Diabetes and cognitive decline

According to the American Diabetes Association, 27 percent of people aged 65 and older in the United States have diabetes and about half have prediabetes. Numerous studies have found that individuals with diabetes, especially type 2 diabetes, have a lower level of cognitive function and are at higher risk for dementia than individuals without diabetes. The studies discussed below provide additional evidence supporting the recommendation that a healthy lifestyle to reduce risk from heart disease and diabetes may also help prevent Alzheimer's disease.

In the October 2013 issue of the *Journal of Alzheimer's Disease*, researchers reported a strong correlation between Alzheimer's disease and high blood sugar levels. The study found that people with high blood sugar levels, such as those linked with type 2 diabetes, had a dramatic increase in beta-amyloid protein, a protein toxic to cells in the brain.

A study published in the July 2013 issue of *Alzheimer's & Dementia®: The Journal of the Alzheimer's Association* was the first to show that people in the early stages of type 2 diabetes have signs of brain dysfunction. Study participants showed high levels of insulin resistance in the brain and a reduced ability to use glucose to fuel normal brain function.

Research presented at the Alzheimer's Association International Conference® 2013 (AAIC®) showed that a diabetes drug may be associated with reduced risk of dementia. In a study of nearly 15,000 people with type 2 diabetes who were aged 55 and older, those who took metformin, an insulin sensitizer, had a significantly reduced risk of developing dementia compared with people who took other standard diabetes therapies. Further research is being conducted to evaluate metformin as a potential therapy for dementia and mild cognitive impairment.

In another study, researchers found that the amyloid precursor protein gene, known to be involved in some cases of Alzheimer's, affects the insulin pathway. Disruption of this pathway is a hallmark of diabetes. The finding could point to a therapeutic target for both diseases. The researchers reported their findings in the June 2012 issue of the journal *Genetics*.

A study published in *Diabetologia* in 2007 reported that the early effects of diabetes on the brain were related to levels of a blood protein called hemoglobin A1C (HbA_{1C}). The HbA_{1C} blood test provides a snapshot of how well blood sugars have been managed in the past two to three months. The researchers tested memory, attention and other cognitive skills of people with diabetes and compared the results to healthy subjects without diabetes. They found that even people who had diabetes for less than 10 years had deficits in memory function typically associated with a brain region called the hippocampus. Using brain imaging techniques, they found that people with diabetes had smaller hippocampal sizes than people without diabetes. Finally, they found that the decreases in hippocampal size were correlated to HbA_{1C} blood levels, suggesting that HbA_{1C} could be used to indicate the onset of memory loss and/or hippocampal function.

A study relating type 2 diabetes and cognitive function was published in the June 2013 edition of the journal *Diabetes Care*. The researchers followed 1,290 people for 12 years, collecting cognitive measures at baseline, 6 years later and 12 years later. Even when correcting for

factors such as age, gender and alcohol consumption, subjects who had diabetes at the start of the study performed worse on all cognitive measures and showed a decline in executive function four times larger than persons without diabetes. Additional analyses using data from people who were healthy at the start but later developed diabetes by the either the 6-year or 12-year follow-up, found that these individuals showed a decrease in information-processing speed. In sum, individuals with type 2 diabetes show accelerated cognitive decline, specifically in information-processing speed and executive function.

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