Reversal Learning Task

What is it?

Reversal learning (RL) task is a two-phase cognitive paradigm that assesses cognitive flexibility dependent on problem solving and reasoning. The task challenges cognitive flexibility by forcing the rat to switch from a previously rewarded rule to an opposite one which used to be irrelevant. Cognitive flexibility, and its underlying pathways of problem solving and reasoning, are commonly impaired domains in a wide range of central nervous system (CNS) disorders. Hence, the RL task is widely used for investigating cognitive deficits in rat models relevant to a variety of human CNS disorders.

How does it work?

Following habituation and an initial training on associating a lever press with getting a food reward, the rats are trained to respond to two opposite rule contingencies with no particular order (i.e. half of the rats start training with one rule contingency, and the remaining half with the other contingency to avoid any bias). These two rules are:

1) The cue light above the ***active*** lever is lit shortly every time the levers are introduced.
2) The cue light above the ***inactive*** lever is lit shortly every time the levers are introduced.

During this stage of training, the active lever randomly varies from one training day to the other (between left and the right lever), but the rule contingency stays the same until the rats successfully complete their training and move onto learning the opposite rule contingency. After the rats meet the necessary criteria in their response to both rule contingencies, the RL test is introduced.

The RL task consists of two phases with a time-out period in between. The rats complete a training session with a randomly chosen rule contingency the day prior to the testing. On the test day, the rats are placed into the operant chambers and the first phase starts with the same rule contingency and the same active lever as the previous day's training. This is called the **initial phase**, and it lasts for 5 minutes. Following this, the rats stay in the operant chambers, with no levers to press, for 2 minutes called the time-out period. The second phase of the task begins after the time-out; this is the **reversal phase**, and it consists of the opposite rule contingency with the opposite lever being active (e.g. if in the initial phase the right lever was active with the right cue light flashing, then in the reversal phase it will be the left lever active with right cue light flashing). The reversal phase also runs for 5 minutes, after which the rats return back to their home cages. This test is repeated (~4-6 times) to obtain a stabilised performance prior to any drug treatments.

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Two types of data collected from the RL task are percent correct responding values and total number of lever presses in each phase. The mean percent correct responding of rats in both the initial and the reversal phases of the task are measured and reflect cognitive flexibility. The mean total number of lever presses is measured for both phases, and is used as a measure of motor activity, to ensure that any effects seen in the percent correct responding data are not due to an effect on motivation and/or motor activity that could be affecting the number of lever presses.

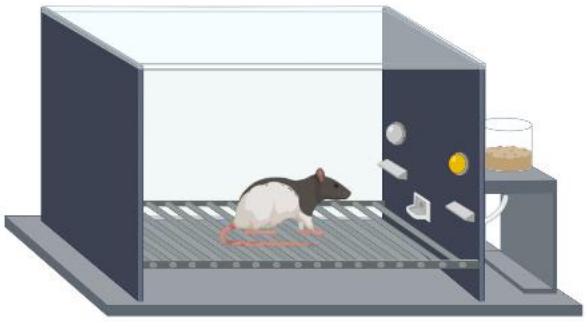

Figure 1: Reversal learning operant chamber.

The effect of subchronic Phencyclidine (scPCP) in the Reversal Learning test

The b-neuro laboratory has demonstrated a selective, long lasting and robust deficit in this task induced following the scPCP treatment regimen. The deficit is only observed in the reversal phase of the task, where scPCP treated rats obtain a significantly lower percent correct responding data compared to the vehicle treated rats. The percent correct responding in the initial phase is not affected by scPCP treatment. The mean total number of lever presses in both phases of the task also do not show a change following scPCP administration. Therefore, the decrease in percent correct responding observed within the reversal phase in scPCP treated rats can represent a selective deficit in switching from a previously rewarded rule contingency to the opposite one, with no apparent effects on motivation and/or motor activity.

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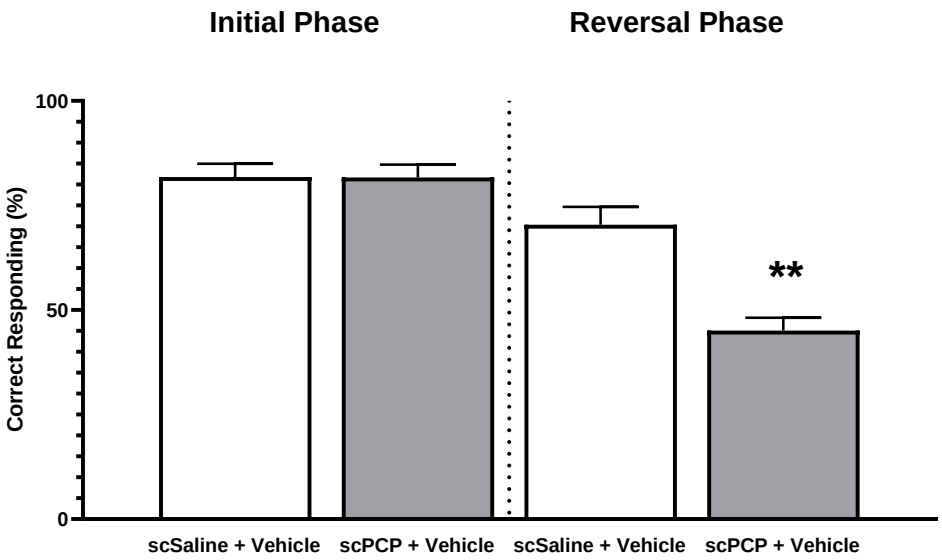

Figure 2: The effect of scPCP treatment (2 mg/kg, i.p. twice daily for seven days, followed by at least a 7-day washout period) on performance in the reversal learning task. The dashed line separates the initial phase (left) from the reversal phase of the task (right).

Reversal of the scPCP RL deficit by a reference compound

At b-neuro we have demonstrated the ability of a range of compounds in this paradigm. Reproducibility and validation data can be shared upon request. We work with clients to pick the most relevant reference compound.

For further information, please see review articles below.

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Cadinu D, Grayson B, Podda G, Harte MK, Doostdar N, Neill JC (2017) NMDA receptor antagonist rodent models for cognition in schizophrenia and identification of novel drug treatments, an update. Neuropharmacology; S0028-3908(17)30584-1.

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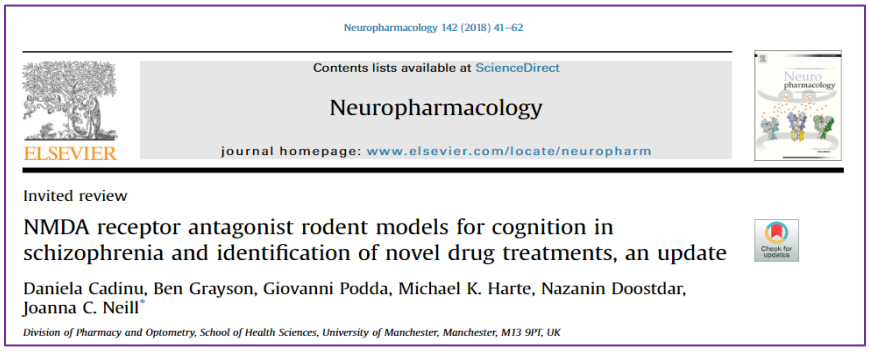

Neuropharmacology 142 (2018) 41–62

Contents lists available at ScienceDirect

Neuropharmacology

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Invited review

NMDA receptor antagonist rodent models for cognition in schizophrenia and identification of novel drug treatments, an update

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Neill, JC, Barnes, S, Cook, S, Grayson, B, Idris, NF, McLean, SL, Snigdha S, Rajagopal, L, Harte, MK. (2010) Animal models of cognitive dysfunction and negative symptoms of schizophrenia: focus on NMDA receptor antagonism. Pharmacology and Therapeutics, 128(3):419-32.

Pharmacology & Therapeutics 128 (2010) 419–432

Contents lists available at ScienceDirect

Pharmacology & Therapeutics

journal homepage: www.elsevier.com/locate/pharmthera

Associate Editor: F. Tarazi

Animal models of cognitive dysfunction and negative symptoms of schizophrenia: Focus on NMDA receptor antagonism

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