

# Anesthesia increases risk of developing Alzheimer's disease in patients with genetic predisposition

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The use of repetitive anesthesia with isoflurane (one of the most common anesthetics by inhalation) increases the risk of developing changes similar to those observed in AD brains in mice with mutations of the amyloid precursor protein. This is the main conclusion of Spanish researchers coordinated by Doctors Maria Angeles Mena and Justo Garcia de Yebenes, from Centro de Investigacion Biomedica en Red de Enfermedades Neurodegenerativas. The work has been published in the *Journal of Alzheimer's Disease*.

Dr. María Ángeles Mena, Researcher at Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED) and Director of the Neuropharmacology Laboratory at Hospital Ramón y Cajal (Madrid, Spain), coordinated the study performed by predoctoral student Juan Perucho and others.

The study "Anesthesia with isoflurane increases long lasting behavioral changes and amyloid pathology of [Alzheimer's disease](#) in mice" confirms that anesthesia is safe for normal mice but potentially harmful for mice with genetic risk factors for Alzheimer's disease (AD).

Over several months, investigations have focused on analyzing the effects of the anesthesia in normal mice and in mice with mutations that produce AD.

Madrid, March 16, 2010.- The use of repetitive anesthesia with isoflurane (one of the most common anesthetics by inhalation) increases the risk of developing changes similar to those observed in AD brains in mice with mutations of the [amyloid precursor protein](#) (APP). This is the main conclusion of Spanish researchers coordinated by Doctors Maria Ángeles Mena and Justo García de Yébenes, from CIBERNED (Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas). The work has been published in an authoritative publication in this area of pathology: *Journal of Alzheimer's Disease*. Other participants in the study are Juan Perucho, Isabel Rubio, María J. Casarejos, Ana Gómez, José A. Rodríguez-Navarro, Rosa M. Solano, from the Neurobiology and Neurology Departments at Hospital Ramón y Cajal in Madrid.

The findings suggest a possible mechanism of developing Alzheimer. Some epidemiological studies have shown an increased prevalence of AD in patients undergoing anesthesia and surgery. Doctor Justo García de Yébenes states that "before surgery requiring anesthesia, it may be ideal to know the genetic background of the patients so that the drugs used and the pattern of anesthesia may be personalized accordingly."

The linkage between the repetitive use of isoflurane anesthesia and the development of AD changes in mice with mutations indicates the advisability of testing for genetic risk factors for AD in patients prior to surgery. Until recently, the most important genetic risk factor for AD was the presence of the allele E4 of the apolipoprotein E, but recently other genetic polymorphisms of risks have been identified. Once these polymorphisms of risks are identified and their relative impact on the pathogenesis of AD are known, a simple, automatic test for risk of AD should be performed in patients, namely the elderly, undergoing surgery under general anesthesia and the anesthetic procedure should be modified accordingly. A personalized clinical model that would enable the reduction of the patient's potential risk for AD would reduce the risk

of anesthesia.

#### Study conclusions:

The study "Anesthesia with isoflurane increases long lasting behavioral changes and amyloid pathology of Alzheimer's disease in mice", confirms that anesthesia is safe for normal mice but risky for asymptomatic carriers of mutations which produce AD.

The research has been based on the application of anesthesia twice a week during three months in normal mice and in mice with mutations (7-10 months old) that produce AD (known as APP<sup>swe</sup>). The results show alterations produced in the brain of mice with mutations very similar to those observed in patients that have already developed Alzheimer's disease.

#### Study highlights:

- Application of repetitive anesthesia in genetically altered mice increased their death rate.
- Mutant mice showed less reactivity after anesthesia was over. Their time for recovery after anesthesia was also increased.
- Repetitive anesthesia produced persistent disorders affecting behavior of mutant mice.
- Neuronal death increased in [brain](#) areas critical for cognition.
- Increased inflammatory response and deposition of beta-amyloid peptides.

- Isoflurane [anesthesia](#) of mutant mice altered the levels of chaperones (proteins which regulate the processing of abnormal proteins)

AD usually is the main cause of dementia for people over 65

Currently, over 5 million people in the first world suffer from AD, a neurodegenerative pathology that lacks a specific diagnostic test. The prevalence of this disease is also increasing in developing countries. Currently, there is no therapy that stops or reverts the progression of AD, although there are several treatments that partially improve symptoms. Researchers predict that Spain will experience a 75% increase of AD patients in 25 years.

Memory loss, language problems, incapacity for decision making and discernment are some of the main traits of this disease.

**More information:** Full study published in volume 19:4 Journal of Alzheimer's Disease, 2010. [DOI:10.3233/JAD-2010-1318](https://doi.org/10.3233/JAD-2010-1318)

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