

## **Genetic differences of exploratory and learning behavior reproduce reliably across labs and cohorts in mice housed under enriched conditions**

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Standard animal housing conditions as typically used in biomedical research impose constraints on behavior that alter brain function and may question the validity of conclusions drawn from behavioral experiments. Enriched housing could solve this problem but is suspected to increase variability and to reduce the reliability of results. To address this question, we tested 432 mice in a multi-lab study. DBA/2 and C57BL/6 mice and their F1 cross were compared in tests of exploratory behavior and anxiety (open-field, O-maze, object exploration) as well as in a water-maze place navigation task. Each of three labs (Anatomy Zurich, Psychiatric Research Zurich, Animal Welfare Giessen) tested three cohorts of mice using standardized procedures. In each lab, one half of the mice was housed under standard conditions, the other in enriched cages.

Marked strain differences were observed in all tests. Strain ranking was stable across labs in all tests despite some variation of effect sizes. Enriched housing did not alter the strain ranking, nor did it reduce reproducibility across labs and cohorts. In absence of increased within group variability, enriched animals displayed improved exploratory activity and better physical performance in the water-maze. We conclude that the employed behavioral procedures allow reliable detection of genetic differences by different labs and teams and that the reliability of results is not negatively affected by enriched housing. Further, our results show that the analysis of exploratory behavior benefits from enriched housing, in particular in strains with low base-line activity.

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