EJN fens EUROPEAN JOURNAL OF NEUROSCIENCE

European Journal of Neuroscience, Vol. 33, pp. 2272–2273, 2011 doi:10.1111/j.1460-9568.2011.07716.x

BEHAVIORAL NEUROSCIENCE

COMMENTARY
Neuronal correlates of normal and drug-potentiated Pavlovian–instrumental transfer (Commentary on Saddoris *et al.*)

EJN FEATURED ARTICLE

Kyle S. Smith
McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, MA, USA

As Saddoris *et al.* (2011) emphasized in their exciting new study, reward-directed actions are often initiated or facilitated by conditional stimuli that have been independently associated with the reward. The influence of conditional cues over action is also thought to play a major role in drug addiction. Yet, vital as this process may be to learned behavior, it is a difficult one to isolate experimentally, and little is known about its mechanism at the level of neuronal activity.

Here, the authors make new headway on the issue by measuring neural firing correlates of Pavlovian–instrumental transfer (PIT) in rats. The basic effect of PIT can perhaps be traced back to Estes (Estes, 1943, 1948), and is revealed by a three-phase protocol: (i) train an animal to associate a Pavlovian positive conditioned stimulus (CS+) cue, such as a tone, with reward; (ii) separately train the animal to associate an instrumental action, such as a lever press, with the reward; and (iii) present the CS+ with the levers available. In this last test phase, the animal will press the lever much more when the CS+ is presented, despite never having 'learned' this cue-press sequence as a means of obtaining a reward. Thus, the PIT test is able to isolate the invigoration of actions by independently learned Pavlovian stimuli.

Saddoris *et al.* (2011) trained rats following this protocol, and also included a non-predictive CS− cue and an unrewarded lever as controls. On the PIT test day, firing of projection neurons was recorded in the nucleus accumbens core and shell, which are key substrates for the effect (Wyvell & Berridge, 2000; Corbit *et al.*, 2001; Hall *et al.*, 2001; Lex & Hauber, 2008). Behaviorally, the CS+ increased lever pressing, as confirmation of PIT. Neurally, many interesting accumbens firing differences are reported between direction of responses, stimuli evoking them, and recording sites, further building a view of substantial heterogeneity and information multiplexing in accumbens firing. A main finding to highlight was that PIT performance levels correlated with the number of core neurons that fired more to the CS+ than to the CS− or pre-cue baseline and with the number of shell neurons that fired during lever pressing more robustly when the CS+ was present (i.e. PIT-modulated). This potentially indicates a distinct contribution for the core in assigning motivational value to reward-predictive cues to arouse behavior, and for the shell in integrating learned cue and action information to guide PIT performance.

In a separate experiment, rats underwent a period of cocaine self-administration after the learning phases, which led them, in the PIT test, to press even more during the CS+ than control groups. The clear PIT enhancement coincided with a similarly clear increase in the number of shell (but not core) neurons firing more to rewarded versus unrewarded stimuli and actions, as well as in the number of PIT-modulated neurons in both shell and core. Food cup entry and related firing was unaffected, bolstering the conclusion that firing reflected PIT rather than general reward pursuit or psychomotor activation. Thus, it would seem that these data reveal elements of firing plasticity that could contribute to the influence of dopamine on PIT (Dickinson *et al.*, 2000; Wyvell & Berridge, 2000; Lex & Hauber, 2008), and to the inflated capacity of independently learned cues to motivate reward seeking in addiction states (Wyvell & Berridge, 2001).

One suspects, on the basis of the many brain sites implicated in PIT, that the accumbens is contributing particular component features. Determining what functional coding features emerge in these other sites would be key to fleshing out the effect at a circuit level (Homayoun & Moghaddam, 2009), but it is a challenge, as sites for PIT span mesocorticolimbic and sensorimotor circuitry (e.g. see Holland & Petrovich, 2005; Yin *et al.*, 2008). This effort might be aided by multisite recordings or targeted online manipulations of key firing patterns to causally control PIT, as well as task designs to dissociate general from outcome-specific forms of PIT (Blundell *et al.*, 2001; Corbit & Balleine, 2005). For now, however, this work represents an important and 'motivating' step forwards.

References

Blundell, P., Hall, G. & Killcross, S. (2001) Lesions of the basolateral amygdala disrupt selective aspects of reinforcer representation in rats. *J. Neurosci.*, **21**, 9018–9026.

Corbit, L.H. & Balleine, B.W. (2005) Double dissociation of basolateral and central amygdala lesions on the general and outcome-specific forms of pavlovian–instrumental transfer. *J. Neurosci.*, **25**, 962–970.

Corbit, L.H., Muir, J.L. & Balleine, B.W. (2001) The role of the nucleus accumbens in instrumental conditioning: evidence of a functional dissociation between accumbens core and shell. *J. Neurosci.*, **21**, 3251–3260.

Dickinson, A., Smith, J. & Mirenowicz, J. (2000) Dissociation of Pavlovian and instrumental incentive learning under dopamine antagonists. *Behav. Neurosci.*, **114**, 468–483.

Estes, W.K. (1943) Discriminative conditioning I. A discriminative property of conditioned anticipation. *J. Exp. Psychol.*, **32**, 150–155.

Estes, W.K. (1948) Discriminative conditioning; effects of a Pavlovian conditioned stimulus upon a subsequently established operant response. *J. Exp. Psychol.*, **38**, 173–177.

Hall, J., Parkinson, J.A., Connor, T.M., Dickinson, A. & Everitt, B.J. (2001) Involvement of the central nucleus of the amygdala and nucleus accumbens core in mediating Pavlovian influences on instrumental behaviour. *Eur. J. Neurosci.*, **13**, 1984–1992.

Holland, P.C. & Petrovich, G.D. (2005) A neural systems analysis of the potentiation of feeding by conditioned stimuli. *Physiol. Behav.*, **86**, 747–761.

Homayoun, H. & Moghaddam, B. (2009) Differential representation of Pavlovian–instrumental transfer by prefrontal cortex subregions and striatum. *Eur. J. Neurosci.*, **29**, 1461–1476.

Lex, A. & Hauber, W. (2008) Dopamine D1 and D2 receptors in the nucleus accumbens core and shell mediate Pavlovian–instrumental transfer. *Learn. Mem.*, **15**, 483–491.

Saddoris, M.P., Stamatakis, A. & Carelli, R.M. (2011) Neural correlates of Pavlovian-to-instrumental transfer in the nucleus accumbens shell are selectively potentiated following cocaine self-administration. *Eur. J. Neurosci.*, **33**, 2274–2287.

Wyvell, C.L. & Berridge, K.C. (2000) Intra-accumbens amphetamine increases the conditioned incentive salience of sucrose reward: enhancement of reward ‘wanting’ without enhanced ‘liking’ or response reinforcement. *J. Neurosci.*, **20**, 8122–8130.

Wyvell, C.L. & Berridge, K.C. (2001) Incentive sensitization by previous amphetamine exposure: increased cue-triggered ‘wanting’ for sucrose reward. *J. Neurosci.*, **21**, 7831–7840.

Yin, H.H., Ostlund, S.B. & Balleine, B.W. (2008) Reward-guided learning beyond dopamine in the nucleus accumbens: the integrative functions of cortico-basal ganglia networks. *Eur. J. Neurosci.*, **28**, 1437–1448.