

Physical Activity Throughout the Adult Life Span and Domain-Specific Cognitive Function in Old Age: A Systematic Review of Cross-Sectional and Longitudinal Data

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Abstract

Background A growing body of literature suggests that physical activity might alleviate the age-related neurodegeneration and decline of cognitive function. However, most of this evidence is based on data investigating the association of exercise interventions or current physical activity behavior with cognitive function in elderly subjects.

Objective We performed a systematic review and hypothesize that physical activity during the adult life span is connected with maintained domain-specific cognitive functions during late adulthood defined as age 60+ years. **Methods** We performed a systematic literature search up to November 2017 in PubMed, Web of Science, and Google Scholar without language limitations for studies analyzing the association of leisure physical activity during the adult life span (age 18+ years) and domain-specific cognitive functions in older adults (age 60+ years).

Results The literature review yielded 14,294 articles and after applying inclusion and exclusion criteria, nine cross-sectional and 14 longitudinal studies were included. Moderate- and vigorous-intensity leisure physical activity was associated with global cognitive function and specific cognitive domains including executive functions and memory but not attention or working memory. Most studies assessed mid- to late-adulthood physical activity, thus information concerning the influence of young adult life-span physical activity is currently lacking.

Conclusions Observational evidence that moderate- and vigorous-intensity leisure physical activity is beneficially associated with maintained cognitive functions during old age is accumulating. Further studies are necessary to confirm a causal link by assessing objective physical activity data and the decline of cognitive functions at multiple time points during old age.

Key Points

Leisure physical activity during early, mid, and late adulthood seems to be favorably associated with performance and alleviated the decline of global cognitive function, executive functions, and memory during old age.

Evidence on the impact of light-intensity activities and the influence of physical activity during early adulthood on cognitive function in old age is limited.

Higher intensity leisure physical activities seem to be of particular relevance for maintaining cognitive function in old age.

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1 Introduction

A growing body of literature suggests that physical activity (PA) might alleviate the age-related neurodegeneration and decline of cognitive function [1, 2]. Most of this evidence is based on data investigating the association of current PA behavior with cognitive function in elderly subjects. Based

on these findings, it might be hypothesized that PA during an earlier adult life span could be a relevant factor for maintained cognitive functions and therefore attenuates the decline of cognitive performance during late adulthood.

Whereas the body of evidence for a connection between PA during the adult life course and mental illnesses closely related to cognitive decline is increasing [3, 4], less evidence seems to be available concerning the association between life-course PA and specific cognitive functions or performance. Focusing on such long-term PA effects, some authors have previously analyzed the influence of frequency [5, 6], duration [7, 8], intensity [5, 9, 10], or energy expenditure [11] of PA during the adult life span. Leaving aside notable differences in these PA modalities and their assessment, the underlying datasets vary in the age periods during which leisure PA was assessed as well as the follow-up periods. A systematic overview of available data is currently lacking. Within such an approach, the influence and interrelationships of PA modalities (such as duration and intensity) need to be differentiated.

Evidence concerning the effects of current PA behavior concludes that the beneficial influence on cognitive function might be domain specific [2]. However, a large number of recent studies on adult life-course PA assessed cognitive function primarily via indices for global cognitive function based on *z*-scores of multiple outcomes [5, 6, 10, 11]. Based on current reviews, attention, processing speed and executive function [12], memory, and working memory [2] can be identified as areas of interest. A differentiated view on domain-specific neurocognitive measures [2, 13] is thus crucial for a thorough understanding of specific long-term PA effects.

Taken together the available data are heterogeneous concerning study types, cognitive and PA assessment methods, as well as timeframes during which dependent and independent variables were assessed. Consequently, gathering information through a systematic analysis of the currently available evidence is of great relevance. Within such an approach, particular attention should be paid to both study quality, including design, applied statistics, and assessments, as well as to the systematic analysis and differentiation of PA modalities and relevant domains of cognitive function.

We performed a systematic review of the associations between adherence to leisure PA during adulthood and domain-specific cognitive function in old age. We hypothesized that PA over the adult life span (age 18+ years) is connected with maintained domain-specific cognitive functions during late adulthood (age 60+ years).

2 Methods

2.1 Search Strategy

The present systematic review was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [14]. Two independent researchers (T.I. and T.E.) performed the literature search between June and November 2017 (final search date 8 November, 2017). We performed a systematic literature search in PubMed, Web of Science, and Google Scholar without publication language limitations. We used a search strategy including the terms for PA, life span, cognitive function, and older participants. Search terms and algorithms for the respective databases are listed in Table 1. We also performed hand searching in the reference citations of identified articles.

2.2 Study Selection

The identified studies were initially screened by the two independent reviewers (T.I. and T.E.) to determine whether they met the selection criteria. To be included in our analysis, studies had to assess (1) leisure PA during a time point or time span of adulthood (age 18+ years), and (2) cognitive function during a time point or time span of old age, defined as a sample mean age of 60+ years (either in the overall sample or a subsample analysis). Leisure PA included all activities that people participated in during their free time and that were not work related and did not involve life maintenance tasks such as housecleaning [15]. Physical activity could be assessed via objective (e.g., accelerometry) or subjective methods (e.g., questionnaires). To define long-term effects, ≥ 10 years should separate at least one time point of leisure PA behavior and cognitive function assessment. Participants (either the overall sample or a subsample that was analyzed separately) should have no cognitive impairments or mental illnesses. Cognitive function was defined as an assessment/outcome that indicates the performance or decline in (1) a definable cognitive domain, or (2) multiple cognitive domains, or (3) overall/global cognitive function.

Studies were excluded if cognitive assessments were solely used to define a mental illness (such as mild cognitive impairment or dementia) using cut-off values or scoring systems. Furthermore, studies assessing larger samples including participants across a wide age span (including participants aged 60+ years) without assessing PA effects for a subsample fitting our inclusion criteria (mean age ≥ 60 life-years) were excluded. Study selection was performed independently and in duplicate by two researchers (T.I. and T.E.). Differences in opinion relating

Table 1 Literature search terms and algorithms for the respective databases

Physical activity	Life span	Cognitive function	Older participants
“Physical activity”	Lifelong	Psych*	Old*
Exercis*	Lifetime	Cognit*	Elderly
Sport	Lifespan	Mental	Age*
	Lifecourse	Neuropsych*	Geriat*
	“Life long”	Academic	Aging
	“Life time”	Intellect*	Elder*
	“Life span”	Attention	Senior*
	“Life course”	Executive	
	Earl*	Memory	
Search terms for MEDLINE and Web of Science	(Lifelong OR lifetime OR lifespan OR lifecourse OR “life long” OR “life time” OR “life span” OR “life course” OR “earl*”) AND (“physical activity” OR exercise OR exercis* OR sport) AND (psych* OR cognit* OR mental OR neuropsych* OR academic OR intellect* OR attention OR executive OR memory) AND (old* OR elderly OR age* OR geriat* OR aging OR elder* OR senior*)		
Search terms for Google Scholar	(Psychological OR neuropsychological OR cognitive OR mental OR academic OR intellectual OR attention OR executive OR memory) AND (“physical activity” OR exercise OR sport) AND (old OR elderly OR age OR geriatric OR aging OR elder OR senior) AND (life)		

to inclusion and exclusion were discussed until a consensus was reached. Persisting disagreements were discussed in a consensus meeting of all coauthors to make the final decision.

2.3 Data Extraction

Data extraction from the selected studies was performed by two independent reviewers (T.I. and T.E.) using a preformatted spreadsheet. We extracted the following descriptive information from the studies included: authors and year of publication, study quality rating, PA measurement (primary independent variable), other independent (e.g., leisure time cognitive activity) or dependent outcomes/variables (e.g., electroencephalography data), sample size and characteristics of study participants, domain-specific cognitive outcomes (dependent variables), statistical methods, covariates included in statistical models, and major findings (concerning associations between leisure PA and cognitive outcomes). For PA, the specification and type of the applied measurement, the timeframe during which PA was assessed, PA normatives (frequency, intensity, type, timing), and information about the test quality were gathered. Information on participant characteristics included age, sex, and other characteristics such as ethnic group (if applicable). Inclusion criteria for subgroup analyses were reported. Cognitive outcomes and domains were listed as reported in the original data. Further information included assessment type and information on test quality (if reported in the reference). Major findings were

defined as results of statistical analyses assessing associations between adult life-span leisure PA and cognitive outcomes. We did not include data on findings related to secondary independent or dependent variables.

2.4 Assessment of Study Quality

We applied a method for developing a suitable quality assessment tool used in an earlier systematic review by our workgroup [16]. Using this approach, we analyzed the currently available literature on reporting and quality assessment tools for comparable observational studies [16–20].

Because items on PA assessment and other specific quality characteristics were missing, we adapted the 12-item list of Füzeki et al. [16]. Consequently, study quality was determined by answers to the questions listed in Table 2. Domains were identified based on a systematic review of assessment tools [18], and specific items were formulated based on Ariëns et al. [21] and Cliff et al. [22].

Information on study quality for each study was extracted by two reviewers (T.I. and T.E.) and differences were discussed until a consensus was attained. Persisting disagreements were discussed in a consensus meeting of all coauthors to make the final decision. Items were coded as “present” (1) or “absent/unclear” (0). A cut-off value of 50% of the total possible points has previously been used to distinguish high- or moderate-quality studies from low-quality studies [21]. Because we applied a 14-item check list for cross-sectional studies and a 16-item checklist for

Table 2 Assessment of study quality**Study purpose**

1. Was the study purpose clearly stated?

Study design and methods

2. Were eligibility criteria and the sources and methods of selection of participants clearly defined?

3. Were all outcomes, exposures, predictors, potential confounders, and effect modifiers clearly defined using standardized methods of acceptable quality?

4. Was exposure measurement (physical activity) carried out using standardized methods and measures and with acceptable quality (FITT scheme)?

5. Was physical activity with low-to-moderate and moderate-to-vigorous intensity analyzed separately?

6. Differentiation of physical activities (household, commuting, workplace, leisure) and/or sport?

7. Were the effects controlled for current (from physical activity assessment to cognitive function assessment) physical activity behavior?

8. Were results adjusted for sedentary behavior?

Statistical methods

9. Was choice of confounders adjusted for, and in the case of subgroup analysis, definition of subgroups appropriate (sex, age, education or IQ, social surroundings, chronic diseases, alcohol, and smoking)?

10. Were all statistical methods, including those used to control for confounding and to examine subgroups and interactions, appropriate (i.e., sample size, statistical power)?

11. Were methods dealing with missing data appropriate?

Results

12. Were descriptive data and results of inductive analysis clearly stated?

13. Were unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval) given?

Discussion

14. Were study limitations clearly stated?

Longitudinal studies

15. Were estimates of relative risk given and ideally translated into absolute risk for a meaningful time period; precision of estimates reported (e.g., 95% confidence interval)?

16. Were outcomes for cognitive function tested at multiple time points and change of cognitive function analyzed?

Items were coded as “present” (1) or “absent/unclear” (0)

FITT frequency, intensity, type, time

longitudinal studies, we further subdivided the upper 50% range into two categories. Accordingly, cross-sectional studies scoring 12 points and above were classified as high, those scoring 8–11 points as moderate, and those below 8 points as low quality. Longitudinal studies scoring 13 points and above were classified as high, those scoring 9–12 points, as moderate and those below 9 points as low quality.

2.5 Assessment of Domain-Specific Cognitive Functions

To differentiate the domain-specific influence of PA on cognitive performance, we separated four cognitive domains based on Smith et al. [2]. The domains were attention, executive function, working memory, and memory. Because some studies applied global scores for multiple cognitive domains or applied the Mini-Mental State Examination (MMSE) [23], we added the domain global cognitive function. Cognitive tests not listed by

Smith et al. [2] or not clearly defined as assessing one of the five cognitive domains (based on the original article or references) were summarized as ‘various’. Table 3 provides an overview of all cognitive tests applied to assess domain-specific cognitive functions.

3 Results

3.1 Characteristics of the Included Studies

The literature review yielded 14,294 articles. After applying inclusion and exclusion criteria, 23 studies were included in the analysis (Fig. 1). Of the included studies, nine were cross-sectional and 14 were longitudinal. The characteristics of the included cross-sectional and longitudinal studies are summarized in Tables 4 and 5, respectively. The sample sizes varied widely across cross-sectional ($n = 32$ –9344) and longitudinal ($n = 196$ –16,466) studies depending on inclusion and exclusion criteria and

Table 3 Overview of domain-specific cognitive tests included in this review

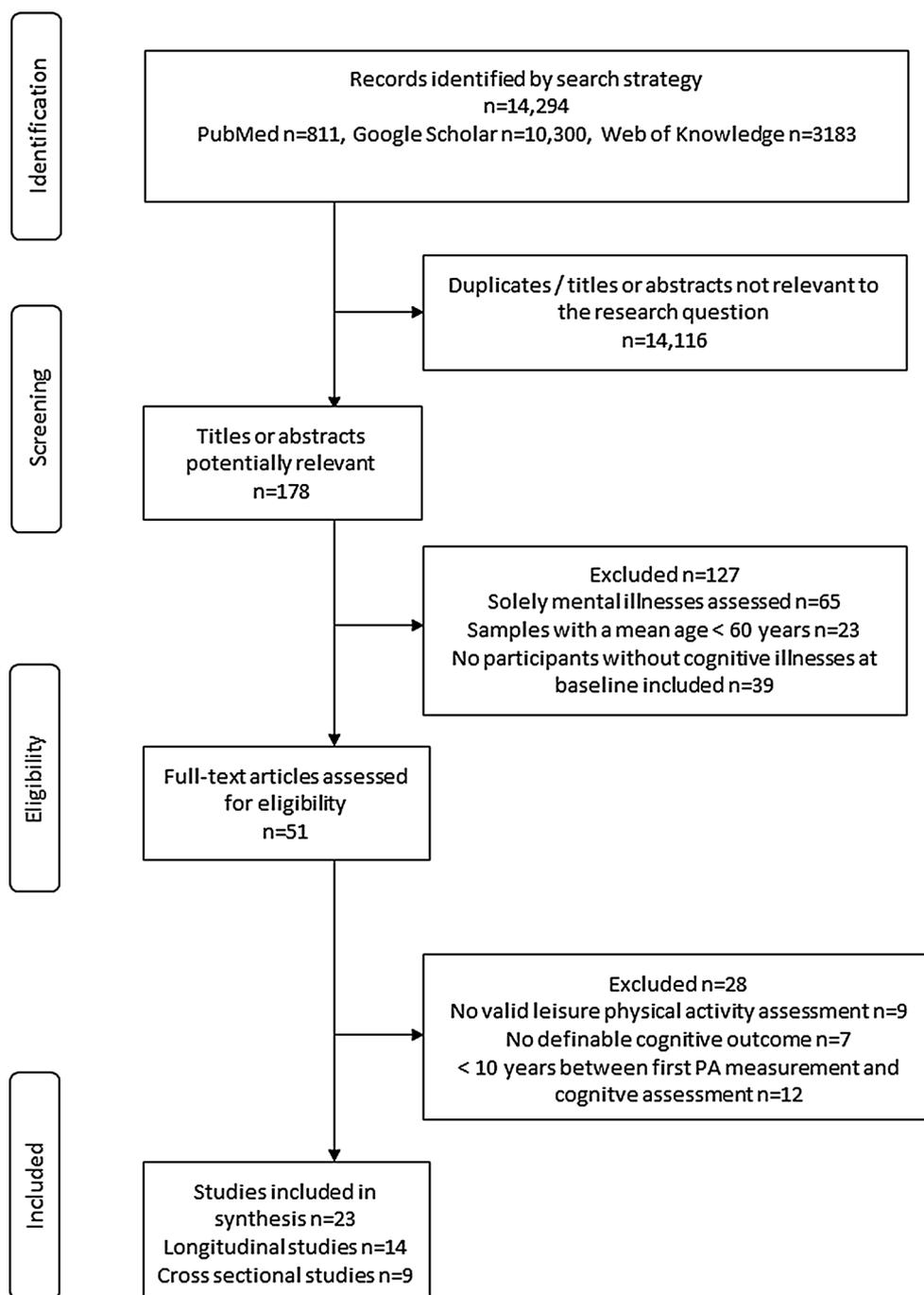
Attention	Executive function	Working memory	Memory	Global cognitive function	Various
Trail Making Test A [25, 26, 29, 31]	Trail Making Test B [25, 26, 31]	Wechsler Adult Intelligence Scale Digit-Span Test [25, 26]	Verbal Learning and Memory Test [25, 26]	MMSE [24–26, 31, 41]	Multiple Choice Word Test [25, 26]
Stroop Color and Word Test (word reading and color naming condition) [25, 26]	Stroop Color and Word Test (interference condition) [8, 25, 26, 29]	Digit-Span Backward Test [9, 34]	Wechsler Memory Scale Logical Memory [6, 31]	Modified MMSE [28]	Raven's Standard Progressive Matrices [6]
Symbol Digit Modalities Test [8, 11]	Phonemic Fluency Test [6, 8, 9]	Visual-Span Backward Test [9]	California Verbal Learning Test II Immediate Recall and Delayed Recall [29, 36]	Telephone Interview for Cognitive Status [34]	Primary Mental Abilities—Reasoning Measure [38]
Choice reaction time task [8, 33]	Word Fluency Test [25, 26]	Running Span Memory Task [8]	Rey Auditory Verbal Learning Test [8]	Cognitive Performance Scale [10]	Adult Development and Enrichment Project Letter Series [38]
Wechsler Adult Intelligence Scale Digit-Symbol Test [25, 26]	Category Fluency Test [8, 34]	Automated Neuropsychological Assessment Metrics Battery [29]	Spatial Span Test [33]	Wechsler Test of Adult Reading [29]	Word series [38]
D2 Test [25, 26]	Alphabet Coding Task-15 [24]	Spatial Working Memory Test [33]	Paired Associates Learning Test [33]	10-Item Short Portable Mental Status Questionnaire [40]	Educational Testing Service Number Series [38]
Attention Network Test [11]	Wilde Test of Intelligence—Mirrored Figures [11]		Delayed Matching to Sample Test [33]	Mattis Dementia Rating Scale [8]	Nürnberger Altersinventar [31]
Auditory Consonant Trigram Test [11]	D-KEFS Card-Sorting Test [11]		Pattern Recognition Memory Test [33]		Leistungsprüfsystem [31]
Judgment of Line Orientation Test [8]	D-KEFS Color-Word Interference Test [11]		Delayed Word List Recognition Task [31]		MMSE subtest—registration, repeating and orientation [32]
Letter Search Test [35]	D-KEFS Verbal Fluency Test [11]		Immediate Word List-Recall [31]		Pattern recognition memory [33]
Automated Neuropsychological Assessment Metrics Battery [29]	Modified Wisconsin Card Sorting Task [8]		Immediate Recall [38]		Delayed Matching to Sample Task [33]
MMSE subtest for attention/concentration [32]			Word fluency [38]		
Simple reaction time task [33]			20-Word Short-Term Verbal Free Recall [36]		
			Word Learning Task [35]		
			East Boston Memory Test Immediate Recall, Delayed Recall [34]		
			Medical College of Georgia Complex Figures Test [11]		
			Selective Reminding Test Memory, Cued Recall, Multiple Choice Recognition, Oral Delayed Recall [11]		
			Picture association [9]		
			Object naming [9]		
			Multitrial Word-List-Learning Task [9]		

Domains include attention, executive functions, memory, working memory, and global cognitive function. A 'various' category, which includes tests lacking description of the assessed cognitive domain, was also included. References indicate studies that applied the assessment *D-KEFS* Delis–Kaplan Executive Function System, *MMSE* Mini-Mental State Examination

research questions. The earliest cross-sectional study was published in 2007 [10] and the earliest longitudinal study was published in 2003 [24].

3.2 Main Findings of the Quality Assessment

Of the nine cross-sectional studies included, three [25–27] were of low quality, five [8, 10, 28–30] were of moderate quality, and one [11] was of high quality. Of the 14

Fig. 1 Flow chart for selection of studies. *PA* physical activity

longitudinal studies included, four [24, 31–33] were of low quality, eight [6, 9, 34–39] were of moderate quality, and two [40, 41] were of high quality.

3.3 Physical Activity Assessments

One cross-sectional study assessed the history of endurance training by national or regional sport rankings (runners) [29]. Three cross-sectional studies applied PA questionnaires or interviews that had not been previously used or

validated [25–27]. Two cross-sectional studies used questionnaires that had been used before but had not been validated or tested for reliability [10, 30] and one [28] applied a modified (and therefore not validated) version of the Paffenbarger questionnaire [42]. Gill et al. [11] used the Lifetime Total Physical Activity Questionnaire developed and tested for reliability by Friedenreich et al. [43]. Rouillard et al. [8] used the French version of the Historical Leisure Activity Questionnaire, which was developed and tested for reliability in English by Kriska et al. [44].

Table 4 Characteristics of the included cross-sectional studies

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Gajewski et al. 2015 [25] 6/14	<p>1. Two unspecified questionnaires for lifetime (1) and current PA (2)</p> <p>2. Time span not specified</p> <p>3. Duration, intensity, type, and age participants started activity</p> <p>4. Two groups (low active vs. active; cut-off: 290 min/4.4 sessions/week)</p> <p>5. No</p>	<p>Dependent variable: electroencephalography (event-related potentials)</p>	<p>40 (male)</p> <p>Education: (rating scale ranging from 1 = primary school to 5 = high school diploma)</p> <p>low active 3.6 ± 1.2</p> <p>vs. active 4.0 ± 0.6 (SD)</p> <p>73.2 ± 4.5 (SD)</p>	<p>Memory-based task switching paradigm</p> <p>General cognitive status: MMSE [23]</p> <p>'Big Five' personality traits [61]</p> <p>Attentional endurance: D2 Test [62]</p> <p>Speed of processing and vigilance: Digit Symbol Test [63]</p> <p>Short-term and working memory: Digit Span Test [63]</p> <p>Interference control: Stroop Color and Word Test [64]</p> <p>Verbal Memory: Verbal Learning and Memory Test [65]</p> <p>Divergent thinking: Word Fluency Test [66]</p> <p>Crystallized intelligence: Multiple Choice Word Test [67]</p> <p>Mental rotation: mirrored figures from the Wilde Test of Intelligence [68]</p> <p>Psychomotor speed of task switching: Trail Making Test [69]</p>	<p>T-test, analysis of variance</p> <p>No covariates but groups were matched regarding sex, age, education, and no-smoking status</p>	<p>No relationship between PA and performance in almost all cognitive tests</p> <p>Interference index of the Stroop Test was significantly higher for non-active than active participants (t value 2.24, p value 0.031)</p> <p>'Big Five' personality traits agreeableness was higher in the active than in the non-active seniors (t value 3.11, p value 0.005)</p> <p>Memory-based task switching paradigm mixing costs of accuracy as well as speed variability were larger and response times were slower in the low-activity group compared with the active group</p>

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Gajewski et al. (2015) [26] 7/14	1. Two unspecified questionnaires for lifetime (1) and current PA (2) 2. Time span not specified (whole lifespan) 3. Age participants started activity, duration, intensity, and type 4. Divided cohort into 2 groups (low active vs. active 290 min/4.4 sessions/week) 5. No	Dependent variable: electroencephalography (event-related potentials)	40 (male) Education: (rating scale ranging from 1 = primary school to 5 = high school diploma) low active 3.6 ± 1.2 vs. active 4.0 ± 0.6 (SD) 73.2 ± 4.5 (SD)	General cognitive status: MMSE [23] 'Big Five' personality traits [61] Attentional endurance: D2 Test [62] Speed of processing and vigilance: Digit Symbol Test [63] Short-term and working memory: Digit Span Test [63] Interference control: Stroop Color and Word Test [64] Verbal memory: Verbal Learning and Memory Test [65] Divergent thinking: Word Fluency Test [66] Crystallized intelligence: Multiple Choice Word Test [67] Mental rotation: mirrored figures from the Wilde Test of Intelligence [68] Psychomotor speed of task switching: Trail Making Test [69]	T test No covariates but groups were matched regarding sex, age, education, and no-smoking status	Almost all cognitive tests showed no effects of PA Interference index of the Stroop Test was significantly higher for non-active than active participants (<i>t</i> value 2.24, <i>p</i> value 0.031) 'Big Five' personality traits: agreeableness was higher in the active than in the non-active seniors (<i>t</i> value 3.11, <i>p</i> value 0.005)

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Gill et al. (2015) [11] 12/14	<p>1. Interviewer-administered Lifetime Total Physical Activity Questionnaire</p> <p>2. Four time spans (age < 20, 21–35, 36–50, 51–65 years)</p> <p>3. Type, duration; and intensity (0–3 MET: low, 3–6 MET: moderate, and > 6 MET: vigorous [70])</p> <p>4. MET hours per week per year, additional analyses for type, intensity, and age period</p> <p>5. Reliability approved but not tested for validity [43]</p>	<p>Dependent variable: cerebrovascular blood flow</p>	<p>226 (118 female)</p> <p>Education in years: male 16.3 ± 2.8, female 15.7 ± 2.2 (SD)</p> <p>English speaking, healthy, community-dwelling, currently inactive, BMI < 35</p> <p>66.5 ± 6.4 (SD)</p>	<p>Global cognition score as sum of equally weighted domain z-scores</p> <p>Complex attention: Attention Network Test [71], Auditory Consonant Trigram Test [72]</p> <p>Processing speed: Symbol Digit Modalities Test oral and written [13]</p> <p>Verbal knowledge: D-KEFS Verbal Fluency Test (category fluency score) [73]</p> <p>Verbal memory: Buschke Selective Reminding Test for Memory (cued recall, multiple choice recognition, and oral delayed recall) [74]</p> <p>Visual memory: Medical College of Georgia Complex Figures Test [75]</p> <p>Executive function: D-KEFS Card Sorting Test; Color Word Interference Test; Verbal Fluency Test [73]</p> <p>Spatial reasoning: Medical College of Georgia Complex Figures Test [75]</p>	<p>Multiple (stepwise) linear regression</p> <p>North American Adult Reading Test [76] as a measure of premorbid verbal intellectual ability, age, sex, VO_{2max}, BMI, interaction terms (age-sex, age-predictor, sex-predictor, age-sex predictor)</p>	<p>With every unit increase in yearly MET hours/week of lifetime total PA, there was a 0.40 increase in global cognition z-scores</p> <p>Male individuals have an increasing cognition score as levels of lifetime PA increase, female individuals do not</p> <p>For every unit increase in MET hours/week/year of lifetime recreational PA, there was a 1.18 increase in global cognition z-scores</p> <p>For vigorous-intensity PA over a lifetime, there was a 9.85 increase in global cognition s-scores for every hour/week of PA</p> <p>For every unit increase in yearly MET hours/week of PA from early childhood to age 20 years, there was a 0.47 increase, and for activity between the ages of 21 and 35 years, there was a 0.36 increase in global cognition z-scores</p>

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Landi et al. (2007) [10] 10/14	<ol style="list-style-type: none"> 1. Questionnaire 2. Three time spans: age 20–40 years; 41–60 years, and last year before assessment 3. Combination of frequency and intensity (1 = light-intensity PA such as walking three or fewer times a week to 4 = participation in high PA or sports more than twice a week) 4. Four-point ordinal scale classified into two groups: group one included light- or moderate-intensity activity (scores 1 and 2), group two included regular to moderate- to high-intensity activity (scores 3 and 4) 5. Applied before; not validated or tested for reliability [77, 78] 	<p>Dependent variable: cognitive impairment</p>	<p>364 (244 female) Education in years 5.1 ± 1.5 (SD) 85.9 \pm 4.9 (SD)</p>	<p>Cognitive Performance Scale (6-item, 7-category scale) [79] Higher score = worse cognitive performance, cognitive impairment > 1 point</p>	<p>Analysis of covariance Age, sex, education, depression, ADL Scale score, number of diseases, alcohol abuse, and smoking habits</p>	<p>Participants with a history of high-intensity PA had lower Cognitive Performance Scale scores compared with participants with a history of light-intensity PA Subjects reporting light-intensity PA during young and adult life had a higher Cognitive Performance Scale score (1.24 \pm 0.09, indicating worse performance) compared with those reporting high-intensity PA for at least one age period (0.81 \pm 0.21) and those reporting high-intensity PA throughout their lives (0.75 \pm 0.12)</p>
Middleton et al. (2010) [28] 11/14	<ol style="list-style-type: none"> 1. Modified Paffenbarger Questionnaire 2. Four time points: teenage, age 30, 50 years, and current life year 3. Frequency and type (low intensity = walking, gardening, moderate intensity = jogging or skiing) 4. Dichotomized at each age: active or inactive (no regular participation in any PA or sport at the relevant age) 5. Modified version; therefore not validated or tested for reliability [42] 	<p>Dependent variable: significant cognitive impairment was defined as a modified MMSE score of 22 or less</p>	<p>9344 (female) Education in years 12.6 ± 2.8 (SD) Primarily white, US metropolitan areas: included, when able to walk, excluded, when bilateral hip replacement 71.6 \pm 5.2 (SD)</p>	<p>26-point modified MMSE [80]</p>	<p>Multiple linear regression Age, years of education, smoking history, marital status, medical history (diabetes mellitus, hypertension), BMI, depressive symptoms (15-Point Geriatric Depression Scale [81])</p>	<p>For all time points (except for age 30 years): women who were physically active had a higher average modified MMSE score than those who were physically inactive When PA measures for all four ages were entered into a single model, adjusted for variables associated with PA status at any age, only teenage PA status remained significantly associated with cognitive performance in old age</p>

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Rouillard et al. (2016) [8] 9/14	<p>1. Historical Leisure Activity Questionnaire (French version)</p> <p>2. Four time spans: age 6–18, 19–34, 35–54, > 55 years</p> <p>3. Type, duration, intensity (based on a list of activities > 6 MET)</p> <p>4. Mean hours per week over four time spans</p> <p>5. Tested for reliability but not validated [44]</p>	<p>Independent variables: level of education, decisional latitude, psychological job demands, leisure activities (non-physical)</p>	<p>Healthy: 47 (24 female)</p> <p>Education in years 13.32 ± 3.33</p> <p>Total Mattis Dementia Rating Scale score [82] lower than 130 or lower than 27 in the MMSE</p> <p>Sub-analysis for Parkinson vs. healthy (Parkinson's disease <i>n</i> = 49, 22 female) 63.9 ± 8.2 (SD)</p>	<p>Global cognitive efficiency: Mattis Dementia Rating Scale [82]</p> <p>Visuospatial perception: Judgment of Line Orientation [83]</p> <p>Episodic memory: Auditory Verbal Learning Test [84]</p> <p>Processing speed: Choice Reaction Time Task [85]</p> <p>Attention/perceptual speed: Symbol Digit Modality Test [86]</p> <p>Executive Functions: Updating of working memory: computerized version of the Running Span Memory Task [87]</p> <p>Interference resolution: Golden's version of the Stroop Test [88]</p> <p>Strategic search in memory: Phonemic and Category Fluency Tasks [89]</p> <p>Cognitive flexibility: modified version of the Wisconsin Card Sorting Test [90]</p>	<p>Hierarchical linear regression Age, sex, Hospital Anxiety and Depression Scale (for both groups), duration of disease, levodopa equivalent daily dose (for the Parkinson's disease group)</p>	<p>The number of hours of PA per week practiced over a lifetime was not associated with better cognitive functions</p>

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Tseng et al. (2013) [29] 8/14	<p>1. History of endurance training (nationally or regionally ranked runners)</p> <p>2. > 15 years (and still engaged in endurance exercise at time of study)</p> <p>3. Master athletes = nationally or regionally ranked runners; sedentary = moderate/high-intensity aerobic exercise < 30 min 3 times per week</p> <p>4. Grouped in master athletes and sedentary</p> <p>5. No</p>	<p>Dependent variable: magnetic resonance imaging-based brain volume measurements</p>	<p>Master athletes: 12 (3 female); sedentary: 12 (4 female); youth control: 9 (4 female)</p> <p>Education in years: master athletes: 16.2 ± 2.2; sedentary: 15.8 ± 2.3; youth control: 14.7 ± 1.6 (SD)</p> <p>Master athletes: 72.4 ± 5.6; sedentary: 74.6 ± 4.3; youth control: 27.2 ± 3.6 (SD)</p>	<p>Exclusion of dementia: Montreal Cognitive Assessment</p> <p>Global intelligence: Wechsler Test of Adult Reading</p> <p>Executive function: Subtests from D-KEFS; Trail Making Test (A and B); Stroop Color and Word Test</p> <p>Declarative memory: California Verbal Learning Test-II</p> <p>Working memory, processing speed, reaction time: Automated Neuropsychological Assessment Metrics Battery</p>	<p>1. <i>T</i> test</p> <p>2. Analysis of covariance</p> <p>Global intelligence</p>	<p>No differences in performance on Montreal Cognitive Assessment between master athletes and sedentary</p> <p>1. Master athletes outperformed sedentary on Wechsler Test of Adult Reading</p> <p>2. After controlling for global intelligence level, master athletes performed better than sedentary in Category Fluency Test (<i>F</i> value 3.45, <i>p</i> < 0.005) and both (sedentary and youth control) in Letter Fluency Test (<i>F</i> value 5.72, <i>p</i> < 0.01) [both D-KEFS subtests]</p>
Pesce et al. (2011) [27] 6/14	<p>1. History of aerobic training (cyclist, long-distance runners, rowers mountaineers vs. non-trained controls/sedentary)</p> <p>2. ≥ 10 years (and still engaged in endurance exercise at time of study)</p> <p>3. Frequency, type (aerobically trained non-cyclists = training ≥ 3 times per week; cyclist = cycling ≥ 3 times per week; sedentary = none of the sports ≥ 3 times per week)</p> <p>4. Grouped in cyclists, aerobically trained non-cyclists, and sedentary</p> <p>5. No</p>	<p>Independent variable: acute effects of exercise (cycle ergometer 60% heart rate reserve)</p>	<p>48 (9 female)</p> <p>No data on education available</p> <p>Fully independent and non-institutionalized lifestyle</p> <p>60–80 (range)</p>	<p>Attention: reaction time for local and global targets in milliseconds</p>	<p>Analysis of variance</p> <p>No covariates but age- and sex-matched groups</p>	<p>No significant differences for attention performance between the three groups during the resting condition</p> <p>Significantly better attention performance (faster reaction times) for cyclists and aerobically trained non-cyclists during exercise on a cycle ergometer (group × physical exercise interaction, <i>F</i> value 4.17, <i>p</i> value 0.022)</p>

Table 4 continued

Reference and rating	Physical activity measurement (1) Name; (2) time frame; (3) FITT; (4) measure (scale); (5) previously applied or validated	Other outcomes	Sample size characteristics Age (years) at cognitive assessment	Cognitive domains	Statistics covariates/confounders	Major findings
Wouters et al. (2017) [30] 8/14	<ol style="list-style-type: none"> Exercise History Questionnaire Four time spans: age 18–29, 30–49, 50–64, ≥ 65 years Time, intensity (min/day; intensity in MET: low = 2.5, moderate = 4.5, high = 8.5) MET min/day and groups based on MET min/day tertiles (low ≤ 90, moderate = 91–206, high ≥ 207) Applied before; not validated or tested for reliability [91] 	<p>Independent variables: current PA, training walking speed</p>	<p>209 (67 female)</p> <p>No descriptive data on education available</p> <p>Overall sample: participants of a 4-day March sport event and their relatives and friends</p> <p>Relevant subsample: senior study participants aged ≥ 60 years 66.4 \pm 4.7 (SD)</p>	<p>Brain Aging Monitor—Cognitive Assessment [92]</p> <p>Working memory: The Lost Artefacts (recall a list of items, 7 levels)</p> <p>Executive function: Temple of Wisdom (solving a labyrinth, 5 levels)</p> <p>Visuospatial short-term memory: Nebo's Amulet (pattern recognition, 8 levels)</p> <p>The number of levels reached were used as the dependent variable</p>	<p>Multiple linear regression (standardized regression coefficients), chi-squared test, analysis of variance</p> <p>Sex, age, education (low to moderate vs. high), BMI, cognitive stimulating activities, smoking, alcohol, sleep</p>	<p>No significant associations of lifelong PA with all three Brain Aging Monitor—Cognitive Assessment tests were found in participants ≥ 60 years</p>

ADL activities of daily living, BMI body mass index, D-KEFS Delis–Kaplan Executive Function System, FITT frequency intensity type time, MET metabolic equivalents of task, MMSE Mini-Mental State Examination, PA physical activity, SD standard deviation, VO_{2max} maximal oxygen uptake

Six longitudinal studies applied PA questionnaires that had not been previously used or validated [9, 24, 31, 32, 36, 37]. Three longitudinal designs used comprehensive lifestyle questionnaires that had been used before but had not been validated or tested for reliability concerning PA data assessment [6, 38, 41]. One study applied a standardized interview and reported measures for validity [34] and two studies applied self-developed questionnaires and reported measures for validity [33] or validity and reliability [40]. One study [35] applied the validated Minnesota Leisure Time Activity Questionnaire [45] and one study [39] applied the French version of the validated Modifiable Activity Questionnaire [46].

None of the validated and formerly applied questionnaires was developed for the analysis of the association between PA and cognitive function. Furthermore, none of the questionnaires was applied by more than one author.

Most of the included studies assessed one or two relevant PA normatives such as duration, frequency, or intensity of PA. However, only two cross-sectional [11, 30] studies and one longitudinal [34] study used metabolic equivalents of tasks (MET) and/or MET hours [47] as standardized measures for PA intensity and energy expenditure. Furthermore, only two longitudinal studies [24, 37] differentiated less active and higher active participants related to current activity guidelines (150 min of moderate-intensity PA, or 75 min of vigorous-intensity PA).

3.4 Physical Activity Influence on Global Cognitive Function

Overall, no study found a detrimental association between leisure PA during the life span and cognitive function in older age. Both longitudinal studies of high quality [40, 41] revealed a significant association between PA during higher ages (64+ years) and alleviation of cognitive decline up to the age of 84 years. Leading in the same direction, the only high-quality cross-sectional study [11] was able to report a beneficial association between PA over a time span of < 20–65 years and global cognitive function of participants with a mean age of 66 years.

Six cross-sectional [8, 10, 11, 25, 26, 28] and nine longitudinal studies [6, 24, 31–34, 39–41] assessed global or general cognitive function by building scores as an overall measure for multiple cognitive assessments or by applying a test for general cognitive status such as the MMSE [23]. Two cross-sectional studies [25, 26] of low quality analyzed the association between lifetime PA, using 290 min per week as a cut-off value and MMSE scores, and found no differences in scores between active and less active participants. In contrast, one cross-sectional study [28] of moderate quality reported an association between

activities during teenage years and scores on a modified version of the MMSE. The results of three out of four longitudinal studies of low [24, 31] or moderate quality [32] showed no association between lifetime PA and MMSE scores. The fourth longitudinal study of high quality however used MMSE scores to indicate cognitive decline in considerably older participants (age 84 years) and showed a beneficial association with PA intensity at age 74 years [41].

Cross-sectional studies of high [11] and moderate quality [10] based on other measures of global cognitive function found associations between PA and cognitive scores based on multiple tests. However, a moderate-quality study [8] found no association with global cognitive efficiency assessed via a single testing procedure. Three longitudinal studies of moderate [33, 34] and low quality [6] showed an association between PA and cognitive performance or cognitive decline based on scores built on multiple cognitive domains. However, one longitudinal study of moderate quality [39] was not able to confirm an association between PA and cognitive performance. One longitudinal study used a questionnaire in a design of high quality [40] and reported associations between cognitive function and mid-life and later adult life PA.

3.5 Physical Activity Influence on Domain-Specific Cognitive Functions

3.5.1 Executive Functions

Executive functions were tested and analyzed as separate cognitive domains in five cross-sectional [8, 25, 26, 29, 30] and six longitudinal studies [9, 24, 31, 34, 37, 38]. Table 3 provides an overview of the tests applied to measure domain-specific cognitive functions. Two cross-sectional studies of low quality, based on the same dataset [25, 26], tested multiple executive functions and found an association between Stroop test performance and PA. In contrast, three cross-sectional studies of moderate quality showed no associations between PA and multiple executive functions [30] including Stroop tests [8, 29]. Three longitudinal studies of moderate quality [9, 34, 37] assessing multiple tests and one low-quality study [24] using one cognitive assessment showed significant associations between PA and executive functions. However, one longitudinal study of moderate [38] and one of low quality [31] were not able to confirm these results.

3.5.2 Attention

Attention was tested and analyzed as a separate domain in five cross-sectional [8, 25–27, 29] and two longitudinal studies [31, 35]. All tests applied for attention assessment

are listed in Table 3. With the exception of one moderate-quality longitudinal study assessing the decline of attention performance via multiple time points [35], cross-sectional (five of low-to-moderate quality) [8, 25–27, 29] and longitudinal (one of low quality) [31] studies showed no associations between attention performance and PA.

3.5.3 Memory

Five cross-sectional studies of low [25, 26] and moderate [8, 29, 30] quality assessed verbal, episodic, and visuospatial memory and found no associations with PA. In contrast, five out of six longitudinal studies of moderate quality found significant associations between PA and semantic [9], verbal [35–37], and auditory [34, 36] memory. One longitudinal study of low quality [31] and one of the above-mentioned studies of moderate quality [9] were not able to confirm an association between PA and verbal memory.

3.5.4 Working Memory

Working memory was assessed in two low-quality [25, 26] and three moderate-quality [8, 29, 30] cross-sectional and two moderate-quality longitudinal studies [9, 34]. Only one longitudinal study of moderate quality found an association between PA and working memory assessed via digit spans [34]. No other studies were able to confirm an association between PA and working memory assessed with item and card sorting tests or digit spans (for a list of applied tests see Table 3).

3.6 Influence of Physical Intensity

Whereas three cross-sectional [8, 10, 30] and four longitudinal studies [6, 34, 37, 39] assessed PA using a combined measure based on intensity, duration, and frequency, only one cross-sectional [11] and four longitudinal studies [9, 24, 33, 41] analyzed the influence of PA intensity as a separate factor. All five studies found significant associations between high-intensity PA and global cognitive function [11], global cognitive decline [33, 41], and memory as well as executive functions [9, 24]. One study analyzed the influence of high-intensity PA duration using a mean value for an age span ranging from 6 to > 55 years and failed to confirm the association between higher intensity PA and cognitive function [8].

3.7 Influence of Physical Activity During Specific Age Periods

Most of the cross-sectional studies included in this review analyzed PA as an overall measure across a time span

including most of the adult lifetime [8, 10, 11, 30] or failed to define the assessed time span [25, 26]. Two cross-sectional studies focused on participants aged 60+ years engaged in endurance training > 10 years and were able to report better performance in global intelligence and executive function (indicating relevance of PA during higher ages) [29] but not attention performance [27]. One cross-sectional study assessed and separately analyzed multiple time points during the life span [28] and reported an association between overall mean and teenage PA and MMSE scores.

The majority of longitudinal studies assessed the influence of PA from mid-life (> age 35 years) to late adult life using one [9, 32, 33, 38, 39] or multiple time points [34–37] and were able to report significant associations with global cognitive function, memory, and executive functions. One longitudinal study assessed the influence of PA during age 15–25 years and found significant associations with executive functions but not with MMSE scores [24]. Three studies focused on late-life PA (age 60–85 years) and reported associations with less cognitive decline in higher ages [6, 40, 41]. Only two studies [6, 31] assessed life-span PA as an overall mean measure. Both studies failed to confirm associations with global cognitive function [6] or multiple cognitive domains [31].

4 Discussion

We found evidence concerning the association between adult life-span PA and global cognitive performance measures, attention, executive functions, working memory, and memory. Most of the studies analyzed PA via measures of duration or energy expenditure and were able to report associations with global cognitive function and decline, executive functions, and memory. Attention and working memory in participants aged 60+ years seem not to be associated with earlier adult life PA. No study found detrimental effects of adult life-span PA on cognitive functions. Activities during mid- and late adult life and measures of mean lifetime PA were analyzed frequently. In contrast, valid information concerning the impact of early adult life PA on domain-specific cognitive functions in old age is sparse.

4.1 Findings in Relation to Previous Studies

4.1.1 Global Cognitive Function

One of the most frequently applied cognitive measures was the MMSE. We are able to report evidence based on six low- to moderate-quality studies indicating no associations between PA and cognitive status assessed by the MMSE.

Table 5 Characteristics of the included longitudinal studies

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Brewster et al. (2014) [9]	1. Life Experiences and Activities Form 2. Time point age 40 years (assessed at age 74 ± 7 years) 3. Frequency and intensity (PA included light and heavy activities during work, house or yard work, and exercise) 4. 5-point rating scale frequency rating from 1 = never to 5 = almost every day 5. No	Independent variables: recreational activities, language, literacy/education, morphometrics, APOE genotyping, childhood socioeconomic status	333 (220 female) Education in years: African: 13.54 ± 3.03 (SD), Hispanic: 8.39 ± 5.48 (SD), Caucasian: 14.40 ± 3.05 (SD) North Americans African (<i>n</i> = 120, 73% female), Hispanic (<i>n</i> = 109, 66% female), and Caucasian (<i>n</i> = 104, 58% female) North Americans One time point: 74.4 ± 7.1 (SD)	Episodic memory: Multitrial Word List Learning Test [93] Semantic memory: verbal (object-naming); nonverbal (picture association) [93] Executive function: category fluency, phonemic fluency (letter) [93] Working memory: Digit Span Backward Test, Visual Span Backward Test, List Sorting Test [93]	Mixed-effects regression Basic demographic variables, APOE 4 status	Heavy PA at age 40 years was positively associated with semantic memory (parameter estimate 0.056, standard error 0.022, <i>p</i> value 0.011) and executive function (parameter estimate 0.060, standard error 0.025, <i>p</i> value 0.017) Heavy PA at age 40 years was positively associated with a positive trend for episodic memory (parameter estimate 0.038, standard error 0.022, <i>p</i> value 0.086)
Dik et al. (2003) [24]	1. Unspecified questionnaire 2. Time span age 15–25 years (assessed at age 62–85 years) 3. Intensity (did the activity cause them to sweat or make them exhausted) and frequency 4. Four groups based on time per week: no regular PA (never or sometimes); low (less than 1–2 h/week); moderate (3–9 h/week); high (10 h/week or more) 5. No	None	1241 (673 female) [985 full datasets including all assessments at time points] No education assessment but verbal intelligence score 13.2 ± 3.7 (SD) [range 0–20] One time point: 74.9 ± 6.4 (SD)	General cognitive function: MMSE [23] Information processing speed: Alphabet Coding Task-15 [94]	Generalized estimating equations [95] Model 1: time adjusted sex, verbal intelligence Model 2: adjusted for age, socioeconomic status, early life physical work demands, current PA, smoking, alcohol, diabetes mellitus, cardiac disease, depression	Information processing speed differed significantly between PA levels, with the lowest scores in both the inactive and highly active groups (a physically active working history may have influenced these effects) Sex-specific analysis revealed a significant association of early-life PA with information processing speed, but not with general cognitive function only in men

Table 5 continued

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Gow et al. (2016) [6]	<p>1. Retrospective questionnaire booklet</p> <p>2. Three time spans: age 20–35; 40–55; 60–75 years (assessed at age 83 years)</p> <p>3. General level of PA assessed as combination of duration type and intensity per week (1 = necessary household; 2 = walking or other outdoor activities 1–2 times; 3 = walking or other outdoor activities several times per week; 4 = exercising 1–2 times with perspiring and heavy breathing; 5 = exercising several times with perspiring and heavy breathing; 6 = heavy exercise or competitive sport several times per week)</p> <p>4. 6-point rating scale</p> <p>5. Applied before but not validated or tested for reliability [96]</p>	<p>Independent variables: non-physical leisure activity</p>	<p>550 (58.2% female) [376 full datasets]</p> <p>Education in years 10.9 ± 2.5 (SD)</p> <p>Lothian birth cohort (Scotland) 1921</p> <p>Four time points: 79, 83, 87, and 90</p>	<p>Latent general cognitive ability based on all cognitive domains</p> <p>Intercept = level of general cognitive ability at age 79, 83, 87, and 90 years</p> <p>Slope = change in general cognitive ability from age 79 to 83, 83 to 87, and 87 to 90 years</p> <p>Executive function: Phonemic Verbal Fluency Test [13]</p> <p>Verbal declarative memory: logical memory from the Wechsler Memory Scale-Revised [97]</p> <p>Nonverbal fluid ability: Raven's Standard Progressive Matrices [98]</p>	<p>Latent growth curve models [99]</p> <p>Sex, number of years in full-time education, social class, smoking, estimated weekly alcohol consumption</p>	<p>No associations with intercept</p> <p>After inclusion of the covariates, the association between PA at 60–75 years of age and slope became significant (slope path coefficient 0.265, <i>p</i> value 0.045). Individuals who were more physically active in later life experienced less cognitive decline over the 11 years of follow-up from age 79 to 90 years</p>

Table 5 continued

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Weuve et al. (2004) [34] 11/16	1. Standardized interview 2. Time span of 8–15 years during mid-life via multiple reports (with a mean of five reports) 3. Duration, type (including running, jogging, walking, hiking, racquet sports, swimming, bicycling, aerobic dance, exercise machines, other vigorous and light-intensity activities, and stairs climbed daily) and intensity (outdoor walking pace) 4. Quintiles based on MET hours per week and quartiles based on walking MET hours per week 5. Tested for validity but not for reliability [34]	None	18766 (female) (16466 data sets for cognitive change assessment) Education 22% with bachelor's, master's, or doctorate degree US women registered as nurses in 1976 Two time points: 74.2 ± 2.3 (SD) and 2 years later	Initial interview: Telephone Interview for Cognitive Status [100] Later interviews: immediate recall using the East Boston Memory Test [101] Category fluency [102] Working memory and attention: Digit Span Backwards [13] Tests were analyzed separately and for women given all 6 tests a global score was calculated by averaging the z-scores from all tests For overall verbal memory, a combination of the immediate and delayed recalls of the first interview and 10-word list of the later interviews, for women given all 4 tests a global score was calculated	Multiple linear and logistic regression Model 1: age at cognitive assessment, education, husband's education, alcohol consumption, smoking, aspirin use, ibuprofen use, vitamin E supplementation, mental health on the mental health scale of the Short Form-36, history of osteoarthritis, history of emphysema or chronic bronchitis, low vitality on the energy fatigue scale, problems with balance, moderate to severe bodily pain and health limitations in walking a block Model 2: Model 1 + high blood pressure, elevated cholesterol level, type 2 diabetes mellitus, coronary heart disease, coronary artery bypass graft surgery, congestive heart failure, transient ischemic attack, and carotid endarterectomy (women with stroke had already been excluded from participation in the baseline cognitive testing) For analysis of walking: stair-climbing and other low-intensity activities	Statistically significant trends of increasingly higher mean scores on all the cognitive measures with higher levels of long-term PA Significantly higher cognitive scores for women in the third and fourth quartiles of walking on all cognitive measures Higher levels of PA were associated with less decline over 2 years in all cognitive measures aside from category fluency

Table 5 continued

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Cadar et al. (2012) [35] 9/16	<p>1. Minnesota Leisure Time PA Questionnaire (age 36 years) and open questions during interview (age 43 years)</p> <p>2. Two time points (age 36 and 43 years)</p> <p>3. Frequency as number of activities per month</p> <p>4. Categorization at each age and mean for both ages as: inactive = no participation; moderate = 1–4 times per month; most active = 5 or more times per month.</p> <p>Score for change: inactive at all ages; increased activity; decreased activity; moderate or most active at both ages</p> <p>5. Tested for validity [45]</p>	<p>Independent variables: smoking, and dietary behavior</p>	<p>1018 (528 female)</p> <p>Education: 451 participants with advanced ('A level', taken during the final year of secondary/high school) or higher (university or equivalent) education and 567 below this educational level</p> <p>Born in England, Scotland, and Wales in March 1946</p> <p>Two time points: 43 years, and 60+ years (range of 60–64 years)</p>	<p>Verbal memory: 15-item word learning task devised by the National Survey of Health and Development [103] research team</p> <p>Speed and concentration: letter search task</p>	<p>Multivariable analysis of covariance</p> <p>Model 1: (raw associations for) sex, social class of origin, cognitive ability at age 8, educational attainment, occupational class, symptoms of anxiety and depression</p> <p>Model 2: Model 1 + smoking status, dietary choice, PA</p> <p>Model 3: Model 2 + cumulative scores of lifestyle behaviors</p>	<p>Significant differences for verbal memory at age 60+ years between physical activity group categories (PA at age 36 and 43 years, PA mid-life score and change in PA). No influence of PA on memory decline from age 43 to 60+ years</p> <p>Significant differences for speed and concentration at age 60+ years between activity groups for age 43 years, mid-life score and change in PA (no significant differences for PA at age 36 years)</p> <p>High-intensity PA at 43 years was associated with a slower search speed decline after full adjustment</p> <p>Most active at both 36 and 43 years and those who increased their level of PA also had a slower search speed decline</p>
Ku et al. (2012) [40] 13/16	<p>1. Unspecified questionnaire</p> <p>2. Five time points (age 64, 67, 70, 74, and 78 years)</p> <p>3. Frequency per week (no sessions, 1–2 sessions, 3–5 sessions, 6+ sessions)</p> <p>4. Lower and higher activity group (cut-off 3.83 sessions/week)</p> <p>5. Tested for validity and reliability [40]</p>		<p>1160 (574 female)</p> <p>Educational status data not reported</p> <p>Taiwanese adults</p> <p>Two time points: ≥ 67 years, and ≥ 78 years</p>	<p>5 items of the 10-item Short Portable Mental Status Questionnaire [104]</p>	<p>Latent growth models: unconditional model without controlling for covariates and conditional model controlling for covariates</p> <p>Sex, age, education level attained, cohabitation status, self-perceived social support, alcohol drinking, smoking, number of chronic diseases, activities of daily living</p>	<p>Higher level of PA at baseline was significantly related to a slower decline in cognitive performance, as compared with a lower level of activity ($\beta = 0.22$)</p> <p>Association between changes in PA and changes in cognitive performance ($\beta = 0.36$)</p>

Table 5 continued

Reference and rating	Physical activity measurement 1. Name; 2. time frame; 3. FITT; 4. measure (scale); 5. previously applied or validated	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Szoeke et al. (2016) [36] 10/16	1. Unspecified questionnaire 2. Four time points (subjects age range 45–55, 50–60, 55–65, and 60–70 years) 3. Frequency by active days a week 4. Groups non-active vs. active (at least 1 active day) 5. No	Independent variables: sociodemographic factors, lifestyle factors, and clinical and vascular risk factors	387 (female) Educational status data not reported Four time points: 49.6 ± 2.5 (SD), 55, 60, and 65 years	Verbal episodic memory: Modified version of the CERAD assessments [105], delayed recall of the CERAD 10-item Supraspan Word List score [106] Auditory verbal memory: CERAD immediate recall sum of 3 trials, California Verbal Learning Task—II—immediate and delayed recall [107]	Mixed linear regression Age, education	Mean PA across all time points from baseline until the third follow-up: each mean day of PA was associated with an increase of delayed recall CERAD performance of 0.136 points (95% CI 0.058–0.214) All auditory verbal memory test scores were associated with cumulative PA (statistical model not clearly described)
Sabia et al. (2009) [37] 10/16	1. Unspecified questionnaire 2. Three time points (mean age: 44, 55, and 61 years) 3. Frequency, intensity and duration (hours per week spent with mildly energetic, moderately energetic, and vigorous PA) 4. Groups “low risk” vs. “high risk” (low risk: > 2.5 h/week of moderate PA or > 1 h/week of vigorous PA) 5. No	Independent variables: smoking status, alcohol consumption, dietary behavior	5123 (27.9% women) Educational status data not reported Whitehall II study (UK) One time point: 61.1 ± 6.0 (SD)	Executive function: Reasoning by Alice Heim 4-I Test [108] and verbal fluency by phonemic (“S” words) and semantic (“animal” words) verbal fluency tests [109] A composite score of executive function was created using these tests Memory: short-term verbal test (20-word free recall test) “Poor cognition” was defined as cognitive scores in the lowest sex-specific quintile	Logistic regression Age, sex, socioeconomic position	High risk across mid-life (cumulative exposure of all three time points) was associated with greater odds of poor memory (OR 1.29, 95% CI 1.01–1.65) and a significant trend for poor executive function (<i>p</i> value 0.06) No evident association between PA at age 44 years and measures of cognitive function at age 61 years High-risk participants at mid-life and late mid-life were at higher risk of poor executive function (OR 1.19, 95% CI 1.01–1.39) compared with low-risk participants High risk at late mid-life was associated with poor memory (OR 1.28, 95% CI 1.09–1.50)

Table 5 continued

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Yu et al. (2009) [38] 10/16	<p>1. Life Complexity Inventory Questionnaire</p> <p>2. Two time points (mean age 53 years and 7-year follow-up)</p> <p>3. Duration of PA (number of weekly hours spent participating in sports, PA, and outdoor hobbies)</p> <p>4. Hours spent doing PA divided by total hours for all leisure time activities</p> <p>5. Applied before but not validated or tested for reliability concerning measures of leisure time PA [110]</p>	<p>Independent variables: leisure time cognitive activity, self-directed work, and hypertension</p>	<p>626 (56.41% female)</p> <p>Education in years 15.01 ± 2.66 (SD)</p> <p>Participants of the Seattle Longitudinal Study (96% white)</p> <p>Three time points: 53.2 ± 12.8 (SD), 7- and 14-year follow-ups</p>	<p>Verbal memory: word fluency [111], immediate memory [112], delayed memory [112]</p> <p>Composite score was calculated: verbal memory = .005 (word fluency) + .500 (immediate memory) + .495 (delayed memory); score was converted to <i>t</i>-scores (mean = 50, SD = 10)</p> <p>Inductive reasoning: Primary Mental Abilities Reasoning Measure [111], Adult Development and Enrichment Project Letter Series [113], word series [114], Educational Testing Service Number Series [115]</p> <p>Composite score was calculated: inductive reasoning = 0.280 (primary mental abilities reasoning measure) + 0.272 (letter series) + 0.259 (word series) + 0.189 (number series); score was converted to <i>t</i>-scores (mean = 50, SD = 10)</p>	<p>Multi-level modeling</p> <p>Age, sex, education, income</p>	<p>The proportion of weekly hours spent on leisure time PA was not related to verbal memory or inductive reasoning</p>

Table 5 continued

Reference	Physical activity measurement and rating	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Sattler et al. (2011) [31] 4/16	<p>1. Unspecified questionnaire</p> <p>2. Five time spans (age 6–14, 14–20, 20–40, 40–60 years, and at age 62 years) assessed at age 62 years</p> <p>3. Frequency, duration, and type (open-ended questions aiming at current and past sport activities)</p> <p>4. Groups: physically active vs. inactive (active = at least one sport activity for at least once a week for 2 h during all time spans)</p> <p>5. No</p>	<p>Independent variable: objective physical fitness</p> <p>Dependent variables: Alzheimer's disease, vascular dementia, mild cognitive impairment [116], and mild cognitive disorder [117].</p>	<p>Overall sample: 500 subjects initially recruited, 323 reassessed (24 with Alzheimer's disease, 102 with mild cognitive impairment, 174 control subjects)</p> <p>Relevant subsample: 174 control subjects (88 female)</p> <p>Education in years 13.8 ± 3.0 (SD)</p> <p>One time point: 74.1 ± 1.1 (SD)</p>	<p>MMSE [23]</p> <p>Memory, learning, attention and cognitive flexibility: Logical memory of the Wechsler Memory Scale [97], Trail Making Test [69], Nürnbergger-Alters-Inventar [118], Leistungsprüfsystem [119]</p> <p>Memory: immediate word list recall, delayed word list recognition</p> <p>Visuospatial functioning: spatial orientation, block design</p> <p>Verbal comprehension: information subtest</p> <p>Abstract thinking: similarities subtest</p> <p>Speed: number-connection test</p> <p>Attention and concentration: D2 Test [62]</p>	<p>Logistic regression</p> <p>Education, socioeconomic status, depressive symptoms</p>	<p>No significant differences in neuropsychological test performance of self-reported active compared to inactive subjects (data of inductive analysis not provided)</p>

Table 5 continued

Reference and rating	Physical activity measurement 1. Name; 2. time frame; 3. FITT; 4. measure (scale); 5. previously applied or validated	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Gelder van et al. (2004) [41] 14/16	<p>1. Questionnaire</p> <p>2. Two (Finland) or three (the Netherlands and Italy) time points (age 74, 79, and 84 years)</p> <p>3. Type, duration, and intensity (walking, cycling, gardening, hobbies, odd jobs, and sporting activities > 2 kcal/kg/h were summed to obtain total weekly duration of PA)</p> <p>4. Four groups based on duration in 1990 and 2000 (min/day: < 30, 31–60, 61–120, > 120)</p> <p>Mean intensity score (intensity multiplied by duration, summed and divided by the total time spent on all activities, classified in quartiles based on the mean intensity in 1990)</p> <p>Three groups based on change in duration from 1990 to 2000 (increase > 60 min/day, decrease > 60 min/day, stable defined as change < 60 min/day)</p> <p>Three groups based on change in intensity from 1990 to 2000 (increase > 0.8 points, decrease > 0.8 points, stable defined as change < 0.8 points)</p> <p>5. Applied before but not validated or tested for reliability [120]</p>		<p>295 (male) [46 Finnish, 118 Dutch, 131 Italian]</p> <p>Education in years: Finnish 4.6 ± 2.6 (SD), Dutch 11.1 ± 4.2 (SD), Italian 5.0 ± 2.6 (SD)</p> <p>Participants of the 'Finland, Italy, and the Netherlands Elderly' study with no history of myocardial infarction, stroke, diabetes mellitus, or cancer and a MMSE score > 18 in 1990</p> <p>Three time points: 74, 79, and 84 years</p>	MMSE [23]	<p>Multivariate linear regression</p> <p>Age, education, country, alcohol consumption, smoking status, mental intensity and duration, ADL, depression, BMI, use of antihypertensive drugs, HDL, total cholesterol, blood pressure, baseline cognitive functioning</p>	<p>Men in the lowest intensity score quartile at baseline showed the strongest 10-year cognitive decline (1.8 times stronger than the decline among the other quartiles)</p> <p>Cognitive decline was strongest for those whose duration of PA decreased > 60 min/day (2.6 times stronger than for those whose duration of activity remained stable)</p> <p>No cognitive decline among men who increased their duration of PA</p> <p>Men whose intensity of activity decreased more than 0.8 points during 10 years had the strongest cognitive decline (3.6 times stronger than the decline of men, whose intensity remained stable)</p> <p>No cognitive decline in the group with increasing intensity</p>

Table 5 continued

Reference and rating	Physical activity measurement 1. Name; 2. time frame; 3. FITT; 4. measure (scale); 5. previously applied or validated	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Käreholt et al. (2011) [32] 8/16	1. Unspecified questionnaire 2. One time point (age range 46–75 years) 3. Type (sports, gardening and dancing) and frequency (no, sometimes, often) 4. Three-point scale transformed into standardized score (mean = 0, SD = 1) 5. No	Independent variables: political activities, organizational activities, mental activities, sociocultural activities, and social activities	1643 (58.7% women) Education in years 8.4 (interquartile range 6–10) Random samples of Swedish population One time point: 80.2 (range 69–98)	Outcome measure based on items from the MMSE [23]: registration and repeating, orientation, delayed recall, attention/concentration	Ordered logistic regressions Model 1: Age, age-square, sex, follow-up time Model 2: Model 1 + mobility problems, symptoms of mental distress, employment status, education, and adult and childhood socioeconomic status Model 3: Model 3 + all leisure time activities simultaneously	In Models 1 ($\beta = 0.25$, p value < 0.001) and 2 ($\beta = 0.17$, p value 0.017), PA was correlated to better cognition for women but not for men In Model 3, the association between PA and cognition was significant at the 10% level among women ($\beta = 0.14$, p value 0.055)
Stevens et al. (2016) [33] 8/16	1. Unspecified questionnaire 2. One time span (12 mo at mean age: 55 years) 3. Type (home, work, and leisure time) and intensity (four-point Likert scale: inactive, light, moderate, heavy) 4. Weighted average of intensity of all three activity types 5. Not applied before but tested for validity [33]	Independent variable: leg extension muscle power	324 (female) Education described as 63% educated > secondary [121] Twins from the TwinsUK volunteer registry with absence of significant cerebral pathology Two time points: 55.7 ± 7.3 (SD), and 65.7 ± 7.3 (SD)	Seven computerized test from the Cambridge Neuropsychological Test Automated Battery [122]: paired-associates learning, delayed matching to sample, pattern recognition memory, spatial span, spatial working memory, simple reaction time, five-choice reaction time Age-related cognitive change score based on all 7 tests	1. Multivariable linear regression 2. Paired t test for twin-pair analyses Age, birthweight, adult height, adult ability, occupation, household income, mental health score, smoking, alcohol, dietary saturated fat, total vegetables, leg extensor power, PA, blood pressure, waist-hip ratio, glucose, cholesterol to HDL ratio, ischemic heart disease, type 2 diabetes mellitus	1. PA measured at baseline had an independent protective effect on the cognitive change score over the subsequent 10 years (standardised β -coefficient 0.129, p value 0.028) 2. No significant differences in cognitive change scores between physically active twins and their counterparts

Table 5 continued

Reference and rating	Physical activity measurement 1. Name; 2. time frame; 3. FITT; 4. measure (scale); 5. previously applied or validated	Other outcomes	Sample size characteristics age (years) at cognitive assessments	Cognitive domains	Statistics covariates/confounders	Major findings
Kesse-Guyot et al. (2014) [39] 11/14	<p>1. Modifiable Activity Questionnaire (French version)</p> <p>2. One time span (1 years) assessed at a mean age of 55 years</p> <p>3. Frequency, intensity, type, and duration (of each leisure time PA performed at least 10 times for at least 10 min/session over the last year)</p> <p>4. Groups: active vs. inactive (inactive: less than 30 min/day of walking or equivalent PA); summary score: MET h/week</p> <p>5. Applied before and tested for validity [46]</p>	<p>Independent variables: mid-life fruit and vegetable consumption, alcohol intake, fish and seafood consumption, sedentary behavior, and a combination of these factors</p>	<p>1326 male, 1104 female Education: male 21.6% < 6 years, 37.0% 6–11 years, 41.4% ≥ 12 years; female: 20.1% < 6 years, 45.3% 6–11 years, 34.6% ≥ 12 years</p> <p>Healthy adults in France One time point: 65.6 ± 4.5 (SD)</p>	<p>Short-term and working memory: forward and backward digit span [123] Mental flexibility: Delis–Kaplan Trail Making Test [124] Episodic memory: RI-48 Test cued recall [125] Lexical semantic memory: semantic and phonemic verbal fluency task [13] Scores were converted to <i>t</i>-scores (mean = 50; SD = 10) A composite cognitive measure (mean = 50), defined as the mean of the 6 standardized scores was computed and rescaled to an SD of 10</p>	<p>1. Analysis of covariance 2. Structural equation models Model 1: age, sex education Model 2: Model 1 + time lag between baseline and cognitive evaluation, occupational status, intervention group during trial phase, energy intake, number of 24-h records, BMI, depressive symptoms, baseline self-reported memory troubles, history of diabetes mellitus, hypertension, cardiovascular diseases Model 3 (for each unhealthy behavior): Model 2 + other lifestyle behaviors</p>	<p>1. No significant effect of mid-life leisure time PA on late-life cognition 2. Low leisure time PA was one of the main contributors to a latent unhealthy lifestyle factor related to verbal memory</p>

ADL activities of daily living, *APOE4* apolipoprotein E4, *BMI* body mass index, *CERAD* Consortium to Establish a Registry for Alzheimer’s Disease, *CI* confidence interval, *FITT* frequency intensity type time, *HDL* high-density lipoprotein, *kcal* kilocalories, *MET* metabolic equivalent of task, *MMSE* Mini-Mental State Examination, *OR* odds ratio, *PA* physical activity, *SD* standard deviation

One high-quality longitudinal study however showed an association between cognitive decline, assessed by the MMSE, and PA during late adult life. These findings are in contrast to studies focusing on other measures of global cognitive function. These low- to high-quality studies were able to provide evidence for the association of PA with global cognitive function based on scores obtained from multiple cognitive assessments, telephone interviews, or questionnaires. However, one (of six) longitudinal and one (of three) cross-sectional medium-quality studies showed no associations between PA and global cognitive function. In addition to overall evidence on global cognitive function and decline, indicating a significant association with adult life-span PA, three studies were able to confirm the relevance of vigorous-intensity PA. Consistent with earlier reviews [12], our data indicate that the MMSE might be suited to assess PA effects on cognitive decline in longitudinal studies. In contrast, the MMSE appears to be not suitable as a cross-sectional measure of cognitive function and inter-individual comparison in healthy elderly individuals. Taking the evidence from all included studies together, maintenance of global cognitive functions seems to be connected with adult life PA. Thus, our dataset confirms current reviews on the impact of exercise on cognitive aging [48] and neurocognitive performance [2]. Because earlier meta-analytic findings [2] and most of the studies included in this review indicate preliminary evidence for domain-specific effects of PA, further studies on combined cognitive scores should include post-hoc analyses of separate domains.

4.1.2 Attention and Executive Functions

Evidence of the connection between PA and executive functions is equivocal. Whereas three cross-sectional and two longitudinal studies found no associations between PA and multiple executive functions, two cross-sectional studies with overlapping datasets and four longitudinal studies reported significant associations with overall and vigorous-intensity adult life PA. The categorization of executive functions used in this review is not without problems. Based on an earlier high-quality meta-analysis [2], we put various clearly distinguishable functions in one category. However, some studies included in our review applied the same cognitive tests and reported contradictory results in samples with different mean ages. Similarly, evidence relating to attention performance was also heterogeneous. Future studies therefore need to further analyze the interaction between PA and the age-related decline of executive functions and attention.

All studies that assessed cognitive functions at a single time point revealed no association between PA and attention. The only study that assessed the age-related decline in

attention via multiple assessments showed a significant beneficial association with PA during mid-life. Overall, these findings are consistent with recent evidence indicating the effects of current PA primarily on complex executive tasks, which demand greater amounts of both attentional focus and performance in higher cognitive functions such as interference control [48]. Our findings extend the current meta-analytic findings on short-term effects [2], identifying comparable long-term associations between adult life PA and especially vigorous intensity for maintaining executive cognitive abilities in old age. These findings are in contrast to those of some studies of maintained cognitive function in younger ages indicating a detrimental effect of vigorous PA [7]. Future studies should use cognitive assessments that are able to determine the influence of attention and executive functions and furthermore are sensitive to age-related change in cognitive functions, such as the Stroop test [49] or cognitive testing batteries such as the Cogstate system [50]. Furthermore, these studies should adopt longitudinal designs assessing cognitive outcomes at multiple time points throughout the later life span.

4.1.3 Memory

Studies assessing mean lifetime PA and memory at a single time point in late life reported no associations; however, one study assessing mean lifetime PA and change in memory performance (multiple time points) indicated a beneficial association with less decline in memory performance. In a similar vein, longitudinal studies highlighted the relevance of mid- to late-life overall and vigorous-intensity PA for the maintenance of memory function in old age. Again, this is consistent with research on the relevance of current PA for cognitive function. Kramer et al. previously described a favorable association between PA and memory in one of their earlier reviews in 2005 [51]. Later meta-analyses [2] and reviews [48] confirmed these findings for exercise interventions and habitual PA. However, Miller et al. [48] highlighted a potential discrepancy between the physical performance data and PA questionnaire findings, which were stated to be less valid and therefore of limited usefulness. Consequently, future studies should confirm the results of this review evaluating objective data on adult lifetime PA.

4.1.4 Working Memory

The evidence related to working memory is based on a small number of low- to moderate-quality studies and to date only two longitudinal designs have assessed this domain. One of these studies assessed working memory at one time point in late life [9]. This study focused on mid-

life PA and was not able to report a significant association between PA and working memory [9]. In contrast, the second longitudinal design tested cognitive functions at two time points and was able to show significant associations between mid-life PA and both mean working memory performance and alleviated decline of this cognitive function [34]. Keeping these discrepancies in mind, most of the currently available evidence (six out of seven studies) indicates that late-life working memory performance seems not to be related to adult life-span PA. These findings are in contrast to currently available overviews reporting preliminary evidence for a beneficial association [12] or equivocal evidence concerning overall or short-term PA effects [2, 48]. Future studies need to assess working memory performance at multiple time points to analyze a potential influence of PA on the decline of this function.

4.2 Underlying Neurobiological Mechanisms

A growing body of literature shows significant PA effects on neuronal structure and metabolism. In contrast, no study on brain plasticity or biomarkers currently reports findings that could explain domain-specific influences found in this and other reviews. Overall, cognitive function during later life seems to depend on preserved brain functions and plasticity [48]. Based on imaging technologies, current research has been able to find evidence for an association between PA and brain volume measures indicating changes in brain structure and grey or white matter quantity; [48, 52, 53] indications for an influence on metabolic markers of neuronal integrity and viability; [54, 55] and increased angiogenesis and cerebral blood flow [1]. Currently, detected target areas for long-term changes include the frontal cortex [54], the hippocampus as well as the prefrontal [53] and temporal regions [52]. Further adaptive responses that might explain long-term PA effects on maintained cognitive function include the reduction of cardiovascular risk factors and inflammatory markers, which are linked to cognitive decline and neurodegenerative diseases [56]. Another emerging theory is that PA is linked to increased bioavailability of growth factors such as vascular endothelial growth factor [57] and therefore stimulates neurogenesis and angiogenesis in the brain. However, so far, no study was able to report a causal link between these pathways and the long-term effects of PA on cognitive function. Future studies should combine the assessment of PA-induced adaptations of cognitive functions and neurobiological markers within relevant brain areas.

One of the most frequently discussed mechanisms for PA effects are increased levels of neurotrophins such as brain-derived neurotrophic factor (BDNF). Brain-derived neurotrophic factor is discussed as a crucial mediator of

beneficial PA-induced effects on brain plasticity and cognitive function [58]. However, based on current evidence, PA and exercise interventions might influence BDNF differently. A recent review concluded that PA could be negatively associated with plasma BDNF levels while data on acute exercise interventions indicate an enhancing effect on plasma levels [59]. Currently, no study has focused on BDNF and the influence of long-term PA on maintained cognitive function. Therefore, it is of great interest to investigate the effects of lifelong PA on BDNF in old age and its possible role as a mediator of long-term effects on cognitive function and brain metabolism.

4.3 Strengths and Limitations

To the best of our knowledge, this is the first systematic review to focus on the association between adult life-span PA and cognitive function in old age. We followed the rigorous Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and conducted our literature search in three databases without language restriction. To minimize methodological diversity in the assessment of PA and the measurement of cognitive outcomes, we focused on studies that assessed clearly definable cognitive functions and applied objective or subjective PA measures, which are able to assess single or multiple time points during a life span at least 10 years prior to cognitive assessments.

A large proportion of the studies included adopted cross-sectional designs or assessed cognitive functions at one time point and therefore limit our ability to draw causal conclusions. One major limitation for most of the included studies is that information on validity and/or reliability for PA assessments was not available. Currently, no study on leisure PA during the adult life span and cognitive function during old age has analyzed objective PA measures such as accelerometry. For the systematic assessment of PA throughout the life span, two reliable instruments were used, the Lifetime Total Physical Activity Questionnaire [43] and the Historical Leisure Activity Questionnaire [44]. For the analysis of current PA in longitudinal designs, multiple reliable self-developed [33, 34, 40] and established [45, 46] instruments were applied. To date, most longitudinal studies have focused on PA during mid to late life. Consequently, evidence on the influence of early adulthood PA on the change in domain-specific cognitive performance in older age is sparse. Future longitudinal designs could include valid retrospective questionnaires and objective prospective PA assessments such as accelerometry. Available evidence suggests that manual work (occupational PA) could be associated with an increased risk of dementia [60]. Therefore, studies that further delineate the influence of leisure and occupational PA are needed.

Comparable to the assessment of PA, a large number of cognitive measures, analyzing various cognitive domains, were applied. Most studies of global cognitive function based on scores or single measurements showed associations with adult life PA and therefore call for a further assessment of underlying effects. Based on our findings, clinical screening tools such as the MMSE seem to be less suited than cognitive domain-specific assessments. We recommend the application of validated tests or testing batteries. If applicable, digital versions of test instruments such as the Stroop Test or Trail Making Test might facilitate the execution and analysis of testing procedures. Furthermore, our data indicate that measures of cognitive decline appear to be more sensitive for PA effects than cognitive assessment at one time point. Future studies thus need to assess cognitive functions at multiple time points to further analyze the interactions with attention, executive functions, and memory found in this review and confirm the trend for no associations between lifetime PA and working memory.

5 Conclusions

Leisure PA during early, mid, and late adulthood seems to be favorably associated with cognitive functions including global cognitive function and decline, executive functions, and memory in old age. Available evidence on the impact of early adulthood PA and the effect of adherence to current World Health Organization activity recommendations (at least 150 min of moderate-intensity PA, or 75 min of vigorous-intensity PA per week) is limited. To date, only two longitudinal studies used cut-offs comparable to these recommendations for group comparisons [24, 37]. Both studies indicated a positive association between adhering to PA recommendations and executive function [24, 37] as well as memory [37]. More information on the relevance of current PA recommendations and the specific influence of earlier adult life periods is necessary. Preliminary evidence indicates that leisure physical activities with higher intensity seem to be of particular relevance for maintained cognitive function in old age. By contrast, information concerning the specific impact of light-intensity PA is currently missing. Consequently, currently inactive or insufficiently active people should be encouraged to engage in PA of moderate-to-vigorous intensity. The influence of light-intensity PA needs to be further analyzed. In terms of more specific recommendations, future studies should focus on dose–response relationships and underlying mechanisms by further analyzing the influence of PA intensity and duration using standardized measures such as MET and MET hours, and determining the impact of specific activity types.

Compliance with Ethical Standards

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