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Distinct age-related associations for body mass index and cognition in cognitively healthy very old veterans

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Abstract

Objectives—Associations between high body mass index (BMI) and subsequent cognitive decline, reported in elderly averaging below age 75, become less consistent at older ages. We compared the associations of BMI with cognition in moderately old (ages 75–84, N=154) and oldest-old (85+, N=93) samples.

Participants and Measurements—BMI and cognition were assessed cross-sectionally in cognitively intact elderly (mean age=84.5, SD=4.4) male veterans. Regression analyses of three cognitive domains – executive functions/language, attention, and memory – compared relationship with BMI between the moderately old and oldest-old.

Results—Higher BMI was associated with relatively poorer executive functions/language performance in the moderately old, while the opposite relationship, higher BMI associated with relatively better performance, was found in the oldest-old. Associations for the other two cognitive domains did not differ significantly between age groups.

Conclusions—The reversal of association direction for executive functions/language performance with higher BMI is consistent with the protected survivor model. This model posits a minority subpopulation with a protective factor – genetic or otherwise – against both mortality and cognitive decline associated with risk factor status. The very old who remain cognitively intact despite the presence of risk factors are more likely to possess protection.

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Keywords

body mass index; dementia; oldest-old; successful cognitive aging; protected survivor

Introduction

Many risk factors for cardiovascular diseases, such as diabetes, cholesterol, and hypertension, have been identified as risk factors for cognitive decline, dementia, or Alzheimer's disease (AD), particularly in studies of young elderly. For several, associations diminish for survivors who remain cognitively healthy into very old age (Silverman & Schmeidler 2018). The relationship between body mass index (BMI) and cognitive decline has been examined with varying results. Most midlife BMI studies associated high BMI with AD or dementia risk (Emmerzaal, Kiliaan, & Gustafson 2015), with null findings (Gustafson et al. 2009; Stewart et al. 2005) and reverse relationships (Kivimaki et al. 2015; Qizilbash et al. 2015) also reported. The association with AD and dementia appears to diminish as BMI measurement age increases, and low late-life BMI has been associated with increased risk (Emmerzaal, Kiliaan, & Gustafson 2015). Consistent with both, decreasing BMI from mid- to late-life has been associated with increased risk for AD (Tolppanen et al. 2014).

In a study of BMI quartile and risk for dementia measured five years later, participants below age 76 showed a U-shaped relationship – underweight and obese individuals were at higher risk. In contrast, for participants ≥ 76, risk decreased as BMI increased. Thus, for older elderly, the highest quartile had relatively less risk than middle quartiles; for younger elderly, it had relatively more risk (Luchsinger et al. 2007).

The protected survivor model for successful cognitive aging was proposed as an explanation for changes in associations with age for other cardiovascular risk factors (Silverman & Schmeidler 2018). This model posits that risk factor status within an individual (risk for the unprotected majority, no risk for the protected minority) does not change. The proportion protected increases as the population ages due to differential mortality. With increasing age, the average risk in the surviving population declines, and eventually the risk factor may be associated – but not causally – with protection.

Few studies of BMI and cognition have reported findings for the “oldest-old” – ≥ 85. The present study compared samples of moderately old (75–84, N=154) and oldest-old (N=93) cognitively intact men on cross-sectional relationships of BMI with cognitive domains. We hypothesized that an association between higher BMI and poorer cognitive performance in the moderately old group would be diminished or even reversed in the oldest-old.

Methodology

Study sample

The eligibility requirements, recruitment, and cognitive assessment procedures have been described in detail elsewhere (Beeri et al. 2006). Briefly, participants were cognitively intact male veterans recruited from the James J. Peters Veterans Affairs Medical Center (JJP-VAMC) in Bronx, NY, age 75 or older. Criteria for intact cognitive functioning were a score

in the upper three quartiles on the Mini-Mental State Examination (MMSE) based on sex, age, and education norms, and a zero score—no dementia—on the Clinical Dementia Rating scale administered to both the participant and an informant. Note that no neuropsychological tests were used to evaluate intact cognition. All project procedures were approved by the JJP-VAMC and Mount Sinai Institutional Review Boards; all participants provided signed informed consent.

Cognitive Domains

Factor analysis with orthogonal varimax rotation of principal components with eigen values >1 derived uncorrelated cognitive domains providing conceptual clarity. An initial analysis on 11 neuropsychological tests produced three domains labelled by tests for which the weight was highest, Executive functions/language (Shipley Vocabulary, Similarities, Trails: A and B, Letter Fluency, Boston Naming), Attention (Target Cancellation: Shapes and Letters), and Memory (Word List: Delayed Recall, Immediate Recall, and Recognition). Since Boston Naming had low weights on all three factors, the final factor analysis without it yielded three essentially similar domains.

BMI

BMI was weight (kilograms) divided by height (meters) squared measured concurrently with cognitive assessment.

Statistics

For each domain, multiple regression analysis tested the age group by BMI interaction to evaluate whether the association with BMI differed by age group. Additional variables in the analysis were age group and BMI (required to test the interaction), age (i.e., age within age group) and education (years), and age group interaction with age and education (controlling for age group differences in domain associations with age and education). Interpretation of age group by BMI interaction was clarified by comparing age groups' partial correlations of BMI with domains, controlling for age and education.

Results

Descriptive statistics (Table 1) describe the full sample and compare moderately old and oldest-old subgroups. Consistent with cross-sectional—distinguished from longitudinal—comparisons in the general population, the oldest-old group was significantly shorter, lighter, and had lower BMI (Launer and Harris 1996) and lower MMSE (Crum et al. 1993) than the moderately old group. Differences in education and the three domains were not significant.

In interaction analyses, the age groups differed significantly in extent of association of BMI for executive functions/language ($p = 0.032$), but not the other domains (Table 2). Although neither age group association of BMI with executive functions/language was significant, their directions differed – worse performance with higher BMI for moderately old, but better for oldest-old (Supplementary Figure).

Discussion

In these cognitively intact male veterans, there was a significant interaction with age group for the association of BMI with executive functions/language. This reflected the reversal of direction – better executive functions/language performance in the oldest-old with higher BMI, contrasting with poorer executive functions/language performance in the moderately old, consistent with younger samples.

Most studies of BMI association measured cognition over wide age ranges; primarily young elderly samples, only a few very old (Emmerzaal, Kiliaan, & Gustafson 2015). Discrepancy among those results parallels discrepancy in this study comparing narrower age ranges—reduced association with increasing age, eventually reversing. This study differed from many earlier studies by requiring intact cognition, to examine subtle differences in cognitive performance.

In the general population, education and neuropsychological performance are lower for cohorts of increasing age. Restricting the samples to intact cognition may explain the absence of such differences. Nonetheless, consistent with age-based norms for MMSE inclusion criteria, MMSE scores were significantly lower for the oldest-old. Similarly, the decrease in BMI in the very old in the general population (Visser and Harris 2012) was reflected in this study. As body composition changes for the oldest-old, e.g., bone and muscle mass lost, changing meaning of BMI may have contributed to our results. Age, per se, is a very strong risk factor for cognitive decline and dementia. Even within the intact cognition range, an incipient dementia process is more likely in the oldest-old, consistent with their significantly lower MMSE. A supplemental analysis additionally controlling for MMSE (and its interaction with age group) showed a similar age group interaction for executive functions/language ($p=0.027$). Thus, the observed age group interaction for executive functions/language is not readily attributable to incipient dementia for the oldest-old.

Recommended BMI for the general adult population is below 25.0 – 29.9 (overweight), but this may not apply to the elderly, with mortality relatively higher for BMI <22.0 or >32.9 (Winter et al. 2014), suggesting a U-shaped association. Correspondingly, an inverted U-shaped association with BMI was found for good cognition in the elderly (Kuo et al.). In this study, executive functions/language was best for high BMI among the relatively low-BMI oldest-old group, and for the low BMI among the relatively high-BMI moderately old group. In a post-hoc analysis, controlling age and education, there was a significant quadratic BMI component with executive functions/language ($r=-0.194$, $p=0.002$). This provides a more concise model for the relationship of cognition with BMI by conflating the two extremes, although they may represent different underlying mechanisms. For mortality, obesity is associated with cardiovascular disease and obesity-related cancers, although not other cancers, but underweight is associated with noncancer, non-cardiovascular disease causes (Flegal et al. 2007).

The reversal of association direction in this study is also consistent with the protected survivor model for successful cognitive aging that motivated it (Silverman & Schmeidler

2018). “Survival” in this study is the criterion for inclusion – intact cognition. The longitudinal model explains the difference – between two ages – in association of a cognitive risk factor and cognition. This cross-sectional study compares – in two age groups – the associations of BMI, a cardiovascular risk factor, with concurrent neuropsychological performance. The model posits a minority with an unidentified protective factor – genetic or otherwise – associated with survival, and also with good cognition even despite risk factor status. In applying the model to BMI, for the younger age group, lack of association between protection and BMI is assumed. Compared with protected survivors, unprotected survivors tend to have relatively low BMI, but worse cognitive performance. As the population ages, an increasingly larger proportion of survivors is protected, for both low and high BMI. Eventually, the changing composition of survivors may lead to a reversal of the usual association between BMI and cognition.

The study has several limitations. Only association of BMI and concurrent neuropsychological performance could be assessed in this cross-sectional study, not cognitive change over time. Although many studies of cardiovascular risk factors have found midlife assessments predict subsequent cognition better than late-life, midlife BMI was not available. The significance of interaction for one domain could not withstand adjustment – by the Bonferroni inequality – for three.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Characteristics of the study sample

	All Participants 75 years	Moderately old 75–84 years	Oldest old 85 years	p-value*
Number of Participants	247	154	93	-
Mean Age (SD)	83.5 (4.4)	80.7 (2.4)	88.1 (2.8)	-
Mean Years of Education (SD)	13.8 (3.3)	13.8 (3.1)	13.9 (3.6)	0.81
Mean Height in inches (SD)	68.3 (3.3)	68.8 (2.7)	67.5 (2.4)	<0.0005
Mean Weight in lbs. (SD)	177.5 (29.0)	184.4 (30.8)	166.1 (21.5)	<0.0005
Mean BMI (SD)	26.8 (3.9)	27.4 (4.2)	25.7 (3.2)	0.001
Mean MMSE (SD)	28.1 (1.6)	28.4 (1.5)	27.8 (1.7)	0.005
Executive functions/ Language	-0.02 (1.00)	-0.04 (1.00)	0.02 (1.01)	0.69
Attention	0.01 (1.00)	0.02 (1.00)	-0.01 (1.00)	0.86
Memory	-0.01 (1.01)	-0.00 (1.02)	-0.01 (1.01)	0.97

* Student's t-test; df=245

Table 2

Age group associations with BMI for three cognitive domains *

	df	Executive functions/ Language	Attention	Memory			
Interaction analysis, t-test of difference between age group associations (p)							
	239	0.035	0.719	0.786			
Partial correlations							
Age Group		r	p	r	p	r	p
Moderately Old	150	−0.144	0.076	0.005	0.950	0.003	0.968
Oldest Old	89	0.151	0.154	0.048	0.652	−0.031	0.769

* Controlling for age and years of education.