Children with mitochondrial disorders are frequently anesthetized. Anesthetics may interfere with mitochondrial function and alter their response to anesthesia and surgery. There is a lack of evidence on how to most safely treat this population of children undergoing surgery. Mutations in the mitochondrial ND6 gene cause isolated complex I dysfunction and mutations in the CO1 gene cause complex IV dysfunction. We examined sevoflurane, isoflurane, and halothane sensitivity in 3 genotypes of mice (ND6 knockout, CO1 knockout, and wild type (WT)).

Methods

8 mice in each genotype were placed into individual airtight chambers breathing spontaneously while the inhaled anesthetic was administered. The concentration of the anesthetic was measured intermittently at the exhaust port. After equilibration at each anesthetic concentration for 15 minutes, the chambers were rotated 180 degrees so that the mice were flipped onto their backs. If a mouse was unable to turn itself prone onto all 4 feet within 2 minutes, it was considered to have lost righting reflex (LORR) and was considered lost for righting reflex (LORR) and emerged from anesthesia. Plots of log of volatile anesthetic gas concentration vs. percent population having lost righting reflex were generated and fit with a non-linear dose-response curve with a variable slope (using Prism 4.0) to obtain $MAC_{LORR}$ and $MAC_{RORR}$.

Conclusion

Complex I is the most sensitive step in oxidative phosphorylation to inhibition by volatile anesthetics in vitro (1). Morgan et al also found hypersensitivity to volatile anesthetics in a subset of children with complex I defect (2). Our findings support these prior reports and offer additional insight into how volatile anesthetics interfere with mitochondrial function.

References