10-2016

Cardiorespiratory Fitness Is Associated with Better Executive Function in Young Women

Samuel P. Scott
Pennsylvania State University

Mary Jane De Souza
The Pennsylvania State University, mjd34@psu.edu

Karsten Koehler
University of Nebraska-Lincoln, kkoehler3@unl.edu

Dylan L. Petkus
Pennsylvania State University

Laura E. Murray-Kolb
The Pennsylvania State University, lem118@psu.edu

Published in *Medicine & Science in Sports & Exercise* 48:10 (Oct 2016), pp 1994-2002. doi:10.1249/MSS.0000000000000974

Submitted December 2015; accepted April 2016.

Supplemental content follows the **References**.

Cardiorespiratory Fitness Is Associated with Better Executive Function in Young Women

Samuel P. Scott,[1] Mary Jane De Souza,[2] Karsten Koehler,[3] Dylan L. Petkus,[2] and Laura E. Murray-Kolb[1]

1 Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA;
2 Department of Kinesiology, The Pennsylvania State University, University Park, PA; and
3 Department of Nutrition and Health Sciences, University of Nebraska–Lincoln, Lincoln, NE

Corresponding author — Laura E. Murray-Kolb, 219 Chandlee Laboratory, The Pennsylvania State University, University Park, PA 16802; email lem118@psu.edu

Abstract

Purpose: A positive association between cardiorespiratory fitness (CRF) and cognitive function has been demonstrated mainly in children and older adults. Women attending college live in a cognitively demanding setting where optimal cognition matters but often experience declines in CRF. Our aim was to test whether CRF is associated with executive function in young adult women.

Methods: Participants in this cross-sectional study included 120 healthy women age 18–35 yr in a university setting. Each woman completed a maximal treadmill-based exercise test to determine peak oxygen uptake ($\dot{V}O_{2peak}$), computerized tests of executive function, and questionnaires to assess motivation and other factors with potential to influence physical and cognitive performance.

Results: Overall CRF was excellent, with a sample mean $\dot{V}O_{2peak}$ of 44.6 mL·min^{-1}·kg^{-1}. After adjusting for covariates, higher $\dot{V}O_{2peak}$ was associated with better performance on attention ($P < 0.01$), learning/ shifting ($P < 0.01$), working memory ($P < 0.01$), and problem-solving ($P < 0.05$) tasks. Likewise, when women were grouped according to the American College of Sports Medicine fitness classification, performance on executive function tasks was poorest in women with very poor or poor CRF. Women with superior CRF performed best on executive function tasks, and performance was intermediate in women with fair, good, or excellent CRF.

Conclusion: The findings from this cross-sectional study suggest that optimal cognition is related to CRF in young adult women. Future studies are needed to test whether strategies to improve CRF are effective in improving cognitive function.

Keywords: cardiorespiratory fitness, maximal exercise test, women, young adult, behavior, cognition

One-third of adults worldwide are physically inactive (16). The period of transition from high school to college is frequently accompanied by increased inactivity leading to weight gain, with most studies showing a gain of about 4 lb in the first year of college, which may mark the beginning of a trend (15). In 2014, 51% of women attending college in the United States did not meet the physical activity guidelines set by the American College of Sports Medicine (ACSM), and 31% were estimated to be overweight or obese (1). Among the multitude of established ramifications of low fitness, suboptimal cognitive performance secondary to low fitness may jeopardize learning and academic success in college-attending women (19).

The bidirectional association between physical and mental health has been acknowledged for millennia (46). Within research relating fitness to brain and behavior, a focus on life stage extremes—periods during which rapid brain changes occur—has predominated, and little is known about this association during young adulthood. It is now widely recognized that lifelong brain remodeling occurs (14), which has generated interest in how to optimize brain function in young adults. Evidence for an association between fitness and cognition has been identified at the neural level in studies using electroencephalography to examine event-related potentials, suggesting that fitness promotes neural plasticity (34). However, limited evidence at the behavioral level prevents forming implications for real-life scenarios. The lack of data to support behavioral effects also makes it difficult to distinguish whether fitness benefits the whole brain or only certain systems underlying certain behaviors, that is, whether the effects of fitness are general or specific. Furthermore, previous investigations in young adults have involved methodological constraints such as small sample size, assessment of fitness using self-reported or indirect measures, or aggregation of data across different age groups or sexes (18,21,45). Given the changes in fitness and high dependence on optimal cognition in university settings, we sought to better understand relations between cardiorespiratory fitness (CRF) level and executive function in young adult women. Our purpose was to test whether

CRF, as determined in a maximal treadmill-based exercise test, was related to performance on tasks measuring processing speed, sustained attention, learning/shifting, inhibitory control, working memory, and planning/problem solving. We hypothesized that higher CRF would be associated with better executive task performance.

Materials and Methods

Participants and Study Design

Data collection for this observational study occurred between March and November 2014 at The Pennsylvania State University, University Park, PA. The larger scope of the study was to examine interrelations between iron status, fitness, and cognition. Women were specifically focused on instead of men because of the higher prevalence of iron deficiency in women, who experience menstrual iron losses (24). Findings relating iron status to cognition have been published elsewhere (42). Participants were recruited using flyers and online advertisements. Those interested completed an online screening form and, after meeting initial criteria, were invited to the Clinical Research Center on campus, where a blood draw was performed, anthropometric measurements were taken, and cognitive tests were administered. Fitness testing occurred on a subsequent day within 2 wk of the initial visit. Inclusion criteria were the following: female, 18–35 yr of age, nonpregnant/nonlactating, body mass index (BMI) between 18 and 30 $kg \cdot m^{-2}$, hemoglobin (Hb) ≥ 12.0 $g \cdot dL^{-1}$, no chronic illness or disease, no cardiovascular conditions or physical injury, proficient in the English language, and normal or corrected-to-normal vision. Anemic (Hb < 12.0 $g \cdot dL^{-1}$) individuals were excluded given that reduced oxygen transport capacity is known to affect CRF (48) and were informed of their status and referred to their physician for follow-up care. Visits were scheduled at the convenience of the participant between 8 a.m. and 5 p.m.

All women provided written informed consent before testing. All procedures were reviewed and approved by the Institutional Review Board of The Pennsylvania State University.

Fitness Testing

Peak oxygen consumption ($\dot{V}O_{2peak}$), an indicator of CRF, was measured during a progressive treadmill test modified from Astrand and Saltin (2) to volitional exhaustion using breath-by-breath open-circuit spirometry. Participants were instructed to refrain from consuming food, alcohol, and caffeine 3 h before the test, and from strenuous exercise on the day of the test. Compliance to these instructions and use of medications in the previous 24 h were queried at the beginning of each testing session. The test was initiated by the participant selecting a comfortable walking, jogging, or running speed at 0% grade that she believed could be sustained for 10 min. The grade of the treadmill was increased 2% after every 2 min for the first 8 min of the test and 1% for each subsequent minute. $\dot{V}O_2$ and $\dot{V}CO_2$ were measured using a SensorMedics Vmax metabolic cart (Yorba Linda, CA). During each stage of the test, the RPE was used as a subjective measure of exercise intensity (38). $\dot{V}O_{2peak}$ was considered to be achieved if three of the following criteria were met: 1) attainment of age-predicted maximal HR (220 j age); 2) RER Q1.1; 3) plateau in oxygen consumption despite an increase in workload; and 4) attainment of an RPE score of Q18 (4). The data of each participant were independently inspected by two of the authors.

Cognitive Testing

Written questionnaire. Before the computerized tasks, women filled out a questionnaire with information on their most recent menstrual period, parental occupation, handedness, cigarette smoking, and use of oral contraceptives, dietary supplements, and medications. A nine-item measure of work drive was used to assess motivation (26). A small snack of water, juice, and/or a granola bar was offered to each participant as they completed the written questionnaire.

Computerized tasks. Full details of the computerized cognitive testing have been described elsewhere (42). Briefly, five tasks were administered using the Psychology Experiment Building Language platform on laptop computers (28). All sessions, lasting approximately 50 min on average, were monitored by trained research staff, and environmental distractions were minimized. After listening to an initial set of instructions read from a script by the researchers, the women self-administered the tests by following on-screen instructions. They then completed the tests without interruption unless they had questions or the researchers determined that they were deviating from task instructions. The five tasks were chosen based on their wide use in the behavioral sciences, broad coverage of executive functions, and hypothesized association with CRF. The tasks included **1)** the Attentional Network task (ANT), a modified flanker task designed to assess three distinct components of attention: alerting (perceiving that something requires attention), orienting (the shifting of attention to a cued location), and conflict (filtering out irrelevant visual information) (12); **2)** Berg's Card Sorting task (BCST), commonly known as the Wisconsin card sorting task, which involved sorting 64 cards into piles based on one of three unknown rules (number, shape, or color) that changed throughout the task, requiring the participant to adjust her strategy (13); **3)** a Go/No-Go oddball task (GNG) where participants were trained to respond to a Go stimulus but to inhibit their response to a different No-Go stimulus, thereby assessing inhibitory control (3); **4)** Sternberg's Working Memory Search task (SMS), requiring participants to memorize sets of letters (three, five, or eight consonants) and then decide whether subsequent probe letters were either present or absent from the memorized set (43); **5)** the Tower of London task (TOL) used to assess planning and problem-solving ability, requiring women to rearrange stacks of colored discs from a starting point to a goal configuration in as few moves as possible (33). Outcome measures common across ANT, GNG, and SMS tasks included accuracy (the percentage of correct responses), reaction time (RT), and RT variability in milliseconds using the median and interquartile range of the RT distribution, respectively. Alerting, orienting, and conflict difference scores were calculated from the appropriate cue and flanker conditions in the ANT. The primary BCST outcomes were the number of categories completed, where completion of a category required 10 correct sorts, and the number of perseverative errors (incorrect responses according to the current sorting rule that were correct according to the previous sorting rule). The TOL outcomes were excess moves defined as the number of moves made beyond the minimum number of moves required to solve each problem, planning time defined as how long a participant spent planning her responses (time elapsed between problem presentation and picking up the first disc), and solution time defined as time required to achieve the goal configuration.

Statistical Analyses

Two approaches were used in an effort to understand how fitness was associated with cognitive performance: **1)** regression analysis using $\dot{V}O_{2peak}$ as a continuous predictor to use the power of the full spectrum of CRF and **2)** a comparison of fitness groups defined according to the most recent ACSM classifications for women age 20–29 yr (1). Given the limited number of women in our sample with low CRF, we chose to combine the "very poor" and "poor" categories, as well as the "fair" and "good" categories; therefore, we compared four groups: 1) "very poor/poor," 2) "fair/good," 3) "excellent," and 4) "superior." Accuracy variables were transformed using a Fisher logit approximation to avoid ceiling effects, and a Box–Cox transformation was applied to planning time because of the skewed nature of this variable, (40); other dependent variables were left untransformed.

ANOVA and ANCOVA were used for group comparisons, with a *post hoc* Tukey test to further investigate group differences. Task performance is presented as both raw values and *Z* scores. *Z* scores are used to aid readers who may be unfamiliar with these specific outcomes and for practical purposes of displaying results on a common scale in figures. The SMS and TOL outcomes were modeled using mixed procedures with difficulty level specified as a within-participants factor in the repeated measures analysis. For the SMS, the three difficulty levels corresponded to set length. For the TOL, two difficulty levels were created by first ranking each problem in terms of excess moves, planning time, and solution time and then summing the rank scores for each of these outcomes. To gauge the efficiency of handling additional cognitive load, the change in performance from lower to higher difficulty level for TOL and SMS tasks was also used as a dependent variable.

ANOVA or Kruskal–Wallis tests were used for covariate assessment, as appropriate. Age was included in all models given the well-described association between age and executive performance (20,49). Other potential covariates were included in adjusted models if either 1) the groups being compared differed in the variable or 2) the variable was related to the dependent variable, at the $P < 0.1$ level (see Table, Supplemental Content 1, list of variables included as covariates in analyses). All models were run without and with covariates, and are presented accordingly as unadjusted and adjusted analyses with effect sizes (R^2 and η^2) reported. Effect sizes were interpreted as small ($R^2 = 0.01$, $\eta^2 = 0.01$), medium ($R^2 = 0.09$, $\eta^2 = 0.06$), and large ($R^2 = 0.25$, $\eta^2 = 0.14$) based on Cohen's definitions (7).

Power analysis was conducted based on literature relating CRF and cognitive performance among young adults in their 20s (23). Because this study only compared two fitness groups, i.e., "lower fit" versus "higher fit," we chose to unite the two lower CRF groups in our study ("very poor/poor" and "fair/good") and our two higher CRF groups ("excellent" and "superior") before conducting power analyses. Assuming a two-tailed 5% type I error, we estimated that the sample size in the present study ($n = 120$) was sufficient to detect a difference in cognitive performance among individuals with lower and higher CRF at a power of 0.99. Because CRF was lower in our lowest CRF group ("very poor/poor") and higher in our highest CRF group ("superior") when compared with the sample reported by Labelle et al., we are confident that power is in a similar magnitude when comparing the association between CRF and cognitive performance among four fitness groups.

Practice trials for all tasks were excluded before computing performance indices, and the convention of only including correct trials in the calculation of RT measures was followed. Analyses were carried out in SAS for Windows software (version 9.4; SAS Institute, Cary, NC). An alpha level of $P < 0.05$ was used to determine statistical significance.

Results

Sample characteristics and covariate assessment. As shown in Figure 1, 560 women were screened and 120 were included in the final analyses. Table 1 shows characteristics of the overall sample as well as the sample categorized by ACSM fitness groups. With a mean $\dot{V}O_{2peak}$ of 44.6 $mL\cdot min^{-1}\cdot kg^{-1}$, which is above the 80th percentile for women age 20–29 yr (1), overall fitness in the sample was "excellent." Twenty-seven percent of the women were overweight (BMI, 25.0–29.9 $kg\cdot m^{-2}$). As per study design, oxygen transport was uncompromised in all individuals, with a sample mean Hb of 13.1 $mg\cdot dL^{-1}$. The sample mean parental occupation score suggests that the women had above-average socioeconomic status relative to the US population average score of 50 for adults age 16 yr and older (29). Oral contraceptive use was reported by

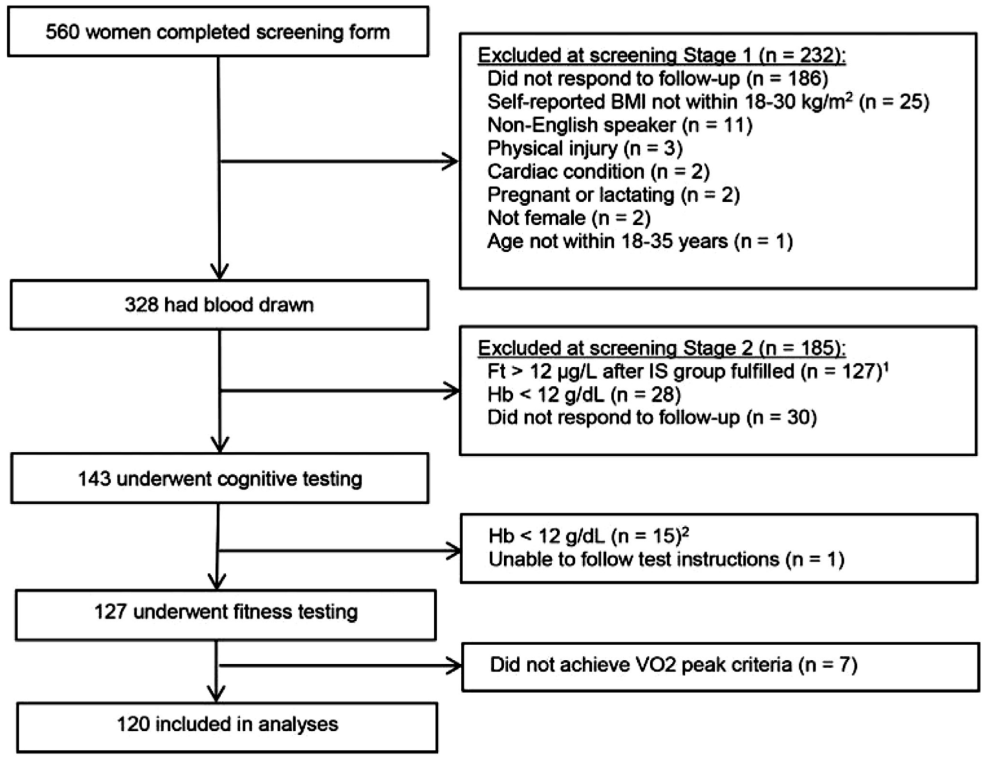

Figure 1. Study flow diagram.
1 The current analyses were part of a study that also examined relations between iron status and cognition; iron-deficient and iron-sufficient (IS) groups were compared, with the screening criterion for the IS group being ferritin (Ft, a biomarker of iron storage) >12 μg·L^{-1}. Once the target sample size for the IS group was achieved, additional IS individuals (n = 127) were excluded.
2 Although anemia was one of the exclusion criteria, 15 anemic (Hb < 12 g·L^{-1}) participants underwent cognitive testing because, until the IS group was fulfilled, the blood draw and cognitive testing occurred at the same visit to minimize participant burden; thus, Hb was not measured until after the cognitive test. These participants were not invited to return for fitness testing.

50% of participants, 32% reported any use of medications, 20% reported using dietary supplements, and none were smokers. Nearly all women were Caucasian.

The ACSM fitness groups differed in age and in percentage of women who were overweight. As per study design, group differences existed for $\dot{V}O_{2peak}$. Associations with some cognitive outcomes at the $P < 0.1$ level were found for oral contraceptive use, parental occupation score, medication use, task order, handedness, and laptop number. Therefore, the appropriate variables were included as covariates in the respective analyses (see Table, Supplemental Content 1, list of variables included as covariates in analyses).

Relations between CRF and cognitive performance measures. In no instance was higher CRF associated with worse cognitive performance. Table 2 contains summary statistics and significance from the regression analyses using $\dot{V}O_{2peak}$ as a continuous predictor of cognitive

Table 1. Descriptive characteristics of overall sample and comparison of fitness groups using ACSM fitness classifications for females age 20–29 yr.

	Overall Sample (n = 120)	ACSM Fitness Classifications: Very Poor/Poor (n = 17)	Fair/Good (n = 40)	Excellent (n = 31)	Superior (n = 32)	P^a
Age (yr)	22.7 ± 0.4	24.1 ± 1.3A	23.7 ± 0.7A	21.7 ± 2.6A	21.6 ± 0.6A	0.049
BMI (kg·m^{-2})	23.0 ± 0.3	24.2 ± 0.6A	23.9 ± 0.5A	22.3 ± 0.5B	22.0 ± 0.4B	0.007
Peak $\dot{V}O_2$ (mL·min^{-1}·kg^{-1})	44.6 ± 0.7	32.0 ± 0.9A	40.3 ± 0.4B	46.9 ± 0.4C	54.4 ± 0.7D	<0.001
Nam–Powers–Boyd Index	68 ±2	64 ±5	68 ±3	68 ±4	71 ± 3	0.36
Work drive (motivation) score	3.6 ± 0.1	3.6 ± 0.2	3.6 ± 0.1	3.4 ± 0.1	3.9 ± 0.1	0.12
Days since last menstrual cycle[b]	16 ±1	18 ±5	17 ±2	17 ±2	14 ± 2	0.49
Oral contraceptive user (%)	50	50	55	53	44	0.80
Medication user[c] (%)	32	38	25	40	31	0.56
Dietary supplement user[d] (%)	20	21	23	13	28	0.57
Right handed (%)	90	88	95	97	78	0.06

Values are expressed as mean ± SE or percentages where specified.
Bold values indicate significance at P < 0.05.
Within a row, groups with different superscript capital letters are significantly different based on post hoc Tukey test (P < 0.05).
a. Overall significance from ANOVA model testing differences between ACSM fitness groups.
b. Number of days between most recent menstrual period and date of cognitive test.
c. Medications primarily included antidepressants, thyroid, and allergy medicines.
d. Dietary supplements primarily included multivitamins and fish oil; others included vitamin D, vitamin C, iron, and biotin.

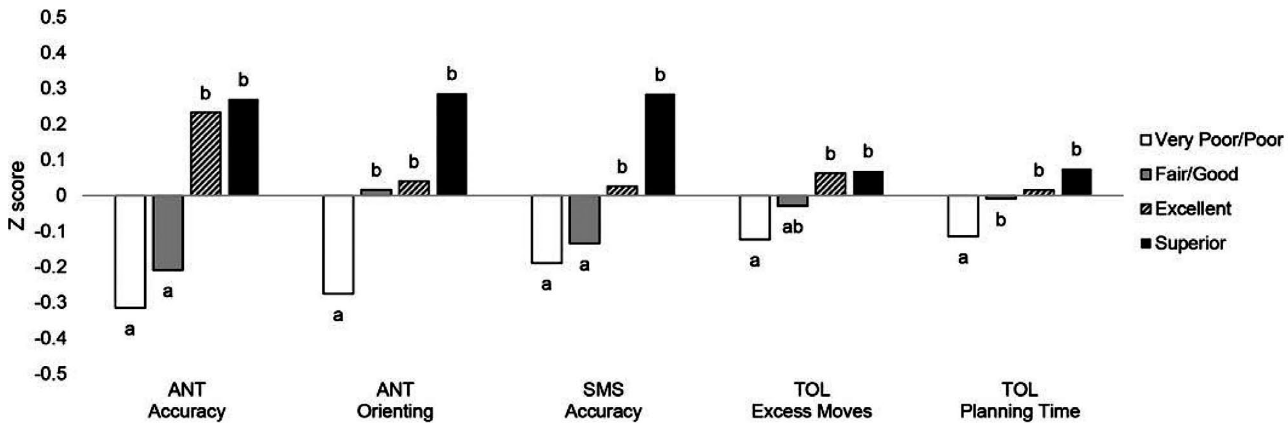

Figure 2. Cognitive task performance by ACSM fitness group in young adult women. A higher Z score indicates better task performance (higher accuracy, higher orienting, lower excess moves, and higher planning time); Z scores were computed using a mean of 0 and SD of 1; bars for a given outcome with different letters are significantly different (*P* < 0.05) in the Tukey post hoc test.

Table 2. Results of regression analyses with continuous $\dot{V}O_{2peak}$ as a predictor of cognitive performance in young adult females before and after adjustment for covariates.

	β (95% CI)		R^2			P	
Outcome	Unadj.[a]	Adj.[a]	Unadj.[a]	Adj.[a]	Adj. – Unadj.[a]	Unadj.[a]	Adj.[a]
ANT							
Accuracy, % correct	0.20 (0.02, 0.38)	0.25 (0.06, 0.43)	0.04	0.08	0.04	**0.030**	**0.009**
RT (ms)	–0.05 (–0.24, 0.13)	–0.04 (–0.23, 0.14)	0.00	0.06	0.06	0.57	0.80
RT variability (ms)	–0.08 (–0.25, 0.09)	–0.07 (–0.26, 0.12)	0.01	0.07	0.06	0.35	0.33
Alerting (ms)	–0.14 (–0.33, 0.04)	–0.07 (–0.26, 0.12)	0.02	0.07	0.05	0.12	0.44
Orienting (ms)	0.20 (0.02, 0.38)	0.21 (0.02, 0.39)	0.04	0.04	0.00	**0.033**	**0.032**
Conflict (ms)	–0.10 (–0.27, 0.08)	–0.10 (–0.28, 0.09)	0.01	0.01	0.00	0.27	0.30
BCST							
Categories completed	0.14 (–0.05, 0.33)	0.16 (–0.04, 0.36)	0.02	0.02	0.00	0.14	0.65
Perseverative errors	–0.16 (–0.35, 0.03)	–0.16 (–0.36, 0.04)	0.02	0.02	0.00	0.10	0.09
GNG							
Accuracy, % correct	–0.02 (–0.20, 0.16)	0.06 (–0.13, 0.25)	0.00	0.14	0.14	0.82	0.54
RT (ms)	0.00 (–0.18, 0.18)	–0.01 (–0.19, 0.18)	0.00	0.09	0.09	0.99	0.64
RT variability (ms)	–0.01 (–0.19, 0.18)	–0.10 (–0.31, 0.10)	0.00	0.18	0.18	0.92	0.32
SMS							
Accuracy, % correct	0.13 (0.02, 0.23)	0.15 (0.04, 0.26)	0.01	0.02	0.01	**0.018**	**0.006**
Change[b]	0.06 (–0.13, 0.24)	0.07 (–0.12, 0.26)	0.00	0.00	0.00	0.53	0.49
RT (ms)	0.01 (–0.09, 0.11)	0.03 (–0.09, 0.15)	0.00	0.09	0.09	0.87	0.58
Change[b]	0.03 (–0.07, 0.13)	0.06 (–0.04, 0.16)	0.00	0.02	0.02	0.57	0.34
RT variability (ms)	–0.04 (–0.15, 0.07)	–0.03 (–0.14, 0.09)	0.00	0.02	0.02	0.88	0.83
Change[b]	0.01 (–0.09, 0.11)	0.05 (–0.05, 0.16)	0.00	0.01	0.01	0.42	0.24
TOL							
Excess moves	–0.07 (–0.13, 0.00)	–0.07 (–0.14, –0.01)	0.00	0.01	0.01	**0.037**	**0.031**
Change[b]	0.09 (–0.09, 0.28)	0.13 (–0.01, 0.08)	0.01	0.03	0.02	0.32	0.19
Planning time (s)	–0.07 (–0.13, 0.00)	–0.09 (–0.15, –0.02)	0.00	0.01	0.01	**0.048**	**0.010**
Change[b]	0.07 (–0.11, 0.26)	0.11 (–0.08, 0.30)	0.01	0.03	0.02	0.45	0.24
Solution time (s)	0.02 (–0.04, 0.09)	0.01 (–0.05, 0.08)	0.00	0.02	0.02	0.27	0.44
Change[b]	0.12 (–0.06, 0.31)	0.7 (0.00, 0.37)	0.01	0.08	0.07	0.19	0.050

Bold values indicate significance at *P* < 0.05.

a. Values are reported before and after adjustment for covariates including age, parental occupation, work drive, days since last menstrual cycle, oral contraceptive use, medication use, dietary supplement use, handedness, task order, and computer number; covariate selection for the regression analyses was based on relation to the outcome at P < 0.1; covariates included in each model can be found in Supplemental Content 1. The difference in R^2 before and after adjustment is also reported.

b. Change in performance from low to high difficulty problems (see Statistical Analyses).

performance, with the significance of all models indicated before and after adjustment for covariates. Positive associations were found between the $\dot{V}O_{2peak}$ and the percentage of correct responses on the attention (ANT) and working memory (SMS) tasks, the ability to shift attention (ANT orienting), and the amount of time spent planning on the problem-solving task (TOL). A negative association was found between the $\dot{V}O_{2peak}$ and the number of TOL excess moves, suggesting that higher CRF was related to more efficient problem-solving ability. The significance level of all models remained unaltered by covariate addition, except for a change in the TOL solution time from lower to higher difficulty problems; the nonsignificant association with $\dot{V}O_{2peak}$ became significant after covariate addition such that higher $\dot{V}O_{2peak}$ was associated with a greater increase in solution time from lower to higher difficulty.

Stepwise patterns were observed for several outcomes when comparing groups based on ACSM fitness classifications. Before adjustment for covariates, the groups differed in ANT orienting (*F* = 3.1, *P* = 0.028) and SMS accuracy (*F* =

3.0, $P = 0.035$), with *post hoc* pairwise comparisons showing greater orienting in the "superior" versus "very poor/poor" group ($P = 0.014$) and greater SMS accuracy in those with "superior" fitness compared with those with "fair/good" ($P = 0.012$) and "very poor/poor" ($P = 0.011$) fitness. Figure 2 shows standardized cognitive scores by fitness group for the outcomes where the adjusted model was significant (P G 0.05). Following adjustment, the ANCOVA for fitness group differences was significant for ANT accuracy ($F = 3.6$, $P = 0.003$) and orienting ($F = 3.4$, $P = 0.005$), BCST perseverative errors ($F = 3.0$, $P = 0.009$), SMS accuracy ($F = 3.4$, $P = 0.021$), and TOL excess moves ($F = 4.8$, $P = 0.031$) and planning time ($F = 4.1$, $P = 0.009$). Those in the "very poor/poor" fitness group exhibited the worst performance, and those in the "superior" fitness group exhibited the best performance for each of these outcomes. In other words, higher CRF was associated with making fewer incorrect responses on attention and working memory tasks, better attentional orienting ability, more efficient problem-solving ability, and more time spent planning responses mentally before task execution.

No associations were found between CRF and response speed across the tasks. In addition, performance on the inhibitory control (GNG) task was not found to be related to CRF. Mean task performance by fitness group and results of the unadjusted and adjusted analyses for the full set of behavioral measures can be accessed in Supplemental Digital Content 2 (see Table, Supplemental Content 2, comparison of cognitive performance between ACSM fitness groups).

Discussion

We sought to examine associations between CRF in healthy young adult women and performance on widely used behavioral tasks assessing different aspects of executive function with relevance to daily well-being. The main finding from this study was that CRF was positively associated with performance on tasks of attention, learning/shifting, working memory, and problem solving. The positive association between CRF and executive function was also observed when women were categorized according to current ACSM criteria. In fact, when significant findings were observed, task performance was always better in women with the highest CRF (ACSM category "superior") when compared with women with the lowest CRF (ACSM category "very poor" or "poor").

We feel that the effects sizes in our study, which ranged from small to medium for most outcomes using the standard definition of magnitude, are meaningful. As would be expected, the models that were adjusted to account for covariates explained a greater proportion of variance compared with the unadjusted models. To put the magnitude of effects we observed into practical terms, it is useful to examine studies involving groups of persons for whom task performance would be expected to greatly differ. For example, compared with a normal healthy population, those with diagnosed conditions involving known executive deficits would be expected to perform more poorly on the tasks used in the current study. In one study comparing ANT performance of patients with schizophrenia to healthy controls, ANT accuracy and orienting effect sizes were medium ($d = 0.46$ or $\eta^2 = 0.05$) and small ($d = 0.29$ or $\eta^2 = 0.02$), respectively (36). Another group found lower ANT accuracy in adults diagnosed with attention-deficit/hyperactivity disorder compared with healthy controls ($d = 0.71$ or $\eta^2 = 0.11$), but no orienting effect (27). When we compared ACSM fitness groups, we found medium effect sizes for both accuracy ($\eta^2 = 0.05$ in the unadjusted model) and orienting ($\eta^2 = 0.07$ in the unadjusted model). Our findings for working memory performance are also important. He et al. (17) reported that the difference between SMS accuracy between patients with schizophrenia and healthy controls was 2.3% ($P < 0.0001$). Comparatively, in our study, the difference in SMS accuracy between women with "very poor/poor" fitness and those with "superior" fitness was 2.9%. These examples suggest that the variation in behavior accounted for by variation in CRF is indeed meaningful.

We failed to observe an association between CRF and performance on the GNG task, which may have been too easy for these educated women in their 20s, the life stage when executive function peaks (49). Similarly, the lack of an association between CRF and response speed across the tasks is likely due to low variability in RT in this highly performing sample of college students, although we cannot rule out the possibility of a truly null finding. A speed accuracy tradeoff is supported by data from the planning and problem-solving task (TOL), where participants with higher CRF took more time to mentally plan their responses to solve problems more efficiently and make fewer excess moves; this phenomenon has been previously reported (47). The instructions in the TOL task specifically asked participants to plan their responses mentally before moving the discs and to solve the problems in as few moves as possible.

Although we are unable to explain the mechanisms behind our observations given the study design, current evidence strongly points to growth factors as the key mediators through which exercise is able to influence synaptic plasticity and behavior (30). These neurotrophins include brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF-1), and vascular endothelial growth factor (VEGF), which act in concert to modulate neurogenesis and angiogenesis in the CNS (9). Human studies have shown increases in peripheral BDNF levels after exercise, with the level of increase corresponding to exercise intensity and duration (39). Rodent studies have also shown BDNF increases in several brain regions, notably in the hippocampus, after exercise (31). Importantly, BDNF is able to cross the blood–brain barrier in both directions, and animal studies point to a direct correlation between plasma and brain levels (22). Although most research has considered BDNF, IGF-1 and VEGF may also explain some of the beneficial effects of exercise on cognition. IGF-1 and VEGF are both produced in the periphery (muscle and liver) but can cross the blood–brain barrier (11,25). Like BDNF, levels of IGF-1 rise rapidly after exercise, with increased IGF-1 gene expression several days after exercise onset (10).

In addition to demonstrations of exercise-induced neurotrophin release, animal studies have shown concomitant neurogenic and behavioral effects. For example, mice conducting wheel running for 50 d exhibited enhanced hippocampal neurogenesis and superior performance on a water maze test when compared with sedentary controls (6). Collectively, the available evidence in both human and animal studies suggests that the brains of exercising individuals are not only well connected in terms of neural network complexity, but also receive an ample supply of nutrients from the periphery via a robust vasculature, and these attributes are likely due to the effect of neurotrophin release after exercise. In terms of executive functioning specifically, which is heavily reliant on the ability of frontal brain regions and their intercommunication with midbrain and posterior regions (37), it is difficult to postulate a precise regional target of neurotrophins. BDNF is widespread in the adult rat brain (8), and postmortem analysis of human brain tissue has demonstrated regional similarity of BDNF mRNA expression in rat and human brains, with basal forebrain cholinergic neurons being a primary BDNF target (32). Furthermore, data suggest that neurons in the basal forebrain mediate executive aspects of attentional performance via projections to the cortex and subthalamic nucleus (5). Thus, one might speculate that exercise-induced BDNF released from muscle tissue crosses the blood–brain barrier, targeting at least the basal forebrain, thus bolstering the neural structures underlying executive processes.

Our findings extend previous work examining relations between fitness and cognition in young adults. Scisco et al. (41) found no differences between groups of low-fit and high-fit mostly female college students and no sex differences in terms of both neuroelectric and behavioral indices on a demanding switching task. The authors suggest that the association between CRF and cognition may only emerge after early adulthood but also note that other executive function tasks with different designs such as an Eriksen flanker task may reveal differences; our finding that attentional accuracy and orienting ability on the ANT, a modified Eriksen flanker task, improve with increasing CRF supports the notion that CRF may benefit executive function in young adults. Many distinct behavioral aspects are encompassed under the umbrella of executive functions, and differences in task design should be taken into account so distinctions are not lost when comparing studies. In another study, where neuroelectric patterns were examined in younger and older male and female adults performing a three-stimulus oddball task, Pontifex et al. (35) found effects of CRF on P3b but not P3a amplitude, hypothesized to be indices of attentional resource allocation and orienting, respectively. They did not, however, observe fitness or sex effects on behavioral performance in terms of accuracy. In contrast, using a different attention task, Fan and Posner's ANT, we found effects of fitness on both attentional accuracy and orienting such that higher CRF was associated with superior behavioral performance. These discrepant findings could be explained by the fact that, although both the three-stimulus oddball task and the ANT gauge attentional control and require filtering out irrelevant information, they are not identical in design.

Our study had several strengths and limitations. The findings here are strengthened by the use of a gold standard assessment of CRF, a treadmill-based exercise test performed until volitional exhaustion. This fitness test was possible in our study given the relatively high fitness of our sample, but in lower-fit populations, submaximal tests or questionnaire measures may be required to assess fitness. In our analyses, we examined fitness categorically according to definitions with public health relevance. We also considered a number of potential confounders of cognitive performance, and it was important to account for these factors because most of our statistically significant findings emerged in the adjusted models. Furthermore, we employed an array of five cognitive tasks in a 1-h testing session to capture a diverse profile of behavior and executive function. Future studies in men, other ethnic groups, lower fitness groups, and individuals with a lower socioeconomic or education background are needed to determine whether CRF is also associated with better executive function in these populations. In addition, longitudinal evidence is needed to causally link fitness to cognitive performance.

In conclusion, we have shown that increasing CRF as assessed using an incremental $\dot{V}O_{2peak}$ test to exhaustion is associated with better performance on three behavioral tasks measuring different aspects of executive function in healthy young adult women. These findings may have implications for academic performance and future well-being, because better executive function may offer an edge in a competitive academic environment and because performance in college has been shown to relate to future employment (44). Although most work to date on the topic of fitness and cognition has been done in children and older adults, this study adds to the available evidence of such a relation in younger adults. Future efforts should continue to explore the link between CRF and behavior in young adults using longitudinal designs that permit causal inference. Finally, more work is needed to determine whether the behavioral benefits of fitness translate into other measures of well-being such as academic and work performance.

Acknowledgments — The authors thank Tracey Allen, Cynthia Flanagan, Karen Clinger, and Filomena Martin for performing the blood draws in this study. We also thank Suzanne Simons, Caterina Myshko, Megan Satterthwaite, Abigail Lathrop, Ruoyi Wang, Jenna Jiang, and Jay Lieberman for assistance in scheduling, test administration, and blood analysis. This work was financially supported through pilot funds from the College of Health and Human Development at The Pennsylvania State University. The authors have no conflicts of interest to disclose. The results of the present study do not constitute endorsement by ACSM.

References

1. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2014.
2. Astrand PO, Saltin B. Maximal oxygen uptake and heart rate in various types of muscular activity. *J Appl Physiol*. 1961; 16:977–81.
3. Bezdjian S, Baker LA, Lozano DI, Raine A. Assessing inattention and impulsivity in children during the Go/NoGo task. *Br J Dev Psychol*. 2009; 27(2):365–83.
4. Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med*. 1970; 2(2):92–8.
5. Burk JA, Sarter M. Dissociation between the attentional functions mediated via basal forebrain cholinergic and GABAergic neurons. *Neuroscience*. 2001; 105(4):899–909.
6. Clark PJ, Brzezinska WJ, Puchalski EK, Krone DA, Rhodes JS. Functional analysis of neurovascular adaptations to exercise in the dentate gyrus of young adult mice associated with cognitive gain. *Hippocampus*. 2009; 19(10):937–50.
7. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale (NJ): Erlbaum; 1988.
8. Conner JM, Lauterborn JC, Yan Q, Gall CM, Varon S. Distribution of brain-derived neurotrophic factor (BDNF) protein and mRNA in the normal adult rat CNS: Evidence for anterograde axonal transport. *J Neurosci*. 1997; 17(7):2295–313.
9. Cotman CW, Berchtold NC, Christie L-A. Exercise builds brain health: Key roles of growth factor cascades and inflammation. *Trends Neurosci*. 2007; 30(9):464–72.
10. Ding Q, Vaynman S, AkhavanM, Ying Z, Gomez-Pinilla F. Insulin-like growth factor I interfaces with brain-derived neurotrophic factor-mediated synaptic plasticity to modulate aspects of exercise-induced cognitive function. *Neuroscience*. 2006; 140(3):823–33.
11. Fabel K, Fabel K, Tam B, et al. VEGF is necessary for exercise-induced adult hippocampal neurogenesis. *Eur J Neurosci*. 2003; 18(10):2803–12.
12. Fan J, McCandliss BD, Fossella J, Flombaum JI, Posner MI. The activation of attentional networks. *Neuroimage*. 2005; 26(2):471–9.
13. Fox CJ, Mueller ST, Gray HM, Raber J, Piper BJ. Evaluation of a short-form of the Berg card sorting test. *PLoS One*. 2013; 8(5):e63885.
14. Fuchs E, Flugge G. Adult neuroplasticity: More than 40 years of research. *Neural Plast*. 2014; 2014:e541870.
15. Gropper SS, Simmons KP, Connell LJ, Ulrich PV. Changes in body weight, composition, and shape: A 4-year study of college students. *Appl Physiol Nutr Metab*. 2012; 37(6):1118–23.
16. Hallal PC, Andersen LB, Bull FC, et al. Global physical activity levels: Surveillance progress, pitfalls, and prospects. *Lancet*. 2012; 380(9838):247–57.
17. He H, Sui J, Yu Q, et al. Altered Small-World Brain Networks in Schizophrenia Patients during Working Memory Performance. *PLoS ONE* 2012; 7(6) e38195. https://doi.org/10.1371/journal.pone.0038195
18. Hillman CH, Kramer AF, Belopolsky AV, Smith DP. A cross-sectional examination of age and physical activity on performance and event-related brain potentials in a task switching paradigm. *Int J Psychophysiol*. 2006; 59(1):30–9.
19. Hötting K, Röder B. Beneficial effects of physical exercise on neuroplasticity and cognition. *Neurosci Biobehav Rev*. 2013; 37(9 Pt B):2243–57.
20. Huizinga M, Dolan CV, van der Molen MW. Age-related change in executive function: Developmental trends and a latent variable analysis. *Neuropsychologia*. 2006; 44(11):2017–36.
21. Kamijo K, Takeda Y. Regular physical activity improves executive function during task switching in young adults. *Int J Psychophysiol*. 2010; 75(3):304–11.
22. Karege F, Schwald M, Cisse M. Postnatal developmental profile of brain-derived neurotrophic factor in rat brain and platelets. *Neurosci Lett*. 2002; 328(3):261–4.
23. Labelle V, Bosquet L, Mekary S, Bherer L. Decline in executive control during acute bouts of exercise as a function of exercise intensity and fitness level. *Brain Cogn*. 2013; 81(1):10–7.
24. Looker AC, Dallman PR, Carroll MD, Gunter EW, Johnson CL. Prevalence of iron deficiency in the United States. *JAMA*. 1997; 277(12):973–6.
25. Lopez-Lopez C, LeRoith D, Torres-Aleman I. Insulin-like growth factor I is required for vessel remodeling in the adult brain. *Proc Natl Acad Sci U S A*. 2004; 101(26):9833–8.
26. Lounsbury JW, Gibson LW, Hamrick FL. The development and validation of a personological measure of work drive. *J Bus Psychol*. 2004; 18(4):427–51.
27. Lundervold AJ, Adolfsdottir S, Halleland H, HalmLy A, Plessen K, Haavik J. Attention Network Test in adults with ADHD—The impact of affective fluctuations. *Behav Brain Funct*. 2011; 7:27.
28. Mueller ST, Piper BJ. The Psychology Experiment Building Language (PEBL) and PEBL Test Battery. *J Neurosci Methods*. 2014; 222:250–9.
29. Nam CB, Boyd M. Occupational status in 2000; Over a century of census-based measurement. *Popul Res Policy Rev*. 2004; 23(4):327–58.
30. Neeper SA, Gómez-Pinilla F, Choi J, Cotman C. Exercise and brain neurotrophins. *Nature*. 1995; 373(6510):109.
31. Neeper SA, Gómez-Pinilla F, Choi J, Cotman CW. Physical activity increases mRNA for brain-derived neurotrophic factor and nerve growth factor in rat brain. *Brain Res*. 1996; 726(1–2): 49–56.
32. Phillips HS, Hains JM, Laramee GR, Rosenthal A, Winslow JW. Widespread expression of BDNF but not NT3 by target areas of basal forebrain cholinergic neurons. *Science*. 1990; 250(4978):290–4.
33. Phillips LH, Wynn V, Gilhooly KJ, Della Sala S, Logie RH. The role of memory in the Tower of London task. *Memory*. 1999; 7(2):209–31.
34. Polich J, Lardon MT. P300 and long-term physical exercise. *Electroencephalogr Clin Neurophysiol*. 1997; 103(4):493–8.
35. Pontifex MB, Hillman CH, Polich J. Age, physical fitness, and attention: P3a and P3b. *Psychophysiology*. 2009; 46(2):379–87.
36. Rubio Gómez JL, Hernández Bellido L, Ruiz Veguilla M, Ferrín Erdozaín M, Pereda Baños A, Gómez Milán E. Attentional network task performance in schizophrenic patients. *Psicothema*. 2010; 22(4):664–8.
37. Rusnakova S, Rektor I. The neurocognitive networks of the executive functions. In: Abud Ajeena IM, editor. *Advances in*

Clinical Neurophysiology. Rijeka, Croatia: InTech; 2012 [accessed January 16, 2015] http://www.intechopen.com/books/references/advances-in-clinical-neurophysiology/the-neurocognitive-networks-of-the-executive-functions

38. Saltin B, Astrand PO. Maximal oxygen uptake in athletes. *J Appl Physiol*. 1967; 23(3):353–8.
39. Schmolesky MT, Webb DL, Hansen RA. The effects of aerobic exercise intensity and duration on levels of brain-derived neurotrophic factor in healthy men. *J Sports Sci Med*. 2013; 12(3):502–11.
40. Schneider-Garces NJ, Gordon BA, Brumback-Peltz CR, et al. Span, CRUNCH, and beyond: Working memory capacity and the aging brain. *J Cogn Neurosci*. 2010; 22(4):655–69.
41. Scisco JL, Leynes PA, Kang J. Cardiovascular fitness and executive control during task-switching: an ERP study. *Int J Psychophysiol*. 2008; 69(1):52–60.
42. Scott SP, Murray-Kolb LE. Iron status is associated with performance on executive functioning tasks in nonanemic young women. *J Nutr*. 2016; 146:1–9.
43. Sternberg S. High-speed scanning in human memory. *Science*. 1966; 153:652–4.
44. Sulastri A, Handoko M, Janssens JMAM. Grade point average and biographical data in personal resumes: predictors of finding employment. *Int J Adolesc Youth*. 2015; 20(3):303–316.
45. Themanson JR, Hillman CH, Curtin JJ. Age and physical activity influences on action monitoring during task switching. *Neurobiol Aging*. 2006; 27(9):1335–45.
46. Torrey J. The Moral Instructor and Guide to Virtue. 25th ed. Philadelphia, PA: Grigg, 1973. p. 202.
47. Unterrainer JM, Rahm B, Kaller CP, et al. Planning abilities and the Tower of London: is this task measuring a discrete cognitive function? *J Clin Exp Neuropsychol*. 2004; 26(6):846–56.
48. Woodson RD, Wills RE, Lenfant C. Effect of acute and established anemia on O2 transport at rest, submaximal and maximal work. *J Appl Physiol*. 1978; 44(1):36–43.
49. Zelazo PD, Craik FIM, Booth L. Executive function across the life span. *Acta Psychol (Amst)*. 2004; 115(2–3):167–83.

SUPPLEMENTAL DIGITAL CONTENT 1. List of variables included as covariates in models relating VO2 peak to cognitive performance in young adult females

Outcome	Covariates included in regression analyses (Table 2)	Covariates included in ACSM group comparisons (SDC Table 2)
ANT		
Accuracy, % correct	Age	Age, handedness, laptop
RT, ms	Age, OC use	Age, handedness, laptop, OC use
RT variability, ms	Age, task order	Age, handedness, laptop, task order
Alerting, ms	Age, laptop	Age, handedness, laptop
Orienting, ms	Age	Age, handedness, laptop
Conflict, ms	Age	Age, handedness, laptop
BCST		
Categories completed	Age	Age, handedness, laptop
Perseverative errors	Age	Age, handedness, laptop
GNG		
Accuracy, % correct	Age, task order	Age, handedness, laptop, task order
RT, ms	Age, OC use, handedness	Age, handedness, laptop, OC use
RT variability, ms	Age, NPB score, DS use, OC use, task order	Age, handedness, laptop, NPB score, DS use, OC use, task order
SMS		
Accuracy, % correct	Age	Age, handedness, laptop
Change[2]	Age	Age, handedness, laptop
RT, ms	Age, NPB score, M use, handedness, task order	Age, handedness, laptop, NPB score, M use, task order
Change[2]	Age	Age, handedness, laptop
RT variability, ms	Age, OC use, M use, laptop	Age, handedness, laptop, OC use, M use
Change[2]	Age	Age, handedness, laptop
TOL		

Excess moves	Age	Age, handedness, laptop
Change[2]	Age	Age, handedness, laptop
Planning time, s	Age	Age, handedness, laptop
Change[2]	Age	Age, handedness, laptop
Solution time, s	Age, handedness	Age, handedness, laptop
Change[2]	Age	Age, handedness, laptop

DS, dietary supplement; M, medication; NPB, Nam-Powers-Boyd parental occupation score; OC, oral contraceptive

SUPPLEMENTAL DIGITAL CONTENT 2. Comparison of cognitive performance between groups using ACSM classifications based on VO2 peak for females aged 20-29 years.

Outcome	Very Poor/Poor (n = 17)	Fair/Good (n = 40)	Excellent (n = 31)	Superior (n = 32)	η^2		*P*	
ANT					Unadj.[1]	Adj.[1]	Unadj.[1]	Adj.[1]
Accuracy, % correct	95.3 ± 1.2[a]	96.5 ± 0.5[a]	97.8 ± 0.4[b]	97.9 ± 0.2[b]	0.05	0.19	0.12	**0.012**
RT, ms	470 ± 15[a]	454 ± 11[a]	451 ± 6[a]	467 ± 11[a]	0.03	0.07	0.10	0.74
RT variability, ms	142 ± 13[a]	139 ± 6[a]	125 ± 4[a]	131 ± 6[a]	0.02	0.13	0.08	0.41
Alerting, ms	57 ± 6[a]	54 ± 5[a]	43 ± 5[a]	49 ± 4[a]	0.04	0.14	0.21	0.13
Orienting, ms	14 ± 7[a]	31 ± 4[b]	31 ± 3[b]	37 ± 4[b]	0.07	0.12	**0.028**	**0.005**
Conflict, ms	118 ± 12[a]	114 ± 7[a]	97 ± 4[a]	101 ± 6[a]	0.03	0.06	0.24	0.50
BCST								
Categories completed	3.7 ± 0.3[a]	3.9 ± 0.2[a]	4.0 ± 0.2[a]	4.2 ± 0.2[a]	0.03	0.05	0.38	0.78
Perseverative errors	9.1 ± 0.6[a]	6.5 ± 0.5[b]	7.1 ± 0.5[ab]	6.6 ± 0.5[b]	0.05	0.15	0.10	**0.009**
GNG								
Accuracy, % correct	91.8 ± 1.2[a]	90.1 ± 0.8[a]	89.8 ± 1.0[a]	92.2 ± 0.6[a]	0.04	0.19	0.06	0.09
RT, ms	413 ± 10[a]	396 ± 7[a]	398 ± 7[a]	411 ± 7[a]	0.01	0.10	0.64	0.77
RT variability, ms	113 ± 5[a]	116 ± 4[a]	120 ± 4[a]	116 ± 5[a]	0.02	0.19	0.31	0.91
SMS								
Accuracy, % correct	92.5 ± 0.9[a]	92.8 ± 0.6[a]	93.8 ± 0.6[b]	95.4 ± 0.4[b]	0.03	0.04	**0.035**	**0.021**
Change[2]	-6.2 ± 0.8[a]	-4.4 ± 0.7[a]	-4.5 ± 0.6[a]	-3.6 ± 0.5[a]	0.02	0.02	0.21	0.49
RT, ms	749 ± 21[a]	696 ± 16[a]	709 ± 16[a]	736 ± 17[a]	0.02	0.09	0.38	0.32

Change[2]	150 ± 22 [a]	122 ± 12 [a]	149 ± 14 [a]	148 ± 16 [a]	0.01	0.03	0.51	0.29
RT variability, ms	322 ± 23 [a]	314 ± 19 [a]	306 ± 20 [a]	328 ± 25 [a]	0.00	0.03	0.92	0.66
Change[2]	204 ± 29 [a]	203 ± 28 [a]	153 ± 20 [a]	224 ± 26 [a]	0.02	0.02	0.32	0.24
TOL								
Excess moves	1.69 ± 0.21[a]	1.36 ± 0.13[ab]	1.15 ± 0.14[b]	1.14 ± 0.12[b]	0.01	0.01	0.16	**0.042**
Change[2]	1.31 ± 0.33 [a]	1.44 ± 0.26 [a]	1.49 ± 0.27 [a]	1.31 ± 0.25 [a]	0.00	0.03	0.96	0.86
Planning time, s	8.3 ± 0.5[a]	9.2 ± 0.5[b]	9.4 ± 0.6[b]	9.9 ± 0.5[b]	0.01	0.01	0.13	**0.013**
Change[2]	3.2 ± 1.4 [a]	5.3 ± 1.2 [a]	3.9 ± 1.3 [a]	5.9 ± 1.2 [a]	0.02	0.06	0.43	0.48
Solution time, s	12.1 ± 0.6 [a]	11.2 ± 0.5 [a]	10.9 ± 0.5 [a]	11.2 ± 0.5 [a]	0.00	0.03	0.45	0.81
Change[2]	8.5 ± 0.9 [a]	9.6 ± 1.0 [a]	9.9 ± 0.7 [a]	10.0 ± 0.9 [a]	0.01	0.08	0.71	0.27

Values are expressed as mean ± SE

Bold values indicate significance at $P < 0.05$

Within a row, groups with different superscript letters are significantly different ($P < 0.05$) in the adjusted analyses

[1] *P* (unadjusted, adjusted) before and after adjustment for covariates including age, parental occupation, days since last menstrual cycle, oral contraceptive use, medication use, dietary supplement use, handedness, task order, and computer number; covariate selection for the regression analyses was based on relation to the outcome at $P < 0.1$; not all covariates were included in all models (see Supplemental Digital Content 1)

[2] Change in performance from low to high difficulty problems (see 'Statistical Analyses' section)