Combined effects of physical activity and obesity on cognitive function: Independent, overlapping, moderator, and mediator models

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Abstract:

This article reviews studies on physical activity, obesity, and cognition to explore how physical activity and obesity may work independently or together in affecting cognitive function. In particular, we propose six hypotheses derived from four conceptual models to advance our understanding of the combined effects of physical activity and obesity on cognition. The four conceptual models are distinguished by the presumed temporal relationship and the presumed correlation between physical activity and obesity and include an independent model, an overlapping model, a moderator model, and a mediator model. Among the 16 studies testing the effects of physical activity and obesity on cognition in a combined approach, the moderator model, viewing either physical activity or obesity as the potential moderator, was most frequently examined ($n = 10$), mediator ($n = 3$) and independent ($n = 2$) models received relatively less attention, and only a single study used an overlapping model. Results were mixed when considering the moderator, independent, and mediator models. The single study that took an overlapping model approach found support for the model hypothesis. One relevant observation from this review is that the variance within the small extant literature with respect to the choice of conceptual model limits our ability to make assertive conclusions relative to the relations among the examined variables. Given the logic supporting a combined effect of physical activity and obesity on cognition, researchers are encouraged to consider the possible models of the relationship as they design studies to further address this research question.

Keywords: Physical Activity | Obesity | Cognitive Function | Executive Function | Physical Inactivity

Article:

Key Points

Six hypotheses were derived from four conceptual models (independent, overlapping, moderator, and mediator) that describe the expected relationship between the independent variables of physical activity and obesity as they relate to cognitive function.
In the extant literature, empirical studies most frequently approached the research question using a moderator model with mixed findings for both obesity as a moderator and physical activity as a moderator.
A smaller number of studies adopted mediator or independent models with results supporting both independent effects of physical activity and obesity on cognition, a role of obesity as a mediator of the effects of physical activity on cognition, and a role of physical activity as a mediator of the effects of obesity on cognition.
Only a single study took the overlapping model approach and this study supported the effects of physical activity and obesity on cognition.
Research examining how physical activity and obesity interact to affect cognition remains in its infancy, and researchers should carefully consider the conceptual model explaining how these two independent variables would be expected to influence cognition as they design studies to test these effects.

1 Introduction

The prevalence of physical inactivity and obesity has been increasing dramatically in recent decades, and both have been described as global pandemics [1, 2]. According to the 2012 Lancet Physical Activity Series Working Group, 31.1 % of adults (aged 15 years or older) and 80.3 % of adolescents (aged between 13 and 15 years) worldwide do not meet public health guidelines for minimal physical activity [3]. In addition, the Global Burden of Disease Study 2013 reported that more than 36.9 % of adults worldwide, along with more than 22 % of adolescents in developed countries, met criteria for being overweight or obese [1]. The pandemics of physical inactivity and obesity have generated substantial public health challenges and a considerable social burden because they are associated with premature mortality and morbidity related to coronary heart disease, type 2 diabetes mellitus, breast cancer, and colon cancer [4, 5]. Indeed, physical inactivity and obesity have been recognized as predictors or even risk factors for negative health outcomes [4].

The adverse health consequences of physical inactivity and obesity are not merely physical. Studies have independently examined and linked physical inactivity and obesity to mental health outcomes, particularly cognitive function. For example, epidemiological studies have observed that physical inactivity is predictive of worse cognitive function [6, 7]. Conversely, the positive relation between physical activity and cognition is well established in studies employing cross-sectional designs in which individuals with higher fitness levels, implying engagement in more physical activity, showed better cognitive performance than individuals with lower fitness levels [8]. These cognitive improvements have been observed using behavioral measures [9, 10] as well as through assessment of structural and functional brain changes [11, 12]. Similar beneficial effects on cognition attributed to physical activity are supported by longitudinal studies. A meta-analytic review of cohort studies revealed that as compared with adults not engaged in physical activity, those with higher levels of physical activity showed 38 % less decline in cognitive performance during a 12-year follow-up [13]. Meta-analyses of randomized controlled trials

(RCTs) have further indicated that physical activity interventions significantly and positively affect cognitive function with effect size indicative of small to large benefits [14, 15].

In addition to physical inactivity, prior research has also identified a negative association between obesity and cognitive function. That is, compared with individuals of normal weight, overweight or obese individuals generally exhibit deteriorated cognitive performance, including problems with general cognitive functioning, attention, executive functioning, memory, and visuospatial performance [16]. Although additional studies exploring the relationship between obesity and cognition are needed, a recent systematic review concluded that obesity is associated with impaired cognitive function across many cognitive domains [17]. Additionally, obesity status is strongly correlated with neurostructural deficits in prefrontal [18] and orbitofrontal cortexes [19], the brain regions associated with executive function.

Considering the above findings, evidence suggests that both physical activity and obesity are associated with cognitive function; however, as most previous studies on cognitive function have examined either physical activity or obesity in isolation, the known relationship between physical activity and obesity has been essentially ignored in this literature. That is, although physical inactivity and obesity are inherently correlated (e.g., obesity results from an imbalance between energy intake and energy expenditure; physical activity directly influences energy expenditure; and obesity leads to reductions in activity) [20, 21], little is known about how these two factors work, either separately or together, in influencing cognition [22]. A better understanding of how the interaction between these two factors affects cognitive function is important.

Accordingly, the present review explores the potential effects of physical activity and obesity on cognitive function. Several models and hypotheses are proposed to differentiate research aiming to elucidate how physical activity and obesity work independently or together in affecting cognitive function. The review comprises four sections. In the first section, the terminology for the primary variables is explained. The second section briefly describes four conceptual models related to physical activity, obesity, and cognitive function, and these include independent, overlapping, moderation, and mediation models. The third section reviews empirical studies exploring the relationships amongst physical activity, obesity, and cognitive function and then categorizes these studies as testing one of six hypotheses based on the previously outlined models. The final section presents a discussion with conclusions drawn from the current research and recommendations for future research directions.

2 Terminology for the Primary Variables

The primary variables included in the current review are two independent/predictor variables, physical activity and obesity, and a dependent/criteria variable, cognitive function.

Physical activity is defined as "*any bodily movement produced by the contraction of skeletal muscles that results in a substantial increase in caloric requirements over resting energy expenditure*" [23]. Exercise is defined as "*a type of physical activity consisting of planned, structured, and repetitive bodily movement done to improve and/or maintain one of more components of physical fitness*" [23]. Although physical activity is defined more broadly than

exercise and includes unstructured activities, whereas exercise is more narrowly defined and refers to structured exercise training, physical activity and exercise have several defining characteristics in common. In particular, frequency (*F*), intensity (*I*), time/duration (*T*), type/mode (*T*), total volume/amount (*V*), and progression (*P*), which collectively compose the FITT-VP principle, have been proposed as characteristics of an exercise prescription [23, 24] and can also be used to describe physical activity behaviors. Another term related to physical activity and exercise is physical fitness, which is defined as "*a set of attributes or characteristics individuals have or achieve that are related to their ability to perform physical activity*" [23]. Typically, aerobic fitness is indexed as maximal or peak oxygen uptak$_e$. In the current review, physical activity and exercise are considered interchangeable terms.

The definition of obesity is based on the level of body mass index (BMI), a value of body mass (in kilograms) divided by the square of the body height (in meters). According to the World Health Organization, adults aged 20 years or older with a BMI between 25 and 29.9 kg/m^2 and a BMI > 30 kg/m^2 are classified as overweight and obese, respectively [25, 26]. This classification has been commonly used to define the prevalence of obesity worldwide [1].

Cognitive function, also known as cognition, is a comprehensive term describing the mental processes of knowing. Although cognitive function comprises many aspects, these aspects differ depending on the framework established. For example, using factor analyses, Carroll [27] concluded that the categories of cognitive function include fluid intelligence, crystallized intelligence, general memory and learning, visual perception, retrieval ability, and processing speed. In research on physical activity and cognition, cognitive function is often operationalized as basic information processing and executive function [14, 28, 29]. Basic information processing involves only limited resources, whereas executive function, a higher level of cognitive function, is believed to represent processing that requires a greater amount of cognitive control. That is, executive processes are described as involving inhibition, cognitive flexibility, updating, or planning, are used to appropriately guide purposeful or goal-directed behavior, and are typically required when performing in a novel environment [9, 30, 31].

3 Conceptual Models

The models being considered all involve three variables (physical activity, obesity, and cognitive function) with physical activity and obesity considered to be predictive factors and cognitive function considered the outcome variable. As a variety of relations can be derived from three or more variables [32, 33], it is not our goal to address all possibilities. Rather, this section describes four models that we believe are guiding research in this area either because the models appropriately address a possible association among physical activity, obesity, and cognitive function or because current empirical studies have directly or indirectly explored these models. These models are categorized according to two dimensions: (1) the correlation between the two predictive factors and (2) the temporal precedence of the two predictive factors (Table 1). Specifically, models of independent, overlapping, moderation, and mediation are proposed (Fig. 1). General descriptions of these models are provided with A and B representing the two predictive factors and C representing the outcome variable.

Table 1. Relationships between factors A and B for each model

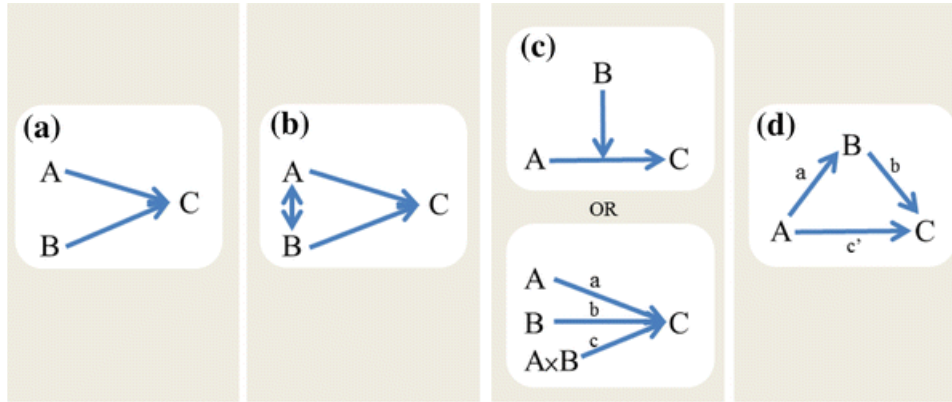| Relationship between factors A and B	Model			
	Independent	Overlapping	Moderator	Mediator
Correlated	No	Yes	No	Yes
Temporal precedence	No	No	Yes	Yes

Figure 1. Illustration of four models for the effect of the relation between two factors on an outcome variable: **a** A and B are independent factors that affect C; **b** A and B are overlapping factors that affect C; **c** B is a moderator of A's effect on C; and (**d**) B is a mediator of A's effect on C. The *lower-case letters* represent paths. In **c**, the level of A affects/predicts the variance of C (path a), the level of B affects/predicts the variance of C (path b), and the product or interaction of levels of A and B affects/predicts the variance of C (path c). In (**d**), the level of A affects/predicts the variance of B (path a), the level of B affects/predicts the variance of C (path b), and the causal/prediction chain shows no significant effects after controlling for paths a and b (path c′)

3.1 Independent Model: A and B Are Independent Factors That Affect C

The independent model is illustrated in Fig. 1a. The independent model assumes that both factors (A and B) are co-dominant in affecting the outcome variable (C). However, the temporal precedence of A and B cannot be identified in the independent model. Additionally, A and B are assumed to be uncorrelated variables, at least to the extent that the empirical studies provide no information regarding the correlation between A and B.

3.2 Overlapping Model: A and B Are Overlapping Factors That Affect C

The overlapping model is illustrated in Fig. 1b. The operational definition of the overlapping model is similar to that of the previous model in which A and B are co-dominant in affecting C and neither A nor B can be identified as exerting temporal precedence. However, to meet the criteria of the overlapping model, the study must have employed correlation analysis to establish a relationship between A and B.

3.3 Moderator Model: B Is a Moderator of the Effect of A on C

The moderator model is illustrated in Fig. 1c. A moderator is a third variable (B in this case) that may be involved in the relation between an independent variable/predictor (A in this case) and a

dependent/criterion variable (C). Specifically, a moderator is defined as a variable that "*changes the sign or strength of the effect of an independent variable on a dependent variable*" [34]. Baron and Kenny [35] defined a moderator as a "*variable that partitions a focal independent variable into subgroups that establish its domains of maximal effectiveness in regard to a given dependent variab*le (p. 1173)*"*. In the moderator model, although A can be uncorrelated with B, A is expected to temporally precede B [32].

Figure 1c illustrates two typical diagrams representing a single moderator model. The upper part of Fig. 1c provides a typical conceptual display of a moderator model; however, the lower part of the figure, involving three pathways, is useful to show how to statistically test moderation.

Path a: The level of A affects/predicts the variance of C.
Path b: The level of B affects/predicts the variance of C.
Path c: The product or interaction of levels of A and B affects/predicts the variance of C.

Although the significant effects in paths a and b are typically observed in this model, they do not have to be significant for a moderator to meet the necessary criteria. That is, to be a moderator, only path c must be significant. Because path c represents the interaction of A and B, a moderator effect can also be considered an interaction effect. Notably, the upper portion of Fig. 1c exhibits the hierarchical rank of the B function over A, reflecting that B serves as the moderator of the effects of A on C.

3.4 Mediator Model: B Is a Mediator of the Effect of A on C

The mediator model is illustrated in Fig. 1d. A mediator is another type of third variable that may be involved in the relation between an independent variable/predictor (A in this case) and a dependent/criterion variable (C). Specifically, a mediator is an intermediate, qualitative, or quantitative variable (B in this case) that causes or directly predicts the effect of an independent variable (A) on a dependent variable (C), with A causing B and B causing C [34]. That is, in terms of temporal position, A is expected to occur before B, and B occurs before C. This is also the main characteristic distinguishing a mediator from a moderator. That is, the mediator is caused by the antecedent whereas the moderator is temporally independent of factor A. A mediator can be described as "*the generative mechanisms through which the focal independent variable is able to influence the dependent variable of interest* [35] "*. In the mediator model, A is not only expected to correlate with B but also to precede B temporally [32].

An examination of a mediator provides information about how or why an effect occurs. Indeed, the effect of a mediator should be considered when a strong relation between A and B is observed. Figure 1d illustrates the path diagram of a single mediator model. To be a mediator, several causal chains should be met. Statistically, a series of regressions is recommended to test for mediation [34, 35, 36].

Path a: The level of A affects/predicts the variance of B.
Path b: The level of B affects/predicts the variance of C.
Path c: The causal/prediction chain shows no significant effects when paths a and b are controlled for.

4 Literature Associated with the Models

In this section, we review empirical studies testing the combined effects of physical activity and obesity on cognitive function based upon the previously outlined models. Studies were identified by using electronic databases including PubMed, Google Scholar, and ScienceDirect. Given that the combined influence of physical activity and obesity on cognitive function has only been considered in recent years, the search covered the period of 15 years prior to September 2015. The search terms related to physical activity included *physical activity*, *exercise*, and *fitness*; those related to obesity included *obese*, *obesity*, *overweight*, *weight status*, *body mass index*, *bioelectrical impedance*, *waist circumference*, and *skinfold measurement*; and those related to cognition included *cognition*, *cognitive function*, *cognitive performance*, *executive control*, and *executive function*. The search criteria excluded studies published in languages other than English, studies examining acute exercise (i.e., a single bout of exercise), and studies examining fitness as a proxy for physical activity. Additionally, studies were entered into the analysis stage if variables related to physical activity, obesity, and cognition were established as primary or at least secondary variables.

Though the search process, 16 studies were identified as meeting the inclusion criteria, and they were categorized according to one of six hypotheses based upon the four previously described models (Table 2; Fig. 2). One limitation regarding the categorization of these studies should be acknowledged. Given their diverse purposes and methodological designs, studies rarely met the precise criteria of the models. Therefore, we categorized the studies based on the aforementioned criteria of the correlation and temporal precedence (Table 1) and upon the specific hypothesis of the models that was most appropriate for a specific empirical study.
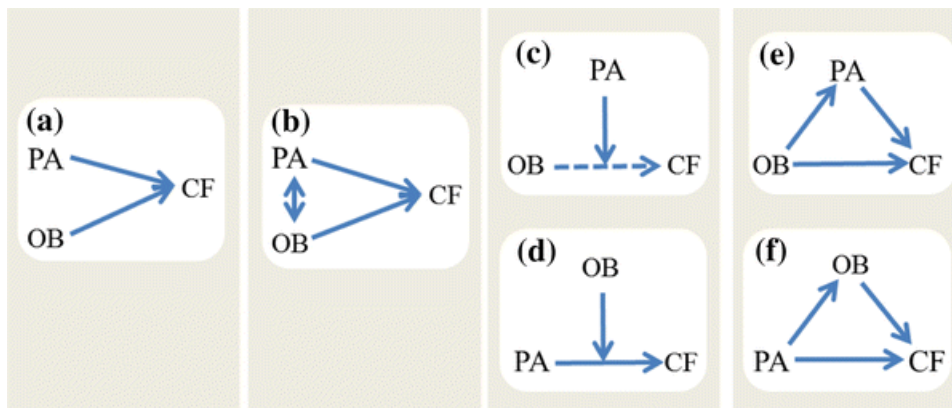

Figure 2. Illustration of six hypotheses based on independent, overlapping, moderator, and mediator models for the effect of the relation between physical activity (PA) and obesity (OB) on cognitive function (CF): (**a**) independent model, PA and OB are independent factors that affect CF; (**b**) overlapping model, PA and OB are overlapping factors that affect CF; (**c**) moderator model, PA is a moderator of OB's effect on CF (the broken line indicates that the relationship between OB and CF was not directly tested in studies included in this review); (**d**) moderator model, OB is a moderator of PA's effect on CF; (**e**) mediator model, PA is a mediator of OB's effect on CF; and (**f**) mediator model, OB is a mediator of PA's effect on CF

Table 2. Studies exploring the relationship between physical activity and obesity on cognition based upon six hypotheses from four conceptual models

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
Independent model Hypothesis 1						
Katz et al. [37] USA	CS	N = 138 SLE (F = 100 %) Age = 47.8 ± 12.5 years Percentage of obese participants: BMI (≥30): 30 % WC (≥84.5 cm): 48 %	PA measure: IPAQ	BMI DXA WC	Episodic memory: CVLT-II RCFT EF: COWAT DKEFS VF-Le DKEFS Car DKEFS CWI DKEFS TMT	Model with BMI + physical inactivity: physical inactivity associated with EF impairment (OR: 9.1 [1.8, 46.7]) Model with DXA + physical inactivity: Physical inactivity associated with EF impairment (OR: 9.4 [1.7, 52.8]) DXA-defined obesity associated with EF impairment (OR: 14.8 [1.4, 151.0]) Model with WC + physical inactivity: physical inactivity associated with EF impairment (OR: 8.4 [1.6, 44.3])
Napoli et al. [38] USA	RCT Groups: CG DG DEG EG	N = 107 OB OA (F = 62.6 %) Age = 69 ± 4 years Weight status (BMI) of groups: CG: 37.3 ± 4.7 DG: 37.2 ± 4.5 DEG: 37.2 ± 5.4 EG: 36.9 ± 5.4	PA program: DEG and EG: 90-min exercise program Frequency: 3 days/week, Duration: 52 weeks	BMI	3MS TMT A/B WFT	Cognitive improvement: 3MS: DEG ≅ EG > DG > CG TMT A/B: DEG > EG ≅ DG ≅ CG WFT: DEG ≅ EG > DG ≅ CG
Overlapping model Hypothesis 2						
Kerwin et al. [39] USA	CS	N = 8745 postmenopausal women Age = 65–79 years Percentage of obese participants: BMI (≥30): 29.27 %	PA measure: Self-report of frequency and duration of four speeds of walking and three other activities	BMI WC WHR	3MSE	PA inversely correlated with cognitive function PA inversely correlated with BMI Women with smaller WC: negative association between BMI and cognitive function Women with highest WC: positive association between BMI and cognitive function Women with lower WHR: negative association between BMI and cognitive function

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
						Women with highest WHR: positive association between BMI and cognitive function

Moderator model
Hypothesis 3: physical activity is a moderator

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
Cancela Carral and Ayan Perez [44] Spain	RCT Groups: Calisthenics Strength	N = 62 OA (F = 100 %) Age = 68.4 ± 3.4 years Weight status (BMI) of groups: Strength: 28.81 ± 3.61 Calisthenics: 29.96 ± 3.98	PA program: calisthenics group: exercise in water + calisthenic exercise Strength group: exercise in water + strength training Frequency: 5 days/week Duration: 5 months	BMI	MMSE	Cognitive improvement: MMSE: Strength group ≅ calisthenics group
Davis et al. [43] USA	RCT Groups: CG High-dose EG Low-dose EG	N = 94 OW children (F = 59.6 %) Age = 9.2 ± 0.84 years Weight status of participants: BMI: 25.8 ± 4.0 BMI-z: 2.1 ± 0.4	PA program: High-dose EG: 40 min exercise Low-dose EG: 20 min exercise Frequency: 5 days/week Duration: 15 weeks PA measure: Questionnaire	BMI BMI-z	CAS	Cognitive improvement: CAS (planning): High-dose EG > CG
Davis et al. [40] USA	RCT Groups: CG High-dose EG Low-dose EG	N = 171 OW children (F = 56.0 %) Age = 9.3 ± 1.0 years Weight status of participants: BMI: 26.0 ± 4.6 BMI-z: 2.1 ± 0.4	PA program: High-dose EG: 40 min exercise Low-dose EG: 20 min exercise Frequency: 5 days/week Duration: 13 weeks	BMI BMI-z	Anti-saccade task CAS WJTA-III	Cognitive improvement: CAS (planning): High-dose EG > low-dose EG > CG WJTA-III (broad math cluster): High-dose EG > low-dose EG > CG Changes in cerebral activation: Anti-saccade task: EG had higher activation in bilateral prefrontal cortex and lower activation in bilateral posterior parietal cortex
Krafft et al. [41] USA	LD Groups: CG EG	N = 18 OW children (F = 50.0 %) Age = 8–11 years Weight status of participants: BMI: ≥85 % percentile	PA program: EG: 40 min/day aerobic exercise Frequency: 5 days/week Duration: 8 months	BMI	CAS BRIEF	Cognitive improvement: CAS: CG ≅ EG BRIEF: CG ≅ EG
Krafft et al. [42]	RCT	N = 43 OW children	PA program:	BMI	Anti-saccade task	Changes in cerebral activation:

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
USA	Groups: EG CG	(F = 65.2 %) Age = 8–11 years Weight status of participants: BMI ≥85 % percentile	EG: 40 min/day aerobic exercise Frequency: 5 days/week Duration: 8 months	DXA	CAS Flanker task	Anti-saccade task: EG had lower activation in precentral gyrus and posterior parietal cortex CG had higher activation in precentral gyrus and posterior parietal cortex Flanker task: EG had higher activation in left medial frontal, superior and middle frontal gyrus, superior temporal gyrus, cingulate gyrus, and insula CG had lower activation in left medial frontal, superior and middle frontal gyrus, superior temporal gyrus, cingulate gyrus, and insula
Moderator model: Hypothesis 4: obesity is a moderator						
Crova et al. [45] Italy	RCT Groups: G-led S-led	N = 70 OW children (F = 50.0 %) Age = 9.6 ± 0.5 years Weight status (BMI) of groups: G-led: 19.3 ± 3.6 S-led: 18.9 ± 3.2	PA program: G-led: 1 PE class S-led: PE class + 2 training classes Duration: 21 weeks	BMI	RNG	Cognitive improvement: RNG (pre-post difference in inhibition of mental routines): Overweight S-led > overweight G-led Overweight S-led > lean S-led Overweight G-led ≅ lean G-led
Galioto et al. [48] USA	CS	N = 85 BSP (F = 68.6 %) Age = 43.3 ± 11.0 years Weight status of participants: BMI: 46.8 ± 6.7	PA measure: MVPA RAPA	BMI	IntegNeuro cognitive test battery: Attention EF Language Memory	Relationships between PA and cognitive function (after adjustment for BMI): Attention: MVPA and RAPA negatively associated with performance EF: RAPA negatively associated with performance Memory: RAPA negatively associated with performance
Galioto Wiedemann et al. [46] USA	CS Groups: Lean OB	N = 72 YA (F = 55.6 %) Weight status of groups (BMI): Lean: 18.5–24.9 OB: > 30	PA measure: IPAQ	BMI	GNG RT RMCPT RT SCPT	Relationships between PA and cognitive function: GNG RT (lean group): IPAQ and total METs negatively associated with performance GNG RT (OB group): IPAQ and total METs positively associated with performance GNG errors (lean group):

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
						IPAQ and total METs positively associated with performance RMCPT RT (lean group): IPAQ negatively associated with performance SCPT (lean group): IPAQ negatively associated with performance
Langenberg et al. [47] Germany	CS	$N = 71$ pre-BSP ($F = 77.5$ %) Age = 41.4 ± 11.9 years Weight status of participants: BMI: 46.9 ± 6.0	PA measure: Mean steps per minute	BMI	IGT CBTT AVLT	Relationship between BMI and cognitive function: BMI was negatively correlated with CBTT Relationships between PA and cognitive function: No association between PA and measures of IGT/CBTT/AVLT
Ruiz et al. [49] Spanish	CS	$N = 1820$ adolescents ($F = 52.6$ %) Age = 13.0–18.25 years	PA measure: Whether participating in PA during leisure time or not	BMI	SRA-TEA	Relationship between BMI and cognitive function: SRA-TEA: BMI not associated with performance Relationship between PA and cognitive function: SRA-TEA: PA associated with better cognitive performance
Mediator model: Hypothesis 5: physical activity is a mediator						
Dore et al. [50] USA	CS	$N = 917$ ($F = 59$ %) Age = 23–98 years WC (M) = 102.3 ± 13.2 WC (F) = 90.7 ± 14.5 WHR (M) = 0.945 ± 0.061 WHR (F) = 0.834 ± 0.077	PA measure: MET hours/week	WC WHR	Global composite MMSE Verbal memory Visual spatial organization Scanning and tracking Working memory Similarities	Negative association between WC and WHR and all measures of cognitive performance Positive association between PA and all measures of cognitive performance PA attenuated the relationship between WC and measures of cognitive performance Only the relationship between WC and similarities test remained significant after adjusting for PA
Mediator model Hypothesis 6: obesity is a mediator						
Dannhauser et al. [52] UK	LD	$N = 67$ MCI OA ($F = 42.0$ %) Age = 73.9 ± 8.3 years Weight status of participants: BMI: 26.3 ± 3.6	PA program: 30–45 min exercise Frequency: 3 days/week Duration: 12 weeks	BMI	MMSE TMT A/B LFT Category fluency DST	Cognitive improvement: DST (backward): 12-week intervention > pre-intervention 12-week intervention > baseline DST(forward): 12-week intervention > baseline

Study	Design	Population characteristics[a]	PA program, frequency, duration, and measures	Obesity measures	Cognitive tasks	Main results
						LFT: 12-week intervention > baseline Category fluency: 12-week intervention > pre-intervention
Smith et al. [51] USA	RCT Groups: DASH DASH + WM UDC	N = 124 HBP OW adults (F = 63.7 %) Age = 52 ± 9.6 years Weight status of participants: BMI: 32.8 ± 3.8	PA program: DASH + WM: 30 min aerobic exercise Frequency: 3 days/week Duration: 4 month	DXA	EFML: TMT A/B Stroop DST VF VPA COWAT Psychomotor speed: Ruff 2 and 7 test Digit Symbol Substitution test	Cognitive improvement: EFML (TMT A/B, VPA and Stroop): DASH + WM > UDC (improvement in DASH + WM was mediated by VO_{2max}) Psychomotor speed (Ruff 2 and 7 test): DASH > UDC DASH + WM > UDC (improvement in DASH + WM was mediated by weight loss)

[a]Age values are mean ± standard deviation except where otherwise stated. [] = 95 % confidence interval

Abbreviations for intervention or group: *CG* control group, *CS* cross-sectional design, *DASH* Dietary Approaches to Stop Hypertension alone, *DASH + WM* Dietary Approaches to Stop Hypertension combined with behavioral weight management program, *DEG* diet and exercise group, *DG* diet group, *EG* exercise group, *F* female, *G-led* generalist-led curricular physical education group, *LD* longitudinal design, *3MSE* modified MMSE, *OA* older adults, *PA* physical activity, *PE* physical education, *RCT* randomized controlled trial, *S-led* specialist-led enhanced physical education group, *UDC* usual diet control, *YA* young adults

Abbreviations for medical conditions: *BSP* bariatric surgery patients, *HBP* high blood pressure, *MCI* mild cognitive impairment, *OB* obese, *OW* overweight, *SLE* systemic lupus erythematosus

Abbreviations for PA or weight assessment: *BMI* body mass index (kg/m^2), *BMI-z* body mass index z-score, *DXA* dual-energy X-ray absorptiometry, *IPAQ* International Physical Activity Questionnaire, *MET* metabolic equivalent, *MVPA* moderate-vigorous physical activity, *RAPA* rapid assessment of physical activity, *VO2 max* maximal oxygen uptake, *WC* waist circumference, *WHR* waist-to-hip ratio

Abbreviations for cognitive task assessment: *3MS* Modified Mini-Mental State Examination, *AVLT* Auditory-Verbal Learning Test, *BRIEF* Behavioral Rating Inventory of Executive Function, *CAS* Cognitive Assessment System (Planning, Attention, Simultaneous and Successive processing scales), *CBTT* Corsi Block Tapping Test, *COWAT* Controlled Oral Word Association Test, *CVLT-II* California Verbal Learning Test-Second Edition, *DKEFS CWI* Delis–Kaplan Executive Function System Color-Word Interference test, *DKEFS Car* Delis–Kaplan Executive Function System Card-Sorting test, *DKEFS TMT* Delis-Kaplan Executive Function System Trail-Making Test, *DKEFS VF-Le* Delis-Kaplan Executive Function System Verbal Fluency subtest (Letter Fluency), *DSS* digit symbol substitution, *DST* digit span test, *EF* executive function, *EFML* executive function-memory-learning, *GNG* Go/No-Go task, *GNG RT* Go/No-Go task reaction time, *HVOT* Hooper Visual Organization Test, *HVLT* Hopkins Verbal Learning Test, *IGT* Iowa Gambling Task, *LFT* Letter Fluency Task, *LMR* logical memory recall, *MMSE* Mini-Mental State Examination, *MR* matrix reasoning, *RCFT* Rey Complex Figure Test Copy Trial, *RMCPT RT* Running Memory Continuous Performance Task Reaction Time, *RNG* random number generation (inhibition of mental routines and working memory updating), *SCPT* Standard Continuous Performance Task, *SRA-TEA* Science Research Associates-Test of Educational Ability, *TMT A/B* Trail Making Test A and B, *VPA* verbal paired association, VF verbal fluency, *VRR* visual reproduction recall, *WFT* Word Fluency Test, *WJTA-III* Woodock–Johnson Tests of Achievement III (Broad Reading and Broad Math clusters)

4.1 Independent Model

Hypothesis 1: physical activity and obesity are independent factors that affect cognitive function. This model assumes that physical activity and obesity independently affect cognitive function, with no correlation or temporal precedence between physical activity and obesity (Fig. 2a). Two studies were best described by this model [37, 38].

Focusing on women who were expected to be vulnerable to cognitive impairment because of having systemic lupus erythematosus, Katz et al. [37] observed that both physical activity and obesity were significantly and independently associated with cognitive dysfunction. Specifically, women who were considered inactive (<600 metabolic equivalent min/week) showed more cognitive impairment on the total cognitive battery and on memory and executive function than women considered active. Impaired cognitive functions were also observed between women who were considered to be obese (BMI > 30 kg/m^2) and women who were not obese. Further multivariate logistic regression analyses confirmed that when entered together, both inactivity and obesity were significantly associated with executive dysfunction, even after adjusting for potential covariates (e.g., education, oral glucocorticoid use, depression). Last, when interaction terms for physical activity and obesity were included in the analyses, none of the interaction terms were significant, suggesting that the effects on cognition were independent.

Similar results were observed in a study employing a 1-year RCT. Napoli et al. [38] randomly assigned frail and obese adults to one of four interventions: (1) diet (energy deficits of 500–750 kcal per day), (2) exercise (90 min of flexibility, aerobic, resistance, and balance exercises), (3) diet and exercise, and (4) control. After the intervention, the three treatment groups had better scores on multiple cognitive tasks than the control group, with more improvements for the diet and exercise group and the exercise-only group relative to the diet-only group. Stepwise multiple regression analysis showed that exercise and weight loss were independent predictors of cognition. That is, obesity-related indices including insulin sensitivity and C-reactive protein predicted cognitive change in the diet group, whereas physical activity-related indices of aerobic fitness and strength predicted cognition change in the exercise group.

4.2 Overlapping Model

Hypothesis 2: physical activity and obesity are overlapping factors that affect cognitive function. This model assumes that physical activity and obesity jointly affect cognitive function but that there is no temporal precedence between physical activity and obesity (Fig. 2b).

One study was categorized as fitting this model. Kerwin et al. [39] examined the relationship between weight (i.e., BMI and waist-hip ratio) and cognitive performance in a large sample of postmenopausal older (aged 65–79 years) women ($n = 8745$), where several covariates (e.g., exercise, waist circumference, hypertension, heart disease) were included in the analysis. When looking at relationships across the entire sample, exercise was not only associated with lower BMI, but was also related to better cognitive performance; while larger waist circumference and higher BMI were associated with worse cognitive performance. These findings support the viewpoint of the overlapping model.

4.3 Moderator Model

This model assumes a theoretical or statistical temporal precedence between the two factors (i.e., physical activity and obesity) as they affect cognitive function, with one of the two factors moderating the prediction or causal chain between the other factor and cognitive function. Given that both physical activity and obesity could act as moderators, the current moderator model includes two possible hypotheses. That is, physical activity as a moderator of obesity's effect on cognitive function (hypothesis 3) would suggest that the effects of obesity on cognitive function are different depending upon physical activity. Obesity as a moderator of physical activity's effect on cognitive function (hypothesis 4) would suggest that the effects of physical activity on cognitive function are different depending upon obesity.

Hypothesis 3: physical activity is a moderator of obesity's effect on cognitive function. No study specifically met the full criteria for this model (Fig. 2c). That is, the moderating effect of physical activity on the direct influence of obesity on cognition has not been tested. There were studies, however, that were designed specifically to test the effect of physical activity on cognitive function in obese samples based upon the assumption that obesity is associated with impaired cognitive function. These studies are included in this discussion with the relationships illustrated in Fig. 2c with a "dotted line" between obesity and cognition indicating that this relationship was not tested in these studies. In the end, this model included the largest number of studies and all of them employed longitudinal interventions [40, 41, 42, 43, 44].

To elucidate the effect of physical activity on cognition, two studies examined the dose–response relationship between physical activity and cognition in overweight and obese students. Davis and colleagues [40, 43] observed that a 3-month exercise intervention facilitated executive function (i.e., planning) and mathematics achievement, increased bilateral prefrontal cortex activation, and reduced bilateral posterior parietal cortex activation in overweight children undergoing the intervention compared with a control group. Notably, linear trends between physical activity dose and performance were identified for both executive function and mathematics achievement. Cancela Carral and Ayan Perez [44] examined whether two high-intensity exercise programs influenced cognitive function in community-dwelling older women. Older overweight women ($n = 65$) were randomly assigned into either an aquatic exercise plus high-intensity strength training (strength training group) or the same exercise plus calisthenic training. The results indicated that although the strength training group had improved strength, both training groups significantly improved in cognitive function, suggesting the beneficial effect of exercise on cognition regardless of exercise modality in an older overweight sample.

The role of physical activity as a moderator was examined in longitudinal studies conducted by Krafft and colleagues [41, 42], who examined an 8-month exercise intervention with several types of cognitive functions (e.g., anti-saccade, flanker tasks) as well as the relation among exercise, brain activation, and brain structure in less fit children who were overweight or obese. Although the two (group: exercise, control) by two (time point: pre-test, post-test) analysis of variance failed to show an interaction effect for either cognitive task, an interaction of group by time was observed for brain activation. Specifically, lower activation in the precentral gyrus and posterior parietal cortex during anti-saccade tasks and higher activation in the anterior cingulate and superior frontal gyrus during flanker tasks were observed in the exercise group compared

with the control group [42]. A similar interaction effect of group by time on the white matter integrity of the superior longitudinal fasciculus was also observed [41]. These findings suggest that the moderator role of exercise may be present when more sensitive imaging techniques are used in children who are overweight or obese.

Hypothesis 4: obesity is a moderator of physical activity's effect on cognitive function.
Hypothesis 4 posits that obesity plays the role of moderator in the relation between physical activity and cognitive function (Fig. 2d). One study employing a RCT design [45] and four studies employing cross-sectional designs [46, 47, 48, 49] are categorized as testing hypothesis 4.

In a study of college students, the positive relation between more self-reported physical activity and better inhibitory control, sustained attention, and vigilance was observed in lean (BMI 18.5–24.9 kg/m^2) but not in obese (BMI > 30 kg/m^2) participants [46]. Galioto et al. [48] examined the correlation between physical activity and cognitive function in morbidly obese individuals eligible for bariatric surgery, where analyses were conducted for the full group (i.e., average BMI 46.8 kg/m^2) and for the subgroup of even more obese individuals (i.e., average BMI 48.6 kg/m^2). The results revealed a weak correlation between self-reported physical activity and cognition (e.g., executive function, attention, memory) after adjustments for BMI in the full group; however, no correlation between objectively reported physical activity and cognition was observed when examining the even more obese subgroup. These studies suggest that the positive relationship between physical activity and cognitive function is moderated by weight status.

To further elucidate the effect of physical activity on cognition, Crova et al. [45] focused on weight status and physical activity. They compared inhibition and working memory between two physical activity programs in children categorized as lean or overweight. One of the physical activity programs was a typical physical education class and the other was an enhanced physical education program that involved specialist-led activities and two additional hours of skill-based and open skill (tennis) training. Results indicated that both physical activity programs benefitted inhibition; however, overweight children, compared with lean children, had larger improvements in inhibition in the enhanced physical education program. Thus, this study also supported the role of obesity status as a moderator of the effects of physical activity on cognitive function, but in contrast to other research [46, 48] this study reported greater cognitive benefits for the overweight group.

Two studies have also found that obesity fails to moderate the relationship between physical activity and cognition. Langenberg et al. [47] examined the relationship between physical activity behavior, BMI, and neurocognitive performance in patients prior to bariatric surgery. Their analyses indicated that although there is an inverse correlation between physical activity and BMI, BMI did not moderate the relationship between physical activity and cognitive performance Similarly, by examining the relationship between physical activity, cognitive performance, and weight status in adolescents, Ruiz et al. [49] indicated that self-reported physical activity during leisure time was positively correlated with cognitive performance; however, weight status (assessed by BMI) did not moderate the relationship.

4.4 Mediator Model

This model assumes a theoretical or statistical temporal precedence between two factors (i.e., physical activity and obesity) in their effect on cognitive function, with one of the two factors mediating the prediction or the causal chain between the other factor and cognitive function. Like the moderator model, either factor could serve as the mediator. Thus, the current mediator model can have either physical activity as the mediator of obesity's effect on cognitive function (hypothesis 5, Fig. 2e) or obesity as the mediator of physical activity's effect on cognitive function (hypothesis 6, Fig. 2f).

Hypothesis 5: physical activity is a mediator of obesity's effect on cognitive function. Only one study has examined these relationships in accord with hypothesis 5. Using a cross-sectional design, Dore et al. [50] investigated the relationship between central adiposity and seven aspects of cognitive function with adjustments for cardiovascular risk factors and physical activity. The multivariate regression analyses demonstrated that central adiposity was inversely associated with cognitive performance, regardless of the anthropometric measure used (waist circumference or waist to hip ratio). The negative relationship was still revealed even after adjusting for many demographic variables (e.g., age, education, sex) and cardiovascular risk factors (e.g., high-density lipoprotein-cholesterol ratio, systolic blood pressure). Interestingly, when taking physical activity into consideration, none of the significant associations between waist-to-hip ratio and cognitive function remained. This was also true for waist circumference and cognitive performance (with the exception of performance on the similarities test). Given that physical activity was positively associated with cognitive function and negatively associated with central adiposity, the attenuation of the relationships between measures of central adiposity and cognitive performance with the inclusion of physical activity was interpreted as suggesting a mediational role of physical activity in the relationship between central adiposity and cognitive performance.

Hypothesis 6: obesity is a mediator of physical activity's effect on cognitive function. Two studies have examined the relations between the studied variables in accord with hypothesis 6. Smith et al. [51] conducted a 4-month RCT to examine the effects of diet and weight management (including exercise) on neurocognition in overweight and obese adults with high blood pressure. In all, 124 participants were assigned either a DASH (Dietary Approaches to Stop Hypertension) diet only, a DASH diet with weight management through exercise and caloric restriction, or a usual diet (the control group). Neurocognitive performance and health status were measured. Although the two DASH diet groups showed improved psychomotor speed relative to the usual diet group, only the DASH diet with weight management group exhibited better performance in executive function, memory, and learning. Additionally, the DASH diet with weight management group, but not the DASH diet only group, showed significantly improved fitness and decreased BMI. Regression results revealed that weight loss played a mediating role in explaining the effects on psychomotor speed observed for the DASH diet with weight management group.

Dannhauser et al. [52] examined the effects of multiple health-promoting activities on cognition in older adults with mild cognitive impairment. After completing the ThinkingFit program, a multimodal intervention involving physical activity and group- and individual-based cognitive stimulation for 12 weeks, participants showed improved cognition and reduced BMI relative to

the baseline. Considering the simultaneous alteration of both cognition and BMI, the authors suggested that BMI played a mediating role in the relation between physical activity and cognition. However, it should be noted that the mediator role was not actually tested in this study.

5 Discussion

Research exploring the relationship between the independent variables of physical activity and obesity and the dependent variable of cognition has typically considered only one independent variable at a time [8, 9, 10, 11, 12, 16, 17]. However, recent research has begun to consider these two independent variables within the same study. Sixteen studies that have adopted this approach were categorized relative to whether their research designs reflected independent, overlapping, moderator, or mediator models of the relationship between physical activity, obesity, and cognition. Among these studies, the moderator model was most frequently examined ($n = 10$), with mediator ($n = 3$) and independent models ($n = 2$) receiving relatively less attention, and only one study using a design that would be considered reflective of the overlapping model.

Although the two studies adopting the independent model used different research designs (cross-sectional and a RCT), both studies concluded that physical activity and obesity independently predict cognitive function [37, 38]. The assessment of physical activity- and obesity-related indexes in isolation as predictor variables is logical if one adopts the independent model as the conceptual model that best describes the relationship between physical activity, obesity, and cognitive function; however, such an approach implies no association between the two predictors, and this is unlikely given our current understanding.

Interestingly, because only one study adopted the overlapping model [39], this suggests that researchers do not view this as a viable model for explaining how the two predictors affect cognition. Perhaps this is because this model prescribes a lack of temporal precedence between physical activity and obesity, which may run counter to common belief that a lack of physical activity causes weight gain. Importantly, there is evidence supporting that the relationship works in the other direction as well. That is, longitudinal evidence with children (aged 7–10 years) indicates that a 10 % higher percent body fat at age 7 years was predictive of a small decrease in physical activity at age 10 years, but the reverse was not true [21]. Another possibility is that this model in which no temporal precedence is assigned is a sensible approach in cross-sectional studies where the primary focus is on the simultaneous effects of physical activity and obesity on cognition at a given point in time. Studies that adopt a more longitudinal approach are not likely to use this model to explain the potential combined effects.

In contrast to these first two models that have not been commonly adopted in the literature, the moderator model has been more frequently adopted with both physical activity and obesity having been tested in the role of moderator (i.e., hypothesis 3 and 4). Notably, the moderator role of physical activity is only indirectly suggested because none of the studies conducted all necessary statistical tests to assess this model. Some studies have assessed the effects of physical activity on cognition in overweight or obese groups based upon the premise that these groups would be expected to have poorer cognitive performance than normal weight individuals. Although this is an indirect approach to considering obesity as a moderator, results show that the

effect of physical activity on cognition is discernable in overweight or obese populations. Further, it should be noted that a higher dose of physical activity may have a larger effect among these obese populations than lower dose programs [40, 43, 44]. For studies that directly tested the moderating role of obesity, results were mixed with one study showing larger effects for those who were more obese [45], and two others showing that obesity did not moderate the results [47, 49]. Notably, some studies included individuals who were morbidly obese (i.e., bariatric surgery candidates), and these findings may not generalize to comparisons between normal-weight, overweight, and obese individuals.

The fact that the current literature reflects a roughly equal distribution amongst studies with physical activity or obesity serving as the moderator is interesting. One possible explanation for this lack of consistency in terms of which variable is viewed as the moderator is that this is actually reflective of limitations in statistical training rather than variance in the conceptual view of the relationship amongst the variables. In other words, it is possible that researchers have operationalized one of these variables categorically and then are choosing to make that variable the moderator in their analysis rather than letting their conceptual view of the relationship drive this distinction. Clearly, this is an important consideration because the categories that have been used to define the moderator are typically arbitrary in that we do not know cut-off points that are relevant with regard to moderating the effect. As a result, we may be negating our ability to observe significant interactions because of a failure to understand how this moderation may express over the continuum of the data. Another possible explanation for this conversion of continuous data to categorical data is that researchers may be motivated to identify ways to improve cognition for people who might be at risk for poor cognitive performance. For example, because overweight/obese children demonstrate worse cognitive performance than normal weight children [16, 17], there are clear implications of a finding that physical activity mostly benefits this group of individuals. Hence, researchers may be deciding to target groups of individuals rather than considering the continuum with respect to weight.

With regard to the mediator model, obesity has been tested as a mediator of the effects of physical activity on cognition in two studies [51, 52], while only one study considered physical activity in the role of mediator [50]. It should be noted however, that although results from these studies were interpreted as providing evidence that BMI, weight loss, or physical activity plays a mediating role, only one study used an appropriate statistical analysis to test the mediator model [51]. The lack of studies testing the hypothesis that physical activity is a mediator between obesity and cognition (hypothesis 5) likely reflects the belief that it is a lack of physical activity that results in obesity rather than the other way around. Nevertheless, there is some evidence to suggest that this relationship can also go the other direction with higher levels of percent body fat being shown to be predictive of a decrease in physical activity over time in children [21], implying that the concept proposed in hypothesis 5 is worthy of exploration.

5.1 Limitations and Future Directions

It is important to note the limitations of this review and of the extant literature. The first limitation is related to our ability to accurately categorize papers into conceptual models. That is, it was sometimes complicated to categorize precisely a study to a specific model because of the study's diverse purposes and methodologies. For example, based upon the description of the

purpose statement ("to determine if physical activity level modified the relationship between measures of central adiposity and cognitive performance", p. 348) and discussion of the findings ("the association between physical activity and cognitive function may be only partially mediated through adipose tissue", p. 348) in the paper by Dore et al. [50], it is possible to categorize this study into either hypothesis 3 of moderator models or hypothesis 6 of mediator models. As mentioned in Sects. 3 and 4, our categorization choice was consistently based upon the specific hypothesis of the model that was most appropriate for a specific empirical study, where the two dimensions (i.e., correlation and temporal precedence of the two factors) presented in Table 1 provided our primary guide and then relationships (e.g., direction of statistical analysis) among factors presented in Fig. 2 further assisted in categorizations.

Furthermore, although we used the term fitness in our searches, we only included in our review studies that included measures of physical activity or exercise and excluded studies that focused exclusively on fitness [22, 53, 54, 55, 56]. This decision was made because physical activity and exercise are behaviors and fitness is partly, but not completely, determined by these behaviors. As such, the inclusion of fitness would have dramatically increased the complexity of this review because fitness (like obesity) could be a predictor of physical activity and also an outcome of physical activity. Given the purpose of this preliminary review, we think it was logical to exclude studies on fitness. It should be noted however that studies have observed that fitness but not physical activity influences cognitive outcomes in children [57] and similar findings were observed with regard to hippocampal volume and memory in older adults [58]. Hence, future research should carefully consider the potential role of fitness in these relationships. Another reason to include a focus on fitness is that fitness is typically assessed using more objective and accurate measures than are available for measures of physical activity and exercise. Hence, fitness may be a more stable variable to influence cognition and investigators designing future studies are encouraged to include fitness in the model.

One important limitation of the extant literature is that studies examining obesity have generally used BMI as the measure of weight [39, 40, 41, 46, 47, 48, 59], and only a few studies have applied measures that consider body adiposity and fat-free mass by using dual-energy X-ray absorptiometry [37, 42] or magnetic resonance imaging, which measure visceral abdominal tissue volume [38]. Additionally, a few studies have employed waist circumference or waist-to-hip ratio to assess central adiposity [39, 50]. Although BMI is a common index of obesity, the accuracy of the index is limited when determining the percentage of body fat and lean mass [60]. This may be important because the association between obesity and cognitive dysfunction appears only when measures of dual-energy X-ray absorptiometry, not BMI, are used, implying that measures of body adiposity may assume a more primary role with respect to cognition [37]. Given that these indices of obesity may be differentially associated with measures of cognitive function, this issue should be considered in future research.

Another commonality in this body of research that can be viewed as a limitation relates to participant characteristics. Many studies have focused on special populations, such as individuals with high blood pressure [51], heart failure or bariatric surgery patents [47, 48], and individuals with systemic lupus erythematosus [37]. Although these special populations were selected because they were assumed to have cognitive dysfunction relative to the general population, no studies included in the current review directly tested this assumption. Of additional importance,

participants with these medical concerns may potentially be dissimilar from the general population with regard to other factors (e.g., nutrition, genetic factors, disease-related physical and mental conditions) that may confound the effect of the relation between physical activity and obesity on cognition. Study designs involving appropriate control groups or statistical control of covariates are required to rule out the effects of confounders.

Another relevant aspect as we review this literature relates to the large number of cognitive tasks that have been used. Multiple cognitive domains have been examined with a variety of cognitive tasks to elucidate the effects of physical activity and obesity. This is important because physical activity and obesity may differentially affect specific cognitive functions [9, 47]. For example, physical inactivity and obesity have been shown to be associated with executive function, but not memory [37]. Pontifex et al. [22] found that physical activity is associated with both inhibition and switching aspects of executive function, whereas obesity is associated with only switching. Similar findings supporting that the effects of physical activity and obesity may be task (or domain) specific were also noted by other studies [38, 48, 53, 55]. However, it appears that the types of cognitive function and tasks have been somewhat arbitrarily selected in prior research. Previous meta-analyses on physical activity and cognition have provided a classification for cognitive function based on theoretical frameworks [9, 29, 61] or underlying common cognitive demands [14, 28, 31]. In future studies, researchers are encouraged to provide a rationale supporting their selection of cognitive tasks.

The examination of studies using the moderator model is further limited because of the failure to use appropriate statistical methods to test underlying premises. In particular, most studies have only assumed a temporal precedence between the two factors, but have not directly tested this relationship. A similar limitation is evident in studies exploring mediating models in that the mediator role for physical activity and obesity has been addressed directly in only one study that used appropriate mediational analysis [51]. Furthermore, while single moderator and mediator models may be appropriate to simplify the relationship between physical activity, obesity, and cognition based upon the extant literature, more complicated models involving more factors, such as a multiple mediator model with two or more mediators [34], may also be possible. For example, Alosco et al. [62] reported that fitness, hypertension status, and type 2 diabetes status all acted as mediators of the relation between obesity and cognition. Furthermore, Etnier [63] encouraged researchers to consider that more complex models may explain the interrelations of physical activity, a third variable that could be obesity, and cognition. In particular, Etnier suggested that while a single micromediational model may explain the link between physical activity and cognition, it was more likely that multiple mediators and/or micromediational chains provide better explanations of this link. Finally, because mediators and moderators may cooperate, a moderated mediator model, which addresses the complicated relations associated with cognition, has been proposed [64, 65].

Similarly, the relationship between exercise and cognition per se might also be influenced by factors or levels associated with the independent variable. For example, dose–response relations between exercise intensity [66, 67] and cognition [40, 68] and between exercise duration and cognition [68] have been identified, suggesting that these particular aspects of exercise may influence the exercise-cognition relation. Additionally, although endurance activity and muscular activity have both been found to improve cognition [69, 70], the brain activation patterns

associated with these two types of physical activity are located in different areas of the brain [71, 72]. Thus, these findings might also imply that physical activity modality may influence the relationship [10, 65].

In addition to the four relatively simple models that have been proposed for understanding the relationships between physical activity, obesity, and cognition, other more complex models incorporating multiple mediators and moderators are also possible. Additionally, the model may be more complex because cognition may also influence physical activity or obesity, resulting in a reciprocal effect (Fig. 3). For example, lower cognitive scores indexed by processing speed, executive function, and overall cognition significantly predict low fitness levels as well as lower hyperinsulinemia and insulin sensitivity in middle-aged adults [73]. In a cross-sectional investigation, Pentz and Riggs [74] showed that executive function level in children is associated with better physical activity status, as assessed by exercising outside of school and exercising with parents, and that it predicted children's status regarding these two physical activities in a 6-month follow-up. Similarly, several domains of cognitive function exhibit an inverse correlation with obesity [16]. Indeed, studies have shown that executive dysfunction or executive function training predicts later weight loss and BMI status [75, 76]. In addition to the role of moderation and mediation that the current review proposes, these findings suggest that the relations among physical activity, obesity, and cognition may be reciprocal [77]. Further study, particularly using a longitudinal design to determine causality, is required to better document this possibility.
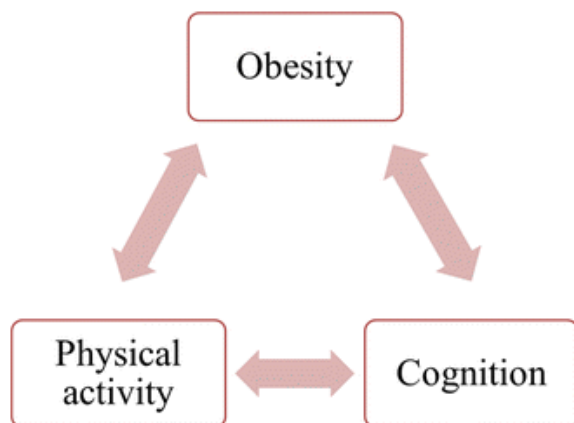

Figure 3. Illustration of reciprocal interaction model among physical activity, obesity, and cognitive function

6 Conclusions

In sum, given the known relationship between physical activity and obesity and that both of these factors have been shown to be predictive of cognitive performance, it is startling to recognize how few studies have actually explored their potential combined effects. This reductionist approach of studying a single variable in isolation is undoubtedly limiting our understanding of how these closely related factors may synergistically influence cognition. The further remarkable fact is that the extant studies have predominantly adopted a moderator model with an equal distribution amongst studies with physical activity and obesity serving as the moderator. It is also notable that only three studies have adopted a mediational model. In two cases, it was presumed that changes in physical activity influence cognition in part through the effect on weight while

the other study took the approach that obesity impacts cognition through its influence on physical activity. Clearly, research on the effects of physical activity and obesity, particularly regarding their joint effects on cognition, remains in its infancy. The models proposed herein as well as the limitations and recommendations regarding the examination of fitness as another primary factor, the measurement of obesity, consideration of participants' health status, the potential moderating role of cognition types, the use of direct testing for moderation and mediation, the employment of more complicated moderation and mediator models, and the investigation of other factors that influence the model proposed by the current studies may inform potential frameworks and guidelines for future research.

Conflicts of interest
Yu-Kai Chang, Chien-Heng Chu, Feng-Tzu Chen, Tsung-Min Hung, and Jennifer L. Etnier declare that they have no conflicts of interest relevant to the content of this review.

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