Neuropsychology of reinforcement processes in the rat

A dissertation submitted for the degree of Doctor of Philosophy

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This thesis investigated the role played by regions of the prefrontal cortex and ventral striatum in the control of rats' behaviour by Pavlovian conditioned stimuli, and in their capacity to choose delayed reinforcement.

First, the function of the anterior cingulate cortex (ACC) in simple Pavlovian conditioning tasks was addressed. The ACC is a subdivision of prefrontal cortex that has previously been suggested to be critical for the formation of stimulus–reward associations. It was found that lesions of the ACC did not prevent rats from learning a simple conditioned approach response to a conditioned stimulus (CS) predictive of food reward, or from utilizing that CS as a conditioned reinforcer subsequently. Additionally, these subjects successfully acquired a conditioned freezing response to a CS predicting footshock. However, the same animals were impaired at the acquisition of autoshaped behaviour, an impairment that has been demonstrated previously. An autoshaping deficit was also observed when lesions were made following training. The phenomenon of Pavlovian–instrumental transfer was intact in these subjects. The hypothesis was developed that the ACC is not critical for the formation of stimulus–reward associations *per se*, but is critical when multiple stimuli must be discriminated on the basis of their differential association with reward. In support of this hypothesis, animals with lesions of the ACC were impaired on a version of the conditioned approach task in which a second, neutral stimulus, perceptually similar to the CS, was added; the lesioned subjects exhibited reduced discrimination.

Second, the role of the nucleus accumbens (Acb) in Pavlovian–instrumental transfer was investigated. The nucleus accumbens core, together with a larger amygdalar–striatal network of which it is a component, has previously been shown to be necessary for the expression of 'simple' Pavlovian–instrumental transfer. Rats with lesions of the nucleus accumbens core (AcbC) and shell (AcbSh) were tested on a 'response–specific' Pavlovian–instrumental transfer task, in which a Pavlovian CS selectively enhances instrumental responding for the outcome with which the CS was originally paired. AcbC lesions impaired the response specificity of this effect, while AcbSh lesions abolished Pavlovian–instrumental transfer entirely. These results are consistent with some — but not all — previous results in suggesting that the shell provides 'vigour' and the core provides 'direction' for the potentiation of behaviour by Pavlovian CSs.

Third, an attempt was made to train rats on a task for assessing preference for delayed reinforcement, using the 'adjusting-delay' paradigm. It was not immediately apparent that the rats reacted to the contingencies operative in this task, and mathematical analysis of their behaviour was conducted to establish whether their behaviour was sensitive to the delay, and what 'molar' features of performance on this task could be explained by delay-independent processes.

Fourth, a different delayed reinforcement choice task was developed, modifying a previously published task in which the subject is repeatedly offered a choice, in discrete trials, of a small reward delivered immediately, and a large reward delivered after a delay, with the delays systematically varied by the experimenter. Rats were trained on versions of this task in which the large, delayed reinforcer was or was not explicitly signalled by a cue present during the delay. The behavioural basis of performance on this task was examined, and *d*-amphetamine, chlordiazepoxide, and a-flupenthixol were administered systemically. It was found that the effects of *d*-amphetamine depended on whether the delayed reinforcer was signalled or unsignalled, increasing preference for signalled delayed reinforcement at some doses, but decreasing preference for unsignalled delayed reinforcement. These results may resolve contradictions in the literature, and are suggested to reflect the known effect of amphetamine to potentiate responding for conditioned reinforcers.

Fifth, rats that had been trained on this task (with no explicit signals present during the delay) were given lesions of the ACC, AcbC, or medial prefrontal cortex (mPFC). ACC-lesioned rats were no different from sham-operated controls in their ability to choose a large, delayed reinforcer. Lesions of mPFC reduced the tendency of subjects to shift from one lever to the other during the course of a session, but mPFC-lesioned subjects responded normally to removal of the delays, suggesting a loss of stimulus control. However, rats with lesions of the AcbC were severely impaired on this task, preferring the small, immediate reward, even though they discriminated the reinforcers. Additionally, the effects of intra-Acb amphetamine were assessed using a different version of the delayed reinforcement choice task, and found to have slight but inconsistent effects to reduce preference for the delayed reinforcer, though this effect did not depend on whether the delayed reward was signalled or unsignalled. These results suggest that the AcbC contributes significantly to the rat's ability to choose a delayed reward, a finding that has important implications for the understanding of Acb function. It is suggested that dysfunction of the AcbC may be a key element in the pathology of impulsivity.