Reliable detection of strain differences and enrichment effects by different teams and labs using the same procedures to assess exploratory behavior and learning in mice

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The reliability of behavioral testing of mice has recently been questioned, especially in the domain of exploratory behavior. Because reliable detection of genetic differences across labs is essential for behavioral phenotyping, we have run a multi-lab study involving 431 mice. We compared DBA/2 and C57BL/6 mice and their F1 cross in tests of exploratory activity and anxiety (O-maze, open-field, novel object test) and in a water-maze place navigation task. Different teams used identical procedures in three labs (Anatomy Zurich, Psychiatric Research Zurich, Animal Welfare Giessen). Each lab tested three cohorts. In each one half of mice was housed under standard conditions, the other in enriched cages.

As expected, the mouse strains showed marked performance differences in all tests and their relative ranking varied between tests. Within each exploration test as well as in the place navigation task, strain ranking was well reproduced across labs despite some variation of the magnitude of the differences. In all labs and independently of strain, enriched housing enhanced exploratory activity in the test arenas, but did not improve performance in the place navigation task. The rank order of strains was not affected by the housing conditions in any of the tests. Effects of strain and housing accounted for up to 40% of variance in the data, while the contribution of lab interactions remained mostly below 5% in both enriched and non-enriched conditions. Consistent detection of small strain differences was limited by within group variability rather than lab effects or interactions.

We conclude that the employed behavioral procedures allow reliable detection of genetic differences by different labs and teams, provided that sample sizes are large enough and statistics interpreted carefully. The analysis of exploratory behavior is likely to benefit from enriched housing, in particular in strains with low base-line activity.

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