

Oxygen treatment hastens memory loss in Alzheimer's mice

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A 65-year-old woman goes into the hospital for routine hip surgery. Six months later, she develops memory loss and is later diagnosed with Alzheimer's Disease. Just a coincidence? Researchers at the University of South Florida and Vanderbilt University don't think so. They suspect that the culprit precipitating Alzheimer's disease in the elderly women may be a routine administration of high concentrations of oxygen for several hours during, or following, surgery - a hypothesis borne out in a recent animal model study.

Dr. Gary Arendash of the Florida Alzheimer's Disease Research Center at USF and Dr. L. Jackson Roberts II at Vanderbilt University used mice genetically altered to develop abnormal levels of the protein beta amyloid, which deposits in the brain as plaques and eventually leads to Alzheimer's-like [memory loss](#) as the mice age. They found that young adult Alzheimer's mice exposed to 100-percent oxygen during several 3-hour sessions demonstrated substantial memory loss not otherwise present at their age. Young adult Alzheimer's mice exposed to normal air had no measurable memory loss, and neither did normal mice without any [genetic predisposition](#) for Alzheimer's disease.

The authors suggest that people genetically predisposed to Alzheimer's disease or with excessive amounts of beta amyloid in their brains are at increased risk of developing the disease earlier if they receive high concentrations of oxygen, known as hyperoxia. Their study is published online this month in *NeuroReport*.

"Although oxygen treatment beneficially increases the oxygen content of blood during or after major surgery, it also has several negative effects that we believe may trigger Alzheimer's symptoms in those destined to develop the disease," said USF neuroscientist Arendash, the study's lead author. "Our study suggests that the combination of brain beta amyloid and exposure to high concentrations of oxygen provides a perfect storm for speeding up the onset of memory loss associated with Alzheimer's Disease."

While postoperative confusion and memory problems are common and usually transient in elderly patients following surgery, some patients develop permanent Alzheimer's-like cognitive impairment that remains unexplained. Recent studies have indicated that general anesthesia administered during surgery may increase a patient's risk of Alzheimer's disease, but the laboratory studies did not use animals or people predisposed to develop the disease.

"Postoperative memory loss can be a fairly common and devastatingly irreversible problem in the elderly after major surgical procedures," said Roberts, an MD who holds an endowed chair in Pharmacology at Vanderbilt University School of Medicine. "There has been much speculation as to the cause of this memory loss, but the bottom line is that no one really knows why it happens. If all it takes to prevent this is reducing the exposure of patients to unnecessarily high concentrations of oxygen in the operating room, this would be a major contribution to geriatric medicine."

The USF-Vanderbilt study looked at 11 young adult mice genetically modified to develop memory problems as they aged, mimicking Alzheimer's disease. After behavioral tests confirmed the mice had not yet developed memory impairment at age 3 months - about age 40 in human years - the researchers exposed half the Alzheimer's mice to 100-percent oxygen for three hours, three times over the next several

months. The protocol was intended to replicate initial and supplemental exposures of elderly patients in hospital operating rooms and recovery suites to high concentrations of oxygen. The other half of the mice were exposed to 21-percent oxygen, the concentration of oxygen in typical room air.

When researchers retested the mice after the final gas exposure, they found that Alzheimer's mice exposed to 100-percent oxygen performed much worse on tests measuring their memory and thinking skills than the Alzheimer's mice exposed to normal room air. In fact, the Alzheimer's mice exposed to room air demonstrated no memory loss. Moreover, exposure of young adult mice without beta amyloid protein deposited in their brains to 100-percent oxygen did not adversely affect their memories. This is consistent with studies in humans showing that exposure of young adults to high concentrations of oxygen has no harmful effects on memory.

The researchers also demonstrated that even a single 3-hour exposure to 100-percent oxygen caused memory deficits in the Alzheimer's mice. Furthermore, when they examined the brains of these mice, they found dramatic increases in levels of isofurans, products of oxygen-induced damage from toxic free radicals. The increase was not present in the brains of normal control mice exposed to the single hyperoxia treatment.

How might high concentrations of oxygen hasten memory impairment in those destined to develop [Alzheimer's disease](#)? The researchers suggest the striking increase of isofurans during surgery may be one triggering mechanism, particularly in cardiac bypass surgery where very high blood oxygen levels are routinely attained and permanent memory loss often occurs months after the surgery. Secondly, exposure to high concentrations of oxygen prompts abnormal swelling of brain cell terminals that transmit chemical messages from one brain cell to another and may further disrupt already frayed nerve cell connections in those at

risk for Alzheimer's. Third, high concentrations of oxygen combined with [beta amyloid](#) plaques constricts blood vessels and decreases blood flow to the brain more than either one alone.

The authors caution that the study in mice may or may not accurately reflect the effects of hyperoxia in human surgery patients.

"Nonetheless, our results call into question the wide use of unnecessarily high concentrations of oxygen during and/or following major surgery in the elderly," Roberts said. "These oxygen concentrations often far exceed that required to maintain normal hemoglobin saturation in elderly patients undergoing surgery."

Source: University of South Florida Health

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