Effects of physical activity on cognitive functioning in middle age: evidence from the Whitehall II prospective cohort study.

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Effects of Physical Activity on Cognitive Functioning in Middle Age: Evidence From the Whitehall II Prospective Cohort Study

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Objectives. We examined the association between physical activity and cognitive functioning in middle age.

Methods. Data were derived from a prospective occupational cohort study of 10 308 civil servants aged 35–55 years at baseline (phase 1; 1985–1988). Physical activity level, categorized as low, medium, or high, was assessed at phases 1, 3 (1991–1994), and 5 (1997–1999). Cognitive functioning was tested at phase 5, when respondents were 46–68 years old.

Results. In both prospective (odds ratio [OR] = 1.65; 95% confidence interval [CI] = 1.30, 2.10) and cross-sectional (OR = 1.79; 95% CI = 1.38, 2.32) analyses, low levels of physical activity were a risk factor for poor performance on a measure of fluid intelligence. Analyses aimed at assessing cumulative effects (summary of physical activity levels at the 3 time points) showed a graded linear relationship with fluid intelligence, with persistently low levels of physical activity being particularly harmful (OR = 2.21; 95% CI = 1.37, 3.57).

Conclusions. Low levels of physical activity are a risk factor for cognitive functioning in middle age, fluid intelligence in particular. (*Am J Public Health.* 2005; 95:2252–2258. doi:10.2105/AJPH.2004.055574)

Poor cognitive functioning is a predictor of mortality at all ages[1–5] and, as such, can be seen as a marker of general health status. Leisure-time physical activity has been shown to have a beneficial impact on cognitive functioning among older adults.[6–12] It also appears to offer protection against cognitive impairment and dementia in the elderly.[13,14] A meta-analysis that focused on randomized aerobic fitness intervention trials with intervention periods of less than a year showed fitness training to be associated with improved cognitive performance.[15]

Despite the wealth of evidence in this domain, questions remain. The most important question relates to whether the association between physical activity and cognitive functioning is specific to old age or evident earlier in adulthood. It also remains unclear whether benefits of physical activity over several years have a cumulative effect on cognitive functioning. This issue is relevant for the elaboration of public health messages on leisure-time physical activity. Cross-sectional studies are not adequate to model long-term effects of physical activity, and, because of their relatively short intervention periods (typically 3–4 months), the same is true of studies involving experimental designs.

We examined the association between physical activity over a span of several years and cognitive functioning in middle age. We contend that it is important to examine the relationship between physical activity and cognitive functioning in younger, healthier populations and to assess whether subtle neuropsychological deficits are evident among members of these age groups who are not physically active. Poor cognitive performance in early adulthood or in middle age is clinically relevant, given studies showing that individuals with mild cognitive impairment progress to clinically diagnosed dementia at an accelerated rate.[16,17]

We also sought to identify specific cognitive domains that might be particularly vulnerable to low levels of physical activity. Different studies have revealed beneficial effects of physical activity on fluid intelligence,[6,7] visuospatial performance,[10] reaction time,[8] and memory.[18,19] However, multiple cognitive domains often have not been examined in the same study. Establishing specific associations would enable elaboration of the pathways and mechanisms through which physical activity influences cognitive functioning.

METHODS

Study Population

The data used in our investigation were derived from the Whitehall II study, established in 1985 (full details on the study are available elsewhere[20]). All civil servants aged 35–55 years in 20 London-based departments were invited to participate in the study by letter. In total, 73% of those invited agreed to take part in phase 1 (n = 10,308 [6895 men and 3413 women]). Baseline examinations (phase 1), which took place during 1985 through 1988, involved clinical examinations and self-administered questionnaires with sections focusing on demographic characteristics, health status, lifestyle factors, work characteristics, social support network, and life events. Clinical examinations included measures of blood pressure, anthropometry, biochemical indicators, neuroendocrine function, and subclinical markers of cardiovascular disease. Subsequent phases of data collection alternated between self-administered questionnaires alone (phases 2 [1989–1990], 4 [1995–1996], and 6 [2000–2001]) and self-administered questionnaires accompanied by clinical examinations (phases 1, 3 [1991–1994], and 5 [1997–1999]).

Assessment of Physical Activity

Physical activity was assessed via questionnaire data from phases 1, 3, and 5. At phases 1 and 3, participants were asked about the frequency and duration of their participation in "mildly energetic" (e.g., weeding, general housework, bicycle repair), "moderately energetic" (e.g., dancing, cycling, leisurely swimming), and "vigorous" (e.g., running, hard swimming, playing squash) physical activity. The frequency and duration measures were combined to compute hours per week of activity at the 3 intensity levels. Subsequently, these intensity categories were used to derive 3 levels of physical activity: high, medium, and low. A high level of activity corresponded to 2.5 hours or more per week of moderate physical activity *or* 1 hour or more per week of vigorous physical activity. A low level of activity corresponded to less than 2 hours per week of moderate activity *and* less than 1 hour per week of vigorous physical activity. Amounts of physical activity that fell between these 2 categories were classified as being at a medium level.

At phase 5, the questionnaire was modified to include 20 items on frequency and duration of participation in walking, cycling, sports, gardening, housework, and home maintenance. Once again, frequency and duration of each activity were combined to compute hours per week of physical activity. A compendium of activity energy costs was then used to assign each of the 20 physical activities assessed a metabolic equivalent (MET).[21] MET values reflected the intensity of each physical activity, 1 MET being approximately equal to the energy cost of lying quietly. Amount of time spent in activities with MET values ranging from 3 to 6 (e.g., cycling, gardening) was summed to allow calculation of total number of hours per week of moderate physical activity. Similarly, amount of time spent in activities with MET values of 6 or above (e.g., sports) was summed to allow calculation of total hours per week of vigorous physical activity. The same criteria employed at phases 1 and 3 were then used to compute high, medium, and low categories of physical activity.

Levels of physical activity at phases 1, 3 and 5 were set at 0, 1, and 2 to represent high, medium, and low levels, respectively. Levels of physical activity at the 3 time points were summed to create a physical activity level summary score. This summary score ranged from 0, representing an activity level of 0 (high) at all 3 points, to 6, representing an activity level of 2 (low) at all 3 points.

Assessment of Cognitive Functioning

Cognitive functioning was assessed as part of the clinical examination at phase 5, when the respondents were between the ages of 46 and 68 years (mean age: 55.6 years). The cognitive test battery consisted of 5 standard tasks (1, the Mill Hill Vocabulary Scale, used as a covariate) selected to provide a comprehensive evaluation of cognitive functioning among middle-aged adults.

The first test was a 20-word free-recall test of short-term memory. Participants were presented a list of 20 words, each of 1 or 2 syllables (ream, latch, hot, skirt, jab, clog, mare, else, wage, jowl, chap, trout, blot, reek, tape, dusk, list, smug, duck, big), at 2-second intervals and then asked to recall in writing as many of the words as they could in any order. They had 2 minutes to do so.

The Alice Heim 4-I (AH 4-I) test is a measure of fluid intelligence composed of a series of 65 verbal- and mathematical-reasoning items of increasing difficulty.[22] It assesses inductive reasoning by measuring individuals' ability to identify patterns and infer principles and rules. Participants had 10 minutes to complete this instrument.

We used two measures of verbal fluency[23]: phonemic and semantic. Phonemic fluency was assessed via "s" words and semantic fluency via "animal" words. Participants were asked to recall in writing as many words beginning with "s" and as many animal names as they could. They were allowed 1 minute to complete each test.

Covariates Measured at Baseline

The following covariates were included in the analyses: age, gender, education, socioeconomic position, self-rated health, vascular risk factors (blood pressure and cholesterol levels), smoking status, mental health status, social network, and a proxy for baseline cognitive functioning. Education was grouped into 5 hierarchical categories: (1) no formal education, (2) lower secondary education, (3) higher secondary education, (4) university degree, and (5) higher university degree. Employment grade, ranging from 1 (highest) to 6 (lowest), was used to assess socioeconomic position. All British civil service jobs have an associated employment grade,[20] and people at different grades differ in terms of salary, social status, and level of responsibility.

Self-rated health was assessed with the question "In general, would you say your health is very good, good, fair, poor, or very poor?" Participants' blood pressure was measured twice, whereas they were in a sitting position (once after 5 minutes' rest), with a Hawksley (Lancing, Sussex, England) random-zero sphygmomanometer. Serum cholesterol level was determined via the cholesterol oxidate peroxidase colorimetric method (BCLkit; Boehringer, Mannheim, Germany). Smoking status was assessed with a question on whether participants currently smoked (cigarettes, hand-rolled tobacco, or cigars), the frequency with which they smoked, and, if they had quit, when they had done so. The 30-item General Health Questionnaire was used to assess mental health status.[24] A social network index was adapted from the Berkman and Syme[25] instrument; scores on items assessing number of people in network, frequency of contacts, group membership, and church attendance were summed to allow calculation of overall index scores.

The Mill Hill Vocabulary Scale, a measure of acquired verbal knowledge that focuses on people's ability to recognize and comprehend the meaning of words, was used as a proxy for baseline cognitive functioning.[26] This instrument assesses crystallized intelligence, an aspect of cognition that is unaffected by age. We used the scale in its multiple choice format, which consists of a list of 33 stimulus words, in order of increasing difficulty, and 6 response choices.

Statistical Analysis

One-way analyses of variance, with gender and age as covariates, were initially used to examine differences in mean cognitive scores as a function of level of physical activity at phases 1, 3, and 5. F tests were used to assess overall effects of physical activity, and additional post hoc tests were conducted to determine differences between groups. Similarly, cognitive tests were examined as a function of summary physical activity scores. Standardized T scores (mean=50, SD=10) were used in these analyses.

The next step involved assessment, through the use of binary logistic regression analyses, of the risk of poor cognitive performance associated with physical activity. In the case of each test, poor cognitive functioning was indicated by categorization in the lowest quintile. The reference group was participants who reported a high level of physical activity. The first set of analyses included levels of physical activity at phases 1 and 5 individually so that analyses of current physical activity (phase 5: cross-sectional analyses) and analyses of baseline activity (phase 1: prospective analyses) could be compared. Next, to assess cumulative effects, risk of poor cognitive performance as a function of summary score was examined, with 0 (high level at all 3 time points) as the reference category. In both of these analyses, 3 models were tested. Model 1 was the basic model, controlling for gender and age alone. Model 2 added education, employment grade, self-rated health, blood pressure, cholesterol, smoking status, mental health status, and social network index score. Finally, model 3 included Mill Hill score (here a proxy for baseline cognitive function) and all of the model 2 variables.

RESULTS

The median length of follow-up from phase 1 to phase 5 was 11 years; 355 individuals died during this period. Of the 10308 baseline participants (1985–1988), 8637 provided data at phase 3 (1991–1994), and 7830 provided data at phase 5 (1997–1999). Cognitive functioning and physical activity data at all 3 phases were available for 6236 respondents. In comparison with baseline data, the data used in our analyses were influenced by age (P=.001) and employment grade (P=.001) but not by gender (P=.61). The attrition rate was higher among older respondents and respondents of low socioeconomic position.

Table 1 presents data on respondents' physical activity levels; it can be seen that approximately half of the respondents reported high levels of activity at the 3 phases (51.3% at phase 1, 46.6% at phase 3, and 44.6% at phase 5). Table 1 also shows age- and gender-adjusted data on high, medium, and low levels of physical activity at the 3 phases (phases 1, 3, and 5). Performance on the memory test was not significantly associated (P=.07) with level of physical activity at phase 1. All other F tests were significant. Post hoc tests showed that the low-activity group, but not the medium-activity group, had lower cognitive-functioning scores than the high-activity group at phase 1. At phases 3 and 5, both of these groups had significantly lower mean scores than the high-activity group on all measures of cognitive function. Table 2 shows that 20.7% of the participants reported high levels of physical activity at all 3 phases and that 5.1% reported low levels at all of the phases. Age- and gender-adjusted mean scores differed significantly between the summary levels of physical activity for all of the cognitive tests examined.

Participants reporting a low level of physical activity at baseline (phase 1) were significantly more likely to have cognitive test scores in the lowest quintile after adjustment for age and gender (Table 3, model A1). After adjustment for measured covariates and confounders, including Mill Hill Vocabulary Scale score (Table 3, model A3), an association remained only between low level of physical activity at baseline and AH 4-I score. Cross-sectional age- and gender-adjusted associations (phase 5 physical activity and phase 5 cognitive functioning) were somewhat stronger (Table 3, model B1) than prospective associations (phase 1 activity and phase 5 cognitive functioning). After further adjustment for education, employment grade, self-rated health, blood pressure level, cholesterol level, smoking status, mental health status, and social network index score, low levels of physical activity remained associated with greater risk of poor cognitive functioning for all outcomes examined (Table 3, model B2). Additional adjustment for Mill Hill score (as a proxy for baseline cognitive functioning) revealed significant effects of low physical activity levels on AH 4-I score and phonemic fluency (Table 3, model B3).

Table 4 presents the odds of being ranked in the lowest quintile of cognitive test scores as a function of summary score (calculated to represent levels of physical activity through the 3 time points). A significant age- and gender-adjusted association was observed between summary score and the odds of being ranked in the lowest quintile on all cognitive tests (Table 4, model C1). Tests for linear

TABLE 1—Mean Scores on Cognitive Tests at Phase 5 and Levels of Physical Activity, by Study Phase: Whitehall II Prospective Cohort Study, 1985–1999 (n = 6236)

	Cognitive Test Mean Score (95% CI)				
	No. (%)	Memory	Alice Heim 4-I	Phonemic Fluency	Semantic Fluency
Phase 1 (1985–1988)					
High	3196 (51.3)	50.10 (49.7, 50.5)	50.49 (50.1, 50.8)	50.19 (49.8, 50.5)	50.27 (49.9, 50.6)
Medium	1654 (26.5)	50.05 (49.6, 50.5)	50.41 (49.9, 50.9)	50.12 (49.6, 50.6)	50.23 (49.7, 50.7)
Low	1386 (22.2)	49.70 (49.2, 50.2)	48.36 (47.8, 48.9)[a]	49.39 (48.8, 49.9)[a]	49.09 (48.5, 49.6)[a]
F test P	.07	<.0001	.05	.001	
Phase 3 (1991–1994)					
High	2906 (46.6)	50.44 (50.1, 50.8)	50.35 (50.0, 50.7)	50.58 (50.2, 50.9)	50.59 (50.2, 50.9)
Medium	1718 (27.5)	49.70 (49.2, 50.2)[a]	49.68 (49.2, 50.1)[a]	49.47 (49.0, 49.9)[a]	49.51 (49.0, 49.9)[a]
Low	1612 (25.8)	49.52 (49.0, 50.0)[a]	49.70 (49.2, 50.2)[a]	49.50 (49.0, 50.0)[a]	49.45 (48.9, 49.9)[a]
F test P	.006	.03	<.0001	<.0001	
Phase 5 (1997–1999)					
High	2783 (44.6)	50.72 (50.3, 51.1)	51.19 (50.8, 51.6)	50.80 (50.4, 51.2)	50.90 (50.5, 51.3)
Medium	2243 (36.0)	49.84 (49.4, 50.3)[a]	50.02 (49.6, 50.4)[a]	49.99 (49.6, 50.4)[a]	50.03 (49.6, 50.4)[a]
Low	1210 (19.4)	48.64 (48.1, 49.2)[a]	47.21 (46.7, 47.6)[a]	48.18 (47.6, 48.8)[a]	47.86 (47.3, 48.4)[a]
F test P	<.0001	<.0001	<.0001	<.0001	

Note. CI = confidence interval. Analyses were carried out on T scores (mean = 50, SD = 10), adjusted for age and gender.
[a]Significantly lower mean (post hoc test; P < .05) than group score at high physical activity level.

TABLE 2—Mean Scores on Cognitive Tests at Phase 5 and Physical Activity Summary Scores, by Study Phase: Whitehall II Prospective Cohort Study, 1985–1999 (n = 6236)

Physical Activity Summary Score	No. (%)	Cognitive Test Mean Score (95% CI)			
		Memory	Alice Heim 4-I	Phonemic Fluency	Semantic Fluency
0	1293 (20.7)	51.14 (50.6, 51.7)	51.47 (50.9, 52.0)	51.26 (50.7, 51.8)	51.28 (50.7, 51.8)
1	1223 (19.6)	50.34 (49.8, 50.9)[a]	50.73 (50.2, 51.3)	50.42 (49.8, 51.0)[a]	50.56 (50.0, 51.1)
2	1136 (18.2)	49.42 (48.8, 50.0)[a]	49.93 (49.4, 50.5)[a]	49.76 (49.2, 50.3)[a]	49.87 (49.3, 50.5)[a]
3	970 (15.6)	49.62 (49.0, 50.3)[a]	49.42 (48.8, 50.0)[a]	49.40 (48.8, 50.0)[a]	49.25 (48.6, 49.9)[a]
4	765 (12.3)	49.62 (48.9, 50.3)[a]	49.29 (48.6, 50.0)[a]	49.55 (48.8, 50.3)[a]	49.91 (49.2, 50.6)[a]
5	528 (8.5)	48.92 (49.0, 50.8)[a]	48.96 (48.1, 49.8)[a]	49.54 (48.7, 50.4)[a]	49.20 (48.3, 50.1)[a]
6	321 (5.1)	48.28 (47.2, 49.4)[a]	46.53 (45.4, 47.6)[a]	47.73 (46.6, 48.9)[a]	46.86 (45.7, 48.0)[a]
F test		<.0001	<.0001	<.0001	<.0001

Note. CI = confidence interval. Physical Activity Summary Scores were calculated by assigning scores of 0, 1, and 2 to high, medium, and low levels of activity at the 3 phases of measurement. These scores were then summed to allow calculation of the summary score, which could range from 0 to 6. A score of 0 represents a high physical activity level across the 3 measurements, and a score of 6 represents a low activity level at all 3 measurements. Analyses were carried out on T scores (mean = 50, SD = 10), were adjusted for age and gender.
[a]Significantly lower mean (post hoc test; $P < .05$) than group score at high physical activity level at the 3 phases.

trend across the summary scale were also significant for all measures of cognitive functioning examined. Adjustment for the covariates assessed (Table 4, model C3) significantly attenuated these relationships. The final model, model C3, showed a linear, cumulative dose–response relationship between levels of physical activity across phases 1, 3, and 5 and poor performance on the AH 4-I. A summary score of 6, representing low levels of physical activity at the 3 time points, also was associated with poor phonemic fluency.

DISCUSSION

Our results, derived from a large prospective cohort study of British civil servants, indicate that physical activity has a beneficial impact on cognitive functioning in middle age. The association between physical activity and cognitive performance previously has been examined in the elderly; in that age group there is considerable evidence that lack of physical activity is a risk factor for poor cognitive functioning. Our results showed a small but significant association between physical activity and cognitive functioning in middle age. The age- and gender-adjusted relationship between physical activity and cognitive performance was greatly attenuated by the addition of education and socioeconomic position to the model (results not shown), both of which have been shown to be critically important confounders of this relationship.[27,28] However, in analyses adjusted for all of the covariates assessed (age, gender, education, employment grade, self-rated health, blood pressure level, cholesterol level, smoking status, mental health status, social network index score), including a proxy for baseline cognitive functioning (Mill Hill Vocabulary Scale), physical activity remained significantly associated with fluid intelligence (AH 4-I score) and phonemic fluency.

We examined prospective, cross-sectional, and cumulative effects, because these effects signify different aspects of the relationship between physical activity and cognitive functioning. The prospective analyses showed that low levels of physical activity at baseline were significantly associated with lower scores on all cognitive tests 11 years later. After adjustment for the covariates, a significant association remained between low levels of physical activity and poor performance on the AH 4-I, a measure of fluid intelligence. The cross-sectional associations were more extensive, particularly before adjustment for baseline cognitive functioning. However, after adjustment for covariates, the cross-sectional associations were significant only for AH 4-I score and phonemic fluency. Dustman et al. suggested that such cross-sectional associations in fact represent cumulative effects of physical activity.[29] Our data allowed us to explore this hypothesis. The cumulative effect of physical activity was evident in a linear dose–response relationship, particularly for AH 4-I score. A significant linear effect also was observed for the measures of verbal fluency, accounted for mostly by the adverse effects of low levels of physical activity throughout the 3 measurement phases.

We examined different aspects of cognitive functioning rather than assessing general impairment with an instrument such as the Mini Mental State Examination, which is widely used in research on the elderly but is inappropriate for use among younger populations owing to ceiling effects (minor variation in scores—all participants score highly). A battery of cognitive tests similar to that used in this study better captures variability in cognitive scores. The disadvantage is the lack of standard criteria with which to judge poor cognitive performance. In keeping with other research in this area, we used lowest-quintile rankings to denote poor performance.[30] Our results indicate that fluid intelligence, as assessed with the AH 4-I, is particularly vulnerable to the negative effects associated with low levels of physical activity. These findings support the suggestion from earlier research that physical activity moderates the decline in cognitive functioning typically associated with aging.[31,32] The aspect of cognitive functioning that declines most with age is fluid intelligence,[33] and our results show that low levels of physical exercise are already a risk factor in middle age. Fluid intelligence is seen to be intrinsically associated with information processing and involves short-term memory, abstract thinking, creativity, ability to solve novel problems, and reaction time.

Our results concerning the association between physical activity and cognitive functioning in middle age add to the body of research showing the protective effect of physical activity on cognitive decline and dementia among the elderly. Identification of risk factors associated with cognitive decline, particularly earlier in the life course, is critical in formulating prevention or intervention strategies. It is highly likely that the relationship between physical activity and cognitive performance is reciprocal; that is, increased

TABLE 3—Odds of Ranking in Lowest Cognitive-Functioning Quintile, by Level of Physical Activity (Prospective and Cross-Sectional Associations): Whitehall II Prospective Cohort Study, 1985–1999

Model and Level of Physical Activity	OR (95% CI) for Ranking in Lowest-Functioning Quintile			
	Memory	Alice Heim 4-I	Phonemic Fluency	Semantic Fluency
Prospective analyses: physical activity assessed at phase 1 (1985–1988)				
Model A1[a]				
High	Reference	Reference	Reference	Reference
Medium	0.92 (0.77, 1.10)	1.09 (0.92, 1.29)	0.88 (0.75, 1.03)	0.93 (0.78, 1.11)
Low	1.21 (1.01, 1.45)*	1.78 (1.51, 2.10)*	1.21 (1.03, 1.41)*	1.38 (1.16, 1.64)*
Test for trend *P*	.09	<.0001	.07	.001
Model A2[b]				
High	Reference	Reference	Reference	Reference
Medium	0.91 (0.75, 1.11)	1.19 (0.97, 1.47)	0.89 (0.75, 1.06)	0.95 (0.78, 1.16)
Low	0.97 (0.79, 1.91)	1.47 (1.19, 1.82)*	0.97 (0.80, 1.16)	1.11 (0.90, 1.36)
Test for trend *P*	.65	<.0001	.53	.41
Model A3[c]				
High	Reference	Reference	Reference	Reference
Medium	0.92 (0.76, 1.12)	1.23 (0.98, 1.54)	0.89 (0.75, 1.06)	0.94 (0.76, 1.16)
Low	0.99 (0.80, 1.23)	1.65 (1.30, 2.10)*	0.99 (0.82, 1.20)	1.15 (0.92, 1.43)
Test for trend *P*	.80	<.0001	.69	.33
Cross-sectional analyses: physical activity assessed at phase 5 (1997–1999)				
Model B1[a]				
High	Reference	Reference	Reference	Reference
Medium	1.17 (0.99, 1.39)	1.46 (1.24, 1.72)*	1.24 (1.07, 1.44)*	1.30 (1.10, 1.54)*
Low	1.53 (1.26, 1.86)*	2.81 (2.35, 3.37)*	1.96 (1.65, 2.32)*	2.08 (1.73, 2.51)*
Test for trend *P*	<.0001	<.0001	<.0001	<.0001
Model B2[b]				
High	Reference	Reference	Reference	Reference
Medium	1.10 (0.91, 1.32)	1.20 (0.98, 1.46)	1.09 (0.93, 1.29)	1.10 (0.91, 1.33)
Low	1.32 (1.06, 1.64)*	1.93 (1.53, 2.44)*	1.42 (1.17, 1.73)*	1.30 (1.04, 1.63)*
Test for trend *P*	.02	<.0001	<.001	.02
Model B3[c]				
High	Reference	Reference	Reference	Reference
Medium	1.11 (0.92, 1.34)	1.19 (0.96, 1.48)	1.10 (0.93, 1.30)	1.10 (0.91, 1.34)
Low	1.19 (0.95, 1.50)	1.79 (1.38, 2.32)*	1.34 (1.09, 1.65)*	1.14 (0.89, 1.45)
Test for trend *P*	.11	<.0001	.006	.25

Note. OR = odds ratio; CI = confidence interval.
[a]Adjusted for age and gender.
[b]Adjusted for age, gender, education level, employment grade, self-rated health, blood pressure level, cholesterol level, smoking status, mental health status, and social network index score.
[c]Adjusted for age, gender, education level, employment grade, self-rated health, blood pressure level, cholesterol level, smoking status, mental health status, social network index score, and Mill Hill Vocabulary Scale score.
*$P < .05$.

physical activity leads to better cognitive functioning *and* brighter people exercise more. However, it is the former pathway that has public health significance. In our data, causal direction is inferred rather than shown directly, in that a proxy for baseline cognitive functioning was controlled. Crystallized intelligence does not decline in middle age,[33] and we used this type of intelligence as a proxy for baseline level of cognitive functioning. Further support for the protective effect of physical activity on cognitive functioning has been provided by the results of fitness trials[15] and a study showing that this association holds even after adjustment for childhood cognitive performance.[34]

Although several viable hypotheses have been proposed, the mechanisms underlying the association between physical activity and cognitive functioning are poorly understood. Physical activity has been shown to sustain cerebral blood flow,[10,35] and it may improve aerobic capacity and cerebral nutrient supply.[36,37] Physical activity also is believed to facilitate neurotransmitter metabolism.[29,37] Cotman and Berchtold suggested that physical activity triggers molecular and cellular changes that support and maintain brain plasticity.[38] For example, 1 investigation revealed greater neuronal plasticity in the larger posterior hippocampi of London taxi drivers, who undertake intensive navigational study of the city as part of their training.[39] Another possibility is that physical activity reduces the risk of conditions or diseases (e.g., hypertension, diabetes, cardiovascular disease) that impair cognitive functioning.[40,41] Evidence from animal studies has shown that physical activity is associated with cellular, molecular, and neurochemical changes.[42–45] The effects observed have been related to increases in cerebral vascularization, increased dopamine levels, and molecular changes in neurotrophin factors that serve neuroprotective functions.[46]

A number of limitations of our study should be noted. First, although the sample covered a wide socioeconomic range, the data were derived from white-collar civil servants and cannot be assumed to represent general populations. Second, physical activity levels were self-reported and may have been underestimated or overestimated. This possibility is mitigated by the fact that comparisons between self-reported physical activity levels and measures of physical fitness have shown little discrepancy in other studies,[47] and the former self-reports of physical activity are more suitable for assessing activity over time.[48,49] Another problem is that the measure of physical activity used at phase 5 was different from that used at phases 1 and 3. However, because we employed broad physical activity categories, this discrepancy is unlikely to have influenced our results.

TABLE 4—Odds of Ranking in Lowest Cognitive-Functioning Quintile, by Level of Physical Activity, by Study Phase (Cumulative Effects): Whitehall II Prospective Cohort Study, 1985–1999

Model and Summary Score	OR (95% CI) for Ranking in Lowest-Functioning Quintile			
	Memory	Alice Heim 4-I	Phonemic Fluency	Semantic Fluency
Model C1[a]				
0	Reference	Reference	Reference	Reference
1	1.06 (0.83, 1.34)	1.28 (1.01, 1.65)*	1.11 (0.90, 1.38)	1.26 (0.99, 1.62)
2	1.16 (0.91, 1.48)	1.61 (1.26, 2.06)*	1.37 (1.11, 1.69)*	1.44 (1.12, 1.84)*
3	1.30 (1.02, 1.67)*	1.96 (1.54, 2.51)*	1.37 (1.10, 1.71)*	1.71 (1.34, 2.20)*
4	1.33 (1.02, 1.73)*	2.20(1.70, 2.85)*	1.51 (1.19, 1.90)*	1.65 (1.26, 2.16)*
5	1.32 (0.98, 1.77)	2.45 (1.85, 3.24)*	1.48 (1.14, 1.93)*	1.86 (1.39, 2.49)*
6	1.91 (1.37, 2.66)*	3.51 (2.56, 4.83)*	2.28 (1.70, 3.07)*	2.87 (2.08, 3.96)*
Test for trend *P*	<.0001	<.0001	<.0001	<.0001
Model C2[b]				
0	Reference	Reference	Reference	Reference
1	1.01 (0.79, 1.31)	1.15 (0.86, 1.55)	1.01 (0.80, 1.27)	1.12 (0.85, 1.47)
2	i	1.50 (1.11, 2.02)*	1.20 (0.95, 1.52)	1.25 (0.95, 1.64)
3	1.14 (0.87, 1.49)	1.44 (1.07, 1.94)*	1.07 (0.84, 1.36)	1.29 (0.97, 1.70)
4	1.24 (0.93, 1.66)	1.65(1.20, 2.28)*	1.17 (0.90, 1.53)	1.25 (0.92, 1.69)
5	1.02 (0.73, 1.43)	1.79 (1.26, 2.55)*	1.11 (0.82, 1.49)	1.31 (0.93, 1.84)
6	1.15 (0.78, 1.72)	2.11 (1.39, 3.18)*	1.50 (1.06, 2.13)*	1.54 (1.04, 2.29)*
Test for trend *P*	.24	<.0001	.05	.02
Model C3[c]				
0	Reference	Reference	Reference	Reference
1	1.02 (0.79, 1.31)	1.11 (0.81, 1.52)	1.02 (0.80, 1.28)	1.12 (0.85, 1.48)
2	1.09 (0.83, 1.42)	1.57 (1.14, 2.15)*	1.24 (0.98, 1.57)	1.29 (0.97, 1.72)
3	1.17 (0.89, 1.53)	1.45 (1.05, 2.01)*	1.10 (0.86, 1.40)	1.33 (0.99, 1.78)
4	1.26 (0.94, 1.69)	1.74 (1.23, 2.48)*	1.19 (0.91, 1.56)	1.25 (0.90, 1.72)
5	1.09 (0.77, 1.54)	2.13 (1.44, 3.16)*	1.17 (0.86, 1.59)	1.42 (0.99, 2.04)
6	1.07 (0.70, 1.62)	2.21 (1.37, 3.57)*	1.52 (1.06, 2.20)*	1.49 (0.97, 2.29)
Test for trend *P*	.23	<.0001	.03	.02

Note. OR = odds ratio; CI = confidence interval. Summary physical activity scores were calculated by assigning scores of 0, 1, and 2 to high, medium, and low levels of activity at the 3 phases of measurement. These scores were then summed to allow calculation of the summary score, which could range from 0 to 6. A score of 0 represents a high physical activity level across the 3 measurements, and a score of 6 represents a low activity level at all 3 measurements.
[a]Adjusted for age and gender.
[b]Adjusted for age, gender, education level, employment grade, self, rated health, blood pressure level, cholesterol level, smoking status, mental health status, and social network index score.
[c]Adjusted for age, gender, education level, employment grade, self, rated health, blood pressure level, cholesterol level, smoking status, mental health status, social network index score, and Mill Hill Vocabulary Scale score.
*$P < .05$.

Third, our findings were probably affected by higher rates of missing data among the older- and lower-grade participants. This pattern of missing data is relatively common in longitudinal studies. Because both older- and lower-grade categories were related to low levels of physical activity and poor cognitive performance, it is likely that the effects reported here have been underestimated. Finally, use of the Mill Hill Vocabulary Scale as a proxy for baseline cognitive functioning is problematic in that it probably led to overadjustment and incomplete resolution of the issue of reverse causation.

In conclusion, our results indicate that physical activity is an important factor in cognitive functioning in middle age and that its effects appear earlier than previously reported. We showed that fluid intelligence is particularly at risk from lack of activity. Physical activity has long been linked to survival[50–52] and well-being among the elderly,[53] and there is evidence suggesting that the effects of physical activity on cognitive functioning are stronger in this age group than in others.[7,8,11,12,15] Further research is required to examine whether fluid intelligence remains at risk as individuals age and whether other aspects of cognitive ability, such as verbal fluency, also become increasingly associated with levels of physical activity. ■

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This article was accepted December 21, 2004.

Contributors

A. Singh-Manoux originated the study, conducted the analyses, and wrote the article. M. Hillsdon categorized the physical activity variables and provided expertise on the interpretation of these categories. E. Brunner and M. Marmot reviewed drafts of the article.

Acknowledgments

Archana Singh-Manoux is supported by a Chaire d'excellence award from the French Ministry of Research. The Whitehall II study has been supported by grants from the British Medical Research Council (MRC); the British Heart Foundation; the British Health and Safety Executive; the British Department of Health; the National Heart, Lung, and Blood Institute (grant HL36310); the National Institute on Aging (grant AG13196); the Agency for Health Care Policy and Research (grant HS06516); and the John D. and Catherine T. MacArthur Foundation Research Networks on Successful Midlife Development and Socioeconomic Status and Health. Michael Marmot is supported by an MRC research professorship.

We thank all of the participating civil service departments and their welfare, personnel, and establishment officers; the British Occupational Health and Safety Agency; the British Council of Civil Service Unions; all participating civil servants in the Whitehall II study; and all members of the Whitehall II study team.

Human Participant Protection

This study was approved by the ethics committee of University College London. Written informed consent was obtained from each participant.

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