

## [N-72] Volatile Anesthetics Disrupt Neuronal Migration in the Developing Rat Brain

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**Background:** Brain development involves a sequence of events including proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis. Volatile anesthetics can cause neurotoxicity, which could be due to disruption of any of the above developmental processes. The mechanisms by which anesthetics cause neurotoxicity are not entirely known, but many studies have shown that animals and children exposed to anesthetics develop subsequent deficits in learning, memory, and behavior. The effects of volatile anesthetics on neuronal migration have not yet been characterized.

**Hypothesis:** Volatile anesthetic exposure during early brain development in the rat disrupts neuronal migration, which alters the final position of neurons in the hippocampus, as well as learning ability later in life.

**Methods:** P1 rats were injected with BrdU to label cells formed on day P1. These rats were then exposed to volatile anesthetics (isoflurane (1.5%), sevoflurane (2.5%), or desflurane (7%)) for 2 hours or to 30% oxygen as a control on day P2. The animals were sacrificed on day P7 or P14, and immunohistochemical assays were performed for BrdU, NeuN, and GFAP, in order to determine the fate of the BrdU-labeled cells after exposure to anesthesia. The cells were then quantified in defined areas of the hippocampal dentate gyrus to determine any differences between anesthetics and controls on neuronal migration. A subset of exposed animals was kept for behavior testing at age 4-6 weeks and age 6 months using the Morris Water Maze (MWM).

**Results:** There were significantly fewer BrdU-positive cells in the hippocampal dentate gyrus in rats exposed to isoflurane or desflurane when compared to controls, while the sevoflurane-exposed rat brains had equal numbers of BrdU-positive cells compared to controls. In the MWM behavior testing at age 4-6 weeks, both the isoflurane-exposed and desflurane-exposed rats showed significantly impaired learning on day 3 of the testing. However, there were no behavioral differences between sevoflurane-exposed rats and controls.

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