Succumbing to instant gratification without the nucleus accumbens

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Animals act to obtain rewards such as food, shelter, and sex. Sometimes, their actions are rewarded or reinforced immediately, but often this is not the case; to be successful, animals must learn to act on the basis of delayed reinforcement. They may also profit by choosing delayed reinforcers over immediate reinforcers, if the delayed reinforcers are sufficiently large. However, individuals differ in their ability to choose delayed rewards. Self-controlled individuals are strongly influenced by delayed reinforcement, and choose large, delayed rewards in preference to small, immediate rewards; in contrast, individuals who are relatively insensitive to delayed reinforcement choose impulsively, preferring the immediate, smaller reward in this situation (*1*). Impulsivity has long been recognized as a normal human characteristic (*2*) and in some circumstances it may be beneficial (*3*), but impulsive choice contributes to deleterious states such as drug addiction (*4-8*) and attention-deficit / hyperactivity disorder (ADHD) (*9*).

Little is known about how the brain learns from or chooses delayed reinforcement. We studied three brain regions previously implicated in other kinds of reinforcement learning: the nucleus accumbens core (AcbC), anterior cingulate cortex (ACC), and medial prefrontal cortex (mPFC) (*10*). The AcbC is a critical site where signals that predict reward have their motivational impact (*11-15*). All three structures are abnormal in humans with ADHD or in animal models of ADHD (*16-20*), and all three receive projections from dopaminergic and

serotonergic neurons; systemically-administered drugs that influence either of these neuromodulator systems affect animals' propensity to make impulsive choices (*3, 21-24*).

To establish whether abnormalities in these regions might cause impulsive choice, we used a task in which hungry rats regularly choose between two levers. Responding on one lever led to the immediate delivery of a small food reward; responding on the other led to a much larger food reward, but this reward was delayed for between 0 and 60 seconds (*24, 25*). Once they had been trained on this task, we selectively destroyed neurons of the AcbC, ACC, or mPFC, and re-tested the rats (*10*).

Rats with AcbC lesions became, and remained, impulsive; they began to choose the immediate, small reward much more often than sham-operated controls. They persisted in choosing impulsively, even though they were made to experience the larger, delayed alternative at regular intervals. Why did they do this? In theory, impulsive choice might arise for a variety of reasons (*1, 21*). Take an abstaining smoker, offered a cigarette. His choice is between a small, immediate reward (a cigarette) and a large, delayed reward (better health in the future). If he acts impulsively where another does not, it could be because he does not perceive the larger reward to be as worthwhile as his self-controlled counterpart does, or because he is simply less influenced by outcomes that are delayed considerably. Which is true of rats whose AcbC has been destroyed? Our findings (*10, 26*) and others' (*27, 28*) suggest the latter. Even those AcbC-lesioned rats who showed an extreme preference for the larger reward when it was not delayed were incapable of choosing it as often as normal rats when it was delayed (*10, 26*). In fact, AcbC-lesioned rats appear just as sensitive to the magnitude of reward as normal rats (*28*), suggesting that their impulsive choice arises not because the large reward is subjectively too small to compensate for the normal effects of the delay, but because they would have to wait too long for it.

In addition to being impulsive, AcbC-lesioned rats are also hyperactive (*10, 29*), but they do not appear to be inattentive (*30, 31*). Destruction of the AcbC does not, therefore,

mimic ADHD in full, but our findings suggest that the behaviour of rats with AcbC damage resembles that of humans with the hyperactive–impulsive subtype of ADHD (*32*).

In contrast, we found that damage to the ACC or mPFC did not produce impulsive choice (*10*); thus, although the ACC and mPFC have been shown to be abnormal in disorders of impulsivity (*16-18*), our findings suggest that dysfunction of these regions is not an important contributor to impulsive choice. The abnormalities of structure or function observed in these regions in ADHD brains may therefore be responsible for other features of the disorder (such as inattention or motoric disinhibition) (*33*), or these regions may have altered as a consequence of a disease process beginning elsewhere. A clearer understanding of the neurochemical and neuroanatomical basis of the symptoms and signs of ADHD may lead to more effective therapy.

This study (*10*) examined the role of the AcbC in choosing delayed rewards, but did not address whether the AcbC is a critical structure in *learning* from delayed reinforcement. In order to learn which actions are the correct ones that eventually lead to reinforcement, and which are not, some mechanism must 'bridge' the delay between action and outcome. We recently took two groups of hungry rats, one with AcbC lesions and one without, and presented them with two levers; one did nothing, while every press on the other lever delivered a single food pellet. For some rats, this pellet was delivered immediately; for others, it was delayed. Normal rats took longer to learn to press the lever when the reinforcement was delayed, which is not surprising (*34*), but they learned successfully with delayed reinforcement. Rats with AcbC lesions were perfectly able to learn this task when there was no delay, but were profoundly impaired when there was a delay between action and outcome (*35*).

Taken together, these results indicate that the AcbC is a reinforcement learning structure specialized for the difficult task of learning with, and choosing, delayed reinforcement. Further understanding of the mechanism by which it does so, or fails to do so, would provide insight into the pathology of a number of neuropsychiatric disorders.

Behavioural neuroscientific techniques may make it possible to distinguish the brain regions that underlie different types of impulsivity (*3*), and to segregate the neural abnormalities that contribute to complex disorders such as ADHD and drug addiction.

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