

Attentional Set Shifting Task

What is it?

The attentional set-shifting task is a cognitive test used to assess a rat's cognitive flexibility – the ability to adapt to changing rules by inhibiting previously relevant information and shifting attention to newly relevant information. This is a core feature of executive function and is often diminished in conditions such as schizophrenia and other CNS disorders. Across a series of trials, the rat learns and responds to different rules to obtain a food reward buried in a bowl of media. These rules can relate to one of two dimensions: the type of media (e.g., sawdust vs sand) or type of odour (e.g., mint vs caramel). As rules change, the rat must adjust its focus and mental strategies according to the relevant dimension.

How does it work?

Starting one week prior to the task, rats are mildly food restricted to maintain motivation to dig for food rewards. The attentional set-shifting task is conducted over two consecutive days: training, followed by testing.

Training

The rat learns to discriminate between two media types over several trials. Next, the rat learns to discriminate between two odours. In each case, the rat is deemed successful (reached criterion) and ready to progress to the next stage when they dig in the correct bowl in 6 consecutive trials.

Testing

Twenty-four hours after training, rats are tested (Figure 1). Testing consists of 7 different 'sets', and as before, the rat must reach criterion in one set before it can pass to the next (Figure 2). Throughout the task and for each set, the number of trials to reach criterion is used as a measure of cognitive performance.

Starting with media type as relevant dimension, the rat progresses through simple discrimination (medium 1 vs medium 2), compound discrimination (medium 1 vs medium 2, with the media being anointed with 'distractor' odours, which should be ignored by the rat), and reversal 1 (medium 1 vs medium 2, but rewarded media is switched), intra-dimensional shift (media 3 vs media 4), and reversal 2 (again, the rewarded media is switched). In the next set, referred to as the extra-dimensional shift, a new pair of media is introduced, and the relevant dimension becomes odour instead of media type. This is a particularly challenging set, requiring a high degree of cognitive flexibility (Figure 3). The final set is reversal 3 (rewarded odour is switched).

Attentional Set Shifting Task

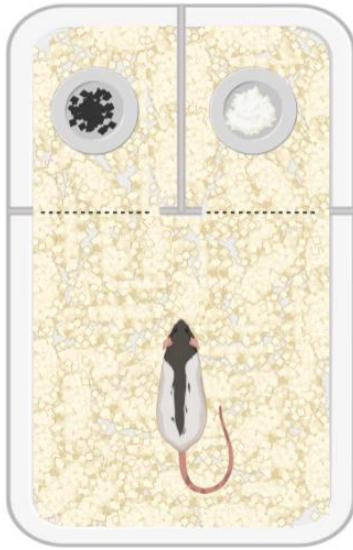


Figure 1: Attentional set-shifting task arena. Before each trial, the rat is placed in the main compartment, and one bowl is placed in each minor compartment. Depending on the current set, the bowl pair will have a combination of media type and odours, and one bowl will be rewarded while the other is not. Dotted lines represent dividing panels which are simultaneously lifted at the beginning of a test trial.

Discriminations	Dimensions		Exemplar combinations	
	Relevant	Irrelevant	Rewarded	Unrewarded
SD	Medium		M1	M2
CD	Medium	Odour	M1/O1	M2/O1
			M1/O2	M2/O2
Rev1	Medium	Odour	M2/O1	M1/O1
			M2/O2	M1/O2
IDS	Medium	Odour	M3/O3	M4/O3
			M3/O4	M4/O4
Rev2	Medium	Odour	M4/O3	M3/O3
			M4/O4	M3/O4
EDS	Odour	Medium	O5/M5	O6/M5
			O5/M6	O6/M6
Rev3	Odour	Medium	O6/M5	O5/M5
			O6/M6	O5/M6

Figure 2: Attentional set-shifting task table, detailing the relevant dimension (medium or odour) and the contents of each bowl according to set.

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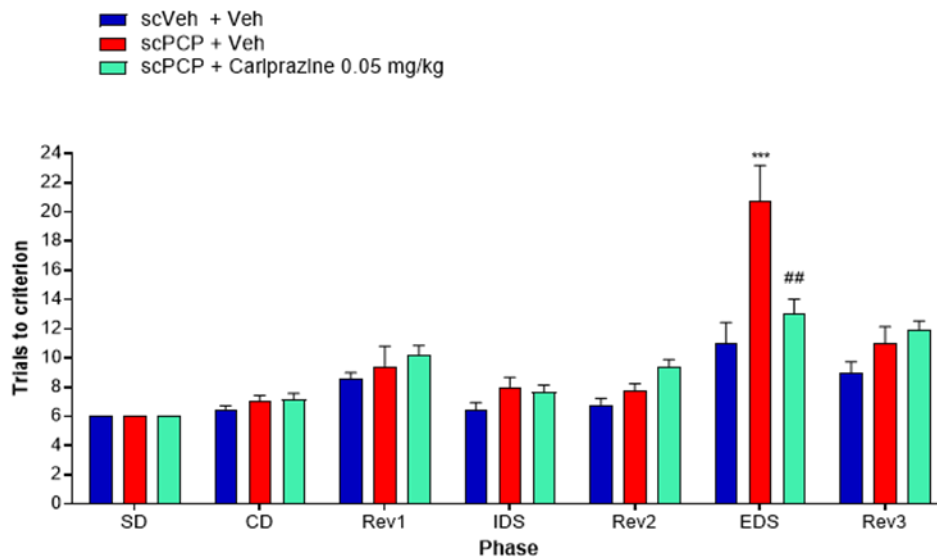



Figure 3: Exemplar attentional set-shifting task results. Sub-chronic PCP treated rats (red bars) took significantly more trials to reach criterion in EDS compared to scVeh (blue bars), owing to the reduced cognitive flexibility seen in these rats. Acute treatment with cariprazine (green bars) reversed the scPCP induced deficits, with these rats having a significant reduction in the number of trials to reach criterion in the EDS compared to scPCP treated animals. *** $P < 0.001$ = significant increase in trials to criterion compared to scVeh; ## $P < 0.01$ = significant decrease in trials to criterion compared to scPCP.

For further information, please see review articles below.

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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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.

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

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