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 cause neurotoxicity, which could be due to disruption of any of the above developmental processes.
- Animals and children exposed to volatile anesthetics have subsequent deficits in learning, memory, and behavior.
- The effects of volatile anesthetics on neuronal migration have not been characterized in vivo.

Hypothesis: Volatile general anesthetics disrupt hippocampal neuronal migration during early brain development, having neurobehavioral consequences later in life.

Methods
- Postnatal Day 1 (P1): Brdu Injection (50 mg/kg x 2)
- Postnatal Day 7, 14 (P7, P14): Brain Tissue Collection, HJC cell quantification
- P2: Anesthetic Exposure (0.75 MAC x 2h)
- P28-P40, P182: Behavior Testing (Morris Water Maze)

Results

Figure 1 – Brdu-positive cell quantification.

Figure 2 – Morris Water Maze: Age 6 weeks.

Figure 3 – Morris Water Maze: Age 6 months.

Conclusions
- Cell counts: There were significantly fewer Brdu-positive cells in the granular layer of the hippocampal dentate gyrus in isoflurane and desflurane treated animals compared to controls at age P7, but no differences after sevoflurane exposure. However, all cell counts were equivalent at age P14.
- Behavior: There were no overall significant differences in any of the behavioral tests at 6 weeks or 6 months post-exposure, though post-hoc tests showed significant differences between isoflurane and desflurane treated animals and controls on some testing days.
- Overall: One-two hour exposure to P2 to either isoflurane or desflurane causes a transient disruption of neuronal migration with no significant long term effect on learning and memory, while the same exposure to sevoflurane has no effects on neuronal migration or behavior.

References