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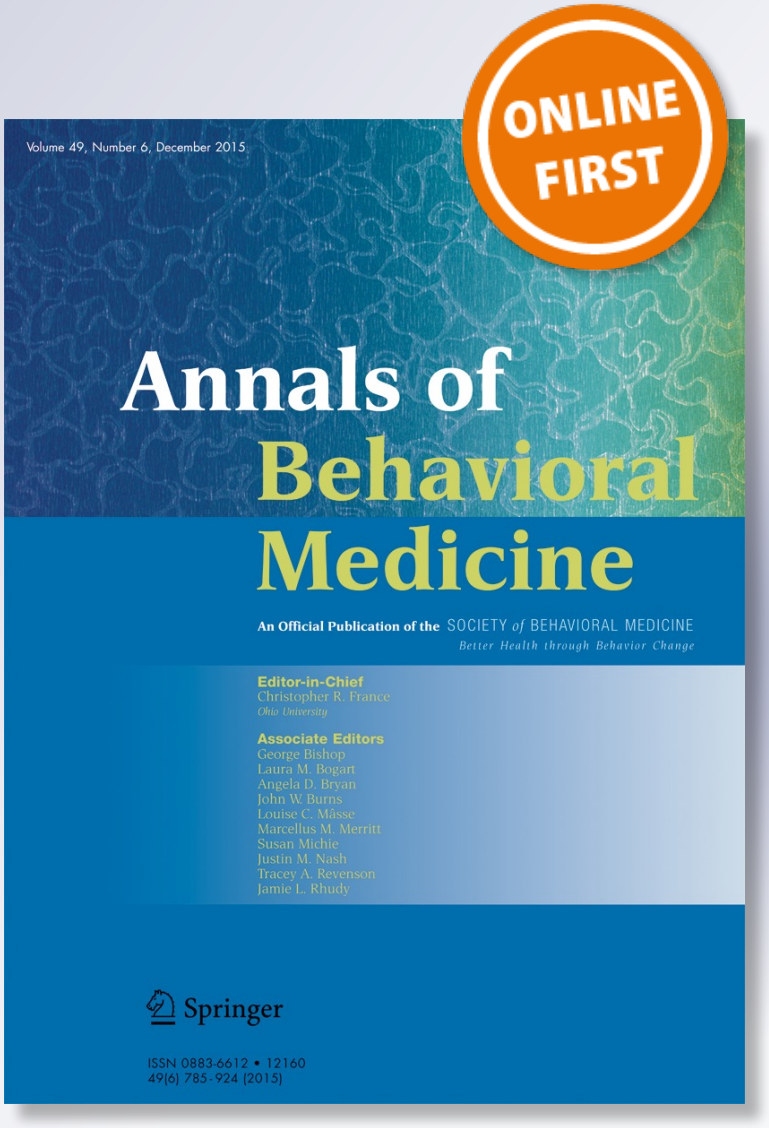

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ORIGINAL ARTICLE

Body Mass and Physical Activity Uniquely Predict Change in Cognition for Aging Adults

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Abstract
Background Physical activity and body mass predict cognition in the elderly. However, mixed evidence suggests that obesity is associated with poorer cognition, while also protecting against cognitive decline in older age.
Purpose We investigated whether body mass independently predicted cognition in older age and whether these associations changed over time.
Methods A latent curve structural equation modeling approach was used to analyze data from a sample of aging adults ($N = 8442$) split into two independent subsamples, collected over 6 years.
Results Lower baseline Body Mass Index (BMI) and higher physical activity independently predicted greater baseline cognition ($p < 0.001$). Decreases in BMI and physical activity independently predicted greater decline in the slope of cognition ($p < 0.001$).
Conclusions Our results support the obesity paradox in cognitive aging, with lower baseline body mass predicting better cognition, but less decline over time protecting against cognitive decline. We discuss how weight loss in the elderly may serve as a useful indicator of co-occurring cognitive decline, and we discuss implications for health care professionals.

Keywords Cognitive aging · Physical activity · Body mass

The world's population of older adults is growing exponentially, with an expected two billion adults over the age of 60 by 2050 [1]. Aging is associated with declines in a range of cognitive abilities including attention, executive functioning, processing speed, and episodic memory [2]. Understanding the factors that contribute to and predict age-related cognitive decline is essential in preserving quality of life in older age, keeping older adults in the workforce for a longer period of time, and minimizing health care costs. Recent research has sparked increased interest in body mass and physical activity, both of which regulate and maintain health throughout life and are associated with cognitive aging [3]. Aerobic physical activity improves cardiovascular fitness, increasing cerebral blood flow and volume, which preserves brain structure and function [4, 5]. Anaerobic resistance training maintains muscle mass and strength, and decreases white matter lesion progression, which preserves cognition as well [6–9]. In the case of body mass, increased fat storage in overweight and obese adults results in inflammation, leptin and insulin resistance, and increased risk for cardiovascular disease [10–12], all of which contribute to decreased cognitive functioning [12].

Physical activity and body mass are closely linked—physical activity and diet play a large role in determining body mass [13]. Despite their association—physical activity reduces the risk of obesity [14] and maintains body mass [15]—recent findings suggest that body mass and physical activity may become *decoupled* during aging. Greater physical activity and lower body mass predict preserved cognition during adulthood, but a decline in body mass during older age may result in negative cognitive consequences. The primary goals of this paper are to determine whether body mass independently predicts cognition in older adults and whether the

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relationship between body mass and cognition changes during older age.

Physical Activity and Cognitive Functioning

In adults over 50, physical inactivity is associated with poorer cognition roughly 2 years later [16]. Increased cardiovascular fitness improves cortical plasticity and delays the onset of age-related cognitive decline [17]. For example, 1 year of aerobic training that included stretching exercises increased memory performance and reversed 1 to 2 years of hippocampal volume loss compared to a control group [18]. In addition, a meta-analysis found a moderate effect size for aerobic fitness training with executive control processes, including planning, working memory, inhibitory processes, and multitasking, receiving the greatest gains [19].

Cognitive reserve theory suggests that physical activity—both aerobic and resistance training—increases the brain's resources and resistance to cognitive decline by promoting neurogenesis and neuronal plasticity [20]. Baseline cardiorespiratory fitness, as measured by peak oxygen consumption (VO_2 max), duration of treadmill exercise, and oxygen uptake efficiency, is associated with maintenance of attention, verbal memory, and verbal fluency across 6 years [21]. Aerobic exercise results in gains in cardiovascular measures of VO_2 max and ratings of perceived exertion [4]. In addition, aerobic fitness contributes to increased resting state cerebral blood flow—a measure of blood supply to the brain, specifically in the anterior cingulate and hippocampus, which play crucial roles in the default network and memory performance [4]. Aerobic exercise increases cerebral blood volume and perfusion in the hippocampus [5] and frontal and superior temporal lobe gray matter volume [22], which is particularly important as lower levels of cerebral blood flow result in the damage and death of neurons, and predict cognitive decline [23]. Thus, aerobic exercise improves cardiovascular fitness and increases blood flow to brain regions responsible for cognitive performance, which leads to sustained cognitive functioning with age.

Resistance training focuses on maintaining and increasing muscle mass and also counteracts age-related declines in muscle mass and reduces the risk for sarcopenia (by increasing muscle mass and strength), improving neuromuscular function and increasing motor neuron firing [6, 24, 25]. In addition, resistance training is tied to cognitive gains in executive control, memory, and attention [7, 8], and loss of skeletal muscle mass is related to lower cognition in older adults [26]. Decreases in white matter lesion progression are also observed with resistance training. For example, older women who performed twice-weekly resistance training sessions demonstrated significantly lower white matter lesion volume after a 12-month trial as compared to a balance and tone control group [9]. Inadequate caloric intake and a protein-deficient diet in older age may contribute to sarcopenia and result in reduced fat-free mass, muscle strength, and size [27, 28]. To assess the benefit of increased protein intake on the maintenance of muscle mass in older age, protein supplementation programs have been implemented alongside resistance training interventions with an overall pattern of gains in fat-free mass, but minimal added benefit in muscle mass or strength [27, 29]. Thus, resistance training may provide unique benefits for physical fitness and cognition in the elderly, with protein supplementation assisting in weight maintenance.

Physical activity also is related to decreased risk for dementia, with an 88 % decrease in risk for more active (physical activity, >4 h/week) women (>85 years) [30]. Similarly, in a sample of 1720 older adults (>65 years), people who were physically active fewer than three times per week were significantly more likely to develop Alzheimer's disease, regardless of genetic predisposition [31]. Exercise reduces age-related chronic low-grade inflammation [32], a mediator of obesity-related cognitive decline [33] that plays a role in Alzheimer's disease [34].

Despite evidence supporting the beneficial effects of physical activity on cognitive aging, null findings do exist. A longitudinal study of Australians (65–98 years) found no association between physical activity and memory performance across a 15-year period [35]. Similarly, a recent meta-analysis found no relationship between fitness and cognition in cross-sectional comparisons, but a significant negative relationship between fitness and cognition for pre-post comparisons [36]. An understanding of physical activity's effects on cognition is still unclear.

Body Mass and Cognitive Functioning

Higher body mass, frequently operationalized using the Body Mass Index (BMI), is associated with poorer cognition in adulthood. For example, middle-aged adults (32–62 years) with higher BMI demonstrated poorer cognition at baseline, as measured by word recall, digit-symbol substitution, and a selective attention task, and greater cognitive decline at a 5-year follow-up [37]. Similarly, overweight and obese adults performed worse on a range of cognitive tasks, including verbal fluency, delayed free recall, and Trail-Making Test A [38].

Body mass may influence cognition through a variety of biological pathways. Obesity is associated with increased cardiovascular risks and diseases, including diabetes, which affects cognitive processes [10]. Due to an increase in adipose tissue secretion for fat storage in obese individuals, inflammatory cytokine levels rise [39], leading to neuronal excitability [40] and an elevation in leptin [41]. Typically, increased leptin is associated with lower rates of cognitive decline [42].

However, obese individuals are more likely to develop leptin resistance [11], which counteracts its protective role in preserving cognitive function in normal weight adults [43]. Further, insulin resistance and impaired insulin regulation are highly correlated with obesity and predict cognitive deficits [12]. Excess insulin production is related to increased beta-amyloid levels, which play a role in the development of Alzheimer's disease [44]. The association between body mass and insulin-like growth factor (IGF-1) is U-shaped, with the highest levels observed in normal weight adults. Higher insulin-like growth factor predicts better task-shifting, psychomotor speed, and decreased cognitive decline [45, 46].

Obesity is also correlated with structural and functional brain changes. Compared to normal weight older adults, obese adults show frontal, anterior cingulate, hippocampal, and thalamic atrophy [47], and a decline in cerebral white matter integrity [48]. These regions are closely linked to executive functioning and memory. BMI is a strong predictor of skeletal muscle mass, which declines with age [49] and predicts cognitive performance [50]. Age-related chronic inflammation, marked by an elevation in two pro-inflammatory cytokines: interleukin-6 and tumor necrosis factor-α, is associated with and can potentially cause decreased muscle mass and function [51] and cognitive decline [52].

Despite these well-established associations, paradoxical findings suggest a shift in older age, through which higher body mass becomes *protective* and thereby preserves health and cognition [53]. Commonly referred to as the obesity paradox, higher BMI is associated with a decreased risk of death in older adults [54], despite an independent association between obesity and all-cause mortality [55]. Optimal weight seems to increase with age, reversing the relationship between obesity and cardiovascular disease [56]. For example, non-obese women (>60 years) who experienced a decline in body mass were more likely than women who maintained their weight to be hospitalized and receive home medical visits [57]. Although higher body mass during midlife predicts a 1.5–3-fold increase in the onset of Alzheimer's disease and other dementias [58], a decline in body mass or the concurrent status of underweight in older age increased the likelihood of a dementia diagnosis [59]. Furthermore, overweight adults aged 65 to 94 demonstrated better reasoning and visuo-spatial processing speed than normal-weight adults of the same age [60].

Few studies have examined body mass longitudinally, with mixed results. One study of Italians (>77 years) found higher baseline body mass increased risk for cognitive decline, as measured by the Mini-Mental State Examination [61]. In contrast, overweight and obese men experienced less steep declines in cognitive ability than normal weight adults [62]. Further work is needed to clarify the association between body mass and cognitive decline in older age and to determine whether body mass is a unique predictor of cognition over-and-above the salubrious effects of physical activity. It is possible that a lower body mass during adulthood protects against cognitive decline, whereas a decline in body mass during older age serves as a risk factor.

The Present Study

Prior research has established the importance of both body mass and physical activity in predicting later cognition. Both factors influence cognition through the preservation of muscle mass and cardiovascular function, and the minimization of negative health consequences from increased fat storage; however, a handful of studies suggest the opposite may be true for body mass, with higher BMI predicting less cognitive decline over time. To explore this paradox, and to test whether body mass and physical activity are *unique predictors* of baseline cognition and change in cognition over time, the present study examined these associations in a sample of older adults ($N = 8442$) with longitudinal data at three time points across 6 years, drawn from the Survey of Health, Ageing, and Retirement in Europe (SHARE) study, a multinational sample of older adults. Using latent curve growth modeling (LCGM), we modeled simultaneous associations of BMI and physical activity with changes in cognition over time. We hypothesized that lower BMI and greater levels of physical activity would predict higher levels of initial cognition, whereas (consistent with the obesity paradox) loss of BMI and less physical activity would both predict steeper cognition decline over time.

Methods

Participants

The SHARE dataset currently has four waves of data collection (2004–2005; 2006–2007; 2008–2009; 2011–2012): three panel waves (2004, 2006, and 2010) and one reporting retrospective life histories (2008). Participants were selected from 19 European Union countries and Israel, with over 80,000 unique participants ages 50 or older, though only 10 countries participated in all waves necessary for the current study. The average retention rate for the first four waves was 81 %. See Börsh-Supan et al. [63] for further description.

The data collection incorporated a variety of variables capturing participants' psychological status, physical health, and cognition. Only the initial participant from each household with at least two complete waves of data (at T0, T1, and T3) over 65 years old were included ($N = 8442$) in the sample. Of the original 83,540 people, 53,985 only had a single wave of data from T0, T1, and T3, and were excluded. Of those excluded, 70.43 % of the participants had been assessed at only T3. Of the 29,555 participants with two waves of data, 9723 people were identified as sharing the same household as

primary respondents and were excluded to maintain independence within the sample. Finally, of the remaining 19,832, 11, 390 were younger than 65, resulting in the final sample of 8442 adults split into two random subsamples.

Measures

Demographic Variables

The SHARE study assessed a variety of demographic variables, including age, gender, height, weight, years of education, number of chronic illnesses, and number of medications. Height was reported in centimeters. Weight was reported in kilograms. Number of chronic illnesses was based on a total of self-reported responses to the following questions, the "doctor told you that you had: a heart attack, high blood pressure or hypertension, high blood cholesterol, stroke, diabetes or high blood sugar, chronic lung disease, asthma, arthritis, osteoporosis, cancer, stomach or duodenal ulcer/peptic ulcer, Parkinson's disease, cataracts, hip fracture or femoral fracture, or other conditions." Self-reported number of medications was based on a total of "drugs for high blood cholesterol, coronary diseases, other heart disease, asthma, diabetes, joint pain, sleep problems, anxiety or depression, osteoporosis, hormonal/other, stomach burns, chronic bronchitis, or other."

Cognition

Cognition was measured using an arithmetic mean of all SHARE participants' scores on three cognitive tasks: verbal fluency, immediate word recall, and delayed word recall. Scores at each occasion were standardized against the grand mean of all cognitive functioning scores across the three waves. This accounted for differences in scaling of the measures while also allowing for variation between occasions. Verbal fluency was assessed using a semantic fluency task. Participants were asked to name as many animals correctly as possible during a 1-min period. Verbal fluency is an assessment of executive functioning, as participants must devise a strategy for recalling category exemplars. It is sensitive to alterations in executive functions [64] and has been used widely as a component of neuropsychological batteries to differentiate between healthy age-related memory change and clinically significant impairments [65]. Immediate and delayed word recall was measured using the Ten-Word Delayed Recall Test. Ten common words were presented and participants were asked to recall the words immediately and then again five minutes later. This assessment was constructed based on similar computerized word recall tasks that have been used extensively to assess immediate and delayed memory performance [66, 67]. The three-item scale showed adequate internal reliability in the current sample ($\alpha = 0.79$). Taken together, these measures provide a brief assessment of executive functioning and memory, indexing changes that may be apparent in everyday cognitive tasks.

Body Mass Index

Body Mass Index was calculated as a continuous variable, based on the following formula: $(\text{weight}/(\text{height})^2) \times 10{,}000$. Height was only measured at the first time point, whereas weight was measured at each time point.

Physical Activity

Physical activity was measured using a single-item self-report question assessing participants' frequency of sports or activities that are "vigorous," including heavy housework or a job that involves physical labor. Responses to the four-point scale were coded from one to four for the responses "hardly ever, or never," "one to three times a month," "once a week," and "more than once a week," with higher scores indicating higher frequency of physical activity [16].

Data Analysis

In the current study, we evaluated the association between cognition, BMI, and physical activity over time using a latent curve growth model (LCGM). The basic LCGM included three time points (T0, T1, and T3), with T2 excluded, as it did not include the necessary measures. All structural equation models (SEMs) were run in M*plus* v. 7.2 [68] using full information maximum likelihood estimation (FIML) for missing data and simultaneous regression for all path models. Standardized regression coefficients were included to allow for direct comparison of effect sizes as the various measures were scaled differently. These values represent the amount standard deviation (SD) within-occasion change in the manifest cognitive functioning variable predicted by a 1 SD change in the predictor. The standardized values are calculated by the formula $\beta = b \times \text{SD}(x)/\text{SD}(y)$ for continuous predictors and $\beta = b/\text{SD}(y)$ for dichotomous variables. Within the LCGM, cognition's slope and intercept were estimated freely and regressed on our variables of interest, BMI and physical activity level. The intercept of cognition was predicted by T0 BMI and physical activity, whereas the slope of cognition was predicted by T0 BMI and physical activity as well as T3 BMI and physical activity (residualizing scores for each variable by their T0 values). Said differently, T3 BMI and physical activity were regressed on T0 BMI and physical activity, respectively, and the slope of cognition was regressed on the T3 variables, as displayed in Fig. 1. Age and gender were included as time-invariant covariates predicting the intercept and slope of cognition.

The main study hypothesis centered on regression of the latent curve parameters of cognition on T0 BMI and physical

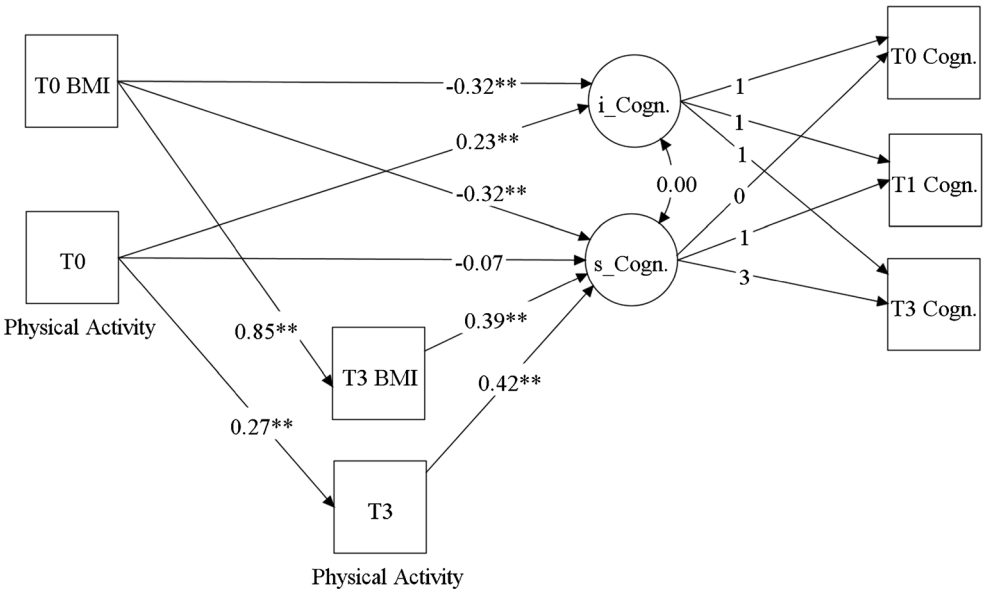

Fig. 1 Associations among the latent curve parameters for cognition and the baseline and residualized change to T3 for BMI and physical activity level among aging adults. The model includes age and gender as covariates, which were not included in the figure for ease of interpretation. The covariation between the slope and intercept of cognition was constrained to 0. All pathways represent the standardized model values. Cogn. = cognition, s_ and i_ = the slope and intercept of the construct described. ** = $p < 0.01$, * = $p < 0.05$

activity and the residualized change for both variables to their T3 scores. We identified the best-fitting LGCM for cognition by comparing nested model specifications using a chi-square difference tests ($\chi^2_{\text{Model 2}} - \chi^2_{\text{Model 1}}$ ($df_{\text{Model 2}} - df_{\text{Model 1}}$)). Elements of the original model (model 1) were constrained and estimated a second time in the nested model (model 2); if constraining different change parameters did not adversely affect model fit, we retained the more parsimonious model. Once the final model was specified, we fit this model to the second subsample to determine if the effects observed in the primary sample would replicate in this second subsample. To assess model fit, we used three main indexes of model fit: standardized root-mean-squared residual (SRMR), root-mean-squared error of approximation (RMSEA), and comparative fit index (CFI). Hu and Bentler [69] suggested that a combination of examining SRMR, supplemented with RMSEA and CFI, is a useful heuristic method to assess comparative model fit. We considered models to have relatively good fit if SRMR values <.08, RMSEA values <.06, and CFI values >.95.

Results

Table 1 displays descriptive statistics for all participants in the current study for the variables of interest estimated using FIML. Table 2 provides a correlation matrix of all variables included in the study, split by subsample.

We first constructed the unconstrained LCGM for cognition. The initial model did not provide an acceptable fit to the data, χ^2 (1, N = 4216) = 25.10, SRMR = 0.016, CFI = 0.99, RMSEA = 0.075. We then constrained the covariation of the intercept and slope cognition to 0. This improved the model fit, and the resulting model fit the data adequately, χ^2 (1, N = 4216) = 25.11, SRMR = 0.016, CFI = 0.99, RMSEA = 0.052. To address our primary research question, we first regressed the intercept of cognition on the T0 scores for BMI and physical activity. We then regressed the slope of cognition on the T0 scores for BMI and physical activity, as well as the T3 BMI and physical activity levels, which were residualized change scores from T0 BMI and physical activity. Finally, we included gender and age as two covariates predicting T0 and T3 BMI and physical activity, as well as the intercept and slope of cognition. This final model fit the data adequately, χ^2 (13, N = 4221) = 87.07, SRMR = 0.025, CFI = 0.99, RMSEA = 0.037. Table 3 displays the full standardized values of the final model, as displayed in Fig. 1.

To assess the primary hypotheses, we examined the regressions of the latent curve parameters of cognition on T0 BMI and physical activity, as well as the T3 residualized change

Table 1 Descriptive statistics for variables of interest for full sample

N = 8442	T0	T1	T3
Cognitive functioning	−0.37 ± 0.89	−0.38 ± 0.97	−0.55 ± 0.79
BMI	26.48 ± 0.88		26.17 ± 0.77
Physical activity level	2.19 ± 0.89		1.77 ± 0.77
Age	75.89 ± 0.98		
Gender	56 % women		
Height	166.25 ± 8.9		
Weight	73.1 ± 13.51		
Chronic Illnesses	2.0 ± 1.54		
Medications	1.94 ± 1.61		
Education	9.15 ± 4.46		

Data are means ± standard deviations. Age was converted to its original metric by multiplying by 10. All means and SDs were calculated using FIML

Table 2 Correlation matrix for all variables used primary and replication subsamples

	1	2	3	4	5	6	7	8	9
Primary subsample									
Cognition T0	–								
Cognition T1	0.72	–							
Cognition T3	0.65	0.67	–						
Phys Act. T3	0.25	0.26	0.32	–					
BMI T3	−0.03	−0.01	0.03	−0.05	–				
Phys Act. T0	0.27	0.27	0.27	0.32	−0.05	–			
BMI T0	−0.05	−0.04	−0.03	−0.08	0.85	−9.07	–		
Age	−0.36	−0.38	−0.44	−0.28	−0.15	−0.25	−0.12	–	
Gender	−0.05	−0.04	−0.05	−0.14	−0.04	−0.16	−0.04	0.11	–
Replication subsample									
Cognition T0	–								
Cognition T1	0.70	–							
Cognition T3	0.63	0.67	–						
Phys Act. T3	0.27	0.26	0.32	–					
BMI T3	−0.05	−0.03	0.03	−0.04	–				
Phys Act. T0	0.21	0.21	0.19	0.36	0.00	–			
BMI T0	−0.06	−0.04	−0.02	−0.08	0.82	−0.04	–		
Age	−0.32	−0.35	−0.41	−0.29	−0.17	−0.25	−0.13	–	
Gender	−0.06	−0.04	−0.01	−0.12	−0.03	−0.10	−0.02	0.08	–

Age was converted to its original metric by multiplying by 10

Phys Act. physical activity

scores. T0 BMI and physical activity independently predicted the intercept of cognition, $\beta = -0.08$, $p < 0.001$ and $\beta = 0.23$, $p < 0.001$, respectively. T0 BMI also predicted the slope of cognition, $\beta = -0.32$, $p = 0.008$, but T0 physical activity did not, $\beta = -0.07$, $p = 0.25$. Participants' baseline cognition was positively associated with their T0 physical activity level, but negatively associated with their T0 BMI score. In addition, the residualized change scores of T3 BMI and physical activity independently predicted the slope of cognition, $\beta = 0.39$, $p < 0.001$, $\beta = 0.42$, $p < 0.001$, respectively. Figure 2 visualizes these effects for BMI. In short, lower BMI is associated with better cognition at baseline, with loss of BMI over time steepening the decline in cognition and an increase in BMI over time weakening the decline in cognition. Decreases in BMI from T0 to T3 are associated with decreases in cognition, independent of BMI at T0.

To replicate the results observed in the primary subsample, we examined the model presented in Fig. 1 in the second replication subsample. We first constrained all parameters of the model to be equivalent to estimates generated in the first subsample (fully-constrained replication). This model specification provided an adequate fit in the confirmatory subsample, χ^2 (29, $n = 4221$) = 141.65, SRMR = 0.038 CFI = 0.98, RMSEA = 0.030. We then freed the constraints in the model from the estimates from the primary subsample. This significantly improved the chi-squared model fit, $\Delta\chi^2$ (16, $N = 4221$) = 51.61, $p < 0.001$. This unconstrained restricted model also fit the data adequately, χ^2 (28, $N = 4221$) = 90.04, SRMR = 0.029, CFI = 0.99, RMSEA = 0.037. This analysis suggests that the result of interest replicate in the replication subsample, though some estimates may differ between the two subsamples. For example, T0 BMI no longer predicted the slope of cognition in this replication sample. The effects of interest, however, replicated such that participants' baseline cognition was positively associated with their T0 physical activity level, but negatively associated with their T0 BMI score, and the residualized change scores of T3 BMI and physical activity independently predicted the slope of cognition. Full results of the replication subsample unconstrained model results are presented in Table 3.

Discussion

In a multinational aging sample, we explored the associations among physical activity, body mass, and cognition across a 6-year period. We specifically tested the obesity paradox and whether physical activity and body mass served as unique predictors of cognitive aging. Baseline physical activity and body mass independently predicted baseline cognition, with higher physical activity and

Table 3 Estimates for model fit and regression coefficients predicting cognition

Primary subsample			
Parameter	Mean		Variance
Cognition intercept	2.31**		0.40**
Cognition slope	0.44**		0.01**
H1 log-likelihood	−42,547.46	SRMR	0.012
No. of parameters	34	RMSEA	0.031
χ^2	180.66	CFI	0.99
Intercept of Cognition	β	95 % CI	B
T0 BMI	−0.08**	(−0.12, 0.04)	−0.01**
T0 Physical activity	0.23**	(0.19, 0.26)	0.11**
Gender	0.02	(−0.01, 0.03)	0.03
Age	−0.38**	(−0.41, 0.06)	−0.04**
Slope of cognition	0.00	(0.00, 0.00)	0.00
Slope of Cognition			
T0 BMI	−0.32**	(−0.56, 0.08)	−0.01**
T0 Physical activity	−0.07	(−0.19, 0.05)	−0.01
T4 BMI	0.39**	(0.15, 0.63)	0.01**
T4 Physical activity	.42**	(0.25, 0.59)	0.03**
Gender	0.06	(−0.04, 0.16)	0.01
Age	−0.29**	(−0.43, 0.15)	−0.00**
Replication subsample			
Parameter	Mean		Variance
Cognition intercept	2.31**		0.40**
Cognition slope	0.44**		0.01**
H1 log-likelihood	−42,547.46	SRMR	0.012
No. of parameters	34	RMSEA	0.031
χ^2	180.66	CFI	0.99
Intercept of Cognition	β	95 % CI	B
T0 BMI	−0.12**	(0.08, 0.15)	−0.18**
T0 Physical activity	0.16**	(0.12, 0.19)	0.08**
Gender	−0.03	(−0.06, 0.01)	−0.03
Age	−0.36**	(−0.40, 0.33)	−0.35**
Slope of cognition	0.00	(0.00, 0.00)	0.00
Slope of Cognition			
T0 BMI	−0.09	(0.27, 0.1)	−0.02
T0 Physical activity	−0.14*	(−0.25, −0.02)	−0.01*
T4 BMI	0.22*	(0.04, 0.41)	0.05*
T4 Physical activity	0.39**	(0.24, 0.53)	0.03**
Gender	0.16**	(0.06, 0.26)	0.03**
Age	−0.27**	(−0.40, −0.14)	−0.04**

*$p < 0.05$; **$p < 0.01$. 0 (=) indicates that the given parameter was constrained to zero

lower body mass at baseline predicting higher cognition. Change in physical activity and body mass over time also independently predicted change in cognition over time. Whereas the pattern between physical activity and cognition remained positive, with greater residualized change in physical activity at T3 (i.e., increases in physical activity over time) predicting positive change in cognition, increases in body mass also predicted positive change in cognition over time. Said differently, a decline in body mass over time predicted greater declines in cognition. These findings provide further evidence for the obesity paradox in cognitive aging, whereby a lower body mass protects against cognitive decline, but losing weight in older age—regardless of one's BMI—results in negative

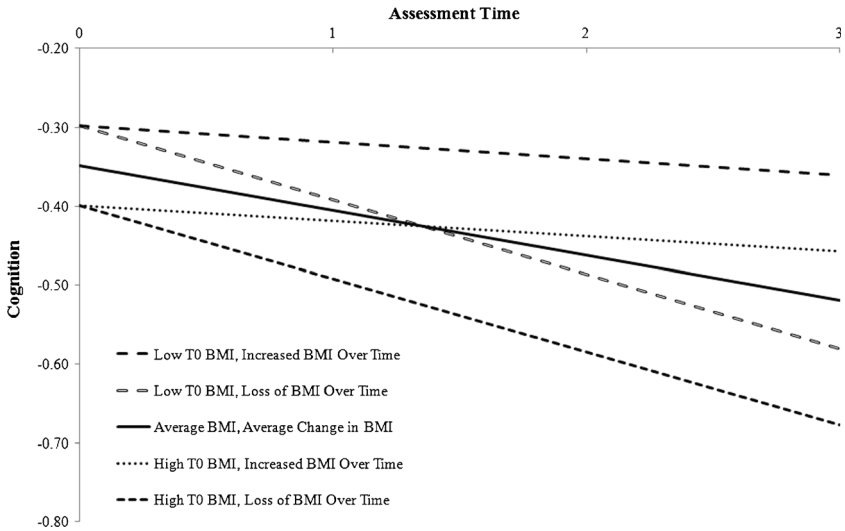

Fig. 2 Fixed effects model representing change in the slope of cognition over time in older adults of low, average, and high T0 BMI (1 SD below, average BMI, and 1 SD above, respectively). For each T0 BMI group, the slope of cognition is broken down into individuals who gain BM over time and those who lose BM over time

health consequences, including accelerated cognitive decline (see 53).

Several potential explanations for the obesity paradox exist. The survival effect suggests that obese adults with the risky accumulation of visceral fat in the abdominal region die earlier, leaving those with less risky obesity in older age groups [70]. Alternatively, third variable explanations cannot be dismissed; weight loss in the elderly may result from disease or chronic illness that negatively influences health and cognitive performance [71]. Obesity is related to increased physical dysfunction and frailty in older age [72]. However, unhealthy weight loss in this population could lead to further declines in age-related muscle mass, resulting in sarcopenia and increased frailty. Intention to lose weight may be a useful predictor of health outcome to differentiate between purposeful weight loss, through exercise and diet, and weight loss due to underlying disease processes [73]. Finally, people experiencing cognitive decline may neglect health-related behaviors, including exercise, medications, and nutritional concerns, resulting in unhealthy weight loss; in this situation, the causal link between the constructs flows from cognitive decline to reduction in body mass. Further work is needed to clarify the nature of the obesity paradox in older adults, with an emphasis on identifying the specific changes in body composition and dietary intake occurring in older adults. Despite the fact that multiple explanations exist for the paradoxical association between BMI and cognitive functioning as adults age, the present findings represent a critical *health surveillance effect*; we may not yet know the causal association between these constructs, but a decline in BMI as adults age is associated with clear decrements in cognitive functioning.

The large, representative nature of the SHARE data is a strength of the current study, but provides the statistical power to detect small and potentially meaningless effects. An important question is whether the current findings have practical significance. One method of benchmarking is comparing effects to other established predictors of the outcome of interest [74]. In the primary subsample, the average slope of cognition was −0.057, which resulted in a loss of −0.18 SD across 6 years, representing the average loss in cognition due to 6 years of chronological aging. In comparison, a 1 SD loss in BMI over the same 6 years (about 15 lbs for men, 13 lbs for women at the average height) predicted an additional change in slope of cognition of −0.037, roughly two thirds of the effect of chronological age. Said differently, men losing 2.5 lbs and women losing 2.2 lbs a year on average experience a decline in cognition approximately 1.67 times that of individuals maintaining the same weight. In the SHARE sample, 13.3 % of people lose 1 SD of weight across the course of the study. Results are similar for physical activity. A 1 SD loss in physical activity over the 6 years predicted an additional change in slope of cognition of −0.040, roughly 70 % of the effect of chronological age. This suggests a 1 point change in physical activity (e.g., moving from "hardly ever, or never" to "one to three times a month") would predict an increase in cognition equivalent to roughly 4.5 years of chronological age. In both cases, the change in body mass and physical activity that predicted the slope of cognition appeared meaningful when benchmarked against prediction by chronological age.

Another important question for understanding the present results is whether changes in cognition as measured by neuropsychological tests relate to changes in everyday functioning. Tomaszewksi et al. [65] addressed this question by comparing neuropsychological results on immediate memory, delayed memory, attention, language, executive functioning, and praxis with a performance-based scale of activities of daily living (DAFS) and a caregiver-based rating scale (IADL) in individuals with early stage Alzheimer's. The DAFS and IADL included

tasks, such as dialing a telephone, selecting shopping items, reading a clock, preparing food, and balancing a checkbook [75, 76]. A significant association existed between daily living measures and neuropsychological test scores, specifically with measures similar to the ones assessed in this study, including immediate memory and executive functioning. This suggests that the cognitive measures used in this paper are valid indicators of declines in everyday functioning in an older population, at least in those experiencing progressive declines in cognition.

The results of this study have clinical implications for the medical care of the elderly. Older adults who are encouraged by their physicians to exercise are significantly more likely to do so, particularly frail populations that may fear injury [77]. A positive attitude toward physical activity improves attendance and adherence [78]. As a result, caretakers and mental health professionals should encourage older adults to explore physical activities that they enjoy. The social component of exercise is especially important to older women [79, 80]; however, all older adults benefit from positive reinforcement and social support from friends, family members, and significant others [81]. As a result, group exercise should be encouraged as an outlet for social support that improves the stress-reducing benefits of exercise [82]. Our findings also suggest that protein supplementation may prevent potentially harmful declines in fat-free body mass and, when combined with aerobic exercise and resistance training, used as a means to preserve cardiovascular fitness, muscle strength, and cognitive function in older age. Physicians and health care professionals should incorporate this information in their feedback and recommendations to patients, particularly older adults who show a pattern of weight loss and increased frailty.

Additionally, the direct relationship between weight loss and declines in cognition may be useful for primary care physicians as an indicator that further assessment of cognition is needed. If older adults experience rapid declines in weight, or gradual declines that occur over several years, physicians should be cognizant of the potential for concomitant cognitive decline: Weight loss may be an early leading indicator of biological changes related to impaired brain function, regardless of BMI. It is essential that further research identify whether actively attempting to lose weight in older age also is associated with greater declines in cognition. It is possible that declines in body mass and cognition reflect frailty and lost health, rather than controllable weight factors. Equally possible, physically active older adults may not be protected from cognitive decline if declines in body mass also occur. As noted above, our analyses do not permit a definitive conclusion that declines in body mass precede and cause declines in cognition; the reciprocal route is plausible—however, because these processes co-occur, weight loss can serve as a useful health surveillance indicator that further examination is warranted.

Several limitations should be considered in interpreting these findings. First, the cognitive measures in this dataset were limited. All three cognitive assessments are widely used in neuropsychological batteries. However, a more expansive battery would have been desirable. Second, the SHARE dataset did not include a variable to indicate whether an individual met criteria for mild cognitive impairment, amnestic or non-amnestic. As a result, changes in cognition are measured across the full representative sample and are not differentiated based upon risk for disease onset and progression. Third, height was only recorded at T0, so changes in BMI result from changes in weight and do not account for age-related declines in height. In addition, BMI does not provide information on body composition changes, namely, whether declines were due to changes in percent body fat or muscle mass. Additional measures of body composition, including percent body fat, muscle mass, and waist circumference would be beneficial in future longitudinal studies to more definitively attribute declines in body mass to specific changes in body composition. Fourth, our measure of physical activity is reliant on self-report, which is susceptible to over and underreporting. Finally, though we have demonstrated a strong relationship between physical activity, body mass, and cognition, it is unknown how much a standard deviation of decline in cognitive ability affects everyday functioning. Future work should measure ecologically relevant outcomes, such as the ability to remember grocery lists, familiar names, and directions. Future research should examine differences in the relationship between physical activity, body mass, and cognition among sub-groups of older adults, including young-old (55–64), old (65–74), and old-old (75+) [35], to better understand the onset and course of the obesity paradox.

Conclusion

The present study identified physical activity and body mass as unique predictors of cognition in older age. Although increased physical activity was associated with better cognition at baseline and a lesser decline in cognition over time, the reverse was true for body mass. Lower body mass predicted better cognition at baseline, but declines in body mass were associated with greater declines in cognition over time. A loss of 1 standard deviation in BMI (2.5 lbs a year for men, 2.2 lbs for women) was comparable to the change in cognition that occurs as a result of 3.9 years of chronological aging. These results provide support for the obesity paradox in cognitive aging and suggest that decreases in body mass should be considered a potential indicator of accelerated cognitive decline in older adults. In light of these findings, physicians and care providers should encourage and prescribe physical activity to older adults and attend with increased awareness to potentially detrimental declines in weight.

Compliance with Ethical Standards

Conflicts of Interest Authors' Statement of Conflict of Interest and Adherence to Ethical Standards Authors Molly Memel, Kyle Bourassa, Cindy Woolverton, and David A. Sbarra declare that they have no conflict of interest. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

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Informed Consent Until July 2011, SHARE has been reviewed and approved by the Ethics Committee of the University of Mannheim. Since then, the Ethics Council of the Max-Planck-Society for the Advancement of Science (MPG) is responsible for ethical reviews and the approval of the study.

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