Clinical studies show that a statistically significant number of people experience long term changes in attention, learning and memory after surgery and anesthesia, raising many questions about why and how the changes that lead to cognitive impairment occur. Animal studies have consistently shown long-term neurocognitive deficits in aged rats following general anesthesia, but the mechanism is still unknown. We hypothesize that postoperative cognitive dysfunction (POCD) may result from anesthetic-induced alteration of adult neurogenesis. To test this hypothesis, we are evaluating the effects of isoflurane and propofol anesthesia on the different stages of adult neurogenesis in young and aged rats by the administration of halogenated thymidine analogs as markers for each stage of new cells development in the dentate gyrus. Alteration of any stage of neurogenesis by anesthesia might explain the postoperative decline experienced in some patients. Even though, the effect of anesthesia has been studied on new cell proliferation, the effect of anesthesia on each stage of neurogenesis has not been studied.

Methods

Three different halogenated thymidine analogs (CldU, IdU, and EdU) were injected intraperitoneally at three different time points corresponding to a stage of adult neurogenesis such as differentiation, migration and integration. While the proliferation stage was assessed by the endogenous marker ki67. Labeling for cell proliferation, the effect of anesthesia on each stage of neurogenesis has not been studied.

Isoflurane affects mature neurons

Two age groups were studied in this experiment young (4 mo old) and aged (21 mo old) F344 rats. Animals in the treatment groups were anesthetized for 3 hours with either 1.5% isoflurane or 35mg/Kg/hr propofol. Additional young and aged rats exposed to room air or intralipid (propofol vehicle) served as controls. Body temperature was maintained at 37°C during the procedure and perioperative parameters such as oxygen saturation, heart rate, and blood pressure were measured throughout the anesthesia period. A day after anesthesia, rats were euthanized and the brains analyzed for immunohistological marker for each time point. Two age groups were studied in this experiment young (4 mo old) and aged (21 mo old) F344 rats. Animals in the treatment groups were anesthetized for 3 hours with either 1.5% isoflurane or 35mg/Kg/hr propofol. Additional young and aged rats exposed to room air or intralipid (propofol vehicle) served as controls. Body temperature was maintained at 37°C during the procedure and perioperative parameters such as oxygen saturation, heart rate, and blood pressure were measured throughout the anesthesia period. A day after anesthesia, rats were euthanized and the brains analyzed for immunohistological marker for each time point.

Propofol affects immature neurons

Anesthesia decreases the number of neurons in the dentate gyrus of rats. Isoflurane decreases the number of mature neurons in the DG of aged rats. Propofol decreases the number of immature neurons in the DG of young rats. The effect of anesthesia in the DG is age and agent dependent. The effect of anesthesia is not on neurogenesis but rather on migration, axon/dendrite targeting and integration.

Conclusion

References