

# The Difference is Droll – Towards a Cognitive Bias Test in Mice

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The quote from Oscar Wilde "The difference is droll /The optimist sees the doughnut /The pessimist, the hole" reflects the fact that that information processing is biased. The term 'cognitive bias' refers to such altered information processing resulting from an individual's background emotional state. Comparable to anxious or depressed humans, animals in a putatively negative emotional state are more likely to judge an ambiguous stimulus as if it predicts a negative event, while animals in a putatively positive emotional state are more likely to judge the same stimulus as if it predicts a positive event. By now, a number of different animal species have been demonstrated to judge ambiguous stimuli dependent upon their proposed emotional state. Thus, tests for cognitive bias have been suggested as a promising new indicator of animal emotion. Mice, including transgenic and knockout lines have become the most widely used species in biomedical research. To date, however, there are no reliable tasks for testing cognitive bias in mice that use reinforcers other than food and therefore would avoid confounding food motivation effects.

In the present study we aimed at establishing a cognitive bias test for mice using different approaches including spatial judgment as well as optical and tactile stimuli. We validated that our set-up can indeed assess different expectations about the outcome related to an ambiguous stimulus: mice having learned to expect something positive within a maze showed a more positive judgment of an unfamiliar location than animals having learned to expect something negative. In a second step, the use of spatial location as discriminatory stimulus was confirmed by showing that the mice's interpretation of an ambiguous stimulus depended on its spatial location, with a position exactly midway between a positive and a negative reference point provoking the highest level of ambiguity. Furthermore, in a pilot study we applied a spatial cognitive bias task to serotonin transporter (5-HTT) knockout mice, a well-established mouse model for the study of anxiety- and depression-related behavior. The anxiety- and depression-like phenotype of the 5-HTT knockout mouse model manifested - comparable to human conditions - also in a trend for a negative distorted interpretation of ambiguous information, albeit this effect was not statistical significant. The results suggest that the present cognitive bias test provides a useful basis to study the emotional state in mice, which may not only increase the translational value of animal models in the study of human affective disorders, but which is also a central objective of animal welfare research.

## Ethical statement

The present work complies with current regulations covering animal experimentation in Germany and the EU (European Communities Council Directive 2010/63/EU). Experiments were announced to the local authorities and were approved by the Universities' 'Animal Welfare Officers' .