

# Sugar High

Evidence linking blood sugar with cognitive problems is on the rise.

BY AMY PATUREL, MS, MPH

Visit your doctor, and no matter what your age, you'll step on the scale, get your blood pressure checked, and receive a lab slip to test your cholesterol levels. But a test for blood sugar? That's a toss-up.

Doctors are short on time, patients don't like being stuck with needles, and the prevailing opinion is that blood sugar (or glucose) isn't an issue until people reach their golden years. Trouble is, a growing body of research suggests that maintaining appropriate blood sugar levels throughout your life could play a key role in preserving your brain.

Research has shown a link between diabetes and dementia for decades. In fact, a November 2012 review in *Experimental Gerontology* reported that people with diabetes have double the risk of developing dementia. Now, scientists are discovering that even modestly elevated blood sugar levels may speed up cognitive decline.

"We know that people with diabetes (whose blood glucose is higher than 125 mg/dL) are at increased risk," says James A. Mortimer, PhD, professor in the department of epidemiology at the University of South Florida and Fellow of the American Academy of Neurology (FAAN). Even pre-diabetes (110 to 125 mg/dL) has shown up in some studies. But this is pre-pre-diabetes, in the 90 to 100 mg/dL range."

These sobering statistics could mean that more than 50 percent of people over age 65 have blood sugar levels that put them at risk for cognitive problems. Plus, with advances in diabetes treatment over the past two decades, people with type 2 diabetes are living longer than ever before. Americans could face a tidal wave of dementia in the coming years. According to some estimates, more than 40 million Americans will have dementia by 2040.

The good news: Blood sugar isn't so difficult to control. A number of lifestyle



strategies—and medications—can keep these all-important levels in check. The key, experts say, is to know your number and intervene before diabetes sets in.

## SUGAR SPIKE

Glucose is the body's main source of fuel. The pancreas produces insulin to convert glucose from food into energy. In people

with insulin resistance, cells do not respond adequately to insulin, prompting the pancreas to produce more of the hormone. Eventually, the pancreas fails to keep up. Without insulin to mop it up, sugar levels rise in the bloodstream, which can damage the kidneys and other organs—including, possibly, the brain, says Dr. Mortimer.

While the brain is responsible for only about two percent of body weight, it consumes about 25 percent of the body's glucose, underscoring the importance of sugar in maintaining normal brain function. Studies show that patients with type 2 diabetes have reductions in brain volume of 0.5 to 2 percent compared to those without the disease—a loss of brain matter equivalent to two to five years of normal aging.

A study published in the February 2013 issue of the medical journal *Diabetes Care*, for example, found that insulin resistance is associated with shrinkage of the hippocampus and amygdala, the same areas of the brain affected by Alzheimer's disease (AD) and other dementias. A second study published in 2012 in the AAN journal *Neurology* suggests that having

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—JAMES A. MORTIMER, PHD

## Are You At Risk of Diabetes?

Controlling risk factors for blood sugar issues may help you stave off diabetes, even if you have a genetic propensity. According to the American Diabetes Association, the following factors increase your risk of diabetes:

- ▶ Impaired glucose tolerance or fasting glucose
- ▶ Older than 45
- ▶ A family history of diabetes
- ▶ Being overweight
- ▶ Not exercising
- ▶ Having low HDL (good) cholesterol, high triglycerides and high blood pressure
- ▶ Smoking

high-normal or pre-diabetic blood sugar levels may have a similar effect.

A third study, published in the August 2013 issue of *The New England Journal of Medicine*, followed more than 2,000 people over the age of 65 for seven years. Among participants with diabetes, those with higher blood sugar (190 mg/dL) were 40 percent more likely to develop dementia than people with diabetes who were at the lower end of the glucose spectrum (160 mg/dL). Even participants who had a fasting blood sugar of 115 mg/dL (so-called pre-diabetes) were 18 percent more likely to be diagnosed with dementia than those with a fasting blood sugar of 100 mg/dL.

Despite these findings, researchers still aren't clear on the mechanism underlying the connection between insulin resistance and cognitive problems. Experts agree, however, that there seems to be a vascular link.

"While there's some suggestion that people who have diabetes have increased plaques and tangles in the brain, the hallmark signs of Alzheimer's disease, most studies show the increased dementia risk is a result of microvascular lesions in the brain," says Dr. Mortimer. Put too much

sugar in the bloodstream, and it begins to glom onto proteins and make them sticky, almost like putting cotton candy in your arteries. Over time, that excess sugar contributes to narrowing and stiffening of the arteries (atherosclerosis). Since the brain is dependent on the arteries to carry oxygen and nutrients, when there are microvascular injuries, the brain suffers.

Indeed, autopsy studies report associations between diabetes and vascular abnormalities. In a recent review

article, researchers showed that people with type 2 diabetes were 2.5 times more likely to develop vascular dementia and 1.5 times more likely to develop AD compared to people without the disease.

### SWING LOW

While people with diabetes and pre-diabetes need to keep blood sugar in check, letting glucose levels sink too low is also dangerous. "Among those with diabetes, both hyperglycemia (elevated blood sugar) and hypoglycemia (low blood sugar) can impact brain function and cognition, and impact dementia risk," says Rachel Whitmer, PhD, senior scientist of dementia epidemiology in the Kaiser Permanente Division of Research in Oakland, CA.

Even one episode of low blood sugar can reduce the brain's supply of sugar to such a degree that brain damage sets in. In a study of more than 16,000 people with type 2 diabetes published in the April 2009 issue of *The Journal of the American Medical Association*, Dr. Whitmer and colleagues found that people who were hospitalized for severe hypoglycemia were more than twice as likely to develop dementia than those

who didn't have bouts of hypoglycemia, even up to 15 years later. And the link appears to go both ways: in a separate study, researchers discovered that those with dementia also had twice the risk of hypoglycemia.

"Someone with diabetes who has even mild cognitive problems, such as small decrements in memory or attention, is at high risk of developing hypoglycemia because they could have difficulty managing their medications, which can lead to dangerously low levels of blood sugar," says Dr. Whitmer.

Hypoglycemia events impair nutrient delivery to the brain, inhibit the development of new neurons, and increase the amount of inflammatory proteins in the brain. In animal models, scientists have shown damage to the hippocampus following a single hypoglycemic episode.

"People with diabetes have mild and moderate low blood sugar episodes all the time, so these findings have big implications," explains Dr. Whitmer. Low blood sugar used to be an issue primarily for people with type 1 diabetes, but with the increased use of insulin secretagogues (medications that increase insulin production) in combination with other diabetes therapies, and the increased use of insulin in advanced type 2 diabetes, low blood sugar events are becoming increasingly common among people with type 2

### BLOOD SUGAR NUMBERS AT A GLANCE

**Normal fasting blood sugar:**  
▶ below 100 mg/dL

**Pre-diabetes:**  
▶ 100 mg/dL to 125 mg/dL

**Diabetes:**  
▶ over 125 mg/dL

diabetes as well.

“With some of the medications that have been introduced over the past decade, the population has had tighter glyce-mic control, but we don’t really know yet whether that’s better for the brain in old age,” says Dr. Whitmer. “The big question is what glycemic control should elderly people who have type 2 diabetes strive for. We know it shouldn’t be too high and it shouldn’t be too low. Beyond that, we don’t know what’s best for the brain.”

### SAFEGUARDING YOUR BRAIN

While none of these studies definitively prove that high or low blood sugar levels cause dementia, they offer more reasons to keep blood sugar levels on even keel. Unfortunately, insulin resistance and pre-diabetes have no symptoms, so it’s important to monitor blood sugar. The American Diabetes Association recom-mends people get screened for diabetes at three-year intervals beginning at age 45. If you are overweight, have a family history of the disease, or have other risk factors, your doctor may advise earlier and more frequent testing.

“There’s this notion that diabetes is something you worry about when you get there, but like all chronic diseases, diabe-tes has a very long latent period,” explains Dr. Mortimer. “You get increases in insulin 8 or 10 years before you ever see any kind of effect on blood sugar levels, so it kind of creeps up on you. If you don’t catch the creep, then you’re going to be in trouble.”

The best way to catch the creep? Diet, exercise, and stress relief (see sidebar). Limit foods that send blood sugar levels soaring (think soda, fruit punch and oth-er sugary foods and beverages), exercise, ideally for 30 to 45 minutes at least five days per week, and engage in stress-re-lieving activities like yoga, massage, and spending time with the people you love.

If you can’t control your blood sugar

## Keep Blood Sugar Levels Even: The Big Six

Research shows that how you take care of yourself during your younger years goes a long way toward staving off chronic disease. But it’s never too late to learn new rou-tines, ditch old habits, and take a sip from the fountain of youth. Try these six strate-gies to keep blood sugar levels on even keel:

- 1. Eat more produce.** An April 2009 study published in the journal *Circulation* found that each additional serving of fruits and vegetables enhanced vascular function among people with hypertension. The more fruits and veggies the subjects ate, the greater the response.
- 2. De-stress.** Chronic stress increases cortisol levels, which in turn create a cas-cade of deleterious effects including insulin resistance. To counteract the ill effects of inevitable day-to-day stress, practice meditation, take a warm bath, or go for a long walk.
- 3. Get moving.** Exercise is one of the most important things you can do to keep blood sugar stable. Even short bouts of brisk walking several times throughout the day can help.
- 4. Ditch the sugar.** Sugar raises insulin levels, which starts a cascade of events that lead to fat storage. High insulin levels also lock fat cells into place, making it dif-ficult to lose weight. And those fat cells don’t just sit on your hips—they’re active hormone factories releasing inflammatory proteins into the bloodstream. Avoid refined carbohydrates like syrups, sodas and sweets in favor of fruits, vegetables, and whole grains.
- 5. Get checked out.** Make sure a doctor stays on top of your body mass index, waist circumference, and lab tests such as fasting glucose and lipid panel. Assessing these levels can identify looming threats early, providing ample opportunity for corrective action. If you have a family history of heart disease, or are overweight or obese, your doctor may want to see you more frequently.
- 6. Don’t skimp on sleep.** If you limit the amount of time you spend in deep sleep, the brain interprets that as insufficient energy stores and increases your appetite ac-cordingly. A November 2006 study published in the *American Journal of Epidemiol-ogy* found that among 68,183 women, those who slept for five or fewer hours each night gained 2.5 pounds more than those sleeping seven hours a night. And losing weight is key to staving off obesity and diabetes.

levels with lifestyle strategies, taking medication is your next best bet, prefer-ably when fasting blood glucose is hov-ering around 100, says Dr. Mortimer. In fact, preliminary research suggests that at least one diabetes drug, metformin, could have brain-boosting benefits.

Metformin makes muscle tissue more receptive to insulin, the hormone needed to help sugar get into the body’s cells and tissues to provide fuel. It also reduces the amount of glucose produced in the liver. And animal studies suggest it may play a role in the development of new brain cells. “It’s hard to make a leap from that kind of science to what happens in hu-mans, but the results are impressive,” says Dr. Whitmer.

Dr. Whitmer’s own research showed

that when people started taking metfor-min, they had a 20 percent reduced risk of developing dementia during the five-year study period compared to those who initi-ated treatment with other medications for diabetes, including sulfonylureas, thiazoli-dinediones or insulin.

“We know that cholesterol and high blood pressure during middle age affects your risk of dementia. Now we’ve estab-lished blood sugar has a similar impact,” says Dr. Mortimer. “Ideally we should all be getting plenty of mental and physical exer-cise, eating a healthy diet with plenty of fruits and vegetables and limited red meat, and getting sufficient sleep.” Take those steps, and you’ll not only lower your risk of blood sugar issues, you’ll also protect your-self from other health pitfalls. 