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Deep brain stimulation may hold promise for mild Alzheimer's disease

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A study on a handful of people with suspected mild Alzheimer's disease (AD) suggests that a device that sends continuous electrical impulses to specific "memory" regions of the brain appears to increase neuronal activity. Results of the study using deep brain stimulation, a therapy already used in some patients with Parkinson's disease and depression, may offer hope for at least some with AD, an intractable disease with no cure.

"While our study was designed mainly to establish safety, involved only six people and needs to be replicated on a larger scale, we don't have another treatment for AD at present that shows such promising effects on brain function," said the study's first author, Gwenn Smith, Ph.D., a professor in the Department of Psychiatry and Behavioral Sciences at the Johns Hopkins University School of Medicine. The research, published in the Archives of Neurology, was conducted while Smith was on the faculty at the University of Toronto, and will be continuing at Toronto, Hopkins and other U.S. sites in the future. The study was led by Andres M. Lozano, chairman of the Department of Neurosurgery at the University of Toronto.

One month and one year after implanting a device that allows for continuous electrical impulses to the brain, Smith and her colleagues performed PET scans that detect changes in brain cells' metabolism of glucose, and found that patients with mild forms of AD showed sustained increases in glucose metabolism, an indicator of neuronal activity. The increases, the researchers say, were larger than those found

in patients who have taken the drugs currently marketed to fight AD progression. Other imaging studies have shown that a decrease in glucose metabolism over the course of a year is typical in AD. Alzheimer's disease cannot be precisely diagnosed by brain biopsies until after death.

The team observed roughly 15 percent to 20 percent increases in glucose metabolism after one year of continuous stimulation. The increases were observed, to a greater extent, in patients with better outcomes in cognition, memory and quality of life. In addition, the stimulation increased connectivity in brain circuits associated with memory.

Deep brain stimulation (DBS) requires surgical implantation of a brain pacemaker, which sends electrical impulses to specific parts of the brain. For the study, surgeons implanted a tiny electrode able to deliver a low-grade electrical pulse close to the fornix, a key nerve tract in brain memory circuits. The researchers — most with the University of Toronto — reported few side effects in the six subjects they tested. Just as importantly, says Smith, was seeing that DBS appeared to reverse the downturn in brain metabolism that typically comes with AD.

AD is a progressive and lethal dementia that mostly strikes the elderly. It affects memory, thinking and behavior. Estimates vary, but experts suggest that as many as 5.1 million Americans may have AD and that, as baby boomers age, prevalence will skyrocket. Smith says decades of research have yet to lead to clear understanding of its causes or to successful treatments that stop progression.

The trial of DBS came about, Smith reports, when Lozano used DBS of the fornix to treat an obese man. The procedure, designed to target the regions of the brain involved in appetite suppression, unexpectedly had significant increases in his memory. Inspired, the scientists persisted through rigorous ethical and scientific approvals before their AD phase I safety study could begin.

Smith, who also is director of the Division of Geriatric Psychiatry and Neuropsychiatry at Johns Hopkins Bayview Medical Center, is an authority on mapping the brain's glucose metabolism in aging and psychiatric disease. It was Smith's earlier analysis of AD patients' PET scans that revealed their distinct pattern of lowered brain metabolism. She determined that specific parts of the temporal and parietal cerebral cortex — memory network areas of the brain where AD's earliest pathology surfaces— became increasingly sluggish with time.

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