# **Abstract**

Categories: Neuroscience in Anesthesiology and Perioperative Medicine

Title: Sevoflurane May Not Induce Long-term Toxicity in Alzheimer's Disease Transgenic

Drosophila

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## **Introduction:**

Some evidences suggested that inhalational anesthetics could damage neurons and may be a potential link to Alzheimer's disease  $(AD)^{1-4}$ . However, there is no study for the effects of inhalational anesthetics on long-term outcome. The advantages of *Drosophila* model are as follow: 1. more than 77% of known human genes are recognizably matched in the genome of *Drosophila*; 2. short life cycle and easily in great quantities breed<sup>5-6</sup>. Therefore, we investigate the long-term effects of sevoflurane, the most commonly used inhalational anesthetic, on the overall survival in AD-transgenic *Drosophila*.

### **Methods:**

We used five- to six-day-old AD-transgenic male flies (*elav*/Y;H29.3/+) and control male flies (*elav*/Y) (n=6). All flies were anesthetized with 2.1% or 3% sevoflurane plus 100% oxygen for 4 and 16 times exposure (1 hour per time). Anesthetic and oxygen concentrations were measured continuously (Dräger Medical AG & Co., Germany). The flies were maintained at a density of 35 per vial under a 12-h light:12-h dark cycle until all AD transgenic male flies dead<sup>7</sup>. Differences between mean values were evaluated using student's t-test and the statistical significance was set at p < 0.05.

### **Results:**

The survival of AD-transgenic flies was significantly lower than control flies on day 50 and 60 (Fig. 1 and 2, p<0.001, respectively). Exposure of 2.1% sevoflurane for 16 times and 3% sevoflurane for 4 times did not further decrease the survival of control flies and AD files (Fig. 1 & Fig.2).

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## **Conclusions:**

We found that sevoflurane in clinically relevant concentrations might not affect the overall survival of control and AD-transgenic flies. This suggests that sevoflurane might not have long-term neurotoxic effects. Stratmann *et al.* demonstrated that no cognitive deficit 4 months after anesthetic treatment in aged rats and supposed the neurologic effect of anesthetics may be transient<sup>8</sup>. Other studies showed that inhalational anesthetics may have neuroprotective effects<sup>9-10</sup>. Therefore, general anesthesia with sevoflurane might be still effective and safe in clinical practices including the elderly and patients with AD. Future studies are necessary to determine whether inhalational anesthetics may induce neurotoxic or neuroprotective effects, which may eventually lead to safer anesthesia care for patients.

### **References:**

- 1. Anesthesiology 110:628-37 (2009)
- 2. Anesthesiology 112:567-75 (2010)
- 3. Arch Neurol 66:620-31 (2009)
- 4. Life Sci 77:2369-83 (2005)
- 5. Neurobiol Dis 40:29-39 (2010)
- 6. Exp Gerontol 46:335-9 (2011)
- 7. J Nutr Biochem 19:376-83 (2008)
- 8. Anesthesiology 112:305-15 (2010).
- 9. Mol Biol Rep 39:5049-57 (2012).
- 10. Eur J Pharmacol 675:40-6 (2012)

# Figure 1.

### 2.1% E16-male AD flies

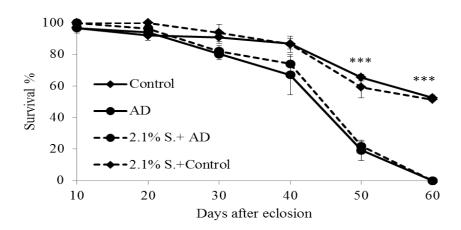


Figure 1. Anesthesia with 2.1% sevoflurane for 16 times (1 hour per time) did not affect the survival on control and AD-transgenic flies. "AD" refers to Alzheimer's disease; "S" indicated 2.1% sevoflurane; "E" indicated exposure. Error bars indicate SEM. Data were evaluated using student's t-test method. \*\*\*p<0.001.

Figure 2.

### 3% E4-male AD flies

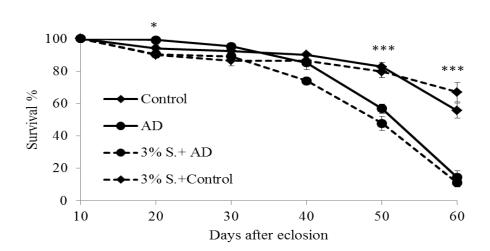


Figure 2. Anesthesia with 3% sevoflurane for 4 times (1 hour per time) did not affect the survival on control and AD-transgenic flies. "AD" refers to Alzheimer's disease; "S" indicated 3% sevoflurane; "E" indicated exposure. Error bars indicate SEM. Data were evaluated using student's t-test method. \*\*\*p<0.001.