COLLEGE OF SCIENCE
THE UNIVERSITY OF ALABAMA IN HUNTSVILLE

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Motor Activity in a Mouse Model of Tyrosinemia Type I

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Introduction

Tyrosinemia Type I is an autosomal recessive genetic disorder which results in a deficiency of FAH, an essential enzyme in the breakdown of tyrosine. The incomplete metabolism of tyrosine results in the accumulation of toxic metabolites in affected individuals. This can be fatal if left untreated. The current therapies for treatment of tyrosinemia type I include liver transplant and treatment with NTBC (nitisinone). NTBC prevents the buildup of the toxic metabolites, but neurological, cognitive and motor impairment issues have been reported in some patients. Whether this is due to treatment with NTBC or a function of the disease itself remains unknown.

Methods

Coordination and balanced were assessed using static rod testing. Mice that fell off of the rod, turned upside down or failed to complete the traversal in the allotted time were assigned a maximum score. The mice were trained on the rods for 10 consecutive days (Deacon, et. al., 2013). Gait was assessed using video taken from below as the mouse traversed a clear Plexiglas® runway. Analysis was carried out using Kinovea© software. Mice were trained to run across the runway for two days prior to video acquisition on the third day (Galante, et. al., 2009). All data are presented as individual data points showing the mean with 95% CI. Eight mice were used for gait and static rod testing, 4 control mice and 4 NTBC mice with 2 of the NTBC mice being FAH deficient.

Results

Figure 1. Mice on NTBC have increased urine HVA levels corresponding to a higher dopamine concentration.

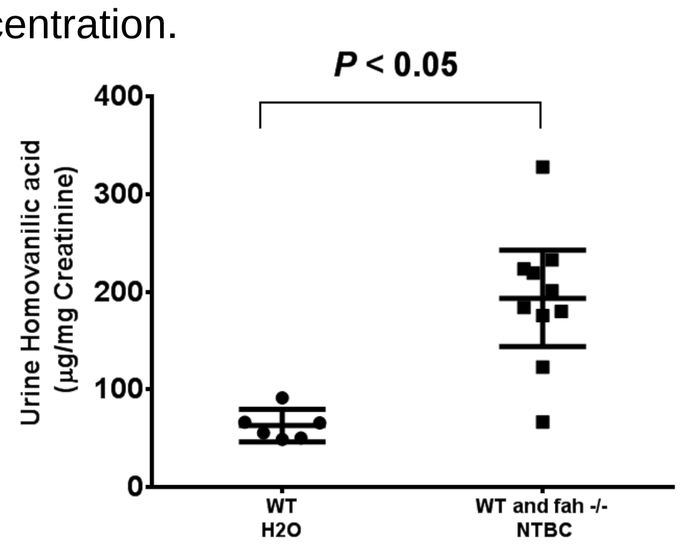
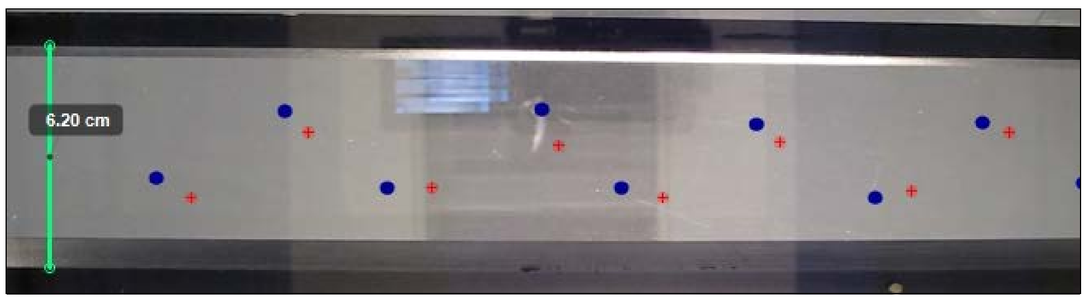


Figure 4. Example of Mouse Gait Analysis Trail



Figures 2 & 3. Mice on NTBC are less coordinated during orientation and traversal on the small static rod after an average of 6-10 days. Control mice are equally coordinated on both rods.

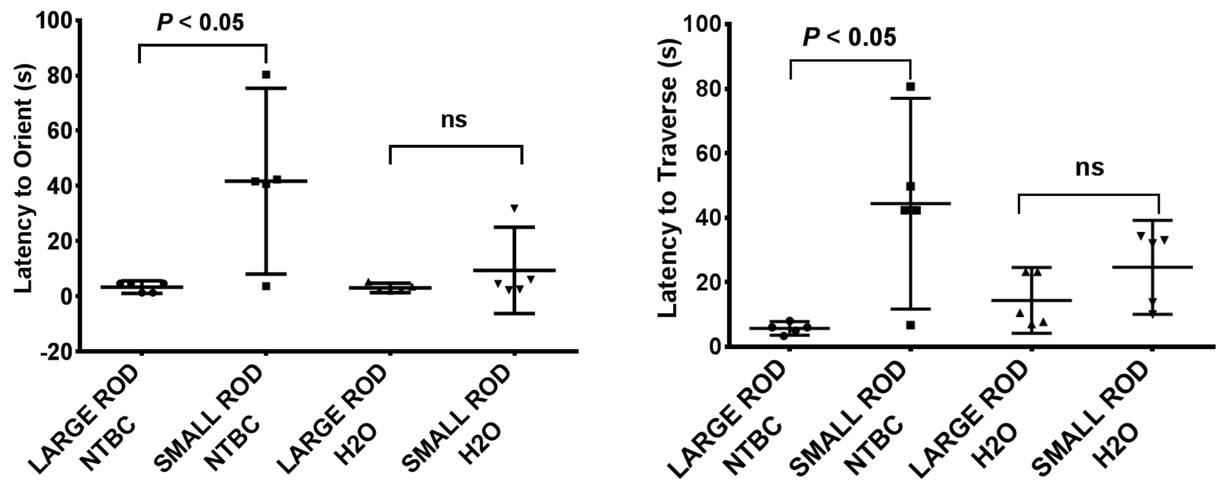
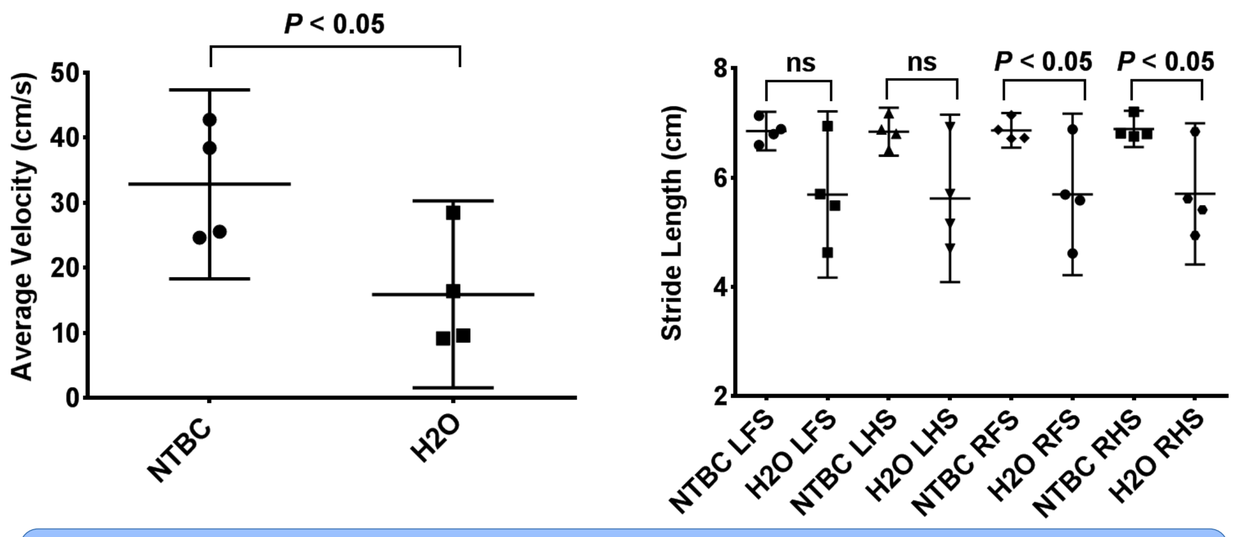


Figure 5 & 6. Mice on NTBC showed increased velocity during gait analysis. Mice on NTBC had greater stride length on the right side.



Conclusions

- Mice being treated with NTBC have increased urine HVA levels corresponding to increased dopamine metabolism.
- Mice on NTBC are significantly less coordinated on the small static rod as compared to the large static rod. Control mice are equally coordinated on each rod.
- Gait can be consistently assessed in mice by filming from below (MouseyGait™) and plotting foot prints. Further assessment is needed to determine whether differences in gait between groups are due to other factors such as size, speed, etc.

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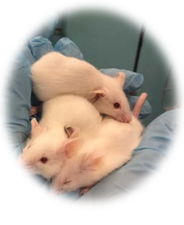

References

Deacon, R. M. J. Measuring Motor Coordination in Mice. *J. Vis. Exp.* (75), e2609, doi:10.3791/2609 (2013).

Galante, M., Jani, H., Vanes, L., Daniel, H., Fisher, E. M. C., Tybulewicz, V. L. J., Morice, E. (2009). Impairments in motor coordination without major changes in cerebellar plasticity in the Tc1 mouse model of Down syndrome. *Human Molecular Genetics*, *18* (8), 1449–1463.

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