

# Diabetes, Impaired Cognitive Function Linked

The few prospective studies that deal with this issue have had conflicting results.

REVIEWED BY KRISTIN YAFFE, MD

**D**iabetic and prediabetic women have impaired cognitive performance, and they have an increased risk of developing cognitive impairment.

“Interventions aimed at early diagnosis and treatment of abnormal glucose metabolism and their effects on prevention of cognitive impairment need to be undertaken,” reported researchers in *Neurology*.<sup>1</sup> Kristine Yaffe, MD, and associates from the University of California, San Francisco, set out to further investigate the link between diabetes and changes in cognitive function. They said prospective studies yielded conflicting results.

Researchers looked at data derived from the Multiple Outcomes of Raloxifene Evaluation trial, a 4-year, randomized clinical study of 7,027 premenopausal women with osteoporosis. The trial took place at 178 sites, and the women had a mean age of 66.3 years.

Diabetic women were identified by history, a fasting blood glucose of  $\geq 7$  mmol/L or use of hypoglycemic agents. A woman was said to have impaired fasting glucose (IFG) if her fasting glucose was  $< 7$  mmol/L but  $> 6$  mmol/L; all others were defined as having normal glucose.

A total of 3.8% (267) of the women had diabetes and 4.2% (297) had IFG.

Dr. Yaffe and colleagues identified the main outcome as the baseline score and the 4-year change on five standardized tests that measure cognitive ability and the risk of developing clinically significant impairment. Lower z scores indicated worse performance, they said, and clinically significant impairment was defined as dementia, mild cognitive impairment or very low cognitive scores.

At baseline, women with IFG had worse cognitive scores versus women with normal glucose but better scores compared to diabetic women. The age-adjusted z scores based on all five tests were as follows: normal glucose 0.40, 95% CI 0.30-0.49; IFG 0.14, 95% CI -0.36-0.64; diabetic patients -0.78, 95% CI -1.50-0.50;  $P=.001$ ).

## DECLINE IN COGNITIVE SCORES

Diabetic patients had a greater 4-year decline in cognitive scores. The age- and treatment-adjusted z scores were: normal glucose -0.05, 95% CI -0.16-0.05; IFG 0.11, 95% CI -0.53-0.75; diabetic patients -1.00, 95% CI -1.50-0.50;  $P=.001$  (Table 1).

When the researchers performed adjustments for other variables such as education, race and depression, the results remained similar. For women with diabetes or IFG, the risk of developing cognitive impairment was almost double. The specific age- and treatment-adjusted ORs were 1.64; 95% CI 1.03-2.61 for IFG and 1.79; 95% CI 1.14-2.81 for diabetic patients.

“Women – and most likely men – with diabetes and with prediabetes are at an elevated risk for developing cognitive impairment,” Dr. Yaffe said in an interview. “Physicians may want to consider screening their elderly diabetic patients for cognitive dysfunction.”

When asked what the implications from this study are for future research, Dr. Yaffe said it has yet to be determined the exact mechanisms that link glucose dysregulation with cognitive impairment. “Also, we need to deter-

**TABLE 1. COGNITIVE FUNCTION SCORE COMPARISON**

	NG	IFG	DIABETIC PATIENTS
	n=6,463	n=297	n=267
Baseline age-adjusted composite z score ( $P<.001$ )	0.40	0.14	-0.78
4-year decline ( $P=.001$ )	-0.05	0.11	-1.00
<i>NG = normal glucose</i> <i>IFG = impaired fasting glucose</i>			

## MOOD, COGNITIVE PERFORMANCE ALTERED BY ACUTE HYPERGLYCEMIA

**Patients were more tired and less energetic during acute hyperglycemia, with higher levels of tense arousal.**

"Acute hyperglycemia in people with type 2 diabetes significantly impaired speed of information processing, working memory and some aspects of attention," researchers reporting in *Diabetes Care* wrote. "It also had a profound detrimental effect on key mood states."

Andrew J. Sommerfield, MRCP and colleagues from the departments of diabetes and psychology at the Royal Infirmary of Edinburgh, UK, studied 12 men and 8 women who had type 2 diabetes to investigate their cognitive function and mood during acute hyperglycemia. Patients – who had diabetes for approximately 6 years – ranged in age from 53.1 to 72 years, and had a median body mass index of 29.8 kg/m<sup>2</sup>. Baseline HbA1c levels were 7.5%. No chronic medical conditions, including microvascular disease, were present in any of the patients.

Blood glucose levels were stabilized during the study, and concentrations were 4.5 ±0.2 mmol/L during euglycemia and 16.7±0.6 mmol/L during hyperglycemia. Information processing speed and working memory were most affected during acute hyperglycemia, researchers wrote. Results showed that acute hyperglycemia did not significantly impair reaction time, however.

Visual attention was also affected, researchers wrote. When compared to the amount of time it took for patients to complete a visual selective attention task during euglycemia, it took them longer to finish the same tasks during acute hyperglycemia. Auditory selective attention, immediate and delayed memory and memory performance were also affected, researchers wrote. Acute hyperglycemia did not affect sustained attention, and researchers noted that results suggested that patients could be accurate, but not speedy.

The moods of type 2 diabetes patients were also affected during bouts of acute hyperglycemia. Researchers wrote that arousal in the forms of alertness and happiness diminished during hyperglycemia. Patients were also more tired and less energetic during acute hyperglycemia. Levels of tense arousal, agitation and anxiety increased during the same period, researchers noted.

Researchers concluded that the adverse effects of acute hyperglycemia in type 2 diabetic patients may interfere with their ability to complete daily activities. ■

Sommerfield AJ, Deary IJ, Frier BM. Acute hyperglycemia alters mood state and impairs cognitive performance in people with type 2 diabetes. *Diabetes Care*. 2004;27:2335-2340.

mine if more aggressive control of diabetes would reduce risk of developing cognitive problems."

**DECLINING MENTAL FUNCTION**

In an accompanying report on *Neurology's Patients Page*,<sup>2</sup> Janet Jankowiak, MD, wrote, "It is well known that too much sugar causes tooth decay, but might it also cause brain decay?" Dr. Jankowiak, of the Jewish Memorial Hospital and Rehabilitation Center in Roxbury, Mass, wrote that people with diabetes may be at a greater risk for a decline in mental function – brain decay – or dementia. "Fortunately, improving eating habits and avoiding excessive weight gain may prevent many cases of diabetes."

In Dr. Yaffe and colleagues' study, 12.1% of the women with diabetes and 10.1% of those with IFG developed a significant decline in mental function versus 5.9% of the women with normal sugar regulation, Dr. Jankowiak said. "From these results, the authors conclude that abnormal regulation of blood sugar is linked to an increased risk of developing cognitive impairment and dementia in elderly women."

There may be several reasons for the association, she said.

One may be that the other typical complications of diabetes like kidney disease, stroke, hypertension, fat deposits in the blood and heart disease might lead to diminished mental capacity. Another possibility is that high blood sugar causes direct nerve cell damage. Nerve cell damage may also be caused indirectly in the brain from atherosclerosis; and a separate study recently showed that levels of an enzyme that helps break down sugar in the blood is reduced in patients with Alzheimer dementia.

"It is important that clinicians figure out who is at risk for neurological complications of diabetes and try to reduce the risk," Dr. Yaffe said. "This is particularly true as the population is aging so quickly." ■

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1 Yaffe K, Blackwell T, Kanaya AM, et al. Diabetes, impaired fasting glucose, and development of cognitive impairment in older women. *Neurology*. 2004;63:658-663.

2 Jankowiak J. Too much sugar may cause brain decay. *Neurology*. 2004;63:E9-E10.