



Anesthetic Sensitivity of Mouse C57BL/6 Substrains to Isoflurane

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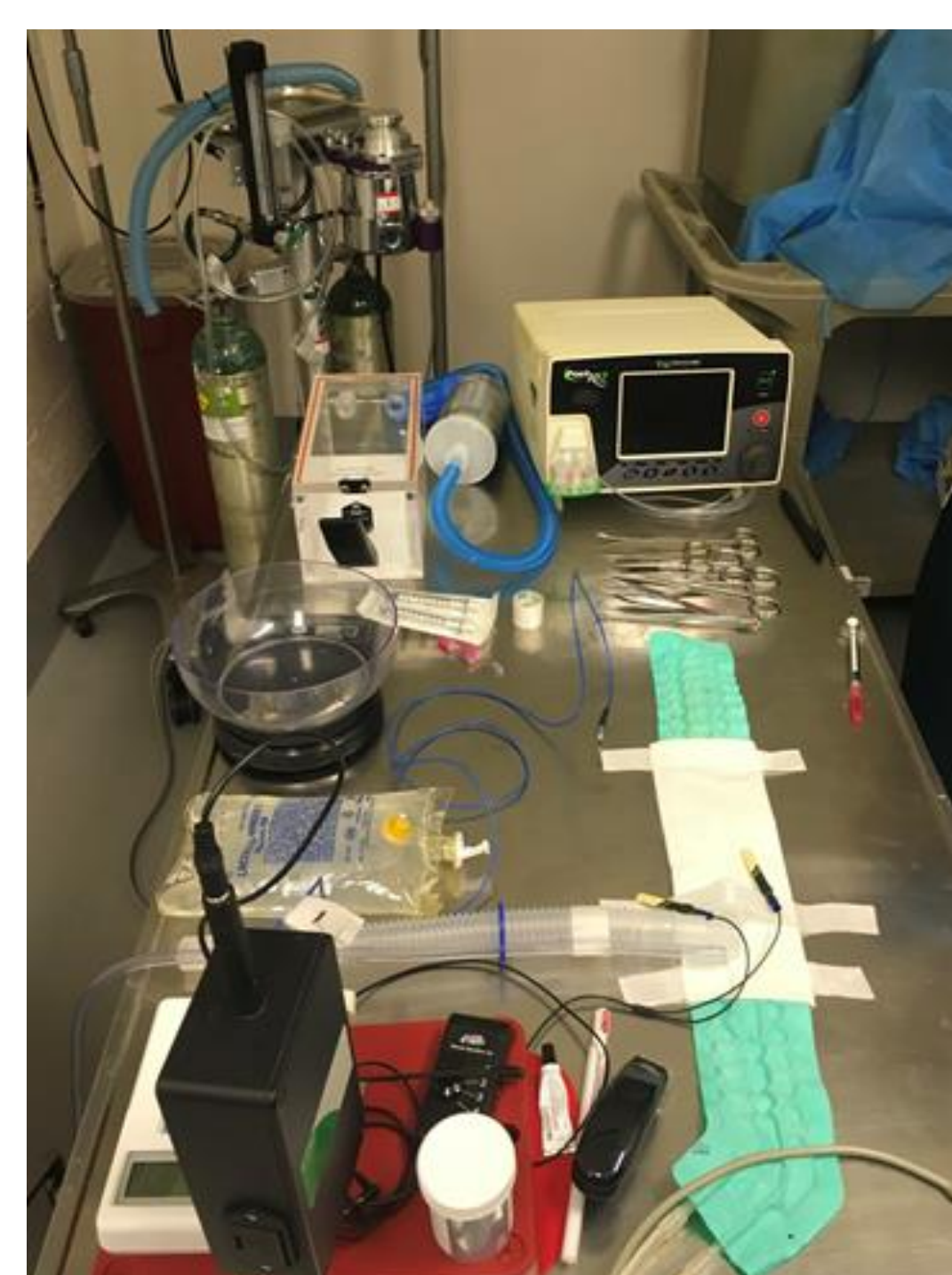
Introduction

While genetically very similar, many physiological differences have been documented between the substrains of C57BL/6 mice that have important impacts on the animals. One study (Roth et al. 2002) demonstrated differences in the duration of sedation between C57BL/6J and C57BL/6N when using ketamine/midazolam. Understanding differences between the substrains of this commonly used strain of mice will aid in the delivery of anesthetics and help to improve the repeatability of studies using these mice. Additionally, sex-differences have been reported to many anesthetics in mice, including sevoflurane, which is closely related to isoflurane, the most commonly used inhalant anesthetic in mice. The goal of this project was to determine the effect of C57BL/6 substrains and sex on isoflurane sensitivity.

Methods

Female and male C57BL/6 mice were obtained from four different vendors: C57BL/6NTac from Taconic (TAC: n=6), C57BL/6J from The Jackson Laboratory (JAX: n=6), C57BL/6NHsd from Envigo (n=6), and C57BL/6NCrI from Charles River Laboratories (CRL: n=6). The minimum alveolar concentration (MAC) for isoflurane was determined for each substrain. Mice were anesthetized with

isoflurane, using 100% oxygen as the carrier gas. Isoflurane concentration was measured using the Poet IQ2 (Criticare Systems, Inc). After 15 minutes of equilibration at 1.7% isoflurane, a 300-gram force (Touch Test Device) delivered to the hind paw. Presence or absence of a motor response was recorded. Isoflurane concentrations were then increased every 10 minutes until the mouse was determined to be at a surgical plane of anesthesia. The surgical plane was defined as the absence of any motor response to the Touch Test



Device. Body temperature, measured by a ThermaWorks rectal thermometer, was maintained at $36\text{ C} \pm 1.0\text{ C}$ using a warm water heating pad (Gaymar T/Pump) and heat lamp. Heart rate and oxygen saturation were monitored using the MouseSTAT Jr Rodent Pulse Oximeter (Kent Scientific). and the respiratory rate was determined by thoracic excursions. The transition point to a surgical plane of anesthesia was defined as half-way between the highest percentage of isoflurane where mice had a positive withdrawal and the lowest percentage with a negative withdrawal. A two-way ANOVA was performed to detect statistical differences on the transition points with substrain and sex as the two main effects.

Results

The MAC for each substrain was: C57BL/6NTac: $2.0\% \pm 0.1$, C57BL/6J: $2.1\% \pm 0.1$, C57BL/6NHsd: $2.0\% \pm 0.2$, and C57BL/6NCrI: $2.0\% \pm 0.1$. None of these differences were significantly different ($p=0.282$). There were no significant differences between males, $2.0\% \pm 0.1$ and females, $2.1\% \pm 0.1$ ($p=0.441$). There was no morbidity or mortality noted in any of the mice.

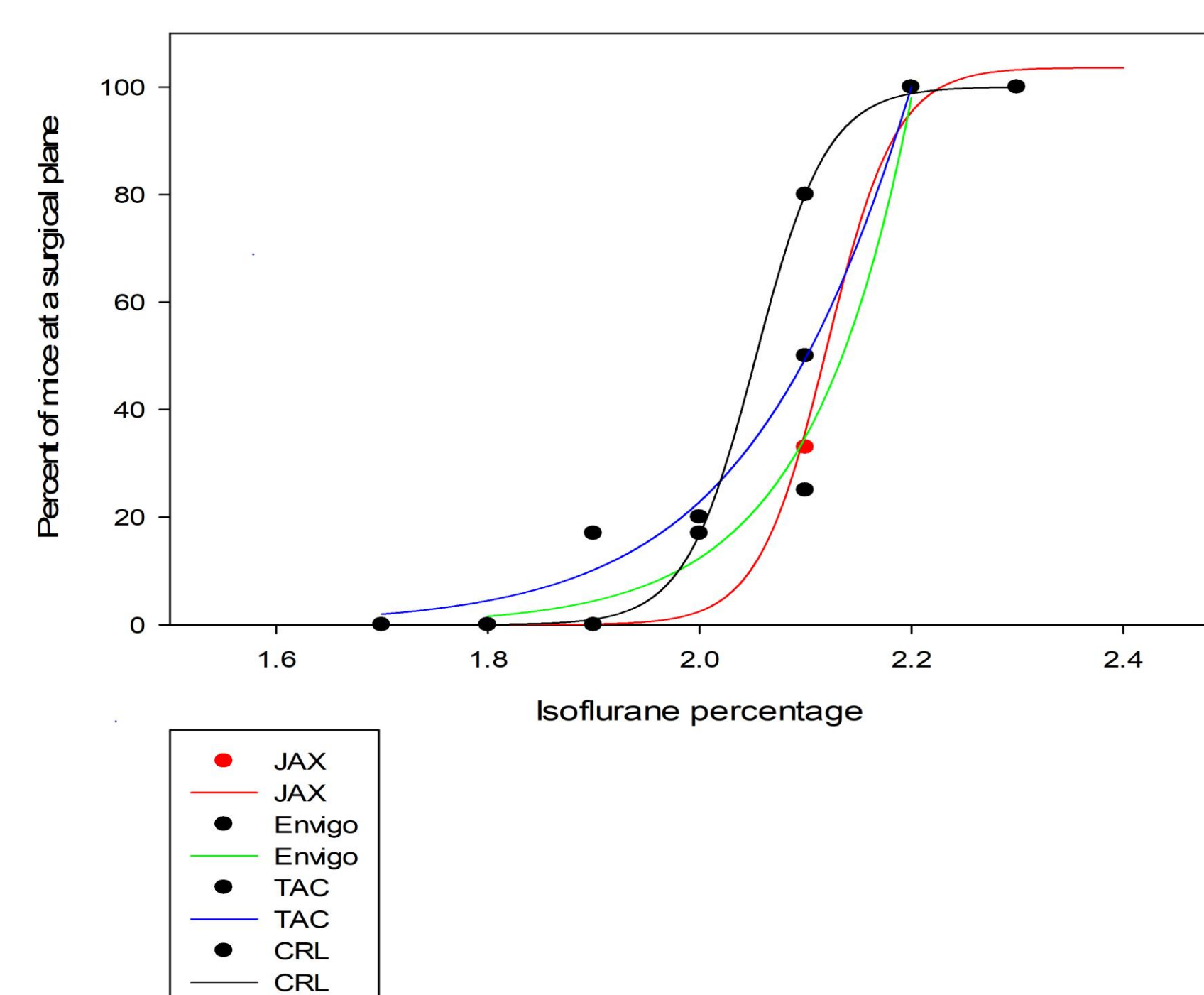


Figure 1. Minimum Alveolar Concentration of Isoflurane by C57BL/6 Substrain ($p=0.282$)

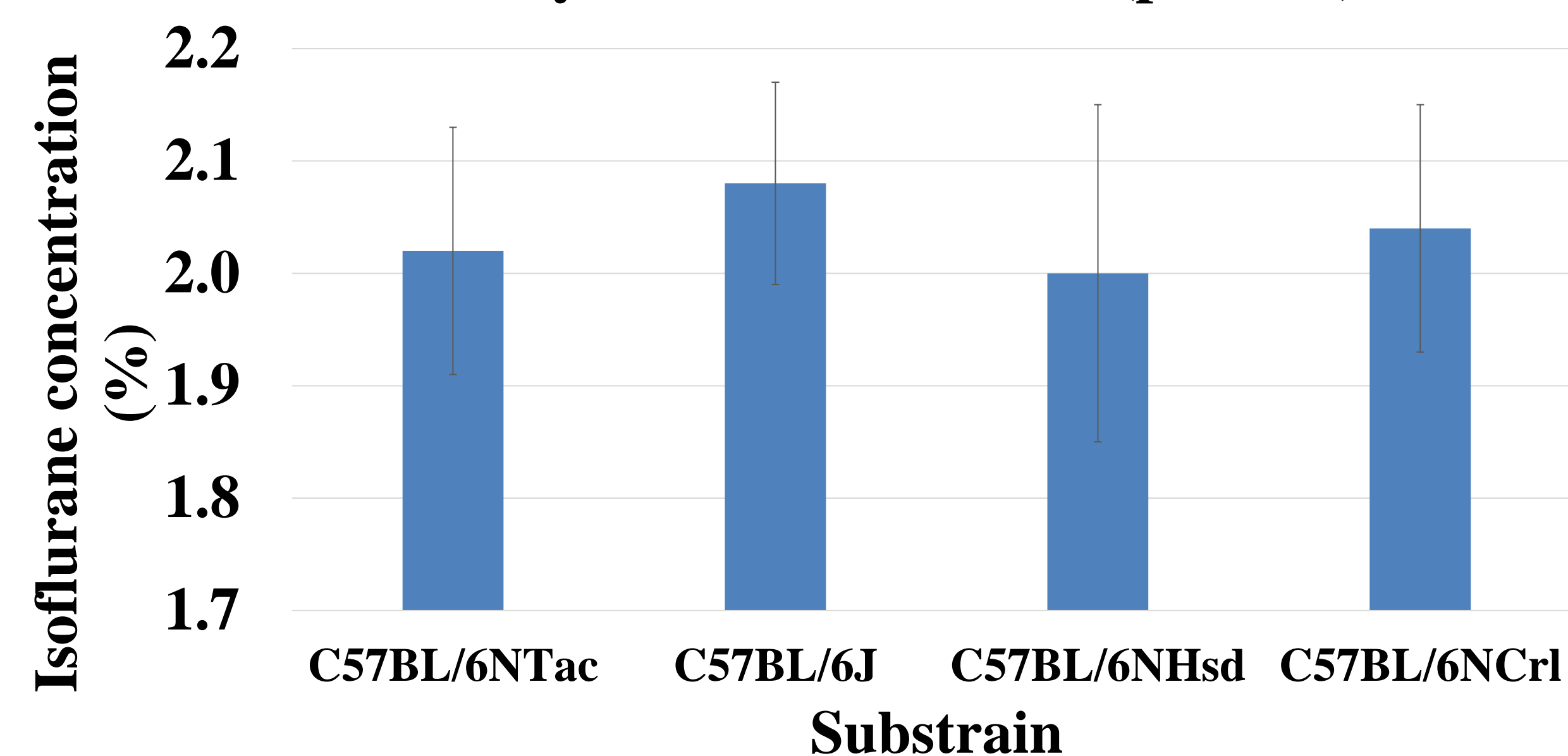
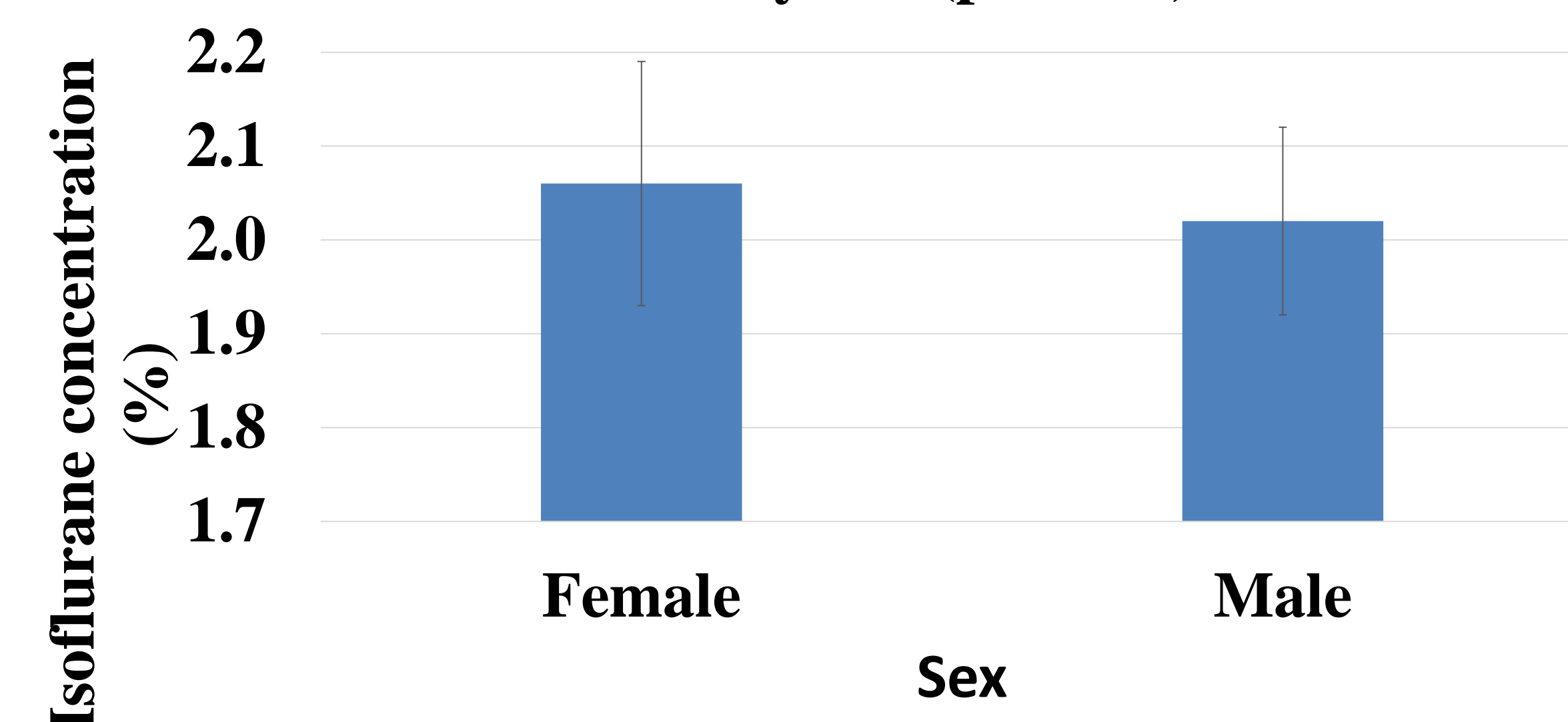


Figure 2. Minimum Alveolar Concentration of Isoflurane by Sex ($p=0.441$)



Discussion

Mouse strain differences in MAC to various inhalant anesthetics have been demonstrated previously and recent work has shown a difference in response to injectable anesthetics between C57BL/6J and C57BL/6N mice. Despite these findings, no differences were detected between the substrains of C57BL/6 mice tested in this study. Further, the small differences in response between male and female mice was not statistically or physiologically different. From an anesthetic safety perspective, isoflurane recommendations do not need to be tailored to the C57BL/6 substrains or sex of the animal being studied.

Future Work

While there are differences between C57BL/6 substrains to some injectable anesthetics, we did not find significant differences for minimum alveolar concentration of isoflurane between substrains. There were also no differences between female and male mice. Future work will examine substrain response to ketamine, xylazine, and acepromazine, a commonly used injectable anesthetic combination.

Acknowledgements

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References

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