

Introduction

Motor coordination and motor learning can be affected by several diseases and disorders as well as certain drug treatments. When developing new therapeutics or transgenic animal models of said diseases and disorders, it is important that their motor behavior is measured properly. Measurement in rodents is most commonly performed on the RotaRod because of its automated features [1]. Animals need to balance on a rotating rod and latency to fall is analyzed. A longer latency is taken to index better coordination while a shorter latency can imply a possible impairment. The most frequently used protocols are the fixed speed paradigm for studying motor coordination and fatigue, and the accelerating paradigm for motor coordination and learning [2]. These protocols are used worldwide but are tested on a wide variety of RotaRods currently on the market. Different systems can vary with respect to rod diameters, surface texture, minimum/maximum speed, and even the possibility to administer shocks when animals fall onto a grid floor. This will influence the reproducibility of results and thus both within as well as between laboratory reliability.

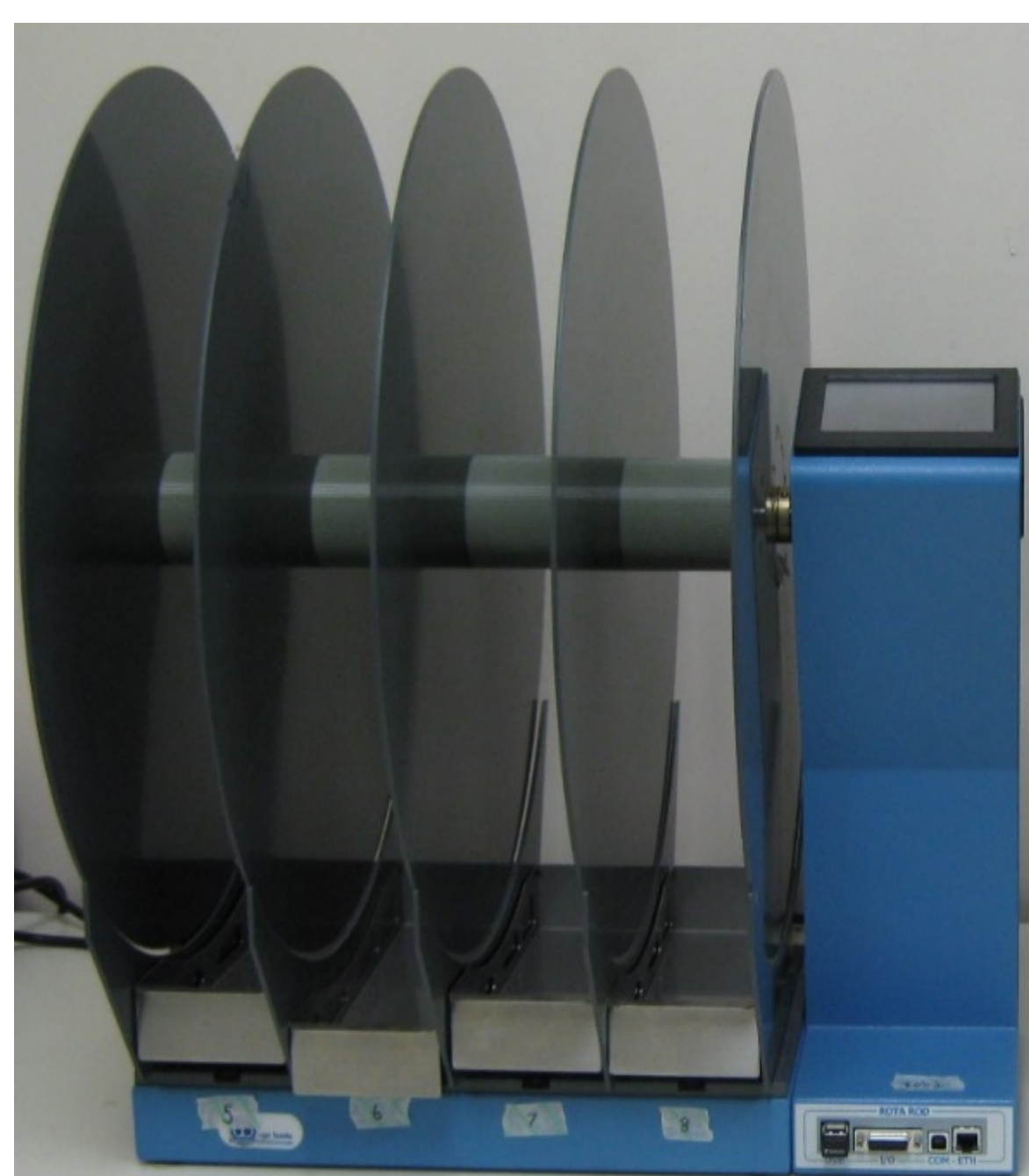
Methods

Animals

- Female NMRI mice (Charles River, UK): 3 (n=35) and 5-6 (n=24) months
- Female C57Bl/6 (Homebred): 3-5 months (n = 20)
- Female 5x FAD (Homebred): 3-5 months (n = 20)

In accordance with the European Communities Council Directive (63/2010/EU) and a project license with local ethical approval under the UK Animals (Scientific Procedures) Act (1986).

RotaRods



Custom-made automated 4-lane accelerating Ugo Basile SRL (Italy) rat RotaRod NG



4-lane accelerating TSE Systems (Germany) Rat RotaRod

Differences

- Grooves on rod: 2mm (UB) vs 1 mm (TSE)
- Divisions between lanes: Rotating (UB) vs fixed (TSE)
- Noise: only present with TSE

Accelerating protocol

- 5-45 rpm over 300 s
- 4 trials/day for 3 days
- Parameter analysed: latency to fall

Statistics

Two-way ANOVA ($\alpha = 0.05$) and Bonferroni post hoc test in GraphPad Prism version 5.04.

Results

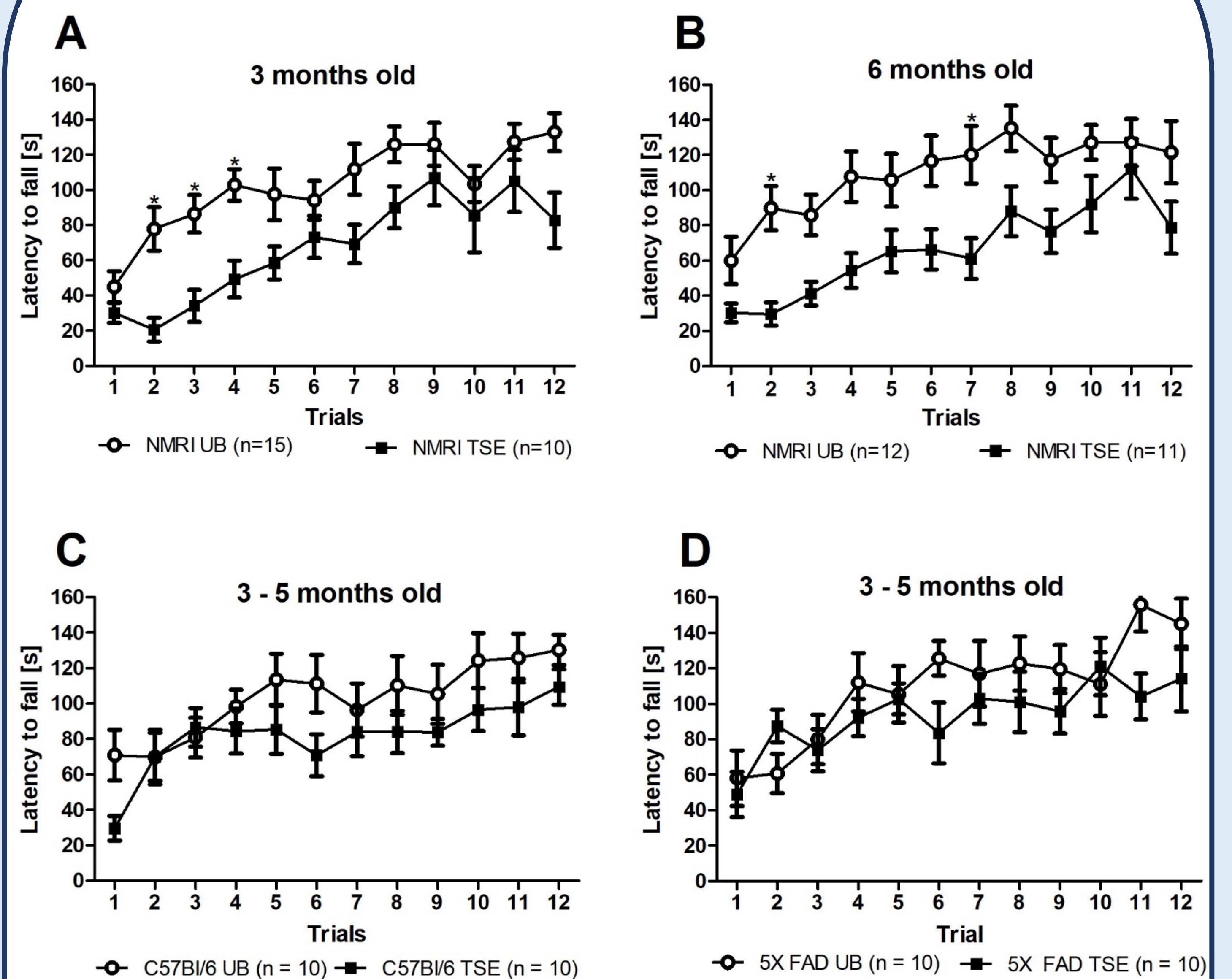


Figure 1: Comparison of Ugo Basile and TSE RotaRod results per strain. (A) A significant main effect of rod ($p = 0.0013$) was found for 3 month old NMRI mice. (B) A similar significant main effect of rod ($p = 0.0002$) was found for 6 month old NMRI mice. (C) C57bl/6 mice of 3 to 5 months old also showed a significant effect of rod ($p = 0.0377$). (D) No significant effect of rod ($p = 0.1776$) was found for the 5x FAD mice (3-5 months old).

- Significant effect of Rod was found for both NMRI and the C57Bl/6 mice but not for the 5x FAD mice
- Performance on TSE RotaRod was lower than on UB
- All animals have similar learning curves on both rods
- Effect is independent of age

Discussion

- Motor coordination, but not motor learning is affected by small differences in RotaRod hardware.
- Can have significant effects on studies using new transgenic models and/or new drugs
- Phenotypes may be overlooked when task is too simple
- Efficacy of drugs may not show if task is too difficult
- Reproducibility of earlier findings may become difficult when changing to newer versions or different manufacturer

References

- Mann, A., & Chesselet, M.-F. (2015) Chapter 8 - Techniques for Motor Assessment in Rodents in LeDoux, M. S. *Movement Disorders (Second Edition)* (pp. 139–157). Boston: Academic Press.
- Rustay, N.R., Wahlsten, D., Crabbe, J.C. (2003). Influence of task parameters on rotarod performance and sensitivity to ethanol in mice. *Behavioural Brain Research*, 141: 237-249.