

Multiple health characteristics on cognitive function in older adults

Paul D. Loprinzi, Meghan K. Edwards, Chelsea Joyner, Elizabeth Crush

Department of Health, Exercise Science and Recreation Management, The University of Mississippi, Oxford, MS, USA

ABSTRACT

Individual health characteristics, namely, physical activity, smoking, and weight status, have a positive effect on cognitive function, especially during the aging process. However, fewer studies have evaluated the combined associations of these health characteristics on cognitive function among older adults, which was this study's purpose. Data from the 1999–2002 National Health and Nutrition Examination Survey were used ($N = 2,370$ adults 60+ years). Clinical measures were assessed using the Digit Symbol Substitution Test (DSST), self-reported physical activity, and smoking status. Weight status was evaluated based on measured body mass index. Being a non-smoker [$\beta = 2.44$; 95% confidence interval (CI): -0.03 – 4.92 ; $P = 0.05$] and meeting the physical activity guidelines ($\beta = 5.73$; 95% CI: 4.34 – 7.12 ; $P < 0.001$) were independently associated with DSST. There was also an evidence of an additive association of these three health characteristics on cognitive function. The highest area under the receiver operating characteristic curve [area under the curve (AUC)] was observed among those who met physical activity guidelines (AUC = 0.59 ; 95% CI: 0.57 – 0.61) compared to smoking status (receiver operator characteristic = 0.51 ; 95% CI: 0.49 – 0.52) or weight status (AUC = 0.49 ; 95% CI: 0.47 – 0.51). Weight status and smoking are independently associated with cognitive function, and individuals with all three evaluated health characteristics (non-smoking, normal weight, and active) had the highest cognitive function.

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Introduction

Cognitive function is inversely associated with age [1], with some degree of cognitive decline being considered as a normal outcome associated with aging [2,3]. However, particularly in the older adult years, reduced cognitive function is also linked with various neurodegenerative diseases, such as dementia [4]. Therefore, maintenance of cognitive function is important, and efforts should be made to attenuate rates of cognitive decline that occur with increasing age. Cognitive function may be partially modifiable via lifestyle behaviors. For instance, certain health characteristics, such as physical activity [5–7], smoking [8], and weight status [9], have all been shown to be individually associated with cognitive function.

Specifically, physical activity has been shown to be positively associated with cognitive function,

with copious evidence supporting both acute and chronic influences of physical activity on cognition [10–18]. Physical activity is believed to enhance constructs such as information processing, attention, and memory [19–23], all of which are important for optimal cognitive functioning. Improvements in these processes may partially result from exercise-induced increases in molecules such as brain-derived neurotrophin factor and insulin-like growth factor-1 [24–26], which ultimately may promote neurogenesis, angiogenesis, and synaptic plasticity [19–23]. Recent animal research on this topic has also identified a new potential mediator of the physical activity-cognitive function relationship, cathepsin B [27].

Previous research investigating the association between smoking status and cognitive function has yielded somewhat mixed findings, though there is

Contact Paul D. Loprinzi ✉ pdloprin@olemiss.edu 📧 Department of Health, Exercise Science and Recreation Management, The University of Mississippi, 229 Turner Center, Oxford, MS 38677, USA.

plentiful evidence to suggest that smoking plays a detrimental role on one's cognitive health. For example, a meta-analysis evaluating smoking status and risk for dementia and cognitive decline [28] found that current smokers (compared to never smokers or individuals who had smoked at one point in time but quit) had an increased risk of cognitive decline or dementia. One proposed mechanism to support this association is that smoking is a risk factor for vascular diseases and therefore could influence cognition (e.g., vascular dementia) via vascular pathways [29]. Additionally, smoking has been shown to be associated with periventricular and subcortical white matter lesion progression, which have been linked with greater cognitive decline [30]. The findings of a review paper [28] also seem to support the notion that smoking cessation may lead to cognitive improvements. For instance, there were no observable differences in the risk of Alzheimer's disease when comparing never-smokers to current non-smokers who had previously smoked. It seems plausible that quitting smoking may reverse some of the potential cognitive damage originally elicited from smoking, considering that smoking cessation has been shown to be associated with a reduction in inflammatory markers, such as C-reactive protein (CRP) [31]. Notably, systemic inflammation may lead to neuro-inflammation in certain areas of the brain (e.g., hypothalamus), promoting hypothalamic neurodegeneration and reduced cognitive function [32].

Similar mechanisms have been proposed to explain the relationship between weight status and cognitive function [9]. For example, the vascular effects of obesity (e.g., increased risk for cerebrovascular diseases) are suggested to influence the development of vascular cognitive impairment among older persons [33], possibly via enhanced atherosclerosis in large cerebral arteries as well as alterations in cerebral microcirculation [34]. Being overweight or obese may also contribute to dysfunction of the blood brain barrier, which has been shown to be associated with both Alzheimer's disease and vascular dementia [9]. With regards to systemic inflammation, overweight and obese individuals have been demonstrated to have higher levels of circulating pro-inflammatory cytokines (e.g., CRP and interleukins 1 and 6) [35], which have been shown to be associated with dementia [36], as well as impaired processing speed and executive function [37].

Importantly, emerging work has begun to investigate the potential combined effects of health

characteristics on various health outcomes [38–40], in addition to their individual effects. Such investigations are noteworthy as they may shed light on potential additive effects of having multiple positive health characteristics and may assist in the development, implementation and evaluation of a precision prevention framework to facilitate and target behavior and health outcome change. Presently, there is limited research evaluating the potential additive effects of multiple health characteristics on cognitive function. Thus, the purpose of this short communication study was to evaluate the individual and combined associations of several health characteristics (namely, physical activity, smoking, and weight status) on cognitive function among older adults.

Methods

Design and participants

Data from the 1999–2002 National Health and Nutrition Examination Survey (NHANES) were used. Study procedures were approved by the National Center for Health Statistics ethics review board, with informed consent obtained prior to data collection. 2,370 adult (60–85 years) participants provided data on the study variables. Participants in this age range were evaluated as this was the age range eligible for the NHANES cognitive testing.

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, multistage, stratified, and 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

Demonstrating evidence of construct validity [41], the Digit Symbol Substitution Test (DSST) was used to assess cognitive function. The DSST, a component of the Wechsler Adult Intelligence Test [42] 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 [43,44].

Participants were asked to copy symbols that were paired with numbers within 2 minutes. Following the standard scoring method, one point is given for each correctly drawn symbol.

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 [13,45].

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) [46]. For example, the MET level for moderate-intensity walking is 3.5 and 5.0 for vigorous-intensity walking; for swimming, the MET level for moderate and vigorous intensity is 6.0 and 8.0, respectively.

Weight status

Measured height and weight were used to calculate body mass index (BMI; kg/m²), with normal weight defined as 18.5–24.9 kg/m².

Smoking

Participants were classified as smokers if they self-reported smoking every day or some days; otherwise, classified as non-smoker. Previous research demonstrates evidence of validity for self-reported smoking assessment [47].

Measurement of covariates

Covariates included: *age*, *gender*, *race-ethnicity* (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and others), *CRP* (mg/dL [48]); energy intake (kcal, continuous), and *comorbid illness* (ordinal variable: range, 0–9 chronic diseases) based on physician-diagnosis of arthritis, coronary artery disease, stroke, congestive heart failure, heart attack, emphysema, chronic bronchitis, diabetes, and hypertension. Energy intake (kcal) was assessed from the mobile examination center (MEC) interview

and the follow-up telephone interview, with the average of these values used; if data was missing from the telephone interview, only energy intake obtained from the MEC interview was used. These covariates were included in all analyses.

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. Specifically, the NHANES sampling weights were applied to render nationally representative estimates. Multivariable linear regression was performed to examine the association between the health characteristics and cognitive function (outcome variable). Two multivariable models were computed:

1. A model evaluating the independent associations of the three evaluated health characteristics on cognitive function. The independent variables in this model included the aforementioned covariates along with the three health characteristics. Smoking was categorized as non-smoker vs. smoker (referent); physical activity was categorized as meeting physical activity guidelines vs. not (referent), with ≥ 2000 MET-min-month defined as meeting physical activity guidelines; and weight status was defined as normal BMI vs. not (referent).
2. An additive multivariable regression model was evaluated by creating a 3-level health characteristic variable, ranging from 0–3. For example, those who were a non-smoker, normal weight, and met physical activity guidelines received a score of “3.” In this model, this health characteristic index variable was regressed on cognitive function, while adjusting for the covariates.

Additionally, receiver operator characteristic (ROC) analysis was used to examine how well the test separates the sample into those with and without “adequate” cognition. Here, participants were stratified as above (DSST = 42) and below the sample DSST median.

Results

Characteristics of the analyzed sample are shown in Table 1. Participants, on average, were 69.9 years, with 55.1% being female.

In the multivariable regression model (Table 2), normal BMI was not significantly associated with

Table 1. Characteristics of the analyzed sample, 1999–2002 NHANES (N = 2370).

Variable	Point estimate	95% CI
Cognitive function, mean DSST	47.7	46.4–49.1
Age, mean years	69.9	69.3–70.4
Gender, % female	55.1	
Race-ethnicity, % white	83.7	
CRP, mean mg/dL	0.51	0.47–0.55
Comorbidities, mean #	1.53	1.45–1.61
Energy intake, mean kcals	1796.2	1752.2–1840.2
BMI, mean kg/m ²	28.1	27.8–28.4
Normal BMI, %	28.1	
MVPA, mean MET-min-month	3593.2	2994.8–4191.6
Meets guidelines, %	37.2	
Non-smoker, %	87.5	

BMI = body mass index, CRP = C-reactive protein, DSST = Digit Symbol Substitution Test, MET = metabolic equivalent of task, MVPA = moderate-to-vigorous physical activity.

Table 2. Multivariable regression results examining the association between the individual health characteristics and cognition.

	β	95% CI	P-value
Model 1			
Normal BMI vs. not	0.43	-1.59–2.45	0.66
Non-smoker vs. smoker	2.44	-0.03–4.92	0.05
Meeting exercise guidelines vs. not	5.73	4.34–7.12	<0.001
Model 2			
1 vs. 0 health characteristics	2.57	-1.18–6.33	0.17
2 vs. 0 health characteristics	6.58	2.58–10.59	0.002
3 vs. 0 health characteristics	8.66	4.29–13.04	<0.001

In both models, covariates included age, gender, race-ethnicity, C-reactive protein, energy intake, and comorbid illness. BMI = body mass index.

the DSST score [$\beta = 0.43$; 95% confidence interval (Ci): -1.59–2.45; $P = 0.66$], but non-smoker ($\beta = 2.44$; 95% CI: -0.03–4.92; $P = 0.05$) and meeting physical activity guidelines ($\beta = 5.73$; 95% CI: 4.34–7.12; $P < 0.001$) were independently associated with DSST. In the additive multivariable regression model, and compared to those with a healthy lifestyle index score of 0, those with an index score of 1 ($\beta = 2.57$; 95% CI: -1.18–6.33; $P = 0.17$), 2 ($\beta = 6.58$; 95% CI: 2.58–10.59; $P = 0.002$), and 3 ($\beta = 8.66$; 95% CI: 4.29–13.04; $P < 0.001$) had a higher DSST score.

As summarized in Figure 1, the highest area under the receiver operating characteristic curve [area under the curve (AUC)] was observed among those who met physical activity guidelines (AUC = 0.59; 95% CI: 0.57–0.61) compared to smoking status (ROC = 0.51; 95%

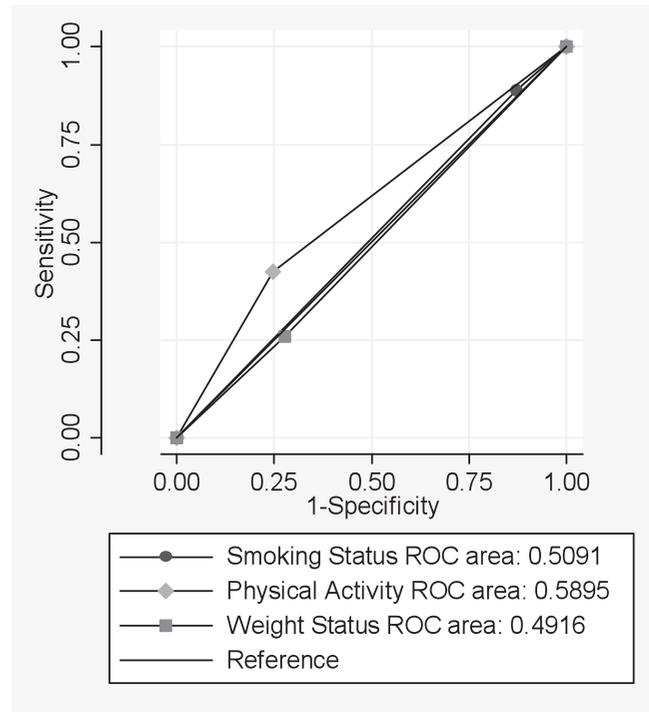


Figure 1. Receiver operator characteristic curve analysis.

CI: 0.49–0.52) or weight status (AUC = 0.49; 95% CI: 0.47–0.51).

Discussion

Previous research has demonstrated that individual health characteristics, such as smoking, weight status, and physical activity, are associated with cognition function. The main findings of the present study were 1) that smoking and physical activity were independently associated with the DSST and 2) there was a significant correlation between highest DSST score and those with three health characteristics (non-smoker, normal BMI, and active). The ROC findings suggest that physical activity status is the best predictor of cognitive function.

With regard to the individual health characteristics, emerging work suggests that smoking may have neurocognitive impairments [49]. Briefly, smoking may negatively influence cognition via alterations in brain structure, connectivity, receptor binding, through hypoxic events, and/or alterations in biochemistry and neurotransmission [50,51]. In alignment with the present study, physical activity has been shown to induce positive cognitive benefits [5–7]. Briefly, physical activity may help to increase cortical plasticity [52], in part, by promoting angiogenesis and increasing levels of brain neurotrophic factors [7]. We did not observe an

independent association of weight status on cognition, which is in contrast to other studies [9]. Other work [9] suggests that overweight/obese individuals who are otherwise healthy have alterations in brain pathology, including reduced volume of a number of brain regions (post-central gyrus, frontal lobe, putamen, and middle frontal gyrus), impaired hippocampal long-term potentiation, decreased hippocampal neurogenesis, decreased levels of dopamine and acetylcholine, increased markers of oxidative stress, and increased central inflammation (stimulated by peripheral cytokines).

In this present study, smoking and physical activity were associated with cognitive function, but weight status was not. Although speculative, the null findings for weight status may be a result of using a proxy measure (BMI) of adiposity, as opposed to a direct assessment of body fat percentage. Interestingly, we observed evidence of an additive association of the three health characteristics on cognitive function, with those having all three (non-smoker, normal BMI, and active) having the best cognitive function.

This study extends the existing literature, but several limitations should be considered. The physical activity assessment was subjective and may be susceptible to recall bias. However, there is evidence of convergent validity for the particular subjective physical activity measure utilized in this study [45]. Given that subjective measures often attenuate results toward the null, it is likely that our physical activity-DSST results are an underestimation of their true effect [53]. Another limitation is using measured BMI as a proxy for weight status as well as only utilizing one measure of cognition. Given that the data was collected from an NHANES sample, a strength of the study is the potential to generalize to United States civilians. Future studies should extend these results longitudinally and experimentally to better inform the temporal relationship between the evaluated parameters.

In conclusion, findings of this study suggest an independent association between smoking, physical activity, and cognitive function. Given these associations, older adults should be informed of the adverse health effects that low physical activity and smoking, in particular, might have a negative impact on cognition. Further, methods of smoking cessation and exercise plans should be available for older adults when addressing these health behaviors. For future research, when assessing the individual health characteristics (namely, physical activity, smoking, and weight status) on cognitive

function among older adults, it would be beneficial to explore further environmental factors (social and built environment) as potential antecedents to these health behaviors. These potential antecedents may have an impact over one's lifetime and may play an important role on the individual and additive effects of multiple negative health characteristics on cognition. Furthermore, future studies should also evaluate other combinations of health characteristics on cognition, such as dietary behavior and sleep.

References

- [1] Glisky EL. Changes in cognitive function in human aging. In: Riddle DR (ed.) *Brain aging: models, methods, and mechanisms*, Boca Raton, FL, CRC Press, 2007.
- [2] Harada CN, Natelson Love MC, Triebel KL. Normal cognitive aging. *Clin Geriatr Med* 2013; 29:737–52.
- [3] Salthouse TA. Selective review of cognitive aging. *J Int Neuropsychol Soc* 2010; 16:754–60.
- [4] Larson EB, Kukull WA, Katzman RL. Cognitive impairment: dementia and Alzheimer's disease. *Annu Rev Public Health* 1992; 13:431–49.
- [5] Loprinzi PD. Epidemiological investigation of muscle-strengthening activities and cognitive function among older adults. *Chronic Illn* 2016; 12:157–62.
- [6] Loprinzi PD, Kane CJ. Exercise and cognitive function: a randomized controlled trial examining acute exercise and free-living physical activity and sedentary effects. *Mayo Clin Proc* 2015; 90:450–60.
- [7] Loprinzi PD, Herod SM, Cardinal BJ, Noakes TD. Physical activity and the brain: a review of this dynamic, bi-directional relationship. *Brain Res* 2013; 1539:95–104.
- [8] Zhang X, Cai X, Shi X, Zheng Z, Zhang A, Guo J, et al. Chronic obstructive pulmonary disease as a risk factor for cognitive dysfunction: a meta-analysis of current studies. *J Alzheimers Dis* 2016; 52(1):101–11.
- [9] Nguyen JC, Killcross AS, Jenkins TA. Obesity and cognitive decline: role of inflammation and vascular changes. *Front Neurosci* 2014; 8:375.
- [10] Gow AJ, Bastin ME, Munoz Maniega S, Valdes Hernandez MC, Morris Z, Murray C, et al. Neuroprotective lifestyles and the aging brain: activity, atrophy, and white matter integrity. *Neurology* 2012; 79:1802–8.
- [11] Fabrigoule C, Letenneur L, Dartigues JF, Zarrouk M, Commenges D, Barberger-Gateau P. Social and leisure activities and risk of dementia: a prospective longitudinal study. *J Am Geriatr Soc* 1995; 43:485–90.
- [12] Loprinzi PD. Epidemiological investigation of muscle-strengthening activities and cognitive function among older adults. *Chronic Illn* 2016; 12:157–62.

- [13] Loprinzi PD. Multimorbidity, cognitive function, and physical activity. *Age (Dordr)* 2016; 38:8.
- [14] Lautenschlager NT, Almeida OP. Physical activity and cognition in old age. *Curr Opin Psychiatry* 2006; 19:190–3.
- [15] Kamijo K, Hayashi Y, Sakai T, Yahiro T, Tanaka K, Nishihira Y. Acute effects of aerobic exercise on cognitive function in older adults. *J Gerontol B Psychol Sci Soc Sci* 2009; 64:356–63.
- [16] Brisswalter J, Collardeau M, Rene A. Effects of acute physical exercise characteristics on cognitive performance. *Sports Med* 2002; 32:555–66.
- [17] Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci* 2008; 9:58–65.
- [18] Kramer AF, Erickson KI, Colcombe SJ. Exercise, cognition, and the aging brain. *J Appl Physiol* (1985) 2006; 101:1237–42.
- [19] Pontifex MB, Hillman CH, Fernhall B, Thompson KM, Valentini TA. The effect of acute aerobic and resistance exercise on working memory. *Med Sci Sports Exerc* 2009; 41:927–34.
- [20] Ratey JJ, Loehr JE. The positive impact of physical activity on cognition during adulthood: a review of underlying mechanisms, evidence and recommendations. *Rev Neurosci* 2011; 22:171–85.
- [21] Cotman CW, Berchtold NC, Christie LA. Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends Neurosci* 2007; 30:464–72.
- [22] Farmer J, Zhao X, van Praag H, Wodtke K, Gage FH, Christie BR. Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult male Sprague-Dawley rats in vivo. *Neuroscience* 2004; 124:71–9.
- [23] van Praag H. Exercise and the brain: something to chew on. *Trends Neurosci* 2009; 32:283–90.
- [24] Kramer AF, Erickson KI. Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function. *Trends Cogn Sci* 2007; 11:342–8.
- [25] Murray PS, Holmes PV. An overview of brain-derived neurotrophic factor and implications for excitotoxic vulnerability in the hippocampus. *Int J Pept* 2011; 2011:654085.
- [26] Ferris LT, Williams JS, Shen CL. The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. *Med Sci Sports Exerc* 2007; 39:728–34.
- [27] Moon HY, Becke A, Berron D, Becker B, Sah N, Benoni G, et al. Running-induced systemic cathepsin B secretion is associated with memory function. *Cell Metab* 2016; 24(2):332–40.
- [28] Anstey KJ, Wood J. Chronological age and age-related cognitive deficits are associated with an increase in multiple types of driving errors in late life. *Neuropsychology* 2011; 25:613–21.
- [29] Sabia S, Elbaz A, Dugravot A, Head J, Shipley M, Hagger-Johnson G, et al. Impact of smoking on cognitive decline in early old age: the Whitehall II cohort study. *Arch Gen Psychiatry* 2012; 69:627–35.
- [30] van Dijk EJ, Prins ND, Vrooman HA, Hofman A, Koudstaal PJ, Breteler MM. Progression of cerebral small vessel disease in relation to risk factors and cognitive consequences: Rotterdam Scan study. *Stroke* 2008; 39:2712–9.
- [31] Bakhru A, Erlinger TP. Smoking cessation and cardiovascular disease risk factors: results from the Third National Health and Nutrition Examination Survey. *PLoS Med* 2005; 2:e160.
- [32] Miller AA, Spencer SJ. Obesity and neuroinflammation: a pathway to cognitive impairment. *Brain Behav Immun* 2014; 42:10–21.
- [33] Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, Iadecola C, et al. Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011; 42:2672–713.
- [34] Zlokovic BV. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders. *Nat Rev Neurosci* 2011; 12:723–38.
- [35] Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. *Nat Rev Immunol* 2011; 11:85–97.
- [36] Koyama A, O'Brien J, Weuve J, Blacker D, Metti AL, Yaffe K. The role of peripheral inflammatory markers in dementia and Alzheimer's disease: a meta-analysis. *J Gerontol A Biol Sci Med Sci* 2013; 68:433–40.
- [37] Trollor JN, Smith E, Agars E, Kuan SA, Baune BT, Campbell L, et al. The association between systemic inflammation and cognitive performance in the elderly: the Sydney Memory and Ageing Study. *Age (Dordr)* 2012; 34:1295–308.
- [38] Loprinzi PD, Branscum A, Hanks J, Smit E. Healthy lifestyle characteristics and their joint association with cardiovascular disease biomarkers in US adults. *Mayo Clin Proc* 2016; 91:432–42.
- [39] Loprinzi PD, Mahoney S. Concurrent occurrence of multiple positive lifestyle behaviors and depression among adults in the United States. *J Affect Disord* 2014; 165:126–30.
- [40] Loprinzi PD. Health behavior characteristics and all-cause mortality. *Prev Med Reports* 2016; 3:276–8.
- [41] Proust-Lima C, Amieva H, Dartigues JF, Jacqmin-Gadda H. Sensitivity of four psychometric tests to measure cognitive changes in brain aging-population-based studies. *Am J Epidemiol* 2007; 165:344–50.
- [42] Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults: a systematic review of longitudinal studies, 1996–2011. *Am J Prev Med* 2011; 41:207–15.

- [43] Vilkki J, Holst P. Mental programming after frontal lobe lesions: results on digit symbol performance with self-selected goals. *Cortex* 1991; 27:203–11.
- [44] Parkin AJ, Java RI. Deterioration of frontal lobe function in normal aging: influences of fluid intelligence versus perceptual speed. *Neuropsychology* 1999; 13:539–45.
- [45] Loprinzi PD. Dose-response association of moderate-to-vigorous physical activity with cardiovascular biomarkers and all-cause mortality: considerations by individual sports, exercise and recreational physical activities. *Prev Med* 2015; 81:73–7.
- [46] Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 2000; 32:S498–504.
- [47] Yeager DS, Krosnick JA. The validity of self-reported nicotine product use in the 2001–2008 National Health and Nutrition Examination Survey. *Medical Care* 2010; 48:1128–32.
- [48] Loprinzi P, Cardinal B, Crespo C, Brodowicz G, Andersen R, Sullivan E, et al. Objectively measured physical activity and C-reactive protein: National Health and Nutrition Examination Survey 2003–2004. *Scand J Med Sci Sports* 2013; 23:164–70.
- [49] Loprinzi PD, Herod SM, Walker JF, Cardinal BJ, Mahoney SE, Kane C. Development of a conceptual model for smoking cessation: physical activity, neurocognition, and executive functioning. *Res Q Exerc Sport* 2015; 86:338–46.
- [50] Durazzo TC, Gazdzinski S, Meyerhoff DJ. The neurobiological and neurocognitive consequences of chronic cigarette smoking in alcohol use disorders. *Alcohol Alcohol* 2007; 42:174–85.
- [51] O'Neill J, Tobias MC, Hudkins M, Oh EY, Hellemann GS, Nurmi EL, et al. Thalamic glutamate decreases with cigarette smoking. *Psychopharmacology (Berl)* 2014; 231:2717–24.
- [52] Colcombe SJ, Kramer AF, Erickson KI, Scalf P, McAuley E, Cohen NJ, et al. Cardiovascular fitness, cortical plasticity, and aging. *Proc Natl Acad Sci U S A* 2004; 101:3316–21.
- [53] Tooze JA, Troiano RP, Carroll RJ, Moshfegh AJ, Freedman LS. A measurement error model for physical activity level as measured by a questionnaire with application to the 1999–2006 NHANES questionnaire. *Am J Epidemiol* 2013; 177:1199–208.