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COGNITIVE AND NEURAL CORRELATES OF AEROBIC FITNESS IN OBESE OLDER ADULTS

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Background/Study Context: Aerobic fitness is associated with preserved cognition and brain volume in older adulthood. The current study investigated whether the benefits of aerobic fitness extend to obese older adults, a segment of the population that is rapidly growing and who exhibit compromised cognition and brain structure relative to their nonobese counterparts.

Methods: Measures of obesity, aerobic fitness, cognition (processing speed, executive function, spatial ability, memory), and regional brain volumes (prefrontal gray, prefrontal white, hippocampus) were obtained from 19 obese older adults aged 65 to 75. Hierarchical linear regression analyses were conducted to examine the proportion of unique variance in cognitive and volumetric measures accounted for by aerobic fitness after controlling for covariates (age, gender, and waist circumference).

Results: Aerobic fitness accounted for a significant amount of unique variance in processing speed (adjusted $R^2 = .44$), executive function (adjusted $R^2 = .34$), and hippocampal volume (adjusted $R^2 = .27$).

Conclusion: This novel pattern of results suggests that obesity does not preclude the benefits of fitness for cognition and brain volume in older adults. Fitness appears to be a beneficial factor for maintenance of processing speed, executive function, and hippocampal volume, which are vulnerable to age- and/or obesity-related decline.

Age-related declines in cognitive processes, including speed, executive control, and memory, in conjunction with atrophy of prefrontal and medial temporal regions of the brain are well documented (e.g., Raz & Rodrigue, 2006; Salthouse & Meinz, 1995). However, growing evidence indicates large individual differences in aging trajectories and the dependence of these changes, in part, on health-related factors (e.g., Raz & Rodrigue, 2006). For example, older adults who engage in aerobic exercise or are aerobically fit show benefits to executive function, processing speed, and spatial ability (Colcombe & Kramer, 2003) as well as memory (Erickson et al., 2009). Importantly, such benefits extend to the structural integrity of older adults' brains (Colcombe et al., 2006). The volume of regions that show the greatest age-related atrophy, including frontal gray and white matter, increases subsequent to older adults' engagement in an aerobic exercise intervention (see also Colcombe et al., 2003, for convergent cross-sectional evidence of an association between aerobic fitness and regional brain volume). Similarly, aerobic fitness is positively associated with the volume of medial temporal structures (Gordon et al., 2008; cf. Bugg & Head, 2011), including hippocampus (Erickson et al., 2009), a region that is compromised in early-stage Alzheimer's disease (Braak & Braak, 1991).

Health-related factors can also deleteriously affect older adults' cognition and brain structure. Here, we focus on the potentially negative effects of obesity (i.e., body mass index [BMI] ≥ 30 kg/m²), which has increased markedly in older populations (e.g., Flegal, Carroll, Kuczmarski, & Johnson, 1998). Recent investigations indicate that relative to normal weight or even overweight, obesity in older adulthood is associated with poorer memory and executive function (Elias, Elias, Sullivan, Wolf, & D'Agostino, 2003; Gunstad et al., 2007; Walther, Birdsill, Glisky, & Ryan, 2010; but see Kuo et al., 2006), and frontal (Raji et al., 2010; Walther 2010) and hippocampal (Raji et al., 2010) atrophy. Central adiposity, the accumulation of adipose tissue in the trunk area, appears particularly harmful. It is associated with an increased risk of cognitive impairment (West & Haan, 2009) and reduced hippocampal volume (Jagust, Harvey, Mungas, & Haan, 2005) after controlling for BMI.

Because the prevalence of obesity is projected to rise in all age categories including older adulthood (e.g., Arterburn, Crane, & Sullivan, 2004), the existence of the above negative outcomes leads to pressing concerns regarding not only the quality of life of obese older adults but also the burden to our health care system. These concerns raise the question of whether the benefits of health-promoting factors such as aerobic fitness are offset by health conditions such as obesity. That is, can obese older adults reap the benefits of fitness for cognition and brain volume, or does obesity preclude the obtainment of these benefits? Some existing research suggests that the benefits of fitness more generally are observed for obese older adults. For example, the risks of all-cause mortality and mortality related to cardiovascular disease are lower for fit as compared with unfit individuals in all categories of body weight, including obesity (Lee, Blair, & Jackson, 1999). However, other evidence suggests that the benefits of fitness may be attenuated or nonexistent in an obese older adult sample. For example, it has been shown that obesity is associated with increased cardiovascular disease risk factors regardless of fitness level (Christou, Gentile, DeSouza, Seals, & Gates, 2005). Furthermore, because obesity is negatively associated with aerobic fitness (e.g., Ross & Katzmarzyk, 2003), it is possible that the fittest obese older adults may not be fit enough, and obesity may represent a boundary condition for the cognitive and brain benefits of fitness.

The purpose of the present study was to address the important and novel question of whether aerobic fitness is predictive of cognition and regional brain volume in a sample that consists entirely of obese older adults. If fitness is beneficial in the context of obesity, then fitness should account for a significant amount of unique variance

in processing speed, executive function, and spatial ability (cf. Colcombe & Kramer, 2003) and use of controlled recollection during memory retrieval, with a positive association between fitness and these outcomes. In contrast, higher fitness should be associated with less reliance on automatic processes (i.e., familiarity) in memory. Similarly, if the benefits of fitness extend to obese older adults, then fitness should account for a significant amount of unique variance in regional brain volumes that have been sensitive to fitness effects in previous studies, including hippocampus, prefrontal gray, and prefrontal white matter (Colcombe et al., 2003, 2006; Erickson et al., 2009). These a priori regions of interest have prominence in both the aging and obesity literatures.

METHODS

Participants

The sample consisted of 19 obese older adults (74% female; 84% Caucasian) aged 65 to 75 ($M = 68.4$, $SD = 2.7$) with an average education level of 2.79 ($SD = .85$; range = 1 [less than high school] to 4 [graduate school]). The inclusion criteria were age ≥ 65 ; obesity ($BMI \geq 30 \text{ kg/m}^2$); sedentary lifestyle (did not participate in regular exercise more than twice a week); stable body weight ($\pm 2 \text{ kg}$) over past year; and no change in medications for at least 6 months prior to enrollment. The exclusion criteria were current smoking history; Type I or II diabetes; dyspnea or angina at rest with minimal exertion; stage III or IV renal failure (glomerular filtration rate [GFR] $< 30 \text{ ml/min}$); severe anemia (hemoglobin [Hb] $< 8 \text{ g/dl}$); visual/hearing impairment interfering with daily tasks; cognitive impairment (Mini-Mental State Examination [MMSE] ≤ 24); history of malignant neoplasm; and corticosteroid agents or sex-steroid use within 3 months. No participant reported use of antidepressants or current history of depression. Participants consented to participation in accordance with the Washington University Human Research Protection Office.

Materials and Procedure

BMI was calculated as measured weight (kilograms)/height² (meters). Waist circumference was the measure of central adiposity. Lean body mass (nonbone fat-free mass), appendicular lean mass, and fat mass were measured via dual x-ray absorptiometry (DEXA)

(Hologic Delphi 4500/w; Waltham, MA). Enhanced Whole Body 11.2 software (Hologic) was used to obtain the measure of lean mass in legs and arms. The bone mineral-free portion of the appendicular extremity represents primarily skeletal muscle (Heymsfield, Gallagher, Visser, Nunez, & Wang 1995).

Peak aerobic capacity (VO_2 peak) was assessed during a symptom-limited, graded treadmill test (see also Villareal, Banks, Sinacore, Siener, & Klein, 2006). Warm-up was at 0% grade, at the fastest comfortable walking speed, and varied from 3 to 5 min to produce approximately 70% of each subject's peak heart rate. Speed was then held constant and elevation was progressively increased by 2% to 3% every 2 min based on clinical judgment (i.e., consideration of physical limitations, sedentary lifestyle, chronic conditions). The test was terminated when subjects became too fatigued to continue (Kohrt et al., 1991). The highest average O_2 uptake from four consecutive 15 s was designated as VO_2 peak. The primary measure of aerobic fitness was VO_2 peak normalized by appendicular lean mass as determined by the DEXA scan (cf. Burns et al., 2008). We refer to this measure as VO_2 adjusted. VO_2 adjusted was chosen as the aerobic fitness measure because 95% of the O_2 consumed during a treadmill test is in exercising muscles (i.e., lean mass) (Fleg et al., 2005), with most of it being used by limb muscles (i.e., appendicular lean mass) (Proctor & Joyner, 1997). Furthermore, VO_2 adjusted is independent of age-associated changes in body composition (Proctor & Joyner, 1997), which was important given our obese sample, and minimizes gender differences. One subject's adjusted score was ≥ 4 SD from the mean and was replaced using regression imputation. Descriptive data for the VO_2 measures and corresponding physiological variables are presented in Table 1.

The cognitive data were obtained prior to the magnetic resonance imaging (MRI) scan on a separate day within 2 months of the body composition and aerobic fitness assessments. The cognitive tasks were administered in the same order for all participants. Scores from two tasks in the processing speed, executive function, and spatial ability domains were standardized via z -score transformation and summed to derive a composite. This approach weights each task equally rather than allowing each measure to combine in a maximal fashion. For the memory domain, we administered a single task from which two measures were derived and z -transformed.

For the processing speed domain, Symbol Search (Wechsler, 1997) and Letter Comparison (Salthouse & Meinz, 1995) tasks were administered. The Symbol Search task required participants to determine whether a target symbol matched one of four search symbols. For the

Table 1. Descriptive Data

	Mean	SD	Range
<i>Body Composition</i>			
Height (cm)	166.7	8	156–186
Weight (kg)	99.9	15.9	82–143
BMI (kg/m ²)	36	5.1	30–45
Waist Circumference (cm)	115.2	14.3	93–148
Fat Mass (kg)	40.7	9.3	24–60
Lean Body Mass (LBM) (kg)	56.7	11.5	42–85
Appendicular Lean Mass (ALM) (kg)	24.2	5.8	16–37
<i>Fitness Measures</i>			
Absolute VO ₂ (VO _{2 peak}) (L/min)	1.66	.32	1.11–2.14
VO _{2 peak} relative to ALM (mL/kg ALM /min)	68.3	9.4	49–80
Respiratory Exchange Ratio (RER)	1.1	.05	1.02–1.21
Maximum HR (beats/min)	137.9	17.2	104–166
<i>Cognitive Measures</i>			
Symbol Search	28.2	6.3	18–43
Letter Comparison	7.3	1.4	4–10
Stroop	35.6	10.8	21–54
Operation Span	10.4	4.6	4–19
Spatial Relations	66.8	7.5	54–77
Judgment of Line Orientation	23.6	5	11–30
Familiarity	0.61	0.13	.30–.75
Recollection	0.36	0.16	.09–.61
<i>Regional Brain Volumes</i>			
Hippocampus (cm ³)	8	0.8	6–9
Prefrontal Gray (cm ³)	69.6	4.7	63–80
Prefrontal White (cm ³)	57.9	6.8	40–71

Note: (1) VO_{2 peak} relative to ALM = VO_{2 adjusted}; (2) The mean maximum HR increases to 142 when 4 subjects taking beta-blockers or calcium channel blockers, which can lead to less reliable HR estimates, are removed.

Letter Comparison task, participants visually compared two letter strings (e.g., XCVJNE and XCVJHE) to determine whether the two were the same or different. In both tasks participants were instructed to work as rapidly as possible and the index of performance was the number correct within a time limit. For the executive function domain, Stroop color naming and Operation Span (OSPAN; Turner & Engle, 1989) tasks were administered. For Stroop, the paper version was used where participants first read the names of color words (e.g., RED, GREEN, BLUE) printed in black ink, then named the ink color of XXXXX strings printed in red, green, or blue ink (i.e., neutral condition), and finally named the ink color of words in the incongruent condition (e.g., the word RED printed in blue ink). The index of performance was interference, defined as residual

performance in the incongruent condition after controlling for performance in the neutral condition. For OSPAN, a working memory capacity task was used involving the concurrent solving of mathematic equations and memorization of words. The index of performance was absolute span, which refers to the total number of words correctly recalled across all 12 trials of the task. Working memory capacity tasks such as OSPAN have been shown to reflect domain-general executive attention, the ability to maintain goal-relevant information in the face of interference (Kane et al., 2004). For the spatial ability domain, the measures were the Woodcock-Johnson III Spatial Relations subtest (Woodcock, McGrew, & Mather, 2001) and Benton Judgment of Line Orientation (Benton, Varney, & Hamsher, 1978) tasks. For the Spatial Relations task, participants were shown a complex spatial pattern, and asked to determine which pieces would be needed to construct the pattern (e.g., select the pattern's constituent parts). For the Judgment of Line Orientation task, participants were asked to select a line from an array of 11 lines that matched the orientation of a target line. The index of performance for both tasks was the number correct.

For the memory domain, a proactive interference task was administered in which participants studied and attempted to recall cue-target pairs (e.g., KNEE-BEND; KNEE-BONE) (see Jacoby, Debner, & Hay, 2001, for procedural details). Following Jacoby et al. (2001), our indices of performance were estimates of familiarity (accessibility bias), a relatively automatic retrieval process, and recollection, a controlled retrieval process.

Imaging was performed using a Siemens 3.0 Tesla Trio scanner (Erlangen, Germany). Cushions and a thermoplastic mask were used during scanning to reduce head movement. A scout image (TR = 20 ms, TE = 5 ms, flip angle = 40°, 2.2 × 1.7 × 8 mm resolution) was acquired first in order to center the field of view on the brain. Two T1-weighted sagittal MP-RAGE scans (TR = 2400 ms, TE = 3.16 ms, flip angle = 8°, TI = 1000 ms, 1 × 1 × 1 mm resolution) were acquired. Image processing steps (see Buckner et al., 2004, for details) included inter- and intrascan motion correction, atlas transformation, averaging, and inhomogeneity correction resulting in registered structural data in 1 mm³ voxels in atlas space (Talairach & Tournoux, 1998). Atlas normalization is equivalent to normalization based on intracranial volume (Buckner et al., 2004). The Freesurfer image analysis suite (Desikan et al., 2006) was used to obtain automated regional volume estimates of hippocampus, prefrontal gray matter, and adjacent prefrontal white matter. This technique assigns a

neuroanatomical label to each voxel in the MR image. There is high correspondence between the volumes generated by this technique and manually generated volumes (Desikan et al., 2006).

Analytic Approach

A series of hierarchical linear regression analyses were conducted to examine the proportion of unique variance in cognitive and volumetric measures accounted for by VO_2 adjusted after controlling for theoretically relevant covariates. The covariates were age, gender, and waist circumference.¹ Bivariate correlations between age, gender, waist circumference, and the predictor and outcome variables are reported prior to the results of the regression analyses. An alpha level of .01 was used.

RESULTS

Descriptive data from the body composition, aerobic fitness, cognitive, and MRI assessments are presented in Table 1.

Bivariate Correlations

There were no significant associations between age and the predictor (VO_2 adjusted) or outcome variables (all $ps > .122$), possibly because of the restricted age range. Gender was significantly associated with the recollection estimate ($r(17) = .55, p < .007$), but not with any other outcome or the predictor variable (all $ps > .132$, with the exception of a trend for gender and prefrontal white matter volume, $r(17) = -.41, p = .039$). The relationship between waist circumference and the predictor variable, VO_2 adjusted, approached significance ($r(17) = -.51, p = .013$). Waist circumference was not significantly related to any of the outcome measures (all $ps > .105$).

¹There were two measures of obesity, BMI and waist circumference, in the present study. The measures were strongly correlated ($r(17) = .82, p < .001$). Therefore, we elected to treat one as a potential covariate rather than both so as not to restrict power. We chose waist circumference because of prior studies showing negative effects of this measure of obesity on cognition (West & Haan, 2009) and brain volume (Jagust et al., 2005), independent of BMI. Controlling for obesity (i.e., waist circumference) in the regression analyses permits one to conclude that any observed relationships between aerobic fitness and cognition or brain volume relate to varying degrees of fitness and not obesity, which has been shown in past studies to covary with fitness.

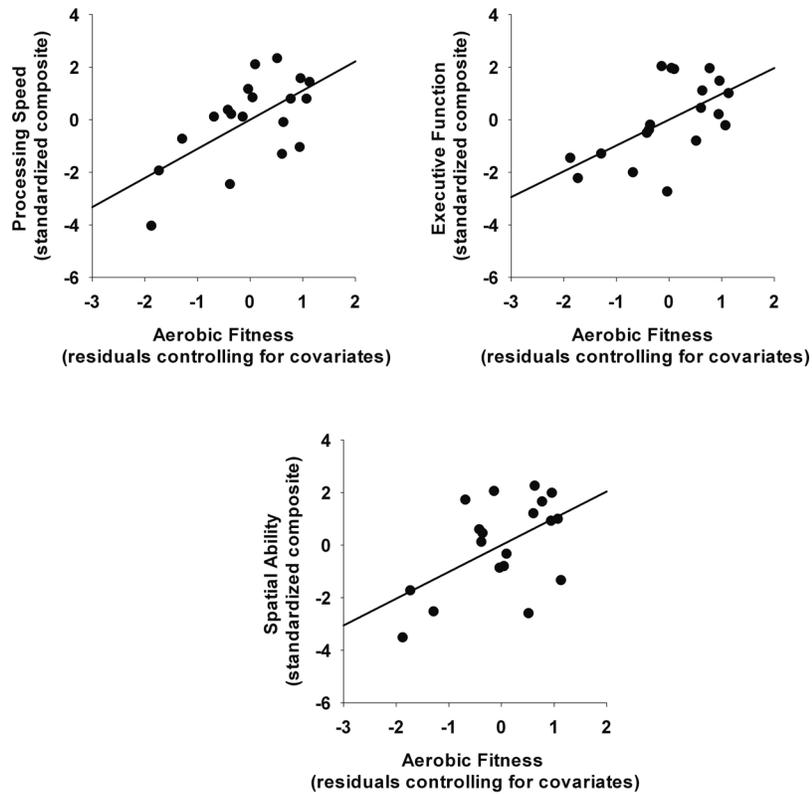


Figure 1. Associations between aerobic fitness (VO_2 adjusted) and cognitive composites after controlling for covariates (i.e., age, gender, and waist circumference).

Regression Analyses²

VO_2 adjusted accounted for unique variance in processing speed (adjusted $R^2 = .44$, R^2 change = .39, $\beta = .13$, $p = .003$) and executive

²The minimum sample sizes needed to observe a significant relationship between aerobic fitness and the following outcomes were computed based on a model in which power was specified at .80, three covariates and one predictor variable were included, and effect sizes were estimated to be equivalent to those obtained in the current study. Sample sizes were calculated for alpha levels of .01, .05, and .10, respectively: spatial ability ($ns = 36, 25, 20$); recollection estimate ($ns = 132, 89, 70$); familiarity estimate ($ns = 65, 44, 35$); prefrontal gray matter volume ($ns = 84, 57, 45$); prefrontal white matter volume ($ns = 71, 48, 38$). We thank an anonymous reviewer for suggesting the inclusion of these estimates.

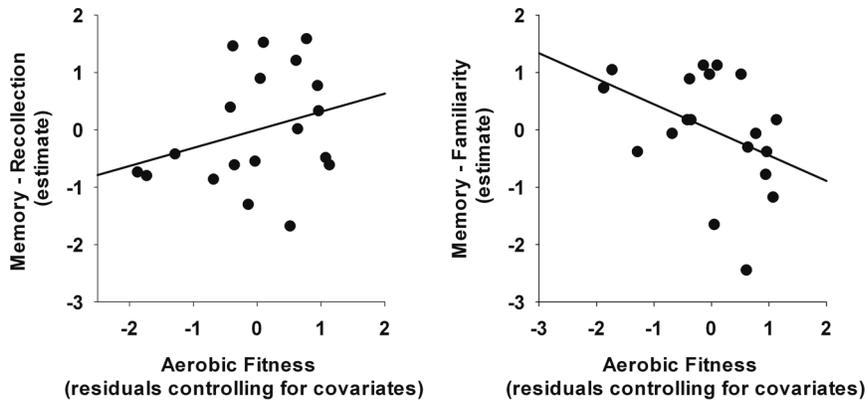


Figure 2. Associations between aerobic fitness (VO_2 adjusted) and memory process estimates after controlling for covariates (i.e., age, gender, and waist circumference).

function (adjusted $R^2 = .34$, R^2 change = .35, $\beta = .11$, $p = .008$), with a nonsignificant trend for a positive association with spatial ability (adjusted $R^2 = .19$, R^2 change = .29, $\beta = .12$, $p = .024$) (see Figure 1). For the memory task, aerobic fitness did not account for significant, unique variance in recollection (adjusted $R^2 = .40$, R^2 change = .08, $\beta = .01$, $p = .137$) or familiarity (adjusted $R^2 = .07$, R^2 change = .17, $\beta = -.01$, $p = .094$), although associations were in the expected direction (see Figure 2).

VO_2 adjusted also accounted for unique variance in hippocampal volume (adjusted $R^2 = .27$, R^2 change = .39, $\beta = 62.09$, $p = .008$) (see Figure 3). VO_2 adjusted did not account for significant, unique variance in prefrontal gray matter volume (adjusted $R^2 = -.04$, R^2 change = .13, $\beta = 210.42$, $p = .155$) or prefrontal white matter volume (adjusted $R^2 = .17$, R^2 change = .15, $\beta = 330.94$, $p = .089$), although associations were in the expected direction (see Figure 3).

DISCUSSION

The current investigation examined the novel question of whether aerobic fitness is associated with better cognitive performance and larger regional brain volumes in a sample that consisted entirely of obese older adults. A promising pattern of results was revealed indicating that fitness is a beneficial factor for maintenance of cognition and brain volume in this population. In particular, aerobic fitness

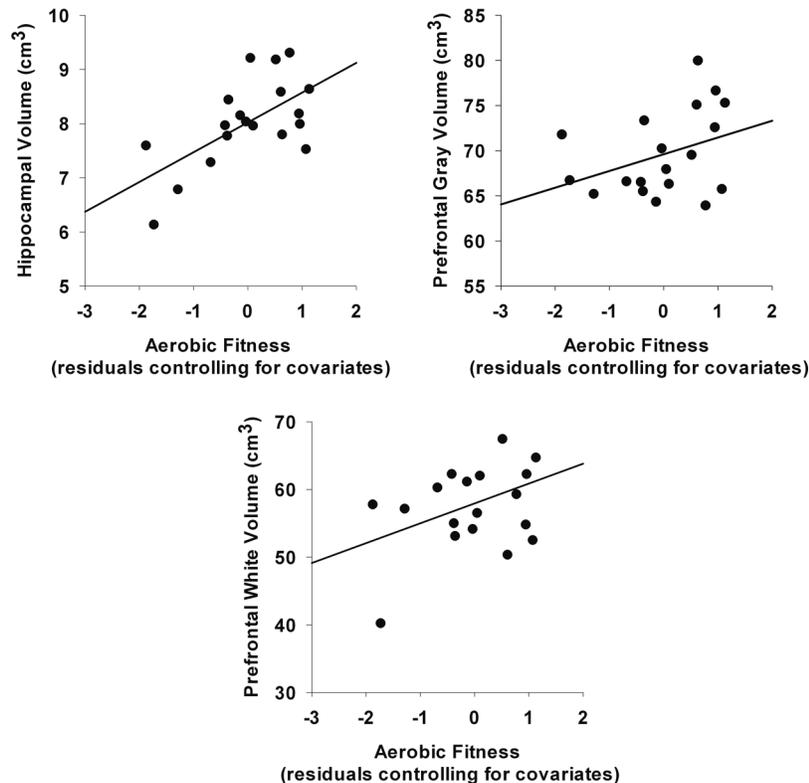


Figure 3. Associations between aerobic fitness (VO_2 adjusted) and regional brain volumes after controlling for covariates (i.e., age, gender, and waist circumference).

accounted for a significant amount of variance in two domains of cognition that are known to be vulnerable to age-related decline, processing speed and executive function. These findings converge with prior reports of such benefits in healthy older adults (Colcombe & Kramer, 2003). In addition, there was a trend ($p = .024$) for aerobic fitness to account for unique variance in spatial ability. This trend may reflect our relatively small sample size, as a power analysis based on a desired power of .80 indicates that an effect of this size would have met the more stringent alpha level if the sample size were 36.

Aerobic fitness also accounted for a significant amount of variance in hippocampal volume, a region that is compromised by obesity (Jagust et al., 2005; Raji et al., 2010). This is the first demonstration of this finding in an older adult sample that is obese and is consistent

with recent reports of such an association in a healthy older adult sample (Erickson et al., 2009) and older adults with early-stage Alzheimer's disease (Honea et al., 2009). This finding may be especially significant because prior work shows that obese older adults (as defined by waist circumference) are at an increased risk of cognitive impairment (West & Haan, 2009), and baseline hippocampal volume predicts convergence from mild cognitive impairment to Alzheimer's disease, with reduced rates observed for those with larger volumes (Grundman et al., 2002).

In contrast to a prior finding in a healthy older adult sample (Erickson et al., 2009; see also Blumenthal & Madden, 1988, for an association between fitness and reaction time in memory search in healthy middle aged to older men), aerobic fitness was not significantly related to memory performance. Also, in contrast to prior findings (Colcombe et al., 2003, 2006), aerobic fitness did not account for a significant amount of variance in prefrontal gray or prefrontal white matter volume. Obesity may represent a boundary condition for the benefits of fitness in select cognitive processes or brain regions. Alternatively, differences in methodology may contribute to the discrepant patterns. For example, Erickson et al. (2009) used a spatial memory paradigm, whereas our memory task involved verbal paired-associates. Further, we extracted neuroanatomically defined brain regions for analysis, whereas Colcombe et al. (2003, 2006) identified regions via voxel-based morphometry (for elaboration, see Bugg & Head, 2011; Kennedy et al., 2009).

Although this investigation has the limitations of a relatively small sample size and a predominantly female and Caucasian composition, the current cross-sectional results provide initial evidence of a direct relationship between aerobic fitness and select measures of cognition and brain volume in the context of obesity and aging. Obese older adults with higher levels of fitness are at an advantage relative to their less fit peers on measures of processing speed, executive function, and hippocampal volume. One potential implication is that obese older adults who are unable to lose weight, but can increase their aerobic fitness, may experience benefits to cognition and brain volume (cf. Lee et al., 1999). To establish that increased fitness leads to increases in processing speed, executive function, and hippocampal volume, an intervention study is needed in which these measures are obtained from obese older adults prior to and following an aerobic exercise program. An open question is whether aerobic fitness benefits cognition and brain volume similarly in obese older adults with diabetes or those who would not otherwise have met the inclusion/exclusion criteria in the current study.

Another implication of the current findings concerns factors that mediate effects of obesity on cognition and brain structure. Prior studies have shown that cardiovascular and metabolic risk factors are partial, but not complete, mediators (e.g., Elias et al., 2003; Jagust et al., 2005). Our findings suggest that poor aerobic fitness may contribute to cognitive impairment and volumetric reductions in obese older adults. The current findings are therefore important in supporting the inclusion of aerobic fitness measures in future studies that attempt to model obesity-related effects.

REFERENCES

- Arterburn, D. E., Crane, P. K., & Sullivan, S. D. (2004). The coming epidemic of obesity in elderly Americans. *Journal of the American Geriatric Society, 52*, 1907–1912.
- Benton, A. L., Varney, N. R., & Hamsher, K. (1978). Visuospatial judgment: A clinical test. *Archives of Neurology, 35*, 364–367.
- Blumenthal, J. A., & Madden, D. J. (1988). Effects of aerobic exercise training, age, and physical fitness on memory-search performance. *Psychology and Aging, 3*, 280–285.
- Braak, H., & Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica, 82*, 239–259.
- Buckner, R. L., Head, D., Parker, J., Fotenos, A. F., Marcus, D., Morris, J. C., & Snyder, A. Z. (2004). A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: Reliability and validation against manual measurement of total intracranial volume. *Neuroimage, 23*, 724–738.
- Bugg, J. M., & Head, D. H. (2011). Exercise moderates age-related atrophy of the medial temporal lobe. *Neurobiology of Aging, 32*, 506–514.
- Burns, J. M., Cronk, B. B., Anderson, H. S., Donnelly, J. E., Thomas, G. P., Harsha, A., Brooks, W. M., & Swerdlow, R. H. (2008). Cardiorespiratory fitness and brain atrophy in early Alzheimer disease. *Neurology, 71*, 210–216.
- Christou, D. D., Gentile, C. L., DeSouza, C. A., Seals, D. R., & Gates, P. E. (2005). Fatness is a better predictor of cardiovascular disease risk factor profile than aerobic fitness in healthy men. *Circulation, 111*, 1904–1914.
- Colcombe, S. J., Erickson, K. I., Raz, N., Webb, A. G., Cohen, N. J., McAuley, E., & Kramer, A. (2003). Aerobic fitness reduces brain tissue loss in aging humans. *Journals of Gerontology, 58A*, 176–180.
- Colcombe, S. J., Erickson, K. I., Scaif, P. E., Kim, J. S., Prakash, R., McAuley, E., Elavsky, S., Marquez, D. X., Hu, L., & Kramer, A. F. (2006). Aerobic exercise training increases brain volume in aging humans. *Journals of Gerontology, 61A*, 1166–1170.
- Colcombe, S., & Kramer, A. F. (2003). Fitness effects on the cognitive function of older adults: A meta-analytic study. *Psychological Science, 14*, 125–130.

- Desikan, R. S., Segonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., Buckner, R. L., Dale, A. M., Maguire, R. P., Hyman, B. T., Albert, M. S., & Killiany, R. J. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*, *31*, 968–980.
- Elias, M. F., Elias, P. K., Sullivan, L. M., Wolf, P. A., & D’Agostino, R. B. (2003). Lower cognitive function in the presence of obesity and hypertension: The Framingham Heart Study. *International Journal of Obesity*, *27*, 260–268.
- Erickson, K. I., Prakash, R. S., Voss, M. W., Chaddock, L., Hu, L., Morris, K. S., White, S. M., Wojcicki, T. R., McAuley, E., & Kramer, A. F. (2009). Aerobic fitness is associated with hippocampal volume in elderly humans. *Hippocampus*, *19*(10), 1030–1039.
- Fleg, J. L., Morrell, C. H., Bos, A. G., Brant, L. J., Talbot, L. A., Wright, J. G., & Lakatta, E. G. (2005). Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation*, *112*, 674–682.
- Flegal, K. M., Carroll, M. D., Kuczmarski, R. J., & Johnson, C. L. (1998). Overweight and obesity in the United States: Prevalence and trends, 1960–1994. *International Journal of Obesity and Related Metabolic Disorders*, *22*, 39–47.
- Gordon, B. A., Rykhlevskaia, E. I., Brumback, C. R., Lee, Y., Elavsky, S., Konopack, J. F., McAuley, E., Kramer, A. F., Colcombe, S., Gratton, G., & Fabiani, M. (2008). Neuroanatomical correlates of aging, cardiopulmonary fitness level, and education. *Psychophysiology*, *45*, 825–838.
- Grundman, M., Sencakova, D., Jack, C. R., Jr., Peterson, R. C., Kim, H. T., Schultz, A., Weiner, M. F., DeCarli, C., DeKosky, S. T., van Dyck, C., Thomas, R. G., & Thal, L. J. (2002). Brain MRI hippocampal volume and prediction of clinical status in a mild cognitive impairment. *Journal of Molecular Neuroscience*, *19*, 23–27.
- Gunstad, J., Paul, R. H., Cohen, R. A., Tate, D. F., Spitznagel, M. B., & Gordon, E. (2007). Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Comprehensive Psychiatry*, *48*, 57–61.
- Heymsfield, S. B., Gallagher, D., Visser, M., Nunez, C., & Wang, Z. M. (1995). Measurement of skeletal muscle: Laboratory and epidemiological methods. *Journals of Gerontology Series A: Biological Sciences Medical Sciences*, *50*, 23–29.
- Honea, R. A., Thomas, G. P., Harsha, A., Anderson, H. S., Donnelly, J. E., Brooks, W. M., & Burns, J. M. (2009). Cardiorespiratory fitness and preserved medial temporal lobe volume in Alzheimer’s disease. *Alzheimer Disease & Associated Disorders*, *23*, 188–197.
- Jacoby, L. L., Debner, J. A., & Hay, J. F. (2001). Proactive interference, accessibility bias, and process dissociations: Valid subjective reports of memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *27*, 686–700.
- Jagust, W., Harvey, D., Mungas, D., & Haan, M. (2005). Central obesity and the aging brain. *Archives of Neurology*, *62*, 1545–1548.
- Kane, M. J., Hambrick, D. Z., Tuholski, S. W., Wilhelm, O., Payne, T. W., & Engle, R. W. (2004). The generality of working memory capacity: A latent-variable approach to verbal and visuospatial memory span and reasoning. *Journal of Experimental Psychology: General*, *133*, 189–217.

- Kennedy, K. M., Erickson, K. I., Rodrigue, K. M., Voss, M. W., Colcombe, S. J., Kramer, A. F., Acker, J. D., & Raz, N. (2009). Age-related differences in regional brain volumes: A comparison of optimized voxel-based morphometry to manual volumetry. *Neurobiology of Aging, 30*, 1657–1676.
- Kohrt, W. M., Malley, M. T., Coggan, A. R., Spina, R. J., Ogawa, T., Ehsani, A. A., Bourey, R. E., Martin, W. H., & Holloszy, J. O. (1991). Effects of gender, age, and fitness level on response of $\dot{V}O_{2\max}$ to training in 60–71 yr olds. *Journal of Applied Physiology, 71*, 2004–2011.
- Kuo, H., Jones, R. N., Milberg, W. P., Tennstedt, S., Talbot, L., Morris, J. N., & Lipsitz, L. A. (2006). Cognitive function in normal-weight, overweight, and obese older adults: An analysis of the advanced cognitive training for independent and vital elderly cohort. *Journal of the American Geriatric Society, 54*, 97–103.
- Lee, C. D., Blair, S. N., & Jackson, A. S. (1999). Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *American Journal of Clinical Nutrition, 69*, 373–380.
- Proctor, D. N., & Joyner, M. J. (1997). Skeletal muscle mass and the reduction of $\dot{V}O_{2\max}$ in trained older subjects. *Journal of Applied Physiology, 82*, 1411–1415.
- Raji, C. A., Ho, A. J., Parikshak, N. N., Becker, J. T., Lopez, O. L., Kuller, L. H., Hua, X., Leow, A. D., Toga, A. W., & Thompson, P. M. (2010). Brain structure and obesity. *Human Brain Mapping, 31*, 353–364.
- Raz, N., & Rodrigue, K. M. (2006). Differential aging of the brain: Patterns, cognitive correlates, and modifiers. *Neuroscience and Biobehavioral Reviews, 30*, 730–748.
- Ross, R., & Katzmarzyk, P. T. (2003). Cardiorespiratory fitness is associated with diminished total and abdominal obesity independent of body mass index. *International Journal of Obesity and Related Metabolic Disorders, 27*, 204–210.
- Salthouse, T. A., & Meinz, E. J. (1995). Aging, inhibition, working memory, and speed. *Journals of Gerontology Series B, 50*, 297–306.
- Talairach, J., & Tournoux, P. (1998). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme Medical Publishers.
- Turner, M. L., & Engle, R. W. (1989). Is working memory capacity task dependent? *Journal of Memory and Language, 28*, 127–154.
- Villareal, D. T., Banks, M., Sinacore, D., Siener, C., & Klein, S. (2006). Effects of weight loss and exercise on frailty in obese older adults. *Archives of Internal Medicine, 166*, 860–866.
- Walther, K., Birdsill, A. C., Glisky, E. L., & Ryan, L. (2010). Structural brain differences and cognitive functioning related to body mass index in older females. *Human Brain Mapping, 31*(7), 1052–1064.
- Wechsler, D. (1997). *WAIS-II administration and scoring manual*. San Antonio, TX: The Psychological Corporation.
- West, N. A., & Haan, M. N. (2009). Body adiposity in late life and risk of dementia or cognitive impairment in a longitudinal community-based study. *Journals of Gerontology Series A: Biological Sciences, 64A*, 103–109.
- Woodcock, R. W., McGrew, K. S., & Mather, N. (2001). *Examiner's manual*. Itasca, IL: Riverside Publishing.