

A Biethnic Community Survey of Cognition in Participants With Type 2 Diabetes, Impaired Glucose Tolerance, and Normal Glucose Tolerance

The New Mexico Elder Health Survey

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OBJECTIVE — To determine whether elderly individuals with type 2 diabetes or impaired glucose tolerance are at increased risk for cognitive impairment compared with individuals with normal glucose tolerance.

RESEARCH DESIGN AND METHODS — Elderly Hispanic individuals ($n = 414$) and non-Hispanic white individuals ($n = 469$) aged ≥ 65 years, randomly selected from the Medicare rolls of Bernalillo County (Albuquerque), NM, were recruited for an interview/examination that included an evaluation of glucose tolerance. Information on nine tests of cognitive function and two measures of depression allowed comparisons between diabetic status and these functions. Comparisons also were made between glycosolated hemoglobin concentrations and these cognitive tests in the 188 participants with diabetes.

RESULTS — None of the mean scores on the tests of cognitive function was significantly lower in the participants with diabetes compared with those participants with normal glucose tolerance after adjustments for ethnicity, sex, age, level of education, and presence of depression, with or without elimination of those with dementia (Mini-Mental State Exam < 18). Interestingly, participants with impaired glucose tolerance tended to score higher than those with normal glucose tolerance. No significant associations were found between glycosolated hemoglobin concentrations and cognitive test scores in participants with diabetes.

CONCLUSIONS — We could not show any increased risk for cognitive impairment in participants with diabetes compared with those with normal glucose tolerance after adjustments for ethnicity, sex, age, education, and presence of depression, before or after elimination of dementia in this random sample from a biethnic population of predominantly community-dwelling elders.

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Abbreviations: GDS, Geriatric Depression Scale; GHb, glycosolated hemoglobin; GLM, generalized linear regression model; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; MMSE, Mini-Mental State Exam; NHW, non-Hispanic white.

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

Extensive literature has been published describing the effects of type 2 diabetes on cognitive ability and the interaction with depression. A review article analyzing 19 studies with appropriate control groups reported that in 13 of these studies, significantly lower scores on at least one aspect of cognitive function testing were observed in subjects with diabetes compared with subjects without diabetes (1). Widespread inconsistencies exist in the conclusions drawn from these reports. Reasons for these discrepancies include use of noncomparable patient populations, insufficient sample sizes, and failure to control or adjust for variables such as age, sex, ethnicity, educational and socioeconomic status, presence of depression, inclusion or exclusion of subjects with vascular or Alzheimer's type dementia, and use of different cognitive test batteries. Studies also have considered the impact of metabolic derangements (hyperglycemia, recurrent hypoglycemia, hyperinsulinemia, elevation of glycosolated hemoglobin [GHb], and dyslipidemia) on cognitive function (2,3).

Although much of the variance in human mental ability is attributable to general intelligence, in clinical practice, it is useful to examine a variety of cognitive domains (4). These domains include attention and concentration, memory (both verbal and nonverbal), abstract thinking, constructional ability, and speed of information processing. Full assessment of cognitive function, therefore, requires structuring of a battery of psychometric tests to ensure that sufficient cognitive domains are examined to detect any deficits or decrements in ability.

The New Mexico Elder Health Survey is a study of health and health-related issues in nearly equal numbers of elderly (≥ 65 years of age) Hispanic and non-Hispanic white (NHW) men and women randomly selected from the Health Care

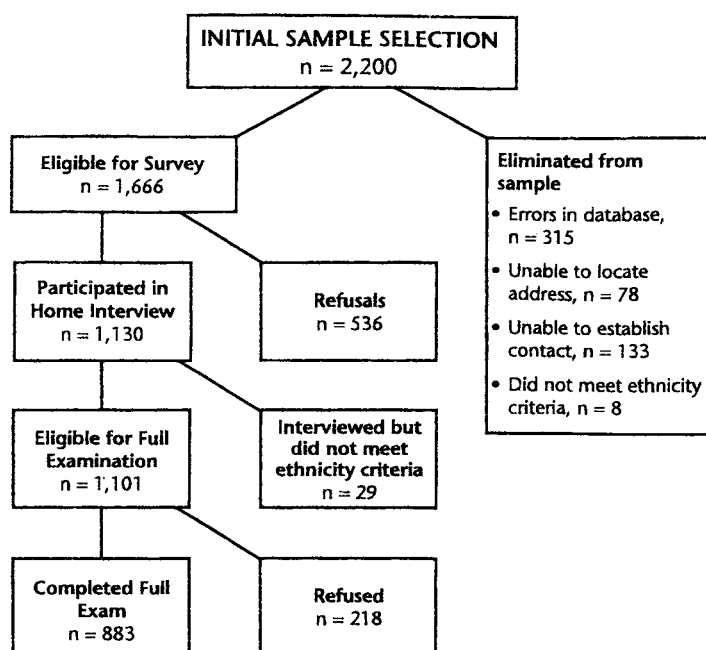


Figure 1—Participation rates after random selection of 2,200 prospective candidates using the GUESS (Generally Useful Ethnic Search System) program on 50,700 Medicare recipients in Bernalillo County, NM.

Financing Administration (Medicare) rolls of Bernalillo County (Albuquerque), NM (5,6). One of the objectives of the New Mexico Elder Health Survey was to compare the prevalence of type 2 diabetes and impaired glucose tolerance in the two ethnicities, along with the prevalence of atherosclerotic disease and aberrations in cardiovascular risk factors associated with diabetes. Our database included evaluations of cognitive and affective (depression) functions, which allowed comparisons between diabetic status and these functions. Also, in the participants with diabetes, the relation between GHb concentration and cognitive function has been studied.

RESEARCH DESIGN AND METHODS

Study design/subjects

A total of 2,200 prospective participants (equal numbers of Hispanic and NHW men and women) were randomly selected from 50,700 Health Care Financing Administration registrants (Medicare recipients), ≥ 65 years of age, residing in Bernalillo County (Albuquerque), NM, using the GUESS (Generally Useful Ethnic Search System), which separates individuals primarily by surname (Fig. 1).

After eliminating individuals who had died, moved from the county, or could not be located, and individuals who were ineligible because they clearly did not meet criteria to qualify as Hispanic or NHW, 1,666 eligible participants were contacted. A total of 1,130 individuals (67.8%) participated in paid home interviews. Thereafter, it was determined that an additional 29 interviewees were not qualified for the survey because they either did not meet ethnicity standards (self-identification and three of four grandparents Hispanic or NHW) or had died or moved after the home interview and before an examination could be completed. Of the 1,101 individuals interviewed at home and determined to be eligible, 883 individuals (80.2%) participated in a paid 4-h interview/examination by a nurse practitioner, nurse, and nutritionist. All participants were offered transportation to the University of New Mexico Senior Health Center (clinic), where 88.9% of the interviews/examinations were performed. Individuals who were unwilling or unable to travel were interviewed and examined at home (9.7%) or in a nursing home (1.4%). A total of 96% of the interviews were performed directly with the participant, and 4% of the interviews were conducted with the aid of a

spouse, relative, or caregiver. There were no other exclusionary criteria as long as informed consent could be obtained from the participant or legal guardian. All participants gave written informed consent, and the research was approved by the Human Research Review Committee of the University of New Mexico Health Sciences Center. Further details on the design and survey instruments used in this study and demographic characteristics of the recruited participants are published elsewhere (5,6).

Diabetes evaluation

Blood samples were collected between 8:00 and 8:30 A.M. after an overnight fast and assayed for serum glucose and GHb as part of a larger battery of tests. Unless the participant was on insulin and/or oral hypoglycemic agent or had a fasting glucose level >8.3 mmol/l (150 mg/dl) (Hemo Cue B-glucose; Hemo Cue, Mission Viejo, CA), the individual was asked to ingest 75 g of glucola during a 10-min period, and a blood sample was obtained 2 h later for serum glucose determination. Glucose was determined by a hexokinase enzymatic assay using a Roche-Cobas Bio instrument (Roche Analytical Instrument, Nutley, NJ) and reagents from Beckman Instruments (Carlsbad, CA). GHb was determined by a radioimmunoassay from Endocrine Science Products (Calabasas Hill, CA).

Participants were placed in one of four categories based on World Health Organization recommendations recently modified by the American Diabetes Association's Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (7). Participants were considered to have diabetes if they were taking insulin (serum C-peptide determinations were used to document type 2 diabetes) and/or oral hypoglycemic agents. They also were considered to have diabetes if their fasting serum glucose level was ≥ 7.0 mmol/l (126 mg/dl) or their 2-h postglucola glucose level was ≥ 11.1 mmol/l (200 mg/dl). Participants were considered to have impaired glucose tolerance (IGT) if their fasting serum glucose level was ≥ 6.1 mmol/l (110 mg/dl) but <7.0 mmol/l or their 2-h glucose level was ≥ 7.8 mmol/l (140 mg/dl) but <11.1 mmol/l. Participants were considered to have normal glucose tolerance (NGT) if their fasting serum glucose level was

Table 1—Distribution of participants by glucose tolerance status with mean \pm SEM age and level of education, total GDS score adjusted for age, ethnicity, and sex, and the results of the nine tests of cognition adjusted for age, level of education, ethnicity, and sex

| | Diabetes | IGT | NGT |
|--------------------------------|------------------|------------------|-----------------|
| n | 188 | 175 | 476 |
| Age (years) | 73.4 \pm 0.4 | 74.6 \pm 0.5 | 73.8 \pm 0.3 |
| Education (years of schooling) | 10.9 \pm 0.3* | 11.7 \pm 0.3 | 12.3 \pm 0.2 |
| GDS (15) | 2.66 \pm 0.18* | 2.33 \pm 0.19 | 2.00 \pm 0.11 |
| MMSE (29) | 25.6 \pm 0.23 | 26.0 \pm 0.23 | 25.6 \pm 0.14 |
| Pentagon drawing (10) | 8.67 \pm 0.13 | 9.06 \pm 0.14† | 8.73 \pm 0.08 |
| Fuld—number retrieved (10) | 6.67 \pm 0.12 | 6.83 \pm 0.12 | 6.67 \pm 0.07 |
| Fuld—total recalled (10) | 7.27 \pm 0.13 | 7.46 \pm 0.13 | 7.37 \pm 0.08 |
| Fuld—number of names | 16.0 \pm 0.35 | 16.2 \pm 0.36 | 15.6 \pm 0.02 |
| Digits forward (8) | 5.66 \pm 0.13 | 5.93 \pm 0.14 | 5.95 \pm 0.08 |
| Clock face (8) | 5.95 \pm 0.11 | 6.17 \pm 0.11 | 6.07 \pm 0.07 |
| Color Trail 1 (25) | 20.9 \pm 0.33 | 21.6 \pm 0.34 | 21.0 \pm 0.21 |
| Color Trail 2 (25) | 12.6 \pm 0.32 | 13.6 \pm 0.33 | 13.0 \pm 0.20 |

Data are mean \pm SEM. Numbers in parentheses represent the maximum scores for each test. *Difference between diabetes and NGT significant at $P < 0.01$; †difference between IGT and NGT significant at $P < 0.05$.

<6.1 mmol/l and their 2-h glucose level was <7.8 mmol/l. The remaining participants were listed as indeterminate, generally because permission was not obtained for blood sampling or the participant had not fasted overnight.

Neuropsychological assessment

Cognitive test measures used (and the functions they were intended to estimate) were 1) the Mini-Mental State Exam (MMSE) (orientation, recall, attention, language, and visual graphic ability), 2) Wechsler Adult Intelligence Scale-Revised Digits Forward (attention and immediate memory), 3) Fuld Object Memory Evaluation (learning and secondary memory), 4) clock drawing (visuoconstruction), and 5) two Color Trail Making Tests (psychomotor speed and cognitive flexibility). How these tests were administered and scored in this population is described in more detail elsewhere (8).

Two indicators of depression were obtained. First, a self-report of a history of depression was available from the interview. Second, the 15-question short version of the Yesavage Geriatric Depression Scale (GDS) was administered (in either Spanish or English). Both the means of the number of questions answered to indicate depression and the percentage of participants with more than six answers indicating depression were available.

Statistical analyses

Descriptive statistics including means \pm SEM were generated. Participants for whom any component of the necessary database was missing were excluded from that analysis. Differences in mean test scores between participants with diabetes and those with NGT were examined using analysis of variance. For this testing, only significant differences of $P < 0.05$ are reported. Continuous variables were tested for normality in distribution. A logarithmic transformation was applied to skewed variables, e.g., GHb in diabetic participants. For continuous variables, e.g., scores on each of the nine cognitive function tests and total GDS scores, group comparisons between participants with diabetes or IGT versus those with NGT were conducted using a generalized linear regression model (GLM) adjusting first for age and education (years) for each sex/ethnicity group and then for ethnicity, sex, age, and education for all participants (Table 1). Added to subsequent models were "history of depression" and total GDS scores as indicators of the presence of depression. Finally, the models were rerun after eliminating participants with an MMSE score <18 to avoid very low cognitive scores from participants with probable dementia. GLM was also used to examine the associations between each of the cognitive tests and GHb concentrations as continuous variables adjusting for ethnicity, sex, age, level of education, and

evidence of depression (history of depression and total GDS scores). Power analyses were used to determine the smallest differences (deltas) in each cognitive test score between paired glucose tolerance groups that would be significant assuming the alpha level was fixed at 0.05 and power at 0.80. All analyses were made using SAS software (SAS Institute, Cary, NC) (9).

RESULTS— Diabetes occurred significantly more in Hispanic participants than in NHW individuals ($P < 0.001$) and more often in men than in women ($P < 0.05$). A further description of the survey participants, their diabetic status, and aberrations in other metabolic parameters, along with types of medications they were taking, has been published elsewhere (5).

A preliminary analysis of the significance of differences between participants with diabetes and those with NGT from each of the four ethnicity/sex groups using two-sided Student's *t* tests showed only two significant differences in unadjusted cognitive scores ($P < 0.05$). Hispanic men with diabetes scored higher on Color Trails 1 ($P = 0.04$), whereas NHW women with diabetes scored lower on the Digits Forward test ($P = 0.04$). Considering the number of comparisons made, this number of significant differences could be explained by chance alone.

Scores for the cognitive tests were consistently lower in Hispanics than in NHW individuals, which can be explained, at least in part, by lower levels of formal education and by language barriers. The lower mean level of education (years of schooling) in participants with diabetes compared with those with NGT is explained by the fact that the prevalence of diabetes was almost twice as great in Hispanics than in NHW individuals, emphasizing the need to take into account differences in ethnicity and educational levels in glucose tolerance groups. Age, sex, and the presence of depression were other covariates that were recognized as potentially affecting these comparisons. Next, we examined the level of significance of differences between participants with diabetes or IGT compared with those with NGT for each of the nine cognitive tests and the total GDS scores using GLM for each of the sex/ethnicity groups adjusting for age and education. Both Hispanic men and NHW women with diabetes had higher GDS scores than their

Table 2—Comparisons of the observed differences in the nine tests of cognitive function adjusted for age, level of education, ethnicity, and sex with the smallest differences (Deltas) in cognitive scores that would be detectable as significant assuming an alpha level fixed at 0.05 and power at 0.80, comparing first the participants with diabetes against those with NGT and then those with IGT and those with NGT

| | Diabetes versus NGT | | IGT versus NGT | |
|----------------------------|---------------------|-------------------------------|---------------------|-------------------------------|
| | Observed difference | Minimum detectable difference | Observed difference | Minimum detectable difference |
| MMSE (29) | 0 | 0.75 | 0.4 | 0.75 |
| Pentagon drawing (10) | −0.06 | 0.43 | 0.33 | 0.45 |
| Fuld—number retrieved (10) | 0 | 0.39 | 0.16 | 0.39 |
| Fuld—total recalled (10) | −0.10 | 0.43 | 0.09 | 0.43 |
| Fuld—number of names | 0.4 | 0.98 | 0.6 | 1.01 |
| Digits forward (8) | −0.29 | 0.43 | −0.02 | 0.45 |
| Clock face (8) | −0.12 | 0.37 | 0.10 | 0.37 |
| Color Trail 1 (25) | −0.1 | 1.10 | 0.6 | 1.12 |
| Color Trail 2 (25) | −0.4 | 1.06 | 0.6 | 1.08 |

Data are *n*. Numbers in parentheses represent the maximum score for that test.

counterparts with NGT ($P = 0.030$ and 0.022 , respectively). Comparisons of the cognitive tests in participants with diabetes and those with NGT showed only one significant difference with NHW women with diabetes scoring lower on the Digits Forward test ($P = 0.026$). Comparing participants with IGT and those with NGT, Hispanic women with IGT scored higher in drawing the pentagon ($P = 0.042$).

Table 1 summarizes the distribution of participants by glucose tolerance status with mean \pm SEM age and level of education; the total GDS score adjusted for age (years), ethnicity and sex; and the results of the nine tests of cognition adjusted for age (years), level of education (years of schooling), ethnicity, and sex. There was a significantly higher mean total GDS score in participants with diabetes compared with those with NGT ($P = 0.002$). The only significant difference in the cognitive tests was that participants with IGT scored higher in the pentagon-drawing test ($P = 0.042$) than those with NGT. No significant interactions between glucose tolerance status and ethnicity and/or sex were observed.

Recognizing that depression can negatively affect cognitive scores, if “history of depression” and total GDS scores are added to a GLM with the previous adjustments, no significant differences in cognitive test scores between participants with diabetes compared with those with NGT were observed. Participants with IGT,

however, had higher scores on Color Trails 2 ($P = 0.039$), MMSE ($P = 0.015$), and pentagon drawing ($P = 0.027$) than participants with NGT.

Because subjects with dementia could have very low cognitive test results, which would lower mean test scores disproportionately and bias the interpretations, GLM were developed not only with all participants included but also after dropping participants with an MMSE score <18 . This meant 12 of 188 participants with diabetes (6.4%), three of 175 participants with IGT (1.7%), and 16 of 476 participants with NGT (3.4%) were no longer included in the statistical models. This further narrowed the small differences in mean cognitive test scores observed between the participants with diabetes and IGT compared with participants with NGT (Table 1). With these models, again, no significant differences were noted between the participants with diabetes or IGT and those with NGT.

Power analyses were performed to determine the smallest differences (deltas) in cognitive scores between glucose tolerance groups that would be detectable as significant, assuming the alpha level was fixed at 0.05 and power was fixed at 0.80 (Table 2). First, the participants with diabetes were compared with participants with NGT, and second, participants with IGT were compared with participants with NGT. Because the observed differences in cognitive scores between the glucose tolerance groups were so small

compared with the minimum differences detectable as statistically significant (deltas) obtained on power analyses, this can be interpreted to mean that, even if we had recruited a much larger number of participants, the conclusions that no significant differences existed in cognitive function between the participants with diabetes and those with NGT would not have changed.

Estimates of the regression coefficients (betas), standard errors of the estimates, and P values were used to examine the associations between serum GHb on the inverse scale (only the 188 participants with diabetes) and each of the nine cognitive tests after adjusting for ethnicity, sex, age, and education as covariates. No significant association was observed between serum GHb concentration and any of the nine cognitive tests after adjustment.

CONCLUSIONS— Our community-based survey of a randomly selected elderly population showed no evidence of impaired cognitive function in participants with diabetes or IGT compared with participants with NGT after adjustments for ethnicity, sex, age, level of education, and presence of depression, either before or after elimination of participants with probable dementia (MMSE score <18). Surprisingly, the group of elderly participants with IGT scored higher on three cognitive function tests after all adjustments than the participants with NGT after further adjustments for the presence of depression. Both animals and humans have improved memory and attention after oral administration of glucose, and this effect is more pronounced in elderly individuals, presumably because the elevation in serum glucose is greater and more prolonged (10,11). Because cognitive testing was performed shortly after glucose ingestion, ~ 1 or 2 h later, depending on random assignment to each of the three examiners, it can be assumed that, as a group, the participants with IGT had higher serum glucose concentrations than those with NGT at the time of their cognitive assessments. This is the only plausible explanation we have for why participants with IGT might do better on cognitive testing than the participants with NGT. Because at least half of the participants with diabetes had been diagnosed with the disease before the survey and were under treatment (so they did

not receive an oral glucose load) we believed it was more appropriate to compare them with the participants with NGT rather than pool the participants with IGT and NGT as the comparison group.

A critical review published in 1997 reported that subjects with type 2 diabetes performed more poorly on at least one aspect of cognitive function testing compared with matched controls without diabetes in 13 of 19 studies (1). The most commonly affected cognitive ability was verbal memory; psychomotor ability and frontal lobe function were less consistently affected. The remaining six studies that reported no differences in cognitive function between subjects with type 2 diabetes and control subjects without diabetes failed to have adequate statistical power, generally because of the small sample size, to detect a medium-sized effect (1). The authors concluded that these findings were consistent with an association between type 2 diabetes and increased risk of cognitive dysfunction. At least four additional studies have been published since reporting an association between type 2 diabetes and impaired cognitive performance (12–15); however, only one study, involving community-dwelling older adults, failed to find any differences in cognitive function between elderly individuals with mild diabetes or IGT compared with those with NGT (16). The most recent study was the large Longitudinal Study of Osteoporotic Fractures, which reported lower baseline cognitive scores and an accelerated decline on repeat testing in women with diabetes compared with women without diabetes (15). The only prior longitudinal study of cognitive function in subjects with diabetes (comparing 52 subjects with diabetes with 610 control subjects without diabetes covaried for age and education) failed to show any accelerated loss of cognitive function in subjects with diabetes (17).

The review and an associated editorial (1,4), however, emphasized that because there were widespread differences in methodology and small sizes of the case-control studies, with only three reports containing >52 case and/or control subjects, one should cautiously interpret the results. Their greatest concerns were the differences in methodology for cognitive testing and the potential for subject selection bias in recruiting participants in case-control studies. We used a broad battery

of neuropsychological tests, as others have recommended (4), to ensure that sufficient cognitive domains were examined to detect any deficits or decrements. Except for the MMSE, the tests were not dependent on language skills. Our experiences with this testing are described in more detail elsewhere (8).

The random selection method used in our study should satisfy much of the concern about patient selection bias, and the number of subjects studied exceeds that reported in most previous publications. Even so, we cannot rule out selection bias, recognizing that in our cross-sectional random sample, there was probably a survival/response bias whereby individuals with both diabetes and lower cognitive scores were potentially at greater risk for death and nonresponse to the study. One of our concerns was whether or not to include individuals with severe cognitive impairment in our models. More participants with diabetes (6.4%) than participants with IGT (1.7%) or NGT (3.4%) showed evidence of severe cognitive impairment (MMSE score <18). It was not surprising to see more individuals with diabetes having more cognitive dysfunction consistent with dementia, because one would expect more atherosclerotic cerebrovascular disease in this cohort. Although others have confirmed that individuals with diabetes have more vascular dementia (18), there is no consensus regarding whether persons with diabetes are at increased risk for development of Alzheimer's-type dementia (18–20). Whether one is justified in omitting these individuals depends on the hypothesis to be tested. Both models failed to show significant differences in cognitive scores between participants with diabetes and those with NGT.

Another concern in a study such as ours, with negative findings, is whether there is sufficient power (sample size) to detect differences in cognitive function between the glucose tolerance groups that might be of clinical importance. Power analyses were performed on each of the cognitive tests, first comparing participants with diabetes against those with NGT and then those with IGT against those with NGT. The observed difference in the scores for each of the cognitive tests was so small compared with the delta computed from the power analysis that it seems reasonable to conclude that failure to detect a difference in cognitive function

between our participants with diabetes and those with NGT would not have been changed by increasing the sample size within reasonable limits.

Only 3 of the 24 studies reviewed for this report comparing subjects with diabetes to those without diabetes had sample sizes as large or larger than ours (13,15,16). Two of these studies (13,15) reported impaired cognitive function in their participants with diabetes compared with those without diabetes, and one (16) did not. In the Framingham study (13), however, only one of seven tests of cognition (logical memory, delayed) showed significantly more participants with a diagnosis of diabetes scoring in the lowest quartile of test scores compared with participants without diabetes (odds ratio 1.49, 95% CI 1.00–2.02, $P = 0.05$). The differences on the other six tests of cognitive function failed to reach levels of statistical significance. In the Study of Osteoporotic Fractures (15), the sample size consisted of 677 women with diabetes and 8,950 women without diabetes. For the MMSE, the mean \pm SEM baseline score for the participants with diabetes was 24.6 ± 0.06 compared with 24.7 ± 0.02 for the participants without diabetes. Because of the large sample size, this small mean difference was significant at the $P = 0.03$ level. As seen in Table 2, our power analysis indicates that we would have needed a much larger sample size to detect that small a difference in our study. It must be questioned whether such a small difference is of any clinical significance. Although one of the other two tests of cognitive function in this study examined a domain similar to ours, the scoring used was different. The Trails B test, comparable to our Color Trails 2, showed a mean baseline score (\pm SEM) of 4.79 ± 0.004 in participants with diabetes compared with 4.86 ± 0.017 in participants without diabetes ($P < 0.001$). The Digit Symbol test, another measure of psychomotor speed, showed a mean baseline score (\pm SEM) of 41.1 ± 0.45 in participants with diabetes compared with 43.6 ± 0.11 in participants without diabetes ($P < 0.001$). Even with these larger differences, the clinical significance must be questioned.

Four studies (2,3,21,22) have reported that poor glycemic control in subjects with diabetes, as evidenced by higher GHb concentrations, was inversely associated with at least one measure of

cognitive function. However, no such association was observed in other studies (23,24). We found no association between GHb concentrations and measures of cognitive function in the 188 subjects with diabetes after adjustments for differences in ethnicity, sex, age, level of education, and evidence of depression.

We believe the criticisms of previous studies because of small sample sizes, the potential for patient selection bias, and the failure of testing to cover a diversity of cognitive domains have largely been addressed in our study. We were unable to demonstrate any significant differences in cognitive function in our elderly participants with diabetes compared with participants with NGT, even though there seemed to be more evidence of depression in the participants with diabetes. Interestingly, the participants with IGT seemed to do better in some cognitive domains than those with NGT. Because cognitive impairment is associated with significant morbidity and mortality, the identification of modifiable risk factors for cognitive decline is a major public health priority, making this concern an important issue to study carefully to obtain a consensus.

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