

Head stability in genetically modified mice

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INTRODUCTION

The vestibular system, made up of the semicircular canals and otolithic organs, contributes to the sense of spatial orientation and balance and to head stability in space. Research has shown that a loss of vestibular functionality may be correlated with aging in humans. Vestibular loss in the elderly can lead to falling events, an increasing problem with the general trend of aging and longer life spans in the world's population today. For example, 33% of elderly adults who fracture a femur die within a year of their fall (Swift, BMJ 2001; 322:855). By quantifying variation in head stability in mice running about a flat surface or on an exercise wheel, we expect to establish a correlation between vestibular functionality and a mouse's ability to keep its head stable in space.

This research should help in the future development of treatments and/or therapies, which might protect against falls in aging humans. Our primary goal is to create the necessary hardware and software to monitor rodent locomotion (normal walking behavior) with the purpose of establishing an animal-to-human model of vestibular function. We will use mice with a genetically altered vestibular system, some of which may have diminished vestibular functionality. Using an Inertial Measurement Unit (IMU) attached to the heads of the mice, we will directly measure the variability of head position in space.

HYPOTHESIS

We hypothesize that mice with genetic changes that may diminish vestibular function will have greater variability in their ability to maintain a stable head position in space.

OBJECTIVES

- Design/Organize hardware and software to develop a test sensitive enough to quantify head stability in mice.
- Evaluate vestibular function in two control mice and in two genetically altered mice that may have some level of vestibular dysfunction (homozygous recessive for the myosin 15 $\Delta N/\Delta N$ gene).
- Establish connection between vestibular dysfunction and greater variability in head position.
- (Further Studies) Extend experiment to determine if higher variability in head stability correlates with increased falling rates in vestibular deficient mice.

METHODOLOGY

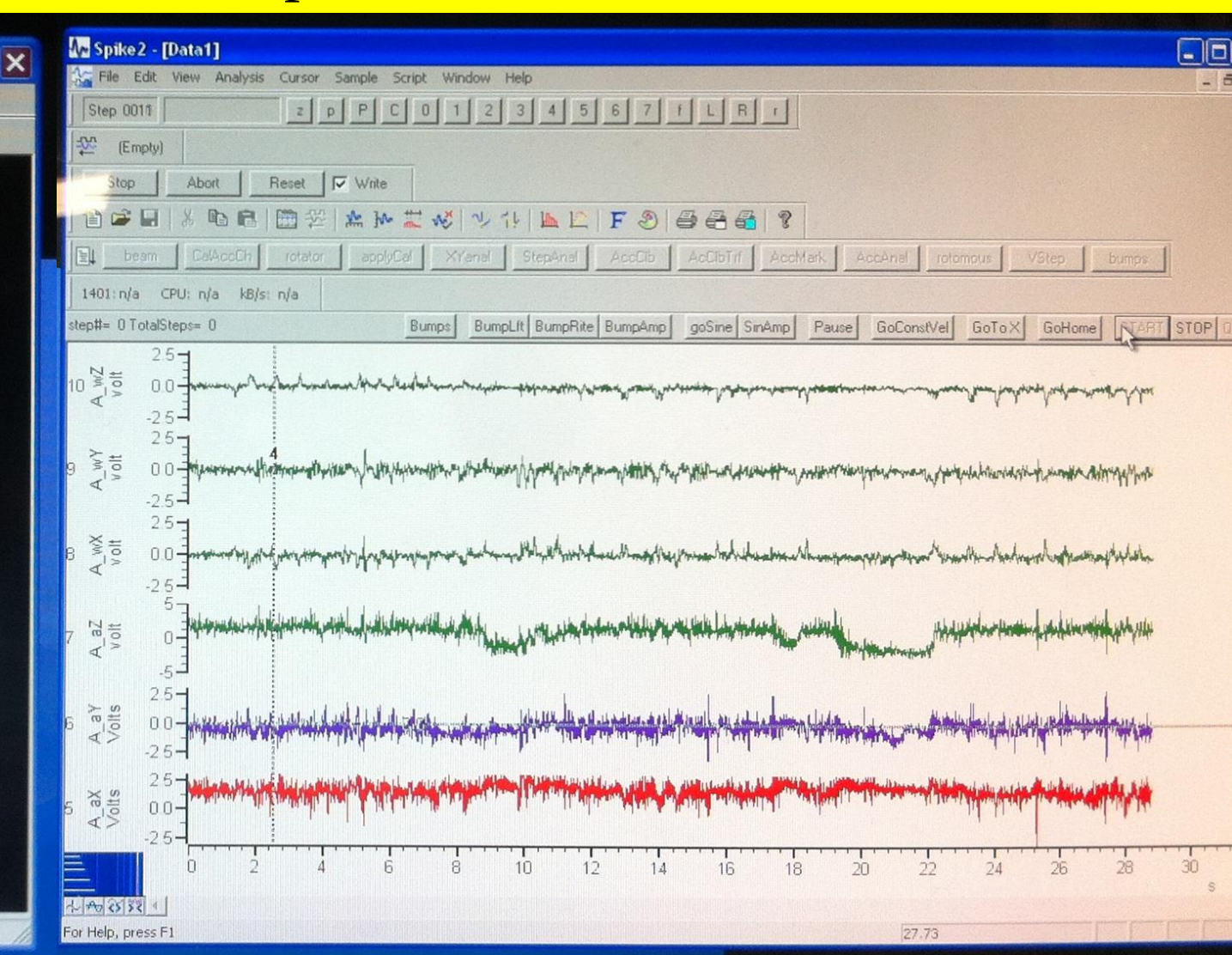
Each mouse was independently placed on an enclosed 12" x 12" flat surface and allowed to run about freely for a period of 6-10 minutes in total darkness on five different days (five trials). An IMU was affixed to the head which measured linear head acceleration and angular head velocity in three dimensions, thus allowing us to quantify the orientation of the head in space as the mice ran.

Data was processed in Spike2 v6.12 (Cambridge Electronic Design) and Matlab 2012 and exported to show the variance of the angular velocity and the linear acceleration of the head of each mouse.

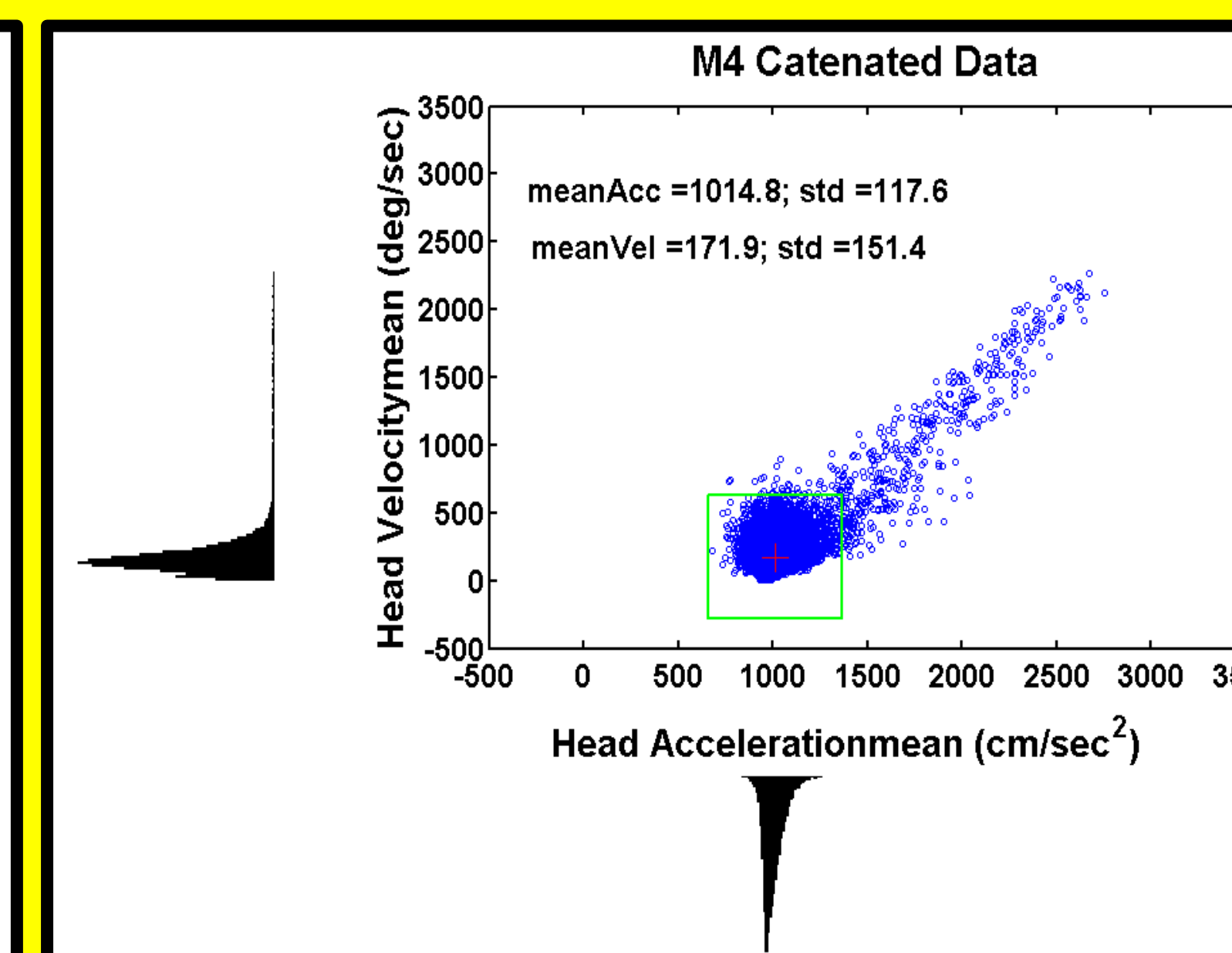
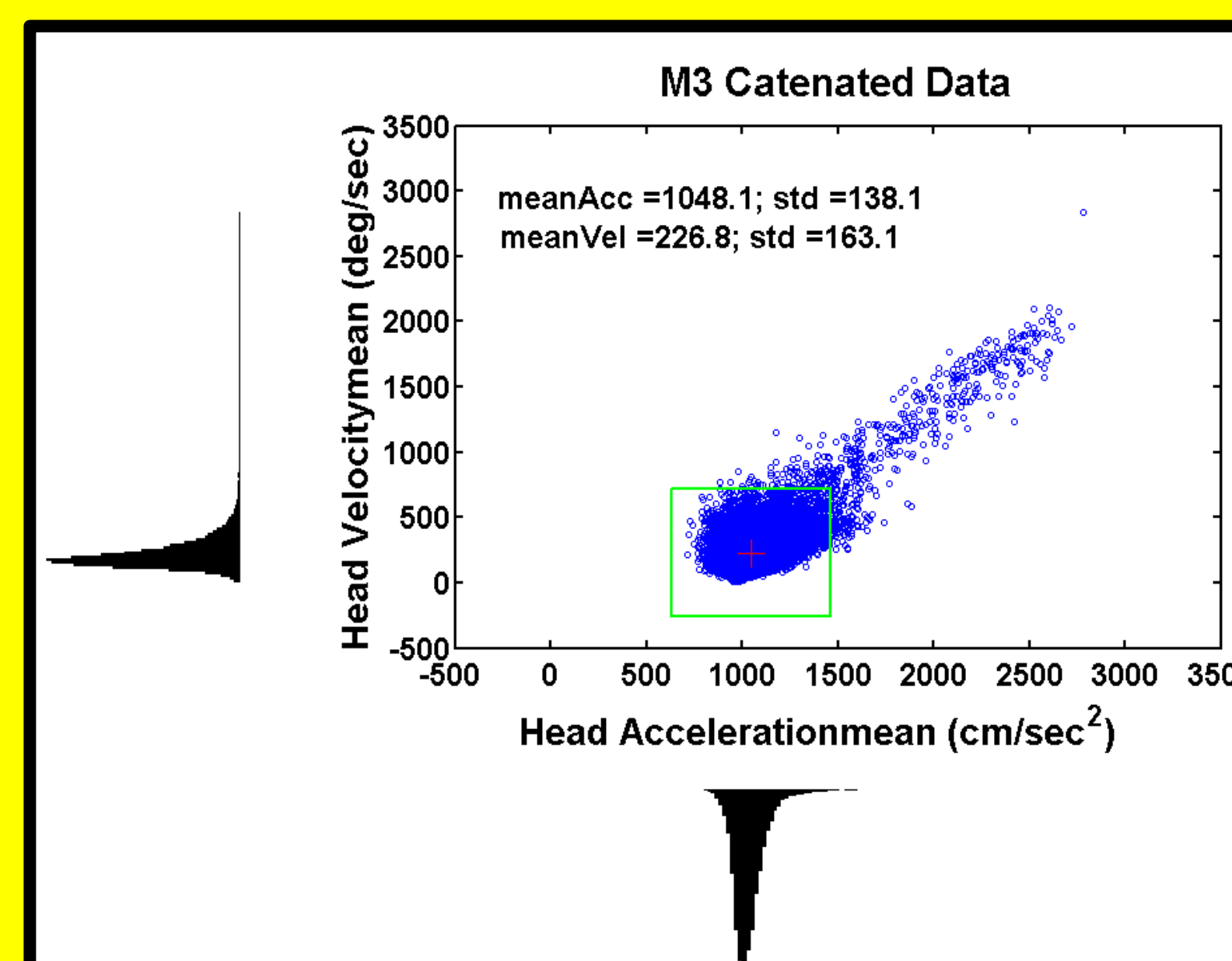
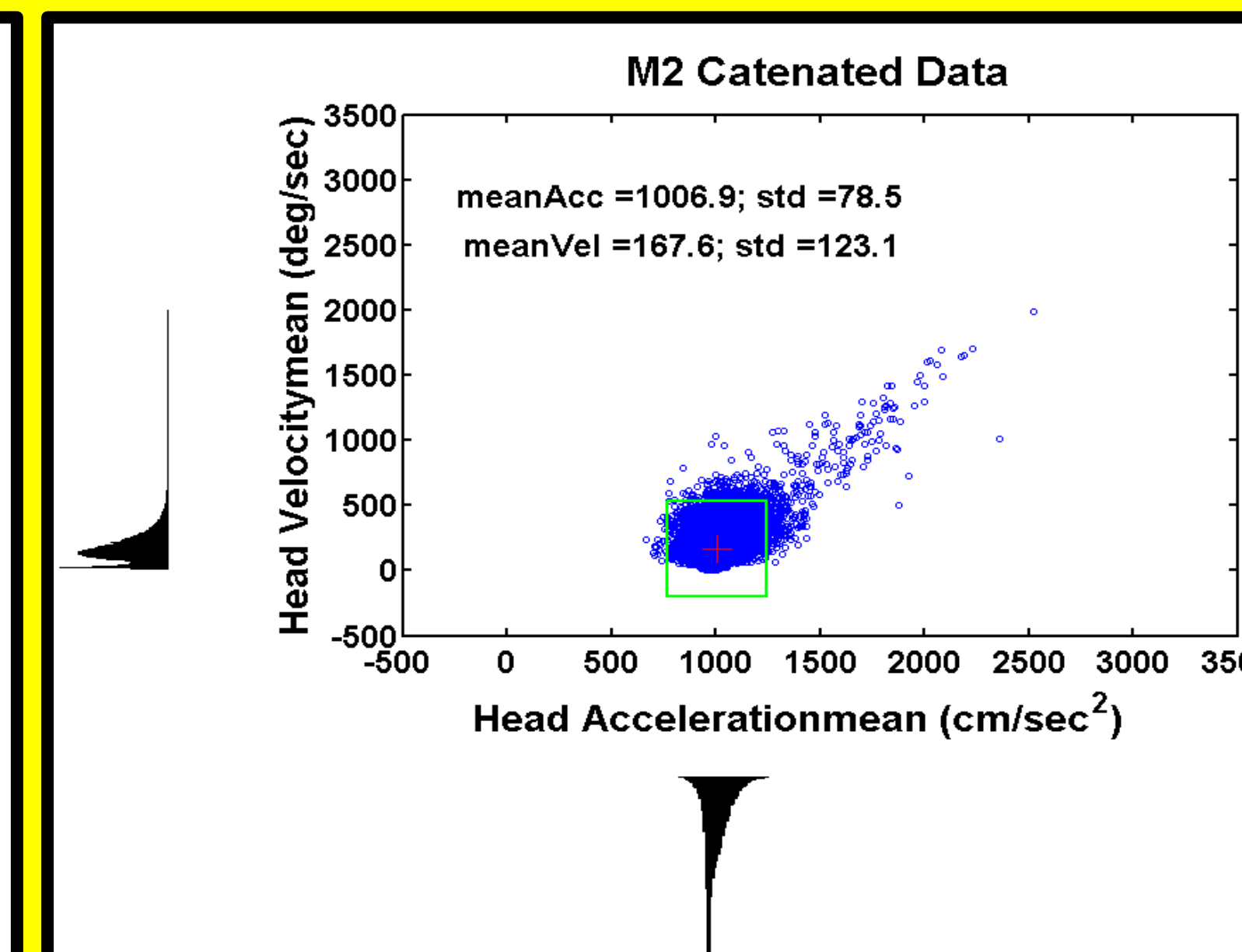
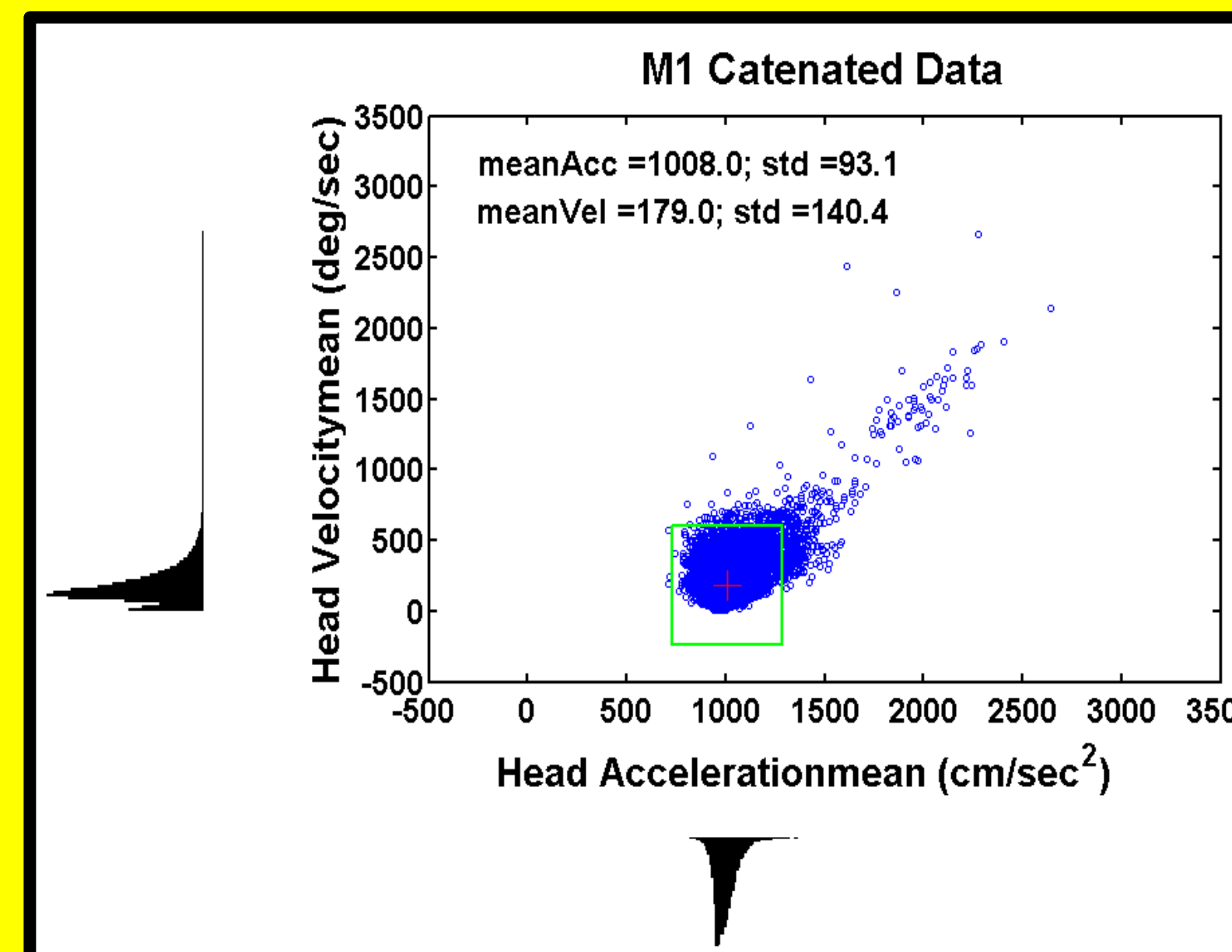
Example of experimental apparatus.



Example of IMU data collection method.

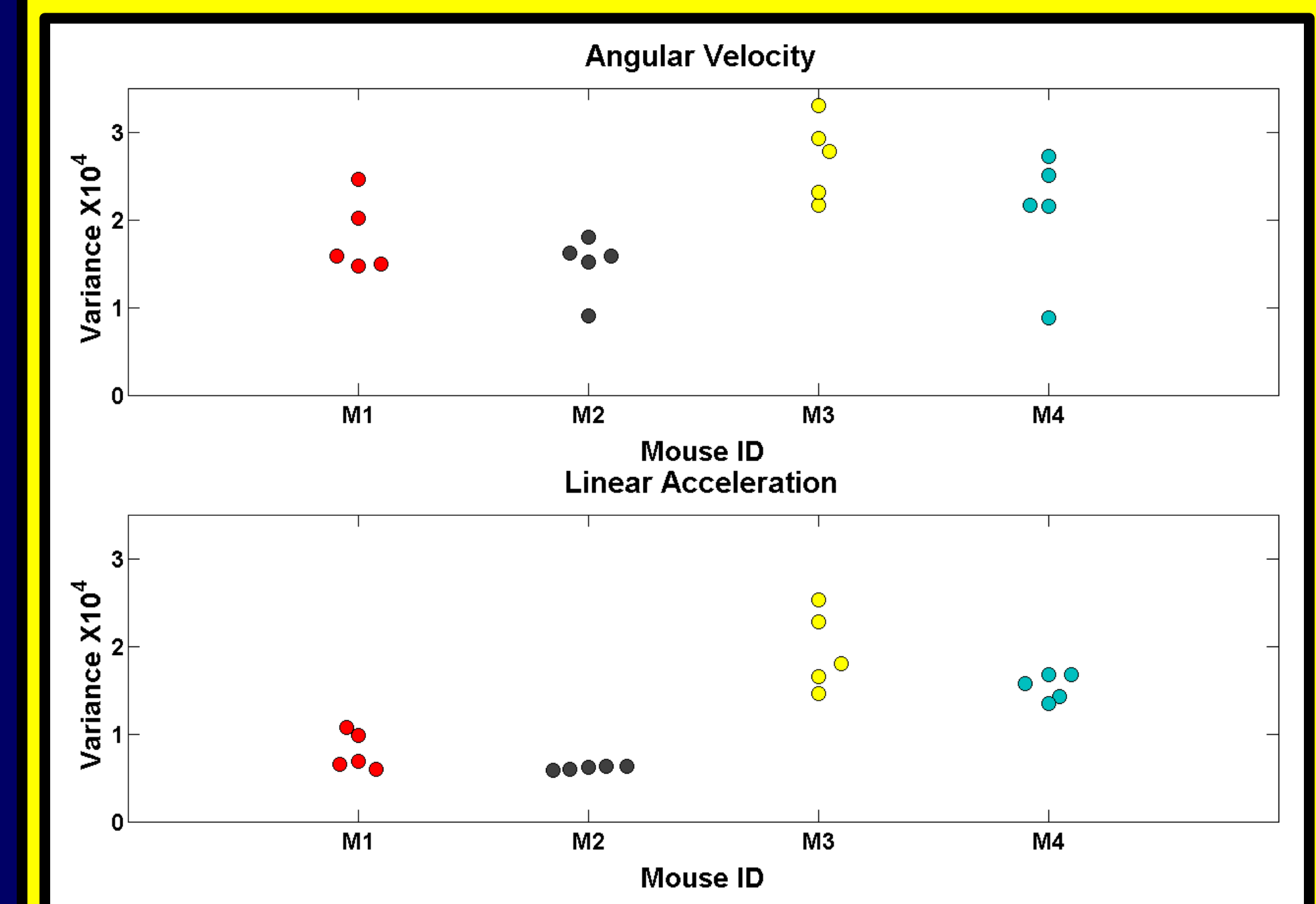


RESULTS



SUMMARY

In order to determine if our test was sensitive enough to isolate vestibular dysfunction, a comparison was done between the control mice (M1 and M2) and our genetically modified mice (M3 and M4). The graphs below show the variance in the linear acceleration and the angular velocity over the course of five trials. Data points are staggered horizontally where needed to prevent overlap and to aid in viewing.



CONCLUSION

1. Both genetically altered mice exhibited more variance in head velocity and head acceleration than the wild type mice (see relative sizes of the green boxes in Results figures).
2. Despite this difference, additional experiments are required to determine if the greater variance can be attributed to vestibular dysfunction or may reflect some other abnormality in these animals.

FUTURE STUDIES

These studies need to be expanded to include

- a) a larger number of control and myosin 15 mice and
- b) additional control mice with known vestibular deficiencies.

ACKNOWLEDGEMENTS

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