MedicalXpress

Role of anesthetics in Alzheimer's disease: Molecular details revealed

January 25 2007

Inhaled anesthetics commonly used in surgery are more likely to cause the aggregation of Alzheimer's disease-related plaques in the brain than intravenous anesthetics say University of Pittsburgh School of Medicine researchers in a journal article published in the Jan. 23 issue of *Biochemistry*. This is the first report using state-of-the-art nuclear magnetic resonance (NMR) spectroscopic technique to explain the detailed molecular mechanism behind the aggregation of amyloid â (Aâ) peptide due to various anesthetics.

Aâ plaques are found in the brains of people with Alzheimer's disease. Many believe that the uncontrolled clumping of Aâ is the cause of Alzheimer's disease and that the similar aggregation of peptides and proteins play a role in the development of other neurodegenerative diseases such as Parkinson's disease.

"Many people know of or have heard of an elderly person who went into surgery where they received anesthesia and when they woke up they had noticeable memory loss or cognitive dysfunction," said Pravat K. Mandal, Ph.D., assistant professor of psychiatry, University of Pittsburgh School of Medicine and lead author of the study. Previous studies by the Pittsburgh researchers found that the inhaled anesthetics halothane and isoflurane and the intravenous anesthetic propofol encouraged the growth and clumping of Aâ in a test tube experiment.

"Our prior research had shown in molecular models that anesthetics may play a role by causing amyloid peptides to clump together—something

that is thought to signal the advancement of Alzheimer's disease. In this study, we set out to see why this was happening and to determine if any one form of anesthesia might be a safer option than another," said Dr. Mandal.

In this study the researchers used NMR spectroscopy to determine how the inhaled anesthetics halothane and isoflurane and the intravenous anesthetics propofol and thiopental interact with Aâ influencing the aggregation of Aâ in forms commonly found in the brains of people with Alzheimer's disease. The results were strikingly different between the inhaled and injected anesthetics. The inhaled halothane and isoflurane had the most potent interaction with Aâ peptides causing the highest levels of Aâ aggregation. The injected anesthetic propofol only interacted and caused aggregation at high concentrations—interaction was not evident at lower concentrations. The intravenous thiopental did not cause the clustering of Aâ peptides even at high concentrations. Additionally, the molecular details for the interaction of these anesthetics with Aâ peptide were revealed.

Dr. Mandal noted that if the same thing occurs in humans, anesthetics could lead to more amyloid plaques which may lead to earlier memory problems, warranting further studies of anesthetics with Aâ both in laboratory and clinical settings.

Source: University of Pittsburgh Medical Center