

Impaired Social Behavior in Mice with Tyrosinemia Type I is Associated with Hypermyelination of the Cerebral Cortex

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Introduction

Social behavior and cognitive issues have recently been observed in individuals with the autosomal recessive disorder Tyrosinemia type I. This inborn error of metabolism leads to a deficiency of a crucial enzyme, FAH, that is involved in tyrosine catabolism. The cause of these neurological problems has not yet been discovered. To gain insight into this we studied social interaction (Moy et al., 2004) and brain histology in mice with tyrosinemia type I.

Results

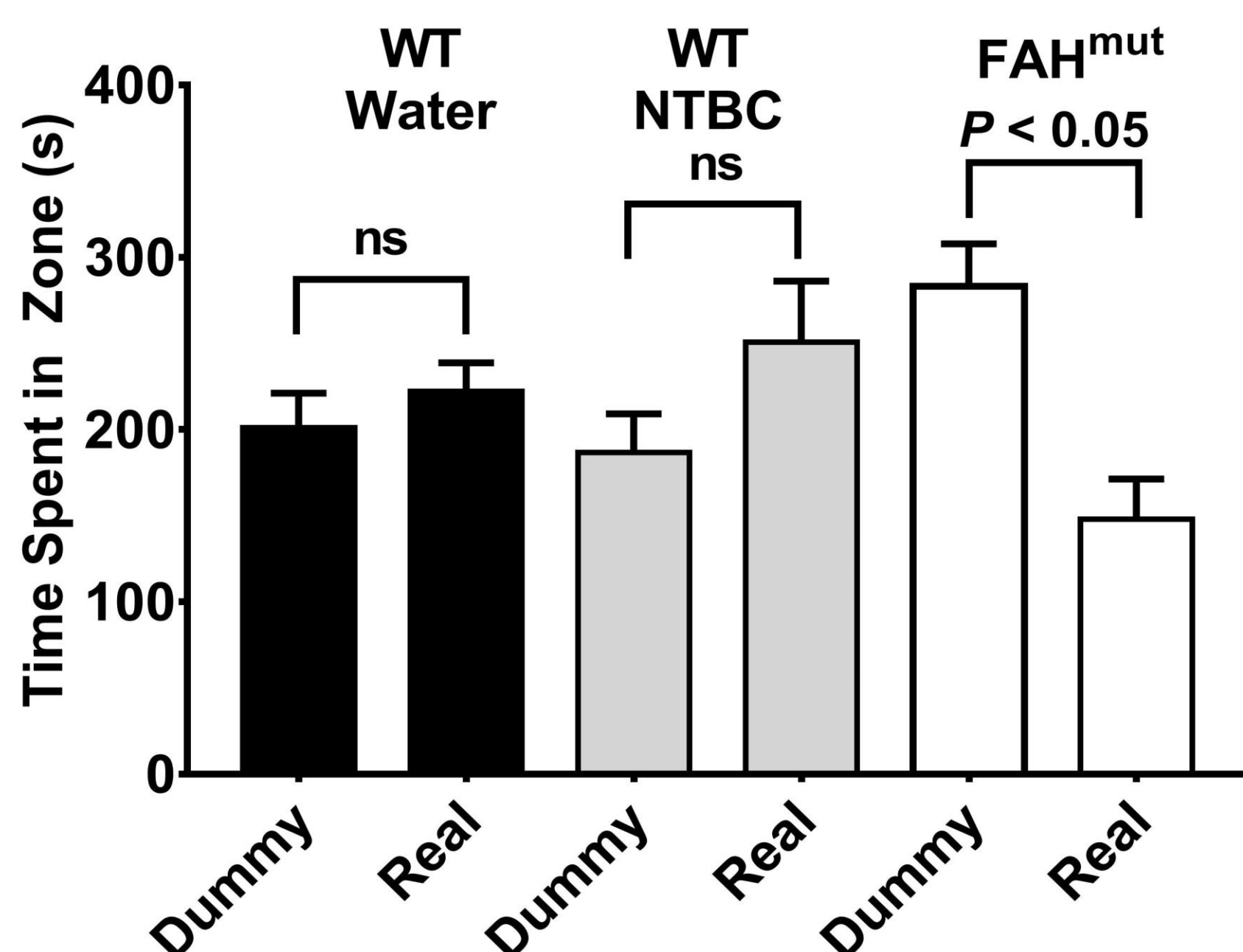
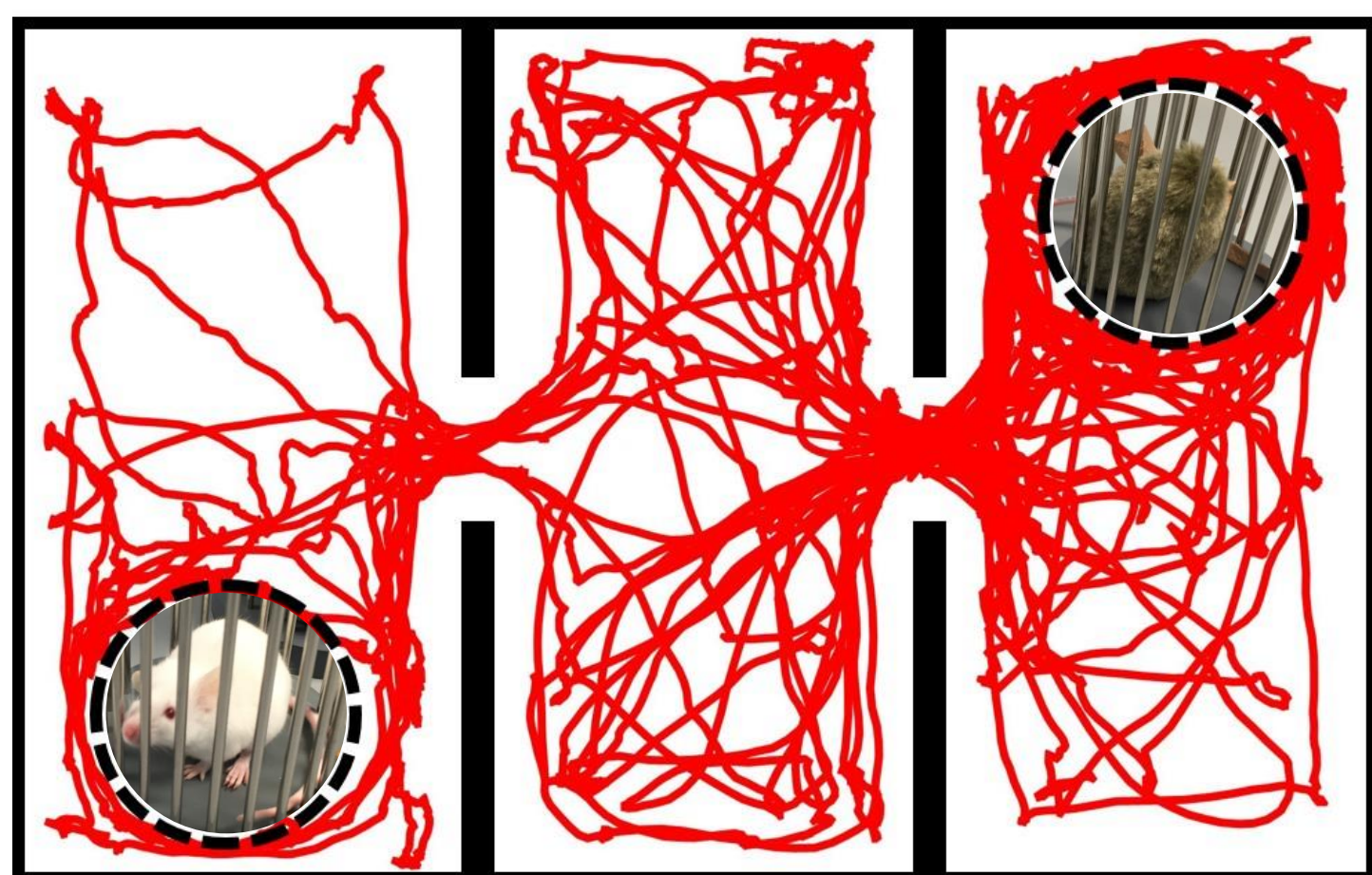


Figure 1. FAH^{mut} mice show abnormal social behavior and spend twice the time investigating a dummy compared to a real mouse.

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FAH^{mut}

WT-NTBC

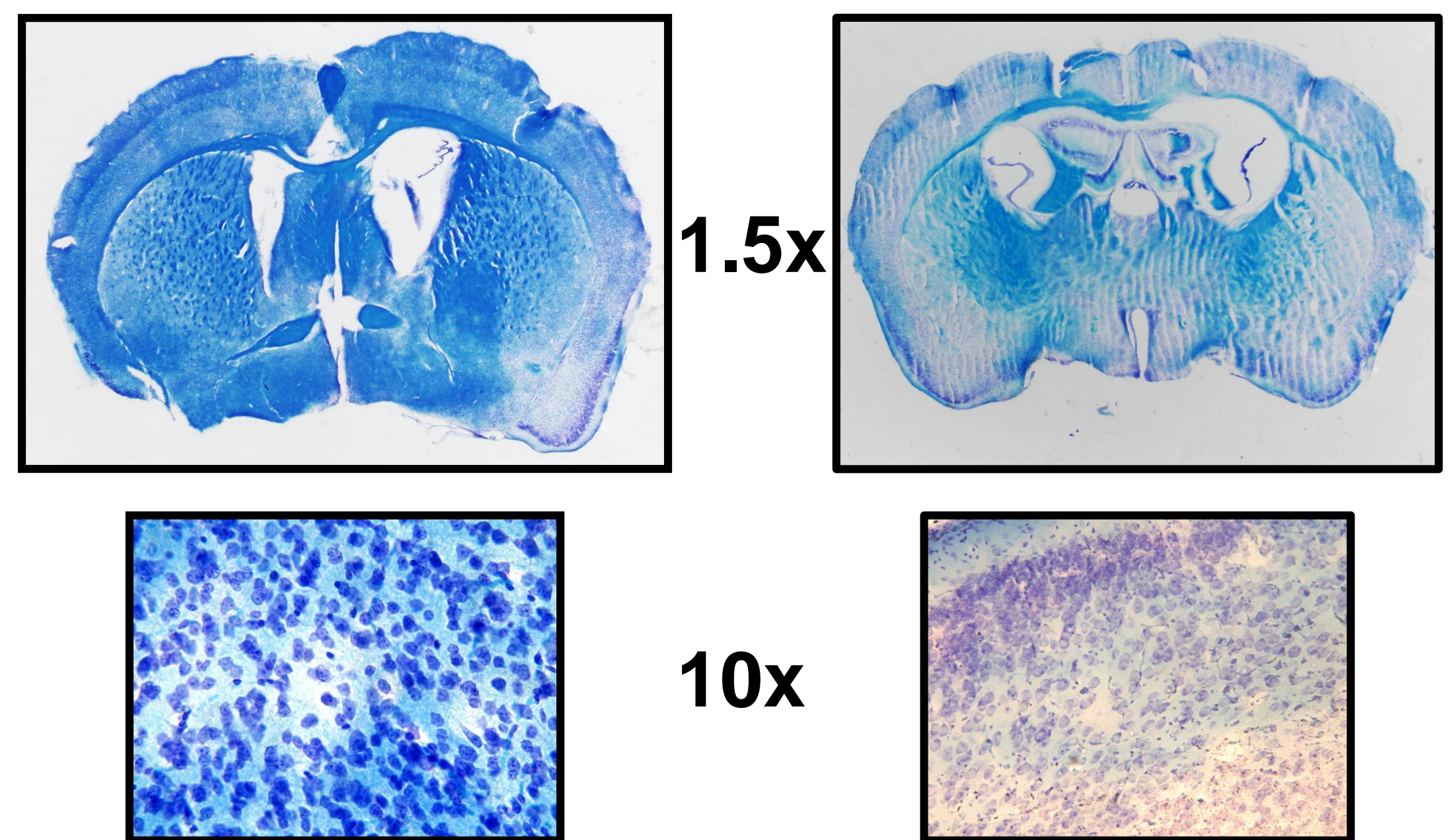


Figure 2. FAH^{mut} mice display hypermyelination of the cerebral cortex. Top image shows a 20 μ m coronal brain slice (1.5x) from Bregma -1.0 and bottom image shows cerebral cortex (10x). Myelin is stained blue and the cell nucleus is stained purple (Kluver and Barrera, 1953).

Conclusions

Mice with tyrosinemia type I show abnormal behavior including slower learning (Hillgartner et al., 2016) and abnormal social interactions with other mice, preferring to spend more time alone. The altered social behavior is caused by the disease (only seen in FAH^{mut} mice) and not treatment with NTBC. Studying the brains of the FAH^{mut} mice showed increased myelin content of the cerebral cortex. This could indicate altered synapse formation and different neurological pathways suggesting a mechanism for the altered behavior.

References

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