Effects of lesions of the nucleus accumbens core and shell on response-specific Pavlovian–instrumental transfer

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Abstract. When an initially neutral stimulus has been paired in Pavlovian fashion with an appetitive outcome such as food, noncontingent presentation of this conditioned stimulus (CS) can enhance ongoing instrumental responding, a phenomenon termed Pavlovian–instrumental transfer (PIT). In its simplest form, PIT is assessed by presenting a CS for food while the subject is responding in extinction on a single lever for the same food. It has previously been shown that the nucleus accumbens, and particularly the core subdivision, is critical for this form of PIT (Hall *et al*., 1999, *Soc. Neuro. Abstr.* 25, P41.2). However, behavioural studies have shown that PIT can be subdivided into a general, motivating effect of the Pavlovian CS, and a response-specific PIT effect, seen as a further enhancement when the Pavlovian and instrumental outcomes are the same (see Dickinson & Balleine, 1994, *Anim. L. Behav.*, 22, 1–18). In the present study, rats received lesions to the core or shell of the nucleus accumbens before being tested on a response-specific PIT task. In the Pavlovian phase, stimulus CS(pel) was paired with pellet delivery, while stimulus CS(suc) was paired with sucrose solution. The subjects were then trained to respond on two levers, with one lever producing pellets and the other producing sucrose. On test, lever-pressing was recorded in extinction while the stimuli were presented noncontingently. Sham-operated subjects (n = 6) showed a selective enhancement of lever-pressing on the lever paired with the same outcome as the Pavlovian CS; this is the response-specific PIT effect. Core-lesioned subjects (n = 4) showed a general enhancement of responding during the CS, but this was not specific to one response. Shell-lesioned animals (n = 4) showed no Pavlovian–instrumental transfer. It is suggested that in this task, the shell is required for the ‘vigour’ and the core for the ‘direction’ of the potentiation of responding by a noncontingent, appetitive stimulus. This pattern closely resembles that previously observed for the potentiation of responding for conditioned reinforcement by psychostimulant drugs injected into the nucleus accumbens (Parkinson et al., 1999, *J. Neurosci.*, 19, 2401–11).

Introduction

- A conditioned stimulus (CS) that has been paired with an appetitive outcome, such as food, can invigorate ongoing instrumental behaviour. This phenomenon is termed **Pavlovian–instrumental transfer (PIT)** (Lovibond, 1983). A simple experimental design is as follows:

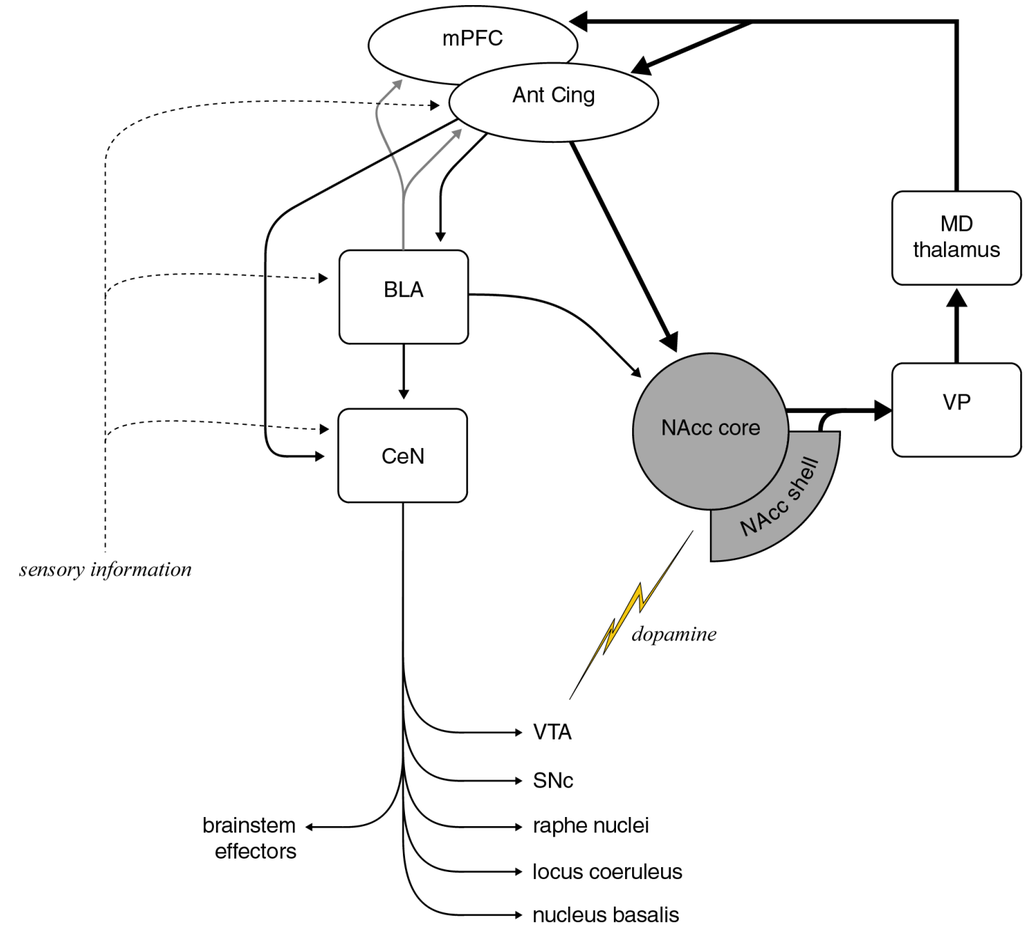
Pavlovian	Instrumental	Transfer test
CS ? food	lever ? food	lever ± CS

- However, PIT has been shown to have at least two components (Dickinson & Balleine, 1994; Dickinson, 1994). The first is a **general, motivating effect** of the CS, in which an appetitive CS can 'boost' instrumental responding, regardless of the outcome of the instrumental response (Dickinson & Dawson, 1987b; Balleine, 1994). The second is a **response-specific effect,** in which the CS further enhances responding if the instrumental outcome is the same as the Pavlovian outcome predicted by the CS (Colwill & Rescorla, 1988).

- It has previously been shown that 'simple' PIT can be impaired by lesions of the nucleus accumbens (de Borchgrave, 1995), or its core subdivision (Hall et al., 1999). However, these studies did not determine whether the 'general' or 'response-specific' components of PIT had been impaired.

- In the present study, therefore, rats with lesions of the core or shell of the nucleus accumbens were trained in a 'response-specific' PIT task. The design is shown below. If response-specific PIT occurs during the transfer test, the CSs will enhance responding selectively on the lever paired with the *same* outcomes.

Pavlovian	Instrumental	Transfer test
CS_1 ? sucrose	$lever_1$? sucrose	$lever_1$ } ± {CS_1
CS_2 ? pellet	$lever_2$? pellet	$lever_2$ } {CS_2



A simplified schematic of part of the 'limbic loop' of the basal ganglia. (*Abbreviations: NAcc – nucleus accumbens; Ant Cing – anterior cingulate cortex; mPFC – medial prefrontal cortex; BLA – basolateral amygdala; CeN – central nucleus of the amygdala; VTA – ventral tegmental area; VP – ventral pallidum.*)

Methods

Subjects and surgery

- Subjects were male hooded Lister rats maintained at 85% of their free-feeding mass.
- They received lesions of the **nucleus accumbens core** (0.09 M quinolinic acid, injected at coordinates AP +1.2 mm, ML ± 1.8, DV –7.1 from skull surface, 0.5 µl per side), the **nucleus accumbens shell** (0.06 M ibotenic acid, injected at three sites, all at AP +1.6, ML ± 1.1, with 0.1 µl at DV –6.4, 0.1 µl at DV –6.9, and 0.2 µl at DV –7.9 relative to skull surface), or **sham** operations.

Behavioural procedure

The task was conducted in standard operant chambers, and involved

- two **reinforcers** (0.05 ml of 20% w/v sucrose solution, and one 45-mg chow pellet);
- two **conditioned stimuli** (lights flashing at 3 Hz, and a clicker operated at 10 Hz);
- two **responses** (left and right levers)

Pavlovian (stimulus/outcome) and instrumental (response/outcome) assignments were counterbalanced.

Phase 1: Pavlovian training. The two stimuli were presented in alternation for 2 min each, separated by a 2-min interstimulus interval. During one stimulus, sucrose was delivered on a random time (RT) 30-s schedule. During the other stimulus, pellets were delivered on an RT 30-s schedule. Five presentations of each stimuli were given in one session. Subjects were trained for 10 sessions.

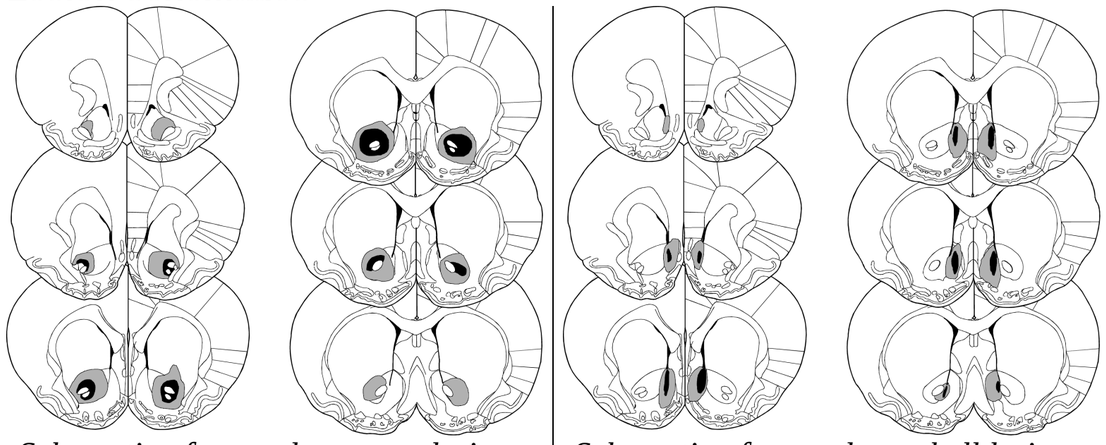
Phase 2: Instrumental training. For six 30-min sessions, animals were presented with a single lever that was reinforced on an RI schedule. No other stimuli were present. Subjects were given the left lever on one day, the right lever on the next, and so on. One lever was consistently reinforced with sucrose; the other with pellets. The parameter of the RI schedule was 2 s for the first pair of sessions, 15 s for the second and 30 s for the third. For a further four sessions, both levers were present and reinforced on independent RI-30s schedules. All sessions began with the insertion of the lever(s) and ended with lever retraction.

Phase 3: Pavlovian reminder. One reminder Pavlovian session was given, using the same schedule as Phase 1.

Phase 4: Instrumental extinction. One 8-min session was given in which both levers were available but not reinforced.

Phase 5: Specific transfer test. The transfer test was conducted in extinction, with both levers present but not reinforced. Two-minute light and clicker stimuli occurred in alternation, with a 2-min interstimulus interval between each, until five of both stimuli had been presented. Two test sessions were given.

Lesion schematics



Schematic of accumbens core lesions. *Schematic of accumbens shell lesions.*

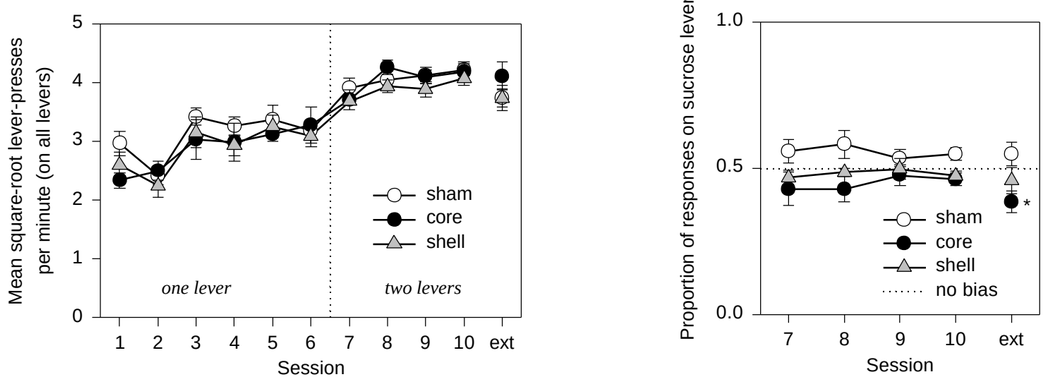
Results

Histology

- Following histological analysis, group sizes were 6 (sham), 4 (core), 4 (shell).

Training

- The groups did not differ in their approach to the food magazine during Pavlovian conditioning.
- Instrumental responding was acquired at the same rate in both groups, though the core group showed a slight preference for the lever producing pellets on the extinction day:

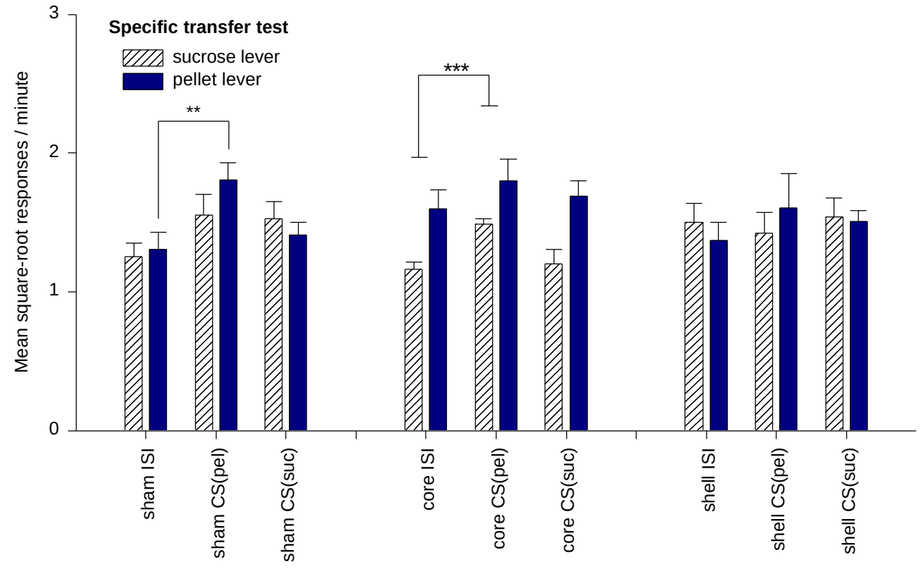


Acquisition of instrumental responding. ***Left:*** *Responses per minute, summed over all levers present. The session length was 30 min; the schedule progressed from RI-2s to RI-30s as described in the Methods. From session 7 onwards, two levers were concurrently available; ext indicates the extinction session.* ***Right:*** *Proportion of responses made on the sucrose lever (* p < .05 relative to shams on the extinction day).*

Transfer test

- Across all groups, the CS paired with pellets was more effective at elevating responding than the CS paired with sucrose.
- The groups differed in their response to the stimuli (significant group × stimulus × lever interaction by analysis of variance, $p = .018$).

- **Sham-operated subjects showed *specific* Pavlovian–instrumental transfer.** The CS paired with pellets selectively elevated responding on the lever trained with the same (pellet) outcome ($p = .007$).
- **Core-lesioned subjects showed Pavlovian–instrumental transfer, but *without response specificity*** ($F < 1$). The CS for pellets elevated responding on both levers equally ($p = .001$). (In addition, these subjects retained the bias towards the pellet lever that was observed during the last stage of training.)
- **Shell-lesioned subjects showed no Pavlovian–instrumental transfer** ($p > .116$).



Discussion and conclusions

Summary of results

- These results demonstrate a Pavlovian–instrumental transfer effect in normal rats that is response-specific, in that Pavlovian stimuli paired with two reinforcers differentially affected instrumental responding for those two reinforcers. Shell-lesioned animals demonstrated no Pavlovian–instrumental transfer, while core-lesioned animals demonstrated some transfer, but this transfer lacked response specificity.

Core and shell: direction and vigour?

- These results support the hypothesis that the nucleus accumbens is involved in the selection and specific invigoration of actions, in response to arousing conditioned stimuli (see Parkinson et al., 2000).

- The simplest model that accommodates the present data is that the shell provides conditioned 'vigour' to enhance ongoing responses, while the core 'directs' this to one of several possible responses.

- These results resemble those of Parkinson et al. (1999), who examined the potentiative effects of D-amphetamine on responding for conditioned reinforcement (Taylor & Robbins, 1984), another phenomenon depending upon Pavlovian conditioned stimuli. They found that shell lesions blocked this potentiation, while core lesions impaired the selectivity of the potentiation, without abolishing potentiation *per se.*

- The effects of shell lesions in the present study also support recent results of Corbit et al. (submitted), who found an abolition of Pavlovian–instrumental transfer in shell-lesioned rats using the same form of task, though there was no significant effect of core lesions in their study.

Neural circuits; analogies with conditioned reinforcement; functional relevance

- Amphetamine's effects to potentiate responding for conditioned reinforcement depend on dopaminergic mechanisms in the nucleus accumbens (Cador et al., 1991), while Pavlovian–instrumental transfer can be blocked by systemic dopamine antagonists (Smith & Dickinson, 1998a). It remains to be seen if PIT depends on nucleus accumbens dopamine, as seems likely.

- It has already been shown that lesions of the central nucleus of the amygdala, which abolish amphetamine potentiation of responding for conditioned reinforcement (Robledo et al., 1996), also abolish the vigour of PIT (Hall et al., 1999).

- Specific information concerning conditioned reinforcers arrives at the nucleus accumbens and depends upon the BLA (Cador et al., 1989; Burns et al., 1993). Although lesions of the BLA do not significantly impair 'simple' PIT (Hall et al., 1999), they have been shown to impair the specificity of PIT (Blundell & Killcross, 2000), as would be expected if the neural system underlying these effects of *noncontingent* Pavlovian CSs (PIT) is the same as that underlying the effects of *response-contingent* CSs (conditioned reinforcement).

- Further work is needed to explore the apparent differences in the effects of accumbens lesions on 'simple' PIT, which survives shell lesions (Hall et al., 1999) and response-specific PIT, which, in the present study, did not.

- This area of research has significant implications for the understanding of drug addiction, including the phenomenon of cue-induced relapse (Gawin, 1991).

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