Original Contribution

Physical Activity Levels and Cognition in Women With Type 2 Diabetes

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Persons with type 2 diabetes have a high risk of late-life cognitive impairment, and physical activity might be a potential target for modifying this risk. Therefore, the authors evaluated the association between physical activity level and cognition in women with type 2 diabetes. Beginning in 1995–2000, cognitive function was assessed in 1,550 Nurses’ Health Study participants aged ≥70 years with type 2 diabetes. Follow-up assessments were completed twice thereafter, at 2-year intervals. Multivariate-adjusted linear regression models were used to obtain mean differences in baseline cognitive scores and cognitive decline across tertiles of long-term physical activity. Initial results from age- and education-adjusted models indicated that greater physical activity levels were associated with better baseline cognition (for a global score averaging scores from 6 cognitive tests, \( P \)-trend = 0.02). However, results were substantially attenuated after adjustment for multiple potential confounders, largely because of physical disability indicators (global score: \( P \)-trend = 0.06); for example, the mean difference for the global score was 0.07 standard units (95% confidence interval: 0.01, 0.15) when comparing extreme tertiles. Results were similar for cognitive decline. These findings indicate little overall association between physical activity and cognition after adjustment for disability factors in older women with type 2 diabetes.

cognition; cohort studies; diabetes mellitus, type 2; exercise; women

Abbreviations: CI, confidence interval; MET, metabolic equivalent; SD, standard deviation; TICS, Telephone Interview for Cognitive Status.

The prevalence of type 2 diabetes is escalating worldwide, and type 2 diabetes currently affects 20 million persons in the United States alone (www.diabetes.org/about-diabetes.jsp). Although cardiovascular disease, kidney disease, and neuropathy are known sequelae, cognitive impairment is increasingly recognized as a further complication at older ages (1, 2). Therefore, identifying strategies to prevent or delay diabetes-related cognitive impairment is a growing public health concern.

Accumulating evidence from animal (3–6) and human (7–19) studies, including several small clinical trials (20, 21), suggests that higher physical activity levels are related to better brain health and cognitive function among generally healthy, nondiabetic older adults. Physical activity also has beneficial effects on vascular health (e.g., lowering blood pressure and improving lipoprotein profiles) and glucose and insulin regulation (22–24), which are important factors in type 2 diabetes that have been associated with a reduced risk of cognitive decline (25). In addition, studies suggest that increased physical activity may positively affect microvascular reactivity (26) and diabetic neuropathy (27, 28) in persons with type 2 diabetes. Still, to our knowledge, increased physical activity has not been explored as a strategy for mitigating diabetes-related cognitive decline; thus, we conducted a prospective study of physical activity and cognitive function among 1,550 women with type 2 diabetes from the Nurses’ Health Study.

MATERIALS AND METHODS

The Nurses’ Health Study began in 1976, when 121,700 US registered nurses aged 30–55 years completed a mailed questionnaire on their health and lifestyle, including type 2 diabetes. Follow-up questionnaires were mailed every
2 years, and women who reported diabetes were sent a supplemental questionnaire for ascertainment of symptoms, diagnostic tests, and treatment. We confirmed type 2 diabetes using standard criteria (29) on the basis of self-reported information from participants; in a validation study, we found that medical records corroborated 98% of self-reported diabetes cases (30). Furthermore, in a random sample of our participants who did not report a diagnosis of diabetes, fewer than 2% had diagnostic evidence of diabetes from blood tests (31). Therefore, underreporting or underdiagnosis of diabetes is likely to have been minimal in this population of health professionals.

Starting in 1995–2000, Nurses’ Health Study participants aged 70 years or older were selected for a study of cognitive function. The first several years were largely devoted to pilot interviews; thus, the majority of women were assessed beginning in 1999–2000. Of the 22,715 women who were initially selected, an initial telephone interview was conducted in community-dwelling women who were free of stroke; 93% of eligible women participated and 7% refused. Follow-up exceeded 90% in the second and third cognitive interviews as well (mean time span over 3 interviews = 4.2 years). Women who participated in the initial cognitive interview had similar characteristics as those who did not participate; for example, mean age (74.6 years vs. 74.8 years) and obesity prevalence (18% vs. 16%) were nearly identical. The institutional review board of Brigham and Women’s Hospital (Boston, Massachusetts) approved this study.

Physical activity assessment

We collected detailed information on participants’ leisure-time physical activity beginning in 1986, and again in 1988, 1992, and biennially thereafter. Specifically, we asked women to estimate the average amount of time per week spent in the following activities during the past year: running (≤10 minutes/mile); jogging (>10 minutes/mile); walking or hiking outdoors; racquet sports; lap swimming; bicycling; aerobic dancing or use of exercise machines; other vigorous activities (e.g., lawn-mowing); and low-intensity exercise (e.g., yoga, stretching, toning). Each activity was assigned a metabolic equivalent (MET) value according to accepted standards, assuming that 1 MET is proportional to the amount of energy expended sitting quietly. MET values assigned were: 12 for running; 8 for stair-climbing; 7 for jogging, racquet sports, lap swimming, and bicycling; 6 for aerobic dancing, use of exercise machines, and other vigorous activities; and 4 for yoga, stretching, or toning. For each participant, we estimated total energy expenditure in MET-hours per week by multiplying each activity’s MET value by the time spent performing that activity and then summing the energy expenditure over all activities.

A validation study (32) was conducted among participants in Nurses’ Health Study II (a similar cohort of women) who responded to these questions on physical activity levels twice, 1 year apart. The reported activity levels were modestly correlated over 1 year ($r = 0.59$), given that true changes in physical activity may have occurred. Furthermore, physical activity levels for the previous year correlated well with those reported for the previous week ($r = 0.79$), as well as those logged in physical activity diaries during the year ($r = 0.62$).

Population for analysis

Among 2,129 participants with type 2 diabetes, we excluded women who were unable to walk ($n = 186$) and women who had been diagnosed with Parkinson’s or Alzheimer’s disease ($n = 26$) prior to the initial cognitive interview; these women were probably unable to engage in regular physical activity. In addition, we excluded women who did not report information on physical activity ($n = 44$) or on specific disability indicators (osteoarthritis, chronic bronchitis/emphysema, fatigue, balance problems, moderate-to-severe body pain, and limitations in walking 1 mile (1.6 km)) ($n = 323$) prior to their initial cognitive interview, because these factors were likely to be important confounders. For analyses of initial cognitive function, we analyzed the 1,550 remaining women with type 2 diabetes as of their first cognitive assessment; analyses of cognitive decline over 2 interviews included 1,352 women who additionally participated in the second cognitive assessment. In preliminary analyses of cognitive decline across 3 interviews conducted over a 4-year period, we included all 1,550 women from our analysis of initial cognitive function, because linear regression models with random effects are able to handle missing follow-up data.

Cognitive assessment

Initially, we administered the Telephone Interview for Cognitive Status (TICS), a telephone adaptation of the Mini-Mental State Examination that is highly correlated with the Mini-Mental State Examination ($r = 0.94$) (33, 34). After high participation rates were established, we gradually added 5 other tests: the East Boston Memory Test—immediate and delayed recalls (added in 1995) (35, 36); category fluency (added in 1996) (37, 38); delayed recall of the TICS 10-word list (added in 1998); and digit-span backwards (added in 1998) (39). Trained nurses administered the cognitive interview and were unaware of participants’ physical activity levels; for each test, more than 90% of baseline data were collected in 1999–2000. Between-interviewer reliability was high across 10 interviewers who scored the cognitive assessments ($r > 0.95$ for each cognitive test). In a validation study, our cognitive battery was administered to 61 highly educated women aged ≥70 years and correlated very well with detailed, in-person interviews ($r = 0.81$). Finally, participation rates were identical across all cognitive tests and remained stable over time.

Our analyses focused on measures of general cognition and verbal memory. For general cognition, we evaluated TICS scores as well as an overall global score that averaged together scores from all 6 of our cognitive tests. For verbal memory (a strong predictor of developing Alzheimer’s disease (40–42)), we averaged together scores from 4 tests: the immediate and delayed recalls of the East Boston Memory Test and the immediate and delayed recalls of the TICS 10-word list. Because point values on the tests are not
equivalent, we used z scores to create composite scores by calculating the difference between each participant’s score and the mean score of the population and then dividing by the standard deviation. Composite scores were constructed only for women who completed all contributing tests.

Statistical analysis

Since pathology underlying both diabetes and cognitive decline is likely to be initiated many years prior to clinical disease, long-term physical activity may be most important (43); thus, our primary predictor was physical activity averaged from all reports, beginning in 1986 (when 34% of participants already had type 2 diabetes) and continuing through the initial cognitive interview. An average of 5 reports was used to calculate the primary exposure over a median time period of 13.3 years (interquartile range, 12.3–13.8) between the first activity assessment and the initial cognitive interview.

We also examined alternative definitions for the exposure. First, to reduce possible confounding by physically disabling conditions, we averaged physical activity only through the first report of a potentially disabling condition, as the onset of such a condition would probably limit a woman’s subsequent physical activity. For these analyses, we defined disability or a disabling condition as a woman’s first report of osteoarthritis, emphysema/chronic bronchitis, fatigue, balance problems, moderate-to-severe body pain, or limitations in walking 1 mile. Second, we explored a greater contrast between extreme physical activity categories (≥26.0 MET-hours vs. <5.2 MET-hours), because women with health conditions such as diabetes might have reduced physical activity levels that would lead to a narrower exposure distribution for analysis. For this purpose, we used cutpoints from a previous study (20) that identified strong relations between physical activity and cognition among the larger, generally healthy cohort of Nurses’ Health Study participants. Third, we separately examined physical activity during the pre- and postdiabetes diagnosis periods, because women might have changed their activity levels upon receiving a diagnosis of diabetes. Finally, we conducted a specific analysis of average walking in relation to cognitive function.

For analysis of baseline cognitive scores, we used multivariate-adjusted linear regression models to obtain mean score differences across tertiles of physical activity. To evaluate cognitive decline over 2 years, we employed the same types of models to obtain mean differences in decline across tertiles of physical activity. For interpretation, a positive mean difference for either baseline scores or decline over 2 years indicates a more favorable cognitive outcome for women in higher tertiles of physical activity. We also conducted preliminary analyses using linear regression with random effects to obtain the slope of decline across 3 cognitive assessments over 4 years. Ninety-five percent confidence intervals were calculated, and linear tests for trend were performed using the median values of the tertiles; all P values were 2-sided.

We considered many potential confounders: age, education, use of antidepressant medication, alcohol intake, smoking, duration of diabetes, use of diabetes medication, body mass index (weight (kg)/height (m)²), and history of high blood pressure, high cholesterol, myocardial infarction, coronary artery bypass graft, transient ischemic attack, carotid surgery, or congestive heart failure. We also controlled for disabling factors in the multivariate models, represented by the following items: osteoarthritis, emphysema, chronic bronchitis, fatigue, balance problems, body pain, and limited walking ability. Although each of these items may not directly determine cognitive status in theory, we believe that multiple disability indicators in aggregate may capture more information than any single indicator, and thus we chose to consider all of these variables. Moreover, the disability variables might also represent underlying health status, in part, and thus be related to cognition. Indeed, we found that the disability indicators were generally related to worse cognitive function in our models. Covariates were derived from a participant’s status at the time of initial cognitive assessment. For models of cognitive decline over 2 years, we additionally adjusted for baseline cognitive scores and time between cognitive interviews; these factors are included implicitly in random-effects models. In models with physical activity curtailed at the time a woman first reported a potentially disabling condition, we did not further adjust for disability indicators.

RESULTS

We examined characteristics of our participants, assessed at the time of initial cognitive interview, across tertiles of long-term physical activity (Table 1). Substantial differences were apparent for self-reported physical disability: specifically, across increasing tertiles of physical activity, we found lower prevalences of women with limitations in walking 1 mile (80% in the lowest tertile of activity, 63% in the middle tertile, and 47% in the highest tertile), moderate-to-severe body pain (39%, 32%, and 27%, respectively), fatigue (45%, 34%, and 23%), and balance problems (24%, 19%, and 17%). Slight differences were observed for alcohol intake and body mass index across tertiles of physical activity, such that women with higher physical activity levels were less likely to abstain from alcohol and less likely to be obese. In addition, TICS, global, and verbal scores from the first cognitive assessment generally increased with increasing tertiles of physical activity.

After adjusting for age and education (Table 2), we found that higher levels of long-term physical activity were associated with better cognitive function across all 3 outcomes at the initial cognitive interview (e.g., for the global score, the mean difference comparing the highest and lowest tertiles of activity was 0.08 standard units (95% confidence interval (CI): 0.01, 0.16; P-trend = 0.02)). When we adjusted for disability indicators, results were generally still positive, yet noticeably attenuated, across all cognitive outcomes. For example, on the global score, the mean difference was 0.07 standard units (95% CI: −0.01, 0.15; P-trend = 0.05) when comparing the highest tertile of physical activity with the lowest. Similar results were also found for TICS and verbal memory after adjustment for disability factors.
although findings did not remain statistically significant for verbal memory. In fully adjusted models, we additionally controlled for use of antidepressant medication, alcohol intake, smoking, diabetes duration, diabetes medication use, body mass index, and existing vascular conditions; these adjustments did not substantially change any of our estimates.

Women with greater levels of long-term physical activity also had less decline in all 3 cognitive measures over approximately 2 years (Table 3) when age- and education-adjusted models were considered (e.g., for the global score, the difference in the slope of decline was 0.02 (95% CI: −0.01, 0.04). Similar results were observed using models adjusted for disability indicators and other health and lifestyle factors.

Since vigorous activity was fairly uncommon in these women, we also specifically considered the relation between walking and cognition (data not shown in tables). However, we did not find an association between walking and cognitive decline in models adjusted for multiple potential confounders (e.g., comparing extreme tertiles of the global score, mean difference = 0.01, 95% CI: −0.09, 0.06; P-trend = 0.8).

In preliminary analyses of cognitive decline across 3 cognitive assessments conducted over 4 years, we found no association between physical activity and decline in models adjusting for age and education (P-trend = 0.2; data not shown); comparing extreme tertiles of the global score, the difference in the slope of decline was 0.02 (95% CI: −0.01, 0.04). Further adjustment for a variety of potential confounders (not including disability factors) did not change these results.

Table 1. Characteristics of Women at Initial Cognitive Assessment (n = 1,550), by Tertile of Average Physical Activitya, Nurses’ Health Study, United States, 1986–2004b

<table>
<thead>
<tr>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 512)</td>
<td>(n = 520)</td>
<td>(n = 518)</td>
</tr>
<tr>
<td>Median no. of MET-hours (range)</td>
<td>3.38 (0.13–6.76)</td>
<td>10.70 (6.77–15.50)</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>74 (2.3)</td>
<td>74 (2.4)</td>
</tr>
<tr>
<td>Education, % with graduate degree</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>No alcohol intake, %</td>
<td>74</td>
<td>68</td>
</tr>
<tr>
<td>History of osteoarthritis, %</td>
<td>56</td>
<td>55</td>
</tr>
<tr>
<td>History of emphysema/chronic bronchitis, %</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>History of fatigue, %</td>
<td>45</td>
<td>34</td>
</tr>
<tr>
<td>History of balance problems, %</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>History of moderate-to-severe body pain, %</td>
<td>39</td>
<td>32</td>
</tr>
<tr>
<td>History of any limitations in walking 1 mile (1.6 km), %</td>
<td>80</td>
<td>63</td>
</tr>
<tr>
<td>Body mass indexd ≥30, %</td>
<td>43</td>
<td>33</td>
</tr>
<tr>
<td>History of high blood pressure, %</td>
<td>79</td>
<td>78</td>
</tr>
<tr>
<td>History of any limitations in walking 1 mile (1.6 km), %</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>TICS, mean (SD)</td>
<td>33.2 (2.6)</td>
<td>33.3 (2.8)</td>
</tr>
<tr>
<td>Global, mean (SD)</td>
<td>−0.03 (0.6)</td>
<td>−0.03 (0.6)</td>
</tr>
<tr>
<td>Verbal, mean (SD)</td>
<td>−0.03 (0.7)</td>
<td>−0.04 (0.7)</td>
</tr>
</tbody>
</table>

Abbreviations: MET, metabolic equivalent; SD, standard deviation; TICS, Telephone Interview for Cognitive Status.

a Physical activity was averaged from 1986 through the initial cognitive interview.
b Percentages are percentages of nonmissing values.
c 1 MET-hour is the amount of energy expended by sitting quietly for 1 hour.
d Weight (kg)/height (m)².
over 2 years compared with those in our main analyses. For age- and education-adjusted models, comparing women with activity levels of $\geq 26.0$ MET-hours and $<5.2$ MET-hours, we found a mean difference in decline in the global score of 0.14 standard units ($95\%$ CI: 0.05, 0.24; $P$-trend = 0.004) (data not shown). When we adjusted for disability indicators, these estimates were noticeably attenuated and no longer statistically significant (mean difference = 0.09 standard units, $95\%$ CI: $-0.01$, 0.19; $P$-trend = 0.07). Additional adjustments for various health and lifestyle factors did not change these results substantially.

We also examined physical activity separately for the periods before and after diabetes diagnosis, because women may have changed their levels of physical activity in response to diagnosis; however, we did not observe significant trends with cognition for either exposure period. The mean duration of time between diabetes diagnosis and initial cognitive interview was 11 years. For the prediabetes analysis, in models adjusted for disability indicators as well as health and lifestyle factors, we found a mean difference in global score decline of $-0.15$ standard units ($95\%$ CI: $-0.17$, 0.10; $P$-trend = 0.03) in fully adjusted models.

### DISCUSSION

In this cohort of women with type 2 diabetes, there was no apparent association between physical activity and cognitive function after adjustment for indicators of physical disability. Although we found a suggestion of an association when we compared women at the extremes of the activity distribution, the overall evidence indicated little relation between physical activity level and cognition in this group of women.

A large body of evidence indicates that higher physical activity levels are associated with healthy brain aging, including cognition, among healthy older adults (3–21). In a previous study (20), we observed that greater levels of physical activity, including walking, were strongly associated with better cognitive function in 18,000 Nurses’ Health

<table>
<thead>
<tr>
<th>Tertile 1 (MET-hours, 3.38 (0.13–6.76)$^{d}$)</th>
<th>Tertile 2 (MET-hours, 10.70 (8.77–15.50))</th>
<th>Tertile 3 (MET-hours, 24.39 (15.54–112.23))</th>
<th>$P$-Trend$^{e}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model $1^{d}$</td>
<td>$0$</td>
<td>0.14 $-0.19$, 0.46</td>
<td>0.45 $0.12$, 0.78</td>
</tr>
<tr>
<td>Model $2^{e}$</td>
<td>$0$</td>
<td>0.07 $-0.27$, 0.40</td>
<td>0.36 $0.01$, 0.70</td>
</tr>
<tr>
<td>Model $3^{f}$</td>
<td>$0$</td>
<td>0.07 $-0.27$, 0.41</td>
<td>0.37 $0.02$, 0.72</td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model $1$</td>
<td>$0$</td>
<td>0.01 $-0.06$, 0.08</td>
<td>0.08 $0.01$, 0.16</td>
</tr>
<tr>
<td>Model $2$</td>
<td>$0$</td>
<td>0.00 $-0.08$, 0.07</td>
<td>0.07 $-0.01$, 0.15</td>
</tr>
<tr>
<td>Model $3$</td>
<td>$0$</td>
<td>0.00 $-0.08$, 0.08</td>
<td>0.07 $-0.01$, 0.15</td>
</tr>
<tr>
<td><strong>Verbal</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Model $1$</td>
<td>$0$</td>
<td>0.01 $-0.08$, 0.09</td>
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</tr>
<tr>
<td>Model $2$</td>
<td>$0$</td>
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<td>$0$</td>
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</tbody>
</table>

**Abbreviations:** CI, confidence interval; MD, mean difference; MET, metabolic equivalent; TICS, Telephone Interview for Cognitive Status.

$^{d}$ Physical activity was averaged from 1986 through the initial cognitive interview.

$^{e}$ Median number of MET-hours (range) in tertile.

$^{f}$ Derived from linear regression models and calculated on the basis of tertile median values.

$^{g}$ Adjusted for age (continuous—years) and education (registered nurse degree, bachelor’s degree, or master’s/double degree).

$^{h}$ Adjusted for age, education, and disability indicators (osteoarthritis, emphysema/chronic bronchitis, fatigue index, balance problems, body pain, and limited walking ability—yes/no).

$^{i}$ Adjusted for age, education, disability indicators, use of antidepressant medication (yes/no), alcohol intake (none, 1–14 g/day, or $\geq 15$ g/day), smoking (never, past, current), duration of diabetes (<5, 5–9, 10–14, or $\geq 15$ years prior to initial cognitive interview), use of diabetes medication (none, oral medication only, insulin), body mass index (weight (kg)/height (m)$^{2}$: <25, 25–29, or $\geq 30$), and vascular factors (high blood pressure, high cholesterol, myocardial infarction, coronary artery bypass graft, transient ischemic attack, carotid surgery, and congestive heart failure—yes/no).
associations between physical activity and cognition; how-
suggested that greater exposure contrast yielded stronger
analysis of generally healthy participants (20). Our results
specifically, the identical cutpoints used in our previous
choosing more extreme cutpoints for physical activity—
women (20). We attempted to explore this concern by
earlier analysis of generally healthy Nurses’ Health Study
detect associations, in contrast with the distribution in our
distribution of physical activity may have been too narrow to
that this may be a less likely explanation.
walking and cognition in the women with diabetes suggests
of disability; however, the lack of association even between
group with diabetes, probably due to their high prevalence
possibility is the generally lower levels of activity in the
stages, and thus even longer-term physical activity may not
persist for the subset of women with type 2 diabetes. One
our current results suggest that this association may not
persist for the subset of women with type 2 diabetes. One
possible explanation is that women with diabetes are likely
to have more advanced brain pathology, even at prediabetes
stages, and thus even longer-term physical activity may not
have cognitive benefits at later pathologic stages. Another
possibility is the generally lower levels of activity in the
group with diabetes, probably due to their high prevalence
of disability; however, the lack of association even between
walking and cognition in the women with diabetes suggests
that this may be a less likely explanation.

Nonetheless, with the higher disability levels, the distri-
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suggested that greater exposure contrast yielded stronger
associations between physical activity and cognition; how-
ever, adjustment for physical disability status attenuated
these findings substantially, and residual confounding is
likely to be even more extensive in these extreme categories
of physical activity. Thus, a cautious interpretation of this
result is warranted for this sample of women with diabetes.

In general, several other limitations are possible. First, we
assume that some random misclassification of physical ac-
tivity and cognitive function occurred, which could have
caused an underestimation of the association we studied.
However, we used validated assessments for both exposure
and outcome, and data on these measures were used to
identify strong relations between physical activity and cog-
nition in the previous study of generally healthy nurse-
participants in this cohort (20). We also averaged physical
activity levels using a mean of 5 assessments and created
composite scores that incorporated multiple cognitive tests,
both of which tend to decrease random error in these mea-
surements (44). Second, women who were lost to follow-up
during the cognitive interviews probably had greater cog-
nitive decline, which may have caused underestimation of our
results; however, given the very high follow-up rates (>90%
at both the second and third interviews), this type of bias is

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Table 3. Mean Difference in Change in Cognitive Function Scores (n = 1,352), by Tertile of Average Physical Activitya, Nurses’ Health Study, United States, 1986–2004

<table>
<thead>
<tr>
<th>Tertile</th>
<th>(MET-hours, 3.38 (0.13–6.76)b) (MD = 0 (Referent))</th>
<th>Tertile 2 (MET-hours, 10.70 (6.77–15.50))</th>
<th>Tertile 3 (MET-hours, 24.39 (15.54–112.23))</th>
<th>P-Trendc</th>
</tr>
</thead>
<tbody>
<tr>
<td>TICS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1a</td>
<td>0</td>
<td>0.16</td>
<td>−0.18, 0.50</td>
<td>0.03</td>
</tr>
<tr>
<td>Model 2c</td>
<td>0</td>
<td>0.03</td>
<td>−0.32, 0.38</td>
<td>0.19</td>
</tr>
<tr>
<td>Model 3b</td>
<td>0</td>
<td>0.06</td>
<td>−0.29, 0.40</td>
<td>0.21</td>
</tr>
<tr>
<td>Global</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>0</td>
<td>0.04</td>
<td>−0.03, 0.11</td>
<td>0.09</td>
</tr>
<tr>
<td>Model 2</td>
<td>0</td>
<td>0.01</td>
<td>−0.06, 0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Model 3</td>
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<td>0.01</td>
<td>−0.06, 0.09</td>
<td>0.05</td>
</tr>
<tr>
<td>Verbal</td>
<td></td>
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<tr>
<td>Model 1</td>
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<td>−0.02, 0.16</td>
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<tr>
<td>Model 2</td>
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<td>0.03</td>
<td>−0.06, 0.13</td>
<td>0.06</td>
</tr>
<tr>
<td>Model 3</td>
<td>0</td>
<td>0.04</td>
<td>−0.05, 0.13</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MD, mean difference; MET, metabolic equivalent; TICS, Telephone Interview for Cognitive Status.

a Physical activity was averaged from 1986 through the initial cognitive interview.
b Median number of MET-hours (range) in tertile.
c Derived from linear regression models and calculated on the basis of tertile median values.
d Adjusted for age (continuous—years), education (registered nurse degree, bachelor’s degree, or graduate degree), initial cognitive score (continuous), and time between cognitive interviews (continuous—years).
e Adjusted for age, education, initial cognitive score, time between cognitive interviews, disability indicators (osteoarthritis, emphysema/chronic bronchitis, fatigue index, balance problems, body pain, and limited walking ability—yes/no).
f Adjusted for age, education, initial cognitive score, time between cognitive interviews, disability indicators, use of antidepressant medication (yes/no), alcohol intake (none, 1–14 g/day, or ≥15 g/day), smoking (never, past, current), duration of diabetes (<5, 5–9, 10–14, or ≥15 years prior to initial cognitive interview), use of diabetes medication (none, oral medication only, insulin), body mass index (weight (kg)/height (m)2; <25, 25–29, or ≥30), and vascular factors (high blood pressure, high cholesterol, myocardial infarction, coronary artery bypass graft, transient ischemic attack, carotid surgery, and congestive heart failure—yes/no).
unlikely to have substantially affected our results. Third, the prevalence of type 2 diabetes in the Nurses’ Health Study (~9%) is lower than in general population studies, and this cohort of health professionals is likely to have good health knowledge and access to health care, suggesting that women in our cohort may also have less severe diabetes. Although this might restrict the generalizability of our results, it also suggests that our results could be less confounded by diabetes severity, thus enhancing the internal validity of our estimates. Finally, we excluded the 15% of women who were missing information on disabling conditions, because this was an important variable in our analyses. The questionnaire items on disabling conditions were only included in the initial mailings of our follow-up questionnaires; thus, the poorer responders (i.e., those who did not reply to the initial mailings) were not included in our analyses. These poorer responders tend to be less healthy and to have greater cognitive decline, thus, we may have somewhat reduced the generalizability of our results by excluding this group. However, importantly, we also minimized the possibility of residual confounding, given the high likelihood that these women were physically disabled as well.

Overall, we found little evidence to suggest that physical activity was associated with cognition after adjustment for potential confounders in women with type 2 diabetes. Moreover, we found high levels of physical disability in this group, and therefore any activity recommendations for other groups, and therefore any activity recommendations for other groups. Nonetheless, further studies should explore modifiable lifestyle factors other than physical activity that may preserve cognitive function among persons with type 2 diabetes—a group at high risk of cognitive impairment.

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