INCREASING ANIMAL WELFARE AND RELIABILITY OF RESULTS FROM PRECLINICAL TRIALS AND ANIMAL STUDIES: ZOOMING IN ON VARIATION IN ADAPTIVE RESPONSE PATTERNS WITHIN AND BETWEEN THREE INBRED MOUSE STRAINS

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Inter-individual differences in behavioral response in mouse inbred strains are often written off as unfortunate noise. We suggest that part of this variation may provide useful information on variation in adaptive capacities in response to aversive or positive stimuli. More insight in these capacities ensures more accurate assessment of which individuals are at risk for compromised welfare. At the same time, on a more fundamental experimental level, capturing part of this variation may better control for confounding variables and thus improve reliability of preclinical results.

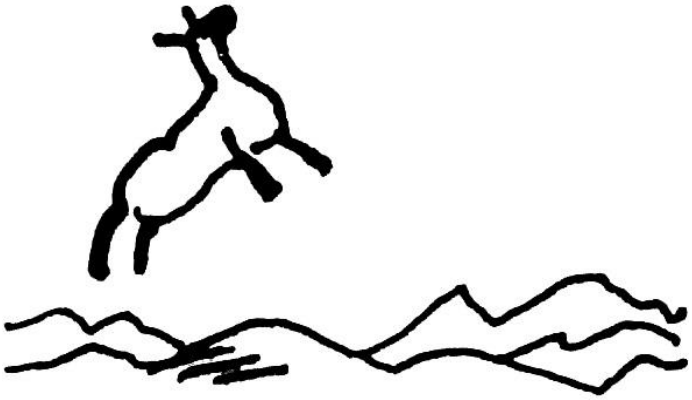
In order to do so we have developed a method that allows for the assessment of temporal behavioral response curves on an individual level. Our approach follows the dynamic concept of animal welfare that states that an animal is likely in a positive welfare state when it is capable and able to react appropriately (i.e. adaptively) to the demands of the environmental circumstances, enabling it to reach a state that it perceives as positive. This view implies that in order to assess which individuals are able to adapt one should measure the temporal progression of a response, alongside the magnitude of that response.

We assessed the level of inter-individual variability in adaptive capacities to an aversive stimulus in three commonly used mouse inbred strains by testing male BALB/cAnNCrl, C57BL/6NCrl and 129S2/SvPasCrl mice [N = 40 per strain] for four consecutive 5-minute trials in an initially unknown environment [the modified Hole Board]. Adaptive capacities were assessed by behavioral responses and corticosterone levels.

For analysis, behavioral responses were summarized in composite variables representing underlying behavioral dimensions: anxiety, avoidance behavior, locomotion, arousal and exploration. Scores on these behavioral dimensions were combined with corticosterone levels for each individual, resulting in six trajectories per mouse. Multivariate approaches subsequently explored whether it was possible to 1. identify homogenous subgroups of individuals that show the same response over time within a single dimension, and 2. Identify response types: subgroups of individuals that consistently group together across multiple dimensions.

The results showed that mice indeed grouped together across multiple dimensions: the analyses yielded two response types of different adaptive value. Interestingly, these types were displayed by individuals of all three strains. Also, some strains showed greater within strain variability than others. We are currently elaborating on these findings in a follow-up experiment that explores whether taking this variation into account indeed increases reliability of results in preclinical trials and animal studies.

Advancing Animal Welfare Science: How Do We Get There? – Who Is It Good For?



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