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## Insulin resistance linked to brain malformations seen in Alzheimer's

August 25, 2010

Japanese researchers combing through the preserved brain samples of 135 men and women who lived and died in the town of [Hisayama](#) have found that those who developed insulin resistance and other metabolic disturbances during their lives were more likely to show plaque deposits in the brain that are a hallmark of [Alzheimer's disease](#).

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The study, published Wednesday in the journal [Neurology](#), sheds light on how Alzheimer's may gain a foothold in the brain -- very likely years before a patient or her family sees any sign of cognitive lapse -- and rob it of memory. The study builds upon mounting evidence that people who develop Type 2 diabetes -- as well as those with diabetes risk factors such as obesity, insulin resistance and high blood pressure -- are at far higher risk for developing dementia later in life.

Of the 135 men and women, whose metabolic function was tracked for 10 to 15 years before their death, only 21 were diagnosed with Alzheimer's disease while living. But scientists found neuritic plaques, which they surmise play an early role in the disease's development, in the brains of 88 participants. Those subjects were more likely than their peers without neuritic plaques to have had Type 2 diabetes or to have shown signs of incipient diabetes while they were alive.

The researchers suggest that three of the signposts of Type 2 diabetes -- [hyperglycemia](#), [hyperinsulinemia](#) and [insulin resistance](#) -- may set in motion the earliest changes in the brain's makeup, helping to initiate the formation of [neuritic plaques](#) -- spiny outcroppings that deform healthy brain cells. The circulation of high levels of glucose and of insulin in the blood may not only damage neurons but also gum up the brain's ability to clear away [amyloid](#), a protein normally produced by the body. Left to languish, pieces of this protein can clump together and form tough plaques in the brain -- the beta-amyloid plaques that are another hallmark of Alzheimer's disease.

Insulin resistance, say the authors, may be the final step in this cascade of metabolic misfortunes, disrupting signaling within and between brain cells. At this point, the symptoms of dementia might begin to become evident. At each step of the way, having a genetic variation associated with higher rates of Alzheimer's disease increased the probability of developing the disease.

-- Melissa Healy / Los Angeles Times

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