The Touchscreen Cognitive Testing Method for Mice and Rats

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Overview

What are the characteristics of the ideal rodent cognitive testing method? In my talk I will suggest the following, which I put forward in a recent publication in a special issue of *Neuropharmacology* (Bussey *et al*., 2011).

"i. It should be automated

Notwithstanding some unique arguments to the contrary (Crabbe and Morris, 2004), most researchers agree that the same type of automation that has paid such dividends in areas like molecular biology is desirable for cognitive testing as well. Certainly the cognitive testing of clinical populations is becoming increasingly automated (e.g., the Cambridge Neuropsychological Test Automated Battery (CANTAB), CogState, Mindstreams), and so automation may help to achieve another desirable: effective translation (discussed in more detail below). But automation of cognitive testing in animal models confers advantages of its own; perhaps the most obvious to researchers 'on the ground' is a reduction in labour: while one experimenter is testing a single mouse in a maze, an experimenter armed with automated apparatus can test many mice simultaneously. Post-docs working in our lab, for example, routinely test 20 animals at a time, adding up to between 1 and 2 hundred a day. This realization negates the argument that some automated tests take more sessions to generate a result, as such tests would have to be 20 times slower before the equivalent non-automated testing methods start to make any time-economical sense. But it is the scientific arguments for automation that are perhaps the most compelling. With an automated test the computer can present many trials to an animal without having to interfere with the animal during testing. Such interference can have a huge effect, not just by introducing variability into the way the task is run, but also by introducing variability and potential confounds relating to the way the experimenter handles the animals, or even the sight or smell of the experimenter (Wahlsten et al., 2003). Finally, because automated tasks are controlled by a computer, parameters such as delays and stimulus presentation are identical on every trial, for every animal, and the measures the computer gets back from the animal, for example latencies, can be accurate to the millisecond. All this adds up to a method that is much more likely to be reliable than non-automated methods.

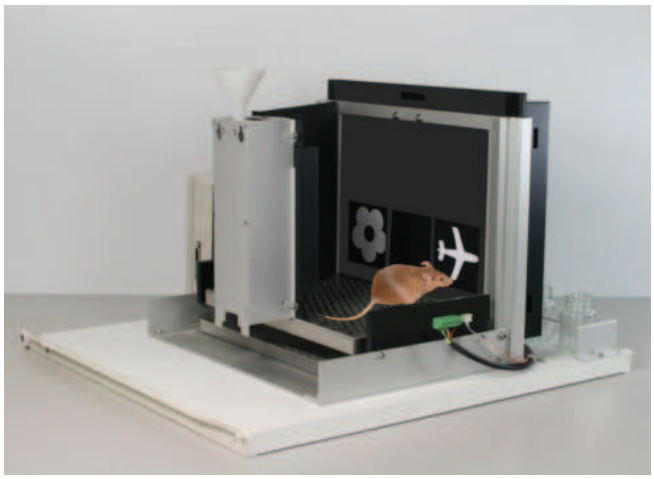

Figure 1. Touchscreen testing setup.

ii. It should be non-aversive and low-stress

Although some animal models, including those of schizophrenia, utilize stress as a manipulation, unnecessary stress as a feature of a cognitive test is best avoided. Everyone knows that stress can interfere with our experimental manipulations, and can have strong modulatory effects on cognition (Joels and Baram, 2009). Unwanted stress can therefore be a major impediment to the accurate assessment of cognition. Yet some of the most popular methods for cognitive testing involve cold water or electric shock. Such unwanted stressors are best avoided if possible, and so we would suggest that the ideal cognitive testing method should if possible be appetitive (reward-based) rather than aversive. Of course the use of appetitive reinforcers is not always problem-free either; some perturbations in experimental animals can affect animals' motivation to perform vigorously to obtain reward. However appetitive reinforcers themselves generally have a less potentially confounding effect on the organism than stressors.

iii. It should assess multiple cognitive domains

Currently we often assess an animal's memory in, say, a pool of water, its ability to extinguish a learned association using, say, foot shock, and its attentional capacities using, say, an operant chamber. Then we try to compare across these tests. Obviously there are difficulties with this approach. Ideally we would be able to investigate all of these aspects of cognition under the same conditions -- in the same apparatus, using the same types of stimuli, and the same rewards and responses. We can then employ a 'battery' of tests to establish a cognitive profile of an animal, in conditions under which the tests can be compared in a less confounded manner.

iv. It should be translational

The goal of all of this is of course translation, from mouse to clinic. Currently the tests we use in animals are usually nothing like the tests we use in clinical populations; some of the test mentioned above provide good examples of this disconnect. In order to translate effectively our findings from animals to humans, the tasks ideally would be as similar as possible. Such 'face validity' does not guarantee construct or predictive validity – further experimentation is needed to do that – but it makes these types of validity, and effective translation, much more likely than when the tests appear on the face of them to have little in common."

In my talk I will describe one method – the touchscreen testing method -- which I and others have been working on for about 20 years now, which we think satisfies this list of desirables and could prove to be very valuable in the cognitive testing of rodent models. I describe that method generally, before describing some of the tests that are currently implemented and providing some examples of how these tests can be used. These tests can be used as part of a 'flexible battery' approach for the cognitive profiling of rodent models.

References

1. Bussey, T.J., Holmes, A., Lyon, L., Mar, A.C., McAllister, K.A.L., Nithianantharajah, J., Oomen, C.A. & Saksida, L.M. (2011) New translational assays for preclinical modelling of cognition in schizophrenia: the touchscreen testing method for mice and rats. *Neuropharmacology,* **62**, 1191-1203.
2. Crabbe, J.C., Morris, R.G. (2004). Festina lente: late-night thoughts on high-throughput screening of mouse behavior. *Nat Neurosci* **7**, 1175-1179.
3. Joels, M., Baram, T.Z. (2009). The neuro-symphony of stress. *Nat Rev Neurosci* **10**, 459-466.
4. Wahlsten, D., Metten, P., Phillips, T.J., Boehm, S. L., 2nd, Burkhart-Kasch, S., Dorow, J., Doerksen, S., Downing, C., Fogarty, J., Rodd-Henricks, K., Hen, R., McKinnon, C.S., Merrill, C.M., Nolte, C., Schalomon, M., Schlumbohm, J.P., Sibert, J.R., Wenger, C.D., Dudek, B. C., Crabbe, J.C. (2003). Different data from different labs: lessons from studies of gene-environment interaction. *J Neurobiol* **54**, 283-311.