Multimorbidity, cognitive function, and physical activity

Paul D. Loprinzi

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Abstract Previous research demonstrates that both physical activity and multimorbidity are associated with cognitive function. However, the extent to which physical activity may moderate the relationship between multimorbidity and cognitive function has not been thoroughly evaluated. Data from the 1999–2002 NHANES were used (60+ years; $N = 2157$). A multimorbidity index variable was created based on physician diagnosis of a multitude of chronic diseases. Physical activity was self-reported and cognitive function was evaluated from the digit symbol substitution test. Multimorbidity was inversely associated with cognitive function for the unadjusted and adjusted models. However, generally, multimorbidity was no longer associated with cognitive function for the majority of older adults who achieved the minimum recommended physical activity level (≥ 2000 MET-min-month), as issued by the United States Department of Health and Human Services. In this national sample of older adults, there was some evidence to suggest that physical activity moderates the relationship between multimorbidity and cognitive function.

Keywords Chronic disease · Executive function · Epidemiology · Health

Introduction

Multimorbidity is defined to have a co-existence of at least two chronic diseases, with approximately 23.2 % of adults having two or more chronic diseases (Barnett et al. 2012). Multimorbidity is associated with premature mortality (Gijssen et al. 2001), reduced functional status (Fortin et al. 2006; Fortin et al. 2004; Kadam et al. 2007), and increased utilization of inpatient and ambulatory health care (Salisbury et al. 2011; Wolff et al. 2002). Although less investigated, emerging research also demonstrates an unfavorable association between multimorbidity and cognitive function (Melis et al. 2013). Emerging research also demonstrates an inverse relationship between physical activity and multimorbidity (Dankel et al. 2015; Loprinzi 2015b, c), and previous research has established a favorable relationship between physical activity and cognitive function (Loprinzi 2015b, d; Loprinzi et al. 2013b, 2015). Taken together, it is thus plausible to suggest that physical activity may moderate the relationship between multimorbidity and cognitive function (i.e., physical activity may have a protective effect on cognitive function among multimorbidity patients). As a result, the question of interest in this study was to determine if multimorbidity continues to be associated with lower cognitive function among those with greater participation in physical activity. This specific question, to my knowledge, has yet to be examined in the literature. This question is addressed using a national sample of older adults from the National Health and Nutrition Examination Survey (NHANES).

P. D. Loprinzi (✉)
Jackson Heart Study Vanguard Center of Oxford, Center for
Health Behavior Research, School of Applied Sciences,
Department of Health, Exercise Science and Recreation
Management, The University of Mississippi, 229 Turner Center,
Oxford, MS 38677, USA
e-mail: pdloprin@olemiss.edu

Methods

Design and participants

Data from the 1999–2002 NHANES were used. Study procedures were approved by the NCHS ethics review board, with informed consent obtained prior to data collection. A total of 2,157 adult (60–85 years) participants provided data on the study variables.

The NHANES is an ongoing survey conducted by the Centers for Disease Control and Prevention that uses a representative sample of non-institutionalized United States civilians selected by a complex, multi-stage, stratified, clustered probability design. The multistage design consists of four stages, including the identification of counties, segments (city blocks), random selection of households within the segments, and random selection of individuals within the households. Further information on NHANES methodology and data collection is available on the NHANES website (<http://www.cdc.gov/nchs/nhanes.htm>).

Measurement of cognitive function

The digit symbol substitution test (DSST) was used to assess cognitive function. The DSST, a component of the Wechsler Adult Intelligence Test (Wechsler 1981) and a test of visuospatial and motor speed-of-processing, has a considerable executive function component and is frequently used as a sensitive measure of frontal lobe executive functions (Parkin and Java 1999; Vilkki and Holst 1991). Participants were asked to copy symbols that were paired with numbers within 2 min. Following the standard scoring method, one point is given for each correctly drawn symbol.

Measurement of multimorbidity

Similar to previous work (Loprinzi 2015b), a multimorbidity ordinal variable was created based on physician-diagnosis of arthritis, coronary artery disease, stroke, congestive heart failure, heart attack, emphysema, chronic bronchitis, hypertension, diabetes, cancer, and obesity (measured body mass index ≥ 30 kg/m²).

Physical activity

Participants were asked open-ended questions about participation in leisure-time physical activity over the past 30 days. Data was coded into 48 activities, including 16 sports-related activities, 14 exercise-related activities, and 18 recreational-related activities; these individual physical activities are published elsewhere (http://wwwn.cdc.gov/Nchs/Nhanes/2005-2006/PAQIAF_D.htm#PADACTIV).

For each of the 48 activities where participants reported moderate or vigorous-intensity for the respective activity, they were asked to report the number of times they engaged in that activity over the past 30 days and the average duration they engaged in that activity.

For each of activity, metabolic equivalent of task (MET)-min-month was calculated by multiplying the number of days, by the mean duration, by the respective MET level (MET-min-month = days*duration*MET level). The MET levels for each activity are provided elsewhere (Ainsworth et al. 2000).

A five-level dose-response physical activity variable was created, with participations classified into one of the following six mutually exclusive categories: (1) <2000 MVPA MET-min-month (current government MVPA guideline threshold; (2) 2000–3999 MVPA MET-min-month; (3) 4000–5999 MVPA MET-min-month; (4) 6000–7999 MVPA MET-min-month; and (5) 8000+ MVPA MET-min-month). These five levels were chosen as they are similar to previous studies (Loprinzi 2015a) and allowed for a sample size of at least 100 per group among this sample.

Measurement of covariates

Covariates included *age*; *gender*; *race-ethnicity* (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other); *poverty-to-income ratio* (range: 0–5; assessment described elsewhere (Lee et al. 2012)); *C-reactive protein* (CRP; mg/dL; assessment described elsewhere (Loprinzi et al. 2013a); and self-reported *smoking status* (current smoker, former smoker, never smoker).

Statistical analyses

All statistical tests (significance set at $P < 0.05$) were performed using Stata (version 12.0), with all analyses accounting for the complex survey design employed in

NHANES. Multivariable linear regression was performed to examine the association between MVPA MET-min-month (5-level categorical variable) and cognitive function (outcome variable). Nine regression models were computed: (1) unadjusted; (2) age-adjusted; (3) adjustment for age, gender, race-ethnicity and poverty level; (4) fully adjusted, with covariates including age, gender, race-ethnicity, poverty level, CRP, and smoking; (5) same as model 4 but only among those engaging in less than 2000 MVPA MET-min-month; (6) same as model 4 but among those engaging between 2000 and 3999 MVPA MET-min-month; (7) same as model 4 but among those engaging between 4000 and 5999 MVPA MET-min-month; (8) same as model 4 but among those engaging between 6000 and 7999 MVPA MET-min-month; and (9) same as model 4 but among those engaging in ≥ 8000 MVPA MET-min-month.

Results

Table 1 displays the weighted characteristics of the study sample. The multivariable regression results examining the association between multimorbidity and cognitive function, stratified by physical activity level, are shown below. As shown below, multimorbidity was inversely associated with cognitive function for the unadjusted and adjusted models. However, multimorbidity was no longer associated with cognitive function for the majority of physical activity doses above the minimum recommended physical activity level (at least 2000 MET-min-month), as issued by the United States Department of Health and Human Services.

Model 1—unadjusted ($N = 2157$)

The comorbid index was significantly inversely associated with cognitive function ($\beta = -2.04$; 95 % CI: -2.5 to -1.5 ; $P < 0.001$).

Model 2—age-adjusted ($N = 2157$)

The comorbid index was significantly inversely associated with cognitive function ($\beta_{\text{adjusted}} = -1.72$; 95 % CI: -2.1 to -1.2 ; $P < 0.001$).

Table 1 Weighted characteristics of the study variables, 1999–2002 NHANES ($N = 2157$)

Variable	Mean/proportion	95 % CI
Age, mean years	70.1	69.4–70.6
% Female	54.9	
% Non-Hispanic white	83.3	
Smoking, %		
Current smoker	12.8	
Former smoker	41.1	
Never smoker	46.1	
Multimorbidity, mean	2.07	1.98–2.15
C-reactive protein, mean mg/dL	0.51	0.46–0.55
Poverty-to-income ratio, mean	2.85	2.66–3.05
Cognitive function, mean	47.4	45.8–48.9
MVPA MET-min-month, mean	3505.7	2905.6–4105.9
% 0–1999 MVPA MET-min-month ($n = 1425$)	62.8	
% 2000–3999 MVPA MET-min-month ($n = 229$)	11.4	
% 4000–5999 MVPA MET-min-month ($n = 134$)	6.8	
% 6000–7999 MVPA MET-min-month ($n = 110$)	5.8	
% 8000+ MVPA MET-min-month ($n = 259$)	13.3	

MVPA moderate-to-vigorous physical activity, *MET* metabolic equivalent of task

Model 3—adjustment for age, gender, race-ethnicity, and poverty level ($N = 2157$)

The comorbid index was significantly inversely associated with cognitive function ($\beta_{\text{adjusted}} = -1.36$; 95 % CI: -1.8 to -0.9 ; $P < 0.001$).

Model 4—fully adjusted, with covariates including age, gender, race-ethnicity, poverty level, CRP, and smoking ($N = 2,157$)

The comorbid index was significantly inversely associated with cognitive function ($\beta_{\text{adjusted}} = -1.34$; 95 % CI: -1.8 to -0.9 ; $P < 0.001$).

Model 5—same as model 4 but only among those engaging in less than 2000 MVPA MET-min-month ($N = 1425$)

The comorbid index was significantly inversely associated with cognitive function ($\beta_{\text{adjusted}} = -1.34$; 95 % CI: -2.0 to -0.7 ; $P < 0.001$).

Model 6—same as model 4 but among those engaging between 2000 and 3999 MVPA MET-min-month ($N = 229$)

The comorbid index was *not* associated with cognitive function ($\beta_{\text{adjusted}} = -1.02$; 95 % CI: -2.3 to 0.3 ; $P = 0.11$).

Model 7—same as model 4 but among those engaging between 4000 and 5999 MVPA MET-min-month ($N = 134$)

The comorbid index was *not* associated with cognitive function ($\beta_{\text{adjusted}} = -0.08$; 95 % CI: -1.6 to 1.4 ; $P = 0.91$).

Model 8—same as model 4 but among those engaging between 6000 and 7999 MVPA MET-min-month ($N = 110$)

The comorbid index was associated with cognitive function ($\beta_{\text{adjusted}} = -1.50$; 95 % CI: -2.7 to -0.2 ; $P = 0.02$).

Model 9—same as model 4 but among those engaging in ≥ 8000 MVPA MET-min-month ($N = 259$)

The comorbid index was *not* associated with cognitive function ($\beta_{\text{adjusted}} = -0.61$; 95 % CI: -1.9 to 0.7 ; $P = 0.34$).

Discussion

Given the burden of multimorbidity, coupled with the debilitating effects of cognitive dysfunction, emerging work has begun to explore the relationship between multimorbidity and cognitive function. Emerging work has demonstrated that regular participation in physical activity is associated with reduced odds of developing multimorbidity. This, taken together, spawned the motivation for the present study, which was to examine

whether physical activity may have a protective effect in preserving cognitive function among multimorbidity patients. Of course, prospective and experimental designs are needed to fully evaluate this possibility, but these preliminary cross-sectional findings support this assertion. That is, the main findings of this study were that multimorbidity was associated with lower cognitive function, but this relationship, for the most part, did not remain among those who engaged in greater amounts of physical activity.

The link between multimorbidity and cognitive function is plausible, given the interrelatedness between physical and cognitive functioning (Wang et al. 2006), as physiological-related chronic diseases include several pathological processes (e.g., amyloid aggregation, vascular damage) interlinked with cognitive dysfunction. Each of the individual chronic diseases included in the multimorbidity index has been previously shown to associate with cognitive dysfunction, including arthritis (Shin et al. 2012), cardiovascular disease (Dardiotis et al. 2012; Waldstein and Wendell 2010), hypertension (Novak and Hajjar 2010), diabetes (Arvanitakis et al. 2006), cancer (Biegler et al. 2009), and obesity (Smith et al. 2011). The possibility of physical activity potentially moderating the multimorbidity-cognitive function relationship is plausible given the established and growing body of research demonstrating physical activity-induced beneficial effects on preserving cognitive function (Loprinzi 2015c; Loprinzi et al. 2013b, 2015) as well as helping prevent and treat multimorbidity (Dankel et al. 2015; Loprinzi 2015c).

The findings of this study need to be interpreted in the context of the study limitations. Inherent in cross-sectional study designs, a limitation of this study is the inability to establish temporal sequence. Thus, future prospective and experimental work on this topic is warranted. Other limitations include the subjective assessment of physical activity; given that subjective assessments of physical activity, as opposed to objective measures (e.g., accelerometry), often attenuate associations (Tooze et al. 2013), it is plausible that the observed findings are underestimated. An additional limitation is the reliance on self-report of physician-diagnosed chronic disease; however, this methodology has demonstrated reasonable clinical sensitivity (Bergmann et al. 1998). Strengths of this study include the novel investigation and national sample of U.S. older adults.

In conclusion, in this national sample of U.S. older adults, multimorbidity was associated with lower cognitive function. However, this association was attenuated toward the null among older adults engaging in most of the higher levels of physical activity. This moderation effect of physical activity provides suggestive evidence that physical activity may have a preservation effect on cognitive function among individuals with multimorbidity. However, this needs to be confirmed with a more robust study design (e.g., prospective/experimental). If confirmed by future work, then these findings will have major clinical implications. In order to help preserve cognitive function and attenuate the cognitive decline that may occur with multimorbidity, clinician promotion of patient physical activity will be of great importance. Making physical activity counseling a priority in clinical practice is of great importance in today's society (Berra et al. 2015). Strategies in integrating physical activity promotion into clinical practice have been discussed elsewhere (Berra et al. 2015), but careful consideration will need to occur when promoting physical activity to multimorbid patients as the combination of different morbidities (e.g., COPD and arthritis) may prove difficulty in initiating and maintaining physical activity (Loprinzi 2015b, c). Future research is needed to inform the best approach to promote physical activity among multimorbid patients.

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