Abstract

This thesis investigated the contribution of the nucleus accumbens core (AcbC) and the hippocampus (H) to choice and learning involving reinforcement that was delayed or unlikely. Animals must frequently act to influence the world even when the reinforcing outcomes of their actions are delayed. Learning with action–outcome delays is a complex problem, and little is known of the neural mechanisms that bridge such delays. Impulsive choice, one aspect of impulsivity, is characterized by an abnormally high preference for small, immediate rewards over larger delayed rewards, and is a feature of attention-deficit/hyperactivity disorder (ADHD), addiction, mania, and certain personality disorders. Furthermore, when animals choose between alternative courses of action, seeking to maximize the benefit obtained, they must also evaluate the likelihood of the available outcomes. Little is known of the neural basis of this process, or what might predispose individuals to be overly conservative or to take risks excessively (avoiding or preferring uncertainty, respectively), but risk taking is another aspect of the personality trait of impulsivity and is a feature of a number of psychiatric disorders, including pathological gambling and some personality disorders.

The AcbC, part of the ventral striatum, is required for normal preference for a large, delayed reward over a small, immediate reward (self-controlled choice) in rats, but the reason for this is unclear. Chapter 3 investigated the role of the AcbC in learning a free-operant instrumental response using delayed reinforcement, performance of a previously learned response for delayed reinforcement, and assessment of the relative magnitudes of two different rewards. Groups of rats with excitotoxic or sham lesions of the AcbC acquired an instrumental response with different delays (0, 10, or 20 s) between the lever-press response and reinforcer delivery. A second (inactive) lever was also present, but responding on it was never reinforced. The delays retarded learning in normal rats. AcbC lesions did not hinder learning in the absence of delays, but AcbC-lesioned rats were impaired in learning when there was a delay, relative to sham-operated controls. Rats were subsequently trained to discriminate reinforcers of different magnitudes. AcbC-lesioned rats were more sensitive to differences in reinforcer magnitude than sham-operated controls, suggesting that the deficit in self-controlled choice previously observed in such rats was a consequence of reduced preference for delayed rewards relative to immediate rewards, not of reduced preference for large rewards relative to small rewards. AcbC lesions also impaired the performance of a previously learned instrumental response in a delay-dependent fashion. These results demonstrate that the AcbC contributes to instrumental learning and performance by bridging delays between subjects' actions and the ensuing outcomes that reinforce behaviour.

When outcomes are delayed, they may be attributed to the action that caused them, or mistakenly attributed to other stimuli, such as the environmental context. Consequently, animals that are poor at forming context–outcome associations might learn action–outcome associations better with delayed reinforcement than normal animals. The hippocampus contributes to the representation of environmental context, being required for aspects of contextual conditioning. It was therefore hypothesized that animals with H lesions would be better than normal animals at learning to act on the basis of delayed reinforcement. Chapter 4 tested the ability of H-lesioned rats to learn a free-operant instrumental response using delayed reinforcement, and their ability to exhibit self-controlled choice. Rats with sham or excitotoxic H lesions acquired an instrumental response with different delays (0, 10, or 20 s) between the response and reinforcer delivery. H-lesioned rats responded slightly less than sham-operated controls in the absence of delays, but they became better at learning (relative to shams) as the delays increased; delays impaired learning less in H-lesioned rats than in shams. In contrast, lesioned rats exhibited impulsive choice, pre-

ferring an immediate, small reward to a delayed, larger reward, even though they preferred the large reward when it was not delayed. These results support the view that the H hinders action–outcome learning with delayed outcomes, perhaps because it promotes the formation of context–outcome associations instead. However, although lesioned rats were better at learning with delayed reinforcement, they were worse at choosing it, suggesting that self-controlled choice and learning with delayed reinforcement tax different psychological processes.

Chapter 5 examined the effects of excitotoxic lesions of the AcbC on probabilistic choice in rats. Rats chose between a single food pellet delivered with certainty (probability $p = 1$) and four food pellets delivered with varying degrees of uncertainty ($p = 1$, 0.5, 0.25, 0.125, and 0.0625) in a discrete-trial task, with the large-reinforcer probability decreasing or increasing across the session. Subjects were trained on this task and then received excitotoxic or sham lesions of the AcbC before being retested. After a transient period during which AcbC-lesioned rats exhibited relative indifference between the two alternatives compared to controls, AcbC-lesioned rats came to exhibit risk-averse choice, choosing the large reinforcer less often than controls when it was uncertain, to the extent that they obtained less food as a result. Rats behaved as if indifferent between a single certain pellet and four pellets at $p = 0.32$ (sham-operated) or at $p = 0.70$ (AcbC-lesioned) by the end of testing. When the probabilities did not vary across the session, AcbC-lesioned rats and controls strongly preferred the large reinforcer when it was certain, and strongly preferred the small reinforcer when the large reinforcer was very unlikely ($p = 0.0625$), with no differences between AcbC-lesioned and sham-operated groups. These results suggest that the AcbC contributes to action selection by promoting the choice of uncertain, as well as delayed, reward.

Key words:

delay
uncertainty
impulsivity
addiction
nucleus accumbens
hippocampus