Evidence Portfolio – Brain Health Subcommittee, Question 1

What is the relationship between physical activity and cognition?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, or socio-economic status?
c. Does the relationship exist across the lifespan?
d. Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)?
e. What is the relationship between physical activity and brain structure and function?

Sources of Evidence: Existing Systematic Reviews and Meta-Analyses

Conclusion Statements and Grades

During the course of the review, it was determined that an accurate description of the state of the science for addressing this question would require several additional subcategories. As such, separate grades were assigned for acute bouts of physical activity (subquestion a), different age groups (subquestion c), and medical conditions with cognitive impairment (subquestion d).

Moderate evidence indicates a consistent association between greater amounts of physical activity and improvements in cognition, including performance on academic achievement tests; performance on neuropsychological tests, such as those involving processing speed, memory, and executive function; and risk of dementia. Such evidence has been demonstrated across numerous populations and individuals representing a gradient of normal to impaired cognitive health status. These effects are found across a variety of forms of physical activity, including aerobic activity (e.g., brisk walking), muscle-strengthening activity, yoga, and play activities (e.g., tag or other simple low organizational games). **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and cognition because of conflicting findings across populations, cognitive outcomes, and experimental approaches. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that acute bouts of moderate-to-vigorous physical activity have a transient benefit for cognition, including attention, memory, crystalized intelligence, processing speed, and executive control during the post-recovery period following a bout of exercise. The findings indicate that the effects are larger in preadolescent children and older adults relative to other periods of the lifespan. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine the effects of moderate-to-vigorous physical activity on cognition in children younger than age 5 years. **PAGAC Grade: Not assignable.**

Moderate evidence indicates an effect of both acute and long-term moderate-to-vigorous physical activity interventions on brain, cognition, and academic outcomes (e.g., school performance, psychometric profile of memory and executive function) in preadolescent children ages 5 to 13 years. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a relationship exists between moderate-to-vigorous physical activity and cognition in adolescents ages 14 to 18 years. **PAGAC Grade: Not assignable.**

Insufficient evidence exists regarding the effect of long-term moderate-to-vigorous physical activity on cognition in young or mid-life adults ages 18 to 50 years. **PAGAC Grade: Not assignable.**

Moderate evidence indicates an effect of long-term moderate-to-vigorous physical activity interventions on cognitive and brain outcomes in adults ages 50 years and older. **PAGAC Grade: Moderate.**

Limited evidence suggests that moderate-to-vigorous physical activity has a stronger effect on cognition in older compared to middle-aged and younger adults. Limited evidence also suggests a stronger effect of moderate-to-vigorous physical activity in older adult women compared to older adult men. **PAGAC Grade: Limited.**

No evidence was observed for an effect of physical activity on cognition as a function of socioeconomic status, race/ethnicity, or weight status. **PAGAC Grade: Not assignable**

Strong evidence demonstrates that greater amounts of physical activity are associated with a reduced risk of developing cognitive impairment, including Alzheimer's disease. **PAGAC Grade: Strong.**

Moderate evidence indicates that moderate-to-vigorous physical activity interventions can improve cognition in individuals with dementia. **PAGAC Grade: Moderate**

Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke. However, data are lacking for several other major conditions that are clinically associated with impaired cognitive function (i.e., autism, cancer). **PAGAC Grade: Moderate.**

Moderate evidence indicates that moderate-to-vigorous physical activity positively affects biomarkers of brain health and cognition. Physical activity-induced changes to these biomarkers have been observed across much of the lifespan, with considerably more evidence in children and older adults than in other age groups. **PAGAC Grade: Moderate.**

Limited evidence suggests that moderate-to-vigorous physical activity has a stronger effect on cognition in older compared to middle-aged and younger adults. Limited evidence also suggests a stronger effect of moderate-to-vigorous physical activity in older adult women compared to older adult men. No evidence was observed for an effect of physical activity on cognition as a function of socioeconomic status, race/ethnicity, or body mass index. **PAGAC Grade: Limited.**

Strong evidence demonstrates that acute bouts of moderate-to-vigorous physical activity have a transient benefit for cognition, including attention, memory, crystalized intelligence, processing speed, and executive control during the post-recovery period following a bout of exercise. The findings indicate that the effects are larger in preadolescent children and older adults relative to other periods of the lifespan. **PAGAC Grade: Strong.**

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Brain Health Subcommittee. Additional searches for original research were not needed.

Existing Systematic Reviews and Meta-Analyses

Overview

A total of 32 existing reviews were included. Of these, 12 were systematic reviews[1-12] and 20 were meta-analyses.[13-32] The existing reviews were published from 2003 to 2016.

The average number of studies included in the systematic reviews was 25, ranging from under 10[2, 6, 7] to 137.[4]

The average number of studies included in the meta-analyses was 28, ranging from under 15[13, 14, 19, 23, 31, 32] to 79.[15]

Exposures

The majority of the included reviews examined physical activity interventions that incorporated aerobic activities as the primary mode of exercise. Many reviews included specific activities such as treadmill and/or biking,[7, 12] active play, or active video-gaming,[2, 4, 5, 8, 30] and Tai Chi.[12, 31] Some studies also examined resistance exercise[9, 15-17, 21] and one study examined sedentary behavior.[6]

Outcomes

Most included reviews addressed changes in test scores on cognitive functions, including executive control, memory, processing speed, and attention. In addition, other studies used neuroimaging tools (e.g., magnetic resonance imaging [MRI], functional MRI [fMRI], or electroencephalogram [EEG]) to measure any changes in brain structure and function.

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Sex	Age	Weight Status	Chronic Conditions	Psychiatric Disorder or Cognitive Impairment
Beckett, 2015		Adults ≥65			
Bustamante, 2016		Youth	Overweight, Obese		
Carson, 2016		Youth 0–5			
Cerrillo-Urbina, 2015		Youth 6–18			Attention deficit hyperactive disorder
Chang, 2012	Male, Female	All ages			
Colcombe, 2013		Adults 55–80			
Den Heijer, 2016		All ages			Attention deficit hyperactivity disorder
Dinoff, 2016	Male, Female	Adults ≥18			
Donnelly, 2016		Youth 5–13			
Esteban-Cornejo, 2015		Youth 13–18			
Etnier, 2006		All ages			
Falck, 2016		Adults ≥40			
Firth, 2016		Adults 22.7–55.0			Schizophrenia
Groot, 2016		Older adults			Cognitive Disability, Dementia
Halloway, 2016		Middle-aged and older adults			
Janssen, 2014		Youth 4–18			
Kelly, 2014		Adults ≥50			
Lambourne, 2010		Adults			
Li, 2016		Adults			
Ludyga, 2016		All ages			
McMorris, 2012		All ages			

	Sex	Age	Weight Status	Chronic Conditions	Psychiatric Disorder or Cognitive Impairment
Morrison, 2016		Adults		Multiple sclerosis	
Murray, 2014		Older adults		Parkinson's disease	
Roig, 2013		Adults			
Sexton, 2016		Older adults			
Smith, 2010		Adults			
Sofi, 2011		Adults			
Spruit, 2016		Youth 10–21			
Tan, 2016		Youth 3–25			Cognitive disability, autism spectrum disorder, attention deficit hyperactivity disorder
Wu, 2013		Adults ≥55 or older			
Zheng, 2016a		Adults ≥60			Mild cognitive impairment
Zheng, 2016b		Adults		Stroke	

Supporting Evidence

Existing Systematic Reviews and Meta-Analyses

Table 2. Existing Systematic Reviews and Meta-Analyses Individual Evidence Summary Tables

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Beckett MW, Ardern CI, Rotondi MA. A meta-analysis of prospective studies on the role of physical activity and the prevention of Alzheimer's disease in older adults. BMC Geriatr. 2015;15:9. doi:10.1186/s12877-015-0007-2.</td></tr>
<tr><td>Purpose: To determine if physical activity (PA) protects against the onset of Alzheimer’s disease in adults over the age of 65.
Timeframe: 1966–2015
Total # of Studies: 9
Exposure Definition: Study participants’ PA was recorded using various methods. Two categories were created for meta-analysis: physically active and physically inactive (or non-active) group.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No
Outcomes Addressed: Incidence of Alzheimer's disease as risk ratio or hazard ratio.
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Abstract: BACKGROUND: The incidence of Alzheimer's disease is increasing as the global population ages. Given the limited success of pharmaceuticals in preventing this disease, a greater emphasis on non-pharmaceutical approaches is needed. The aim of this study was to quantify the association between Alzheimer's disease and physical activity in older adults over the age of 65 years. METHODS: A meta-analytic approach was used to determine if physical activity reduced the risk of Alzheimer's disease in individuals 65 years or older. Some evidence indicates that physical activity may improve cognitive function in older adults, while other evidence is inconclusive. The purpose of this study was to examine if prevention of Alzheimer's disease is possible if started at a later age. The precise brain changes that occur with the onset of Alzheimer's disease are not fully known, and therefore may still be influenced by preventative measures even in advancing age. Determining if physical activity can inhibit the onset of the disease at any age may motivate individuals to adopt an "it's never too late" mentality on preventing the onset of this debilitating disease. Longitudinal studies of participants who were 65 years or older at baseline were included. A total of 20,326 participants from nine studies were included in this analysis. RESULTS: The fixed effects risk ratio is estimated as 0.61 (95% CI 0.52-0.73) corresponding to a statistically significant overall reduction in risk of Alzheimer's disease in physically active older adults compared to their non-active counterparts. CONCLUSION: Physical activity was associated with a reduced risk of Alzheimer's disease in adults over the age of 65 years. Given the limited treatment options, greater emphasis should be paid to primary prevention through physical activity amongst individuals at high-risk of Alzheimer's disease, such as those with strong genetic and family history.</td></tr>
<tr><td>Populations Analyzed: Adults ≥65</td><td>Author-Stated Funding Source: Ontario Brain Institute</td></tr>
</table>

Systematic Review **Citation:** Bustamante EE, Williams CF, Davis CL. Physical activity interventions for neurocognitive and academic performance in overweight and obese youth: A systematic review. *Pediatr Clin North Am.* 2016;63(3):459-480. doi:10.1016/j.pcl.2016.02.004.	
Purpose: To understand the translation (efficacy) of physical activity (PA) interventions for neurologic, cognitive, and academic outcomes in overweight and obese children, with attention to minority representation.	**Abstract:** This article examines cognitive, academic, and brain outcomes of physical activity in overweight or obese youth, with attention to minority youth who experience health disparities. Physically active academic lessons may have greater immediate cognitive and academic benefits among overweight and obese children than normal-weight children. Quasi-experimental studies testing physical activity programs in overweight and obese youth show promise; a few randomized controlled trials including African Americans show efficacy. Thus, making academic lessons physically active may improve inhibition and attentiveness, particularly in overweight youngsters. Regular physical activity may be efficacious for improving neurologic, cognitive, and achievement outcomes in overweight or obese youth.
Timeframe: Inception–2015	
Total # of Studies: 12	
Exposure Definition: Various PA interventions such as treadmill walking, daily sport participation, and aerobic exercise training. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Neurologic (functional magnetic resonance imaging scans), cognitive (flanker test, antisaccade performance, Tower of London), or academic performance (Woodcock Johnson Tests of Achievement). **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Youth, Overweight and Obese	**Author-Stated Funding Source:** None

<table>
<tr><td colspan="2">Systematic Review
Citation: Carson V, Hunter S, Kuzik N, et al. Systematic review of physical activity and cognitive development in early childhood. J Sci Med Sport. 2016;19(7):573-578. Doi:10.1016/j.jsams.2015.07.011.</td></tr>
<tr><td>Purpose: To comprehensively review all observational and experimental studies examining the relationship between physical activity (PA) and cognitive development during early childhood (birth to 5 years).</td><td rowspan="5">Abstract: OBJECTIVES: To comprehensively review all observational and experimental studies examining the relationship between physical activity and cognitive development during early childhood (birth to 5 years). DESIGN: Systematic review. METHODS: Electronic databases were searched in July, 2014. No study design, date, or language limits were imposed on the search. Included studies had to be published, peer reviewed articles that satisfied the a priori determined population (apparently healthy children aged birth to 5 years), intervention (duration, intensity, frequency, or patterns of physical activity), comparator (various durations, intensity, or patterns of physical activity), and outcome (cognitive development) study criteria. Study quality and risk of bias were assessed in December 2014. RESULTS: A total of seven studies, representing 414 participants from five different countries met the inclusion criteria, including two observational and five experimental studies. Six studies found increased or higher duration/frequency of physical activity had statistically significant ($p<0.05$) beneficial effects on at least one cognitive development outcome, including 67% of the outcomes assessed in the executive function domain and 60% in the language domain. No study found that increased or higher duration/frequency of physical activity had statistically significant detrimental effects on cognitive development. Six of the seven studies were rated weak quality with a high risk of bias. CONCLUSIONS: This review provides some preliminary evidence that physical activity may have beneficial effects on cognitive development during early childhood. Given the shortage of the information and the weak quality of available evidence, future research is needed to strengthen the evidence base in this area.</td></tr>
<tr><td>Timeframe: 1895–July 2014</td></tr>
<tr><td>Total # of Studies: 7</td></tr>
<tr><td>Exposure Definition: PA program condition or class, which involved at least moderate-intensity PA. The control group or condition was either usual care or a sedentary condition. Active play during recess, quantified as duration of moderate- to vigorous-intensity physical activity (MVPA), objectively assessed with an accelerometer, was the exposure in one observational study; and frequency of PA, objectively assessed by an actometer, was the exposure in the second observational study.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive development outcomes in the executive function and language domains were most commonly assessed. Children directly completed the assessments or a trained research assistant completed the assessments through direct observation.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Youth 0–5</td><td>Author-Stated Funding Source: Norlien Foundation, Alberta Family Wellness Initiative, Alberta Centre for Child, Family and Community Research</td></tr>
</table>

Meta-Analysis **Citation:** Cerrillo-Urbina AJ, García-Hermoso A, Sánchez-López M, Pardo-Guijarro MJ, Santos Gómez JL, Martínez-Vizcaíno V. The effects of physical exercise in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis of randomized control trials. *Child Care Health Dev.* 2015;41(6):779-788. doi:10.1111/cch.12255.	
Purpose: To examine the evidence for the effectiveness of physical education interventions on symptoms such as inattention, hyperactivity/impulsivity, anxiety, and cognitive functions in children and adolescents with attention deficit hyperactivity disorder.	**Abstract:** OBJECTIVE: The aim of this systematic review and meta-analysis was to examine the evidence for the effectiveness of exercise interventions on attention deficit hyperactivity disorder (ADHD)-related symptoms such as inattention, hyperactivity/impulsivity, anxiety and cognitive functions in children and adolescents. METHOD: Five databases covering the period up to November 2014 (PubMed, Scopus, EMBASE, EBSCO [E-journal, CINAHL, SportDiscus] and The Cochrane Library) were searched. Methodological quality was assessed using the Cochrane tool of bias. Standardized mean differences (SMD) and 95% confidence intervals were calculated, and the heterogeneity of the studies was estimated using Cochran's Q-statistic. RESULTS: Eight randomized controlled trials (n = 249) satisfied the inclusion criteria. The studies were grouped according to the intervention programme: aerobic and yoga exercise. The meta-analysis suggests that aerobic exercise had a moderate to large effect on core symptoms such as attention (SMD = 0.84), hyperactivity (SMD = 0.56) and impulsivity (SMD = 0.56) and related symptoms such as anxiety (SMD = 0.66), executive function (SMD = 0.58) and social disorders (SMD = 0.59) in children with ADHD. Yoga exercise suggests an improvement in the core symptoms of ADHD. CONCLUSIONS: The main cumulative evidence indicates that short-term aerobic exercise, based on several aerobic intervention formats, seems to be effective for mitigating symptoms such as attention, hyperactivity, impulsivity, anxiety, executive function and social disorders in children with ADHD.
Timeframe: Inception–2014	
Total # of Studies: 8	
Exposure Definition: Aerobic physical activity. Intensity was measured with heart rate monitors and maximal oxygen consumption (VO2 max). The mean duration of the interventions was 5 weeks; the mean duration of sessions was 50 minutes, and the average frequency was 2 to 3 times/week. Activities in these interventions included running, motor-driven, and multi-sports. One study used a yoga intervention: one 60 minute session a week for 20 weeks. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Changes in symptoms and/or problems related to attention deficit hyperactivity disorder: attention, hyperactivity, impulsivity, anxiety, executive function, and social disorders. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Youth 6–18, Attention Deficit Hyperactivity Disorder	**Author-Stated Funding Source:** Not Reported

Meta-Analysis

Citation: Chang YK, Labban JD, Gapin JI, Etnier JL. The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Res.* 2012;1453:87-101. doi:10.1016/j.brainres.2012.02.068.

Purpose: To provide an updated comprehensive analysis of the extant literature on acute exercise and cognitive performance and to explore the effects of moderators that have implications for mechanisms of the effects.

Timeframe: Inception–2010

Total # of Studies: 79

Exposure Definition: Acute bouts of exercise, measured by intensity as percentage of heart rate max, maximal oxygen consumption, watts, or power. Very light (<50% heart rate max), light (50–63%), moderate (64–76), hard (77–93), very hard (>93%), and maximal (100%). Also subgroup analysis by type of exercise (aerobic, anaerobic, muscular, combination, or accelerometer). Subgroup analysis by fitness level (low, moderate, and high).

Measures Steps: No

Measures Bouts: No

Examines HIIT: No

Outcomes Addressed: Change in cognitive task scores. Cognitive tasks included information processing, reaction time, attention, crystallized intelligence, executive function, and memory.

Examine Cardiorespiratory Fitness as Outcome: No

Abstract: There is a substantial body of literature related to the effects of a single session of exercise on cognitive performance. The premise underlying this research is that physiological changes in response to exercise have implications for cognitive function. This literature has been reviewed both narratively and meta-analytically and, although the research findings are mixed, researchers have generally concluded that there is a small positive effect. The purpose of this meta-analysis was to provide an updated comprehensive analysis of the extant literature on acute exercise and cognitive performance and to explore the effects of moderators that have implications for mechanisms of the effects. Searches of electronic databases and examinations of reference lists from relevant studies resulted in 79 studies meeting inclusion criteria. Consistent with past findings, analyses indicated that the overall effect was positive and small (g=0.097 n=1034). Positive and small effects were also found in all three acute exercise paradigms: during exercise (g=0.101; 95% confidence interval [CI]; 0.041-0.160), immediately following exercise (g=0.108; 95% CI; 0.069-0.147), and after a delay (g=0.103; 95% CI; 0.035-0.170). Examination of potential moderators indicated that exercise duration, exercise intensity, type of cognitive performance assessed, and participant fitness were significant moderators. In conclusion, the effects of acute exercise on cognitive performance are generally small; however, larger effects are possible for particular cognitive outcomes and when specific exercise parameters are used.

Populations Analyzed: Male, Female, All ages

Author-Stated Funding Source: Office of Research for the School of Health and Human Science at the University of North Carolina at Greensboro

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. Psychol Sci. 2003;14(2):125-130.</td></tr>
<tr><td>Purpose: To examine the extent to which enhancements in aerobic fitness result in improvements in cognition.</td><td rowspan="5">Abstract: A meta-analytic study was conducted to examine the hypothesis that aerobic fitness training enhances the cognitive vitality of healthy but sedentary older adults. Eighteen intervention studies published between 1966 and 2001 were entered into the analysis. Several theoretically and practically important results were obtained. Most important fitness training was found to have robust but selective benefits for cognition, with the largest fitness-induced benefits occurring for executive-control processes. The magnitude of fitness effects on cognition was also moderated by a number of programmatic and methodological factors, including the length of the fitness-training intervention, the type of the intervention, the duration of training sessions, and the gender of the study participants. The results are discussed in terms of recent neuroscientific and psychological data that indicate cognitive and neural plasticity is maintained throughout the life span.</td></tr>
<tr><td>Timeframe: 1966–2001</td></tr>
<tr><td>Total # of Studies: 18</td></tr>
<tr><td>Exposure Definition: Interventions that emphasized cardiovascular fitness in isolation (aerobic) and those that combined cardiovascular fitness training with strength training (combination). The duration of the training sessions was as follows: short, 15–30 minutes; moderate, 31–45 minutes; and long, 46–60 minutes. The length of the exercise intervention was as follows: short, 1–3 months; medium, 4–6 months; and long, 6+ months. Cardiovascular improvement shown in the participants, based on either estimated or actual maximal oxygen consumption (VO2) peak or max scores (unreported; moderate, 5–11%; and large, 12–25%).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive processes identified by the four theoretical positions (speed, visuospatial, controlled processing, and executive control).
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults 55–80</td><td>Author-Stated Funding Source: National Institute on Aging, Institute for the Study of Aging</td></tr>
</table>

<table>
<tr><td colspan="2">Systematic Review
Citation: Den Heijer AE, Groen Y, Tucha L, et al. Sweat it out? The effects of physical exercise on cognition and behavior in children and adults with ADHD: a systematic literature review. J Neural Transm (Vienna). 2017;124(suppl 1):3-26. doi:10.1007/s00702-016-1593-7.</td></tr>
<tr><td>Purpose: To systematically review the effects of cardiovascular and non-cardiovascular exercise types on cognitive, behavioral/socio-emotional, and physical/neuro physiological outcome measures in children with attention deficit hyperactivity disorder, thereby also addressing the duration of these effects (acute or chronic).</td><td rowspan="5">Abstract: As attention-deficit/hyperactivity disorder (ADHD) is one of the most frequently diagnosed developmental disorders in childhood, effective yet safe treatment options are highly important. Recent research introduced physical exercise as a potential treatment option, particularly for children with ADHD. The aim of this review was to systematically analyze potential acute and chronic effects of cardio and non-cardio exercise on a broad range of functions in children with ADHD and to explore this in adults as well. Literature on physical exercise in patients with ADHD was systematically reviewed based on categorizations for exercise type (cardio versus non-cardio), effect type (acute versus chronic), and outcome measure (cognitive, behavioral/socio-emotional, and physical/(neuro)physiological). Furthermore, the methodological quality of the reviewed papers was addressed. Cardio exercise seems acutely beneficial regarding various executive functions (e.g., impulsivity), response time and several physical measures. Beneficial chronic effects of cardio exercise were found on various functions as well, including executive functions, attention and behavior. The acute and chronic effects of non-cardio exercise remain more questionable but seem predominantly positive too. Research provides evidence that physical exercise represents a promising alternative or additional treatment option for patients with ADHD. Acute and chronic beneficial effects of especially cardio exercise were reported with regard to several cognitive, behavioral, and socio-emotional functions. Although physical exercise may therefore represent an effective treatment option that could be combined with other treatment approaches of ADHD, more well-controlled studies on this topic, in both children and adults, are needed.</td></tr>
<tr><td>Timeframe: Inception–2016</td></tr>
<tr><td>Total # of Studies: 29</td></tr>
<tr><td>Exposure Definition: Exercise type (cardiovascular vs. non-cardiovascular) and duration of exercise (acute [<24 hours] and chronic [1–10 weeks]) were looked at. Examples of cardiovascular exercise exposures include treadmill running, cycle ergometer/cycling, swimming and jumping. Examples of non-cardiovascular exercise include yoga, walking, and playground activity.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive outcome measures (intelligence scores, attention, planning, and memory), behavioral and socio-emotional outcomes (parent/teacher questionnaires) and physical and neurophysiological outcomes (physical/physiological effects).
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: All ages, Attention Deficit Hyperactivity Disorder</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Dinoff A, Herrmann N, Swardfager W, et al. The effect of exercise training on resting concentrations of peripheral brain-derived neurotrophic factor (BDNF): A meta-analysis. PLoS One. 2016;11(9):e0163037. doi:https://doi.org/10.1371/journal.pone.0163037.</td></tr>
<tr><td>Purpose: To quantify the magnitude and consistency of the effect of exercise training on resting concentrations of brain-derived neurotrophic factor (BDNF) in peripheral blood.</td><td rowspan="5">Abstract: BACKGROUND: The mechanisms through which physical activity supports healthy brain function remain to be elucidated. One hypothesis suggests that increased brain-derived neurotrophic factor (BDNF) mediates some cognitive and mood benefits. This meta-analysis sought to determine the effect of exercise training on resting concentrations of BDNF in peripheral blood. METHODS: MEDLINE, Embase, PsycINFO, SPORTDiscus, Rehabilitation & Sports Medicine Source, and CINAHL databases were searched for original, peer-reviewed reports of peripheral blood BDNF concentrations before and after exercise interventions >/= 2 weeks. Risk of bias was assessed using standardized criteria. Standardized mean differences (SMDs) were generated from random effects models. Risk of publication bias was assessed using funnel plots and Egger's test. Potential sources of heterogeneity were explored in subgroup analyses. RESULTS: In 29 studies that met inclusion criteria, resting concentrations of peripheral blood BDNF were higher after intervention (SMD = 0.39, 95% CI: 0.17-0.60, $p < 0.001$). Subgroup analyses suggested a significant effect in aerobic (SMD = 0.66, 95% CI: 0.33-0.99, $p < 0.001$) but not resistance training (SMD = 0.07, 95% CI: -0.15-0.30, p = 0.52) interventions. No significant difference in effect was observed between males and females, nor in serum vs plasma. CONCLUSION: Aerobic but not resistance training interventions increased resting BDNF concentrations in peripheral blood.</td></tr>
<tr><td>Timeframe: Inception–2016</td></tr>
<tr><td>Total # of Studies: 29</td></tr>
<tr><td>Exposure Definition: Studies were included if exercise interventions were implemented for ≥2 weeks, at an intensity of ≥50% of peak oxygen uptake (VO2 peak), or if exercise intensity was not reported but exercise was described as running, cycling, or resistance training. Included studies measured BDNF before and after the exercise intervention.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Measured serum, plasma, or whole blood brain-derived neurotrophic factor concentration.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Male, Female, Adults ≥18</td><td>Author-Stated Funding Source: Canadian Institutes of Health Research and Ontario Mental Health Foundation</td></tr>
</table>

Systematic Review **Citation:** Donnelly JE, Hillman CH, Castelli D, et al. Physical activity, fitness, cognitive function, and academic achievement in children: A systematic review. *Med Sci Sports Exerc.* 2016;48(6):1197-1222. doi:10.1249/MSS.0000000000000901.	
Purpose: To answer the following questions: Among children ages 5–13, do physical activity (PA) and physical fitness influence cognition, learning, brain structure, and brain function? Among children ages 5–13, do PA, physical education (PE), and sports programs influence standardized achievement test performance and concentration/attention?	**Abstract:** BACKGROUND: The relationship among physical activity (PA), fitness, cognitive function, and academic achievement in children is receiving considerable attention. The utility of PA to improve cognition and academic achievement is promising but uncertain; thus, this position stand will provide clarity from the available science. OBJECTIVE: The purpose of this study was to answer the following questions: 1) among children age 5-13 yr, do PA and physical fitness influence cognition, learning, brain structure, and brain function? 2) Among children age 5-13 yr, do PA, physical education (PE), and sports programs influence standardized achievement test performance and concentration/attention? STUDY ELIGIBILITY CRITERIA: This study used primary source articles published in English in peer-reviewed journals. Articles that presented data on, PA, fitness, or PE/sport participation and cognition, learning, brain function/structure, academic achievement, or concentration/attention were included. DATA SOURCES: Two separate searches were performed to identify studies that focused on 1) cognition, learning, brain structure, and brain function and 2) standardized achievement test performance and concentration/attention. PubMed, ERIC, PsychInfo, SportDiscus, Scopus, Web of Science, Academic Search Premier, and Embase were searched (January 1990-September 2014) for studies that met inclusion criteria. Sixty-four studies met inclusion criteria for the first search (cognition/learning/brain), and 73 studies met inclusion criteria for the second search (academic achievement/concentration). STUDY APPRAISAL AND SYNTHESIS METHODS: Articles were grouped by study design as cross-sectional, longitudinal, acute, or intervention trials. Considerable heterogeneity existed for several important study parameters; therefore, results were synthesized and presented by study design. RESULTS: A majority of the research supports the view that physical fitness, single bouts of PA, and PA interventions benefit children's cognitive functioning. Limited evidence was available concerning the effects of PA on learning, with only one cross-sectional study meeting the inclusion criteria. Evidence indicates that PA has a relationship to areas of the brain that support complex cognitive processes during laboratory tasks. Although favorable results have been obtained from cross-sectional and longitudinal studies related to academic achievement, the results obtained from controlled experiments evaluating the benefits of PA on academic performance are mixed, and additional, well-designed studies are needed. LIMITATIONS: Limitations in evidence meeting inclusion criteria for this review include lack of randomized controlled trials, limited studies that are adequately powered, lack of information on participant characteristics, failure to blind for outcome measures, proximity of PA to measurement outcomes, and lack of accountability for known confounders. Therefore, many studies were ranked as high risk for bias because of multiple design limitations. CONCLUSIONS: The present systematic review found evidence to suggest that there are positive associations among PA, fitness, cognition, and academic
Timeframe: January 1990–May 2015	
Total # of Studies: 137	
Exposure Definition: PA or fitness assessment methods (e.g., questionnaires, time spent in PE, and FitnessGram). **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Cognitive assessment measures (e.g., reaction time, flanker task, and Cognitive Assessment System), and academic achievement assessment methods	

(e.g., state-administered tests and individualized achievement tests). **Examine Cardiorespiratory Fitness as Outcome:** No	achievement. However, the findings are inconsistent, and the effects of numerous elements of PA on cognition remain to be explored, such as type, amount, frequency, and timing. Many questions remain regarding how to best incorporate PA within schools, such as activity breaks versus active lessons in relation to improved academic achievement. Regardless, the literature suggests no indication that increases in PA negatively affect cognition or academic achievement and PA is important for growth and development and general health. On the basis of the evidence available, the authors concluded that PA has a positive influence on cognition as well as brain structure and function; however, more research is necessary to determine mechanisms and long-term effect as well as strategies to translate laboratory findings to the school environment. Therefore, the evidence category rating is B. The literature suggests that PA and PE have a neutral effect on academic achievement. Thus, because of the limitations in the literature and the current information available, the evidence category rating for academic achievement is C.
Populations Analyzed: Youth 5–13	**Author-Stated Funding Source:** Funding for Szabo-Reed was provided by F32DK103493.

<table>
<tr><td colspan="2">Systematic Review
Citation: Esteban-Cornejo I, Tejero-Gonzalez CM, Sallis JF, Veiga OL. Physical activity and cognition in adolescents: a systematic review. J Sci Med Sport. 2015;18(5):534-539. doi:10.1016/j.jsams.2014.07.007.</td></tr>
<tr><td>Purpose: To systematically review the evidence of association between physical activity (PA) and cognition by differentiating between academic and cognitive performance measures.</td><td rowspan="5">Abstract: OBJECTIVES: The purpose of this report is to perform a systematic review of the evidence on the associations between physical activity and cognition by differentiating between academic and cognitive performance measures. Second-generation questions regarding potential mediators or moderators (i.e., sex, age and psychological variables) of this relationship were also examined. DESIGN: Systematic review. METHODS: Studies were identified from searches in PubMed, Sportdiscus and ERIC databases from 2000 through 2013. The search process was carried out by two independent researchers. RESULTS: A total of 20 articles met the inclusion criteria, 2 of them analyzed both cognitive and academic performance in relation to physical activity. Four articles (18%) found no association between physical activity and academic performance, 11 (50%) found positive association and one showed negative association (5%). Five articles (23%) found positive association between physical activity and cognitive performance and one showed negative association (5%). The findings of these studies show that cognitive performance is associated with vigorous physical activity and that academic performance is related to general physical activity, but mainly in girls. Results of the review also indicate that type of activity and some psychological factors (i.e., self-esteem, depression) could mediate the association between physical activity and academic performance. CONCLUSIONS: Results of the review support that physical activity is associated with cognition, but more research is needed to clarify the role of sex, intensity and type of physical activity and some psychological variables of this association.</td></tr>
<tr><td>Timeframe: 2000–2013</td></tr>
<tr><td>Total # of Studies: 20</td></tr>
<tr><td>Exposure Definition: Weekly self reported PA (one study used objective measurement). Five studies looked just at athletic participation or physical education.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Measures of cognition including Science Research Associates test of educational ability, standardized test scores, Terra Nova test, and other cognitive tests. Academic performance measurements were assessed using self-reported or school-reported grades.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Youth 13–18</td><td>Author-Stated Funding Source: UP&DOWN study</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Etnier JL, Nowell PM, Landers DM, Sibley BA. A meta-regression to examine the relationship between aerobic fitness and cognitive performance. Brain Res Rev. 2006;52(1):119-130.</td></tr>
<tr><td>Purpose: To provide a statistically powerful test of the viability of the cardiovascular fitness hypothesis by examining the dose–response relationship between aerobic fitness and cognition.</td><td rowspan="5">Abstract: Many studies have been conducted to test the potentially beneficial effects of physical activity on cognition. The results of meta-analytic reviews of this literature suggest that there is a positive association between participation in physical activity and cognitive performance. The design of past research demonstrates the tacit assumption that changes in aerobic fitness contribute to the changes in cognitive performance. Therefore, the purpose of this meta-analysis was to use meta-regression techniques to statistically test the relationship between aerobic fitness and cognitive performance. Results indicated that there was not a significant linear or curvilinear relationship between fitness effect sizes (ESs) and cognitive ESs for studies using cross-sectional designs or posttest comparisons. However, there was a significant negative relationship between aerobic fitness and cognitive performance for pre-post comparisons. The effects for the cross-sectional and pre-post comparisons were moderated by the age group of the participants; however, the nature of this effect was not consistent for the two databases. Based on the findings of this meta-analytic review, it is concluded that the empirical literature does not support the cardiovascular fitness hypothesis. To confirm the findings of this review, future research should specifically test the dose-response relationship between aerobic fitness and cognitive performance. However, based upon the findings of this review, we also encourage future research to focus on other physiological and psychological variables that may serve to mediate the relationship between physical activity and cognitive performance.</td></tr>
<tr><td>Timeframe: 1927–October 2005</td></tr>
<tr><td>Total # of Studies: 37</td></tr>
<tr><td>Exposure Definition: Fitness measurement was coded as a maximal measure of oxygen consumption (VO2), a submaximal measure of VO2 used to predict maximal VO2, a submaximal measure of VO2, or a composite measure including a submaximal measure of VO2.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive tests: the categories used were fluid intelligence, crystallized intelligence, general memory and learning, visual perception, auditory perception, retrieval ability, speediness, and processing speed.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: All ages</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Systematic Review
Citation: Falck RS, Davis JC, Liu-Ambrose T. What is the association between sedentary behaviour and cognitive function? A systematic review. Br J Sports Med. 2016;51(10):800-811. doi:10.1136/bjsports-2015-095551.</td></tr>
<tr><td>Purpose: To systematically review the epidemiological evidence regarding how sedentary behavior is associated with cognitive function throughout the adult lifespan.</td><td rowspan="5">Abstract: AIM: The increasing rate of all-cause dementia worldwide and the lack of effective pharmaceutical treatments emphasise the value of lifestyle approaches as prevention strategies. Emerging evidence suggests sedentary behaviour is associated with impaired cognitive function. A better understanding of this association would significantly add to our knowledge of how to best promote healthy cognitive ageing. Thus, we conducted a systematic review ascertaining the contribution of sedentary behaviour towards associated changes in cognitive function over the adult lifespan. STUDY DESIGN: Systematic review of peer-reviewed literature examining the association of sedentary behaviour with cognition. DATA SOURCES: We searched PubMed, PsycINFO, EBSCO and Web of Science, and reference lists of relevant reviews on sedentary behaviour. Two independent reviewers extracted (1) study characteristics and (2) information regarding measurement of sedentary behaviour and cognitive function. We also assessed study quality using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist. ELIGIBILITY CRITERIA: We limited search results to adults >/=40 years, observational studies published in English since 1990 and studies investigating associations between sedentary behaviour and cognitive function. RESULTS: 8 studies examined the association of sedentary behaviour with cognitive function. 6 studies reported significant negative associations between sedentary behaviour and cognitive function. 8 different measures of sedentary behaviour and 13 different measures of cognitive function were used across all eight studies. SUMMARY: Sedentary behaviour is associated with lower cognitive performance, although the attributable risk of sedentary time to all-cause dementia incidence is unclear. Our systematic review provides evidence that limiting sedentary time and concomitantly engaging in regular moderate-to-vigorous physical activity may best promote healthy cognitive ageing.</td></tr>
<tr><td>Timeframe: January 1990–February 2016</td></tr>
<tr><td>Total # of Studies: 7</td></tr>
<tr><td>Exposure Definition: Sedentary behaviors included behaviors as measured by self-reported TV viewing, self-administered French Modifiable Activity Questionnaire, Community Health Activities Model Program for Seniors questionnaire, and Sedentary Behaviour Questionnaire, and self-reported leisure time physical activity. One study used accelerometers to measure sedentary behavior.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive function: five studies measured memory, five measured executive function, four measured processing speed, two measured incidence of cognitive impairment or all-cause dementia, and one measured perceptual organization and planning.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults ≥40</td><td>Author-Stated Funding Source: Jack Brown and Family Alzheimer Research Foundation Society</td></tr>
</table>

Meta-Analysis **Citation:** Firth J, Stubbs B, Rosenbaum S, et al. Aerobic exercise improves cognitive functioning in people with schizophrenia: A systematic review and meta-analysis. *Schizophr Bull.* 2017;43(3):546-556. doi:10.1093/schbul/sbw115. 2	
Purpose: To assess the effect of exercise on global cognition in people with schizophrenia, along with examining which domains of cognitive functioning are most sensitive to exercise interventions. **Timeframe:** Inception–2016 **Total # of Studies:** 10 **Exposure Definition:** Structured and repetitive physical activity (PA) that has an objective of improving or maintaining physical fitness. Examples of exercise protocols include 20 minutes of an interactive PA video game “Move4Health” and 60 minutes of mixed aerobic exercise at 60%–75% peak oxygen uptake. Sessions contain a mixture of treadmill running, elliptical training, and interactive video games. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No **Outcomes Addressed:** Global cognition (change in cognitive functioning), speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving, and social cognition were measured before and after the aerobic exercise intervention program. **Examine Cardiorespiratory Fitness as Outcome:** No	**Abstract:** Cognitive deficits are pervasive among people with schizophrenia and treatment options are limited. There has been an increased interest in the neurocognitive benefits of exercise, but a comprehensive evaluation of studies to date is lacking. We therefore conducted a meta-analysis of all controlled trials investigating the cognitive outcomes of exercise interventions in schizophrenia. Studies were identified from a systematic search across major electronic databases from inception to April 2016. Meta-analyses were used to calculate pooled effect sizes (Hedges g) and 95% CIs. We identified 10 eligible trials with cognitive outcome data for 385 patients with schizophrenia. Exercise significantly improved global cognition (g = 0.33, 95% CI = 0.13-0.53, P = .001) with no statistical heterogeneity (I 2 = 0%). The effect size in the 7 studies which were randomized controlled trials was g = 0.43 (P < .001). Meta-regression analyses indicated that greater amounts of exercise are associated with larger improvements in global cognition (beta = .005, P = .065). Interventions which were supervised by physical activity professionals were also more effective (g = 0.47, P < .001). Exercise significantly improved the cognitive domains of working memory (g = 0.39, P = .024, N = 7, n = 282), social cognition (g = 0.71, P = .002, N = 3, n = 81), and attention/vigilance (g = 0.66, P = .005, N = 3, n = 104). Effects on processing speed, verbal memory, visual memory and reasoning and problem solving were not significant. This meta-analysis provides evidence that exercise can improve cognitive functioning among people with schizophrenia, particularly from interventions using higher dosages of exercise. Given the challenges in improving cognition, and the wider health benefits of exercise, a greater focus on providing supervised exercise to people with schizophrenia is needed.
Populations Analyzed: Adults 22.7–55.0, Schizophrenia	**Author-Stated Funding Source:** Individual author funding sources reported.

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Groot C, Hooghiemstra AM, Raijmakers PG, et al. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized control trials. Ageing Res Rev. 2016;25:13-23. doi:10.1016/j.arr.2015.11.005.</td></tr>
<tr><td>Purpose: To investigate the effect of physical activity (PA) on cognitive function in patients with dementia.</td><td rowspan="5">Abstract: Non-pharmacological therapies, such as physical activity interventions, are an appealing alternative or add-on to current pharmacological treatment of cognitive symptoms in patients with dementia. In this meta-analysis, we investigated the effect of physical activity interventions on cognitive function in dementia patients, by synthesizing data from 802 patients included in 18 randomized control trials that applied a physical activity intervention with cognitive function as an outcome measure. Post-intervention standardized mean difference (SMD) scores were computed for each study, and combined into pooled effect sizes using random effects meta-analysis. The primary analysis yielded a positive overall effect of physical activity interventions on cognitive function (SMD[95% confidence interval]=0.42[0.23;0.62], p<.01). Secondary analyses revealed that physical activity interventions were equally beneficial in patients with Alzheimer's disease (AD, SMD=0.38[0.09;0.66], p<.01) and in patients with AD or a non-AD dementia diagnosis (SMD=0.47[0.14;0.80], p<.01). Combined (i.e. aerobic and non-aerobic) exercise interventions (SMD=0.59[0.32;0.86], p<.01) and aerobic-only exercise interventions (SMD=0.41[0.05;0.76], p<.05) had a positive effect on cognition, while this association was absent for non-aerobic exercise interventions (SMD=-0.10[-0.38;0.19], p=.51). Finally, we found that interventions offered at both high frequency (SMD=0.33[0.03;0.63], p<.05) and at low frequency (SMD=0.64[0.39;0.89], p<.01) had a positive effect on cognitive function. This meta-analysis suggests that physical activity interventions positively influence cognitive function in patients with dementia. This beneficial effect was independent of the clinical diagnosis and the frequency of the intervention, and was driven by interventions that included aerobic exercise.</td></tr>
<tr><td>Timeframe: January 1960–May 2015</td></tr>
<tr><td>Total # of Studies: 18</td></tr>
<tr><td>Exposure Definition: PA was categorized into three categories: aerobic-only, non-aerobic, and combined. A cut-off at 150 minutes of PA per week was used to distinguish between high- and low-frequency interventions.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Changes in cognitive test scores. Cognitive tests, such as the mini mental state examination, clock drawing test, functional assessment of communication skills mental subscale, rapid evaluation of cognitive function, Hopkins verbal learning test, and the Cambridge neuropsychological test automated battery.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Older adults, Cognitive Disablity, Dementia</td><td>Author-Stated Funding Source: Individual author funding (Marie Curie FP7 International Out-going Fellowship) and Alzheimer Nederland and Stichting VUMC</td></tr>
</table>

Systematic Review **Citation:** Halloway S, Wilbur J, Schoeny ME, Arfanakis K. Effects of endurance-focused physical activity interventions on brain health: A systematic review. *Biol Res Nurs.* 2016. pii:1099800416660758.	
Purpose: To identify the effect of endurance-focused physical activity (PA) interventions on the brain as measured by magnetic resonance imaging (MRI) in community-dwelling middle aged or older adults without cognitive impairment. **Timeframe:** Inception–2015 **Total # of Studies:** 6 **Exposure Definition:** Laboratory-based treadmill or supervised bike exercise sessions; one included community-based PA. Interventions consisted of PA training during which participants engaged in aerobic activity for 40–60-minute sessions 2 or 3 times per week. Intervention duration ranged from 12 weeks to 1 year. Researchers most commonly used cardiorespiratory fitness to determine intensity range for each participant during the PA intervention (perceived exertion and heart rate were also used in some studies). **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No **Outcomes Addressed:** Brain volume, cerebral blood flow, cortical plasticity, spatial learning capacity, and brain activation were measured using magnetic resonance imaging. Neuro-cognition assessed by executive function, spatial cognition or spatial memory, verbal memory, and perceptual speed. **Examine Cardiorespiratory Fitness as Outcome:** No	**Abstract:** Physical activity intervention studies that focus on improving cognitive function in older adults have increasingly used magnetic resonance imaging (MRI) measures in addition to neurocognitive measures to assess effects on the brain. The purpose of this systematic review was to identify the effects of endurance-focused physical activity randomized controlled trial (RCT) interventions on the brain as measured by MRI in community-dwelling middle-aged or older adults without cognitive impairment. Five electronic databases were searched. The final sample included six studies. None of the studies reported racial or ethnic characteristics of the participants. All studies included neurocognitive measures in addition to MRI. Five of the six interventions included laboratory-based treadmill or supervised bike exercise sessions, while one included community-based physical activity. Physical activity measures were limited to assessment of cardiorespiratory fitness and, in one study, pedometer. Due to the lack of adequate data reported, effect sizes were calculated for only one study for MRI measures and two studies for neurocognitive measures. Effect sizes ranged from d = .2 to .3 for MRI measures and .2 to .32 for neurocognitive measures. Findings of the individual studies suggest that MRI measures may be more sensitive to the effects of physical activity than neurocognitive measures. Future studies are needed that include diverse, community-based participants, direct measures of physical activity, and complete reporting of MRI and neurocognitive findings.
Populations Analyzed: Middle-aged and older adults	**Author-Stated Funding Source:** National Institute of Nursing Research, National Institutes of Health; Jonas Nurse Leader Scholar; Jonas Center for Nursing and Veterans Healthcare; Midwest Nursing Research Society

Systematic Review **Citation:** Janssen M, Toussaint HM, van Mechelen W, Verhagen EA. Effects of acute bouts of physical activity on children's attention: a systematic review of the literature. *Springerplus.* 2014;3:410. doi:10.1186/2193-1801-3-410.	
Purpose: To describe the effects of acute bouts of physical activity (PA) on attention levels of children.	**Abstract:** The aim of this review was to describe the effects of acute bouts of physical activity on attention levels of children. A systematic review was performed of English studies from searches in PubMed, Sportdiscus and PsycINFO from 1990 to (May) 2014 according to the PRISMA statement. Only prospective studies of children aged 4-18 years old were included, detailing acute effects of physical activity bouts with the primary outcome attention. One reviewer extracted data on the study characteristics. Two reviewers conducted the methodological quality assessment independently using a criteria checklist, which was based on the Downs and Black checklist for non-randomised studies. Overall the evidence is thin and inconclusive. The methodological differences in study sample (size and age), study design and measurement of attention make it difficult to compare results. There is weak evidence for the effect of acute bouts of physical activity on attention. More experimental studies with a comparable methodology, especially in the school setting, are needed to strengthen this evidence.
Timeframe: 1990–May 2014	
Total # of Studies: 12	
Exposure Definition: Short PA bout (i.e., max 45 minutes) and various levels of PA intensity were included. PA bouts could be performed during a physical education lesson, in-between lessons, at the playground, or as an energizer during class. The PA bouts could be performed with or without equipment or apparatus. Examples include PE class, treadmill, and cycle ergometer. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: In a school setting, four different measurements of attention were done (D2-test, observation of on-task behavior or time on task, the Woodcock-Johnson test of Concentration, and the Cognitive Assessment System). In the laboratory studies, the measurement of attention was more comparable; either a computerized visual attention task or (modified) flanker tasks were used. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Youth 4–18	**Author-Stated Funding Source:** Not Reported

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Kelly ME, Loughrey D, Lawlor BA, Robertson IH, Walsh C, Brennan S. The impact of exercise on the cognitive functioning of healthy older adults: A systematic review and meta-analysis. Ageing Res Rev. 2014;16:12-31. Doi:10.1016/j.arr.2014.05.002.</td></tr>
<tr><td>Purpose: To examine the impact of aerobic exercise, resistance training, and Tai Chi on the cognitive function of older adults without known cognitive impairment.</td><td rowspan="5">Abstract: Data from epidemiological, cross-sectional, and neuroimaging research show a relationship between higher levels of exercise and reduced risk of cognitive decline but evidence from randomised controlled trials (RCTs) is less consistent. This review examines the impact of aerobic exercise, resistance training, and Tai Chi on the cognitive function of older adults without known cognitive impairment. We investigate explanations for inconsistent results across trials and discrepancies between evidence from RCTs and other research data. Twenty-five RCTs were included in the review. Meta-analysis results revealed significant improvements for resistance training compared to stretching/toning on measures of reasoning (p<0.005); and for Tai Chi compared to ‘no exercise’ controls on measures of attention (p<0.001) and processing speed (p<0.00001). There were no significant differences between exercise and controls on any of the remaining 26 comparisons. Results should be interpreted with caution however as differences in participant profiles, study design, exercise programmes, adherence rates, and outcome measures contribute to both discrepancies within the exercise research literature and inconsistent results across trials.</td></tr>
<tr><td>Timeframe: 2002–2012</td></tr>
<tr><td>Total # of Studies: 25</td></tr>
<tr><td>Exposure Definition: Aerobic exercise, resistance training, or Tai Chi. Duration of the interventions lasted 12 weeks to 6 months.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cognitive function, divided into the domains of memory and executive function. Memory domain sub-categories were: recognition, immediate recall, delayed recall, face-name recall, and paired associates. Executive function domain subcategories were: working memory, verbal fluency, reasoning, attention, and processing speed. Composite measures of cognitive function were also included.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults ≥50</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Lambourne K, Tomporowski P. The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain Res. 2010;1341:12-24. doi:10.1016/j.brainres.2010.03.091.</td></tr>
<tr><td>Purpose: To examine the effects of acute exercise on cognitive performance.</td><td rowspan="5">Abstract: The effects of acute exercise on cognitive performance were examined using meta-analytic techniques. The overall mean effect size was dependent on the timing of cognitive assessment. During exercise, cognitive task performance was impaired by a mean effect of -0.14. However, impairments were only observed during the first 20min of exercise. Otherwise, exercise-induced arousal enhanced performance on tasks that involved rapid decisions and automatized behaviors. Following exercise, cognitive task performance improved by a mean effect of 0.20. Arousal continued to facilitate speeded mental processes and also enhanced memory storage and retrieval. Positive effects were observed following exercise regardless of whether the study protocol was designed to measure the effects of steady-state exercise, fatiguing exercise, or the inverted-U hypothesis. Finally, cognitive performance was affected differentially by exercise mode. Cycling was associated with enhanced performance during and after exercise, whereas treadmill running led to impaired performance during exercise and a small improvement in performance following exercise. These results are indicative of the complex relation between exercise and cognition. Cognitive performance may be enhanced or impaired depending on when it is measured, the type of cognitive task selected, and the type of exercise performed.</td></tr>
<tr><td>Timeframe: 1900–2008</td></tr>
<tr><td>Total # of Studies: 40</td></tr>
<tr><td>Exposure Definition: Exercise intervention elicited the activation of large muscles and cardiovascular responses. Three different exercise demands were looked at: fatigue, steady state, and inverted U. Subgroup analysis based on running and cycling.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Response time of pre- and post-exercise cognitive function tasks.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

Meta-Analysis **Citation:** Li MY, Huang MM, Li SZ, Tao J, Zheng GH, Chen LD. The effects of aerobic exercise on the structure and function of DMN-related brain regions: A systematic review. *Int J Neurosci.* 2016;127(7):634-649.	
Purpose: To assess the effects of aerobic exercise on the structure and function of the default mode network regions of the brain in adulthood.	**Abstract:** Physical activity may play a role in both the prevention and slowing of brain volume loss and may be beneficial in terms of improving the functional connectivity of brain regions. But much less is known about the potential benefit of aerobic exercise for the structure and function of the default mode network (DMN) brain regions. This systematic review examines the effects of aerobic exercise on the structure and function of DMN brain regions in human adulthood. Seven electronic databases were searched for prospective controlled studies published up to April 2015. The quality of the selected studies was evaluated with the Cochrane Collaboration's tool for assessing the risk of bias. RevMan 5.3 software was applied for data analysis. Finally, 14 studies with 631 participants were identified. Meta-analysis revealed that aerobic exercise could significantly increase right hippocampal volume (SMD = 0.26, 95% CI 0.01-0.51, p = 0.04, I2 = 7%, 4 studies), and trends of similar effects were observed in the total (SMD = 0.12, 95% CI -0.17 to 0.41, p = 0.43, I2 = 0%, 5 studies), left (SMD = 0.12, 95% CI -0.13 to 0.37, p = 0.33, I2 = 14%, 4 studies), left anterior (SMD = 0.12, 95% CI -0.16 to 0.40, p = 0.41, I2 = 74%, 2 studies) and right anterior (SMD = 0.10, 95% CI -0.17 to 0.38, p = 0.46, I2 = 76%, 4 studies) hippocampal volumes compared to the no-exercise interventions. A few studies reported that relative to no-exercise interventions, aerobic exercise could significantly decrease the atrophy of the medial temporal lobe, slow the anterior cingulate cortex (ACC) volume loss, increase functional connectivity within the hippocampus and improve signal activation in the cingulate gyrus and ACC. The current review suggests that aerobic exercise may have positive effects on the right hippocampus and potentially beneficial effects on the overall and other parts of the hippocampus, the cingulate cortex and the medial temporal areas of the DMN. Moreover, aerobic exercise may increase functional connectivity or activation in the hippocampus, cingulate cortex and parahippocampal gyrus regions of the DMN. However, considering the quantity and limitations of the included studies, the conclusion could not be drawn so far. Additional randomized controlled trials (RCTs) with rigorous designs and longer intervention periods are needed in the future.
Timeframe: Inception–2015	
Total # of Studies: 14	
Exposure Definition: The frequencies of aerobic exercise ranged from 2 to 6 sessions weekly. The sessions ranged from 20 to 90 minutes in duration and were conducted for 3 to 12 months. In the included studies, the exercise intensities were described as follows: in nine studies, 60% to 80% maximum heart rate; in two studies, a heart rate that generated a blood lactate concentration of 1.5–2 mmol/L; in two studies, a rating of perceived exertion (RPE) of 12 to 14 (on Borg's 6–20 scale) and in one study, a gas exchange threshold above that of aerobic but below that of anaerobic exercise. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Any structural or connective change in the brain regions related to the default mode network as measured by magnetic resonance imaging. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Adults	**Author-Stated Funding Source:** National Natural Science Foundation of China, Fujian Collaboration Innovation Center for Rehabilitation Technology

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Ludyga S, Gerber M, Brand S, Holsboer-Trachsler E, Pühse U. Acute effects of moderate aerobic exercise on specific aspects of executive function in different age and fitness groups: A meta-analysis. Psychophysiology. 2016;53(11):1611-1626. doi:10.1111/psyp.12736.</td></tr>
<tr><td>Purpose: To investigate transient changes in participants' performance on executive function tasks after a single aerobic exercise session.</td><td rowspan="5">Abstract: Whereas a wealth of studies have investigated acute effects of moderate aerobic exercise on executive function, the roles of age, fitness, and the component of executive function in this relationship still remain unclear. Therefore, the present meta-analysis investigates exercise-induced benefits on specific aspects of executive function in different age and aerobic fitness subgroups. Based on data from 40 experimental studies, a small effect of aerobic exercise on time-dependent measures (g = .35) and accuracy (g = .22) in executive function tasks was confirmed. The results further suggest that preadolescent children (g = .54) and older adults (g = .67) compared to other age groups benefit more from aerobic exercise when reaction time is considered as dependent variable. In contrast to age, aerobic fitness and the executive function component had no influence on the obtained effect sizes. Consequently, high aerobic fitness is no prerequisite for temporary improvements of the executive control system, and low- as well as high-fit individuals seem to benefit from exercise in a similar way. However, a higher sensitivity of executive function to acute aerobic exercise was found in individuals undergoing developmental changes. Therefore, preadolescent children and older adults in particular might strategically use a single aerobic exercise session to prepare for a situation demanding high executive control.</td></tr>
<tr><td>Timeframe: 1995–2015</td></tr>
<tr><td>Total # of Studies: 40</td></tr>
<tr><td>Exposure Definition: A single dose of moderate intensity aerobic exercise (cycling, running, or mixed aerobic activities). Moderate intensity exercise was defined as exercise at 55–70% of maximal heart rate, 40–60% of heart rate reserve, 40–60% maximal oxygen consumption (VO2 max), or rating 11–13 on the perceived exertion scale.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Executive function as assessed by inhibitory control, shifting, and working memory (no units provided).
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: All ages (categorized as pre-adolescent children, adolescents, young adults, and older adults)</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: McMorris T, Hale BJ. Differential effects of differing intensities of acute exercise on speed and accuracy of cognition: A meta-analytical investigation. Brain Cogn. 2012;80(3):338-351. doi:10.1016/j.bandc.2012.09.001.</td></tr>
<tr><td>Purpose: To examine the differential effects of differing intensities of acute exercise on speed and accuracy of cognition.</td><td rowspan="5">Abstract: The primary purpose of this study was to examine, using meta-analytical techniques, the differential effects of differing intensities of acute exercise on speed and accuracy of cognition. Overall, exercise demonstrated a small, significant mean effect size ($g=0.14$, $p<0.01$) on cognition. Examination of the comparison between speed and accuracy dependent variables showed that speed accounted for most of the effect. For speed, moderate intensity exercise demonstrated a significantly larger mean effect size than those for low and high intensities. For speed of processing during moderate intensity exercise, central executive tasks showed a larger effect size than recall and alertness/attention tasks; and mean effect size for counterbalanced or randomized studies was significantly greater than for studies in which a pre-exercise followed by during or post-exercise protocol was used. There was no significant difference between mean effect sizes when testing took place post-exercise compared to during exercise for speed but accuracy studies demonstrated a significantly larger mean effect size post-exercise. It was concluded that increased arousal during moderate intensity exercise resulted in faster speed of processing. The very limited effect on accuracy may be due to the failure to choose tests which are complex enough to measure exercise-induced changes in accuracy of performance.</td></tr>
<tr><td>Timeframe: Not Reported</td></tr>
<tr><td>Total # of Studies: 53</td></tr>
<tr><td>Exposure Definition: Intensity of exercise that activated large muscle groups. Exercise intensity was based on objective measures; low intensity group was <40% of maximum power output, moderate was 40–79%, and high was >80%. When percentage of maximum power output was not available, other indicators were used such as heart rate reserve, heart rate, ventilatory threshold, and maximum aerobic power.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Processing speed and/or accuracy of performing various working memory tasks, such as switch visual attention, Tower of Hanoi, and soccer decision-making.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: All ages</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

Systematic Review **Citation:** Morrison JD, Mayer L. Physical activity and cognitive function in adults with multiple sclerosis: An integrative review. *Disabil Rehabil.* 2016:1-12.	
Purpose: To examine the literature describing the relationship between physical activity (PA) and cognitive function in persons with multiple sclerosis, and review the evidence concerning the effects of physical activity interventions on cognitive function in persons with multiple sclerosis.	**Abstract:** PURPOSE: To identify and synthesize the research evidence concerning (1) the relationship between physical activity and cognitive performance in persons with multiple sclerosis (MS) and (2) to review the reported effects of physical activity interventions on neurocognitive performance conducted in this population. METHODS: Relevant peer-reviewed journal articles were identified by searching PubMed, PsychINFO, and SPORTDiscus through May 2016. Full-text articles meeting the inclusion criteria were evaluated for quality using tools developed by the National Institutes of Health. Studies deemed to be of poor quality were excluded from the review. RESULTS: Nineteen studies meeting the inclusion/exclusion criteria were analyzed. Nine studies reported significant relationships between higher levels of physical activity or cardiorespiratory fitness and measures of cognitive function. Data extracted from 10 physical activity intervention studies reported mixed results on the effectiveness of physical activity to improve selected domains of cognitive function in persons with MS. CONCLUSION: Although correlational studies provide evidence to support a linkage between physical activity and cognitive function in persons with MS, this linkage is confounded by factors that may have influenced the studies' results. Evidence derived from intervention studies that could support a positive effect of physical activity on cognition in persons with MS is equivocal. Implications for Rehabilitation Physical activity has numerous benefits for persons with multiple sclerosis (MS) including improvements in balance, ambulation, depression, fatigue, and quality of life. Structured physical activity programs may contribute to cognitive function stability or improvement in persons with MS.
Timeframe: Inception–2016	
Total # of Studies: 19	
Exposure Definition: The mode of exercise included resistance training, aerobic training (treadmill walking, cycling, rowing, sport climbing, and arm ergometry), and yoga, as well as participation in a web-based PA behavior program. Intervention duration ranged from 8 weeks to 6 months. Exercise session length ranged from 30 to 90 minutes, and the frequency of sessions varied from 1 to 3 times a week. **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Cognition domains including sustained and complex attention, concentration, working and secondary memory, information processing speed, visuospatial skills, verbal fluency, and executive function planning, organization, judgment, reasoning, and problem solving. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Adults, Multiple Sclerosis	**Author-Stated Funding Source:** International Organization of Multiple Sclerosis Nurses; National Institute of Nursing Research, National Institutes of Health

Systematic Review **Citation:** Murray DK, Sacheli MA, Eng JJ, Stoessl AJ. The effects of exercise on cognition in Parkinson's disease: A systematic review. *Transl Neurodegener.* 2014;3(1):5. doi:10.1186/2047-9158-3-5.	
Purpose: To evaluate all original research reports that assessed exercise interventions in human Parkinson's disease or in animal models of Parkinson's disease, with a primary or secondary outcome to examine cognitive function.	**Abstract:** Cognitive impairments are highly prevalent in Parkinson's disease (PD) and can substantially affect a patient's quality of life. These impairments remain difficult to manage with current clinical therapies, but exercise has been identified as a possible treatment. The objective of this systematic review was to accumulate and analyze evidence for the effects of exercise on cognition in both animal models of PD and human disease. This systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. Fourteen original reports were identified, including six pre-clinical animal studies and eight human clinical studies. These studies used various exercise interventions and evaluated many different outcome measures; therefore, only a qualitative synthesis was performed. The evidence from animal studies supports the role of exercise to improve cognition in humans through the promotion of neuronal proliferation, neuroprotection and neurogenesis. These findings warrant more research to determine what roles these neural mechanisms play in clinical populations. The reports on cognitive changes in clinical studies demonstrate that a range of exercise programs can improve cognition in humans. While each clinical study demonstrated improvements in a marker of cognition, there were limitations in each study, including non-randomized designs and risk of bias. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used and the quality of the evidence for human studies were rated from "low" to "moderate" and the strength of the recommendations were rated from "weak" to "strong". Studies that assessed executive function, compared to general cognitive abilities, received a higher GRADE rating. Overall, this systematic review found that in animal models exercise results in behavioral and corresponding neurobiological changes in the basal ganglia related to cognition. The clinical studies showed that various types of exercise, including aerobic, resistance and dance can improve cognitive function, although the optimal type, amount, mechanisms, and duration of exercise are unclear. With growing support for exercise to improve not only motor symptoms, but also cognitive impairments in PD, health care providers and policy makers should recommend exercise as part of routine management and neurorehabilitation for this disorder.
Timeframe: 1966–October 2013	
Total # of Studies: 14	
Exposure Definition: An exercise intervention was defined as any purposeful increase in the subject's physical activity through a single bout of exercise or prolonged exercise over the course of a structured or unstructured program. Examples include tango (dancing), cycling, Wii Fit training, and stretching. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Changes in behavioral or neurobiological markers of cognitive function. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Older Adults, Parkinson's Disease	**Author-Stated Funding Source:** None

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Roig M, Nordbrandt S, Geertsen SS, Nielsen JB. The effects of cardiovascular exercise on human memory: A review with meta-analysis. Neurosci Biobehav Rev. 2013;37(8):1645-1666. doi:10.1016/j.neubiorev.2013.06.012.</td></tr>
<tr><td>Purpose: To review the evidence for the use of cardiovascular exercise to improve memory.</td><td rowspan="5">Abstract: We reviewed the evidence for the use of cardiovascular exercise to improve memory and explored potential mechanisms. Data from 29 and 21 studies including acute and long-term cardiovascular interventions were retrieved. Meta-analyses revealed that acute exercise had moderate (SMD=0.26; 95% CI=0.03, 0.49; p=0.03; N=22) whereas long-term had small (SMD=0.15; 95% CI=0.02, 0.27; p=0.02; N=37) effects on short-term memory. In contrast, acute exercise showed moderate to large (SMD=0.52; 95% CI=0.28, 0.75; p<0.0001; N=20) whereas long-term exercise had insignificant effects (SMD=0.07; 95% CI=-0.13, 0.26; p=0.51; N=22) on long-term memory. We argue that acute and long-term cardiovascular exercise represent two distinct but complementary strategies to improve memory. Acute exercise improves memory in a time-dependent fashion by priming the molecular processes involved in the encoding and consolidation of newly acquired information. Long-term exercise, in contrast, has negligible effects on memory but provides the necessary stimuli to optimize the responses of the molecular machinery responsible for memory processing. Strategically combined, acute and long-term interventions could maximize the benefits of cardiovascular exercise on memory.</td></tr>
<tr><td>Timeframe: 1894–June 2012</td></tr>
<tr><td>Total # of Studies: 41</td></tr>
<tr><td>Exposure Definition: Acute and long-term cardiovascular exercise. Studies included fast walking, jogging, cycling, arm ergometer, and rhythmic muscle strengthening as modes of cardiovascular exercise. Duration of exercise was 30 seconds to 65 minutes, ranging from 4 to 14 weeks. Intensity of the exercise was categorized as light (<40% heart rate reserve), moderate (40–59% heart rate reserve), vigorous (60–89% heart rate reserve) or maximal (≥90% heart rate reserve); duration was categorized as short (<20 min) medium (20–40 min) or long (>40 min).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Changes in scores on tests of human memory: Tests were considered to assess short-term memory if they involved the retention of information over periods of a few seconds to 1–2 minutes; and long-term memory tests were those involving the retention of information over longer periods of time and thus were characterized by a delay (>2 minutes) of the retention test in relation to the exposure to the information to be remembered.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Systematic Review
Citation: Sexton CE, Betts JF, Demnitz N, Dawes H, Ebmeier KP, Johansen-Berg H. A systematic review of MRI studies examining the relationship between physical fitness and activity and the white matter of the ageing brain. Neuroimage. 2016;131:81-90. doi:10.1016/j.neuroimage.2015.09.071.</td></tr>
<tr><td>Purpose: To provide a systematic report of cross-sectional and longitudinal magnetic resonance imaging (MRI) studies that have examined the effects of physical fitness or physical activity (PA) on the white matter of the aging brain.</td><td rowspan="5">Abstract: Higher levels of physical fitness or activity (PFA) have been shown to have beneficial effects on cognitive function and grey matter volumes in older adults. However, the relationship between PFA and the brain's white matter (WM) is not yet well established. Here, we aim to provide a comprehensive and systematic review of magnetic resonance imaging studies examining the effects of PFA on the WM of the ageing brain. Twenty-nine studies were included in the review: eleven examined WM volume, fourteen WM lesions, and nine WM microstructure. While many studies found that higher levels of PFA were associated with greater WM volumes, reduced volume or severity of WM lesions, or improved measures of WM microstructure, a number of negative findings have also been published. Meta-analyses of global measures of WM volume and WM lesion volume yielded significant, but small, effect sizes. Overall, we found evidence for cautious support of links between PFA and WM structure, and highlighted key areas for future research including the extent to which the relationship between PFA and WM structure is anatomically specific, the influence of possible confounding factors, and the relationship between PFA, WM and cognition.</td></tr>
<tr><td>Timeframe: Inception–2015</td></tr>
<tr><td>Total # of Studies: 29</td></tr>
<tr><td>Exposure Definition: Physical fitness and activity was assessed by fitness test, questionnaire, or accelerometry; or administered with an exercise intervention. Examples include questionnaires assessing average metabolic equivalent hours per week over 10 years, a 6-point scale for PA, number of activities per week, peak oxygen uptake, and kilocalories per week over 2 weeks.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Changes in volume of white matter of the brain as measured by magnetic resonance imaging. Lesions and microstructure of white matter.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Older adults</td><td>Author-Stated Funding Source: National Institute for Health Research, Oxford Biomedical Research Centre</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Smith PJ, Blumenthal JA, Hoffman BM, et al. Aerobic exercise and neurocognitive performance: A meta-analytic review of randomized controlled trials. Psychosom Med. 2010;72(3):239-252. Doi:10.1097/PSY.0b013e3181d14633.</td></tr>
<tr><td>Purpose: To understand the effects of aerobic exercise training on specific domains of neurocognitive performance, including attention and processing speed, executive function, working memory, and memory.</td><td rowspan="5">Abstract: OBJECTIVES: To assess the effects of aerobic exercise training on neurocognitive performance. Although the effects of exercise on neurocognition have been the subject of several previous reviews and meta-analyses, they have been hampered by methodological shortcomings and are now outdated as a result of the recent publication of several large-scale, randomized, controlled trials (RCTs). METHODS: We conducted a systematic literature review of RCTs examining the association between aerobic exercise training on neurocognitive performance between January 1966 and July 2009. Suitable studies were selected for inclusion according to the following criteria: randomized treatment allocation; mean age > or =18 years of age; duration of treatment >1 month; incorporated aerobic exercise components; supervised exercise training; the presence of a nonaerobic-exercise control group; and sufficient information to derive effect size data. RESULTS: Twenty-nine studies met inclusion criteria and were included in our analyses, representing data from 2049 participants and 234 effect sizes. Individuals randomly assigned to receive aerobic exercise training demonstrated modest improvements in attention and processing speed (g = 0.158; 95% confidence interval [CI]; 0.055-0.260; p = .003), executive function (g = 0.123; 95% CI, 0.021-0.225; p = .018), and memory (g = 0.128; 95% CI, 0.015-0.241; p = .026). CONCLUSIONS: Aerobic exercise training is associated with modest improvements in attention and processing speed, executive function, and memory, although the effects of exercise on working memory are less consistent. Rigorous RCTs are needed with larger samples, appropriate controls, and longer follow-up periods.</td></tr>
<tr><td>Timeframe: January 1966–July 2009</td></tr>
<tr><td>Total # of Studies: 29</td></tr>
<tr><td>Exposure Definition: Aerobic exercise such as brisk walking, biking, or jogging that lasted more than one month.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Attention and processing speed (Digit Symbol Substitution, Complex/Choice Reaction Time, Ruff 2 & 7 Test, Trail Making Test Section A), executive function (Stroop Interference, Trail Making Test Section B, Animal Naming/Verbal Fluency, Controlled Oral Word Association Test), working memory (Digit Span, WAIS Letter-Number Sequencing), and declarative memory (Logical Memory, Immediate Recall, Rey Auditory Verbal Learning Test).
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: National Institutes of Health, General Clinical Research Center Program, National Center for Research Resources</td></tr>
</table>

Meta-Analysis

Citation: Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: A meta-analysis of prospective studies. *J Intern Med.* 2011;269(1):107-117. doi:10.1111/j.1365-2796.2010.02281.x.

Purpose: To conduct a meta-analysis of all the available prospective cohort studies that investigated the association between physical activity (PA) and cognitive decline in nondemented subjects.

Timeframe: 1966–January 2010

Total # of Studies: 15

Exposure Definition: PA was assessed through questionnaires (with some being self-reported). Some questionnaires assessed intensity levels, whereas others calculated energy expenditure. PA levels were also categorized in different ways, such as "none, low, moderate, high"; <30 minutes, 60, or >60 minutes per day; quartiles; and < or > 4 hours per week.

Measures Steps: No

Measures Bouts: No

Examines HIIT: No

Outcomes Addressed: Cognitive decline or cognitive impairment, defined as decline in cognitive functioning tests at follow-up examination.

Examine Cardiorespiratory Fitness as Outcome: No

Abstract: OBJECTIVE: The relationship between physical activity and cognitive function is intriguing but controversial. We performed a systematic meta-analysis of all the available prospective studies that investigated the association between physical activity and risk of cognitive decline in nondemented subjects. METHODS: We conducted an electronic literature search through MedLine, Embase, Google Scholar, Web of Science, The Cochrane Library and bibliographies of retrieved articles up to January 2010. Studies were included if they analysed prospectively the association between physical activity and cognitive decline in nondemented subjects. RESULTS: After the review process, 15 prospective studies (12 cohorts) were included in the final analysis. These studies included 33,816 nondemented subjects followed for 1-12 years. A total of 3210 patients showed cognitive decline during the follow-up. The cumulative analysis for all the studies under a random-effects model showed that subjects who performed a high level of physical activity were significantly protected (-38%) against cognitive decline during the follow-up (hazard ratio (HR) 0.62, 95% confidence interval (CI) 0.54-0.70; P < 0.00001). Furthermore, even analysis of low-to-moderate level exercise also showed a significant protection (-35%) against cognitive impairment (HR 0.65, 95% CI 0.57-0.75; P < 0.00001). CONCLUSION: This is the first meta-analysis to evaluate the role of physical activity on cognitive decline amongst nondemented subjects. The present results suggest a significant and consistent protection for all levels of physical activity against the occurrence of cognitive decline.

Populations Analyzed: Adults

Author-Stated Funding Source: Not Reported

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Spruit A, Assink M, van Vugt E, van der Put C, Stams GJ. The effects of physical activity interventions on psychosocial outcomes in adolescents: A meta-analytic review. Clin Psychol Rev. 2016;45:56-71. doi:10.1016/j.cpr.2016.03.006.</td></tr>
<tr><td>Purpose: To investigate the effects of physical activity (PA) interventions on four psychosocial outcomes in adolescents: externalizing problems, internalizing problems, self-concept, and academic achievement.</td><td rowspan="5">Abstract: Physical activity interventions are often implemented in the adolescent mental health care practice to prevent or treat psychosocial problems. To date, no systematic review of the effect of these physical activity interventions in adolescents has been conducted. In the current study, four multilevel meta-analyses were performed to assess the overall effect of physical activity interventions on externalizing problems, internalizing problems, self-concept, and academic achievement in adolescents. In addition, possible moderating factors were examined. In total, 57 studies reporting on 216 effect sizes were included, and the results showed significant small-to-moderate effects of physical activity interventions on externalizing problems (d=0.320), internalizing problems (d=0.316), self-concept (d=0.297), and academic achievement (d=0.367). Further, moderator analyses showed that outcome, study, sample, and intervention characteristics influenced the effects of physical activity interventions on psychosocial outcomes. Implications for theory and practice concerning the use of physical activity interventions in adolescent mental health care practice are discussed.</td></tr>
<tr><td>Timeframe: Inception–2015</td></tr>
<tr><td>Total # of Studies: 57</td></tr>
<tr><td>Exposure Definition: PA intervention consisted of sports or (aerobic) exercise activities. The duration of the intervention (in weeks) and the frequency of the intervention (in hours per week) was documented.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Externalizing problems (aggressive or delinquent behavior), internalizing problems, self-concept, and academic achievement.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Youth 10–21</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

Meta-Analysis **Citation:** Tan BWZ, Pooley JA, Speelman CP. A meta-analytic review of the efficacy of physical exercise interventions on cognition in individuals with autism spectrum disorder and ADHD. *J Autism Dev Disord.* 2016;46(9):3126-3143. doi:10.1007/s10803-016-2854-x.	
Purpose: To investigate the efficacy of exercise interventions on individuals with autism spectrum disorder and attention deficit hyperactivity disorder, and explore the practical significance of applying exercise to cognition based on the meta-analytic findings.	**Abstract:** This review evaluates the efficacy of using physical exercise interventions on improving cognitive functions in individuals with autism spectrum disorder (ASD) and/or attention deficit hyperactivity disorder (ADHD). This review includes a meta-analysis based on a random-effects model of data reported in 22 studies with 579 participants aged 3-25 year old. The results revealed an overall small to medium effect of exercise on cognition, supporting the efficacy of exercise interventions in enhancing certain aspects of cognitive performance in individuals with ASD and/or ADHD. Specifically, similar to the general population literature, the cognitive benefits of exercise are not consistent across all aspects of cognitive functions (i.e., some areas are not improved). The clinical significance of the reported effect sizes is also considered.
Timeframe: 1968–2015	
Total # of Studies: 22	
Exposure Definition: Exercise intervention: types of exercises included exergaming, treadmill, cycle ergometers, and mixed-exercises at varying durations (5–70 minutes). **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Cognitive tasks were separated into two broad categories, on-task duration/simple learning tasks (i.e., the length of time individuals stayed engaged on a specific task; or for example, the number of correct responses on the value of various coins presented) and global executive functions. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Youth 3–25, Cognitive Disability, Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder	**Author-Stated Funding Source:** Not Reported

Meta-Analysis **Citation:** Wu Y, Wang Y, Burgess EO, Wu J. The effects of Tai Chi exercise on cognitive function in older adults: a meta-analysis. *J Sport Health Sci.* 2013;2(4):193-203.	
Purpose: To critically assess the effects of Tai Chi exercise on cognitive function in terms of global cognitive, executive, and memory functions in older adults. **Timeframe:** January 1992–July 2012 **Total # of Studies:** 8 **Exposure Definition:** Tai chi; duration of sessions (20–40 minutes), sessions per week (1–3), and duration of intervention (10 weeks to a year) varied among studies. Several different types of Tai Chi were practiced in different studies. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No **Outcomes Addressed:** Neurocognitive tests, including different domains of cognitive function and global cognitive, executive, and memory functions. Mini mental status examination, Alzheimer's disease assessment scale-cognitive subscale, trailmaking test part A, trailmaking test part B, digit span test forward, digit span test backward, visual span test backward, verbal fluency Test, and word delay recall test. **Examine Cardiorespiratory Fitness as Outcome:** No	**Abstract:** Background Cognitive impairment is prevalent among older adults and results in degraded quality of life for older adults. As the population ages, this may cause a huge burden to society. Research has demonstrated that physical exercise is beneficial to cognitive function. The purpose of this meta-analysis was to critically assess the effect of Tai Chi exercise on global cognitive, executive, and memory functions in older adults. Methods After a thorough electronic search and selection, eight studies were included in this meta-analysis with two cross-sectional and six intervention studies. Nine variables included in this meta-analysis were: mini mental status examination (MMSE), Alzheimer's disease assessment scale-cognitive subscale (ADAS-cog), trailmaking test part A (TMA), trailmaking test part B (TMB), digit span test forward (DSF), digit span test backward (DSB), visual span test backward (VSB), verbal fluency test (VFT), and word delay recall test (WDR). The effect sizes and forest plots of these nine variables were generated. Results Four (MMSE, DSB, VSB, and VFT) out of nine variables were significantly improved after Tai Chi exercise with the effect sizes ranged from 0.20 to 0.46 (small to medium). MMSE represented global cognitive function, and DSB, VSB, and VFT represented memory function. Conclusion Tai Chi as a mind-body exercise has the positive effects on global cognitive and memory functions, and more consistent positive effects were found on memory function, especially verbal working memory.
Populations Analyzed: Adults ≥55	**Author-Stated Funding Source:** Not Reported

Meta-Analysis **Citation:** Zheng G, Xia R, Zhou W, Tao J, Chen L. Aerobic exercise ameliorates cognitive function in older adults with mild cognitive impairment: A systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med.* 2016a;50:1443-1450.	
Purpose: To systematically evaluate the effect of aerobic exercise on cognitive function, including global cognitive ability and specific domains of cognition, in older adults with mild cognitive impairment. **Timeframe:** Inception–2015 **Total # of Studies:** 11 **Exposure Definition:** The most commonly used aerobic exercise was regular walking, but handball training, Tai Chi, jogging combined with Tai Chi, cycling, dance-based aerobics, and multicomponent aerobic exercises were also practiced. The frequency of aerobic exercise varied from two to five sessions weekly and 30–60 minutes per session. The duration of the intervention was 6 months or 1 year, with the exception of two studies, which were 6 and 12 weeks, respectively. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No **Outcomes Addressed:** Global cognitive function (Mini-Mental State Examination [MMSE], Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), Montreal Cognitive Assessment [MoCA]), memory (Rey Auditory Verbal Learning Test (AVLT), MMSE), attention (visual span and digital symbol coding), executive ability (Trail-Making Test or part B, Stroop color word test-abridge task, and MoCA [clock drawing]), verbal fluency (verbal fluency test), and visuospatial function (field of view). **Examine Cardiorespiratory Fitness as Outcome:** No	**Abstract:** OBJECTIVE: To evaluate the effect of aerobic exercise on cognitive function in people with mild cognitive impairment (MCI). DESIGN: Systematic review and meta-analysis of aerobic exercise intervention for cognitive function in older adults with MCI. DATA SOURCES: PubMed, EMBASE, SinoMed, China National Knowledge Infrastructure (CNKI), Wanfang and Chinese Science and Technology Periodical (VIP) databases from their inception to 31 January 2015, the Cochrane Central Register of Controlled Trials (Cochrane Library, 2015, Issue 3) and the reference lists of all retrieved articles. ELIGIBILITY CRITERIA: Randomised controlled trials, older adults with MCI, aerobic exercises compared with no specific exercise intervention for global cognitive ability and any specific domains of cognition. DATA SYNTHESIS: Meta-analysis was conducted with RevMan V.5.3 software using the fixed-effect model for the available data without significant heterogeneity, or the random-effect model was used if appropriate. RESULTS: 11 studies were identified involving 1497 participants. Meta-analysis showed that aerobic exercise significantly improved global cognitive ability (Mini-Mental State Examination (MMSE) scores: MD=0.98, 95% CI 0.5 to 1.45, p<0.0001; Montreal Cognitive Assessment (MoCA) scores: MD=2.7, 95% CI 1.11 to 4.29, p=0.0009); weakly, positively improve memory (immediately recall: SMD=0.29, 95% CI 0.13 to 0.46, p=0.0005; delay recall: SMD=0.22, 95% CI 0.09 to 0.34, p=0.0005). No significant improvement was found in other domains of cognition. CONCLUSIONS: Aerobic exercise led to an improvement in global cognitive ability and had a positive effect with a small effect size on memory in people with MCI. However, owing to the limitations of the included studies, these findings should be interpreted cautiously.
Populations Analyzed: Adults ≥60, Mild Cognitive Impairment	**Author-Stated Funding Source:** National Natural Science Foundation of China, Collaboration Innovation Center for Rehabilitation Technology, Fujian provincial rehabilitation industrial institution, and Fujian Key Laboratory of Rehabilitation Technology

<table>
<tr><td colspan="2">Systematic Review
Citation: Zheng G, Zhou W, Xia R, Tao J, Chen L. Aerobic exercises for cognition rehabilitation following stroke: A systematic review. J Stroke Cerebrovasc Dis. 2016b;25(11):2780-2789.doi:10.1016/j.jstrokecerebrovasdis.2016.07.035.</td></tr>
<tr><td>Purpose: To assess the effects of aerobic exercise on cognitive function following stroke.</td><td rowspan="5">Abstract: BACKGROUND: Cognitive impairments are highly prevalent in stroke survivors and can substantially affect their physical rehabilitation and quality of life. The management of these impairments currently remains limited, but increasing studies reported the effect of aerobic exercise on cognitive performance in patients suffering from stroke. The purpose of this review was to assess the effects of aerobic exercise on cognitive function following stroke. METHODS: Seven electronic databases (China National Knowledge Infrastructure [CNKI], Chinese Science and Technology Periodical Database [VIP], Wanfang, China Biology Medicine disc [CBM], Science Citation Index [SCI], EMBASE, and PubMed) were searched from their inception to May 31, 2015, for the effects of aerobic exercise on cognitive ability compared to usual physical activity in stroke survivors. RevMan V5.3 (The Nordic Cochrane Centre) was used to analyze the data and to evaluate the methodological quality of the included studies. RESULTS: Ten eligible studies including 394 participants were identified. Six studies showed that aerobic exercise significantly improved global cognitive ability in stroke survivors. Four studies reported aerobic exercise to be beneficial in improving memory, but only one showed statistical significance. Two studies investigated the effects of aerobic exercise on attention, and one showed a significant improvement. One study reported a significant benefit of aerobic exercise on visuospatial ability in stroke survivors. No adverse events were reported in the included studies. CONCLUSIONS: Aerobic exercise may have a positive effect on improving global cognitive ability and a potential benefit on memory, attention, and the visuospatial domain of cognition in stroke survivors. However, further large, rigorously designed trials are needed to confirm these findings.</td></tr>
<tr><td>Timeframe: Inception–2015</td></tr>
<tr><td>Total # of Studies: 10</td></tr>
<tr><td>Exposure Definition: Aerobic exercises, 1 to 5 sessions weekly and ranged from 20–90 minutes per session, with a varying duration of exercise of 8–24 weeks. The average intensity was controlled to 50%–90% peak oxygen uptake or 60%–80% heart rate reserve. Exercise was cycling (alone or combined with other aerobic exercises), but Tai Chi, yoga, and treadmill exercise were also practiced.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Global cognitive ability or on a specific domain of cognition, such as memory, attention, language, processing speed, execution, verbal fluency, and visuospatial ability, that was measured using objective measurements or scales such as the Montreal Cognitive Assessment, Stroke Impact Scale Domain, the Stroop task, and the Digit Symbol Test.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Stroke</td><td>Author-Stated Funding Source: Fujian Provincial Health and Family Planning Commission, Specialized Research Fund for the Key Disciplines of FJTCM, Fujian Key Laboratory of Rehabilitation Technology</td></tr>
</table>

Table 3. Existing Systematic Reviews and Meta-Analyses Quality Assessment Chart

AMSTARExBP: SR/MA	Beckett, 2015	Bustamante, 2016	Carson, 2016	Cerrillo-Urbina, 2015	Chang, 2012	Colcombe, 2003
Comprehensive literature search performed.	Partially Yes	Partially Yes	Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	No	No	No	Yes	No	No
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No	Yes	Yes	Yes
List of studies (included and excluded) provided.	No	No	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	No	No
FITT defined and examined in relation to outcome effect sizes.	No	N/A	N/A	No	No	No
Scientific quality (risk of bias) of included studies assessed and documented.	No	No	Partially Yes	Yes	No	No
Results depended on study quality, either overall, or in interaction with moderators.	N/A	N/A	No	Yes	N/A	N/A
Scientific quality used appropriately in formulating conclusions.	N/A	N/A	Yes	Yes	N/A	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	N/A	N/A	Yes	Yes	Yes
Effect size index chosen justified, statistically.	Yes	N/A	N/A	Yes	Yes	Partially Yes
Individual-level meta-analysis used.	No	N/A	N/A	No	No	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	No	No	Yes	No	No
Conflict of interest disclosed.	Yes	Yes	No	No	No	No

AMSTARExBP: SR/MA	Den 2016	Dinoff, 2016	Donnelly , 2016	Esteban-Cornejo, 2015	Etnier, 2006	Falck, 2016
Comprehensive literature search performed.	Yes	Yes	Partially Yes	Yes	Yes	Partially Yes
Duplicate study selection and data extraction performed.	Yes	Yes	Yes	Yes	No	Yes
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No	No	Yes	No
List of studies (included and excluded) provided.	No	No	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	No	No	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	N/A	No	N/A	N/A	No	N/A
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	Yes	No	No	Yes
Results depended on study quality, either overall, or in interaction with moderators.	Yes	Yes	Yes	N/A	N/A	Yes
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	Yes	N/A	N/A	Yes
Data appropriately synthesized and if applicable, heterogeneity assessed.	N/A	Yes	N/A	N/A	Yes	N/A
Effect size index chosen justified, statistically.	N/A	Yes	N/A	N/A	Yes	N/A
Individual-level meta-analysis used.	N/A	No	N/A	N/A	No	N/A
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	Yes	No	No	No	No
Conflict of interest disclosed.	No	Yes	No	No	No	Yes

AMSTARExBP: SR/MA	Firth, 2016	Groot, 2016	Halloway, 2016	Janssen, 2014	Kelly, 2014	Lambourne, 2010
Comprehensive literature search performed.	Yes	Partially Yes	Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	No	Yes	No	Yes	No
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No	No	No	No
List of studies (included and excluded) provided.	No	No	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	No	No	N/A	N/A	No	No
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	Partially Yes	Yes	Yes	No
Results depended on study quality, either overall, or in interaction with moderators.	Yes	Yes	No	No	No	N/A
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	No	Yes	Yes	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	No	N/A	Yes	Yes
Effect size index chosen justified, statistically.	Yes	Yes	Yes	N/A	Yes	Yes
Individual-level meta-analysis used.	No	No	N/A	N/A	No	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	Yes	Yes	No	No	No	No
Conflict of interest disclosed.	Yes	Yes	Yes	No	No	No

AMSTARExBP: SR/MA	Li, 2016	Ludyga, 2016	McMorris, 2012	Morrison, 2016	Murray, 2014	Roig, 2013
Comprehensive literature search performed.	Yes	Yes	Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	Yes	No	No	No	Yes
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No	No	No	No
List of studies (included and excluded) provided.	No	No	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	No	No	No	N/A	N/A	No
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	No	Yes	Yes	Yes
Results depended on study quality, either overall, or in interaction with moderators.	No	Yes	N/A	Yes	No	Yes
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	N/A	Yes	Yes	Yes
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	Yes	N/A	N/A	Yes
Effect size index chosen justified, statistically.	Yes	Yes	Yes	N/A	N/A	Yes
Individual-level meta-analysis used.	No	No	No	N/A	N/A	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	Yes	No	No	No	Yes
Conflict of interest disclosed.	Yes	No	No	Yes	Yes	No

AMSTARExBP: SR/MA	Sexton, 2016	Smith, 2010	Sofi, 2011	Spruit, 2016	Tan, 2016	Wu, 2013
Comprehensive literature search performed.	Yes	Yes	Yes	Yes	Yes	Partially Yes
Duplicate study selection and data extraction performed.	Yes	No	Yes	No	No	No
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	Yes	No	No	Yes	No
List of studies (included and excluded) provided.	No	Yes	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	N/A	No	No	No	No	No
Scientific quality (risk of bias) of included studies assessed and documented.	Partially Yes	Partially Yes	No	No	No	No
Results depended on study quality, either overall, or in interaction with moderators.	No	Yes	N/A	N/A	N/A	N/A
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	N/A	N/A	N/A	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	N/A	Yes	Yes	Partially Yes	Yes	No
Effect size index chosen justified, statistically.	Yes	Yes	Yes	Yes	Yes	Yes
Individual-level meta-analysis used.	N/A	No	No	No	No	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	Yes	No	Yes	Yes	Yes	No
Conflict of interest disclosed.	No	No	No	No	No	No

AMSTARExBP: SR/MA	Zheng, 2016a	Zheng, 2016b
Comprehensive literature search performed.	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	Yes
Search strategy clearly described.	Yes	Yes
Relevant grey literature included in review.	Yes	Yes
List of studies (included and excluded) provided.	No	No
Characteristics of included studies provided.	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	No	N/A
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes
Results depended on study quality, either overall, or in interaction with moderators.	No	Yes
Scientific quality used appropriately in formulating conclusions.	Yes	Yes
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes
Effect size index chosen justified, statistically.	Yes	N/A
Individual-level meta-analysis used.	No	N/A
Practical recommendations clearly addressed.	Yes	No
Likelihood of publication bias assessed.	Yes	No
Conflict of interest disclosed.	Yes	No

Appendices

Appendix A: Analytical Framework

Topic Area
Brain Health

Systematic Review Question

What is the relationship between physical activity and cognition?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, or socio-economic status?
c. Does the relationship exist across the lifespan?
d. Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)?
e. What is the relationship between physical activity and brain structure and function?

Population
People of all ages

Exposure
All types and intensities of physical activity, including free-living activities, play, physical fitness, and sedentary behavior

Comparison
People who participate in varying levels of physical activity

Key Definitions

- Cognition: The set of mental processes that contribute to perception, memory, intellect, and action. Cognitive function can be assessed using a variety of techniques including paper-pencil based tests, neuropsychological testing, and computerized testing methods. Cognitive functions are largely divided into different domains that capture both the type of process as well as the brain areas and circuits that support those functions. Working memory, visual attention, and long-term memory are all examples of different cognitive domains that are thought to be dependent on overlapping but yet largely separate neural systems.

Endpoint Health Outcomes

- Attentional control
- Academic achievement
- Brain health and biomarkers of brain health (white matter, gray matter)
- Brain structure
- Brain function
- Cognition
- Cognitive ability
- Cognitive control
- Cognitive function
- Cognitive functioning
- Cognitive health
- Cognitive performance
- Cognitive processing
- Executive control
- Executive function
- Executive functioning
- Executive functions
- Information processing
- Inhibitory control
- Memory
- Mental flexibility
- Mental recall
- Neuro cognitive
- Neurocognitive
- Perceptual processing
- Problem solving
- Scholastic achievement
- Scholastic performance

Appendix B: Final Search Strategy

Search Strategy: PubMed (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: PubMed; Date of Search: 12/13/2016; 294 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Publication Date (Systematic Review/Meta-Analysis)	AND ("2000/01/01"[PDAT] : "3000/12/31"[PDAT])
Limit: Publication Type Include (Systematic Review/Meta-Analysis)	AND (systematic[sb] OR meta-analysis[pt] OR “systematic review”[tiab] OR “systematic literature review”[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR “pooled analyses”[tiab] OR "pooled data"[tiab])
Limit: Publication Type Exclude (Systematic Review/Meta-Analysis)	NOT (“comment”[Publication Type] OR “editorial”[Publication Type])
Cognition	AND (("Academic achievement"[tiab] OR "Academic performance"[tiab] OR "Attentional control"[tiab] OR "Brain health"[tiab] OR "Brain function"[tiab] OR "Cognitive ability"[tiab] OR "Cognitive control"[tiab] OR "Cognitive function"[tiab] OR "Cognitive functioning"[tiab] OR "Cognitive health"[tiab] OR "Cognitive performance"[tiab] OR "Cognitive processing"[tiab] OR "Executive control"[tiab] OR "Executive function"[mh] OR "Information processing"[tiab] OR "Inhibitory control"[tiab] OR "Memory"[mh] OR "Mental flexibility"[tiab] OR "Mental recall"[tiab] OR "Neuro cognitive"[tiab] OR "Neurocognitive"[tiab] OR "Perceptual processing"[tiab] OR "Problem solving"[mh] OR "Problem solving"[tiab] OR "Scholastic achievement"[tiab] OR "Scholastic performance"[tiab]) OR (("Executive function"[tiab] OR "Executive functioning"[tiab] OR "Executive functions"[tiab] OR "Memory"[tiab]) NOT medline[sb]))
Physical Activity	AND (("Exercise"[mh] OR "Exercise"[tiab] OR "Functional Fitness"[tiab] OR "Physical activity"[tiab] OR "Physical fitness"[mh] OR (“Recess” AND ("Child" OR "Youth")) OR “Physical education and Training”[mh] OR Sedentary lifestyle[mh]) OR (("Aerobic activities"[tiab] OR "Aerobic activity"[tiab] OR "Cardiorespiratory fitness"[tiab] OR "Cardiovascular activities"[tiab] OR "Cardiovascular activity"[tiab] OR "Cardiovascular fitness"[tiab] OR "Endurance activities"[tiab] OR "Endurance activity"[tiab] OR "Physical conditioning"[tiab] OR "Physical fitness"[tiab] OR "Resistance training"[tiab] OR "strength training"[tiab] OR “Physical education”[tiab] OR “Sedentary”[tiab] OR "walking"[tiab]) NOT medline[sb]))

Search Strategy: CINAHL (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: CINAHL; Date of Search: 12/22/16; 7 results
Terms searched in title or abstract

Set	Search Terms
Cognition	("Academic achievement" OR "Academic performance" OR "Attentional control" OR "Brain health" OR "Brain function" OR "Cognitive ability" OR "Cognitive control" OR "Cognitive function" OR "Cognitive functioning" OR "Cognitive health" OR "Cognitive performance" OR "Cognitive processing" OR "Executive control" OR "Executive function" OR "Executive functioning" OR "Executive functions" OR "Information processing" OR "Inhibitory control" OR "Memory" OR "Mental flexibility" OR "Mental recall" OR "Neuro cognitive" OR "Neurocognitive" OR "Perceptual processing" OR "Problem solving" OR "Scholastic achievement" OR "Scholastic performance")
Physical Activity	AND ("Aerobic activities" OR "Aerobic activity" OR "Cardiorespiratory fitness" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Cardiovascular fitness" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional Fitness" OR "Physical activity" OR "Physical conditioning" OR "Physical fitness" OR "Resistance training" OR "strength training" OR (Recess AND (Child OR Youth)) OR “Physical education” OR “Sedentary” OR "walking")
Limit: Publication Type Include (Systematic Review/Meta-Analysis)	AND (“systematic review” OR “systematic literature review” OR "metaanalysis" OR "meta analysis" OR metanalyses OR "meta analyses" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Limits	2000-present English language Peer reviewed Exclude Medline records Human

Search Strategy: Cochrane (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: Cochrane; Date of Search: 12/22/16; 35 results

Terms searched in title, abstract, or keywords

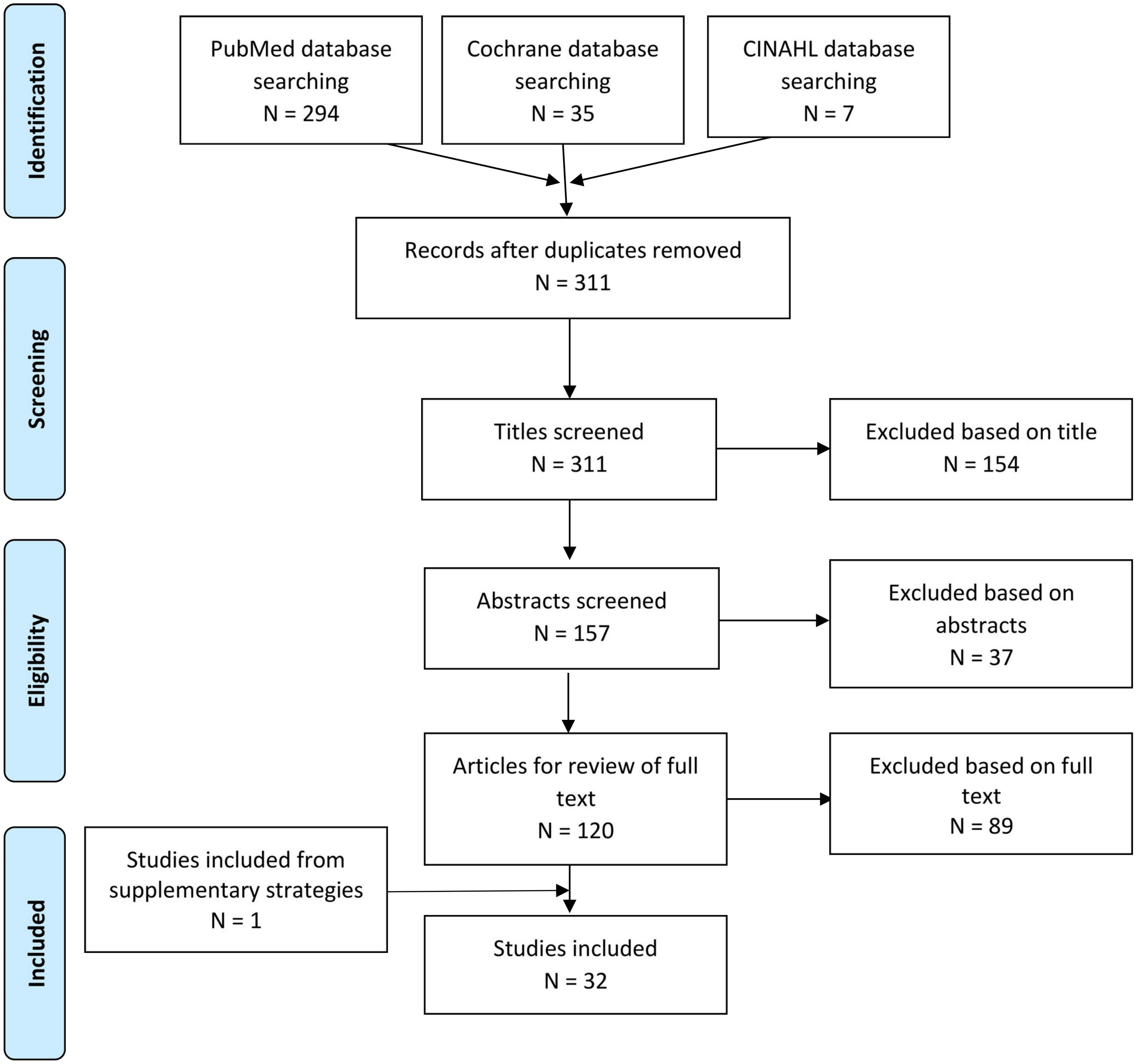
Set	Search Terms
Cognition	("Academic achievement" OR "Academic performance" OR "Attentional control" OR "Brain health" OR "Brain function" OR "Cognitive ability" OR "Cognitive control" OR "Cognitive function" OR "Cognitive functioning" OR "Cognitive health" OR "Cognitive performance" OR "Cognitive processing" OR "Executive control" OR "Executive function" OR "Executive functioning" OR "Executive functions" OR "Information processing" OR "Inhibitory control" OR "Memory" OR "Mental flexibility" OR "Mental recall" OR "Neuro cognitive" OR "Neurocognitive" OR "Perceptual processing" OR "Problem solving" OR "Scholastic achievement" OR "Scholastic performance")
Physical Activity	AND ("Aerobic activities" OR "Aerobic activity" OR "Cardiorespiratory fitness" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Cardiovascular fitness" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional Fitness" OR "Physical activity" OR "Physical conditioning" OR "Physical fitness" OR "Resistance training" OR "strength training" OR (Recess AND (Child OR Youth)) OR “Physical education” OR “Sedentary” OR "walking")
Limits	2000-present Word variations not searched Cochrane Reviews (Reviews) and Other Reviews

Supplementary Strategies

At full text review members of the Physical Activity Guidelines Brain Health Subcommittee identified one relevant article[23] that was not captured by the search strategies.

Appendix C: Literature Tree

Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports Literature Tree



Appendix D: Inclusion/Exclusion Criteria

Brain Health Subcommittee
Q1: What is the relationship between physical activity and cognition?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?

b. Does the relationship vary by age, sex, race/ethnicity, or socio-economic status?

c. Does the relationship exist across the lifespan?

d. Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)?

e. What is the relationship between physical activity and brain structure and function?

Category	Inclusion/Exclusion Criteria	Notes/Rationale
Publication Language	**Include:** • Studies published with full text in English	
Publication Status	**Include:** • Studies published in peer-reviewed journals • Reports determined to have appropriate suitability and quality by PAGAC **Exclude:** • Grey literature, including unpublished data, manuscripts, abstracts, conference proceedings	
Research Type	**Include:** • Original research • Meta-analyses • Systematic reviews • Pooled analysis • Reports determined to have appropriate suitability and quality by PAGAC	
Study Subjects	**Include:** • Human subjects	
Age of Study Subjects	**Include:** • People of all ages	
Health Status of Study Subjects	**Include:** • Healthy people • People with chronic conditions • People with cognitive impairment **Exclude:** • Hospitalized patients only • Athletes only	
Comparison	**Exclude:** • Studies comparing athlete types (e.g., comparing runners to soccer players)	

Date of Publication	**Include:** • Original research published since 2000 • Systematic reviews, meta-analyses, and reports published since 2000	
Study Design	**Include:** • Randomized controlled trials • Non-randomized controlled trials • Prospective cohort studies • Retrospective cohort studies • Case-control studies • Cross-sectional studies • Before-and-after studies • Time series studies • Systematic reviews • Meta-analyses • Pooled analysis • Report **Exclude:** • Narrative reviews • Commentaries • Editorials	
Intervention/ Exposure	**Include studies in which the exposure or intervention is:** All types and intensities of physical activity, including: • Free-living activities • Play • Single, acute bouts of exercise • Physical inactivity • Physical fitness • Sedentary behavior **Exclude:** • Studies that do not include physical activity • Studies of a specific therapeutic exercise delivered by a medical professional (e.g., physical therapist) • Studies of multimodal interventions that do not present data on physical activity alone • Studies where physical activity is only used as a confounding variable	
Outcome	**Include studies in which the outcome is:** • Attentional control • Brain health • Brain function • Cognitive ability	

	• Cognitive control • Cognitive function • Cognitive functioning • Cognitive health • Cognitive performance • Cognitive processing • Executive control • Executive function • Executive functioning • Executive functions • Information processing • Inhibitory control • Memory • Mental flexibility • Mental recall • Neuro cognitive • Neurocognitive • Perceptual processing • Problem solving • Scholastic achievement • Scholastic performance	

Appendix E: Rationale for Exclusion at Abstract or Full-Text Triage for Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Ahlskog JE, Geda YE, Graff-Radford NR, Petersen RC. Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. *Mayo Clin Proc.* 2011;86(9):876-884.					X	
Ahn S, Fedewa AL. A meta-analysis of the relationship between children's physical activity and mental health. *J Pediatr Psychol.* 2011;36(4):385-397. doi:10.1093/jpepsy/jsq107.	X					
Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database Syst Rev.* 2008;(3):Cd005381. doi:10.1002/14651858.CD005381.pub3.					X	
Beydoun MA, Beydoun HA, Gamaldo AA, Teel A, Zonderman AB, Wang Y. Epidemiologic studies of modifiable factors associated with cognition and dementia: Systematic review and meta-analysis. *BMC Public Health.* 2014;14:643. doi:10.1186/1471-2458-14-643.					X	
Bradley BJ, Greene AC. Do health and education agencies in the United States share responsibility for academic achievement and health? A review of 25 years of evidence about the relationship of adolescents' academic achievement and health behaviors. *J Adolesc Health.* 2013;52(5):523-532. doi:10.1016/j.jadohealth.2013.01.008.			X			
Cai Y, Abrahamson K. How exercise influences cognitive performance when mild cognitive impairment exists: a literature review. *J Psychosoc Nurs Ment Health Serv.* 2016;54(1):25-35. doi:10.3928/02793695-20151109-03.					X	
Cai Y, Abrahamson K. Does exercise impact cognitive performance in community-dwelling older adults with mild cognitive impairment? A systematic review. *Quality in Primary Care.* 2015;23(4):214-222.					X	
Carson V, Hunter S, Kuzik N, et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth: an update. *Appl Physiol Nutr Metab.*	X					

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
2016;41(6 Suppl 3):S240-S265. doi:10.1139/apnm-2015-0630.						
Carvalho A, Rea IM, Parimon T, Cusack BJ. Physical activity and cognitive function in individuals over 60 years of age: a systematic review. *Clin Interv Aging.* 2014;9:661-682. doi:10.2147/CIA.S55520.					X	
Castelli DM, Centeio EE, Hwang J, et al. VII. The history of physical activity and academic performance research: Informing the future. *Monogr Soc Res Child Dev.* 2014;79(4):119-148. doi:10.1111/mono.12133.					X	
Caviola L, Faber NS. Pills or push-ups? Effectiveness and public perception of pharmacological and non-pharmacological cognitive enhancement. *Front Psychol.* 2015;6:1852. doi:10.3389/fpsyg.2015.01852.			X			
Chan RJ, McCarthy AL, Devenish J, Sullivan KA, Chan A. Systematic review of pharmacologic and non-pharmacologic interventions to manage cognitive alterations after chemotherapy for breast cancer. *Eur J Cancer.* 2015;51(4):437-450. doi:10.1016/j.ejca.2014.12.017.						X
Chang YK, Pan CY, Chen FT, Tsai CL, Huang CC. Effect of resistance-exercise training on cognitive function in healthy older adults: a review. *J Aging Phys Act.* 2012;20(4):497-517.			X			
Cliff DP, Hesketh KD, Vella SA, et al. Objectively measured sedentary behaviour and health and development in children and adolescents: systematic review and meta-analysis. *Obes Rev.* 2016;17(4):330-344. doi:10.1111/obr.12371.	X					
Clouston SA, Brewster P, Kuh D, et al. The dynamic relationship between physical function and cognition in longitudinal aging cohorts. *Epidemiol Rev.* 2013;35:33-50. doi:10.1093/epirev/mxs004.				X		
Coelho FG, Santos-Galduroz RF, Gobbi S, Stella F. Systematized physical activity and cognitive performance in elderly with Alzheimer's dementia: a systematic review. *Rev Bras Psiquiatr.* 2009;31(2):163-170.						X
Conn VS, Minor MA, Burks KJ, Rantz MJ, Pomeroy SH. Integrative review of physical activity intervention research with aging adults. *J Am Geriatr Soc.* 2003;51(8):1159-1168.	X					
Cox EP, O'Dwyer N, Cook R, et al. Relationship between physical activity and cognitive function in apparently healthy young to middle-aged adults: a systematic					X	

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
review. *J Sci Med Sport.* 2016;19(8):616-628. doi:10.1016/j.jsams.2015.09.003.						
Cramer H, Lauche R, Azizi H, Dobos G, Langhorst J. Yoga for multiple sclerosis: a systematic review and meta-analysis. *PLoS One*. 2014;9(11):e112414. https://doi.org/10.1371/journal.pone.0112414.	X					
Cramer H, Lauche R, Klose P, Langhorst J, Dobos G. Yoga for schizophrenia: a systematic review and meta-analysis. *BMC Psychiatry.* 2013;13:32. doi:10.1186/1471-244X-13-32.					X	
Cumming TB, Tyedin K, Churilov L, Morris ME, Bernhardt J. The effect of physical activity on cognitive function after stroke: a systematic review. *Int Psychogeriatr.* 2012;24(4):557-567.					X	
Cvejic E, Lloyd AR, Vollmer-Conna U. Neurocognitive improvements after best-practice intervention for chronic fatigue syndrome: preliminary evidence of divergence between objective indices and subjective perceptions. *Compr Psychiatry.* 2016;66:166-175. doi: 10.1016/j.comppsych.2016.02.002.						X
Dale H, Brassington L, King K. The impact of healthy lifestyle interventions on mental health and wellbeing: a systematic review. *Mental Health Review Journal.* 2014;19(1):1-26. https://doi.org/10.1108/MHRJ-05-2013-0016.	X					
Dauwan M, Begemann MJ, Heringa SM, Sommer IE. Exercise improves clinical symptoms, quality of life, global functioning, and depression in schizophrenia: a systematic review and meta-analysis. *Schizophr Bull.* 2016;42(3):588-599. doi:10.1093/schbul/sbv164.					X	
Daviglus ML, Bell CC, Berrettini W, et al. NIH state-of-the-science conference statement: Preventing Alzheimer's disease and cognitive decline. *NIH Consens State Sci Statements.* 2010;27(4):1-30.			X			
Denkinger MD, Nikolaus T, Denkinger C, Lukas A. Physical activity for the prevention of cognitive decline: current evidence from observational and controlled studies. *Z Gerontol Geriatr.* 2012;45(1):11-16. doi:10.1007/s00391-011-0262-6.			X			
de Rezende LFMd, Rodrigues Lopes M, Rey-López JP, Matsudo VKR, Luiz Odc. Sedentary behavior and health outcomes: An overview of systematic reviews. *PLoS One.* 2014;9(8):e105620.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Desai R, Tailor A, Bhatt T. Effects of yoga on brain waves and structural activation: A review. *Complement Ther Clin Pract.* 2015;21(2):112-118. doi:10.1016/j.ctcp.2015.02.002.			X			
Devine JM, Zafonte RD. Physical exercise and cognitive recovery in acquired brain injury: a review of the literature. *PM R.* 2009;1(6):560-575. doi:10.1016/j.pmrj.2009.03.015.			X			
Etgen T, Sander D, Bickel H, Förstl H. Mild cognitive impairment and dementia: the importance of modifiable risk factors. *Dtsch Arztebl Int.* 2011;108(44):743-750. doi:10.3238/arztebl.2011.0743.			X			
Farina N, Rusted J, Tabet N. The effect of exercise interventions on cognitive outcome in Alzheimer's disease: a systematic review. *Int Psychogeriatr.* 2014;26(1):9-18. doi:10.1017/S1041610213001385.					X	
Fedewa AL, Ahn S. The effects of physical activity and physical fitness on children's achievement and cognitive outcomes: a meta-analysis. *Res Q Exerc Sport.* 2011;82(3):521-535.	X					
Forbes D, Forbes SC, Blake CM, Thiessen EJ, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev.* 2015;(4):Cd006489. doi:10.1002/14651858.CD006489.pub4.					X	
Forbes D, Thiessen EJ, Blake CM, Forbes SC, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev.* 2013;(12):Cd006489. doi:10.1002/14651858.CD006489.pub3.						X
Garcia JA, Schoene D, Lord SR, Delbaere K, Valenzuela T, Navarro KF. A bespoke kinect stepping exergame for improving physical and cognitive function in older people: A pilot study. *Games Health J.* 2016;5(6):382-388.	X					
Garcia-Soto E, Lopez de Munain Ml, Santibanez M. Effects of combined aerobic and resistance training on cognition following stroke: a systematic review . *Database of Abstracts of Reviews of Effects.* 2013;(2):535-541.					X	
Gates N, Fiatarone Singh MA, Sachdev PS, Valenzuela M. The effect of exercise training on cognitive function in older adults with mild cognitive impairment: a meta-analysis of randomized controlled trials. *Am J Geriatr Psychiatry.* 2013;21(11):1086-1097. doi:10.1016/j.jagp.2013.02.018.					X	

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Grassmann V, Alves MV, Santos-Galduróz RF, Galduróz JC. Possible cognitive benefits of acute physical exercise in children with ADHD: a systematic review. *J Atten Disord.* 2014;21(5):367-371. doi:10.1177/1087054714526041.					X	
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Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
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Tseng CN, Gau BS, Lou MF. The effectiveness of exercise on improving cognitive function in older people: a systematic review. *J Nurs*						X

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