain the validity of stop signal manipulation (Band, van der Molen, & Logan, 2003; Logan, 1994). Further inspection of the mean SSDs indicated that on average in group one a stop signal was presented at 157.5 ms ($SD = 53.2$ ms) or 257.5 ms ($SD = 53.2$ ms; for a shorter and longer delay, respectively) relative to a go signal; in group two, the mean SSDs were 30.5 ms ($SD = 42.9$ ms) and 165.9 ms ($SD = 57.4$ ms). Given the mean response latencies to a go signal of 516.8 ms ($SD = 59.2$; group one) and 603.3 ms ($SD = 64.2$ ms; group two), participants had on average at least 259.3 ms (group one) and 437.4 ms (group two) to override their initial response. Thus, the parameter manipulations failed to reduce the high probability of behavioural inhibition and yielded the overall probability of inhibiting the response of 86.4%. This precluded a valid computation of stop signal reaction time, which requires a chance level accuracy on stop signal trials (Logan 1984; Band et al. 2003). Consequently, task manipulation aimed to elicit behavioural inhibition was deemed invalid and further analyses focused on go mean RT and SDRT on go and stop signal conditions. However, to provide contextual information, performance characteristics of the samples on accuracy measures, and their associations with MVPA and CRF are also presented.

In general, participants had significantly longer mean go RTs on stop signal relative to go condition (group one: $Z = -16.3$, $p < .001$, $r = .61$; group two: $Z = -15.3$, $p < .001$, $r = .61$). Their performance on a stop signal relative to go condition was also more variable as indicated by larger SDRTs (group one: $Z = -8.77$, $p < .001$, $r = -.33$; group two: $Z = -12.47$, $p < .001$, $r = -.61$). Relative to group two (i.e., adolescents who received shorter SSDs), participants in group one (i.e., those who received longer SSDs) responded more quickly ($U = 93,142$, $p < .001$, $r = .59$) and more consistently ($U = 79,270$, $p < .001$, $r = .37$) during the stop signal condition. No significant group differences in performance on go condition were noted (mean RT: $U = 59,685.5$; SDRT: $U = 56,065$, $ps \geq .10$).

4.4.5 Associations between daily MVPA, CRF and cognitive processing

MVPA was moderately related to CRF in both groups: group one $pr = .36$, group two: $pr = .43$, $ps < .001$). Consistent with the predictions, no significant associations were noted between

daily minutes spent in MVPA (log transformed) and either mean RT⁷ (group one: $pr = .02$; group two: $pr = -.01$, $ps > .76$), SDRT (group one: $pr = -.08$; group two: $pr = -.06$, $ps > .11$) or accuracy (group one: $pr = .00$, group two: $pr = .02$, $ps \geq .76$) during the go condition. Contrary to our predictions, however, MVPA was not significantly related to mean RT (group one: $pr = -.04$; group two: $pr = -.01$, $ps > .44$), SDRT (group one: $pr = -.09$; group two: $pr = -.06$, $ps \geq .07$) or accuracy⁸ (group one: $pr = -.06$, group two: $pr = -.08$, $ps \geq .15$) during the stop signal condition (go trials).

Interestingly, in group two CRF was inversely related to mean RT ($r_s = -.15$, $p = .01$), and SDRT ($r_s = -.12$, $p = .03$) during the go condition, suggesting that CRF may yield global benefits to adolescents' cognitive processing speed at least in some adolescents. No such relationships were noted in group one (mean RT: $r_s = -.06$; SDRT: $r_s = -.02$, $ps \geq .26$). In contrast, CRF was significantly and negatively related to accuracy on the go condition in group one ($r_s = -.13$, $p = .01$)⁹ but not in group two ($r_s = -.04$, $p = .45$). CRF was not associated with mean RT, SDRT or accuracy on a more cognitively demanding stop signal condition (go trials) 3 in either group ($ps > .27$).

Based on the a priori hypotheses on the associations between MVPA, CRF and cognitive processing, hierarchical regression models were conducted to further explore the data. In all models CRF and wear time were controlled for and were not statistically significant predictors of either mean RT or variability across task conditions. Consequently, only confounders, which changed depending on the model are further reported. In group one, MVPA did not predict mean RT during go condition, ($\beta = -.01$, $t(349) = .17$, $p = .87$, $\Delta R^2 = .00$, $F(6, 349) = 3.96$, $p = .001$), while controlling for maternal education ($p = .29$), IQ ($\beta = -.18$, $t(349) = 3.28$, $p = .001$) and percent total body fat mass ($\beta = .17$, $t(349) = 2.34$, $p = .02$). As expected, MVPA did not

⁷ In partial correlation analyses with MVPA all cognitive variables were log transformed.

⁸ Due to the limitations of task manipulation and its effects on accuracy measures, our hypotheses focused on the speed and not accuracy of performance. However, further details of the analyses for accuracy measures are provided for interested readers. The analyses of the accuracy data for the stop signal trials revealed a significant correlation in group one for MVPA (log transformed; $pr = .12$, $p = .01$; accounting for accelerometer wear time). However, this association was not significant in a generalized linear model ($B = 3.74$, $SE = .00$, Wald's $\chi^2_{(1, N = 357)} = 0.04$, $p = .84$, LR $\chi^2_{(5, N = 357)} = 8.23$, $p = .14$; accounting for sex, maternal education, CRF and wear time, $ps \geq .06$). The associations were tested using generalized linear models for binary and event data with a probit link function. Accuracy data were expressed as the number of responses correct within a set of 32 stop signal trials. No further significant correlations between MVPA ($p = .64$, group two) or CRF ($ps \geq .06$) and accuracy on stop signal trials were observed.

⁹ The follow-up analyses revealed that CRF was a significant predictor of accuracy on the go condition in group one ($B = -.17$, $SE = .07$, Wald's $\chi^2_{(1, N = 357)} = 6.68$, $p = .01$, LR $\chi^2_{(2, N = 357)} = 7.74$, $p = .02$; after controlling for sex, $p = .35$). The association was tested using a generalized linear model for binary and event data with a probit link function. Accuracy data were expressed as the number of responses correct within a set of 30 trials.

predict response variability (SDRT) on the go condition ($\beta = .02$, $t(352) = .45$, $p = .65$, $\Delta R^2 = .00$, $F(4, 352) = 23.02$, $p < .001$), while controlling for mean go RT ($\beta = .45$, $t(352) = 9.55$, $p < .001$). Inconsistent with the predictions, however, MVPA failed to predict mean RT during the stop signal condition ($\beta = .06$, $t(351) = 1.14$, $p = .25$, $\Delta R^2 = .00$, $F(5, 351) = 1.85$, $p = .10$), when IQ and maternal education were accounted for ($ps > .10$). Furthermore, MVPA also failed to predict response variability during the stop signal condition ($\beta = -.01$, $t(350) = .16$, $p = .87$, $\Delta R^2 = .00$, $F(6, 350) = 16.01$, $p < .001$), while controlling for mean go RT ($\beta = .43$, $t(350) = 9.03$, $p < .001$), IQ and maternal education ($ps > .08$).

In group two, MVPA did not predict mean RT during the go condition ($\beta = .01$, $t(304) = .15$, $p = .88$, $\Delta R^2 = .00$, $F(5, 304) = 2.22$, $p = .052$), while controlling for sex and percent total body fat mass ($ps > .34$). Likewise, MVPA did not predict response variability during the go condition ($\beta = .07$, $t(304) = 1.18$, $p = .24$, $\Delta R^2 = .00$, $F(4, 305) = 14.03$, $p < .001$), while controlling for mean go RT ($\beta = .37$, $t(304) = 6.98$, $p < .001$). Contrary to our hypothesis, MVPA also failed to predict mean RT on the stop signal condition ($\beta = .05$, $t(303) = .78$, $p = .43$, $\Delta R^2 = .00$, $F(6, 303) = 2.12$, $p = .05$), when IQ ($\beta = -.11$, $t(303) = 1.98$, $p = .049$) and percent total body fat mass were accounted for ($p > .26$). No significant relation was found between MVPA and response variability during the stop signal condition ($\beta = .11$, $t(305) = 1.65$, $p = .10$, $\Delta R^2 = .01$, $F(4, 305) = 1.47$, $p = .33$), while controlling for mean go RT ($p = .17$). Thus, our results suggest that in older adolescents from ALSPAC, daily MVPA was not related to the speed or consistency of responding under either task condition.

4.4.6 Cardio-respiratory fitness and cognitive processing speed

Since CRF in group two was significantly correlated with mean RT and SDRT during the go condition, these relations were further inspected with hierarchical regression models. A summary of the models is presented in table 4-6. When CRF was entered as a sole predictor in step one, it accounted for 2.6% of variance in mean RT on the go condition, $F(1, 308) = 8.28$, $p = .004$. In the second step, although CRF, sex, or percent total body fat mass did not predict mean RT ($ps > .40$), together they explained 3.5% of variance in mean RT during the go condition, $R^2 = .035$, $F(3, 306) = 3.66$, $p = .01$. This result may point to a possible interaction effect of sex and adiposity on the relation between CRF and cognitive processing in the group of ALSPAC adolescents who received a stop signal at on average shorter SSDs (i.e., group two). However, when interaction terms between CRF and sex, and CRF and percent total body fat mass were entered into the model, they failed to explain variance in mean go RT ($ps > .77$),

$R^2 = .035$, $\Delta R^2 = .00$, $F(5, 304) = 2.20$, $p = .054$. CRF did not predict response variability during the go condition, when mean go RT and sex were accounted for, $F(3, 306) = 18.1$, $p < .001$.

4.5 Discussion

4.5.1 Summary of findings

To the author's knowledge this study was the first to assess the relation between objectively measured daily MVPA and cognitive function in adolescents while controlling for the effects of CRF. Contrary to our predictions, neither daily MVPA nor CRF was related to task performance (speed or variability in response speed) during the stop signal condition, which required the up-regulation of attention and cognitive control. Daily MVPA was also unrelated to processing speed. Daily MVPA was also unrelated to cognitive performance on attentionally less demanding task. The inclusion of CRF in the models did not modulate these findings. A weak association between CRF and processing speed during the go condition (which required lower levels of cognitive control) was observed in one group of adolescents from ALSPAC (i.e. those who received shorter SSDs). This association was modulated by the inclusion of sex and adiposity to the model. Given the limitations of the stop signal manipulation, the findings related to attentional control need to be interpreted with caution. That is, adolescents employed a strategy of proactive slowing to overcome task manipulation, which substantially decreased task difficulty.

4.5.2 Daily MVPA, attentional control and processing speed

The lack of associations between daily MVPA and attentional control found in our study stands in contrast to the results of Booth and colleagues (2013), who reported positive but weak associations between percent of time spent in MVPA (accelerometry) and normative scores on tasks that require the up-regulation of attention and cognitive control (selective attention and task switching) in younger 11 years old adolescents from ALSPAC. The discrepancy between our findings and those of Booth et al.'s (2013) may be attributed to cognitive maturation between the two samples and/or differences in task characteristics. Congruent with cognitive reserve hypothesis, which posits that the associations between CRF (and by extension daily MVPA) will only emerge in populations with limited cognitive reserve (Stones & Kozma, 1988; Chodzko-Zajko & Moore, 1994), it is plausible that null associations between daily MVPA and cognitive performance found in our study reflect the lack of such associations in a more cognitively mature sample. Alternatively, the lack of the association between daily MVPA and attentional control observed in the current study could be related to the limitation

of the task manipulation, which substantially decreased task difficulty. Booth et al. (2013) utilised a cognitive task that was normalised for use in young adolescents of similar age (Test of Everyday Attention, TEA-Ch; Manly et al., 2001). In contrast, the mean RT on the go trials within the stop signal condition in the current study may have failed to differentiate between higher and lower active adolescents due to issues in the experimental manipulation as indicated by high rates of response inhibition and substantially longer RTs on go trials on the stop signal relative to the go condition. Specifically, high accuracies on the stop signal trials indicate that response inhibition was dominant over response execution. In combination with significantly longer latencies on the go trials within the stop signal relative to the go condition, these results suggest that participants slowed their responses in proactive anticipation of a stop signal (Bissett & Logan, 2011; Logan, 1994). The adoption of this strategy can be related to the fact that older adolescents are more likely to employ proactive over reactive control than children (Munakata, et al., 2012). Therefore, the results of this study emphasise the need to tailor task parameters specifically to the cognitive abilities of the sample. Consequently, inhibitory control could not be adequately assessed in the current study, which might have contributed to the null results. It also remains possible that this measure is not sensitive enough to differentiate between higher and lower physically active individuals. In confirmation, in a recent study employing a stop signal paradigm, Padilla et al. (2013) observed the differences between lower and higher physically active young adults (self-report) on the speed of the inhibition (stop signal reaction time) but not on the latency of responses to the go trials.

These results must be interpreted with caution, however, as both studies (Booth, Tomporowski, et al., 2013; Padilla, et al., 2013) present methodological considerations. Specifically, Booth and colleagues (2013) did not control for the effects of CRF. This is an important limitation, as it is unclear whether the associations between the percentage of time spent in MVPA and the indices of cognitive control could not be accounted for by CRF. Further, in the cross-sectional analyses the authors used only normative scores to assess cognitive control, which were derived from a small sample of children (approximately 100 children over two age bands; Manly, et al., 2001; Manly, et al., 1998). The results of Padilla et al. (2013) are also limited in their conclusive power, as the authors based their physical activity groupings (passive versus active) on self-reported physical activity over the past four years. Inaccuracies in recall, and self-report bias render these measures inaccurate methods for the quantification of intensity or volume of physical activity (Adamo et al., 2009; Prince, et al., 2008), thus limiting the interpretability of the reported relations between daily MVPA and cognitive control. As such,

further research examining the relation between daily MVPA and cognitive control in developing populations is warranted.

4.5.3 Cardio-respiratory fitness and processing speed

In parallel to findings with MVPA, mostly null associations between CRF and adolescents' cognitive performance have been observed. A weak positive association (2.6% of variance explained; Cohen's $f^2 = .027$) between CRF and processing speed was observed in one group of ALSPAC adolescents (who were on average less aerobically fit). The magnitude of this association is comparable to a previous report in a younger sample of pre-adolescent children ($\Delta R^2 = 3\%$; Cohen's $f^2 = .03$, Scudder et al., 2014). This association was reduced to non-significance once adiposity and sex were included in the model. However, the inclusion of these two predictors did not significantly improve the model fit ($\Delta R^2 = .008$, $p = .26$), while the overall model remained statistically significant. Since the correlations between adiposity, sex and CRF were moderate ($r = .63$ to $.66$), and the follow-up analyses using simple regression models indicated that each predictor alone explained 2.6 to 2.8% of variance in processing speed, it is possible that a single characteristic shared by all these predictors could account for the weak association with processing speed (e.g. fat free mass, which is related to CRF, sex and adiposity). Nonetheless, these findings need to be interpreted with caution given that selective and weak associations in one group of ALSPAC adolescents were observed.

Previous findings in children and adults related adiposity (Kamijo, et al., 2012; Li, et al., 2008) and sex (Der & Deary, 2006; Tun & Lachman, 2008) to cognitive control and choice RT, respectively. Therefore, it is important that future research accounts for these associations. Specifically, higher adiposity was associated with a cognitive disadvantage in children. Likewise, sex differences in choice reaction time have been consistently reported in adult studies, indicating that men have shorter RT latencies than women across the lifespan (Der & Deary, 2006; Tun & Lachman, 2008). Together with the inverse associations of CRF to adiposity in adolescents (Burns, Hannon, Brusseau, Shultz, & Eisenman, 2013; Carnethon, Gulati, & Greenland, 2005; Ortega, Ruiz, Castillo, & Sjostrom, 2007; Rodrigues, Leitão, & Lopes, 2013), and sex differences in CRF among children and adolescents (Dencker & Andersen, 2011; Tremblay et al., 2010), these studies suggest that sex and adiposity may help explain the associations between CRF and cognitive processing speed observed in wider literature.

4.5.4 Strengths and limitations

The strengths of our study include a large sample size, objective measurement of daily MVPA, CRF and adiposity, and controlling for important confounders (IQ, maternal education, objectively assessed adiposity, ADHD status based on clinical assessments). This study is also one of a few (Hillman, Kramer, Belopolsky, & Smith, 2006) to inspect the relations of physical activity to cognitive function in older adolescents and to the author's knowledge the first to inspect these associations using objective monitoring of physical activity. The main limitation of the current study is the compromised validity of the Stop Signal task, which did not allow for the adequate assessment of response inhibition. It also resulted in inconsistent application of task parameters within the ALSPAC sample from the research clinics at 15 years.

4.6 Conclusion

In conclusion, this was the first study to assess the relations of objectively measured MVPA to cognitive function in adolescents whilst controlling for the effects of CRF. Although compromised task validity limits the interpretation of some results, we were able to assess the associations between adolescents' daily MVPA, CRF, and processing speed during less attentionally demanding task condition. Our inferences on attentional control suggest that neither daily MVPA nor CRF were significantly related to attentional control in 15 years old adolescents from ALSPAC. However, these inferences are limited by the cognitive strategy of proactive slowing adopted by ALSPAC adolescents. Further research into these associations across developmental spectrum (childhood and adolescence) would help elucidate whether daily MVPA may be selectively associated with cognitive control in cognitively less mature samples, or whether daily MVPA, which is largely intermittent, is insufficient to promote cognitive benefits in young people. Notwithstanding the limitations of the study, our results add to the scant body of evidence on the associations between objectively measured MVPA, CRF and processing speed, which may have implications for cognitive development and academic achievement (Rohde & Thompson, 2007).

Table 4-1. Descriptive characteristics of 15 years old ALSPAC participants who received stop signals at longer delays (group one)

	Males (<i>n</i> = 166, 46.5%)		Females (<i>n</i> = 191, 53.5%)		Overall Sample (<i>N</i> = 357)	
	M (SD)	Range	M (SD)	Range	M (SD)	Range
Age (yrs)	15.4 (.16)	[15.0 – 15.9]	15.4 (.17)	[15.0 – 15.8]	15.4 (.17)	[15.0 – 15.9]
Height (cm)	174.4 (7.0)**	[151.5 – 192.3]	164.5 (5.9)	[146.8 – 177.3]	169.1 (8.1)	[146.8 – 192.3]
Weight (kg)	63.0 (11.2)**	[37.6 – 111]	57.8 (9.3)	[39.2 – 95.5]	60.2 (10.5)	[37.6 – 111.0]
BMI (kg/m ²)	20.6 (3.02)*	[14.7 – 33.1]	21.3 (3.0)	[14.9 – 33.0]	21.0 (3.0)	[14.7 – 33.1]
% OW/OB	15.7		17.8		16.8	
% TBFM	16.9 (8.28)**	[5.9 – 42]	30.1 (7.5)	[13.2 – 50.2]	24.0 (10.3)	[5.9 – 50.2]
Maternal education						
University (%)	19.3		23		21.3	
Ethnicity (% Non-white)	2.4		3.1		2.9	
IQ	102.1 (10.92)	[85 – 131]	101.4 (10.2)	[85 – 129]	101.7 (10.5)	[85 – 131]
CRF (W*kg ⁻¹)	2.54 (.52)**	[1.2 – 4]	1.72 (.42)	[.92 – 3.3]	2.10 (6.2)	[.92 – 4.0]
CPM	490.2 (197.2)*	[147.6 – 1729.9]	399.9 (145.4)	[100.1 – 962.8]	441.9 (177.0)	[100.1 – 1729.9]
Wear time (min)	829.0 (54.8)	[674.6 – 952.6]	822.8 (60.7)	[676.5 – 1031.2]	825.7 (58.1)	[674.6 – 1031.2]
Sedentary time (min)	476.4 (81.5)**	[161 – 671]	499.2 (79.7)	[298 – 728.4]	488.6 (81.2)	[161.0 – 728.4]
LPA (min)	288.4 (65.2)	[146.1 – 466.2]	275.0 (65.0)	[92.9 – 471.2]	281.2 (65.3)	[92.9 – 471.2]
MVPA (min)	64.2 (33.4)**	[12 – 280.2]	48.6 (24.1)	[8.17 – 139.3]	55.8 (29.8)	[8.2 – 280.2]

Note: ** $p \leq .001$, * $p < .05$, † $.05 < p < .1$ OW / OB, overweight / obese; TBFM, total body fat mass; IQ, intelligence quotient; CRF, cardio-respiratory fitness; CPM, counts per minute; LPA: light physical activity ($100 < \text{LPA} < 1,963$ CPM); MVPA: moderate-to-vigorous physical activity ($\geq 1,963$ CPM).

Table 4-2. Descriptive characteristics of 15 years old ALSPAC participants who received stop signals at shorter delays (group two)

	Males (<i>n</i> = 132 , 42.6%)		Females (<i>n</i> = 178, 57.4 %)		Overall Sample (<i>N</i> = 310)		Mean difference
	M (SD)a	Range	M (SD)	Range	M (SD)	Range	(Gr1 –Gr2)
Age (yrs)	15.4 (.16)	[15.1 – 16.0]	15.4 (.15)	[15.1 – 16.0]	15.4 (.16)	[15.1 – 16.0]	-.00 (.01)
Height (cm)	174.8 (7.1)**	[155.3 – 196.0]	164.6 (5.8)	[150.0 – 181.2]	168.9 (8.1)	[150.0 – 196.0]	.16 (.63)
Weight (kg)	63.0 (10.3)**	[42 – 93.8]	59.0 (10.0)	[35.2 – 113.7]	60.7 (10.3)	[35.2 – 113.7]	-.51 (.81)
BMI (kg/m ²)	20.6 (2.7)**	[15.3 – 28.9]	21.8 (3.3)	[14.9 – 39.0]	21.2 (3.1)	[14.9 – 39.0]	-.24 (.24)
% OW/OB	13.7		18.5		16.4		
% TBFM	16.5 (7.9)**	[5.1 – 40.5]	31.1 (7.5)	[14.1 – 54.7]	24.9 (10.5)	[5.1 – 54.7]	-.93 (.81)
Maternal education							
% University	24.2		22.5			23.2	
Ethnicity							
% Non-white	2.4		.6			1.2	
IQ	100.8 (8.4)	[85 – 127]	99.0 (9.1)	[85 – 126]	99.8 (8.8)	[85 – 127]	1.97 (.75)*
CRF (W*kg ⁻¹)	2.39 (.53)**	[1.24 – 4.0]	1.63 (.41)	[.80 – 3.3]	1.9 (.60)	[.80 – 4.0]	.15 (.05)*
CPM	484.3 (168.1)**	[160.1 – 1008.2]	385.6 (128.6)	[113.2 -931.3]	427.6 (154.4)	[113.2 – 1008.2]	14.2 (13.0)
Wear time (min)	828.4 (72.1)	[672 – 1302.7]	826.0 (60.0)	[698.6 – 1042.6]	827.0 (65.3)	[672.0 – 1302.7]	-1.32 (4.8)
Sedentary time (min)	484.9 (82.6)**	[261.7 – 896.5]	515.4 (71.1)	[328.8 – 751.1]	502.4 (77.6)	[261.7 – 896.5]	-13.1 (5.5)*
LPA (min)	278.4 (60.5)*	[140.8 – 452.7]	262.3 (56.2)	[134.3 – 479.5]	269.2 (58.5)	[134.3 – 479.5]	12.4 (4.6) ¹ *
MVPA (min)	64.9 (30.5)**	[2.43 – 152.2]	48.2 (23.0)	[6.43 – 130.4]	55.3 (27.7)	[2.4 – 152.2]	.63 (2.2) ¹

Note: ** $p \leq .001$, * $p < .05$; OW / OB, overweight / obese; TBFM, total body fat mass; IQ, intelligence quotient; CRF, cardio-respiratory fitness; CPM, counts per minute; LPA, light physical activity ($100 < \text{LPA} < 1963$ CPM); MVPA, moderate-to-vigorous physical activity (≥ 1963 CPM); ¹Adjusted for wear time.

Table 4-3. Performance of 15 years old ALSPAC participants on the Stop Signal task

	Group 1			Group 2		
	SSD = MRT – 150 / - 250 ms			SSD = MRT – 250 / - 400 ms		
	M (SD)	Min	Max	M (SD)	Min	Max
Go condition						
MRT (ms)	407.5 (53.2)	296.6	566.0	415.9 (57.4)	279.1	586.9
SDRT (ms)	88.0 (28.7)	37.9	192.7	88.5 (27.4)	41.5	180.8
Accuracy (%)	90.3 (10.5)*	53.3	100	86.1 (11.9)	53.3	100
Stop signal condition						
Go MRT (ms)	516.8 (59.2)*	360.0	693.0	603.3 (64.2)	393.7	799.1
SDRT (ms)	102.7 (21.7)*	56.7	187.2	119.0 (19.7)	62.3	177.4
SSD short (ms)	157.5 (53.2)*	46.7	316.0	30.5 (42.7)	0.0	186.9
SSD long (ms)	257.5 (53.2)*	146.7	416.0	165.9 (57.4)	29.1	336.9
Overall accuracy (%)	86.2 (10.6)*	53.1	100	78.8 (10.3)	51.0	97.9
Accuracy						
(stop signal trials; %)	88.8 (10.8)*	40.6	100	83.8 (13.0)	31.2	100
Accuracy (go trials; %)	84.8 (16.5)*	29.7	100	76.3 (16.6)	31.2	100

Note: *Mean difference between groups significant at: $p < .001$; SSD, stop signal delay; MRT, mean reaction time; SDRT, standard deviation of the reaction time.

Table 4-4. Spearman's rank order correlations between the performance of ALSPAC adolescents on Stop Signal task, demographic characteristics, cognitive and anthropometric variables and cardio-respiratory fitness (group one)

	Age	Sex	SES	IQ	CRF	%TBFM	BMI
Go condition							
MRT (ms)	-.06	.09†	-.12*	-.19***	-.06	.13**	.10†
SDRT (ms)	-.06	.04	-.05	-.05	-.02	.01	-.01
Stop signal condition							
Go MRT (ms)	-.02	.09†	-.11*	-.09†	-.02	.10†	.11*
Go SDRT (ms)	-.05	-.07	-.10†	-.12*	.06	-.01	.04

Note: *** $p \leq .001$, ** $p \leq .01$, * $p < .05$, † $.051 > p > .074$; Sex coded as 1 = male, 2 female; SES, socio-economic status; IQ, intelligence quotient; CRF, cardio-respiratory fitness; TBFM, total body fat mass.

Table 4-5. Spearman's rank order correlations between the performance of ALSPAC adolescents on Stop Signal task, demographic characteristics, cognitive and anthropometric variables and cardio-respiratory fitness (group two)

	Age	Sex	SES	IQ	CRF	%TBFM	BMI
Go condition							
MRT (ms)	-.04	.15**	-.01	-.09	-.15**	.15**	.07
SDRT (ms)	-.07	.11†	-.01	.01	-.12*	.12*	.09
Stop signal condition							
Go MRT (ms)	.04	.13*	.01	-.12*	-.09	.13*	.06
SDRT (ms)	-.02	.05	-.03	-.05	-.04	.06	.02

Note: ** $p \leq .01$, * $p < .05$; † $p = .06$; Sex coded as 1 = male, 2 female; SES, socio-economic status; IQ, intelligence quotient; CRF, cardio-respiratory fitness; TBFM, total body fat mass; MRT, mean reaction time; SDRT, standard deviation of the reaction time.

Table 4-6. A summary of regression analyses for variables predicting mean RT and response variability on Stop Signal Task (group two)

<u>Mean Go MRT</u>				<u>Mean SDRT</u>			
Step/ Predictors	ΔR^2	<i>B</i>	<i>t</i>	Step/ Predictors	ΔR^2	<i>B</i>	<i>t</i>
Step 1	.026*			Step 1	.15**		
CRF ($W \cdot kg^{-1}$)		-.16	2.88*	Mean Go RT		.38	7.28**
Step 2	.01			Step 2	.00		
CRF ($W \cdot kg^{-1}$)		-.07	.84	Mean Go RT		.37	7.00**
Sex		.07	.92	CRF ($W \cdot kg^{-1}$)		-.06	1.18
% TBFM		.07	.79	Step 3			
				Mean Go RT	.00	.37	6.96**
				CRF ($W \cdot kg^{-1}$)		-.06	.91
				Sex		.00	.02

Note: ** $p < .001$; * $p < .01$; CRF, cardio-respiratory fitness; TBFM, total body fat mass; MRT, mean reaction time; SDRT, standard deviation of the reaction time.

Chapter 5

The associations among daily moderate-to-vigorous physical activity, indices of cognitive control and academic achievement in preadolescent children

5.1 Study 2 context

The findings of study 1 indicated that daily MVPA was not related to either processing speed or attentional control in 15 years old British adolescents from ALSPAC. Based on executive function hypothesis, the relationship between cardio-respiratory fitness, aerobic exercise and by extension, daily MVPA, is stronger (therefore more likely to be observed) for these task conditions, which require the up-regulation of cognitive control (Colcombe & Kramer, 2003; Kramer, et al., 1999). Since adolescents employed a strategy of proactive slowing to gain greater control over task requirements, their attentional control was likely insufficiently challenged. This could have contributed to the lack of associations in study 1. In a similar vein, although their cognitive control still undergoes fine tuning, older adolescents are relatively advanced in cognitive development (Luna, et al., 2004; Luna, et al., 2010). Based on the cognitive reserve hypothesis (Stones & Kozma, 1988; Chodzko-Zajko & Moore, 1994), which posits that the associations between cardio-respiratory fitness and cognitive function are more likely to be observed in populations with limited cognitive reserve, it is plausible that in older adolescents the influence of health-related factors, including daily MVPA, on cognitive outcomes are minimised. In contrast, cognitive control undergoes dynamic development until late childhood (10-11 years), where gains in accuracy and speed can be observed (Davidson et al., 2006). Since consistent associations between cardio-respiratory fitness and cognitive tasks (which did and did not up-regulate cognitive control) have been observed in older children (8-9 years old), it is plausible that individual differences in health-related factors such as daily MVPA, are associated with cognitive performance in childhood. To the author's knowledge these relationships have not been inspected in pre-adolescents. Therefore, study 2 aimed to investigate the relationship between objectively measured daily MVPA and cognitive control in a sample of younger (8-9 years old) children.

The data for study 2 was collected as part of the FITKids2 trial, across two cohorts tested during the summer of 2013 and 2014. The study was the result of a collaboration between the author and Professor Hillman at the University of Illinois at Urbana-Champaign, the Principal Investigator of the FITKids2 trial. The collaboration was initiated by the author, who suggested the implementation of objective physical activity monitoring into the trial and contributed a novel research question on daily MVPA and cognitive control in pre-adolescent children. The collaboration resulted in a 14-month scholarly visit at the Neurocognitive Kinesiology Laboratory headed by Professor Hillman. The author contributed an amendment to the study, collected and co-supervised data collection on the trial in collaboration with the FITKids2

research team, and oversaw the implementation of accelerometry part of the trial (which included staff training, data collection, reduction and analyses). Study 2 presents the results based on the cross-sectional analyses (pre-randomisation).

5.2 Introduction

Physical inactivity has become a global pandemic (Kohl, et al., 2012), which adversely affects children's health (Janssen & LeBlanc, 2010) and psychosocial well-being (Biddle & Asare, 2011). Only a third of boys and a fifth of girls in Western countries are physically active at the levels optimal for their health (i.e. engage in at least 60 minutes of moderate-to-vigorous physical activity (MVPA) daily; Colley, et al., 2011; Esliger & Hall, 2009; Troiano, et al., 2008). These trends are further emphasised by the erosion of physical activity from schools motivated by academic pressures (IOM, 2013). For example, since the No Child Left Behind Act (2003) 44 percent of schools in the USA reported significantly reducing the time allocated to physical education (PE) in favour of academic instruction (McMurrer, 2007; Scott, 2008). However, increasing time in PE and physical activity during school hours (e.g. active breaks, increased time and quality of PE) at the very least does not negatively affect academic performance (Singh, et al., 2012), and can potentially benefit it (Carlson et al., 2008; Donnelly et al., 2009; Katz et al., 2010; Sallis et al., 1999).

In confirmation, evidence suggests that structured, daily moderate-to-vigorous physical activity of at least 20 minute duration may benefit children's cognitive functions, which are implicated in academic performance (Davis, et al., 2011; Hillman, et al., 2014). Specifically, emergent evidence from randomised controlled trials (RCTs) suggests that regular engagement in aerobic exercise of nine months duration benefits children's inhibitory control (resisting distractions; Chaddock-Heyman, et al., 2013; Hillman, et al., 2014), working memory (manipulating information in mind; Fisher, et al., 2011; Kamijo, et al., 2011), and task switching (Hillman, et al., 2014), namely higher order cognitive functions implicated in goal directed behaviour and learning, termed jointly cognitive control (Braver, et al., 2009; Miller & Cohen, 2001; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004). For example, prepubescent children who engaged in 60 minutes of daily after-school structured MVPA showed greater improvements on measures of inhibitory control (assessed with a modified Eriksen flanker task; Eriksen & Eriksen, 1974) than waitlist control group (Hillman, et al., 2014). Kamijo et al. (2011) and Fisher et al. (2011) also reported positive effects of physical activity interventions on working memory in older (8-9 years) and younger (6 years) children, respectively. Specifically, Kamijo et al. (2011) evaluated a sub-sample of participants from the FITKids trial (described by Hillman et al., 2014), while Fisher et al. (2011) evaluated a 10-week of 2 hours weekly PE intervention of increased intensity. Working memory was assessed with a verbal (Kamijo, et al., 2011) and a spatial working memory task (Fisher, et al., 2011)

using accuracy and error rates, respectively. Taken together the results of these RCTs suggest that regular aerobic exercise of 60 minutes duration has positive effects on aspects of children's cognition, which require inhibitory control of attention and working memory. This is important since inhibitory control and working memory underpin higher order processes of learning and reasoning, and are closely related to academic achievement (Best, et al., 2011; Blair & Razza, 2007; Espy, et al., 2004; St Clair-Thompson & Gathercole, 2006).

However, implementing aerobic exercise interventions can be costly and not easily incorporated into a school day. An initially more feasible approach may be to increase physical activity across the whole day (e.g. increasing time spent in moderate-to-vigorous physical activity (MVPA)), as recently advocated by the Institute of Medicine in the US (IOM, 2013). At present it remains unknown whether chronic aerobic exercise is necessary for cognitive and / or academic benefits to emerge. Although the field of physical activity and exercise is driven by the cardiovascular fitness hypothesis (Chodzko-Zajko & Moore, 1994; Etnier, 2006), which posits that the effects of chronic aerobic exercise on cognitive performance are mediated by cardio-respiratory fitness (CRF), its tenets are yet to be confirmed (Etnier, 2006).

It is conceivable that daily MVPA (i.e. accumulated across all aspects of the day) may also positively contribute to children's cognitive and scholastic performance. In confirmation, Booth et al. (2013) found positive associations between objectively measured (accelerometry) proportion of time spent in MVPA and tasks of executive attention in a large sample of 4,755 11 and 13 years old adolescents from the Avon Longitudinal Study of Parents and Children (ALSPAC). However, the positive results were greater on a Stroop like task, which required greater up-regulation of cognitive control and involved the change in response mappings and thus inhibitory control of prepotent response (responding one to number 1 in place of two, and vice versa when number 2 was presented) as compared to a visual search task (identifying identical pairs of objects amongst distracters) or a dual task (which required dividing attention between visual and auditory counting tasks). These results are congruent with findings of Pontifex et al. (2011) related to CRF, who observed that high aerobically fit children (i.e. those above 70th percentile on VO_{2max} relative to published norms) maintained accuracy across task conditions which up-regulated cognitive control by changing response mappings on Eriksen flanker task (i.e. responding with right rather than left key to left pointing arrow and vice versa for right pointing arrow), while the accuracy of low aerobically fit children (those below 30th percentile on VO_{2max}) decreased. Booth and colleagues (2013) did not statistically control for either the effects of CRF or intelligence quotient (IQ) in their analyses. In contrast, Pindus et

al. (2014) did inspect these relations while statistically controlling for CRF in a sample of older (15 years old) adolescents from ALSPAC using a computerised Stop Signal task but found no associations between accelerometer assessed MVPA and attentional control. However, since the task design did not allow for adequate up-regulation of cognitive control, their results need to be interpreted with caution. Therefore, it remains unclear from these studies if observed associations between proportion of time spent daily in MVPA and inhibitory control could not be explained by differences in CRF or inter-individual variation in adolescents' intelligence.

To our knowledge only two studies assessed the relationship between objectively measured physical activity (accelerometry) and working memory. The study by Syväoja and colleagues (2014) showed that accelerometer assessed MVPA was not related to spatial working memory (measured with a Corsi block task from Cambridge Neuropsychological Test Automated Battery (CANTAB), which required replicating a spatial sequence) in 12 years old adolescents. Likewise, van der Niet and colleagues (2014) found no associations between accelerometer assessed MVPA and spatial working memory (assessed with visual memory span from Wechsler Memory Scale-Revised; Wechsler, 1987) in a group of 8 to 12 year olds. However, also in these studies important confounders were not controlled for (e.g. BMI, IQ or CRF), which might have occluded the underlying associations. Since age was found to moderate the associations between physical fitness, aerobic exercise and cognitive functions in young people (Fedewa & Ahn, 2011), it is also possible that the effects of MVPA on working memory are specific to younger populations whose cognitive control is less well developed (Davison & Lawson, 2006). Indeed, the effects of chronic aerobic exercise interventions on children's working memory were found in a younger sample (ages 8-9 years; Kamijo, et al., 2011). Given the paucity of data on the associations between objectively measured MVPA and cognitive control, it is important to inspect these relationships across the domains of cognitive control, which are closely related to academic achievement.

To the author's knowledge only one study assessed the relationship between objectively measured physical activity and academic achievement in children, while also statistically controlling for inter-individual differences in CRF in the analyses (Lambourne et al., 2013). CRF mediated a positive association between physical activity (counts per minute) and academic achievement in mathematics in 7-9 year olds (Lambourne, et al., 2013). In two older samples (12 and 14 years) of Dutch adolescents, van Dijk et al. (2014) found positive associations between total volume of physical activity (expressed as step counts) and academic achievement in mathematics in older adolescents, while this association in a younger group

was negative. In contrast, Syväoja et al. (2013) found no associations between objectively measured MVPA (assessed with accelerometers and expressed as daily minutes spent in MVPA) in 12 years old Finnish adolescents. However, these authors did not statistically control for CRF, which could have occluded the underlying associations. Analyses were also limited to associations with the grade point average, while the effects of MVPA on academic achievement may differ depending on the academic domain (Harrington, 2013; Howie & Pate, 2012; Van Dijk, De Groot, Savelberg, et al., 2014). None of the studies statistically controlled for the effects of IQ, which is strongly associated with academic performance (Mayes, et al., 2009; Rohde & Thompson, 2007; Steinmayr, Ziegler, & Träuble, 2010). Taken together, the results of these studies suggest that the associations between objectively measured MVPA and academic achievement are likely complex, can depend on age of the sample, and can be confounded or mediated by the effects of CRF. Thus, in order to make meaningful inferences the associations between CRF and cognitive control must be statistically controlled for in the analyses.

In the present study we chose to focus on a younger sample of prepubescent children whose cognitive control functions are less well developed (Davidson, et al., 2006) and who therefore may experience greater cognitive benefits from MVPA (Fedewa & Ahn, 2011). The study aimed to address the limitations of previous research by evaluating the associations between accelerometer assessed daily MVPA and multiple indices of cognitive control (inhibitory control of attention and working memory) and academic achievement (reading, mathematics, and spelling) while statistically controlling for the effects of CRF and IQ in addition to other important covariates. The mediating effects of CRF on the relationship between daily MVPA and cognitive control were not inspected as the focus of the study was to first establish whether a direct association between daily MVPA and cognitive control existed, while controlling for inter-individual variation in important confounders (e.g., CRF, IQ). Following the study of Lambourne et al. (2013), the study aimed to assess the mediating effects of CRF on the associations between daily MVPA and academic achievement in mathematics. Lastly, based on consistent associations ($ES = .30$; Jacob & Parkinson, 2015) between inhibitory control, working memory and academic achievement in reading and mathematics, the study aimed to assess the mediating effects of cognitive control functions on the relationship between daily MVPA and academic performance in reading and mathematics. Congruent with previous research on CRF and aerobic exercise (Hillman, et al., 2014; Scudder, et al., 2014), we hypothesised that greater accelerometer assessed MVPA will be associated with better

inhibitory control of attention (expressed as shorter mean reaction times and greater accuracy on task conditions requiring up-regulation of cognitive control) and working memory (assessed by greater accuracy) once CRF is statistically controlled for in the models. However, children are more likely to trade accuracy for speed (Davidson, et al., 2006) and therefore we expected greater differences between the groups on measures of accuracy rather than reaction time, which is consonant with previous reports (Chaddock, Erickson, et al., 2012; Hillman, et al., 2014; Pontifex, et al., 2011). Likewise, we expected greater effects of MVPA on working memory when the scoring method required greater up-regulation of cognitive control (e.g. a correct recall of all rather than some words in a given sequence; Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014). Based on previous research, it was further hypothesised that: a) the relationship between daily MVPA and academic achievement will be stronger for mathematics than reading and spelling (as measured by standardised test scores; Howie & Pate, 2012; Van Dijk, De Groot, Savelberg, et al., 2014); b) this relationship will be at least partly mediated by CRF; and c) indices of cognitive control (accuracy and / or reaction time on task of inhibitory control and accuracy on working memory task).

5.3 Methods

5.3.1 Design and participants

One hundred and three 7 to 9 years old children (45.7% girls; $M_{age} = 8.64 \pm 0.57$) were recruited from seven schools in East Central Illinois during summer 2013 and 2014. To be included in the study children had to 1) have a composite score greater than 85¹⁰ on the Brief Intellectual Ability of Woodcock-Johnson III Tests of Cognitive Abilities (Woodcock, McGrew, & Mather, 2001), 2) be free of neurological disorders (as indicated by parental ratings on the ADHD Rating Scale IV (DuPaul, et al., 1998) in a telephone interview), 3) physical disability, 4) or clinical diagnosis of the Attention Deficit Hyperactivity Disorder (ADHD, as disclosed by parents; in addition, legal guardians completed ADHD Rating Scale IV; DuPaul, et al., 1998), 5) free of any physical disabilities that may limit their participation in the intervention, and 6) provide at least one day of valid accelerometer data (≥ 10 hours of accelerometer wear; Rich, et al., 2013). Twenty two children were excluded due to either missing cognitive data ($n = 3$), less than chance accuracy ($n = 13$) on the modified Eriksen flanker task (Eriksen & Eriksen, 1974; Eriksen, 1995; Scudder, et al., 2015) or Operation Span Task (OSPAN; Turner

¹⁰ One child had an intelligence quotient of 84, which only just missed one standard deviation threshold and was therefore retained for the analyses to conserve the sample size.

& Engle, 1989), missing academic achievement ($n = 1$), physical activity ($n = 3$), pubertal stage ($n = 1$; as assessed by a pubertal questionnaire completed by a parent (Taylor, et al., 2001) based on criteria described by Tanner (Tanner, 1962), or ADHD ($n = 1$) data. The data of 81 children (45.7% girls, $M_{age} = 8.64 \pm .57$) were retained for the analyses. In addition, socioeconomic status (SES) was taken using a trichotomous index based on parental reports of: 1) child's participation in free or reduced price lunch programme at school, 2) the highest level of education obtained by mother and father, and 3) the number of parents who work full time (Birnbaum, et al., 2002).

Data collection was conducted between June and September 2013, and June and October 2014. Children visited a laboratory at the University of Illinois at Urbana-Champaign on two separate occasions to complete neuropsychological and cognitive testing. Accelerometers were issued on one of the testing days, and returned by a parent upon completion of wear. The study was approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign. Parents provided written consent and children provided written assent.

5.3.2 Measures

5.3.2.1 Anthropometric assessment

Height and weight were measured while children were in lightweight clothing and with running shoes on. Standing height was assessed with a Seca telescopic stadiometre model 220 (Seca, Birmingham, UK) to the nearest millimetre. Weight was measured with a Seca 769 electronic column scale (Seca, Birmingham, UK). BMI ($\text{weight (kg)/height(m)}^2$) percentiles were calculated based on Centers for Disease Control growth charts (Kuczmarski et al., 2002).

5.3.2.2 Accelerometry

Physical activity was directly measured over seven consecutive days using a triaxial ActiGraph accelerometer model wGT3X+ (ActiGraph, Pensacola, FL, USA). Although the wGT3X+ detects acceleration in all three axes, given the limitations in current intensity thresholds, this research focused on vertical acceleration within the full scale range of ± 6 g with a frequency response of 0.25–2.50 Hz. Participants wore the devices on the waist at the right anterior axillary line on a nylon belt. Data were collected at 100 Hz resolution. Raw .gt3x+ data files were integrated into 15 s epochs using ActiLife software (versions 6.7.1 to 6.10.0 and a firmware version 2.2.1; ActiGraph, Pensacola, FL, USA). Epoched data files were subsequently processed to derive outcome variables using a custom made data reduction software (KineSoft, version 3.3.76, Loughborough, UK; <http://www.kinesoft.org>). Data were

cleaned and screened following procedures described by Sherar et al. (2011). After screening for duplicates ($n = 5$) and spurious files ($n = 0$; based on a plateau in accelerometer counts with 3 consecutive counts at the same number at a count ≥ 10), 103 files were available for the analyses. Non-wear was defined as 60 minutes of consecutive zero counts, allowing for 2 minutes of non-zero interruptions (Troiano, et al., 2008). Files with at least one day and ≥ 10 hours of accelerometer wear ($n = 101$) were included in the analyses. To account for the overnight wear, the analyses were limited to physical activity data from 6am to 11pm. The following variables were analysed: MVPA defined based on age specific cut points for 8 years old children developed by Freedson and reported by Trost et al. (2002), using four metabolic equivalents (MET) as a threshold to account for a higher resting energy expenditure in children (Harrell, et al., 2005; Roemmich, et al., 2000). Sedentary time was defined as < 100 CPM, and light physical activity as $\geq 100 < 4$ METs.

5.3.2.3 Cardio-respiratory fitness

Maximal oxygen consumption (VO_{2max}) was measured during a maximal graded treadmill exercise test, using a computerised indirect calorimetry system (ParvoMedics True Max 2400, Sandy, UT, USA). Averages of VO_{2max} and respiratory exchange ratio (RER) were taken every 20 seconds. A modified Balke Protocol was employed, while children were walking or running on a motor driven treadmill (LifeFitness 92T, Schiller Park, IL, USA). The speed was kept constant, while a gradient was increased by 2.5° every 2 minutes until volitional exhaustion. Heart rate (HR) was monitored throughout the test with a polar HR monitor (Polar WearLink+31; Polar Electro, Finland). Ratings of perceived exertion were taken every two minutes with the children's OMNI scale (Utter, Robertson, Nieman, & Kang, 2002). Maximal oxygen consumption relative to body weight was expressed in $mL \cdot kg^{-1} \cdot min^{-1}$. VO_{2max} was determined based on maximal effort as indicated by a plateau in oxygen consumption defined as less than $2 mL \cdot kg^{-1} \cdot min^{-1}$ despite an increase in workload (Whaley, et al., 2006) or at least one of the following indicators: 1) a $HR \geq 185$ beats per minute (Whaley, et al., 2006), 2) a HR plateau (Freedson & Goodman, 1993); 3) $RER \geq 1.0$ (Bar-Or, 1983); and/or 4) a score of ≥ 8 on the children's OMNI scale (Utter, et al., 2002). VO_2 peak was used as an indicator of aerobic capacity for one child. VO_{2max} percentiles were computed based on normative data provided by Shvartz and Reibold (1990). High and low fit groups were defined as those above or below 70th and 30th percentile, respectively.

5.3.2.4 Inhibitory control

Inhibitory control was assessed with a modified Eriksen flanker task (Eriksen & Eriksen, 1974). This task provides a measure of children's ability to suppress distractors and attend to relevant information (Eriksen & Eriksen, 1974; Friedman & Miyake, 2004; Mezzacappa, 2004). Participants were asked to respond as quickly and as accurately as possible with a corresponding thumb press to the directionality (left or right) of centrally positioned fish amid an array of four flankers (fish). All the stimuli subtended a horizontal visual angle between two outside positions of 14.8° and a vertical visual angle of 3.2°. Stimuli were presented focally on a computer screen from a distance of one meter using Neuroscan Stim 2 software (Compumedics, Charlotte, NC). On congruent trials, the flankers pointed in the same and on incongruent trials in the opposite direction to the target fish. Congruent and incongruent trials were equiprobable and randomly distributed. Upon completion of 40 practice trials, participants were presented with 168 (2 x 84) experimental trials. The stimulus duration was 250 ms with randomly distributed and equiprobable inter-stimulus intervals of 1600, 1800 and 2000 ms. Individual reaction times (RTs) shorter than 200 ms were discarded. The congruent condition leads to faster and more accurate responses as it places lower demands on cognitive control (Eriksen & Eriksen, 1974; Eriksen & Schultz, 1979; Hillman, et al., 2009). The incongruent trials place higher demands on cognitive control, due to the interference from the flanking stimuli, which compete for attentional resources with the target (Eriksen & Eriksen, 1974; Kramer, Humphrey, Larish, & Logan, 1994; Spencer & Coles, 1999). This is reflected in longer response latencies and lower accuracies. In the current study, we measured mean RT and accuracy on congruent and incongruent trials. In addition, two measures of interference control (i.e., a measure of performance decrement associated with the presence of distractors) were computed (i.e., mean RT and accuracy interference scores) by subtracting the congruent from incongruent values (RT) and incongruent from congruent (accuracy). Higher values indicate greater interference. The flanker paradigm has been well established as a robust measure of inhibitory control (Botvinick, et al., 2001; Eriksen, 1995; Friedman & Miyake, 2004; Gratton, et al., 1992; Rueda, et al., 2004; Salthouse, 2010) and has shown high factor loadings on the resistance to interference factor ($\beta = .82$; Friedman & Miyake, 2004). Performance on this task is sensitive to both age-related (Checa & Rueda, 2011; Ridderinkhof & van der Stelt, 2000; Ridderinkhof, et al., 1999; Rueda, et al., 2004; Rueda, et al., 2005; Salthouse, 2010; Stins, et al., 2004; Stins, et al., 2007; van Leeuwen, et al., 2007) as well as

CRF-related differences in children (Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011).

5.3.2.5 Working memory

Working memory was assessed with the Operation Span Task (OSPAN; Turner & Engle, 1989). OSPAN is a working memory span task, which evaluates the ability to maintain memory representations and control attention in face of distractions (Conway, et al., 2005). In the OSPAN task participants were presented with individual words printed on a computer screen, followed by a simple arithmetic problem (for example, $1 + 2 = 3$), which constituted a single trial. Participants were instructed to read both aloud and to indicate whether a solution to an arithmetic problem was correct by a corresponding thumb press on a response pad (left for incorrect, right for correct). The task set concluded with a recall phase where participants were required to write down all to-be-remembered words in the order of presentation. The number of trials per set varied between one and four. All participants completed four blocks of four sets of trials, one for each set size (1, 2, 3 and 4-trial sets) presented at random; in total 40 word-arithmetic operation trials across 16 sets. Stimuli were presented focally on a computer screen from a distance of one meter using Neuroscan Stim 2 software (Compumedics, Charlotte, NC). Words were presented for 1000 ms, followed by an interstimulus interval of 1100 ms and the onset of an arithmetic problem presented for up to 10 s. A cut-off of 50% accuracy on arithmetic problems was set to ensure that arithmetic task successfully prevented mental rehearsal. Albeit lower than recommended accuracy cut-off for young adults (Conway, et al., 2005), the adopted accuracy cut-off allowed to preserve a sample size and proved to be adequate in previous research with children of similar age (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014). In the present study both scoring methods based on all-or-nothing as well as partial credit score criteria were used (see: Conway, et al., 2005, for a detailed review of working memory span scoring methods). In all or-nothing scoring, the points were only awarded for the task sets where all items were correctly recalled in a correct serial order. Two different scores were calculated: all-or-nothing unit score (ANU) was expressed as the proportion of correctly recalled items per set averaged across sets in which all items were correctly and sequentially recalled; all-or-nothing load score (ANL), which is the sum of all correctly recalled elements from task sets in which all items were correctly and sequentially recalled divided by the total number of trials. Thus, only the latter method accounts for the size of the task set. In contrast, the partial credit scoring methods also awards points for task sets in which only a subset of items were correctly recalled and does not penalise for incorrect recall

sequence. For example, if a participant correctly recalled three out of four to-be-remembered words, three points would be awarded for this set according to a partial credit scoring method but no points would be awarded according to all-or-nothing scoring method. In analogy to ANU and ANL, in partial-credit unit scoring (PCU) no weights were assigned to larger sets, while the set size was accounted for in partial-credit load scoring (PCL). ANL and ANU scoring methods are more demanding and thus more robust in differentiating performance at the higher end of cognitive demands. That is, the all-or-nothing scoring methods are better at representing performance during these task conditions, which require highest engagement of executive attention and cognitive control. Prior research in children indicated that CRF specifically differentiated individuals based on their ANL (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014). OSPAN has high test-re-test reliability ($r = .88$; Klein & Fiss, 1999) and good convergent validity as assessed against other working memory span tasks ($r_s = .40$ to $.60$; Kane et al., 2004).

5.3.2.6 Academic achievement

Academic achievement in reading, mathematics and spelling was assessed with five sub-tests from the Kaufman Test of Educational Achievement, Second Edition (KTEA II; Kaufman & Kaufman, 2004), and included the following sub-tests: word recognition, reading comprehension, math concepts and applications, math computation and spelling. Word recognition sub-test involved reading the graded list of phonetically regular and irregular words. On a reading comprehension sub-test, participants read a number of 50-225 words passages ($Mdn = 110$ words) and answered three to four questions per passage. The test included a combination of narrative and expository passages, which were specific and relied on the structure and sequence of ideas, phrasing and sentence syntax rather than vocabulary complexity (which was kept consistent) to test reading ability. Scores on word recognition and reading comprehension formed a composite reading score. Math concepts and applications tested participant's ability to understand and apply mathematical concepts such as number patterns and operations, averages, probability, and higher concepts including algebra, analytical geometry, quadratic equations, and trigonometry. Math computation consisted of 72 problems testing progressively more advanced concepts from operations on whole numbers to binomials and factorial. The two sub-tests compounded a composite math score. Spelling subscale from the written language scale was used as an indicator of written language ability. The standardised composite scores ($M = 100$, $SD = 15$), for reading and mathematics, and a standardised score for spelling were used as measures of domain specific academic

achievement. KTEA II (Kaufman & Kaufman, 2004) has superior psychometric properties with internal consistencies of sub-tests ranging from .93 to .97, high inter-rater reliabilities: .91-.97, and internal validity of .93-.95.

5.3.3 Statistical analyses

Group differences between study participants included and those who were excluded from the study, as well as sex differences on demographic, anthropometric, physical activity, cognitive and academic achievement variables were evaluated using Mann-Whitney U tests, analyses of covariance (time spent in physical activity intensities while adjusting for wear time) and chi-square statistics. Pearson and Spearman's correlation coefficients were used to inspect the bivariate associations. The associations between daily MVPA, cognition and academic achievement were inspected with partial correlation coefficients controlling for wear time. The relationships were further inspected with multiple hierarchical regression models adjusting for these demographic (e.g. age, sex, IQ, pubertal stage, SES, ADHD ratings) or anthropometric variables (BMI), which were significantly related to cognitive and academic achievement outcomes in bivariate correlations. CRF was statistically controlled for in all the models. All models were assessed for multi-collinearity and normal distribution of error terms. Where appropriate, variables were log or square root transformed to conform to the assumption of normality of distribution. IBM SPSS Statistics version 20.0.0.1 was used to conduct all the analyses. The significance level was set at .05.

5.4 Results

5.4.1 Descriptive statistics

Descriptive statistics are presented in table 5-1. Children were on average 8.64 years old (SD = .57). The sample was ethnically diverse and included approximately 27% children of non-white descent. 34.5% of children were classed as overweight or obese. A large proportion of children ($n = 42$; 51.9%) were unfit (i.e. below the 30th VO_{2max} percentile relative to published norms). No differences were noted between those excluded ($n = 22$) and those included ($n = 81$) in the study in demographic (age, sex, ADHD ratings) or anthropometric (height, weight, BMI) variables, pubertal stage, CRF, percent low or high fit, or overweight and obese ($ps \geq .22$). However, those included in the analyses had on average higher IQ ($U = 1,010.5$, $Z = 3.25$, $p < .001$), spent more time sedentary ($U = 816$, $Z = 2.61$, $p = .01$), but had lower CPM ($U = 350$, $Z = 2.28$, $p = .02$), less light physical activity ($U = 248$, $Z = 3.35$, $p = .001$) and MVPA ($U = 341$, $Z = 2.37$, $p = .02$) than those who were excluded from the study. The majority of those

excluded from the study were of low SES ($n = 10$, 62.5%), compared to 27.6% ($n = 23$) of study participants ($\chi^2(1) = 7.33$ $p = .03$).

5.4.2 Sex differences

No significant sex differences were noted for age, ADHD ratings ($ps \geq .34$), anthropometric (BMI, BMI percentile, height, weight; $p \geq .29$) or physical activity variables (CPM, wear time, sedentary time, MVPA; $ps \geq .06$). Boys had higher weight relative values of VO_{2max} ($\Delta M = 4.29$, $SE = 1.72$, $t(79) = 2.49$, $p = .015$) but did not differ from girls on VO_{2max} percentile ($ps \geq .28$). No sex differences were noted for SES, overweight/obese status, pubertal stage or percent of high and low fit ($ps \geq .15$).

Descriptive data for boys and girls' physical activity levels are presented in table 5-1. The majority of participants ($n = 64$, 79.1%) wore an accelerometer for five or more days. Nine participants (11.2%) yielded data for less than four days of wear. Eight (9.9%), 16 (19.8%), 26 (32.1%) and 22 (27.2%) yielded data for 4, 5, 6 and 7 days of wear. Participants wore an accelerometer on average 13.2 hours a day (6am-11pm; $M = 793.4$, $SD = 56.1$ minutes). Participants spent on average 450.9 ($SD = 64.8$) minutes sedentary, 254.1 ($SD = 40.8$) minutes in light, 88.3 ($SD = 30.0$) in MVPA. Physical activity was positively and moderately related to CRF: CPM: $r_s = .54$, $p = .001$, MVPA¹¹: $pr = .38$, $p = .001$.

5.4.3 Cognitive task performance and academic achievement

Participants' performance on modified Eriksen flanker task, OSPAN and tests of academic achievement are summarised in table 5-2. Boys were more accurate ($Mdn = 83.3$ percent, $IQR = 14.9$) on congruent condition of the flanker task than girls ($Mdn = 77.4$ percent, $IQR = 13.7$), $U = 1,086$, $Z = 2.58$, $p = .01$, $r = .29$. No further sex differences were noted for performance on either cognitive tasks or academic achievement tests ($ps \geq .09$). As expected, participants responded, on average, faster and more accurately on congruent (mean RT: $Mdn = 522.5ms$, $IQR = 126.9$; accuracy: $Mdn = 83.3$ percent, $IQR = 15.5$) relative to incongruent trials (mean RT: $Mdn = 578.9ms$, $IQR = 153.3$, accuracy: $Mdn = 72.6$ percent, $IQR = 16.7$) on the flanker task (mean RT: $Z = 7.56$, $p < .001$, $r = .84$; accuracy: $Z = -4.25$, $p < .001$, $r = -.47$). Overall children in the current study showed an average level of academic performance (mathematics: $M = 110.5$, $SD = 15.4$, spelling: $M = 111.4$, $SD = 15.8$, and reading: $M = 115.8$, $SD = 14.1$).

¹¹ Log transformed

5.4.4 Moderate-to-vigorous physical activity, cognitive control and academic achievement

No significant bivariate correlations between MVPA (partial correlations adjusting for wear time) and either cognitive or academic achievement variables were noted ($ps \geq .10$). CRF was negatively related to accuracy interference ($r_s = -.36, p = .03$) but not to other cognitive variables or academic achievement ($ps \geq .10$). A summary of the final steps from the hierarchical regression models predicting inhibitory control, working memory and academic achievement from MVPA are presented in table 5-3¹².

In hierarchical regression models, MVPA did not explain variance in any of the measures of inhibitory control (accuracy, mean RT on the incongruent condition or measures of interference: accuracy and mean RT) on the flanker task ($ps \geq .16$). Taken together these results suggest that MVPA was not a good predictor of inhibitory control. Likewise, MVPA did not explain variance in any of the working memory measures: PCU, PCL, ANU or ANL scores on the OSPAN ($ps \geq .58$). When academic achievement measures were considered, MVPA did not predict performance on reading, spelling or mathematics ($ps \geq .21$). Given the null findings on the relationship between daily MVPA and cognitive control as well as academic achievement, hypothesised mediation analyses (whereby cognitive control was hypothesised to mediate the relationship between daily MVPA and academic achievement) were not performed. Although CRF was not a significant predictor of cognitive or academic achievement variables in any of the models once MVPA was entered in the model (table 5-3), it significantly predicted interference accuracy on a flanker task (Step 2: $\Delta R^2 = .049, p = .049; \beta = -.21, t(77) = 2.00, p = .049, F(3, 77) = 3.40, p = .022$). Therefore, a follow-up multiple hierarchical regression model with CRF as the main predictor and interference accuracy as outcome was performed. After controlling for ADHD ($\beta = -.26, t = 2.46, p = .016$), CRF explained 4.7% of variance in accuracy interference ($\Delta R^2 = .047, p = .045; \beta = -.22, t(78) = 2.03, p = .045, F(2, 78) = 4.95, p = .009$). Since no significant associations between MVPA and academic achievement variables were noted mediation analyses (whereby the associations

¹² For OSPAN (working memory task), only PCU and ANU scores were included, as loading scores were highly correlated with unit scores within partial and all-or-nothing score categories ($rs = .98$ and $.97$, respectively, $ps < .001$).

between daily MVPA and academic achievement in mathematics were mediated by CRF) were not performed¹³.

5.5 Discussion

5.5.1 Summary of findings

To the authors' knowledge this study is the first to assess the associations between objectively measured MVPA and multiple indices of cognitive control using sensitive computerised tasks of inhibitory control and working memory, while also controlling for directly measured CRF and other important confounders including IQ, BMI, ADHD and pubertal status. The associations between daily MVPA and academic achievement were also evaluated using well-validated standardised tests.

Contrary to the hypotheses, the study found predominantly null associations. Specifically, daily MVPA was not significantly related to either inhibitory control of attention or working memory. That is, MVPA was not associated with either the latency or accuracy on incongruent trials of the flanker task or to the indices of interference control. MVPA was also not related to working memory measures in our study as no associations were observed between daily MVPA and either of the OSPAN scoring criteria, which differed in the requirements to up-regulate cognitive control. Likewise, contrary to the hypotheses daily MVPA was not related to academic achievement in mathematics, reading or spelling. The null associations between daily MVPA, cognitive and academic achievement variables paired with null associations between CRF and academic achievement precluded hypothesised mediation analyses. However, CRF was significantly and positively related to greater interference control on a measure of accuracy on the inhibitory flanker task.

5.5.2 Daily MVPA and cognitive control

The results from the current study suggest that daily intermittent MVPA was not associated with cognitive control in typically developing pre-adolescent children from Midwest of the USA. This study is not the first to report null findings in paediatric physical activity and cognition literature. Our results align with those of study 1 (Pindus et al., 2014), which tested the associations between daily MVPA and attentional control in an older (15 years old) sample

¹³ For the mediation to occur, a path from an independent variable (MVPA) to a hypothesised mediator (cardio-respiratory fitness), as well as that from a mediator to the outcome (e.g. academic achievement in mathematics) has to be significant (Hayes & Preacher, 2014; Preacher & Hayes, 2008).

of British adolescents from ALSPAC, while also statistically controlling for CRF. Although the results of Pindus et al. (2014) in relation to attentional control need to be interpreted with caution due to the limitations of the cognitive task, the conclusions of both studies suggest that daily intermittent MVPA is not related to cognitive control in young people. The current study employed sensitive cognitive measures, which adequately up-regulated cognitive control demands, tested multiple cognitive control functions, and assessed younger children, whose cognitive control undergoes dynamic development. Nonetheless, the study found no associations between daily MVPA and cognitive control. Similarly, Syväoja et al. (2014) reported null associations between objectively measured MVPA and several indices of cognitive control: working memory and task switching (measured with attention shift task) in 12 years old Finnish adolescents. However, these authors did not control for either CRF or IQ and therefore, it is unclear whether their results may not have been confounded by inter-individual variability in intellectual ability, especially on measures of working memory, which are most strongly associated with IQ (Conway, Cowan, Bunting, Theriault, & Minkoff, 2002; Conway, et al., 2003; Kane & Engle, 2002; Oberauer, Süß, Wilhelm, & Wittmann, 2008).

Our results stand in contrast to those of Booth et al. (2013) who reported significant associations between the proportion of time spent in MVPA and indices of attentional control (selective attention and interference on a Stroop like task) in a large birth cohort. Since these authors did not control for CRF or IQ, it remains unclear whether the reported associations would hold when these variables were included in the regression models. In our study, we were able to ascertain that exclusion of CRF from the models did not modulate the findings. Since Booth et al. (2013) used a high intensity cut point (3,600 CPM; Mattocks, et al., 2007), and higher intensity of physical activity shows stronger relationship with CRF in young people (Dencker & Andersen, 2011), it is possible that CRF could partly or fully explain their results. Alternatively, it may be argued that the intensity cut point used in our study was lower than that adopted by Booth et al. (2013) and could have captured light physical activity as well as MVPA. However, when we performed the same analyses with a higher intensity threshold (3,000 CPM), the results remained materially unchanged.

The results of our study also stand in contrast to findings from the RCTs, where positive effects of chronic aerobic exercise (i.e. engagement in a nine-month afterschool physical activity programme consisting of at least 70 minutes of daily MVPA) on children's cognitive control were observed for both inhibitory control (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014) and working memory (Kamijo, et al., 2011). The divergent results can relate to the

differences in measured physical activity concepts. In the RCTs children engaged in regular aerobic exercise (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014; Kamijo, et al., 2011), while we focused on daily engagement in MVPA expressed as the accumulation of time spent in MVPA across the whole day. Children's daily MVPA is highly intermittent (Bailey, et al., 1995; Baquet, et al., 2007) and therefore, on average, unlikely to engender increments in aerobic fitness (Dencker & Andersen, 2011). In confirmation, aerobic exercise of at least 10 minute duration (at the intensity of 80% of maximum heart rate and the frequency of at least 3 times a week over a minimum of at least four week duration) seems to be necessary to engender increase in CRF in children and adolescents (Baquet, Van Praagh, & Berthoin, 2003). However, in our study, the majority of children (79%) did not accumulate MVPA in bouts of at least 5 minutes (allowing for a minute interruption) on any of the sampled days (data not shown). Thus, it is possible that regular aerobic exercise is necessary for cognitive benefits to accrue.

In confirmation, we found a positive association between CRF and interference control on a measure of accuracy. That is, higher CRF was associated with better ability to suppress distractions. This result aligns with the findings of Voss et al. (2011) who also reported a positive association between CRF and a measure of accuracy interference control on the flanker task among prepubescent children. Since CRF is posited as the main mechanism for the effects of chronic aerobic exercise on cognitive control (Etnier, 2006; Kramer, et al., 1999), our results suggest that regular aerobic exercise is likely needed to benefit cognition. The effects whereby increased CRF can positively affect cognitive performance could be explained by its positive effects on increased cerebral blood flow (Brown et al., 2010; Zimmerman et al., 2014). Such interpretation is consonant with the results of a recent study in young adults where regulation of cerebral blood flow (measured with cerebrovascular CO₂ reactivity) mediated the associations between regular engagement in MVPA accumulated in at least 15 (vigorous) or 30 (moderate) minute bouts (Guiney, Lucas, Cotter, & Machado, 2015). Cerebral blood flow is tightly coupled to neuronal metabolism, and stimulates increases in the levels of brain-derived neurotrophic factor (BDNF). BDNF is the main mechanism posited to mediate the effects of aerobic exercise on cognitive and brain function (Gomez-Pinilla, et al., 2008; Vaynman, Ying, & Gomez-Pinilla, 2004). In turn, BDNF increases synaptic plasticity, neurogenesis and angiogenesis (Gomez-Pinilla, et al., 2008), namely these neurophysiological processes, which support neural memory formation and learning and lead to increased cognitive performance (Gomez-Pinilla & Feng, 2012; Gomez-Pinilla & Hillman, 2013).

It could be argued that the sample size in the current study was insufficient for small effects to emerge. However, there is no evidence to suggest that with a greater sample our results would change. In all but one of the models with daily MVPA, R^2 change was equal to 0, which suggests no observable statistical effect of daily MVPA on cognitive and academic achievement constructs. In one model, the change in R^2 after the inclusion of daily MVPA was equal to 2% (for incongruent accuracy on a modified Eriksen Flanker task). Indeed, the calculated post-hoc power for the multiple regression analyses with 3 predictors, the sample size of 81 and an alpha level of .05 was 16% and a sample size of 543 would be needed to detect a small effect ($f^2 = .02$, based on $(R^2/(1-R^2))$ Cohen's formula (Cohen, 2003; Soper, 2014)). However, such an effect is practically trivial. In our study for each millisecond decrease in mean RT on the incongruent task condition, a 3.6 minute increase in MVPA would be needed. A between-group difference of approximately 50 milliseconds in performance on the incongruent task condition can differentiate between low and high aerobically fit children (e.g. Chaddock, Hillman, et al., 2012). Thus an increase of 180 minutes daily in MVPA would be needed to attain a 50 ms decrease in mean RT on the incongruent task condition. This would equate to approximately a twofold increase in MVPA, which is unrealistic given that physical activity interventions specifically designed to increase daily MVPA in children achieve an average increase of four minutes (Metcalf, et al., 2013). Therefore, the practical meaning of our findings remains.

Research into the associations between objectively measured MVPA and cognitive control is sparse and to the author's knowledge, ours is the first study to inspect these associations while controlling for CRF, IQ and a number of other important confounders in a younger sample of pre-adolescent children. We used sensitive and objective measures of both daily MVPA and cognitive control, as well as a gold standard measure of CRF and standardised tests of IQ and academic achievement. Thus, although it may be premature to state whether the relationship between daily MVPA and children's cognitive control exists, our results contribute quality evidence on the null associations. In contrast, the positive relationship between CRF and interference control found in the current study aligns with multiple reports on such positive associations between CRF and the indices of inhibitory control from the literature (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Hillman, et al., 2009; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011). Paired with the emergent evidence on the positive effects of aerobic exercise interventions on children's cognitive

control (Chaddock-Heyman, et al., 2013; Davis, et al., 2007, 2011; Hillman, et al., 2014; Kamijo, et al., 2011), our results suggest that aerobic exercise rather than intermittent daily MVPA may be necessary to benefit cognitive control in young people.

5.5.3 Daily MVPA and academic achievement

In parallel to the observed cognitive findings, we found no significant associations between daily MVPA and the standardised achievement scores in mathematics, reading and spelling. Thus far the research into the associations between objectively measured physical activity and academic achievement yields conflicting findings, with some studies reporting positive associations with at least one domain of academic achievement (Booth, Leary, et al., 2013; Davis, et al., 2011; Donnelly, et al., 2009; Lambourne, et al., 2013), some noting negative associations (Tremblay, Inman, & Willms, 2000), while others still reporting null findings (LeBlanc et al., 2012; Syväoja, et al., 2013). Our findings further contribute to this body of research by examining the associations between daily MVPA and academic achievement in younger preadolescent children as assessed with well validated standardised tests.

Our findings in relation to academic achievement align with those by LeBlanc et al. (2012) who reported no associations between accelerometer measured MVPA and domain specific academic achievement in English and mathematics (as assessed by criterion referenced tests) in 10 years old children. Likewise, Syväoja et al. (2013) found no associations between accelerometer measured MVPA and grade point average in Finnish adolescents ($M_{\text{age}} = 12.2$ years). Of note, these researchers observed a significant and curvilinear relationship between self-reported engagement in MVPA (defined as engagement in at least the total of 60 minutes of MVPA daily) and grade point average. This discrepancy can be related to inaccuracies in recall and self-report bias (Adamo et al., 2009; Prince, et al., 2008). However, in alignment with the interpretation of cognitive findings, it is also possible that the discrepancy in findings between objectively assessed and self-reported MVPA reflect different associations between intermittent MVPA and MVPA of the duration, which is sufficient to stimulate aerobic metabolism. MVPA in the study of Syväoja et al. (2014) was expressed as the number of days in the past week that a teenager engaged in at least a total of 60 minutes of daily MVPA. Since structured bouts of MVPA of longer duration are more likely to be remembered (as they are embedded in a concrete context, which forms a specific memory event), this measure might have captured aerobic MVPA.

In confirmation, studies where significant associations between physical activity and academic achievement were observed focused primarily on regular aerobic exercise (Davis, et al., 2011) or engagement in structured MVPA bouts of at least 10 minute duration in addition to children's usual (school) activities (Donnelly, et al., 2009). Davis et al. (2011) found a dose-response effect of chronic aerobic exercise (accumulated in 40 and 20 minute bouts, and performed as the part of daily 3-month after-school physical activity intervention) on children's achievement in mathematics, which aligned with the effects on planning (i.e. higher order cognitive functions sub-served by cognitive control, which are key for academic success). However, their sample included only overweight and obese children who could have benefited from aerobic exercise interventions to a greater extent than healthy weight children. As such, their results are not readily generalised to the whole population of children and adolescents. Donnelly et al. (2009) found significant improvements in academic achievement (on standardised tests of reading, mathematics and spelling) in a sample of 203 7-9 year olds, following a 3-year intervention, which aimed to increase children's weekly MVPA during school hours by 90 minutes through engagement in active breaks (structured MVPA bouts of approximately 10 minutes duration). As observed in the discussion of the associations between daily MVPA and cognitive control, 10 minutes of aerobic exercise three times a week is already sufficient to increase CRF in young people (Baquet, Van Praagh, et al., 2003). Therefore, the results of Donnelly et al. (2009) are likely due to the effects of aerobic exercise rather than daily MVPA. However, the interaction effect of aerobic exercise and increments in daily MVPA on academic achievement could not be ruled out, as authors did not control for the increments in MVPA.

Given mixed results of the studies within objectively measured physical activity and academic achievement literature (Booth, Leary, et al., 2013; Harrington, 2013; Lambourne, et al., 2013; LeBlanc, et al., 2012; Syväoja, et al., 2013; Van Dijk, De Groot, Savelberg, et al., 2014), where few studies controlled for important confounders such as CRF and IQ (e.g. (Lambourne, et al., 2013; Van Dijk, De Groot, Savelberg, et al., 2014) only controlled for CRF, while none of the studies controlled for IQ), further research is needed to elucidate the relationship between objectively measured physical activity and academic achievement.

5.5.4 Strengths and limitations

Our findings add to the scant body of evidence on the relations between objectively assessed daily MVPA, children's cognitive control and academic achievement. To the author's

knowledge this was the first study to assess the relationship between objectively measured MVPA and cognitive control in preadolescent children. In contrast to previous studies of daily MVPA and cognition, we controlled for CRF using the gold standard measure of the peak oxygen uptake (Whaley, et al., 2006) and a number of other important confounders including IQ assessed with standardised tests. Therefore, we were able to ascertain if the results of our study could not be confounded by either variability in CRF or IQ, which previous studies did not. Further strengths of our study include an objective assessment of physical activity, which afforded the capture of the majority of children's daily MVPA, detailed assessment of those domains of cognitive control, which are most consistently associated with academic achievement, using sensitive tasks of inhibitory control and working memory. Further, assessment of academic achievement as well as cognitive control functions enabled us to assess potential differences in these associations between direct and applied measures of cognition. We also used standardised tests of academic achievement and tested a number of academic domains.

Several limitations of the current study have to be recognised. First, the cross-sectional design precludes causal inferences relative to findings on CRF and interference control, which could best be addressed through a randomised controlled trial. Second, we used one day of accelerometer wear as an inclusion criterion and it could be argued that this introduced larger error of measurement and therefore confounded the findings. However, when analyses were repeated excluding nine children with less than four days of wear, the results remained materially unchanged. Further, the majority of children in our study were tested during summer holidays, when the levels of physical activity are higher compared to autumn or winter months (Kristensen et al., 2008). Thus, the results may not be representative of the school year. Due to the limitations of accelerometry, we were unable to capture swimming and cycling, namely sustained aerobic physical activities, which are more prevalent during summer months due to organised summer camps and weather. Thus, our measure likely underestimated children's daily MVPA.

5.5.5 Future directions

Given the null associations between daily MVPA and cognitive control were observed in the current study, and a positive finding on the association between CRF and an indicator of inhibitory control (control of distractions), further research in the area of paediatric physical activity and cognition could be best directed into testing the effects of regular aerobic exercise

on cognitive control in young people. Such research should account for individual differences in child's daily MVPA, which can moderate its effects on cognition in alignment with the dose-response curves of the effects of MVPA on multiple health outcomes (PAGAC, 2008). At present no such studies exist, as extant RCTs did not assess baseline levels of daily objectively measured physical activity.

Table 5-1. Mean (SD) values for participants' demographic, anthropometric, CRF and physical activity data

	Girls (<i>n</i> = 37)		Boys (<i>n</i> = 44)		Combined (<i>N</i> = 81)	
	M (SD)		M (SD)		M (SD)	
Age (yrs)	8.62 (.55)		8.65 (.60)		8.64 (.57)	
SES Low (<i>n</i> , [%])	9 [24.3]		14 [31.8]		23 [28.4]	
Ethnicity (White <i>n</i> , [%])	26 [70.3]		25 [56.8]		51 [63]	
IQ ¹	110.4 (11.6)		111.9 (12.5)		111.2 (12.0)	
Height (cm)	135.5 (6.68)		135.4 (7.18)		135.4 (6.91)	
Weight (kg)	35.9 (11.8)		33.5 (8.90)		34.6 (10.3)	
BMI (kg/m ²)	19.2 (4.85)		18.1 (3.66)		18.6 (4.26)	
OW/OB (<i>n</i> , [%])	14 [37.8]		14 [31.8]		28 [34.5]	
VO _{2max} (mL*kg ⁻¹ *min ⁻¹)	40.8 (8.10)		45.1 (1.11)		43.2 (7.95)	
VO _{2max} percentile	39.4 (8.10)		35.9 (7.36)		37.5 (31.7)	
	M (SD)	Range	M (SD)	Range	M (SD)	Range
CPM	537.6 (154.9)	[289.9, 925.7]	559.0 (169.5)	[285.1, 996.7]	549.2 (162.3)	[285.1, 996.7]
Monitor wear (minutes/day)	785.0 (53.2)	[657.7, 891.7]	800.5 (58.1)	[607.0, 909.6]	793.4 (56.1)	[607.0, 909.6]
Sedentary (minutes/day)	443.0 (58.0)	[328.5, 554.2]	457.6 (69.9)	[338.9, 637.5]	450.9 (67.8)	[328.5, 637.5]
LPA (minutes/day)	259.1 (44.0)	[138.7, 339.7]	250.0 (37.8)	[162.5, 346.6]	254.1 (40.8)	[138.7, 346.6]
MVPA (minutes/day)	82.9 (26.7)	[43.2, 137.5]	92.9 (32.0)	[36.2, 158.7]	88.3 (30.0)	[36.2, 158.7]

Note. SES, socio-economic status; IQ, a composite standardized score of intelligence quotient from Woodcock-Johnson III Tests of Cognitive Abilities, Brief Intelligence Assessment (Woodcock, et al., 2001); ¹ IQ minimum = 84 (*n* = 1); OW/OB, overweight or obese category defined based on the CDC growth charts (Kuczmarski, Ogden, Grummer Strawn, & al., 2000); CPM, counts per minute; sedentary time < 100 CPM; LPA, light physical activity ≥ 100 , < 1638; MVPA, moderate-to-vigorous physical activity ≥ 1638 CPM; intensity cut points were based on age specific cut points for 8 year-olds (using a four METs threshold) developed by Freedson and first published by Trost et al. (2002).

Table 5-2. Performance on flanker task, OSPAN and academic achievement

	Mdn (IQR)	Range
Flanker Congruent		
Mean RT (ms)	506.6 (106.1) ^a	[399.1, 827.0]
Response Accuracy (%)	79.8 (16.7) ^a	[53.6, 98.8]
Flanker Incongruent		
Mean RT (ms)	571.7 (113.6) ^b	[420.9, 939.6]
Response Accuracy (%)	70.2 (18.7) ^b	[51.2, 91.7]
Flanker Interference		
Mean RT (ms)	56.8 (50.5)	[-27.6, 203.0]
Response Accuracy (%)	7.74 (12.2)	[-10.7, 34.5]
OSPAN		
Mean RT (ms)	4609.8 (1603.1)	[2093.4, 7354.4]
Response Accuracy (%)	87.5 (13.7)	[52.5, 100.0]
PCU	.73 (.25)	[.36, 1.0]
PCL	.65 (.24)	[.30, .10]
ANL	.26 (.31)	[.05, .10]
ANU	.44 (.23)	[.13, .10]
	M (SD)	Range
Academic Achievement		
Spelling	111.4 (15.8)	[79.0, 151.0]
Reading	111.5 (13.7)	[70.0, 142.0]
Math	110.5 (15.4)	[82.0, 150.0]

Note. Superscripts a, b, denote significant within-group differences across congruent and incongruent conditions ($ps < .001$); OSPAN, Operation Span Task (Turner & Engle, 1989); PCU, partial-credit unit score; PCL, partial-credit load score; ANU, all-or-nothing unit score; ANL, all-or-nothing load score; Academic achievement was assessed with the Kaufman Test of Educational Achievement, Second Edition (KTEA II; Kaufman & Kaufman, 2004) and expressed as standardised scores with the mean of 100 and an SD of 15.

Table 5-3. A summary of regression models predicting cognitive and academic performance from moderate-to-vigorous physical activity and cardio-respiratory fitness

Predictors	<i>F</i>	df1, df2	ΔR^2	<i>B</i>	SE <i>B</i>	β	<i>t</i>	95% <i>CI</i>
<i>Model 1: Incon Acc</i>	2.05	3, 77	.02					
VO _{2max}				.16	.17	.11	.93	-.18, .50
MVPA				-.06	.04	-.17	-1.42	-.15, .03
<i>Model 2: Incon MRT¹⁴</i>	1.88	5, 75	.00					
VO _{2max}				-.00	.00	-.27	-1.86†	-.01, .00
MVPA				.00	.00	.07	.60	.00, .01
<i>Model 3: Acc Interference</i>	2.54*	4, 76	.00					
VO _{2max}				-.21	.12	-.20	-1.72	-.45, .03
MVPA				-.01	.03	-.03	-.28†	-.07, .06
<i>Model 4: MRT Interference¹⁵</i>	1.65	4, 76	.00					
VO _{2max}				-.04	.02	-.22	-1.81†	-.09, .00
MVPA				-.00	.01	-.05	-.38	-.01, .01
<i>Model 5: OSPAN PCU</i>	3.99**	6, 72	.00					
VO _{2max}				-.00	.00	-.12	-1.06	-.01, .00
MVPA				.00	.00	.02	.22	-.00, .00

¹⁴ Log transformed¹⁵ Square root transformed

<i>Model 6:</i>	1.37	4, 73	.00					
<i>OSPAN ANU</i>								
VO _{2max}				.00	.00	-.02	-.14	-.01, .00
MVPA				.00	.00	-.07	-.56	-.00, .00
<i>Model 7: Spelling</i>	4.87***	5, 73	.00					
VO _{2max}				-.38	.22	-.19	-1.70	-.83, .06
MVPA				-.01	.06	-.02	-.19	-.13, .11
<i>Model 8: Reading</i>	8.73***	4, 76	.01					
VO _{2max}				-.08	.18	-.05	-.46	-.45, .28
MVPA				-.06	.05	-.13	-1.25	-.16, .04
<i>Model 9: Mathematics</i>	5.73***	6, 74	.00					
VO _{2max}				-.20	.21	-.10	-.98	-.61, .21
MVPA				-.03	.06	-.06	-.52	-.14, .08

Note. The results present third step of hierarchical regression models, where all predictors were included. All models were adjusted for wear time and CRF; Model 1 only adjusted for wear time and CRF; Model 2 adjusted for gestational age and BMI, Models 3 and 4 adjusted for ADHD ratings (ADHD Rating Scale IV; DuPaul, et al., 1998); Model 5 adjusted for age, sex and intelligence quotient (IQ; Brief Intellectual Ability index of Woodcock-Johnson III Tests of Cognitive Abilities; Woodcock, et al., 2001); Model 6 adjusted for IQ; Model 7 adjusted for birth weight and IQ; Model 8 adjusted for IQ; Model 9 adjusted for age, IQ and pubertal stage (according to secondary sex staging on pubertal questionnaire: stage I denotes pre-pubertal state and stages II and III the progression of pubertal development (Taylor et al., 2001). Incon Acc, incongruent accuracy on modified Eriksen flanker task (Eriksen & Eriksen, 1974); Incon MRT, incongruent mean reaction time, PCU, partial credit unit score on operation span task (OSPAN, (Turner & Engle, 1989); ANU, all-or-nothing unit score on OSPAN; Spelling, Reading and Mathematics assessed with the Kaufman Test of Educational Achievement, Second Edition (KTEA II; Kaufman & Kaufman, 2004); *** $p \leq .001$, ** $p \leq .01$, * $p < .05$; † $p < .09$

Chapter 6

Effects of an after-school physical activity programme on cardio-respiratory fitness and cognitive control: Preliminary findings from the FITKids2 RCT

6.1 Study 3 context

The null results from studies 1 and 2 based on two developmentally distinct samples suggested that daily MVPA is not related to cognitive control in either children (study 2) or adolescents (study 1). In contrast, positive findings on the associations between cardio-respiratory fitness and interference control in pre-adolescent children (study 2), suggested that child's aerobic capacity could benefit their attentional control, and more precisely, their ability to control distractions. Therefore, aerobic exercise rather than intermittent daily MVPA is likely needed to engender cognitive benefits in children. This hypothesis was tested in study 3 within a randomised controlled trial.

Extant but nominal studies into the effects of aerobic exercise on children's cognitive function either did not control for child's baseline physical activity (Chaddock-Heyman et al., 2013; Hillman et al., 2014; Kamijo et al., 2011) or used self-reports to assess child's physical activity (Davis et al., 2007). Self-reports are, however, inaccurate measures of physical activity in children (Adamo et al., 2009). They are also not suited for use with children younger than 10 years (Kohl et al., 2000). The effects of aerobic exercise on cognition could be confounded or moderated by the baseline levels of physical activity, as baseline physical activity has been found to moderate the effects of aerobic exercise on cardio-respiratory fitness (Baquet et al., 2007). Study 3 was uniquely designed to control for such confounding effects of objectively measured MVPA (and time sedentary) when testing the effects of an aerobic exercise intervention on cognitive control in pre-adolescent children.

The study was the result of a collaboration between the author of the thesis and Professor Hillman, a principal investigator of the FITKids2 trial. The author contributed a unique aspect to the trial, namely the inclusion of the research question on and objective monitoring of daily physical activity, which included both novel technology and expertise in accelerometry data collection, reduction and analyses. The implementation of accelerometry to the trial afforded an answer to the question whether the effects of aerobic exercise on cognitive control occur irrespective of child's baseline daily MVPA and time sedentary. The author contributed an amendment to the research protocol and was responsible for the implementation, deployment, staff training, and accelerometry data reduction on the trial. To the author's knowledge, FITKids2 was the first RCT into the effects of aerobic exercise on cognitive control in children, which controlled for objectively measured daily MVPA and time spent sedentary.

6.2 Introduction

Approximately 80% of children in Western societies are physically inactive (Currie, et al., 2012), that is not engaging in at least 60 minutes of moderate-to-vigorous physical activity (MVPA) daily; (Department of Health, 2011; U.S. Department of Health and Human Services, 2008). Physical inactivity is the main antecedent of the non-communicable diseases (Lee et al., 2012) and is crucial to children's physical (Janssen & LeBlanc, 2010) and psychological (Biddle & Asare, 2011) health. At the same time, childhood and adolescence represent the most opportune periods within which to intervene, as healthy behavioural patterns (increased physical activity and limited sedentary time) established in childhood track into adulthood (Basterfield et al., 2011; Biddle, et al., 2010; Telama, 2009).

Importantly, accumulating evidence from neurocognitive sciences also suggests that consequences of inactive lifestyle can adversely affect brain and cognitive function in children and youth (Hillman, et al., 2011; Verburgh, et al., 2014). This evidence is largely based on the cross-sectional data showing that children who are more aerobically fit also perform better on cognitive tasks, which require the up-regulation of cognitive control (i.e. higher order cognitive functions of inhibitory control, working memory (WM) and shifting which underpin learning and goal-directed behaviour; (Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Diamond, 2013; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011; Wu, et al., 2011). However, the limitation of these studies is that they cannot ascertain whether there is a causal relationship between engagement in physical activity and cognitive function. Experimental evidence from randomised controlled trials (RCTs) is needed to ascertain whether positive effects can be accrued through behavioural modification such as regular aerobic exercise.

Few studies have attempted to inspect causal effects of regular aerobic exercise on children's cognition. The results from these RCTs (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014; Kamijo, et al., 2011), which employed nine-month after-school physical activity interventions (with at least 70 minutes of MVPA) designed to improve cardio-respiratory fitness (CRF) in general population of children, suggest small to moderate increments to children's cognitive control ($ds = 0.25-0.65$). Specifically, children's performance on cognitive tasks tapping inhibitory control (a modified flanker task (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014), WM (a modified Sternberg task; Kamijo, et al., 2011) and task switching (Hillman, et

al., 2014)) showed modest to medium size improvements following participation in a nine-month after-school aerobic exercise intervention.

Although the effects of regular aerobic exercise on cognitive function are posited to be driven by the increments in CRF (Stones & Kozma, 1988; Chodzko-Zajko & Moore, 1994), the tenets of this hypothesis are yet to be confirmed (Etnier, 2006). In two of the intervention studies, the cognitive increments were paralleled by an increase in CRF (directly assessed with maximal oxygen uptake) in intervention but not the control group (Hillman, et al., 2014; Kamijo, et al., 2011). However, Chaddock et al. (2013) noted no differences between the intervention and control groups in the pre- to post-test increments in CRF. The mixed findings from these intervention studies, which used similar duration and intensity of physical activity (at least 70 minutes of MVPA during a 120 minute daily after-school aerobic exercise intervention over nine months) may partly be explained by baseline differences in daily MVPA amongst participants. However, none of these studies controlled for children's objectively measured daily MVPA at baseline, which may have confounded the results.

More data are needed to establish whether the effects of aerobic exercise interventions hold across cognitive control functions and whether they are indeed driven by increments in CRF. For example, only one study examined the effects of an after-school aerobic exercise intervention on multiple indices of cognitive control (Hillman, et al., 2014) but did not include a pure measure of WM. That is, the switch task employed in this study engages WM, as well as inhibitory control and cognitive flexibility. Therefore the task design precludes inferences specific to WM. Based on the executive function hypothesis, which posits that the effects of CRF are specific to these cognitive functions, which up-regulate cognitive control (Kramer, et al., 1999), the effects of an aerobic exercise intervention should hold across tasks, which engage different aspects of cognitive control (e.g., inhibitory control, WM, task switching). Only one study inspected such effects in relation to WM, the cognitive construct, which is closely related to academic performance in children (Alloway & Alloway, 2010; Borella, et al., 2010; St Clair-Thompson & Gathercole, 2006). However, this study found only partial effect of the chronic aerobic exercise intervention on these task conditions, which required minimal or relatively low cognitive load.

The modified Sternberg task used by Kamijo et al. (2011) is a delayed recognition task and therefore may facilitate active rehearsal of the material held in memory. In contrast, dual tasks prevent rehearsal by engaging participants in a distraction task (e.g., reading, math operations)

during the delay period. Thus, the latter tasks likely require greater engagement of executive attention in order to correctly recall the material despite the distraction.

In the present study we investigated the effects of a nine-month after-school aerobic exercise RCT: Fitness Improves Thinking 2 (FITKids2, NCT01334359) on two indices of cognitive control (i.e., inhibitory control and WM), which are most consistently related to academic achievement (Alloway & Alloway, 2010; Blair & Razza, 2007; Borella, et al., 2010; Espy, et al., 2004; St Clair-Thompson & Gathercole, 2006) and CRF (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Moore, et al., 2013; Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011). In contrast to previous studies, we also controlled for objectively measured baseline daily MVPA and time sedentary. FITKids2 trial was specifically designed to increase CRF by engaging children in daily 120 minutes of mostly aerobic, age appropriate physical activities, with at least 70 minutes spent in MVPA (recorded with heart rate monitors) and to inspect its effects on children's cognitive function. The programme curriculum was based on Coordinated Approach to Child's Health (CATCH; McKenzie et al., 1994) and included a combination of aerobic, muscular strength and endurance activities, physically active games, a brief educational component, a snack with a water break, and elements of goal setting. We hypothesised that participation in the FITKids2 after-school aerobic exercise intervention would result in increments in cognitive control (as indicated by faster response latencies and higher accuracies on the task of inhibitory control, and greater accuracy on a WM task) and CRF. Furthermore, consonant with the cardiovascular fitness hypothesis (Chodzko-Zajko & Moore, 1994; Etnier, 2006), we hypothesised that the improvement in cognitive control will be related to pre- to post-test increase in CRF.

6.3 Methods

6.3.1 Study design

Eight to nine year-olds (grades 2 to 4) from seven schools in the east-central Illinois, USA were targeted for recruitment. Those who expressed interest were further screened for physical disabilities, learning difficulties, the use of medication that could affect metabolism or cognitive function, and the presence of neurological or psychiatric disorders, including clinical diagnosis of the attention deficit and hyperactivity disorder (ADHD; as disclosed by parents). In addition, legal guardians completed the ADHD Rating Scale IV (DuPaul, et al., 1998). Following the recruitment, 44 eligible children were pair randomised by an independent

researcher (pairs were matched on age, sex, parental socio-economic status (SES), and VO_{2max}) to either the FITKids2 aerobic exercise intervention ($n = 22$) or a waitlist control group ($n = 22$; figure 6-1). To be included in the study children had to: 1) have an intelligence quotient (IQ) of ≥ 85 as assessed by the Woodcock-Johnson III Tests of Cognitive Abilities, Brief Intelligence Assessment (Woodcock, et al., 2001), 2) be pre- or peri-pubescent (as indicated by parental ratings of child's pubertal stage not greater than 2 on a pubertal assessment scale (Taylor, et al., 2001) according to the criteria described by Tanner (1962)), 3) contribute at least one day of valid accelerometer data (≥ 10 hours of wear). Socio-economic status (SES) was assessed with a trichotomous index based on parental reports of: 1) child's participation in free or reduced price lunch programme at school, 2) the highest level of education obtained by mother and father, and 3) the number of parents who work full time (Birnbaum, et al., 2002).

FITKids2 is an aerobic exercise RCT (trial identifier NCT01334359), which followed from FITKids trial initiated in 2009. FITKids2 started in 2013 and incorporated revised cognitive methods (for example, a new WM task and new neuroimaging methods were included). The data for the present study were collected between June 2013 and May 2014. Immediately after randomisation parents of the control participants were requested in writing that their child maintained his or her regular after-school routine. All children completed a two-day testing protocol pre- and post-intervention and were provided with a \$100 incentive at pre-test and post-test. Following baseline assessments the control group was not contacted again until the post-test. The FITKids2 after-school aerobic exercise intervention was provided at no cost and children received free transport to the intervention centre at the University of Illinois at Urbana-Champaign. The study was conducted over the fall and spring semesters of the 2013/2014 school year. The Institutional Review Board of the University of Illinois at Urbana-Champaign approved the study. Parents provided written consent and children provided written assent.

6.3.2 Participants

Out of 44 study participants, 32 children (16 in intervention group; 18 girls, $M_{age} = 8.64$, $SD = .58$) were retained for the analyses (figure 6-1). Four dropped-out, three were excluded due to missing cognitive data, four performed at or below chance on cognitive tasks and one child was excluded based on a ≥ 85 cut-off on the Brief Intellectual Ability of Woodcock-Johnson III Tests of Cognitive Abilities (Woodcock, et al., 2001). All children provided at least one valid day of accelerometer data (i.e. ≥ 10 hours of wear).

6.3.3 FITKids2 physical activity intervention

A 2-hour after-school aerobic exercise intervention was offered on 157 (92%) out of 170 school days (between August 2013 and May 2014). The intervention was designed to improve CRF through engagement in a variety of age appropriate physical activities. The sessions were held in a gymnasium on the University premises and included at least 70 minutes of intermittent MVPA (recorded by E600 Polar heart rate [HR] monitors; Polar Electro, Finland and values were inspected daily by the staff). Sessions commenced with 25 minutes of physical activities focused on specific health-related fitness component (i.e., CRF, muscular strength). A 10-15 minute educational component followed (topics included for example, goal setting, self-management) during which children were provided with a healthy snack. Following the educational component, children engaged in approximately 45-50 minutes of moderate-to-vigorous intensity physical activities, which included instant activities designed to increase the heart rate (e.g. jumping jacks, gallop, hopping), game play (e.g. tag, mingle mingle similar to musical chairs, fitness scavenger hunt, etc.) or sport activities (e.g., dribbling a basketball, catch fly balls) and concluded with a cool down. The programme curriculum followed the protocol used in Child and Adolescent Trial for Cardiovascular Health (CATCH; Luepker, et al., 1996; McKenzie, et al., 1994; Nader, et al., 1999). CATCH is based on a social learning theory (Bandura, 1977) and combines educational, behavioural and environmental elements to promote physical activity engagement in children and adolescents. The FITKids2 intervention was led by trained research staff. The atmosphere was cooperative but included self-challenges to maintain motivation (Luepker, et al., 1996).

6.3.4 Measures

6.3.4.1 Anthropometric assessment

Height and weight were measured while children were in lightweight clothing and with running shoes on. Standing height was assessed with a Seca telescopic stadiometre model 220 (Seca, Birmnigham, UK) to the nearest millimetre. Weight was measured with a Seca 769 electronic column scale (Seca, Birmnigham, UK). BMI ($\text{weight (kg)/height(m)}^2$) percentiles were calculated based on Centers for Disease Control growth charts (Kuczmarski, et al., 2002).

6.3.4.2 Accelerometry

Physical activity was directly measured over seven consecutive days at baseline (between 12 and 0 weeks prior to the start of the intervention) using a triaxial ActiGraph accelerometer model wGT3X+ (ActiGraph, Pensacola, FL, USA). Although the wGT3X+ detects

acceleration in all three axes, given the limitations in current intensity thresholds, this research focused on vertical acceleration within the full scale range of ± 6 g with a frequency response of 0.25–2.50 Hz. Participants wore the devices on the waist at the right anterior axillary line on a nylon belt. Data were collected at 100 Hz resolution. Raw .gt3x+ data files were integrated into 15 second epochs using ActiLife software (versions 6.7.1 to 6.10.0 and a firmware version 2.2.1; ActiGraph, Pensacola, FL, USA). Epoched data files were subsequently processed to derive outcome variables using a custom made data reduction software (KineSoft, version 3.3.76, Loughborough, UK; <http://www.kinesoft.org>). Non-wear time was defined as 60 minutes of consecutive zero counts, allowing for 2 minutes of non-zero interruptions (Troiano, et al., 2008). Files with at least one day and ≥ 10 hours of accelerometer wear were included in the analyses. To account for the overnight wear, the analyses were limited to activity data from 6am to 11pm. The variables of interest were: MVPA, defined based on age specific cut points for 8 years old children developed by Freedson and published by Trost et al. (2002), using four metabolic equivalents (MET) as a threshold to account for a higher resting energy expenditure in children (Harrell, et al., 2005; Roemmich, et al., 2000). Sedentary time was defined as < 100 CPM, and light physical activity as $\geq 100 < 4$ METs.

6.3.4.3 Cardio-respiratory fitness

The maximal oxygen consumption (VO_{2max}) was measured during a maximal graded treadmill exercise test, using a computerised indirect calorimetry system (ParvoMedics True Max 2400, Sandy, UT, USA). Averages of VO_{2max} and respiratory exchange ratio (RER) were taken every 20 seconds. A modified Balke Protocol was employed, while children were walking or running on a motor driven treadmill (LifeFitness 92T, Schiller Park, IL, USA). The speed was kept constant, while a gradient was increased by 2.5° every 2 minutes until volitional exhaustion. Heart rate (HR) was monitored throughout the test with a polar HR monitor (Polar WearLink+31; Polar Electro, Finland). Ratings of perceived exertion were taken every two minutes with the children's OMNI scale (Utter, et al., 2002). Maximal oxygen consumption was expressed in $mL \cdot kg^{-1} \cdot min^{-1}$. VO_{2max} was determined based on maximal effort as indicated by a plateau in oxygen consumption defined as less than $2 mL \cdot kg^{-1} \cdot min^{-1}$ despite an increase in workload (Whaley, et al., 2006) or one of the following indicators: 1) a HR ≥ 185 beats per minute (Whaley, et al., 2006), 2) a HR plateau (Freedson & Goodman, 1993); 3) RER ≥ 1.0 (Bar-Or, 1983); and/or 4) a score of ≥ 8 on the children's OMNI scale (Utter, et al., 2002). VO_{2max} percentiles were computed based on normative data provided by Shvartz and Reibold (1990). High and low fit groups were defined as below the 30th and above the 70th percentile,

respectively. Pre- to post-test change scores were also computed for VO_{2max} relative and VO_{2max} percentile (i.e. post-test – pre-test).

6.3.4.4 Inhibitory control

Inhibitory control was assessed with a modified Eriksen flanker task (Eriksen & Eriksen, 1974). This task provides a measure of children's ability to suppress distractors and to attend to relevant information (Eriksen & Eriksen, 1974; Friedman & Miyake, 2004; Mezzacappa, 2004). Participants were asked to respond as quickly and accurately as possible with a corresponding thumb press to the directionality (left or right) of centrally positioned fish amid an array of four flankers (fish). All the stimuli subtended a horizontal visual angle between two outside positions of 14.8° and a vertical visual angle of 3.2° . Stimuli were presented focally on a computer screen from a distance of one meter using Neuroscan Stim 2 software (Compumedics, Charlotte, NC). On congruent trials, the flankers pointed in the same and on incongruent trials in the opposite direction to the target fish. Congruent and incongruent trials were equiprobable and randomly distributed. Upon completion of 40 practice trials, participants were presented with 168 (2 x 84) experimental trials. The stimulus duration was 250 ms with randomly distributed and equiprobable inter-stimulus intervals of 1600, 1800 and 2000 ms. Individual reaction times (RTs) shorter than 200 ms were discarded. The congruent condition leads to faster and more accurate responses as it places lower demands on cognitive control (Eriksen & Eriksen, 1974; Eriksen & Schultz, 1979; Hillman, et al., 2009). The incongruent condition places higher demands on cognitive control, due to the interference from the flanking stimuli, which compete for attentional resources with the target (Eriksen & Eriksen, 1974; Kramer, et al., 1994; Spencer & Coles, 1999). This is reflected in longer response latencies and lower accuracies. In the current study, we measured mean reaction time (RT) and accuracy on congruent and incongruent conditions at both pre- and post-test. In addition, mean RT and accuracy interference scores were computed by subtracting the congruent from incongruent values (RT) and incongruent from congruent values (accuracy). Last, change scores in cognitive performance on the reaction time (pre-test – post-test) and accuracy measures (pre-test – post-test) were also calculated. The flanker paradigm has been well established as a robust measure of inhibitory control in cognitive psychology based on multiple replications of the congruency effect (Botvinick, et al., 2001; Eriksen, 1995; Friedman & Miyake, 2004; Gratton, et al., 1992; Rueda, et al., 2004; Salthouse, 2010) and has shown high factor loadings on resistance to interference in the latent variable analyses ($\beta = .82$; Friedman & Miyake, 2004). Performance on this task is sensitive to both age-related (Checa &

Rueda, 2011; Ridderinkhof & van der Stelt, 2000; Ridderinkhof, et al., 1999; Rueda, et al., 2004; Rueda, et al., 2005; Salthouse, 2010; Stins, et al., 2004; Stins, et al., 2007; van Leeuwen, et al., 2007) as well as CRF-related differences in children (Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011).

6.3.4.5 Working memory

WM was assessed with the Operation Span Task (OSPAN; Turner & Engle, 1989). OSPAN is a WM span task, which evaluates the ability to maintain memory representations and control attention in face of distractions (Conway, et al., 2005). In the OSPAN task participants were presented with individual words printed on a computer screen, followed by a simple arithmetic problem (for example, $1 + 2 = 3$), which constituted a single trial. Participants were instructed to read both aloud and to indicate whether a solution to an arithmetic problem was correct by a corresponding thumb press on a response pad (left for incorrect, right for correct). The task set concluded with a recall phase where participants were required to write down all to-be-remembered words in the order of presentation. The number of trials per set varied between one and four. All participants completed four blocks of four sets of trials, one for each set size (1, 2, 3 and 4-trial sets) presented at random; in total 40 word-arithmetic operation trials across 16 sets. Stimuli were presented focally on a computer screen from a distance of one meter using Neuroscan Stim 2 software (Compumedics, Charlotte, NC). Words were presented for 1000 ms, followed by an inter-stimulus interval of 1100 ms and the onset of an arithmetic problem presented for up to 10 seconds. A cut-off of 50% accuracy on arithmetic problems was set to ensure that arithmetic task successfully prevented mental rehearsal. Albeit lower than recommended accuracy cut-off for young adults (Conway, et al., 2005), the adopted accuracy cut-off preserved a sample size and proved to be adequate in previous research with children of similar age (Drollette, Scudder, Raine, Moore, Pontifex, et al., 2014). In the present study two scoring methods based on partial credit unit score and all-or-nothing unit score criteria were employed (see (Conway, et al., 2005) for a detailed review of WM span scoring methods). Partial credit unit (PCU) scoring method awards points for task sets in which at least some items were correctly recalled and does not penalise for incorrect recall sequence. PCU was expressed as the average of proportions of items correct to a set size, across all sets. In contrast, in all-or-nothing unit scoring the points were only awarded for the task sets where all items were correctly recalled in a correct serial order. All-or-nothing unit score (ANU) was expressed as the proportion of correctly recalled items per set averaged across sets in which all items were correctly and sequentially recalled. The PCU scoring method was chosen due to its superior

reliability over other scoring methods (Conway, et al., 2005). In contrast, ANU is a more demanding scoring method and therefore more robust in differentiating performance at the higher end of cognitive demands, namely during these task conditions which require highest engagement of cognitive control. Although two other scoring methods are available (based on load weighted scoring), they are highly correlated with credit unit scoring within each scoring category (partial or all-or-nothing). Therefore, the analyses were limited to unit-load scoring methods. Change scores were computed by subtracting pre- from post-test performance. OSPAN has high test-re-test reliability ($r = .88$; Klein & Fiss, 1999) and good convergent validity as assessed against other WM span tasks ($r_s = .40$ to $.60$; Kane, et al., 2004).

6.3.5 Statistical analyses

The significance level was set at .05. The primary outcomes assessed were mean RT and accuracy on congruent and incongruent task conditions on the flanker task and PCU and ANU scores on OSPAN task of WM. Group differences at pre- and post-test on demographic and anthropometric variables were analysed with Mann-Whitney U-tests, chi-square and Fisher's exact tests, where appropriate. Pre- to post-test changes in BMI and VO_{2max} were evaluated with Wilcoxon signed rank test. Pre- to post-test changes in cognitive variables were examined with repeated measures analyses of variance with Time (pre- and post-test) as within subject factor. Intervention effects on cognitive outcomes were inspected with 2 (Group: Intervention vs Control) x 2 (Time: pre- vs post-test), and 2 (Group: Intervention vs Control) x 2 (Time: pre- vs post-test) x 2 (Congruency: congruent vs incongruent) mixed effects repeated measures ANOVAs. Missing values at post-test on OSPAN task for one subject in the intervention group were replaced with a carry-forward method. Spearman rank correlation coefficients were used to assess whether adherence to the intervention was related to change in BMI, and cognitive outcomes. IBM SPSS Statistics version 20.0.0.1 was used to conduct all the analyses.

6.4 Results

6.4.1 Baseline characteristics

Baseline demographic characteristics are presented in table 6-1. Children in the intervention group were on average 8.73 years old ($SD = .64$; 62.5% girls), while those in the control group were 8.55 years old ($SD = .52$; 50% girls). The mean age at post-test was 9.50 years ($SD = .67$) and 9.27 years ($SD = .50$), respectively. At pre-test, four children (25%) in the intervention and seven children in the control group (43.8%) were overweight or obese. However, no statistically significant between-group differences in either BMI or the proportion of

overweight/obese were noted ($ps > .26$). Similar proportions of overweight and obese in both groups were observed at post-test (intervention: 31.3%, $n = 5$ and control: 50%, $n = 8$, $ps \geq .32$). At pre-test, a large proportion of children in both intervention (50%, $n = 8$) and control (43.8%, $n = 7$) groups were classified as unfit (i.e. below the 30th percentile relative to published norms; $p = .80$). No significant change in the levels of CRF was observed at post-test (50%, $n = 8$ versus 53.3%, $n = 9$; $p \geq .56$). The samples came from families with predominantly medium or high SES (81.3%, $n = 13$, and 62.6%, $n = 10$, intervention and control group, respectively; $p = .21$).

Children in both groups wore an accelerometer for a median of six days. Intervention and control groups did not differ in the number of days of wear ($ps > .27$). All children in the intervention group and 93.7 % ($n = 15$) of controls contributed at least 4 days of accelerometer data ($p = 1.0$). Children wore an accelerometer for an average of 13.4 hours ($SD = .93$) and 13.2 hours ($SD = .91$) between 6am and 11pm in the intervention and control group, respectively ($p = .59$). Groups did not differ on demographic (age, sex, SES), anthropometric variables, IQ or pubertal stage at pre-test ($ps \geq .11$). There were no significant differences at pre-test between intervention and control groups in VO_{2max} (absolute, relative and percentile), time sedentary or physical activity (wear time, CPM, sedentary time, light physical activity and MVPA; $ps \geq .26$). Intervention and control groups also did not differ in performance on cognitive tests at pre-test ($ps > .18$; table 6-4).

6.4.2 Programme evaluation

No significant differences between intervention and control groups were noted at post-test on SES, pubertal stage ($ps > .15$), BMI, or VO_{2max} (absolute, relative and percentile; $ps \geq .30$). Cognitive performance characteristics of both groups at pre- and post-test are presented in table 6-3. No group differences were observed at post-test on any of the cognitive measures ($ps > .21$; table 6-4).

Attendance. Participants attended a median of 90.3% of the sessions offered ($IQR = 23.1$ percent), which equated to a median of 135.5 days ($IQR = 33.2$ days) out of 157 total days of the intervention. The median number of days when participants were present at the intervention was 106 ($IQR = 49$; i.e. 67.5% of the total intervention days offered).

Intensity of physical activity during the FITKids2 intervention sessions. During intervention sessions, children maintained an average heart rate (HR) of 146.1 beats per minute (bpm; $SD = 6.82$), which corresponds to moderate intensity of physical activity (Whaley, et al.,

2006). The majority of time during an intervention session was spent either in ($Mdn = 26.1$ minutes, $IQR = 19.2$, $Mdn = 58.3\%$, $IQR = 20.1$) or above ($Mdn = 18.0$ minutes, $IQR = 13.6$, $Mdn = 34.2\%$, $IQR = 28.4$) the target heart rate zone (i.e. the HR within 55-80% of the maximum HR, which was ascertained during a maximal graded treadmill exercise test at pre-test).

Changes in cardio-respiratory fitness and adiposity. Pre- to post-test within group differences in anthropometric and VO_{2max} variables are presented in table 6-2. No significant changes from pre- to post-test were noted on VO_{2max} relative or VO_{2max} percentile in the intervention group ($ps \geq .48$). However, a trend for a decline in VO_{2max} relative ($Z = -1.5$, $p = .13$) and percentile ($Z = -1.76$, $p = .078$) was observed in the control group (table 6-2). BMI increased in both, the intervention ($\Delta Mdn = .50$, $Z = 2.48$, $p = .013$) and the control group ($\Delta Mdn = .90$, $Z = 3.21$, $p = .001$); groups did not differ in the magnitude of this increase ($\Delta Mdn = -.29$, $Z = 1.02$, $p = .32$). In contrast, BMI percentile significantly increased in the control ($Z = 2.17$, $p = .03$) but not in the intervention group ($p = .53$).

6.4.3 Changes in cognitive performance and treatment effects

Table 6-3 presents within group comparisons for cognitive variables. No pre- to post-test differences in mean RT on the congruent task condition of the flanker task were noted for either the control ($p = .69$) or the intervention group ($p = .06$) and no significant Group by Time interaction for mean RT on the congruent trials of the flanker task was observed ($p = .079$; figure 6-2). Both control ($\Delta M = 9.23$, $SE = 3.27$, $F(1,15) = 7.97$, $p = .01$, $\eta_p^2 = .35$) and the intervention ($\Delta M = 9.60$, $SE = 3.32$, $F(1,15) = 8.35$, $p = .01$, $\eta_p^2 = .36$) group improved their accuracy on the congruent task condition and no Group by Time interaction was observed ($p = .94$).

In contrast, on the incongruent task condition, only intervention group showed increments in accuracy ($\Delta M = 13.5$, $SE = 3.76$, $F(1,15) = 13.0$, $p = .003$, $\eta_p^2 = .46$; Control: $p = .07$) and speed ($\Delta M = 59.9$, $SE = 24.2$, $F(1,15) = 6.15$, $p = .025$, $\eta_p^2 = .29$; Control: $ps = .78$). For the mean RT, a significant Group by Time interaction ($F(1, 30) = 4.69$, $p = .038$, $\eta_p^2 = .13$) indicated that intervention had a positive effect on mean RT (figure 6-3). When formally tested, a three-way interaction of Group by Time by Congruency on the mean RT was not statistically significant ($p = .44$), suggesting that the effect of the intervention on mean RT was not specific to the incongruent task condition (figures 6-4 and 6-5). No effect of Group by Time interaction was observed for accuracy ($p = .27$).

Intervention, but not the control group ($p = .06$), significantly improved on WM when partial ($\Delta M = .11$, $SE = .04$, $F(1,15) = 6.96$, $p = .02$, $\eta_p^2 = .32$) but not all-or-nothing credit scores were considered (Intervention: $p = .09$, Control: $p = .12$). However, Group by Time interaction in the mixed effects ANOVAs was not statistically significant ($p = .99$).

6.4.4 Attendance, changes in adiposity and task performance

Percent attendance, total days in the intervention or days when a child was present at the intervention were not related to changes in BMI ($ps \geq .19$). The total number of days in the intervention was positively related to the increase in accuracy on the congruent condition of the flanker task ($r_s = .50$, $p = .049$). Attendance at the intervention (percent of time, total days or the number of days present) was not further related to cognitive performance ($ps \geq .07$).

6.5 Discussion

6.5.1 Summary of findings

This, to the author's knowledge, is the first study to inspect the effects of an aerobic exercise intervention on cognitive control in children while also controlling for the baseline levels of objectively measured physical activity. The engagement in a nine-month FITKids2 after-school aerobic exercise intervention had a positive effect on one indicator of children's inhibitory control but not on WM. That is, relative to the control group, intervention group showed greater improvement on the speed of responding while also improving in accuracy from pre- to post-test on the incongruent condition of the flanker task. As no significant increments in CRF were noted in either group, these effects were not driven by the increments in CRF. However, compared to the intervention participants, the control group increased in BMI percentile, which suggests an overall protective effect of the FITKids2 aerobic exercise intervention against increases in BMI.

6.5.2 The effects of the FITKids2 aerobic exercise intervention on measures of cognitive control

Our findings on the effects of the FITKids2 intervention on a measure of inhibitory control align with the previous research testing the effects of the prior FITKids intervention in a separate group of participants (Hillman, et al., 2014). Hillman et al. (2014) evaluated the effect of the FITKids intervention in 221 children. The intervention group increased in accuracy of the incongruent task condition of the modified flanker task, but no differences were noted in the change in reaction time between the two groups. In our study, the increase in speed of

performance was accompanied by an increase in accuracy, thus indicating no accuracy by time trade off. Both measures are indicative of the efficiency of inhibitory control (Davidson, et al., 2006), therefore our findings are congruent with the effects observed by Hillman et al. (2014). Since only the intervention group improved in the accuracy on the incongruent task condition, it is also possible that the lack of the intervention effect on the measure of accuracy was due to the small sample and insufficient power to detect the effect. Alternatively, reaction time may have been an overall better marker of intervention effect on child's cognitive performance in this study. That is, a similar trend for an interaction effect was observed for congruent mean RT, where intervention group increased in speed (figure 6-2 and 6-5), while no change in mean RT was observed in the control group for either task condition (figure 6-4). In confirmation, we noted no effects of intervention on the task of WM, where performance was purely based on accuracy of recall (time of recall is not measured in the OSPAN task; table 6-3). This would suggest an overall generalised effect of aerobic exercise intervention on speed of performance across congruent and incongruent task conditions in our sample of pre-adolescents. Paired with increments in accuracy, this finding suggests an overall increase in performance efficiency. However, due to the small sample size and only a trend for significance on the congruent condition of the flanker task, this interpretation remains speculative and needs to be evaluated with a larger sample size.

Our findings cannot confirm or refute the executive function hypothesis (Kramer, et al., 1999), which posits that the effects of aerobic exercise are specific to executive functions (cognitive control is another term used to denote executive functions), as the interaction between Time, Group and Congruency was not significant. As already explained, evident from the interaction plots for both congruent (figures 6-2) and incongruent trials (figures 6-3), intervention group showed similar pattern in the decrease in mean RT also on the congruent trial, while no such pattern was observed in the control group. Previous studies on CRF and cognitive control in children found both general and specific effects on cognitive function (Hill, Williams, Aucott, Thomson, & Mon-Williams, 2011; Scudder, et al., 2014), with a stronger effect emerging for incongruent relative to congruent trials. Thus, it is possible that the lack of the effect of the intervention on mean RT to congruent trials in our study was due to the limited power. Consequently, based on current findings the inferences on the specificity of the aerobic exercise intervention on cognitive control cannot be made.

The main finding that aerobic exercise intervention had a positive effect on an indicator of inhibitory control (mean RT on the incongruent task condition) could have implications for

children's scholastic performance, and self-regulation, which is important to future behavioural adaptation in terms of job success and health (Moffitt, et al., 2011). That is, inhibitory control is most closely related to self-regulation (Rueda, et al., 2005; Sarkis, et al., 2005; Sporer, Brunstein, & Glaser, 2006; White, et al., 2011). In turn, children's ability to self-regulate cognition, behaviour and emotions can define their future job and health outcomes (Moffitt, et al., 2011). Moffitt et al. (2011) investigated how observed levels of self-control (a combined score from observations by researchers, teachers and parents) predicted health and job success, amongst other indicators of 1,037 children from 3 years of age until mid-adulthood (32 years). Poorer self-control during childhood predicted a gradient of worse health and less earnings in adulthood, after controlling for socio-economic background and intelligence. That is, children with poorer self-control were less able to plan effectively and were more prone to poor health choices. Importantly, children who improved their self-control from childhood to adulthood also had better outcomes in adulthood. Our measure of inhibitory control closely relates to effortful control, namely this aspect of self-regulation, which helps children regulate emotional responses to conflict and frustration (Rueda, et al., 2005). Likewise, inhibitory control has been positively associated with and predictive of academic performance in mathematics and reading in early school years (Blair & Razza, 2007; Espy, et al., 2004). In sum, our findings from the FITKids2 intervention confirm the positive effect of the FITKids intervention reported by Hillman et al. (2014) on this measure of cognitive control, which has relevance to academic achievement, and self-regulation.

In contrast, no effects of the FITKids2 intervention were noted on measures of WM, which were based on accuracy. As explained earlier, the null findings may reflect the specificity of intervention effect on reaction time in our sample. Both intervention and control groups improved their performance on the WM task and no group differences in the degree of this improvement were noted. Thus, the observed performance increments are likely due to cognitive development. Our findings stand in contrast to those reported by Kamijo et al. (2011), and Fisher et al. (2011), who found significant effects of physical activity interventions (FITKids after-school aerobic exercise programme and a 10-week physical education programme, respectively) on digit and spatial span tasks. The discrepant findings could be due to the small sample size and insufficient statistical power of our study to detect the effect. Alternatively, the discrepancy in findings could also result from differences in the cognitive tasks. For example, the operation span task used in the current study relies on verbal memory for words, which is more prone to the greater ability to cluster verbal material with

development. In contrast, both tasks used by Kamijo et al. (2011) and Fisher et al. (2011) do not depend on verbal memory and thus are independent of child's ability to conceptually cluster words. A modified Sternberg task used by Kamijo et al. (2011) involves remembering digit sequences, while the Spatial Memory Task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) used in the study by Fisher et al. (2011) requires tracing the sequence of visual patterns on the screen. Given the importance of WM for children's academic performance (Alloway & Alloway, 2010; Borella, et al., 2010; St Clair-Thompson & Gathercole, 2006), further research is needed to elucidate the effects of aerobic exercise interventions on verbal and non-verbal aspects of WM.

6.5.3 Evaluation of the FITKids2 intervention: Effects on cardio-respiratory fitness

Contrary to our hypothesis, we found no significant improvements on the measures of CRF. Thus, the null findings limit the inferences from our study on the underlying mechanisms, which could drive the effect of the nine-month aerobic exercise intervention designed to improve CRF on cognitive control in children. However, ours is a pilot study and the null findings are likely related to the low power (48% in the current study) to detect the hypothesised effects. In the current study a sample of 62 participants would be necessary to detect the effects of the intervention on CRF (assuming the effect size of 0.3, alpha level of .05 and 80% power and mixed effects design; Soper, 2014). Based on the previous recruitment of the cohorts to the FITKids RCT, the expected sample size in the present cohort was 75 participants. Assuming a 15% drop out rate, our study would have been sufficiently powered to detect the hypothesised effects (81% power, assuming the same parameters). In confirmation, findings from the literature generally suggest that increments in cognition are paralleled by increments in CRF (Davis, et al., 2007; Hillman, et al., 2014; Kamijo, et al., 2011). Only one other study (Chaddock-Heyman, et al., 2013) based on a subsample of children from the previous FITKids trial found no significant increase in CRF but their study was also underpowered ($n = 23$). In contrast, published results from the entire FITKids trial ($n = 221$) indicate that the FITKids intervention had a positive effect on children's CRF, which paralleled the positive effects on cognition. Due to the lower intake of participants to the study, the present FITKids2 trial provides pilot data with the ongoing data collection, which will allow for future properly powered analyses (with $n = 58$ subjects at the intake, assuming 15% drop out, the combined sample size of 83 participants in the future analyses will yield 91% power) to further answer the important questions on the mediating role of CRF in these associations.

Lastly, the inclusion of baseline data of objectively measured physical activity allowed us for the first time to assess if the differences in the intervention outcomes were not confounded by the group differences in baseline levels of daily MVPA. This is an important strength of the study, as some evidence suggests a positive association between objectively measured MVPA and selective and executive attention (which both require cognitive control) in adolescents (Booth, Tomporowski, et al., 2013). In addition, we evidenced no differences between intervention and the control group in the time spent sedentary at baseline. This is important, because if such differences were noted, it could be argued that children, who are more sedentary may have also responded better to the intervention (Tremblay, et al., 2011). By controlling for the baseline levels of physical activity and time spent sedentary we evidenced that this was not the case.

6.5.4 Strengths and limitations

This study used a gold-standard experimental design, the RCT, which afforded the assessment of causal relationships between FITKids2 aerobic exercise intervention and cognitive function. The measures used in our study were carefully chosen and specifically designed to up-regulate cognitive control requirements in the population of preadolescent children, which proved valid as measure of inhibitory control in previous research with children (Drollette, Scudder, Raine, Moore, Saliba, et al., 2014; Hillman, et al., 2014; Rueda, et al., 2005; Scudder, et al., 2015; Stins, et al., 2004; van Leeuwen, et al., 2007). Another strength of the study is high adherence to the intervention. We also objectively measured the intensity of the physical activity during the intervention and evidenced fidelity of the intervention as indicated by heart rate recordings and no increases in BMI percentile in the intervention group. Further, we included multiple measures of cognitive control, as such an approach allows for stronger inferences about the effects of aerobic exercise intervention on the tasks, which engage cognitive control. Accordingly our findings contribute to the scant body of literature on the effects of aerobic exercise intervention on WM in children.

Our study also has several limitations. The most important limitation is related to the small sample size and consequently insufficient power to detect small effects. Therefore, the results of this study must be interpreted with caution. Replication of the study with a larger sample size will afford testing of the possible mediating effects of CRF on children's cognitive control. It is also possible that other factors could mediate the effect of the intervention on children's cognition, such as potential increases in self-efficacy, attention to instruction, and the overall

effect of the enriched intervention environment (e.g., social interactions with peers and the University staff, stimulating environment). These effects could be best assessed with an addition of another intervention arm, an attention control group, which would involve similar interactions with staff and peers but in the context of sedentary activities. A three-arm intervention was not feasible in the current study based on the projected participant intake. Last, no follow-up measures were taken, therefore inferences on the sustainability of the intervention effects on cognition cannot be made.

6.6 Conclusions

Participation in a nine-month FITKids2 aerobic exercise intervention improved children's inhibitory control. Although based on limited sample, our findings replicated the results of previous research (Hillman, et al., 2014) and provide further evidence for the potential of a structured aerobic exercise intervention to improve some cognitive indicators in pre-adolescent children. As such, these findings may have implications for policies and initiatives advocating increasing structured MVPA (akin to aerobic exercise) at school, through the inclusion of MVPA breaks and quality PE with 50% time dedicated to MVPA (IOM, 2013). Our findings cannot elucidate the underlying mechanisms of these increments. Although no effects of the FITKids2 intervention on CRF were noted, the intervention had a positive effect on off-setting an increase in BMI percentile. Future research should attempt to provide further insights into the possible mediating mechanisms of the effects of aerobic exercise intervention on cognitive control in children.

6.7 Acknowledgements

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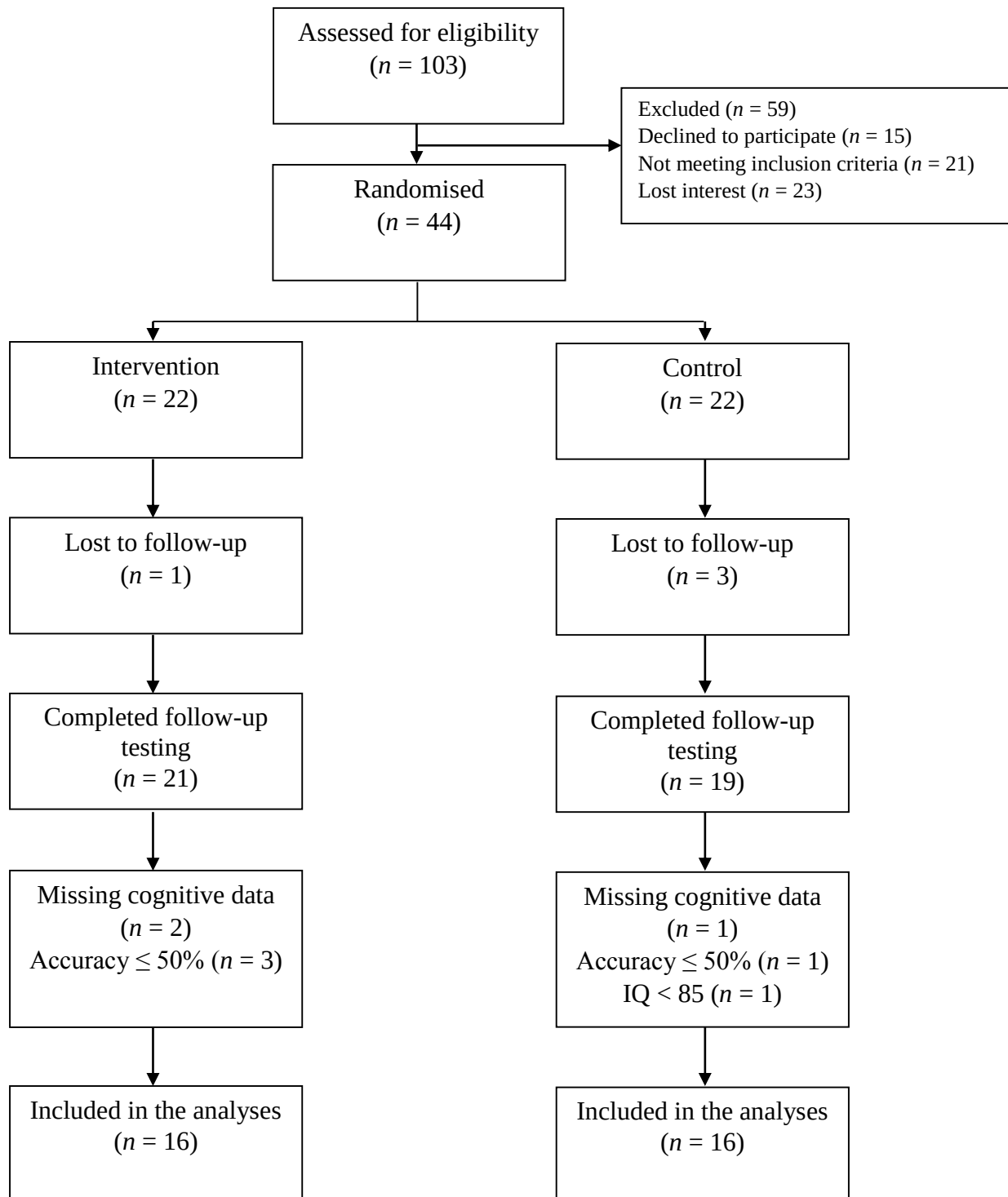


Figure 6-1. The flow of participants through the randomised controlled trial.

Table 6-1. Baseline characteristics of intervention and control groups

	Intervention	Control
	M (SD)	M (SD)
	<i>n</i> = 16	<i>n</i> = 16
Age	8.73 (± .64)	8.55 (± .52)
Gender (boys, girls)	6, 10	8, 8
Sexual maturation (<i>n</i> , [%])		
Pubertal Stage 1	13 [81]	15 [94]
Pubertal Stage 2	3 [19]	1 [6]
SES (<i>n</i> , [%])		
High	5 [31]	1 [6]
Medium	8 [50]	9 [56]
Low	3 [19]	6 [38]
Race (<i>n</i> , [%])		
White	11 [69]	10 [63]
Black or African American	1 [6]	0
Asian	1 [6]	1 [6]
Other and multiracial	3 [19]	4 [25]
IQ	111.7 (± 13.1)	113.7 (± 9.96)
BMI (kg/m ²)	18.3 (± 4.35)	19.2 (± 4.58)
BMI percentile	61.4 (± 32.0)	69.2 (± 29.3)
Overweight (<i>n</i> , [%])	0	3 [19]
Obese (<i>n</i> , [%])	4 [25]	4 [25]
VO _{2max} (L*min ⁻¹)	1.39 (.38)	1.55 (.36)
VO _{2max} (mL*kg ⁻¹ *min ⁻¹)	43.6 (± 9.42)	44.2 (± 7.53)
VO _{2max} percentile	43.8 (± 37.6)	42.2 (± 33.7)
Accelerometer wear (days)	6.25 (± .86)	5.37 (± 1.59)
≥ 4 days (<i>n</i> , [%])	16 [100]	15 [94]
Wear time (min/day)	801.6 (± 55.6)	787.5 (± 54.9)
CPM	567.9 (± 196.4)	541.8 (± 129.6)
Sedentary time ¹ (min/day)	450.7 (± 62.5)	453.5 (± 71.2)
Light PA ¹ (min/day)	263.0 (± 32.0)	248.3 (± 30.6)
MVPA ¹ (min/day)	87.9 (± 33.4)	85.6 (± 24.4)

Note. ¹ Unadjusted means; CPM, accelerometer counts per minute; PA, physical activity; MVPA, moderate-to-vigorous physical activity.

Table 6-2. Comparisons of pre- and post-test measures of cardiorespiratory fitness among intervention and control group participants

	Intervention (<i>n</i> = 16)						Control (<i>n</i> = 16)					
	Pre		Post		<i>Z</i> ¹	<i>p</i>	Pre		Post		<i>Z</i> ¹	<i>p</i>
	Mdn	IQR	Mdn	IQR			Mdn	IQR	Mdn	IQR		
Height (cm)	131	9.0	136	8.00	2.63	.007	134	10.5	141	11.0	3.14	.002
Weight (kg)	29.0 [†]	17.0	32.0	18.7	2.74	.006	32.6	14.9	36.0	17.2	3.52	.000
BMI (kg/m ²)	16.6	8.42	17.1	6.96	2.48	.013	18.2	5.97	19.1	5.19	3.21	.001
BMI percentile	61.5	49.1	64.4	48.4	.62	.53	81.8	50.1	85.0	37.9	2.17	.030
VO _{2max} (L* min ⁻¹)	1.28	.57	1.47	.45	2.48	.013	1.47	.61	1.58	.66	2.43	.015
VO _{2max} (mL*kg ⁻¹ *min ⁻¹)	42.4	15.1	43.2	16.0	-.47	.64	46.6	12.6	42.8	7.90	-1.5	.13
VO _{2max} percentile	27.5	82.0	35	73.5	-.71	.48	33	71.2	27.5	40.2	-1.76	.078

Note. ¹Post-test – pre-test; [†] Variables normally distributed thus means and standard deviations reported.

Table 6-3. Comparisons of pre-test and post-test measures of cognitive control and academic achievement among intervention and control groups

	Intervention (<i>n</i> = 16)						Control (<i>n</i> = 16)					
	Pre-test		Post-test		<i>F</i> (1,15)	<i>p</i>	Pre-test		Post-test		<i>F</i> (1, 15)	<i>p</i>
	M	SD	M	SD			M	SD	M	SD		
Flanker												
Congruent												
Mean RT (ms)	543.0	120.4	498.6	73.3	2.24	.057	514.0	58.1	521.4	58.9	.16	.69
Accuracy (%)	80.6	12.5	90.2	8.34	8.35	.01	77.3	10.2	86.5	10.1	7.97	.01
Flanker												
Incongruent												
Mean RT (ms)	613.4	136.4	553.4	88.1	6.15	.025	569.5	68.5	574.6	63.9	.08	.78
Accuracy (%)	71.0	14.4	84.5	9.84	13.1	.002	73.4	12.1	83.0	11.5	3.79	.07
OSPAN												
Math	84.7	9.95	94.4	4.03	18.4	.001	86.4	10.9	85.6	8.73	.08	.78
Accuracy (%)												
Math MRT (ms)	4374.9	1240.7	3563.7	957.5	7.17	.02	5065.3	976.4	3811.6	883.5	17.9	.00
PCU	.61	.14	.72	.17	6.96	.02	.55	.17	.66	.17	3.97	.06
ANU	.39	.14	.50	.24	3.39	.09	.32	.19	.42	.20	2.64	.12

Note. Significant differences at the alpha level < .05 are presented in bold; ¹Post-test – pre-test; PCU, partial unit credit score; ANU, all-or-nothing unit score as measured with Operation Span Task (OSPAN; Turner & Engle, 1989).

Table 6-4. Comparisons of intervention and control groups at pre-test and post-test on measures of cognitive control

	Pre-test			Post-test		
	Median Difference (Control – Intervention)	Mann-Whitney U	<i>p</i>	Median Difference (Control – Intervention)	Mann-Whitney U	<i>p</i>
Flanker Congruent						
Mean RT (ms)	11.1	129.0	.97	15.1	105.0	.89
Accuracy (%)	-7.14	148.5	.44	-4.17	161.0	.21
Flanker Incongruent						
Mean RT (ms)	-26.7	154.0	.33	32.8	109.0	.47
Accuracy (%)	8.93	115.0	.62	-1.79	150.5	.40
OSPAN						
PCU	-0.04	155.0	.31	-.057	155.0	.31
ANU	-0.06	164.0	.17	-.062	153.0	.34

Note. PCU, partial unit credit score; ANU, all-or-nothing unit score as measured with Operation Span Task (OSPAN; (Turner & Engle, 1989).

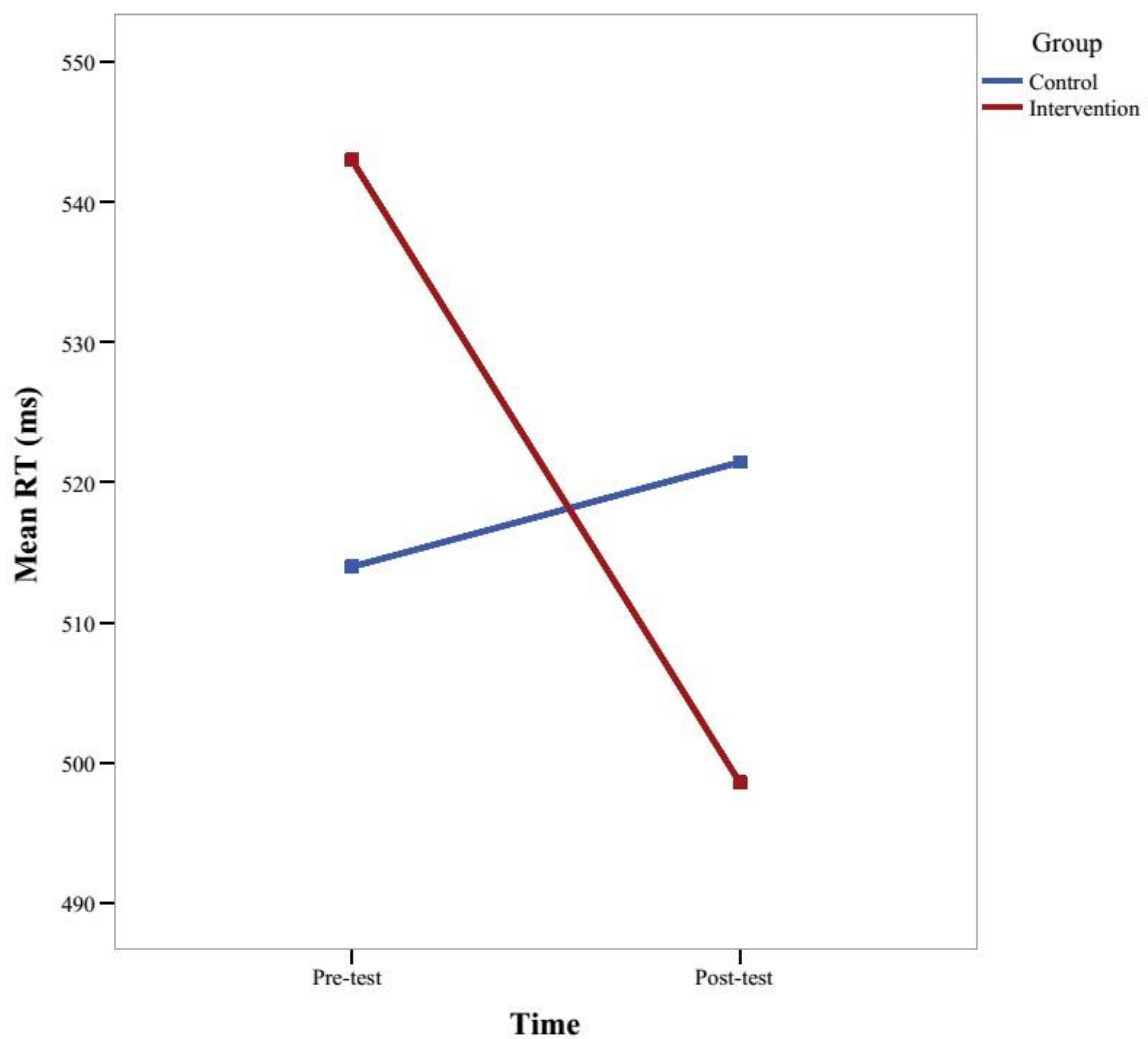


Figure 6-2. The effect of Intervention by Time interaction on the mean RT to congruent trials on the flanker task ($p = .08$).

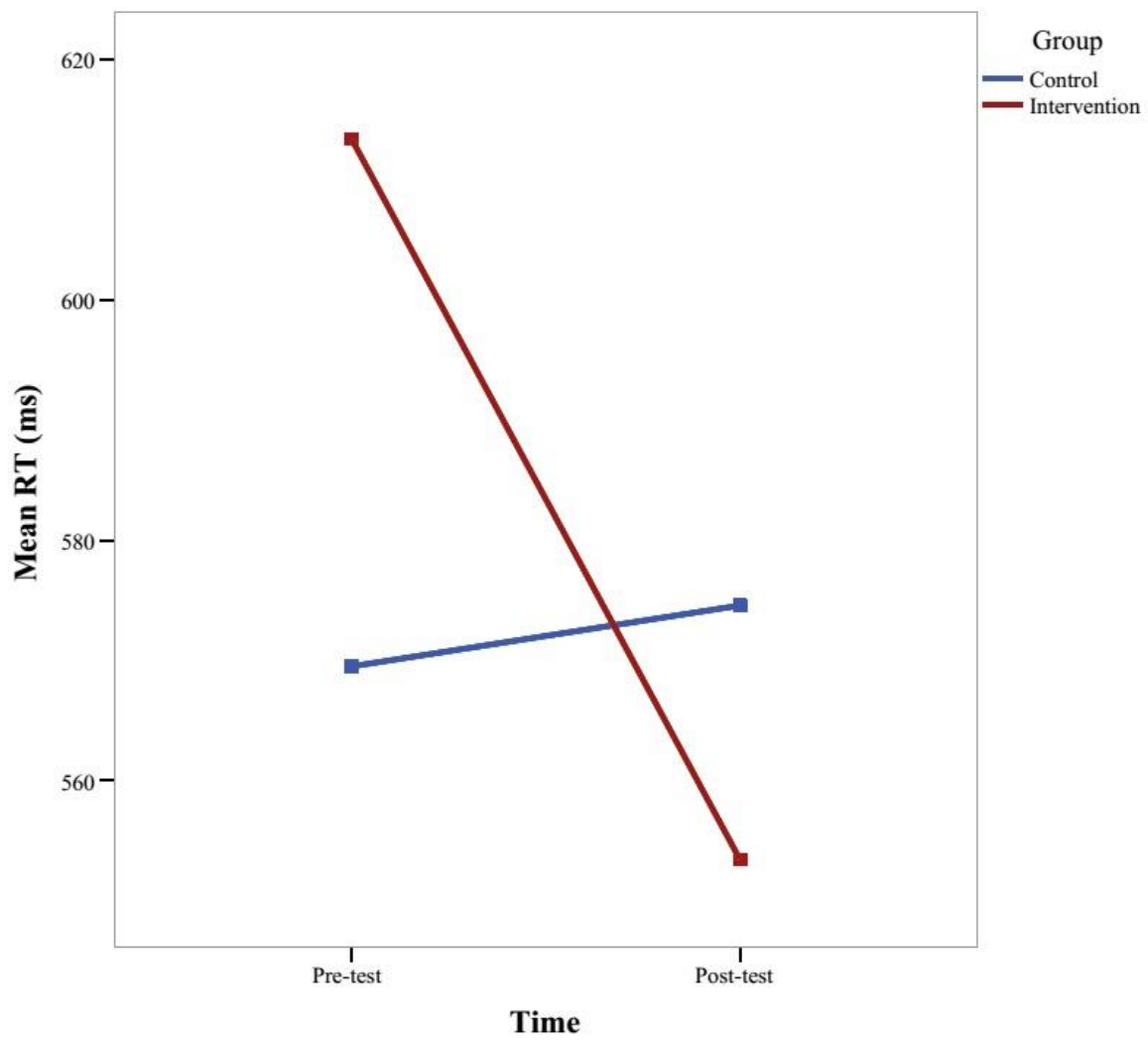


Figure 6-3. The effect of Intervention by Time interaction on the mean RT to incongruent trials on the flanker task ($p = .038$).

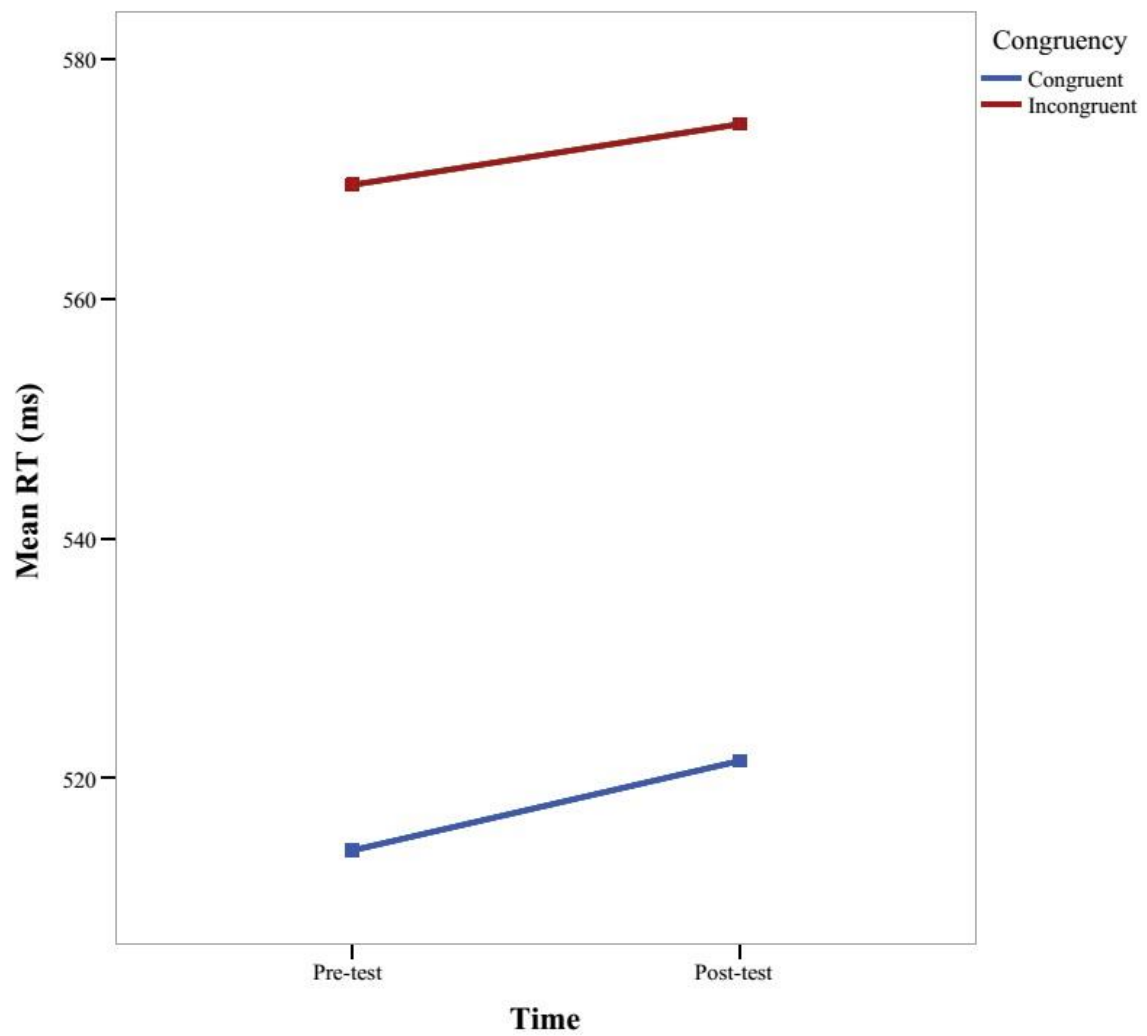


Figure 6-4. The effect of Time by Congruency interaction on the mean RT on the flanker task in the control group ($p = .69$).

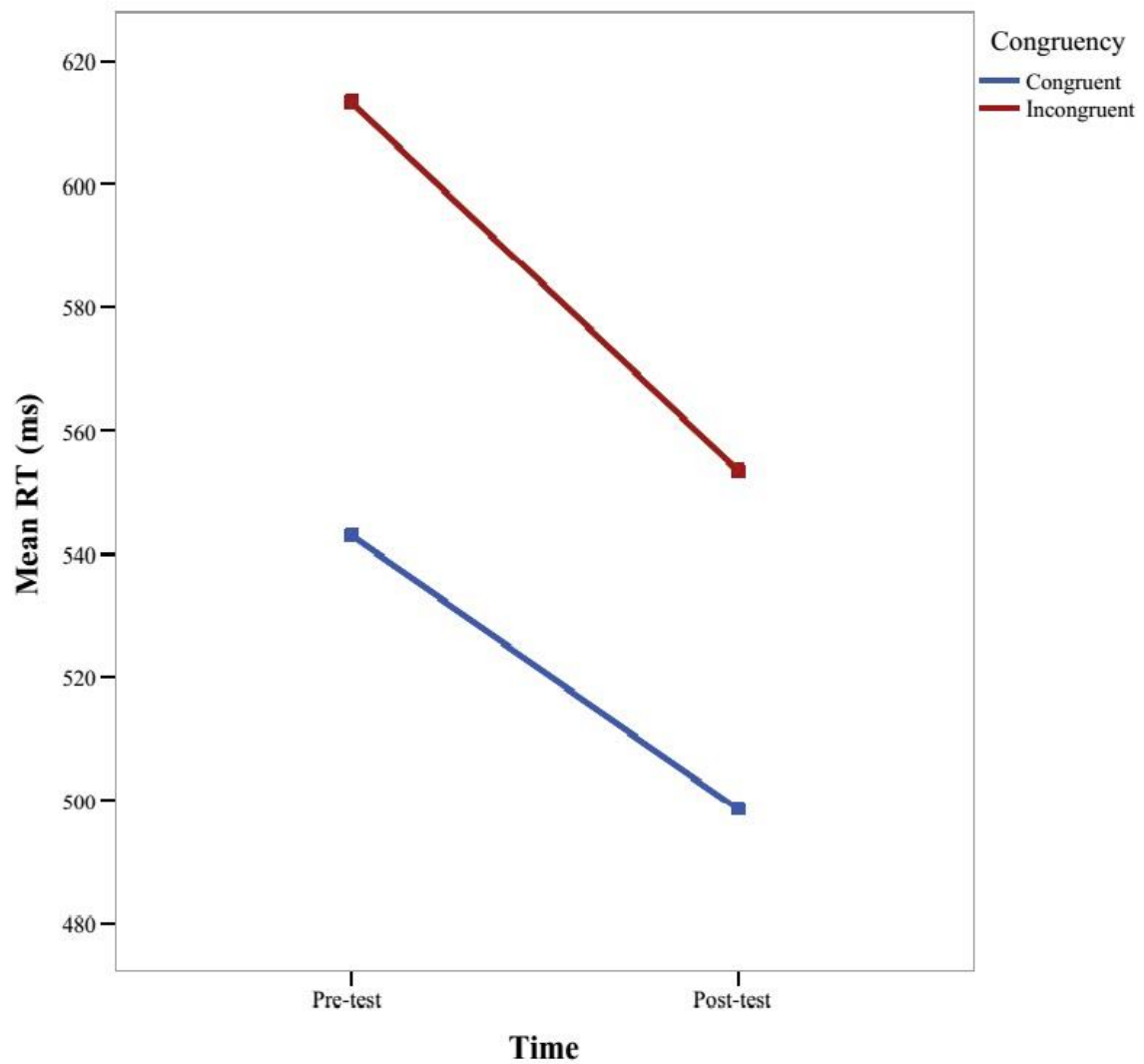


Figure 6-5. The effect of Time by Congruency interaction on the mean RT on the flanker task in the intervention group ($p = .057$).

Chapter 7

General Discussion

This thesis has presented three studies which: (1) investigated the associations between accelerometer assessed MVPA and attentional control, processing speed and variability in processing speed in older adolescents using a cross-sectional design and a large sample ($n = 667$), while statistically controlling for CRF, IQ and other important confounders; (2) investigated the associations between accelerometer assessed daily MVPA, cognitive control (inhibitory control and WM) and applied forms of cognition (academic achievement) in preadolescents; while also statistically controlling for CRF, IQ and other important confounders, and (3) using a randomised controlled trial, evaluated the effects of a nine-month aerobic exercise intervention on children's cognitive control (inhibitory control and WM), and CRF while controlling for objectively assessed daily MVPA and time sedentary at baseline. The thesis posed the question if (1) daily MVPA was associated with cognitive control in two distinct populations of older adolescents (research question 1a) and preadolescent children (1b), who vary in cognitive reserve, and if these associations were independent of CRF and variability in IQ. Second, the thesis investigated the association between daily MVPA and applied forms of cognition (academic achievement; research question 2). Last, the thesis evaluated if a chronic aerobic exercise intervention designed to increase CRF had a positive effect on inhibitory control and WM, while controlling for baseline levels of MVPA and time sedentary (research question 3). This chapter summarises the main findings reported within this thesis and discusses implications of these findings for future research.

7.1 Summary of findings

In answer to research question (1a), based on the results from study 1 we found that:

- neither objectively measured MVPA nor CRF were related to attentional control in older adolescents;
- adolescents employed a cognitive strategy of proactive slowing on a stop signal condition in order to maximise accuracy (successfully inhibiting a response), which limited the conclusions relevant to attentional control;
- there was limited evidence of a weak positive association between CRF and processing speed, which was selective for one group of adolescents from ALSPAC. This association was reduced to non-significance once sex and adiposity were accounted for.

In answer to the research questions (1b) and (2), based on the results from study 2, we found that:

- objectively measured daily MVPA was not associated with either inhibitory control or WM in preadolescent children;
- daily MVPA was also not associated with achievement in any of the academic domains (reading, mathematics and spelling);
- higher CRF was associated with better ability to suppress distractions (expressed as lower cost in response accuracy between task conditions, which varied in cognitive demands) in pre-adolescent children.

Lastly, in answer to research question 3, based on the results from study 3 we found that:

- a nine-month after-school aerobic exercise intervention FITKids2 benefited inhibitory control but not WM in preadolescent children;
- FITKids2 intervention did not increase CRF in preadolescent children;
- only the control group showed an increase in BMI percentile from pre- to post-test (nine months), suggesting a potentially protective effect of the intervention on adiposity in preadolescent children.

7.2 Objectively measured daily MVPA and cognitive control in children and adolescents (studies 1 and 2)

At the conception of this thesis no published study inspected the associations between objectively measured MVPA and cognitive functions in young people. At present a paucity of data exist on the relations of objectively measured MVPA to cognitive control in young people, which present mixed results as both positive (Booth, Tomporowski, et al., 2013) and null associations have been reported (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014; van der Niet, et al., 2014). The main limitations of the past research are: 1) not controlling for CRF and IQ, which does not allow one to ascertain whether the differences in results between these studies are due to the confounding and /or mediating effects of these variables; 2) the focus on a narrow age group of young adolescents (11-12 years), which precludes generalisations of the results across children and adolescents who differ in the degree of cognitive development and thus cognitive reserve (Davidson, et al., 2006); 3) the lack of information on how the associations between daily MVPA and cognitive control compare to those with applied forms of cognition (academic achievement). These limitations were addressed in studies 1 and 2 by 1) controlling for both CRF and IQ, which were measured with gold standard (study 2) and validated tests of CRF (study 1), and standardised tests of IQ (studies 1 and 2); 2) assessing these relationships in older (15 years) adolescents and younger preadolescent (8-9 years old)

children; 3) including standardised measures of academic achievement (study 2). Overcoming the limitations of previous research was important as both CRF (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Hillman, 2005; Moore, et al., 2013; Pontifex, et al., 2011; Pontifex, et al., 2012; Scudder, et al., 2014; Voss, et al., 2011) and IQ (Demetriou, et al., 2014; Giofrè, Mammarella, & Cornoldi, 2013; Hornung, Brunner, Reuter, & Martin, 2011; Tillman, Nyberg, & Bohlin, 2008), are directly linked to cognitive control in children and adolescents. Second, covering these two distinct age groups helps answer the question if such associations generalise across populations with varied degree of cognitive development or are specific to younger populations. Cognitive functions continue to develop in older adolescents, when gains in efficiency can be observed (Luna, et al., 2004; Luna, et al., 2010). Older adolescents are also at risk of impulsive behaviours (e.g. poorer regulation of affect and behaviour, risk taking; Steinberg, 2005). Physical activity interventions yield promise in decreasing impulsive behaviour as indicated by better performance on tasks of response inhibition in children with ADHD (Smith, et al., 2013; Verret, et al., 2012) who have specific problems with behavioural regulation (inhibition, impulsivity; Nigg, 2001). Thus, looking at the link between physical activity behaviour and inhibition in older adolescents is of public health importance.

Likewise, none of the previous studies on objectively measured MVPA and cognitive function investigated these associations in preadolescent children. This is a limitation, as cognitive control is still dynamically developing in children while in adolescents smaller increments in cognitive development (i.e. gains in accuracy, speed and consistency) can be observed (Davidson, et al., 2006). Thus, due to their limited cognitive reserve, children are likely to benefit more from daily MVPA than adolescents (Chodzko-Zajko & Moore, 1994; Fedewa & Ahn, 2011). In confirmation, the most consistent associations between CRF, chronic aerobic exercise, and cognitive control have been evidenced in younger age groups, namely preadolescent children (e.g., Buck, et al., 2004; Buck, et al., 2008; Chaddock-Heyman, et al., 2013; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Davis & Cooper, 2011; Davis, et al., 2007; Hillman, 2005; Hillman, et al., 2014; Kamijo, et al., 2011; Moore, et al., 2013; Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011).

The cross-sectional findings of this thesis suggest that accumulation of daily MVPA as measured with accelerometers does not relate to processing speed and cognitive control in children and processing speed in adolescents. This lack of associations could not be explained by age of the sample, as no associations for processing speed or cognitive control were

observed either in adolescents (study 1) or pre-adolescent children (study 2). It is possible that task limitation in study 1 may have contributed to the null findings relevant to attentional control. However, when limitations of this task were overcome and a younger sample was assessed in study 2 (a stronger association should be expected in younger sample due to limited cognitive reserve), still no associations between daily MVPA and two indices of cognitive control (inhibitory control of attention or working memory) were observed. Study 2 employed computerised tasks, which proved sensitive to CRF-related inter-individual differences in healthy and typically developing children of similar age. Thus task characteristics were unlikely to account for these null results. In both studies, the effects of important confounders were statistically controlled for and confounders were assessed using objective, standardised and/or validated methods. Therefore the lack of the associations is also unlikely due to the confounding effects of such factors as CRF, IQ, SES, adiposity or symptoms of ADHD. Consequently, given the methodological rigour in the assessment of a predictor, confounders and outcomes, the results of studies 1 and 2 contribute quality evidence on the null associations between daily MVPA, cognitive control (study 2) and processing speed (studies 1 and 2) in children and adolescents. The results of study 1 in relation to attentional control provide limited evidence on the lack of such association in an older sample.

Our findings from studies 1 and 2 corroborate those of van der Niet et al. (2014) who found no associations between accelerometer assessed daily MVPA and multiple indices of cognitive control in 8-12 year olds. The results of study 2 also partly corroborate the null findings of Syväoja et al. (2014) in relation to WM but together with the null findings from study 1 stand in contrast to positive associations reported by these authors on a measure of impulsivity (which is an aspect of inhibition; Bari & Robbins, 2013). Our results from studies 1 and 2 also differ from findings reported by Booth et al. (2013), as they suggest that daily accelerometer measured MVPA was not associated with either indices of cognitive control in children or adolescents. The lack of these associations could not be accounted for by CRF, as excluding CRF from the models did not materially change the findings. In contrast, CRF was positively associated with the ability to resist distractions (as indexed by smaller decrements in response accuracy between two task conditions, which placed lower and higher demands on cognitive control). The potential reasons behind equivocal findings within the physical activity and cognition literature in young people will be further discussed.

7.2.1 Potential role of confounders

The associations between daily MVPA and cognitive control are complex, as both physical activity and cognitive control are influenced by a multitude of factors (for example, age, sex, adiposity status, CRF, IQ), which can interact in producing these behavioural outcomes (Tomprowski, Lambourne, & Okumura, 2011). Thus, the associations between daily MVPA and cognition in young people may be confounded (e.g. occluded, amplified or reduced), mediated or moderated by one or multiple of these factors. For example, the associations between daily MVPA and cognitive function can vary with age (Fedewa & Ahn, 2011), sex (Booth, Tomporowski, et al., 2013; Van Dijk, De Groot, Van Acker, Savelberg, & Kirschner, 2014), but also with weight status (Kamijo, et al., 2012; Li, et al., 2008; Yu, Han, Cao, & Guo, 2010); and CRF (Lambourne, et al., 2013; Tomporowski, et al., 2011). Since extant studies rarely accounted for all of these factors, the equivocal findings may reflect the heterogeneity of influences on the relationship between daily MVPA and cognition in children and adolescents.

7.2.1.1 Age

We found no evidence of age-specific associations between daily MVPA and cognitive measures, as daily MVPA was not related to cognitive processing speed or variability in processing speed in older adolescents (study 1) or cognitive control in younger, preadolescent children (study 2). In contrast, Booth et al. (2013) and Syväoja et al. (2014) found such associations in young adolescents on measures of selective attention (Booth, Tomporowski, et al., 2013), which is related to inhibitory control (Bari & Robbins, 2013), and impulse control (Syväoja, et al., 2014). It is possible that such relationships could also emerge for older adolescents, if cognitive control is properly challenged. Based on the limitations of the task employed in study 1, we cannot discount this possibility. The associations between daily MVPA and inhibition may also be particularly salient during the period of heightened emotional arousability and reward seeking, which is characteristic of early adolescents (Steinberg, 2005). Physical activity could therefore provide context to both help manage emotional arousability and to draw social rewards from physical activity participation through interactions with peers, adults, increasing physical competence and self-efficacy (Ashford, Edmunds, & French, 2010; Dishman et al., 2005). Therefore, more physically active children may draw context driven cognitive benefits from physical activity participation (Tomprowski, et al., 2011).

7.2.1.2 Sex

The potential moderating effects of sex on the associations between physical activity and cognition have been noted in adult literature (Spirduso, Poon, & Chodzko-Zajko, 2008), and included as a hypothetical moderator in the study of physical activity and cognition in children (Tomprowski, et al., 2011). Kwak et al. (2009) observed a moderating effect of sex on the associations between CRF, accelerometer measured vigorous physical activity and academic achievement (which is an applied form of cognition and therefore used as a proxy for cognitive function). That is, academic achievement was associated with vigorous physical activity in girls, after controlling for CRF, but not in boys who benefited only from increased CRF but not vigorous physical activity. The results of study 1 partly corroborate these findings, as we observed that CRF (but not daily MVPA) was associated with processing speed but that both sex and adiposity also contributed to these associations. In a follow-up simple regression model, sex explained a similar proportion of variance as CRF in processing speed, suggesting a small advantage for boys. Moderating effects of sex on the associations between daily MVPA (accelerometry) and cognitive control (selective attention, task switching) were observed by Booth et al. (2013). The associations between MVPA and cognitive control were more consistent in boys, where MVPA was related to selective attention as well as task switching. In girls, these associations were marginal and emerged for task switching only. However, the authors did not control for CRF, which could have modified their findings (e.g. CRF could have explained the effects of MVPA on cognitive control in boys). Van Dijk et al. (2014) observed moderating effects of sex on the associations between active commuting (measured with ActiPAL) and selective attention, such that active commuting benefited cognitive performance in girls but not in boys, congruent with the results of Kwak et al. (2009). Since, similarly to Booth et al. (2013), these authors did not control for CRF, they were unable to ascertain whether the associations between active commuting and selective attention would hold after accounting for CRF. The reason why sex can act as a modifier of the relationship between daily MVPA could be related to sex differences in physical activity levels (boys are on average more active than girls; Jago, et al., 2005; Kimm et al., 2000; Riddoch, et al., 2004), which amplify during and after puberty (Nader, et al., 2008; van Mechelen, Twisk, Post, Snel, & Kemper, 2000). Sex differences in physical activity can further interact with sex differences in cognitive performance. Both adult men and boys are on average faster than women and girls on cognitive tasks (Der & Deary, 2006; Dykiert, Der, Starr, & Deary, 2012; Tun & Lachman, 2008). This basic advantage could therefore prime boys for better performance on the measures of speed and on tasks, which require performance within a limited time, such as those included

in studies of cognitive control (Booth, Tomporowski, et al., 2013; Van Dijk, De Groot, Van Acker, et al., 2014). Thus, girls could benefit more from increased physical activity as they start off at a lower level for both physical activity and response speed. However, at present it remains unclear whether such sex differences emerge only for certain cognitive tasks (e.g. those which engage cognitive control versus those which do not), are amplified with age, and whether they could further interact with factors such as differences in CRF and adiposity.

7.2.1.3 CRF

In contrast to previous research (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014; van der Niet, et al., 2014), we accounted for potentially confounding effects of CRF in both studies 1 and 2. We were therefore able to ascertain that the relationships between CRF and daily MVPA, as well as cognitive control did not occlude (by attenuating) potential associations between daily MVPA and cognition. Not only did we control for CRF but we also selectively excluded CRF from the models, which did not change our findings. This is an important contribution, as CRF as a confounder could have a potentially suppressing effect on the associations between daily MVPA and cognitive control or, alternatively, it could mediate this relationship. For example, Lambourne and colleagues (2013) reported such suppressing effect of the CRF on the association between daily physical activity (expressed as CMP) and academic achievement in mathematics in preadolescents. Specifically, CRF changed the directionality (from negative to positive) of this association.

In contrast to the null associations between daily MVPA and cognitive control, we found an association between CRF and interference control (i.e. the ability to suppress distractions), which were specific to pre-adolescents (study 2). CRF contributed a small proportion of variance in interference control (4.7%, corresponding to a small effect size as measured with Cohen's $f = .10$), which is larger than that reported for incongruent accuracy (1%, incongruent accuracy is another measure of inhibitory control) in children of similar age (Scudder et al. 2014). The results of study 2 thus further replicate previous findings on positive associations between CRF and interference control in children (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Voss et al., 2011). As such, the finding from study 2 can have implications for intervention research as they suggest that aerobic physical activity (e.g. such as chronic aerobic exercise, which aims to increase CRF) rather than intermittent daily MVPA may be needed to benefit cognition in young people. The practical meaning of these findings could best be assessed in an RCT, where the magnitude of changes in CRF would be related to increments in interference control. The results of study 3 indicated that changes in CRF were not a

prerequisite to improvements in another indicator of inhibitory control (mean RT on incongruent trials), which were driven by an aerobic exercise intervention. However, the results of study 3 also suggested that aerobic exercise intervention had a protective effect against increments in BMI percentile, and possibly decrements in CRF, as a trend for a decrease in CRF in a control but not intervention group was also observed. Although due to a small sample size the results relevant to CRF need to be interpreted with caution, together with findings from study 2, these results suggest that both adiposity and CRF can contribute to child's inhibitory control and thus should be considered in future studies investigating the relationships between MVPA, aerobic exercise and cognition.

CRF was not related to attentional control in older adolescents. However the conclusion on such association in older sample need to be cautious due to the limitations of the task. In study 1 stop signal condition (go trials) proved to be more cognitively challenging than the go condition, as participants showed decrements in speed, accuracy and increased variability in performance on the stop signal condition. However, the dominance of response inhibition over execution on stop signal trials suggested that the task was less challenging than its design intended. However, response inhibition requires greater levels of cognitive control, as an already initiated response must be inhibited (Logan, 1994). Cognitive gains on this task were observed in older adolescents under optimal task parameters (Williams, 1999). Thus, the possibility that the relationship between CRF and attentional control could have been observed, should the task have properly challenged response inhibition, cannot be discounted. Limited evidence from study 1 suggests that a factor which underlies the associations between CRF, adiposity and sex (e.g. fat free mass) could marginally contribute to processing speed in older adolescents. However, the selective nature of this small effect, which was found for one group of ALSPAC adolescents, precludes definite conclusions.

7.2.1.4 Adiposity

Similar to CRF, differences in weight status can also influence the relationship between physical activity and cognition. Li et al. (2008) found a negative association between child's overweight status (normal weight, at risk of overweight, and overweight) and visuospatial organisation (measured with block design) in 2,519 children and adolescents from NHANES III (8-16 years). Further, meta-analytical findings suggest an inverse association between childhood obesity and general intellectual capacity (IQ) across childhood and adolescence (Yu, et al., 2010). Cognitive differences in inhibitory control related to weight status were also reported (Kamijo, et al., 2012). Kamijo et al. (2012) found an inverse relationship between

obesity and inhibitory control in preadolescent children. Since all these studies controlled for either CRF (Kamijo, et al., 2012; Yu, et al., 2010) or physical activity (Li, et al., 2008), their results indicate that adiposity can confound the associations between these variables and cognitive function. Out of three studies on objectively measured daily MVPA and cognitive control (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014; van der Niet, et al., 2014), only Booth et al. (2013) adjusted the analyses for adiposity (measured with BMI z-scores as a proxy) but did not disclose if BMI significantly contributed to the regression models. In our studies 1 and 2, adiposity was controlled, either through objective measurement of percent body fat mass (study 1) or with BMI as a proxy (study 2). As discussed in relation to CRF, positive associations between CRF and cognitive processing speed in study 1 were coupled with negative associations between percent body fat mass (and body fat mass was negatively related to processing speed in a simple regression model), our results also point to the need to control for adiposity in the study of physical activity, CRF and cognition in young people.

One potential mechanism, which could mediate the associations between overweight and obesity and cognition in children are adverse metabolic changes associated with obesity (e.g. altered lipid profile, insulin regulation, and inflammatory biomarkers; Steinberger et al., 2009). In confirmation, 7-years old children who had one or more risk factors for metabolic syndrome were less able to control distractions on a flanker task of inhibitory control (Scudder, et al., 2015). In addition, higher levels of high density lipoprotein (HDL) cholesterol were associated with greater cognitive flexibility (i.e. faster responses across cognitively more and less demanding task conditions; Scudder, et al., 2015). These findings underscore the importance of considering the effects of other health-related factors as potential mediators (or moderators) of the associations between physical activity and cognition (Hötting & Röder, 2013; Tomporowski, et al., 2011).

7.2.2 MVPA: Measurement, patterns and variability

The equivocal findings across the studies of daily MVPA and cognitive control may also be related to the measurement of physical activity. Although accelerometry provides a sensitive and objective measure of children's daily MVPA, it may underestimate the total volume of MVPA in some individuals due to its inability to capture activities, which involve minimal vertical displacement (e.g. such as cycling) and swimming. Since physical activity was measured during summer months in study 2, when children are more likely to engage in swimming and cycling, this limitation may have contributed to the lack of associations. Also

swimming and cycling are sustained aerobic activities, which could represent the effects of aerobic exercise on cognitive control in preadolescent children. Thus, the limitation of accelerometry to capture such activities may have contributed to our null findings. In contrast, Booth et al. (2013) assessed physical activity across the whole year, thus seasonal variability would have been accounted for in their study. Given that specific effects of chronic aerobic exercise have been observed in relation to both cognitive control (Chaddock-Heyman, et al., 2013; Davies, Segalowitz, Dywan, & Pailing, 2001; Davis, et al., 2007; Hillman, et al., 2014; Kamijo, et al., 2011) and academic achievement (Davis, et al., 2011; Donnelly, et al., 2009), it is also possible that the lack of associations in study 2 was due to the intermittency of children's daily MVPA (Bailey, et al., 1995; Baquet, et al., 2007; Riddoch, et al., 2004). For example, 79% of children in our sample did not accumulate even one MVPA bout of at least 5 minutes duration. Thus, on average their physical activity was insufficient to increase CRF, for which regular aerobic exercise of at least 10 minute duration three times a week is necessary (Baquet, Praagh, & Berthoin, 2003). In contrast, in study 1 adolescents accumulated on average 22 minutes in MVPA in bouts lasting at least 10 minutes.

Most studies observed the associations between daily MVPA and tasks, which engaged inhibitory control (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014). As previously discussed, it is possible that the lack of associations between daily MVPA and attentional control observed in study 1 was due to the limitation of the cognitive task, which minimised the engagement of attentional control. That is adolescents in our study proactively slowed their responses to maximise accuracy. Therefore, their reaction time on the stop signal condition was likely unrepresentative of attentional control. Since other authors (Booth, Tomporowski, et al., 2013; Syväoja, et al., 2014; van der Niet, et al., 2014) did not report on the patterns of daily MVPA in their samples, it is difficult to make inferences about possible contribution of physical activity patterns (i.e. the proportion of daily MVPA accumulated in longer bouts) to the observed relationships between daily MVPA and cognitive control. Given the emergent evidence on the positive effects of chronic aerobic exercise on children's cognitive control (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Kamijo, et al., 2011), comparing the associations between daily MVPA volume and MVPA patterns (e.g., MVPA accumulated in bouts of at least 10 minutes duration) would help elucidate the associations between MVPA and cognitive control in young people.

Lastly, physical activity is a highly variable behaviour (Mattocks, 2007) and therefore a brief period of at most 7 days of physical activity monitoring is unlikely to capture child or

adolescent's habitual physical activity, which shows day to day (Fairclough, et al., in press; Nilsson, et al., 2009; Rowlands, Pilgrim, & Eston, 2008), as well as seasonal variability (Carson & Spence, 2010). Such variability introduces a large error of measurement (Mattocks, 2007), which may occlude the underlying associations. Therefore, it is perhaps not surprising that studies, which reported significant associations between accelerometer measured MVPA and cognitive control either employed a large sample ($n > 4,500$), where differences in seasonality would be accounted for as physical activity was sampled across the whole year (i.e. different participants were assessed at different times of year; Booth, Tomporowski, et al., 2013), or used structural equation modelling, which excludes error-related variance (Syväoja, et al., 2014). As previously stated, the lack of associations observed in study 1 may have been related to task limitations rather than assessment of physical activity, as we used both a large sample size, 4 days of wear as an inclusion criterion, and the majority (68%) of participants wore the device for at least 6 days. It is conceivable that the lack of associations in study 2 was related to a greater variability in physical activity and the measurement period of one day, which was not representative of child's habitual physical activity. However, when analyses were repeated excluding children with less than 4 days of wear, the results remained materially unchanged. Future studies should strive to inspect these associations in larger samples to allow for more stringent inclusion criteria in relation to the number of days of accelerometer wear.

7.2.3 Cognitive measures

One of the limitations of research in physical activity and cognition in young people, which can contribute to disparate findings, is the heterogeneity of methods used to assess cognitive functions (Etnier, 2012; Tomporowski, 2009). Inconsistent terminology (e.g. selective attention (Booth, Tomporowski, et al., 2013) versus inhibition (Van Dijk, De Groot, Van Acker, et al., 2014) to denote performance on similar tasks) and differences in tasks employed to assess the same cognitive construct (e.g. inhibitory control assessed with paper and pencil Stroop task (van der Niet, et al., 2014) or Test of Everyday Attention for Children (Booth, Tomporowski, et al., 2013; Manly, et al., 2001)) and computerised laboratory task as in study 2) may contribute to equivocal findings and make comparisons across the studies difficult. First, paper and pencil tasks include larger measurement error due to human error and lower resolution in recording reaction times. Consequently, the associations on these tasks may be more difficult to observe with smaller samples (e.g. van der Niet, et al., 2014). This could have contributed to disparate findings between the studies of van der Niet et al. (2014) and Booth et al. (2013), which both used paper and pencil tasks but considerably differed in the sample size

($n = 80$ versus $n > 4,500$, respectively). Second, tasks, which were predominantly developed for clinical assessment of cognitive deficits (such as CANTAB employed by Syväoja et al. (2014), or Trail Making Test (Reynolds, 2002) used by van der Niet et al. (2014)) may have limited sensitivity to differentiate between healthy children and adolescents based on the levels of physical activity. For example, Syväoja et al. (2014) observed overall high scores on multiple tasks in their sample, suggestive of limited sensitivity of these tasks. In study 2 we used laboratory tasks specifically designed to challenge inhibitory control and WM in children of similar age, which also proved sensitive to CRF-related differences and the effects of chronic aerobic exercise interventions in past research (e.g., Hillman, et al., 2014; Scudder, et al., 2014; Voss, et al., 2011). However, similar to van der Niet et al. (2014), we also did not observe the associations between inhibitory control and daily MVPA. In contrast, the observed associations between daily MVPA and impulsivity found by Syväoja et al. (2014) may be related to the more powerful statistical technic (structural equation modelling), which controlled for variance due to measurement error, and a larger sample size ($n = 224$ compared to $n = 80$ (van der Niet, et al., 2014) and 81, study 2). Thus, future research should attempt to use both sensitive cognitive measures and latent variable analyses to further elucidate the associations between physical activity and cognitive function in young people.

7.2.4 Academic achievement

The literature on physical activity and academic achievement presents equivocal findings. Based on the results of a systematic review, Singh et al. (2012) concluded that evidence in support of positive effects of physical activity on academic achievement in youth is strong. However, this conclusion was drawn based on only two studies with high quality ratings (large sample, low attrition, superior data collection and analyses; Donnelly, et al., 2009; Nelson & Gordon-Larsen, 2006). However, Nelson et al. (2006) used self-report to assess physical activity, which is an inaccurate measure of physical activity (Adamo et al., 2009; Prince, et al., 2008). In contrast, evidence based on objective monitoring of physical activity presents equivocal results, as both positive (Booth, Leary, et al., 2013; Lambourne, et al., 2013) and null findings have been reported (Harrington, 2013; LeBlanc, et al., 2012; Syväoja, et al., 2013). For example, Booth et al. (2013) and Lambourne et al. (2013) noted positive associations between accelerometer assessed physical activity volume (MVPA and CPM, respectively), and academic achievement in at least one domain, while LeBlanc et al. (2012), Syväoja et al. (2013) and Harrington et al. (2013) reported null findings. Our findings contrast those of Booth et al. (2013) and Lambourne et al. (2013) but corroborate findings by Syväoja

et al. (2013) and Harrington et al. (2013), who found no associations between accelerometer assessed MVPA and academic achievement (expressed as grade point average or standardised scores for achievement in mathematics and reading, respectively) in young adolescents and children. Although Booth et al. (2013) found positive associations between the proportion of time spent daily in MVPA and achievement in English and mathematics in adolescents (in both cross-sectional and prospective analyses, when MVPA at 11 years was related to academic achievement at the ages of 11, 13 and 16 years), these authors did not control for CRF. Given that the authors used a high intensity cut point to denote MVPA (3,600 CPM; Mattocks, et al., 2007), it is possible that these results are representative of vigorous physical activity, which shows stronger associations with CRF (Dencker & Andersen, 2011). Thus, it is unclear whether the reported associations in Booth et al.'s (2013) study could not be explained by the effect of CRF on the achievement in English and mathematics. In study 2, despite the use of standardised measures of academic achievement and partialling out the effects of IQ (which is strongly correlated with academic achievement in general population of typically developing children $r = .83$ (Kaufman et al., 2012) and moderately in the current study, $r_s = .41-.54$), we found no associations between daily MVPA and either reading, mathematics or spelling. Consequently, study 2 contributes quality evidence to the extant literature (Howie & Pate, 2012) in support of null associations. Such quality evidence in larger samples is needed, as despite the progress in research into physical activity and academic achievement over the past three decades, this relationship has not been unequivocally established (Howie & Pate, 2012; Singh et al., 2012). Methodological limitations (e.g. self-reports of physical activity, lack of control for one or multiple important confounders) likely contribute to these discrepant findings. Given that this relationship is of greatest interest to policy makers, educators and parents alike, such quality evidence on the relationship between daily MVPA and academic achievement in larger samples is further needed.

A pertinent question in the literature is whether the associations between daily MVPA and academic achievement are mediated by its associations with cognitive functions, and cognitive control in particular. The results of study 2 suggest that the lack of associations between daily MVPA and academic achievement could not be explained by possible mediating effects of inhibitory control or working memory, as daily MVPA was also not related to either of the indices of cognitive control. One other study attempted to answer this question and found evidence of partial mediation. Specifically, selective attention (measured with d2 test; Brickenkamp & Zillmer, 1998) mediated a positive relationship between total physical activity

volume (assessed with ActivPAL) and adolescents' grades in mathematics. Due to differences in physical activity, cognitive, academic achievement measures and age of the samples, these two studies are not comparable. Future studies should explore this potential mechanism, whereby physical activity may affect academic performance. In addition to cognitive control, which is the main focus in physical activity and cognition literature, other cognitive functions could also help explain such associations. For example, a small number of studies investigated the associations between CRF and the effects of chronic aerobic exercise on children's relational memory (Chaddock, Hillman, Buck, & Cohen, 2011; Monti, Hillman, & Cohen, 2012), namely the cognitive function, which allows one to form relations and representations between experiences, people, places, objects as well as concepts (Cohen et al., 1999), which is also dependent upon cognitive control (Chaddock, et al., 2011). Evidence from these studies suggests that both CRF and chronic aerobic exercise benefit relational memory in preadolescent children (Chaddock, et al., 2011; Monti, et al., 2012). These results are of significant value, as relational memory is a marker of hippocampal function, namely this brain structure, which underlies learning and is responsible for the transfer of information to and from long term memory (Cohen, et al., 1999). Thus, the inclusion of a measure of relational memory into the study of physical activity, cognition and academic achievement in children could increase evidence base on the associations between physical activity and cognitive functions, which are important to learning and academic achievement.

7.3 The effects of aerobic exercise intervention on cognitive control in children (study 3)

In summary, findings from study 2 revealed that only CRF but not intermittent daily MVPA as measured with accelerometers was positively related to cognitive functions in children, and limited evidence on the associations of CRF to processing speed was found in study 1. Importantly, children with higher CRF were better able to control distractions than less aerobically fit peers. No such associations were observed for daily MVPA despite controlling for IQ and other important sources of variance in cognitive performance. Such findings suggested that it may be appropriate to design interventions, which specifically engage children in regular aerobic exercise to increase their CRF rather than focusing on increasing daily but intermittent MVPA. This contention aligns with emergent evidence on the efficacy of chronic aerobic exercise interventions in improving cognitive control in children (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Kamijo, et al., 2011).

Only a paucity of RCTs focused on the effects of chronic aerobic exercise to improve cognition, and the extant evidence has several limitations. First, findings from a large proportion of chronic aerobic exercise intervention studies (Davis, et al., 2007; Davis, et al., 2011; Krafft, et al., 2014) are limited in their generalisability as they were designed specifically for overweight and obese children, who may benefit more with respect to cognition from daily aerobic exercise than children of normal weight. This is because overweight and obesity have been independently related to poorer cognitive function in children and adolescents (Kamijo, et al., 2012; Li et al., 2009; Yu, et al., 2010). Thus, these children may start off with a lower cognitive reserve. Second, some studies did not report the effects of chronic aerobic exercise interventions on CRF (Davis, et al., 2011). Amongst those which did, not all studies noted intervention-related increments in CRF (e.g. Chaddock-Heyman, et al., 2013). Not including CRF in the analyses is an important limitation, as CRF is posited to be the main mediator of the effects of chronic aerobic exercise on cognitive function (Chodzko-Zajko & Moore, 1994; Etnier, 2006; Hötting & Röder, 2013). Third, none of the published chronic aerobic exercise intervention studies controlled for baseline levels of objectively assessed MVPA. Since greater health gains across multiple health outcomes have been observed at the lower end of physical activity continuum (PAGAC, 2008), inactive children could potentially benefit more cognitively from participation in chronic aerobic exercise intervention. Therefore, it was important to ascertain whether any differences between intervention and control groups could not in part be explained by differences in baseline levels of MVPA (and time sedentary). Last, a nominal number of studies have considered multiple domains of cognitive control when testing the effects of chronic aerobic exercise interventions on children's cognition (Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Krafft, et al., 2014). Considering multiple domains of cognitive control simultaneously is needed as at present it remains unknown to what extent the effects of chronic aerobic exercise interventions are specific to a cognitive function under investigation (i.e. inhibition, WM, task switching) or to the engagement of cognitive control in general (i.e. based on the common cognitive control factor; Miyake & Friedman, 2012).

7.3.1 Evaluation of FITKids2 intervention in relation to other RCTs

Overall the intervention was successfully implemented, and measures confirmed its fidelity. That is, children attended 90% of the intervention sessions, spent the majority of the monitored time (92.5%) in MVPA, and achieved an average heart rate of 146 bpm, which corresponds to moderate intensity physical activity (~70% of a maximum heart rate for a 9 year old child;

Pescatello & ACSM, 2014). The fidelity of our intervention is comparable to that of other RCTs, albeit we noted a higher attendance rate than the average of 80.6% across other studies using subsets of participants from the same intervention (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Kamijo, et al., 2011; Krafft, et al., 2014). The mean HR achieved by the participants in our study is slightly below the 158 average for 4 studies, which reported mean HR (Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Krafft, et al., 2014). This likely reflects the differences in intervention content and HR targets employed in FITKids2 (study 3) and aerobic exercise intervention reported by the group of Davis and colleagues (2007, 2011; Krafft, et al., 2014). That is, in FITKids2 (study 3, and FITKids; Hillman, et al., 2014) a target HR was defined as 55-80% of child's maximum HR, which is on average lower than 150 bpm target employed by Davis and colleagues (2007, 2011; Krafft, et al., 2014). Further, Davis et al. (2007, 2011) focused only on aerobic activities, which were easy to perform and did not require skill building, whereas FITKids and FITKids2 incorporated elements of skill building into curriculum. Nonetheless, both intensity levels correspond to MVPA (Whaley, et al., 2006) and therefore the results of Davis et al.'s (2007, 2011), Hillman et al.'s (2014) and those reported in study 3 in relation to cognition are comparable. In addition, a higher dose of MVPA was adopted in FITKids trials to exceed physical activity recommendations (Hillman, et al., 2014).

Based on the preliminary evidence of a dose-response on children's cognition reported by Davis et al. (2011; as indicated by the duration of aerobic exercise bouts of 20 versus 40 minutes), future studies should inspect these effects in more detail. A meta-analysis of findings on the effects of chronic exercise interventions (including aerobic as well as resistance and perceptual-motor training) on cognition (general intellectual capacity and academic achievement) indicated that the highest cognitive gains were achieved within 36 to 70 hours of training, with smaller gains thereafter (Fedewa & Ahn, 2011). Reviewed chronic aerobic exercise interventions (Chaddock-Heyman, et al., 2013; Davis, et al., 2007; Davis, et al., 2011; Hillman, et al., 2014; Kamijo, et al., 2011; Krafft, et al., 2014; including study 3), offered aerobic exercise in excess of 70 hours. Thus, a pertinent question would be how much (e.g. how many sessions and of how long duration) of aerobic exercise is enough to benefit children's cognition. Leading from that, an equally important but thus far not examined question is the sustainability of the effects of chronic aerobic exercise on cognition in young people. The results from functional neuroimaging studies indicate that cognitive changes instigated by chronic aerobic exercise interventions are paralleled by greater efficiency in brain

networks sub-serving attentional control (including prefrontal and parietal regions; Davis & Cooper, 2011; Hillman, et al., 2014). However, these studies do not provide evidence on structural brain changes, which would support long term cognitive benefits. Thus, one of the limitations of the current literature is the lack of follow-up assessments, which could address the question on sustainability of the intervention effects on cognitive function in children. Such studies are needed as their results would inform future interventions as well as policy.

7.3.2 The effects of chronic aerobic exercise on cognitive control

The findings from study 3 indicated that FITKids2 intervention had a positive effect of medium magnitude ($\eta_p^2 = .13$) on one indicator of cognitive control in children, inhibitory control of attention. This effect was independent of child's daily MVPA or time sedentary, thus suggesting that aerobic exercise intervention can be beneficial to child's inhibitory control, regardless of their initial levels of physical activity. In contrast, no intervention effects were observed on WM. However, due to the small sample size and limited power, the null results in relation to WM need to be interpreted with caution. For example, previous work by Hillman et al. (2014) based on a large sample of 221 pre-adolescents and similar intervention content provided evidence for positive effects of the 9-month after-school aerobic exercise intervention on task switching, which engages both inhibitory control and WM. As previously explained in chapter 6 (p. 131), this selective effect may be related to the cognitive indicators used in the task of WM. A selective effect of the intervention was found for RT measure on the flanker task but not accuracy, as both intervention and the control group improved in accuracy of the performance. In contrast, the indicator of WM as assessed with OSPAN task relies on accuracy but not speed of performance. Consequently, it is possible that in our sample the effects of aerobic exercise intervention were specific to speed of performance but not accuracy which showed developmental but not intervention related increments.

It may also be possible that the selective effect of the FITKids2 intervention observed in study 3 could partly be driven by these aspects of the intervention, which were not measured in the study. For example, during the organisational games children were required to pay attention to instruction and to respond appropriately in a fast paced and dynamically changing environment. To respond, a child would need to selectively attend to salient (for example, a sponge ball, a tagger chasing after a child) and ignore distracting elements of the environment (for example, a friend). Therefore they would also practice attentional skills, and fast responding. Although keeping and updating rules of the game would require WM, it is possible that concise and clear

instruction paired with simple rules (many games were based on adaptations of a tag game) placed relatively small demands on WM. Alternatively, increments in WM may require a more focused cognitive training. Since psychological (including cognitive) aspects of the intervention were not measured, such interpretation remains speculative.

Our results on the positive effect of align with those reported by Hillman et al. (2014). This is an important finding, which suggests that chronic aerobic exercise intervention benefited children's ability to suppress distractions and goal focused behaviour independent of baseline physical activity levels (MVPA) and time sedentary. The implications of these findings are better understood in the context of the relationship between inhibitory control and child's ability to self-regulate emotions and behaviour (Rueda, et al., 2005), its associations with higher academic achievement (Blair & Razza, 2007; Espy, et al., 2004) and predictive value in forecasting future health and financial well-being (Moffitt, et al., 2011). That is, children with better self-regulatory skills grow up to be healthier (expressed as a combined index for cardiovascular, inflammatory, respiratory, sexual and dental health) and more financially planful adults, as indicated by greater financial capital and less money related difficulties (Moffitt, et al., 2011). Likewise, inhibitory control during childhood is both associated (Espy, 1997) and predictive of (Blair & Razza, 2007) academic achievement in mathematics and reading (Borella, et al., 2010). Our findings make a significant contribution to the field as they clearly show that such skills can be improved. Together with the extant body of literature on the effects of chronic aerobic exercise intervention on inhibitory control in children (Chaddock-Heyman, et al., 2013; Hillman, et al., 2014), our findings convey an important public health message whereby engaging children in regular aerobic exercise can foster these cognitive skills, which are instrumental to academic success and important to developing life skills.

The comparison of our findings in relation to inhibitory control with those reported by Davis et al. (2007, 2011) is difficult, as these authors used composite cognitive score across multiple cognitive control tasks (Attention scale of CAS; Naglieri & Das, 1997). The tasks included measures of interference control, selective attention and task switching. Thus, their conclusions on the null effects of chronic aerobic exercise intervention on attention may be occluded by the heterogeneity of measures. For example, it is possible that such effects could be observed on one measure (e.g. interference control) but not others. Likewise, we cannot easily compare our results to the positive effects of chronic aerobic exercise intervention reported by these authors on planning. Although planning is a higher order cognitive function subserved by the interactions between inhibition and WM (Asato, et al., 2006), it is a distinct cognitive construct

which is more akin to measures of mental flexibility rather than inhibitory control or WM alone (Naglieri, Prewett, & Bardos, 1989). This example clearly illustrates that heterogeneity of measures and constructs used to assess cognition, which prevails in physical activity and cognitive literature, makes the comparison of the study results challenging. For the field to move forward, studies, which replicate current findings are needed. Further, to facilitate the comparisons of findings between studies using laboratory cognitive tasks (where measures of reaction time and accuracy on multiple task conditions are used as indicators of cognitive function) and those employing cognitive test batteries such as CAS (where composite and standardised scores are reported; Naglieri & Das, 1997), it would be helpful if authors who employ the latter measures also reported mean reaction times and accuracies for the tasks which contributed to the scale composites.

In contrast to inhibitory control, we found no effects of the intervention on WM. Our results differ from those of Kamijo et al. (2011), found a positive effect of FITKids intervention on some aspects of a WM memory task (a 3-letter compared to a 1-letter condition). The discrepancy between our findings and those of Kamijo et al. (2011) could be related to the differences in cognitive tasks (for example, Sternberg task used by Kamijo et al. (2011)) does not include a dual task component and relies on recognition of letters, while operation span task employed in our study requires recall of word sequences and thus may be more cognitively demanding), as well as to the issue of limited power in our study. Given the paucity of data on chronic aerobic exercise interventions and WM, and the limited power of our study, at present the inferences on the effects of aerobic exercise interventions on WM in children would be premature.

7.3.3 Potential mediating mechanisms

The results of study 3 could not confirm or refute the ‘cardiovascular fitness hypothesis’ (Chodzko-Zajko & Moore, 1994) as we observed no increments in CRF due to FITKids2 intervention. However, a protective effect of the intervention on BMI percentile was paired with a trend ($p = .078$) towards a decline in CRF (VO_{2max} percentile) in the control but not the intervention group ($p = .48$), thus suggesting a possible protective effect of the intervention on two correlated physiological markers. Hillman et al. (2014) found significant effects of the prior FITKids intervention on CRF in children of similar age. Since the intervention content in terms of intensity, volume and frequency of aerobic exercise was very similar in both trials, it is likely that the lack of observed increments was due to the small sample size and thus the low

power of our pilot study to detect these effects. Consequently, our results in relation to both WM and CRF are tentative and should be further evaluated with larger samples. We plan such evaluation with a larger sample following the data collection in spring/summer 2015 when the next cohort of FITKids2 will complete the intervention.

Since the effects of the aerobic exercise intervention on inhibitory control emerged in the absence of such effect on CRF, the results of study 3 also suggest that other potential mediators could also help explain the observed effect. Several studies in older adults were able to discern the contribution of CRF to the effects of chronic aerobic exercise intervention on cognition in contrast to other non-specific factors (e.g. taking up a new activity and its effects on cognitive enhancement) by including a stretching/coordination control group (Colcombe et al., 2004; Hötting et al., 2012; Kramer, et al., 1999). Changes in CRF explained a relatively small variance in cognitive improvement (8-10%; Colcombe, et al., 2004; Hötting, et al., 2012; Kramer, et al., 1999). Therefore, other than CRF factors likely also account for positive cognitive changes following aerobic exercise intervention in both children and adults (Hötting & Röder, 2013).

7.3.3.1 Physiological mechanisms

Such mechanisms can include changes to brain structure and function, which are supported by the positive effects of aerobic exercise on neurogenesis, synaptogenesis and angiogenesis in animal models (Wang & van Praag, 2012). Multiple studies in rodents evidenced positive effects of wheel running on neurogenesis, synaptic plasticity and long-term potentiation (a neural substrate of learning) in the dentate gyrus of the hippocampus (a brain structure subserving memory and learning; Marlatt, Potter, Lucassen, & van Praag, 2012; van Praag, Christie, Sejnowski, & Gage, 1999; van Praag, Kempermann, & Gage, 1999). These effects were specific to running, after controlling for environmental enrichment and water maze learning (van Praag, Kempermann, et al., 1999). The structural changes corresponded to improved performance on tasks of spatial learning and memory (Marlatt, et al., 2012). There is evidence to suggest that neurogenesis is likely supported by changes to brain vasculature (Christie et al., 2008; Pereira et al., 2007). For example, exercise induced angiogenesis correlated with increased neurogenesis in the dentate gyrus in mice (Pereira, et al., 2007). In a human study of young adults, increments in VO_{2max} following a chronic aerobic exercise intervention correlated with increased cerebral blood volume in the dentate gyrus, entorhinal cortex and CA1 area of the hippocampus, and improved long term memory (Pereira, et al., 2007). These structural changes in the brain are mediated by the up-regulation of brain derived

neurotrophic factor (BDNF), which promotes synaptic transmission and long-term potentiation, namely a neural form of learning (Gomez-Pinilla & Feng, 2012; Gomez-Pinilla, et al., 2008). In children, such effects may be especially potent as they coincide with critical maturational events in brain development such as peaking synaptic density and subsequent synaptic pruning (Casey, Galvan, et al., 2005; Casey, Tottenham, Liston, & Durston, 2005; Gomez-Pinilla & Feng, 2012; Luna et al., 2001). In turn, increased synaptic density is positively related to cognitive performance (Bibb, Mayford, Tsien, & Alberini, 2010). Therefore, chronic aerobic exercise may positively affect cognitive control by promoting maintenance of synaptic connections, which subserve cognitive control (Gomez-Pinilla & Feng, 2012). Further, preliminary evidence suggests that in children chronic aerobic exercise promotes efficiency in these brain networks, which underlie cognitive control (Davis, et al., 2011; Hillman, et al., 2014). That is, Hillman et al. (2014) found that in parallel to positive cognitive changes, participation in the FITKids intervention resulted in better attention allocation and efficiency in response selection, as indexed by higher amplitude and shorter latencies of a P3 component of event related potentials, which originates from a fronto-parietal brain network. Similarly, Davis et al. (2011) noted intervention-related improvements (following a three-month after-school aerobic exercise intervention) in planning, which coincided with increased activation of prefrontal brain regions. Further evidence is needed to elucidate the physiological mechanisms (e.g. structural changes in brain regions underpinning cognitive control, increments in the levels of BDNF, increased cerebral blood volume), which underpin the effects of chronic aerobic exercise on brain function and cognition.

7.3.3.2 Psycho-social mechanisms

Apart from physiological factors, which can drive the effects of chronic aerobic exercise on cognitive control, psycho-social variables may also act as potential mediators (Tompsonski, et al., 2011). Chronic aerobic exercise interventions provide children with an enriched context for learning and practicing physical but also cognitive (e.g. paying attention, problem solving, reacting to a fast paced and changing environment during organisational games) skills through interactions with peers and staff by engaging children in physical activities based on teamwork, or with elements of skill development. However, the effects of such psychological (e.g. attention, motivation, self-efficacy) and social (e.g. interaction with peers, staff) factors have not been assessed or controlled for in the studies of chronic aerobic exercise and children's cognition.

This is a limitation as the content of such interventions partly draws upon social cognitive theory, which emphasises the importance of self-efficacy (i.e. individual's belief in their own capacity to successfully manage behaviour to obtain desired outcomes) on motivation and behaviour (Bandura, 1977, 1993). For example, the content of study 3 as well as the FITKids trial has been modelled on the CATCH trial, which draws upon social cognitive theory (Bandura, 1977, 1993). Indeed, within the FITKids2 intervention evaluated in study 3, children were faced with multiple opportunities to foster self-efficacy through social modelling (e.g., observing and learning from intervention staff and peers), verbal persuasion (e.g., encouragement from the staff), and mastery experience (e.g. mastering a new skill), namely the main processes, which increase self-efficacy (Bandura, 1977, 1993). Increases in self-efficacy within the physical activity context could foster child's self-regulatory skills. For example, increased self-efficacy has been associated with better self-regulatory skills developed within academic context (Pintrich, 1999). Further, chronic aerobic exercise sessions have a predefined structure with the emphasis on on-task behaviour, which are supported by the strategies developed by staff to keep children engaged. The modelling of positive behaviours (e.g., keeping on task, listening to the instruction) may generalise to other contexts, including cognitive testing environment. For example, a positive effect of a chronic aerobic exercise intervention on behavioural ratings of inattention (alongside its effects on sustained attention) were reported for children with ADHD (Verret, et al., 2012). None of the chronic aerobic exercise intervention studies analysed the effects of chronic aerobic exercise intervention on such contextual (modelling) and psychological (motivation, on task behaviour) variables. Likewise, the majority of the studies (5 out of 6) did not include attentional control group (e.g. with elements of structured and on-task sedentary or non-aerobic activities under instruction of qualified staff). One that did (Krafft, et al., 2014) noted no intervention effects on behavioural measures but observed decreased activation in brain regions sub-serving cognitive control (fronto-parietal regions), which authors interpreted as evidence of more efficient brain activation pattern in the exercise relative to attentional control group. Since these changes did not correlate with behavioural performance, it is difficult to make inferences on how these effects could generalise to cognitive measures. Therefore, at present the influence of psychosocial variables on the effects of chronic aerobic exercise interventions on cognition in healthy children cannot be assessed. Preliminary evidence from chronic aerobic exercise interventions in children with ADHD suggests that cognitive benefits from chronic aerobic exercise interventions are paralleled with positive effects of the intervention on children's self-esteem (assessed with parental, teacher and staff ratings), improvements in social skills (Smith, et al.,

2013) and decrease in inattention and interruptions (Smith, et al., 2013; Verret, et al., 2012). Since these interventions were not specifically developed to target psycho-social outcomes, their results suggest a generalised effect of chronic aerobic exercise interventions on psycho-social variables for children with ADHD. Although, these results may not generalise to a healthy population of children, they suggest that a possibility of such effects needs to be considered. Future research should attempt to include psycho-social outcome measures (e.g. self-efficacy, self-esteem, motivation, social skills) of the intervention as well as attentional control group to elucidate potential mediating effects of psychological variables and social context inherent in chronic aerobic exercise interventions, on the effects of chronic aerobic exercise interventions on young people's cognition.

7.4 Strengths and limitations

7.4.1 Study 1

The key strengths of study 1 include: 1) to the author's knowledge this is the first study to: a) assess the posited relationships in older adolescents, b) inspect the associations with response variability as opposed to only the measures of central tendency, c) control for CRF and IQ; 2) a large sample size ($n = 667$); 3) objective monitoring of physical activity with accelerometers; 4) objective measurement of attentional control using a computerised task; 5) objectively assessed CRF with PWC-170, which shows high validity; 6) inclusion of objectively measured important covariates such as: a) IQ assessed with a validated and standardised test, b) clinical assessments of ADHD, c) objective assessment of adiposity (Dual X-ray Absorptiometry).

The main limitation of study 1 is related to the experimental manipulation in Stop Signal task applied in the ALSPAC research clinics at 15 years, and a cognitive strategy employed by adolescents to overcome the uncertainty of the stop signal. That is, due to the manipulation of the task parameters in ALSPAC research clinics at 15 years, it was necessary to bifurcate the cohort based on the set of task parameters, which was used. This precluded unitary analyses of the whole cohort. Second, adolescents slowed their responses on the stop signal condition to maximise accuracy on stop signal trials. This could have been avoided if the task was pilot tested prior to deployment. Specifically, several adjustments to task parameters could be recommended: 1) a lower proportion of stop signal trials (25% as opposed to 33%), 2) greater number of trials within a stop signal condition (~ 400 trials compared to 96) and 3) dynamically adjusted stop signal delays (i.e. the timing of stop signal in relation to go signal) based on participant's individually tracked performance (Band, et al., 2003). The limitation of physical

activity measurement pertain to studies 1, 2 and 3 and therefore will be jointly discussed in the following section (7.4.4).

As with every epidemiological study there is a question of generalisability of findings due to study attrition and missing data. In general, 37% of all ALSPAC participants attended research clinics at 15 years and 12% were included in the current study. The sample characteristics in study 1 predominantly reflected the inclusion criteria. The study sample had higher socio-economic status and lower BMI than the remainder of the cohort. However, the characteristics of our sample reflect those of the ALSPAC cohort in general, which is predominantly White, less likely to come from low socio-economic backgrounds, and has higher educational attainment as compared to the national UK average (Boyd, et al., 2013). Last, the cross-sectional design precludes conclusions on causality of findings relevant to CRF.

7.4.2 Study 2

The key strengths of study 2 include: 1) to the author's knowledge this is the first study to: a) inspect the associations between objectively measured MVPA and cognitive control specifically in younger preadolescent children, b) to look at two indices of cognitive control (inhibition and WM), which have been most consistently associated with CRF, and chronic aerobic exercise in children (Buck, et al., 2004; Buck, et al., 2008; Chaddock-Heyman, et al., 2013; Chaddock, Erickson, et al., 2012; Chaddock, Hillman, et al., 2012; Davis, et al., 2007; Davis, et al., 2011; Hillman, 2005; Hillman, et al., 2014; Kamijo, et al., 2011; Krafft, et al., 2014; Moore, et al., 2013; Pontifex, et al., 2011; Scudder, et al., 2014; Voss, et al., 2011), c) to control for CRF and IQ; d) to consider the associations between objectively measured MVPA and academic achievement in the context of multiple indices of cognitive control; 2) objective monitoring of physical activity with high resolution (15 second epochs) using state of the art equipment (wGT3X+ accelerometers, sampling rate of 100Hz), which ensured that intermittent MVPA was adequately captured; 3) a gold standard measure of CRF (i.e., maximal exercise test on the treadmill; Whaley, et al., 2006); 4) sensitive laboratory tasks to measure cognitive control; 5) tightly controlled research environment during cognitive testing, which included: a) the same sound proof testing chamber with ambient light used across all participants; b) instructions delivered by trained staff emphasising both speed and accuracy, which minimised adoption of a cognitive strategy of selectively favouring one dimension; c) a cut-off of 70% on accuracy on the practice trials with feedback from the researcher to ensure that a child

understood the task; 6) the use of validated and standardised tests of intelligence and academic achievement.

In study 2 many of the limitations of study 1 were overcome with more sensitive measurement of cognitive control and physical activity using higher resolution and smaller epochs. The limitations of study 2 include: 1) cross-sectional design, which precluded causal inferences relevant to findings on CRF; 2) inclusion of only a single day of physical activity limits inferences on the relationship of habitual MVPA to cognitive control; 3) assessment of physical activity during summer months when physical activity levels are on average higher; 4) a relatively small sample.

7.4.3 Study 3

The key strengths of study 3 include: 1) a robust research design (RCT); 2) low attrition (11%); 3) multiple objective measures of intervention fidelity (gold standard measure of CRF, tracking attendance, HR monitored during each session); 4) the use of multiple strategies to ensure intervention fidelity (e.g. self- and staff monitoring of physical activity intensity; staff training in the use of strategies to keep children engaged, physically active at the moderate-to-vigorous level, and on task); 5) high intervention fidelity (90% attendance, 92.5% of the tracked session time was spent in MVPA, as objectively measured with HR telemetry; no increase in BMI percentile in the intervention group); 6) adopting a higher dose of MVPA (70 minutes) during aerobic exercise sessions than in previous studies in overweight and obese children (20 and 40 minutes); 7) providing free after-school care and transportation to the intervention centre, thus limiting logistical barrier to participation, especially for children from lower socio-economic backgrounds, who are known to selectively drop-out from research causing sample bias (Brannon et al., 2013); 8) controlling for baseline levels of objectively assessed daily MVPA (and time sedentary); 9) inclusion of multiple measures of cognitive control (inhibition, WM); 10) the use of sensitive laboratory tasks to measure cognition.

The main limitation of study 3 was a small sample size and therefore limited power to make inferences relevant to changes in CRF and WM. Second, the effects of the intervention on psychological outcomes such as self-efficacy, motivation, or the effects of interactions with peers and the University staff were not assessed, and therefore their impact on cognitive changes could not be controlled for. Third, the inclusion of an active control group, which would be involved in sedentary but also interactive activities under the instruction of the University staff would ensure that such effects could be controlled for. Fourth, the lack of

follow-up assessments of the intervention precludes conclusions on sustainability of the intervention effect on cognitive control. Last, the lack of assessment of physical activity following the completion of the intervention precluded conclusions on the intervention effects on changes in physical activity behaviour.

7.4.4 Limitations of accelerometry

Accelerometers underestimate energy expenditure as they cannot measure activities such as cycling and swimming. In addition, the ability of extant regression equations to accurately classify the intensity of physical activities is limited by inter-individual variability in age, body size, and clothing (Alhassan et al., 2012; Crouter, et al., 2013; Esliger, 2005). The devices would need to be calibrated to each individual in order to provide the most accurate estimate. Alternatively, a combination of accelerometry and HR monitoring could be used, however such approach could be too costly in the scope of a large epidemiological study (study 1). In addition, MVPA in study 1 may have been underestimated because of a larger epoch used to sample the data (60 s). Thus, shorter MVPA bouts could have been accounted as light activity. Further, a short assessment period of 7 days provides limited information on habitual physical activity, with large intra-individual variation (Mattocks, 2007). Between-day stability increases with the number of days assessed, and in study 1, 70% of participants provided at least 6 days of data therefore reducing the intra-individual variability. Nonetheless, even seven days of accelerometer wear provide only a limited representation of child or adolescent's regular physical activity levels, which vary across the entire year (Mattocks, 2007). Although, it could be argued that the lack of associations between objectively measured MVPA and cognitive control in study 2 could be due to including those participants who had less than 4 days of accelerometer wear, to conserve the sample and to allow for meaningful multiple hierarchical regression analyses with multiple predictors, we included 9 children with less than 4 days of wear (including 5 children (6% of the sample) with one day of wear). However, when analyses were repeated excluding these children, the results remained materially unchanged.

7.5 Future directions

Findings presented within this thesis have implications for future research and practice relevant to the associations of physical activity and cognition in young people. These implications have been organised into two themes focused on 1) observational research on daily MVPA and cognitive function, and 2) chronic aerobic exercise interventions. At present scant evidence on these associations exists, and with the exception of study 2, it is limited to adolescents and does

not include measures of CRF or IQ. Based on equivocal and nominal findings on the associations between daily MVPA and cognition, further research is necessary to elucidate these associations.

7.5.1 Daily MVPA and cognitive function

- (1) Any future studies on the associations between daily MVPA and cognitive functions in young people should include information on physical activity patterns as well as volume.
- (2) Studies need to account for important confounders in the relationship between physical activity and cognition, which as a minimum should include age, sex, CRF, IQ and measures of adiposity and SES. The potential mediating and moderating effects of such variables should be evaluated.
- (3) Further research is needed to assess the relationship between physical activity and multiple cognitive functions including those specifically pertinent to learning such as memory (e.g., relational memory). Studies should attempt to either include multiple measures of the same cognitive construct to facilitate latent variable analyses or to measure multiple cognitive constructs concurrently to increase the evidence base.
- (4) Further quality evidence is needed on the associations between objectively measured physical activity and academic achievement and the role of various cognitive functions in this relationship.
- (5) Prospective studies into the associations between physical activity and cognitive function are needed. Such studies should include multiple measures of physical activity to account for the mode of physical activity, duration, frequency and intensity, as well as objective measures of cognitive function and academic achievement.

7.5.2 Chronic aerobic exercise interventions

- (1) Future studies should endeavour to inspect the dose-response effects of chronic aerobic exercise on children's cognition. To adequately assess dose-response effects studies should include objective baseline measures of physical activity.
- (2) Studies into the mechanisms behind the effects of chronic aerobic exercise on cognition in children are necessary. Such mechanisms should include both physiological (e.g., neurocognitive structural changes, measures of cerebral blood volume) as well as potential effects of psycho-social variables.

(3) Future research should endeavour to assess the long term effects of chronic aerobic exercise interventions on cognitive control in young people by including follow-up assessments.

(4) Future studies using experimental design should attempt to elucidate whether the increments in intermittent MVPA compared to chronic aerobic exercise benefit cognitive control in children and adolescents. Such studies should ideally include chronic aerobic exercise condition, intermittent MVPA condition (matched on MVPA volume), attentional control condition.

7.6 Overall conclusions

There is a need to further understand what aspects of physical activity (e.g. chronic aerobic exercise versus patterns of habitual physical activity) are specifically related to improved cognitive performance and to what degree. Importantly, there is a need to understand what dose of sustained physical activity is needed for such benefits to accrue across childhood and adolescence to inform policy and possibly physical activity recommendations to benefit cognitive performance. This thesis has found that objectively measured daily MVPA was not related to either cognitive control or academic performance in children, and to cognitive performance in adolescents. In contrast chronic nine-month aerobic exercise intervention benefited children's inhibitory control, which is closely related to the ability to self-regulate cognition, behaviour and emotions. Such findings add considerably to the existing literature as they suggest that regular aerobic exercise could bring some cognitive benefits to preadolescent children in this aspect of cognition, which is closely related to academic performance and important to self-regulation. These benefits accrued regardless of children's initial physical activity levels or changes in CRF. Therefore engaging children in regular structured aerobic exercise in a group setting holds promise as one of the means to improve specific aspects of cognitive performance.

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APPENDIX A:

Journal publications and conference presentations related to work presented in
this thesis

Journal articles

(A copy of the front page of the article is included)

Pindus, D. M., Moore, R. D., Hillman, C. H., Bandelow, S., Hogervorst, E., Biddle, S. J. H., & Sherar, L. B. (in press). The relationship of moderate-to-vigorous physical activity to cognitive processing in adolescents: Findings from the ALSPAC birth cohort. *Psychological Research*. Advance online publication. doi: 10.1007/s00426-014-0612-2.

Conference presentations

Pindus, D.M., Moore, R.D., Hillman, C.H., Hogervorst, E., Biddle, S.J.H. and Sherar, L.B. (2014, August). The relations of aerobic fitness and physical activity to cognitive processing: Findings from the ALSPAC birth cohort. *North American Society for Pediatric Exercise Medicine (NASPEM) Biennial Conference*, Minneapolis, United States (oral presentation).

Pindus, D.M., Khan, N., Drollette, E. S., Moore, R.D., Scudder, M., Raine, L., Sherar, L.B., Hillman, C.H. (2014, May). Physical activity intervention and changes in cognitive control in pre-pubertal children: Does intensity matter? Insights from the FITKids randomized controlled trial. *International Society of Behavioral Nutrition and Physical Activity (ISBNPA) 2014 Annual Meeting*, San Diego, CA, United States (invited oral presentation).

Pindus, D.M., Bandelow, S., Hogervorst, E., Biddle, S.J.H., and Sherar, L.B. (2013, May). The association between cardio-respiratory fitness and attention in a birth cohort of British children: Findings from the Avon Longitudinal Study of Parents and Children (ALSPAC). *2013 Annual Meeting of the Society of Behavioral Nutrition and Physical Activity*, Ghent, Belgium (oral presentation).

The relationship of moderate-to-vigorous physical activity to cognitive processing in adolescents: findings from the ALSPAC birth cohort

Dominika M. Pindus · Robert D. Moore Davis ·
Charles H. Hillman · Stephan Bandelow · Eef Hogervorst ·
Stuart J. H. Biddle · Lauren B. Sherar

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Abstract The aim of this study was to assess the relations of daily moderate-to-vigorous physical activity (MVPA) to cognitive functions in 15-year-old adolescents from the Avon Longitudinal Study of Parents and Children while controlling for aerobic fitness. A sub-sample of 667 adolescents ($M_{age} = 15.4 \pm 0.16$ years; 55 % females) who provided valid data on variables of interest, were used in the analyses. MVPA was objectively assessed using an Actigraph GT1M accelerometer and aerobic fitness was expressed as physical work capacity at the heart rate of 170 beats per minute from a cycle ergometer test. A computerized stop-signal task was used to measure mean reaction time (RT) and standard deviation of RT, as indicators of cognitive processing speed and variability during an attention and inhibitory control task. MVPA was not significantly related to cognitive processing speed or variability of cognitive performance in hierarchical linear regression models. In simple regression models, aerobic

fitness was negatively related to mean RT on the simple go condition. Our results suggest that aerobic fitness, but not MVPA, was associated with cognitive processing speed under less cognitively demanding task conditions. The results thus indicate a potential global effect of aerobic fitness on cognitive functions in adolescents but this may differ depending on the specific task characteristics.

Introduction

The adverse physical health consequences of physical inactivity in youth are well understood (Gutin & Owens, 2011; Hallal, Victora, Azevedo, & Wells, 2006; Iannotti, Kogan, Janssen, & Boyce, 2009). However, the relations of daily (i.e. accumulated throughout the entire day) physical activity to cognitive functions in youth are less well understood. Thus far, the majority of research has focused on aerobic fitness as a proxy for regular physical activity. The results of these studies indicate that relative to lower fit children, higher fit children modulate attention more efficiently in relation to task demands (Pontifex et al., 2011); demonstrate greater inhibitory control over pre-potent responses (Chaddock et al., 2012a); and are less affected by task difficulty and conditional manipulations (Voss et al., 2011). That is, higher fit children demonstrate greater performance on tasks requiring cognitive control, particularly for tasks that modulate attentional demands. Cognitive control (also known as executive control or executive function) refers to higher order computational processes underlying perception, memory and action, which serve to regulate and optimize goal-directed behaviors (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Norman & Shallice, 1986; Meyer & Kieras, 1997). Its core processes include: planning and mental flexibility, working memory and

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APPENDIX B:

Consent to collect diagnostic interview information in the ALSPAC study
research clinics at 15.5 years

TF3 File – Interview Session

Teen Focus 3 Visit Number _____	WASI Consent _____	TF3WC	Version 1 10.10.06	 CHILDREN OF THE 90s TeenFocus3 24 Tyndall Avenue Bristol BS8 1TQ (correspondence only) Tel: 0117 928 8900 (answer phone) e-mail: focus-admin@bristol.ac.uk
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Permission to record interviews

In order for us to collect the best quality information, we need to make sure that our staff are trained to the highest standard.

To do this we need to have some of our interviews recorded on tape for other members of the team to listen to. The interviews will have no names attached to them and no one outside the research team will listen to the tapes.

We are therefore asking for permission to record your interview. If you agree now and then change your mind during or after the interview, just let us know and we will stop recording and wipe the tape

STUDY TEENAGER CONSENT

I agree to my interview being taped, and I understand that I can ask for the recording to be stopped and the tape to be wiped at any point.

Signature Date signed / / 2 0 0

Initial Last Name

PARENTAL CONSENT

The purpose of recording the interview has been explained to me. I agree to my son/daughter having their interview recorded for the 'Children of the 90s' study.

I am his/her parent (or guardian) or have parent's permission to give consent.

Signature Date signed / / 2 0 0

Initial Last Name

Office use: Parent/guardian permission: Obtained by phone and form attached ☐ Not required (age 16) ☐

The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University
15880 

Page 1

APPENDIX C:

Consent to cycle ergometer test in the ALSPAC study research clinics at 15.5
years

APPENDIX D:

Data collection sheet: Cycle ergometer test in the ALSPAC study research
clinics at 15.5 years

TF3 File – Activity Session

Teen Focus 3	Activity Session	FORM TF3AC	Version 1	10.10.06
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Visit Number

AC1 Session Start Time : (24 hrs)

AC2 Visit Date / / 2 0 0

AC3 Room 1 ☐ 2 ☐ **AC4 Staff**

AC5 Room temp . °C

RESTING BLOOD PRESSURE

AC6 Salbutamol taken during lung function N ☐ Y ☐

AC8 Infection present/recent (3 weeks) N ☐ Y ☐

AC9 When? / / 2 0 0

AC11 Medication N ☐ Y ☐

AC13 Vaccine within last week? N ☐ Y ☐

AC14 Fried food in last 2 hrs N ☐ Y ☐

AC15 Caffeine in last 2 hrs N ☐ Y ☐

AC16 BP Done done not done refusal
1 ☐ 2 ☐ 3 ☐

AC7 Max Heart rate

AC10 Details

AC12 Details

AC17 Not done code

Result 1 AC18 AC19 AC20

Result 2 AC21 AC22 AC23 AC24 Demeanour

AC25 GP referral letter given? Y ☐ N ☐

AC26 Arm used R ☐ L ☐ AC27 Cuff used small adult adult adult plus
1 ☐ 2 ☐ 3 ☐

SAFETY

AC28 Asthma Y ☐ N ☐

AC31 Bone/Joint probs (serious restriction of movement) Y ☐ N ☐

AC33 Cardiovascular (exercise induced chest pains, dizziness/fainting) Y ☐ N ☐

AC35 Any other reason Y ☐ N ☐

if yes, acute attack
AC29 in last 3 wk, req. oral steroid Y ☐ N ☐

AC30 if yes; PEF > 70% Y ☐ N ☐

AC32 Details

AC34 Details

AC36 Details

Page 1 of 2

33919

TF3 File – Activity Session

Teen Focus 3	Activity Session	FORM TF3AC	Version 1	10.10.06
---------------------	-------------------------	-------------------	------------------	-----------------

EXERCISE TEST

AC37 Ex Test Started ☐ Y ☐ N ☐ AC38 Not done code

d d m m y y staff initials number

AC39 Final downloaded Polar file number

start AC40 Start work load Watts

2m 30s AC41 Systolic AC42 Diastolic AC43 Heart Rate

3m 00s AC44 Increased work load Watts

5m 30s AC45 Systolic AC46 Diastolic AC47 Heart Rate

6m 00s AC48 Increased work load Watts

8m 30s AC49 Systolic AC50 Diastolic AC51 Heart Rate

end AC52 Test Completed ☐ Y ☐ N ☐ if no, time stopped AC53 mins : secs AC54 code

post ex AC55 Systolic AC56 Diastolic AC57 Heart Rate

AC58 Session Comments

STAFF RATINGS - please complete this section for every child

ACR1 COOP	ACR2 SHY	ACR3 FIDG	ACR4 ACTIV	ACR5 ATTN	ACR6 RAP	ACR7 ANX
1 ☐	1 ☐	1 ☐	1 ☐	1 ☐	1 ☐	1 ☐
2 ☐	2 ☐	2 ☐	2 ☐	2 ☐	2 ☐	2 ☐
3 ☐	3 ☐	3 ☐	3 ☐	3 ☐	3 ☐	3 ☐

ACR8 Behaviour Comments

ACR9 Unusual behaviour / reactions ☐ Y ☐ Q ☐ N ☐

ACR10	ACR11	ACR12	ACR13	ACR14	ACR15	ACR16	ACR17	ACR18	ACR19	ACR20
☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y	☐ Y
☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q	☐ Q

33919

APPENDIX E:

Accelerometer data collection sheet: ALSPAC Research Clinics at 15.5 years

TF3 File – Activity Session

Teen Focus 3	Activity Monitor	TF3AM	Version 1	10.10.06
Visit Number A1 Visit Date / / A2 Grid Slot A3 Staff A4 Room 1 ☐ 2 ☐				
A5 Child/Carer happy to participate? Yes 1 ☐ No 2 ☐ If no, A6 Code A7 CSA given out today? Yes 1 ☐ No 2 ☐ If no, A8 Code A9 CSA Serial No. A10 Next 7 days to be typical activity? Yes 1 ☐ No 2 ☐ If no, A11 Code A12 Requires CSA at later date? Yes 1 ☐ No 2 ☐ If yes, A13 New start date / /				
DOWNLOAD DETAILS (for researcher use only) A14 Downloaded? Yes 1 ☐ No 2 ☐ Not returned 3 ☐ A16 Download Date / / A17 Staff Initials A18 Download Comments 				

TF3 File – Activity Session

	Teen Focus 3	Activity Monitor	TF3AM	Version 1	10.10.06	
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Activity monitor codes

Box A6

1. Child refused
2. Carer refused
3. No time to do this
4. Child not able

Box A8

1. Going away on Holiday
2. Illness or injury
3. No monitor available
4. More info to family needed
5. Timing inconvenient

Box A11

1. Going away on Holiday
2. School holidays
3. Illness or injury
4. Extra sporting activity (lasting more than 1 day)

	Page 2 of 2	 4365	
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APPENDIX F:

Stop Signal Task instructions at ALSPAC Research Clinics at 15.5 years

TF3 File – Interview Session

Inhibition Experimenter Instructions

The Inhibition task requires the young person to press the X button when they see an X on screen, and to press an O button when they see an O on screen. If a beep coincides with the presentation of either an X or O, then the young person must try NOT to press the button (inhibit). The young person receives four blocks of trials. The first block consists of Xs and Os with no beeps (30 trials in total) – the young person practices the button presses here. The second block consists of Xs, Os and beeps (24 trials in total 8 of which have a beep) – the young person practices the button presses with beeps here. The third and fourth blocks are the actual experimental trials. Each experimental block consists of 48 trials total in each. 32 of those trials are without beeps, and 16 trials are with beeps.

Instructions for setting priority of Inhibition (Flash Inhibition):

1. Input the participant identifier code twice.
2. Un-mute the volume on the monitor.
3. Explain the instructions to the young person and ensure they understand them before continuing. These instructions will be supported on screen by an example of what the young person is about to see (X or O).

“The computer will show a smiley face in the middle of the screen. You need to look at the smiley face as it acts as a target for you to watch. Then the computer will show either the letter O or the letter X. If you see the letter O come up on the screen, then you should press the button marked O. If you see the letter X come up on the screen, then you should press the button marked X. You should try and do this as fast as you can. If you make any mistakes – do not worry and just carry on. Do you understand what you have to do? OK – get ready for the smiley face.”

4. Make sure the young person uses **both hands** and their **right hand position** **the on ‘X’ button and left on the ‘O’ button**.
5. First block – young person receives 30 trials of Xs and Os.
6. Explain the next set of instructions to the young person and ensure they understand before continuing. These instructions will be supported on screen by an example of what the child is about to see and hear (X or O and beep).

“The next part of the game is a bit different. You will still see either the letter O or the letter X come up on the screen. BUT, sometimes you will also hear a beep. Let’s listen to the beep now! When you hear the beep you should try NOT to press the O or X buttons. When you do not hear a beep, you should press the O and X buttons just as you did in the first part of the game. Again do not worry if you make any mistakes – just keep going. Do you understand what you have to do? OK – get ready for the smiley face.”

7. Second block – young person receives 24 trials of Xs, Os and beeps.
8. A screen then appears to ask them to attempt the next block. **Experimenter** presses continue. At this point the Experimenter can explain that the game now stays the same – “the next blocks will still just be Xs, Os and beeps”.
9. Third block – young person receives 48 trials of Xs, Os and beeps.

TF3 File – Interview Session

10. A screen then appears to ask them to attempt the next block. **Experimenter** presses continue.
11. Fourth block – young person receives 48 trials of Xs, Os and beeps.
12. Read the following debrief aloud to the young person:

“You have now finished and you did really well! Thank you for completing the game. It will tell me how quickly you can respond to the letters and how quickly you do not respond to the letters when you hear a beep!”

13. The program closes down automatically and saves the data to a results file to be found in c:\inhibition\results.

APPENDIX G:

An example of a raw excel file with Stop Signal task data

APPENDIX H:

Parental Consent Form (Studies 2 and 3)

APPENDIX I:

Child Assent Form (Studies 2 and 3)

APPENDIX J:

Health History & Demographics Questionnaire (Studies 2 and 3)

APPENDIX K:

ADHD IV Rating Scale

APPENDIX L:

Tanner Staging Questionnaire (Girl)

APPENDIX M:

Tanner Staging Questionnaire (Boy)

APPENDIX N:

Physical Activity Readiness Questionnaire

APPENDIX O:

VO_{2max} Run Sheet

APPENDIX P:

The Children's OMNI scale of perceived exertion (OMNI Scale)

APPENDIX Q:

Accelerometer Information Sheet

Parent Information Sheet

PLEASE BRING BACK TO FIT KIDS

Issued: _____

Returned: _____

Your child may take the monitor off on: _____

Physical Activity Monitor Information

What is an activity monitor?

An activity monitor is a small device that records information about physical activity patterns. It uses a watch battery to power the monitor. The monitor records body movements during everyday activities such as walking, running, skipping and jumping. The monitor is safe and comfortable to wear. Most people forget that they are wearing it because it is light weight and quite small. Many studies with children and adolescents have successfully used activity monitors.



What is your child supposed to do with the activity monitor?



We ask that your child wears the activity monitor every day for 8 full days. He should put the monitor on when he gets up in the morning and takes it off just before he / she goes to bed. Your child may find it difficult to remember to put the activity monitor back on in the morning. In the past children have found it useful to place the activity monitor by an alarm clock or place a reminder note on a bathroom mirror. It may be helpful if you and your child determine a strategy to help him / her remember to put the monitor back on in the mornings. It is important that he / she does not alter his / her normal physical activity behavior while wearing the activity monitor – we are interested in his / her normal level of activity. He / she should not need to take the monitor off during the day apart from when he / she is engaging in water sports (e.g. swimming).

How is your child supposed to wear the activity monitor?

The monitor is worn on an elastic belt (which is provided with the monitor). The belt fits snugly around the waist so that the monitor is positioned on the right side of the body – over the right hip. Your child can wear the monitor over or under his / her clothes.

However, we ask that he / she keeps the monitor fastened on the belt to reduce the chance of losing it as these are expensive pieces of research equipment.

He / she is asked to wear the monitor at all times during waking hours apart from when he / she is engaging in water sports (e.g. swimming).

When does he / she return the activity monitor?

We will collect the accelerometer from your child at his / her next visit to the Neurocognitive Kinesiology Laboratory at the UIUC. We have asked your child to bring the device on this day. If he / she has no visit scheduled, please return the accelerometer in a pre-stamped and addressed envelope that we provided with the accelerometer.

If you have questions about the monitor please call Dominika or Bonnie at 217-333-3893 or e-mail: d.m.pindus@lboro.ac.uk

APPENDIX R:

Cognitive Tasks Run Sheet

APPENDIX S:

Flanker Task Instructions

APPENDIX T:

Flanker Stimuli

Congruent Condition

Incongruent Condition

APPENDIX U:

OSPAN Instructions

APPENDIX V:

OSPAN Stimuli

APPENDIX W:

OSPAN Record Sheet

APPENDIX X:

FITKids2 Physical Activity Programme Registration Form

APPENDIX Y:

FITKids2 - Telephone screening criteria

APPENDIX Z:

FITKids2 – Telephone ADHD Screening Protocol

APPENDIX AA:

FITKids2 Intervention Schedule

APPENDIX BB:

FITKids2 Content: Matching Illinois Learning Standards

APPENDIX CC:

Examples of strategies used by staff to assure intervention fidelity

