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## Physical activity and cognitive function in bariatric surgery candidates

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### Abstract

Cognitive impairment is common in severe obesity. Lack of physical activity is a likely contributor to impairment in this population, as many obese persons are inactive and physical activity has been positively and independently associated with cognitive function in healthy and medically-ill samples. This study investigated whether physical activity, measured by self-report of aerobic physical activity in 85 bariatric surgery candidates, was associated with cognitive function. A subset of 31 participants also completed objective activity monitoring. Steps/d and high-cadence min/week, representative of ambulatory moderate to vigorous physical activity (MVPA), were calculated. Approximately one quarter of participants self-reported at least 30 min/d of aerobic MVPA, at least 5 d/week. Median steps/d was 7949 (IQR = 4572) and median MVPA min/week was 105 (IQR = 123). Cognitive deficits were found in 32% of participants (29% memory, 10% executive function, 13% language, 10% attention). Controlling for demographic and medical factors, self-reported aerobic physical activity was weakly correlated with lower attention ( $r = -0.21$ ,  $p = 0.04$ ) and executive function ( $r = -0.27$ ,  $p < 0.01$ ) and both self-reported aerobic physical activity and objectively-determined MVPA min/week were negatively correlated with memory ( $r = -0.20$ ,  $p = 0.04$ ;  $r = -0.46$ ;  $p = 0.02$ , respectively). No other correlations between physical activity measures and cognitive function were significant. Contrary to expectations, greater levels of physical activity were not associated with better cognitive functioning. Such

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Declaration of Interest

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findings encourage future studies to clarify the association among cognitive function and physical activity in obese persons.

## Keywords

exercise; obesity; attention; executive function; memory

Obesity is increasingly recognized as an independent risk factor for adverse neurocognitive outcomes. Elevated body mass index (BMI) is associated with increased risk for neurologic disorders such as stroke [1], Alzheimer's disease, and vascular dementia [2–4]. Elevated BMI is also associated with structural and functional abnormalities on neuroimaging in the absence of these disorders, including decreased blood flow [5], reduced white matter integrity [6,7], and smaller grey matter and total brain volume relative to normal weight [8]. Consistent with these adverse brain changes, persons with elevated BMI often exhibit cognitive dysfunction on testing [9–14], with the most common deficits being the domains of memory and executive function [9,10,14]. Cognitive impairment is particularly prevalent in severely obese persons, with up to 25% of individuals demonstrating clinically meaningful levels of impairment on neuropsychological testing [10].

Past studies have shown multiple factors contribute to cognitive dysfunction in obese persons, including severity of obesity and comorbid conditions like hypertension and type 2 diabetes [15]. Though not previously examined, another likely contributor to cognitive impairment in adults with severe obesity is low levels of physical activity [16–18]. Bariatric surgery patients are often sedentary [19] and numerous studies show regular physical activity reduces risk for dementia [20–23] and cognitive decline [24]. Much of the research in this area has demonstrated an association between improved cardiovascular fitness and participation in moderate- to high-intensity exercise on structural and functional neurocognitive outcomes. For example, increased cardiorespiratory fitness is associated with reduced brain atrophy [25], preservation of gray and white matter [26,27], and greater hippocampal volumes [28]. Similarly, moderate- to high-intensity aerobic exercise is associated with increased gray and white matter volume [29] and functional connectivity in the prefrontal cortex [30]. Consistent with these findings, moderate-to high-intensity aerobic exercise has also been shown to improve cognitive functioning, including executive functioning, attention, visuospatial functioning, and processing speed, across patient and healthy samples [30–33].

This preliminary study examined the contribution of physical activity to cognitive function in severely obese adults. Specifically, we examine whether physical activity is associated with memory, attention, executive function, and/or language among adults undergoing bariatric surgery. Based on previous findings, we hypothesized that higher levels of physical activity would be associated with better performance on tests of cognitive function.

## Methods

All procedures were approved by the appropriate Institutional Review Boards and all participants provided written informed consent prior to study involvement.

## Trial design and participants

The original sample included 122 adults who were recruited for an ancillary study focused on cognitive function from the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) parent project [34]. Of the original sample, 17 participants were excluded from analyses due to missing cognitive function data ( $n = 14$ ) or self-reported physical activity data ( $n = 3$ ). Inclusion criteria for the ancillary study included age between 20–70 years and being English-speaking. Exclusion criteria included a history of neurological disorder or injury (e.g. dementia, stroke, seizures), history of moderate to severe head injury (defined as  $> 10$  min of loss of consciousness) [35], past or current history of alcohol or drug abuse (DSM-IV criteria) [36], history of a learning disorder or developmental disability (defined by DSM-IV criteria) [36], or impaired sensory function that precluded computerized testing. Some analyses were further limited to a subset of 31 of these individuals with valid objective physical activity data. All measurements were completed prior to bariatric surgery. Medical and demographic characteristics of the sample are presented in Table 1.

## Measures

**Cognitive function**—The Integneuro cognitive test battery is a standardized and semi-automated computerized battery that estimates intellectual abilities and assesses performance in multiple cognitive domains. Tests are administered in a fixed order using pre-recorded instructions and a touch-screen computer. For each test, the task is introduced and the participant is provided with sample items to ensure comprehension. The battery has demonstrated good construct validity in comparison to standard neuropsychological measures and has been shown to have good test-retest reliability [37,38]. For this study, tests were categorized into four domains: Attention, Executive Function, Memory and Language. These tests included:

### Attention

**Digit span backward**—Digit span assesses basic auditory attention. Participants are presented with a series of digits on the touch-screen, separated by a 1-s interval. Participants are then immediately asked to enter the digits on a numeric keypad on the touch-screen in the reverse order of presentation. The number of digits in each sequence is gradually increased from 3 to 9, with two sequences at each level. The score for this task is the total number of correct trials.

**Span of visual memory**—This task is similar to Spatial Span from the Wechsler Memory Scales [39]. Participants are asked to recreate highlighted forward and backward patterns on the screen. The score is the total number of correct trials.

**Switching of attention – digits**—This test is a computerized adaptation of the Trail Making Test A [40]. Participants are presented with a pattern of 25 numbers in circles and asked to touch them in ascending order. This test assesses attention and psychomotor speed. The score is time to completion.

**Verbal interference – word**—This test is similar to the Word trial on the Stroop Color Word Test [41]. Participants are presented with color words one at a time. Below each

colored word is a response pad with the four possible words displayed in black and in a fixed format. During a 1-min period participants are required to identify the name of each word as quickly as possible after it has been presented on the screen, providing a measure of attention. The score is the number of words correctly identified.

### Executive function

**Switching of attention – digits and letters**—This test is a computerized adaptation of the Trail Making Test B [42]. Participants are presented with an array of 13 numbers (1–13) and 12 letters (A–L). Participants are asked to touch numbers and letters alternately in ascending order. This test taps both attentional abilities and executive function. The score is time to completion.

**Verbal interference – color**—This test is similar to the Color Word trial of the Stroop Color Word Test [43]. Participants are presented with colored words one at a time. To measure executive function, the subject is required to name the color of the ink rather than the target word as quickly as possible during a 1-min period. The score is the number of words correctly identified.

**Maze task**—The maze task assesses executive function and is a computerized adaptation of the Austin Maze [44]. Participants are presented with an  $8 \times 8$  matrix of circles and are asked to identify the hidden path through the grid. Unique auditory and visual cues are presented for correct and incorrect responses. When participants have completed the maze twice without error, or after 10 min has passed, the trial ends. The score is the total number of errors committed.

### Memory

**Verbal list – learning**—This test has two components. Participants are read a list of 12 words a total of four times and asked to recall as many words as possible following each trial. Following presentation and recall of a distraction list, participants are asked to recall target words (i.e. words from the original list). After a 20-min delay, participants are again asked to recall target words. Finally, a recognition trial comprised of target words and foils is completed. The first score is the number of words recalled after a short delay. The second score is the number of words recalled after the 20-min delay. The third score is the number of words correctly identified as a target or foil word.

### Language

**Verbal fluency**—This test has two components. For the letter fluency task, participants are asked to generate words beginning with a given letter of the alphabet (F, A and S), for 60 s. The test is done three times. The first score is the number of correct words generated across all three trials. For the animal fluency task, participants are asked to generate as many animal names as they can in 60 s. The second score is the total number of correct animal names.

## Computing composite scores for cognitive domains

Raw scores for each measure were transformed into z-scores based on age, gender and estimated intelligence to promote generalizability and facilitate clinical interpretation. A composite score for each domain of cognitive function (memory, attention, executive function, and language) was created by averaging the z-scores from each of the specific tests within that domain.

## Physical activity

**Objective assessment of ambulatory physical activity**—Detailed procedures for measuring physical activity for this study have been described elsewhere [16]. Participants were asked to wear the StepWatch™ 3 Activity Monitor (OrthoCare Innovations, Washington, DC) [45], a microprocessor-controlled biaxial activity monitor, fastened above the ankle, that combines acceleration, position and timing information to count steps per minute, for 7 d prior to surgery. Participants returned monitors via mail. Nonwear periods were identified by intervals of at least 120 min with no activity [46]. Daily wear time was calculated as 24 h minus the duration of nonwear periods. Days with less than 10 h of wear time were excluded. Step counts at the minute level were used to calculate mean daily steps and mean daily minutes of ambulatory moderate-vigorous activity (MVPA) (i.e. estimated from the number of minutes with 80 steps or more), as well as mean daily minutes of bout-related ambulatory MVPA (a bout was established when 8 min out of a 10 min window met the threshold of 80 steps or more. A bout ended with three consecutive minutes below this threshold) [47]. Daily MVPA values were standardized to 1-week periods by multiplying the mean daily values by 7.

**Rapid assessment of physical activity (RAPA)**—The RAPA is a nine-item self-report questionnaire designed to easily assess usual physical activity levels of adults 50 and older, which has been found to be comparable to other validated physical activity surveys among older adults [48]. It was selected for this study because the physical activity patterns of severely obese adults are similar to older adults [16]. For the current effort, we utilized the aerobic activity score, determined from responses to seven yes or no items, which are arranged in ascending order based on duration, frequency and level of usual aerobic activity (e.g. “I do 30 minutes or more a day of moderate physical activities, 5 or more days a week” is a score of 6). The highest item with an affirmative response equals the participant’s score (range 0 to 7). Higher scores reflect greater levels of physical activity. A score of 6 or above is considered to be active [48].

## Other measures

Height and weight were measured by trained research staff using standardized protocols. BMI was calculated as height in meters divided by weight in kilograms squared. Age was determined from participant’s self-reported date of birth. Participants also self-reported sex and currently having or having a history of a diagnosis of asthma, diabetes or hypertension by a health care professional.

## Statistical analyses

Descriptive statistics were used to characterize the sample. Pearson and partial correlations, controlling for BMI, diabetes, hypertension and asthma status, were conducted to test associations among the indices of physical activity and the four cognitive function domain scores (attention, executive function, memory and language), which were already adjusted for age, gender and estimated intelligence. Statistical significance was defined as  $p < 0.05$ . The statistical software package used for all analyses was SPSS version 20.

## Results

### Low rates of physical activity in the sample

Among the subset of individuals with valid objective physical activity data ( $n = 31$ ), median steps per day was 7949 steps/d (IQR = 4572). Using standard step per day indices [49], 16.1% of individuals were sedentary (less than 5000 steps/d), 29.0% were low active (5000 to 7499 steps/d), 32.3% were somewhat active (7500 to 9999 steps/d), 12.9% were active (10 000 to 12 499 steps/d) and 9.7% were highly active (12 500+ steps/d). Ambulatory MVPA for this sample ranged from 4 to 650 min/week (median = 105.0; IQR = 123.2). Bout-related MVPA ranged from 0 to 584 min/week (median = 0.0; IQR = 48). Only 41.9% of participants ( $n = 13$ ) achieved any bout-related ambulatory MVPA; 35.5% ( $n = 11$ ) achieved at least 30 min/week of bout-related MVPA, 19.2% ( $n = 6$ ) achieved at least 60 min/week, and only 2 participants (6.4%) achieved at least 150 min/week.

Scores on the aerobic subscale of the RAPA ranged from 2 to 7, with the average being 3.9 (SD = 1.4). Based on this self-report measure, 21.9% of participants were considered active.

### Cognitive impairment is prevalent among obese persons

Clinically meaningful levels of cognitive impairment ( $< 1.5$  SD below the mean) were found in all domains. In this sample, 32.3% ( $n = 10$ ) exhibited deficits in at least one domain. Nine individuals (29.0%) demonstrated impairment in memory; composite scores ranged from  $-2.38$  to  $2.65$  (median =  $-0.72$ , IQR =  $2.70$ ). Four individuals (12.9%) demonstrated impairment in language; composite scores ranged from  $-1.99$  to  $2.76$  (median =  $0.01$ , IQR =  $1.25$ ). Three individuals (9.7%) demonstrated impairment in executive function; composite scores ranged from  $-2.74$  to  $1.94$  (median =  $-0.03$ , IQR =  $1.60$ ). Three individuals (9.7%) demonstrated impairment in attention; composite scores ranged from  $-2.06$  to  $1.40$  (median =  $0.04$ , IQR =  $1.46$ ).

### Physical activity is unrelated to cognitive function

Pearson and partial correlations between measures of physical activity and cognitive function, are presented in Table 2. After controlling for BMI, diabetes, hypertension and asthma status, there were weak negative correlations between RAPA scores and executive function ( $r = -0.27$ ,  $p = 0.006$ ), attention ( $r = -0.21$ ,  $p = 0.04$ ) and memory ( $r = -0.20$ ,  $p = 0.04$ ). Among the subsample, minutes of ambulatory MVPA per week was negatively associated with attention ( $r = -0.46$ ,  $p = 0.02$ ). No other significant correlations between physical activity and cognitive function emerged.

## Discussion

The current study examined the association between physical activity and cognitive function among severely obese individuals. Similar to previous work in this population, including the larger LABS-2 cohort from which participants were selected, [16, 50] physical activity levels were low, with nearly one-quarter (self-report) to less than one-tenth (objective monitoring) of bariatric surgery candidates meeting the national recommendation of at least 150 min MVPA/week [51]. The current findings are also consistent with previous research demonstrating that cognitive impairment is prevalent among obese individuals [9, 10, 14] with cognitive deficits exhibited in 22% of participants. However, contrary to expectations and findings in other samples, [20, 22, 52, 53] after adjusting for potential covariates, there was not a significant association between steps/day and bout-related min/week of MVPA and any of the cognitive function scores. More surprising, self-reported aerobic physical activity was weakly correlated with lower attention and executive function, and both self-reported aerobic physical activity and objectively-determined min/week of MVPA (not bout-related) were negatively correlated with memory performance. Such findings suggest that there is little association between physical activity and cognitive function among severely obese adults in an observational, naturalistic setting. Several aspects of these findings warrant brief discussion.

Though several possibilities exist, the most likely explanation for the current findings involves the low levels of physical activity observed in the sample. Previous research has suggested that cognitive function can be improved through physical activity that enhances cardiovascular fitness [54], and that intensity of physical activity (rather than duration) is most important for cognitive benefits [55, 56]. Similarly, much of the research supporting the association between activity and cognitive function examines the effects of moderate-to high-intensity aerobic training programs [29, 30]. However, low levels of bout-related MVPA (the type of physical activity to most likely improve levels of cardiovascular fitness [29, 30]) were observed in our sample (i.e. only 41.9% of participants achieved any bout-related ambulatory MVPA, only 2 (6.4%) of which achieved the suggested minimum of 150 min/week of bout-related MVPA) and it is possible that no (or very few) participants were above the threshold of physical activity duration or intensity needed to provide cognitive benefits.

Because this was an exploratory study with a small sample size we did not adjust for multiple comparisons, but this did make the study more susceptible to type I errors. Given this fact, coupled with the very low levels of MVPA exhibited by the current sample, it appears likely that the observed associations between some measures of physical activity and cognitive function, which were weak to low, are due to statistical artifact instead [57] of a possible adverse effect of physical activity in this population. Finally, given the known adverse effects of elevated BMI on cognitive function, it is possible that, in this sample, the adverse effects of severe obesity out-weigh the potential benefits of low levels of physical activity on cognitive function.

The mechanisms by which higher levels of physical activity may lead to improved cognitive function among obese are not entirely understood and are likely to be multifactorial. One

likely possibility is that increased levels of physical activity may lead to improvement or resolution of obesity-related medical conditions that are known to impair cognition such as type 2 diabetes mellitus [58], heart disease [59] and sleep apnea [60]. Additionally, greater physical activity and cardiovascular fitness are related to reduced systemic inflammation and circulating biomarkers (e.g. brain derived neurotrophic factor (BDNF) [61], leptin [62], ghrelin [63]) which are implicated in obesity and related to cognitive dysfunction. Finally, increased physical activity levels are likely related to improved cognitive function through their association with improved structural and functional brain outcomes [25–30]. Future studies are needed to clarify the possibility that physical activity can attenuate the adverse neurocognitive effects of obesity.

Several aspects of this preliminary, naturalistic study may limit generalizability. A primary limitation involves the small sample size and use of cross-sectional data. Past studies of physical activity and cognitive function often follow individuals for periods of several weeks to months [52, 64] and it is possible that activity levels over an extended period of time are better predictors of neurocognitive outcomes than briefer periods of monitoring. Thus, another possible explanation for the limited findings involves the short duration of objective physical activity assessment (i.e. 3–7 d), which may not be fully representative of typical physical activity among these individuals. To address this limitation, a self-report measure of usual aerobic physical activity was also evaluated. However, given the bias of subjective physical activity assessment [65], it is not clear whether it better represented actual usual physical activity behavior compared to the objective monitor. Furthermore, despite having an adequate range of values, it appears likely that many individuals were not physically active enough to improve cognitive function. In effect, it is likely that a threshold exists for the benefits of physical activity on cognitive function. Randomized clinical trials of physical activity interventions which promote a high level of MVPA would provide clearer insight into the cognitive benefits of physical activity in this population. Larger, prospective studies may also clarify the association between physical activity and cognition, especially in light of findings that suggest both physical activity and cognition improve following bariatric surgery [66,67].

## Conclusions

The current study supports previous research demonstrating low levels of physical activity and high rates of cognitive impairment among severely obese individuals. Although higher physical activity levels were not associated with better cognition in this study, future research should examine this relationship using randomized clinical trials designed to evaluate the effect of MVPA on change in cognitive function over time. Such findings would directly determine the contribution of improved physical activity and cardiovascular fitness to cognitive impairment in obese persons.

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**Table 1.**

Demographic and medical characteristics of the study sample.

	<b>Full sample (<i>n</i> = 105)</b>	<b>Subsample (<i>n</i> = 31)</b>
	Mean (SD) [range] or%	Mean (SD) [range] or%
Age, years	43.3 (11.0) [20–66]	43.5 (11.1) [21–61]
BMI, kg/m <sup>2</sup>	46.8 (6.7) [35.7–75.0]	48.6 (8.7) [35.7–75.0]
Female	68.6%	67.7%
Diabetes	22.9%	32.3%
Hypertension	42.9%	51.6%
Asthma	15.2%	12.9%
RAPA	3.9 (1.4) [2–6]	4.2 (1.7) [2–6]

Note: RAPA – Rapid Assessment of Physical Activity

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**Table 2.** Unadjusted bivariate and partial correlations between physical activity and cognitive function.

	Cognitive function <sup>a</sup>											
	Attention			Executive function			Memory			Language		
	Unadjusted	Adjusted <sup>b</sup>	Adjusted <sup>b</sup>	Unadjusted	Adjusted <sup>b</sup>	Adjusted <sup>b</sup>	Unadjusted	Adjusted <sup>b</sup>	Adjusted <sup>b</sup>	Unadjusted	Adjusted <sup>b</sup>	Adjusted <sup>b</sup>
<i>Self-reported physical activity (n = 105)</i>												
RAPA score	-0.22*	-0.21*	-0.27**	-0.27**	-0.24*	-0.20*	0.11					-0.09
<i>Objective physical activity (n = 31)</i>												
Steps/d	-0.36*	-0.34	-0.28	-0.17	.07	-0.13						0.07
MVPA min/week	-0.50**	-0.46*	-0.41*	-0.17	-0.08	-0.16						0.04
Bout-related MVPA min/week	-0.43*	-0.36	-0.27	-0.24	-0.22	-0.20						< 0.01

Note: MVPA = moderate-vigorous intensity physical activity; RAPA = Rapid Assessment of Physical Activity;

<sup>a</sup>Cognitive function measures adjusted for age, gender and estimated intelligence;

<sup>b</sup>Correlation adjusted for body mass index, asthma, diabetes and hypertension;

\*  $p < 0.05$ ,

\*\*  $p < 0.01$ .