

Type 2 Diabetes Linked to Poor Cognitive Function in Middle Age

Findings from the Whitehall II study expand on previous research that demonstrated poorer cognitive performance in older adults with type 2 diabetes.

REVIEWED BY MEENA KUMARI, PhD

Type 2 diabetes is associated with poor performance in some aspects of cognition in a middle-aged cohort from the UK's Whitehall II study.

According to a study reported in *Neurology*, the association between diabetes and cognitive function extends to middle-aged adults. Study authors Meena Kumari, PhD, and Michael Marmot, FRCP, from the International Centre for Health and Society, London, said that the findings are important for two reasons. First, diabetes itself is associated with cognitive decline. Second, as the incidence of diabetes in younger age groups increases, there are implications for the management of diabetes in these groups, they said.

ASSOCIATION IN YOUNGER ADULTS

While the association between type 2 diabetes and poorer cognitive function was demonstrated in a number of studies among older participants, the association in younger cohorts is not well examined, the investigators wrote. "With the Whitehall II study we were able to expand on the research associating diabetes and impaired glucose tolerance [IGT] with cognitive performance, by examining this relation in a younger sample, a mostly middle-aged cohort of men and women."

The Whitehall II study looked at cognition across various domains and assessed diabetes by oral glucose tolerance test (OGTT) on two separate occasions. Patients were recruited between 1985 and 1988 from 20 London-based civil service departments. Diabetes status was determined from OGTT performed in 1992 to 1993 and 1997 to 1999 (phases 3 and 5, respectively) and from self-reported diagnosis of diabetes in a baseline

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questionnaire in 1989 (phase 2), phase 3, 1995 (phase 4) and phase 5 of the study.

The researchers administered cognitive tests that were measured at phase 5 in 4,020 men and 1,627 women. These patients were free of stroke and had a mean age of 56 years. The cognitive tests involved five standard tasks, including a verbal memory test, the Alice Heim 4 inductive reasoning test, the Mill Hill verbal meaning test, and phonemic and semantic fluency tests (Table 1).

LACK OF STANDARD CRITERIA

"There is a lack of standard criteria to judge poor performance in standard cognitive tests and assign clinical significance," the investigators wrote. "We have adopted a previously used approach that identifies poor cognitive performance as that being in the worst sex-specific quintile."

At phase 5, a total of 208 men (5%) and 101 women (6%) had diabetes and 405 men (10%) and 192 women (12%) had IGT. The patients with diabetes had an increased risk of poor performance on the Alice Heim 4 test compared with those without diabetes (men: OR 2.45; 95% CI, 1.77-3.38; women: OR, 1.83; 95% CI 1.09-3.08).

The researchers said these effects were independent

TABLE 1. COGNITIVE BATTERY: FIVE STANDARD TESTS

- **Verbal Memory Test**

This test was a 20-word free recall test of short-term memory. Patients were presented with a list of 20 single- or double-syllable words at 2-second intervals and asked to recall them in writing within 2 minutes (maximum score 20; mean \pm standard error 6.86 \pm 2.45).

- **Alice Heim 4 (AH4)**

The AH4 is a test of inductive reasoning that consists of 65 verbal and mathematical reasoning items of increasing difficulty. It measures the ability to identify patterns and infer principles and rules. Participants were given 10 minutes to complete the items (maximum score = 65; 46.47 \pm 11.32).

- **The Mill Hill**

Assesses knowledge of verbal meaning. It is a test of verbal functioning and assesses the patient's vocabulary and ability to recognize and comprehend words. The participants were given 33 stimulus words, each containing a word in capital letters and six other words. The participants had 10 minutes to choose from the six words in each group the word that had the same meaning as the word in capital letters (maximum score 33; 24.87 \pm 4.64).

- **Phonemic and Semantic Fluency Tests**

These two tests require the participant to recall in writing as many words beginning with the letter "S" in 1 minute (mean, 16.85 \pm 4.53) and as many animal words in 1 minute as he or she can (mean, 16.39 \pm 4.23).

of age, social position, vascular problems and health-related behaviors (Table 2). IGT was not related to any measure of cognition.

"Our observations suggest that effects on cognitive performance become apparent in as little as 2.5 to 5 years following diagnosis [of type 2 diabetes]," Drs. Kumari and Marmot wrote. "The timing of the diagnosis was particularly accurate in the study due to repeated administration of the OGTT."

TABLE 2. ADDITIONAL COVARIATES IN PHASE 5

Physical activity. The physical activity questionnaire included 20 items on the amount of time spent on physical activities and was derived from the Minnesota leisure time activity questionnaire. Participants were asked about their activity in the last 4 weeks and a metabolic equivalent value was assigned using a compendium of activity energy costs to categorize the activities as vigorous or not.

Smoking. Current smoking was assessed by the question, "Do you smoke cigarettes now?"

Alcohol. Alcohol intake in the past week was assessed by the question, "Have you had an alcoholic drink in the last 7 days?"

Minor psychiatric disorder. This was measured by the 30-item general health questionnaire (GHQ) and "GHQ caseness" was defined as a score of ≥ 5 . Factor analysis of the GHQ allowed identification of a depression subscale which is divided into scores of 0 to 3 and 4+.

The investigators found that, although type 2 diabetes is associated with poorer cognition, there are no universal effects. Therefore no cross-sectional effects were apparent for memory, semantic or categorical fluency. However, the strongest effects were for inductive reasoning.

DIABETES, POOR COGNITIVE FUNCTION

Comorbidities and health behaviors were associated with diabetes and poor cognition. While vascular problems, hypertension, lack of vigorous activity and no alcohol consumption were associated with poor cognitive performance, they did not explain the increased risk of poor cognitive performance associated with diabetes, the investigators said.

"Our findings suggest that lipids and other metabolic markers play a role in the association between diabetes and cognitive performance," Drs. Kumari and Marmot wrote. "A number of mechanisms have been postulated to play a role in this relationship." Follow-up of the Whitehall II cohort – when the metabolic syndrome variables will be reassessed – will allow the investigators to study the effects of chronic exposure to the metabolic syndrome, they added. ■

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