

Type 2 Diabetes and Cognitive Function in Community-Dwelling Elderly Women

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OBJECTIVE — To examine the relationship of type 2 diabetes to cognitive function in community-dwelling women.

RESEARCH DESIGN AND METHODS — From 1995 to 1999, we administered four tests of cognitive function (Telephone Interview of Cognitive Status [TICS], immediate and delayed recall of the East Boston Memory Test, and verbal fluency) by telephone to 2,374 participants (70–78 years of age) of the Nurses' Health Study. Information on diabetes was collected biennially beginning in 1976; 82 women reported type 2 diabetes before their cognitive testing. We used linear and logistic regression models to calculate multivariate-adjusted mean differences in scores and relative risks of a low score (bottom 10% of the distribution) for diabetic women compared with nondiabetic women.

RESULTS — After multivariate adjustment, women with type 2 diabetes scored lower on all our cognitive tests than women without diabetes. On the general test of cognition (TICS), the mean difference in score between women with and without diabetes was -0.60 (95% CI -1.18 to -0.03 , $P = 0.04$) and the relative risk of a low TICS score was 1.98 (95% CI 1.06 to 3.69). On a global score combining results of the four tests, the mean for diabetic women was lower than that among women without diabetes (adjusted difference in score -0.73 , 95% CI -1.42 to -0.04 , $P = 0.04$), and the relative risk of a low global score was 2.16 (95% CI 1.10 to 4.21). Relative to women without diabetes, longer duration of diabetes was associated with lower scores. Few diabetic women were pharmacologically treated ($n = 31$), but those taking medication had scores similar to those of women without diabetes.

CONCLUSIONS — In these women, diabetes was related to lower scores on several aspects of cognitive function. Longer duration of diabetes may be associated with poorer scores, but hypoglycemic therapy may ameliorate scores.

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D iabetes is common among the elderly individuals, with a wide variety of sequelae. Recently, several large-scale epidemiological studies of the relationship between type 2 diabetes and cognitive function have suggested that

there may be a higher risk of poor cognition among those with diabetes (1,2) or hyperinsulinemia (2,3), but data are not consistent (4). Inability to adequately control for comorbid conditions and differences in populations studied have been

suggested as possible explanations for the discrepant results (5,6). The Nurses' Health Study is a homogeneous cohort of community-dwelling women who have provided extensive information on health and lifestyle over the past 25 years, providing the opportunity to address these issues among 2,374 participants aged 70–78 years who were administered cognitive tests.

RESEARCH DESIGN AND METHODS

The Nurses' Health Study began in 1976, when 121,701 female married registered nurses aged 30–55 years and living in 11 U.S. states completed a questionnaire about lifestyle and medical history, including numerous diseases and risk factors (7). Every 2 years, follow-up questionnaires are sent to the participants to update information; >92% of the original participants are still being followed.

In 1995, we chose the 2,769 eldest participants of the Nurses' Health Study (aged 70–74 years) to participate in a study of cognitive function. These women were community-dwelling, were free of diagnosed cardiovascular diseases, and had responded to the most recent questionnaire (sent in 1994). From 1995 to 1999, we telephoned each of the women for an interview of cognitive function; 2,402 women (88%) completed the telephone interview, 4% refused, and 8% could not be reached because telephone numbers were not accurate. These response rates were identical in women with and without diabetes. Additional characteristics of the study population are described in Table 1.

Cognitive tests

To maximize comparability of conditions across interviews, we asked the women if they were alert (and rescheduled if they were not) and instructed them to eliminate any distractions (i.e., turn off the television). The initial interview consisted of the Telephone Interview for Cognitive Status (TICS) (8), which is modeled on the Mini-Mental State Examination (MMSE). In 1997, after we established high acceptance by participants for telephone interviewing, we added immediate

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F.G. has received honoraria or has been paid in the past as a temporary consultant by pharmaceutical companies that produce diabetes medications (i.e., Novo Nordisk, Schering-Plough, Wyeth-Ayerst); however, neither the honoraria nor the temporary consulting fees were related to research on diabetes medications.

Abbreviations: EBMT, East Boston Memory Test; MMSE, Mini-Mental State Examination; TICS, Telephone Interview of Cognitive Status.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—Characteristics of Nurses' Health Study participants according to diabetes status

Characteristic	Type 2 diabetes		P
	No	Yes	
n	2,292	82	—
Age at interview (years)	74.2 (2.7)	74.3 (1.8)	>0.5
Mental health index*	81.2 (12.8)	77.9 (13.6)	<0.0005
Energy fatigue index*	64.7 (18.3)	55.9 (18.4)	<0.0005
Education after high school (years)	4.0 (1.5)	3.5 (0.9)	0.0005
Age at menopause (years)	48.4 (5.9)	46.5 (6.4)	<0.0005
Current use of postmenopausal hormone	34.2	25.7	0.1
Use of antidepressants	4.8	8.5	>0.1
Cigarette smoking	8.8	8.5	>0.5
BMI ≥ 30 kg/m ²	14.3	39.5	<0.0001
High blood pressure	45.3	64.6	<0.001
Use of aspirin use ≥ 4 times per week	24.8	27.6	>0.5
Use of vitamin E supplementation of ≥ 350 IU	16.3	12.2	0.1

Data are n, means (SD), or %. *Mental health and energy-fatigue indices are taken from Medical Outcomes Short Form-36 and are scored from 0 to 100 points.

and delayed verbal recalls (9) and verbal fluency (10).

Telephone Interview of Cognitive Status. Like the MMSE, the TICS (8) assesses areas such as orientation, registration, immediate verbal memory, and attention. Brandt et al. (8) reported a correlation of 0.94 between TICS and MMSE scores. Test-retest reliability is estimated to be high ($r = 0.97$) (8). In our population, TICS scores ranged from 17 to 41 (41 is a perfect score; the mean score was 33.7, SD = 2.6), and 9.8% of women scored below 31, which has been established as a cut point for cognitive impairment.

Because it has been suggested that diabetes may be particularly associated with poor verbal memory (6), we also separately examined one TICS subtest, immediate recall of a 10-word list. Scores on this item ranged from 0 to 10, with a mean of 4.6 (SD = 1.6) words recalled.

East Boston Memory Test. In the East Boston Memory Test (EBMT) (9), a short paragraph is read to the participant; scoring is based on ability to repeat 12 elements (one point is awarded for each). A test of delayed recall is given at the end of the interview (~15 min later). Scores for the immediate recall ranged from 2 to 12 (mean = 9.7, SD = 1.8). For the delayed recall, scores ranged from 0 to 12 (mean = 9.4, SD = 2.2).

Verbal fluency. To test verbal fluency (10), women are asked to name as many animals as they can during 1 min; this assesses verbal skills, set formation, and

sequencing. Scores ranged from 6 to 32 animals named; the mean score was 16.7 (SD = 4.5).

Global score. To estimate overall cognitive performance, a global cognitive score was calculated by combining the results from each of the primary tests administered: TICS, immediate and delayed recalls of the EBMT, and verbal fluency. The global score was only calculated for women to whom all four tests were administered ($n = 1,625$). We could not simply add the four scores together, because a point is not equivalent for each test; therefore, we created z-scores by taking the difference between the participant's score on each test and the mean score and then dividing that number by the standard deviation. We added the four z-scores to acquire a global score.

Two registered nurses trained to conduct these interviews completed all telephone assessments; a small study of interviewer reliability found correlations >0.95 between the interviewers' scoring for each test included in our battery. Substantial data support the validity of telephone cognitive tests containing items similar to those in our interview. Roccaforte et al. (11) compared results from telephone and in-person administrations of a telephone version of the MMSE; a correlation of 0.85 was found. Kawas et al. (12) gave the Blessed Information-Memory-Concentration test by telephone and in person; they found a correlation of 0.96.

Ascertainment of type 2 diabetes

All diabetes was reported before the cognitive interview and at 30 years of age or older; women with type 1 diabetes or gestational diabetes only were excluded from the study. We limited our definition of type 2 diabetes to women with confirmed or probable diagnoses, based on information collected on a supplementary questionnaire sent to participants at their report of diabetes; this questionnaire included items regarding symptoms, diagnostic tests, and treatment. Confirmed and probable diabetes were defined under guidelines established by the National Diabetes Data Group (13); all cases reported before 1997 were identified without regard to revised criteria endorsed by the American Diabetes Association in 1997. We chose registered nurses as participants because we believe their self-reported diagnostic information to be accurate; in support of this, we previously conducted a validation study (14) among a random sample of participants who reported diabetes and returned a supplementary questionnaire. The ascertainment of diabetes was compared with examination of medical records; self-reports were positively confirmed in 98%.

We identified 82 women who met criteria for type 2 diabetes before their cognitive interview. We estimated duration of diabetes by subtracting the year of diagnosis from the year of cognitive interview. Information on recent medication was taken from the Nurses' Health Study biennial questionnaire immediately before the cognitive assessment.

Population for analysis

Of 2,402 women who completed a cognitive assessment, 1 was excluded because she had type 1 diabetes, and 27 were excluded because they reported diabetes but did not return a supplementary questionnaire providing diagnostic details; thus, analyses are based on 2,374 individuals who completed the TICS ($n = 82$ diabetic subjects) or 1,625 individuals who also completed the East Boston Memory Tests and verbal fluency test ($n = 64$ diabetic subjects).

Statistical analysis

We analyzed the relationship of diabetes to scores on each cognitive test and to the global score combining results of the four primary tests (immediate and delayed recall of the EBMT, TICS, and verbal fluency).

cy). We used linear-regression models to quantify differences in mean scores between women with diabetes and women who never reported diabetes, after adjusting for age and other potential confounders (see below). Linear regression was conducted using Proc Reg in SAS software (SAS Institute, Cary, NC).

We also examined results of each test and the global score as categorical outcomes. For the TICS, we used <31 points to define low scorers (based on an established cutoff) (8); for the remaining tests, we defined a low score as the bottom 10th percentile and compared low scorers with women in the top 90th percentile. For the immediate and delayed recalls of the EBMT, the lower cut point was ≤7; for verbal fluency, the cut point was ≤11; and for the TICS 10-word immediate recall, the cut point was 3. We used logistic regression to estimate age- and multivariate-adjusted relative risks of low scores (calculated from odds ratios) and 95% CIs; logistic regression was conducted using Proc Logistic in SAS software.

In regression models, we considered the following potentially confounding variables: age at interview (continuous), age at menopause (continuous), years of education after high school (1–4 or >4), history of high blood pressure (yes or no), use of aspirin (yes or no), use of vitamin E supplements (yes or no), use of postmenopausal hormone therapy (current, past, or never), BMI (<22, 22–24.9, 25–29.9, 30+ kg/m²), cigarette smoking (current, past, or never), use of antidepressants (yes or no), and mental health index (0–79 or 80–100) and energy-fatigue index (0–65 or 66–100) from the Medical Outcomes Short Form-36. Information on these variables was taken from the first biennial questionnaire before each woman’s cognitive assessment, except for the use of antidepressants, which we began requesting in 1996, and data from the Medical Outcomes Short Form-36, which were included on the 1992 and 1996 questionnaires. In the final models, we did not include the following variables because adding them to the model had no appreciable influence on our estimates of effect for the relationship of diabetes to cognitive function: age at menopause, use of aspirin, cigarette smoking, and mental health index. We separately examined women with confirmed (82%) and probable (18%) diabetes; because results for

Table 2—Mean differences in scores on six measures of cognitive function according to diabetes status, Nurses’ Health Study

	Type 2 diabetes*	
	No	Yes
TICS (n = 2,374)		
Mean score (SD)	33.8 (2.6)	33.1 (3.2)
Age-adjusted difference in score	0	−0.73
Multivariate-adjusted difference in score† (95% CI)	0	−0.60 (−1.18 to −0.03)
P		0.04
TICS 10-word list (n = 2,374)		
Mean score (SD)	4.6 (1.6)	4.3 (1.9)
Age-adjusted difference in score	0	−0.33
Multivariate-adjusted difference in score† (95% CI)	0	−0.28 (−0.64 to 0.08)
P		0.12
Test of verbal fluency (n = 1,625)		
Mean score (SD)	16.8 (4.5)	15.8 (4.3)
Age-adjusted difference in score	0	−1.00
Multivariate-adjusted difference in score† (95% CI)	0	−0.70 (−1.82 to 0.43)
P		0.22
East Boston Memory Test—immediate recall (n = 1,625)		
Mean score (SD)	9.7 (1.8)	9.4 (1.8)
Age-adjusted difference in score	0	−0.33
Multivariate-adjusted difference in score† (95% CI)	0	−0.30 (−0.75 to 0.15)
P		0.19
East Boston Memory Test—delayed recall (n = 1,625)		
Mean score (SD)	9.4 (2.2)	8.8 (2.4)
Age-adjusted difference in score	0	−0.39
Multivariate-adjusted difference in score† (95% CI)	0	−0.52 (−1.07 to 0.04)
P		0.07
Global score‡ (n = 1,625)		
Mean score (SD)	0.10 (2.7)	−0.81 (3.3)
Age-adjusted difference in score	0	−0.92
Multivariate-adjusted difference in score† (95% CI)	0	−0.73 (−1.42 to −0.04)
P		0.04

Data are means (SD) or adjusted means difference (95% CI). *All analyses combine confirmed and probable diabetes because results were similar for both; †Covariates include age at interview, education, vitality index of the Medical Outcomes Short Form-36, high blood pressure, BMI, use of vitamin E, and use of antidepressants, and use of postmenopausal hormones. ‡Global score combines TICS, test of verbal fluency, and East Boston Memory Test—immediate and delayed recalls.

both groups were virtually identical, we only present combined results.

RESULTS— The mean duration between diabetes diagnosis and our cognitive assessment was 12 years; 70% of the diabetes cases were diagnosed >5 years before cognitive testing. Recent use of medication (insulin or oral hypoglycemic agents) was reported by 38% of the women with diabetes (71% oral agents). The average age did not vary by diabetes status (Table 1), although women with type 2 diabetes in particular tended to be

obese and had high blood pressure substantially more often than those without diabetes.

In analyses of the cognitive tests as continuous data (Table 2), women with type 2 diabetes had lower mean scores than those without diabetes on all tests. Women with diabetes scored almost 1 point lower on the TICS than did those without diabetes (multivariate-adjusted linear regression estimate of the mean difference in score −0.60, 95% CI −1.18 to −0.03, P = 0.04). Although similar differences were observed on the verbal

fluency test and immediate and delayed recalls of the EBMT (multivariate-adjusted difference in mean score -0.70 , -0.30 , -0.52 , respectively), none achieved statistical significance, probably due to the smaller sample size to whom these additional tests were administered. On the global score combining results of the four tests, the overall poorer performance was significantly lower among women with type 2 diabetes than among those without diabetes (multivariate-adjusted linear regression estimate of the difference in score -0.73 , 95% CI -1.42 to -0.04 , $P = 0.04$).

Performance on our tests seemed worse among women diagnosed with diabetes >5 years before their cognitive assessment than among women with more recent diagnoses. On the TICS, the mean score of women with diabetes for ≤ 5 years was similar to those without diabetes (multivariate adjusted linear-regression estimate 0.21 , 95% CI -0.80 to 1.22 , $P = 0.7$), whereas those who had diabetes >5 years scored significantly lower than healthy women (estimate of the difference -0.96 , 95% CI -1.64 to -0.28 , $P = 0.006$). On the global score, women with a recent diabetes diagnosis performed similarly to healthy women (multivariate-adjusted linear regression estimate of the difference in score 0.17 , 95% CI -1.03 to 1.37 , $P = 0.5$), but performance was worse in those with longer-term diabetes than in healthy women (estimate of the difference -1.13 , 95% CI -1.95 to -0.31 , $P = 0.002$).

We separately examined women with type 2 diabetes who reported recent treatment ($n = 31$) and those who were not taking medication ($n = 51$). Our results suggested that women not taking medication performed worse than women who were treated, although we had little power to accurately distinguish these results. For example, on the TICS, there was little difference in mean scores for pharmacologically treated diabetic women and for women without diabetes (multivariate-adjusted linear regression estimate 0.29 , 95% CI -0.62 to 1.20 , $P = 0.5$), whereas for nonmedicated diabetic women compared with women without diabetes, this difference was -1.14 (-1.86 to -0.42 , $P = 0.002$). For the global score, the mean among women with type 2 diabetes who reported recent use of medication was similar to women without diabetes (multivariate-adjusted linear-regression estimate 0.64 , 95% CI -0.46 to 1.74 , $P = 0.2$), whereas diabetic women not taking

Table 3—Risk of a low score on six cognitive measures according to diabetes status, Nurses' Health Study

	Type 2 diabetes*	
	No	Yes
TICS		
Low Scorers (<31 points)	208	14
Age-adjusted relative risk	1.0	2.09
Multivariate relative risk† (95% CI)	1.0	1.98 (1.06–3.69)
TICS 10-word list		
Low scorers (<3 words)	549	30
Age-adjusted relative risk	1.0	1.87
Multivariate relative risk† (95% CI)	1.0	1.71 (1.07–2.73)
Test of verbal fluency		
Low scorers (<12 animals)	172	12
Age-adjusted relative risk	1.0	1.86
Multivariate relative risk† (95% CI)	1.0	1.61 (0.82–3.16)
East Boston Memory Test—immediate recall		
Low scorers (<8 points)	171	7
Age-adjusted relative risk	1.0	1.02
Multivariate relative risk† (95% CI)	1.0	0.96 (0.42–2.17)
East Boston Memory Test—delayed recall		
Low scorers (<8 points)	227	13
Age-adjusted relative risk	1.0	1.53
Multivariate relative risk† (95% CI)	1.0	1.51 (0.79–2.87)
Global score†		
Low scorers	150	13
Age-adjusted relative risk	1.0	2.44
Multivariate relative risk† (95% CI)	1.0	2.16 (1.10–4.21)

Data are n or relative risk (95% CI). *For the TICS, the total number of subjects tested was 2,374. For the remaining measures, the total number of subjects tested was 1,625. Low scorers are defined as the bottom 10% and are compared with those scoring in the top 90%, except for TICS, which has an established cutpoint. All analyses combine confirmed and probable diabetes because results were similar for both. †Covariates include age at interview, education, vitality index of the Medical Outcomes Short Form-36, high blood pressure, BMI, use of vitamin E, use of antidepressants, and use of postmenopausal hormones. ‡Global score combines results of TICS, test of verbal fluency, and East Boston Memory Test—immediate and delayed recalls.

medication scored lower than women without diabetes (estimate of the difference in score -1.54 , 95% CI -2.40 to -0.68 , $P = 0.004$).

In analyses of the cognitive tests as categorical outcomes comparing the lowest scorers to women who performed better (Table 3), results were consistent with the continuous data. After adjusting for confounders, we found greater risk of a low score among women with type 2 diabetes relative to healthy women on all tests we administered. For example, on the global score, women with diabetes had a twofold greater risk of a low score (relative risk 2.16, 95% CI 1.10–4.21) than women without diabetes; this rose to a threefold higher risk for women with diabetes >5 years (relative risk 3.18, 1.53–6.61). In addition, diabetic women who received treatment seemed to have a

risk of a low global score comparable with women without diabetes (relative risk 0.83, 0.19–3.71), but this risk was 3.04 (1.43–6.44) for nonmedicated diabetic women compared with women without diabetes.

We were concerned that hearing loss could be related to both diabetes and poor performance on the cognitive tests; this might be responsible for the lower cognitive scores we found among women with diabetes. However, all participants were asked about any difficulty with hearing at the start of their interview. We conducted an analysis excluding the 23% of women who reported any hearing problems; the relationships between type 2 diabetes and cognitive function were similar to those we observed in the entire cohort. For example, on the global score, the multivariate-adjusted mean difference in score

between women with type 2 diabetes and those without diabetes was -0.60 (95% CI -1.51 to 0.31), and women with diabetes were more than twice as likely to have a low global score than were women without diabetes (relative risk 2.13 , $0.91-4.96$).

CONCLUSIONS— We found consistent relationships between diabetes and several aspects of cognitive function among 2,374 women aged 70–78 years in the Nurses' Health Study. Women with type 2 diabetes performed worse than those without diabetes on tests measuring general cognitive function, immediate and delayed verbal recall, and verbal fluency. Overall, when we combined results of our four cognitive tests in a global score, women with diabetes were twice as likely to have a low score as those without diabetes. Longer duration of diabetes and recent lack of pharmacological treatment seemed to be associated with worse performance.

Several limitations should be considered. Information on diabetes diagnosis was self-reported, perhaps leading to misclassification. However, all participants are registered nurses with a demonstrated interest in medical research. We limited our definition of diabetes to confirmed and probable cases based on extensive information provided by participants on a supplementary questionnaire; a validation study comparing diabetes diagnosis from the supplementary questionnaire with medical records demonstrated the data to be highly accurate. However, undiagnosed diabetes may be present in some women, and diagnostic criteria for diabetes changed recently (15), such that some women who would not have received a diagnosis before 1997 would now be considered to have type 2 diabetes. Both of these problems would lead to underestimation of the true association between diabetes and cognitive function.

In addition, the prevalence of diabetes is somewhat low in this select group of women, probably due to 1) our conservative definition of diabetes (27 women who reported diabetes but did not provide adequate information for confirmation were excluded), 2) elimination of women with cardiovascular disease, many of whom have diabetes, and 3) the nature of our participants (registered nurses with good health practices and relatively low prevalence of risk factors for

diabetes). This would not likely affect the validity of our results but may limit generalizability; however, we have found in the past that many of the risk relationships for diabetes that we observed in the Nurses' Health Study (16,17) are quite similar to those reported by studies of more general populations (18,19).

Our cognitive assessment is relatively brief. We administered four tests to encourage high participation (we achieved 96% response among the women we reached by telephone). In a validation study we conducted among 61 nuns from the Rush Religious Order Study (20) with age and educational status similar to Nurses' Health Study participants, we compared the global score from our four telephone-administered tests with the global score from a set of 21 cognitive tests administered in person to the same women; the correlation was 0.81 . Furthermore, we have observed strong relationships between established predictors of cognitive function (age at interview and educational level) and the nurses' performance on each of our cognitive tests (21), confirming the validity of the individual tests.

Other large population-based studies have found associations between diabetes or hyperinsulinemia and cognitive function in nondemented elderly subjects. Recently, Gregg et al. (22) administered two tests of perceptual speed and one test of general cognitive function (modified MMSE) twice to 9,679 community-dwelling elderly women from the Study of Osteoporotic Fractures; on all three tests, greater decline was observed among diabetic women from the first interview to the second interview 3–6 years later. In the Framingham study, which included 1,811 men and women given a single cognitive assessment, Elias et al. (1) reported increased risk of a low score (bottom 25%) for those with diabetes on five of eight tests (immediate and delayed logical memory, digit span forward, word fluency, and similarities); relative risks ranged from 1.22 to 1.49 . Similarly, in the Zutphen Elderly Study (2) of 462 men, diabetic individuals scored significantly lower on the MMSE than men with normal glucose tolerance; among nondiabetic individuals, those with higher insulin levels made more errors than those with lower levels.

Some studies, however, have not found similar results. Significantly, in the

Rancho Bernardo cohort (4), there was no relationship between type 2 diabetes and cognitive function (measured by 10 tests, including several comparable to ours) among 634 men or 876 women. Considering our finding regarding the duration of diabetes, one explanation may be the predominance of recently diagnosed diabetes in that cohort: most of their female participants had diabetes for ≤ 3 years.

This suggestion that longer duration of diabetes seems to be related to worse cognitive performance is consistent with limited data from other studies. In the Study of Osteoporotic Fractures (22), trends were observed of increasing risk of cognitive decline with increasing duration of diabetes, and in the Framingham study (1), each 5-year increment between diabetes diagnosis and cognitive assessment was associated with lower scores on tests of logical memory, word fluency, and similarities.

Most women with type 2 diabetes in our study were not taking medication (many were probably using dietary treatment); therefore, it is difficult to conclude whether pharmacological treatment affected performance. Nonetheless, our data suggested that women who received treatment (largely oral agents) performed better on the cognitive measures than did diabetic women who reported no recent use of medication. It is possible that the reason for using or not using medication may be related to cognitive function; for example, women beginning to experience cognitive impairment may stop taking their medications. However, most women who were not taking medication were long-term nonusers; based on questionnaire data from 1988, 86% of diabetic women not taking medication immediately before their cognitive assessment were also not taking medication 7–10 years before. Furthermore, in the Zutphen Elderly Study (3), poor glycemic control in individuals with diabetes was associated with worse performance on the MMSE, and small treatment studies have found that administration of oral hypoglycemic agents to nondemented patients with type 2 diabetes resulted in improved performance on cognitive tasks (23). Interestingly, in the Study of Osteoporotic Fractures (22) and the Framingham study (1), insulin treatment was related to poorer cognitive performance, and in the Framingham study, diabetic patients treated with oral medications or diet per-

formed similarly to nondiabetic patients. Unfortunately, we did not have enough women using insulin to examine this group separately.

In conclusion, type 2 diabetes was related to poor performance on several aspects of cognitive function in our cohort of community-dwelling women, and use of pharmacological treatment seemed to attenuate these relationships. The absolute mean differences in test scores that we observed between the women with and without diabetes were modest; however, it is likely that even small cognitive effects in a generally healthy "young-old" population (such as ours) carry substantial public health implications over time (24). Based on calculations within the women in our study, we found that having diabetes was equivalent to aging 4 years in terms of scores on our general cognitive test (the TICS). Clearly, further investigation is warranted because both diabetes and poor cognitive function are common conditions among elderly individuals.

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References

- Elias K, Elias ME, D'Agostino RB, Cupples LA, Wilson PW, Silbershatz H, Wolf PA: NIDDM and blood pressure as risk factors for poor cognitive performance: the Framingham study. *Diabetes Care* 20:1388–1395, 1997
- Kalmijn S, Feskens EJM, Launer LJ, Stijnen T, Kromhout D: Glucose intolerance, hyperinsulinaemia and cognitive function in a general population of elderly men. *Diabetologia* 38:1096–1102, 1995
- Stolk RP, Breteler MMB, Ott A, Pots HAP, Lamberts SWJ, Grobbee DE, Hofman A: Insulin and cognitive function in an elderly population: the Rotterdam study. *Diabetes Care* 20:792–795, 1997
- Scott RD, Kritz-Silverstein D, Barrett-Connor E, Wiederholt XC: The association of non-insulin-dependent diabetes mellitus and cognitive function in an older cohort. *J Am Geriatr Soc* 46:1217–1222, 1998
- Stewart R, Liolitsa D: Type 2 diabetes mellitus, cognitive impairment and dementia. *Diabet Med* 16:93–112, 1999
- Strachan MWS, Deary IJ, Ewing FME, Frier BM: Is type II diabetes associated with an increased risk of cognitive dysfunction? *Diabetes Care* 20:438–445, 1997
- Colditz GA, Manson JE, Hankinson SE: The Nurses' Health Study: 20-year contribution to the understanding of health among women. *J Women's Health* 6:49–62, 1997
- Brandt J, Spencer M, Folstein M: The telephone interview for cognitive status. *Neuropsych Neuropsychol Behav Neurol* 1:111–117, 1988
- Albert M, Smith LA, Scherr PA, Taylor JO, Evans DA, Funkenstein HH: Use of brief cognitive tests to identify individuals in the community with clinically diagnosed Alzheimer's Disease. *Int J Neurosci* 57:167–178, 1991
- Morris JC, Edland S, Clark C, Galasko D, Koss E, Mohs R, van Belle G, Filtenbaum G, Heyman A: The Consortium to Establish a Registry for Alzheimer's Disease (CERAD): rates of cognitive change in the longitudinal assessment of probable Alzheimer's disease. *Neurology* 43:2457–2465, 1993
- Roccaforte WH, Burke WJ, Bayer BL, Wengel SP: Validation of a telephone version of the Mini-Mental State Examination. *J Am Geriatr Soc* 40:697–702, 1992
- Kawas C, Karagiozis H, Resau L, Corrada M, Brookmeyer R: Reliability of the Blessed Telephone Information-Memory-Concentration Test. *J Geriatr Psychiatry Neurol* 8:238–242, 1995
- National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
- Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE: Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 338:774–778, 1991
- Gavin JR, Alberti KGMM, Davidson MB, DeFronzo RA, Drash A, Gabbe SB, Genuth S, Harrison I, Kahn R, Keen H, Knowler WC, Lebowitz H, Maclaren NK, Palmer JP, Raskin P, Rizza RA, Stern MP: Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 22:S5–S19, 1999
- Colditz GA, Willett WC, Rotnitzky A, Manson JE: Weight gain as a risk factor for clinical diabetes mellitus in women. *Ann Intern Med* 122:481–486, 1995
- Hu FB, Manson JE, Liu S, Hunter D, Colditz GA, Michels KB, Speizer FE, Giovannucci E: Prospective study of adult onset diabetes mellitus and risk of colorectal cancer in women. *J Natl Cancer Inst* 91:542–547, 1999
- Holbrook TL, Barrett-Connor E, Wingard DL: The association of lifetime weight and weight control patterns with diabetes among men and women in an adult community. *Int J Obes* 13:723–729, 1989
- Will JC, Galusha DA, Vinicor F, Calle EE: Colorectal cancer: another complication of diabetes mellitus? *Am J Epidemiol* 147:816–825, 1998
- Mufson EJ, Chen E-Y, Cochran EJ, Beckett LA, Bennett DA, Kordower JH: Entorhinal cortex beta-amyloid load in individuals with mild cognitive impairment. *Exp Neurol* 158:469–490, 1999
- Grodstein F, Chen J, Pollen DA, Albert MS, Wilson RW, Folstein MF, Evans DA, Stampfer MJ: Postmenopausal hormone therapy and cognitive function in healthy older women. *J Am Geriatr Soc* 48:746–752, 2000
- Gregg EW, Yaffe K, Cauley JA, Rolka DB, Blackwell TL, Narayan KM, Cummings SR: Is diabetes associated with cognitive impairment and cognitive decline among older women? *Arch Intern Med* 160:174–180, 2000
- Gradman TJ, Laws A, Thompson LW, Reaven GM: Verbal learning and/or memory improves with glycemic control in older subjects with non-insulin-dependent diabetes mellitus. *J Am Geriatr Soc* 41:1305–1312, 1993
- Bennett DA: Diabetes and change in cognitive function (Editorial). *Arch Intern Med* 160:141–143, 2000