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Animal personality and the reproducibility crisis: Addressing unexplained variation in preclinical animal research

The reproducibility crisis has shifted research focus toward improving the methodological integrity of animal experiments. Contributing factors to replication failure are being addressed, prompting the reassessment of fundamental methodological principles. For instance, rigorous standardization may restrict inference space and compromise external validity. To counter this, heterogenization strategies have been developed, systematically introducing variation to increase the representativeness of the sample, thus enhancing reproducibility. This involves adding variance sources, common experimental factors that may influence the outcome measure but are not of primary interest, such as the batch effect and testing time. While these factors account for some of the total variation, a significant proportion remains unexplained. We propose that this unexplained variation in animal experiments may be attributed –at least partly - to animal personality, widely used in evolutionary biology to describe individual differences in behavior that are consistent across time/or context. Moreover, we hypothesize that controlling for personality in an experimental design would improve reproducibility. Through a series of experiments, we aim to explore stable personality traits in laboratory mice and develop predictive marker tests for efficient trait quantification - an essential step for integrating personality in an experimental design - (e.g., boldness, explorativeness). Using a balanced design, mice of two strains first undergo predictive marker tests followed by a battery of classic behavioral tests to assess personality. Each test sequence is repeated three times with a 3-week interval between rounds, allowing for evaluation of repeatability – the proportion of the observed variance that attributable to individual differences. To capture different variance sources, our design incorporates experimental factors such as the batch, strain, cage and housing enrichment. Our goal is to break down various sources of variance that influence outcome measures, determine the role of animal personality in residual variance, and evaluate whether its inclusion in the experimental design enhances reproducibility.

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