

Do Outbred ICR:CD1 Mice Form Attentional Sets in a Bait Digging Attentional Set-Shifting Procedure?

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In order to analyze prefrontal function after pharmacological treatments, we wanted to use an attentional set shifting test for the outbred albino ICR:CD1 mice. The attentional set shifting test is successfully used in rats, and recently also in mice, although there has been controversy whether the mice can form attentional sets. Also, the methods used for mice vary a lot between laboratories. Here, we used a food bait digging procedure described for the rats [1] and later adapted for the C57Bl/6J mice [2].

In our procedure, the adult male ICR:CD1 mice (Harlan) were food restricted to 85-90% of their normal weight, habituated to testing arenas and trained to dig scented materials in cups before receiving a bait. During the testing phase, the mice were trained to receive the bait by digging materials in a correct cup based on cue which was either digging material (tactile, visual cue) or odor (olfactory cue) added in the materials. Thus, the bait was not hidden but given after a correct choice. The procedure consisted tasks of simple discrimination (day 1), compound discrimination and compound discrimination reversal (day 2), intradimensional shifts 1-5 (day 3-5) and intradimensional shift 6 and an extradimensional shift (day 6). The procedure took 6 days to perform, each day started with a repetition of the last stage of the previous day. A criterion to pass each stage was 8 out of 10 and last 6 consecutively correct choices. If the mouse did not complete stages of one day within 60 min or if the latency to make a choice was longer than 3 minutes, it was returned to home cage at least for one hour. The animal experimentation was approved by Animal Experiment Board of the Regional State Administrative Agency for Southern Finland.

The ICR mice could perform the discrimination tasks, and as expected the reversal task required significantly more trials than the preceding compound discrimination. We found intradimensional shifts easier when odors were used as relevant cues compared to material cues. Consistently, an extradimensional shift from odor to material was more difficult than the preceding intradimensional shift, while this was not the case for the extradimensional shift from material to odor.

Currently, we are testing for conditions to refine the protocol in order to be able to use the ICR:CD1 mice in pharmacological studies in this test measuring cognitive flexibility. As a conclusion, this test may be useful to analyze mouse prefrontal function. However, it is time consuming and a low throughput method limiting its applicability.

References

1. Birrell, J.M., Brown, V.J. (2000). Medial frontal cortex mediates perceptual attentional set shifting in the rat. *Journal of Neuroscience* **20**, 4320-4324.
2. Bissonette, G.B., Martins, G. J., Franz, T.M., Harper, E.S., Schoenbaum, G., Powell, E.M. (2008). Double dissociations of the medial and orbital prefrontal cortical lesions on attentional and affective shift in mice. *Journal of Neuroscience* **28**, 11124-11130.