Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *Critical Contributions of the Orbitofrontal Cortex to Behavior*

The orbitofrontal cortex, predicted value, and choice

Bernard W. Balleine,[1] Beatrice K. Leung,[1] and Sean B. Ostlund[2]

[1]Brain & Mind Research Institute, University of Sydney, Sydney, Australia. [2]Semel Institute, University of California, Los Angeles, Los Angeles, California

Address for correspondence: Bernard Balleine, BMRI, 100 Mallet St, Camperdown, NSW 2050, Sydney, Australia. bernard.balleine@sydney.edu.au

Considerable evidence suggests that choice between goal-directed actions depends on two incentive processes encoding the reward value of the goal or outcome and the predicted value of an action based on outcome-related stimuli. Although incentive theories generally assume that these processes are mediated by a common associative mechanism, a number of recent findings suggest that they are dissociable; the reward value of an action is derived from consummatory experience with the outcome itself, whereas the predicted value of an action is based on the presence of outcome-associated stimuli from which estimates of the likelihood of an outcome are derived. Importantly, the orbitofrontal cortex (OFC) in rodents appears to mediate the effect of outcome-related stimuli on choice; OFC lesions disrupt the influence of Pavlovian stimuli on choice in tests of outcome-specific Pavlovian-instrumental transfer. However, the influence of outcome-related stimuli on choice involves a larger circuit including the OFC, the ventral striatum, and the amygdala. How these structures interact, however, is not yet fully understood and is an important question for future research.

Keywords: basal ganglia; reward; decision making

Incentive theory and the motivation of action

Choice between goal-directed actions is determined by both the capacity to encode the consequences associated with specific actions and the relative incentive value assigned to those consequences.[1] Although incentive values can be influenced by a range of variables, including effort and temporal delay,[2,3] they are most commonly derived from two forms of learning that underlie reward-guided and stimulus-guided decisions and through which animals encode the experienced reward value of the goal or outcome of an action, that is, the value assigned to an action based on consummatory contact with the outcome, and the predicted value of an action based on the presence of stimuli associated with a specific outcome.[4,5]

In the lab, these forms of incentive learning are typically studied using distinct experimental procedures; outcome revaluation has generally been used to assess the effect of changes in reward value, whereas Pavlovian-instrumental transfer is used to assess the effect of outcome-related stimuli on choice.[5,6] Nevertheless, historically, theories of incentive motivation have generally supposed that these forms of incentive learning influence performance through a common representation of the instrumental outcome,[5,7,8] a view enshrined within various two-process theories of instrumental conditioning .[9,10] Indeed, most forms of incentive theory claim that motivational factors influence the performance of specific actions via changes in the activation of the outcome representation with which those actions are associated rather than by indirect effects on motor output through, say, changes in drive.[4,11,12] On this view, therefore, changes in reward-based and stimulus-based decisions affect choice because they have a common influence on the activation of a specific outcome representation; if both alter outcome activation, then both should similarly alter the performance of any actions associated with that outcome.

One prediction derived from this kind of incentive theory is that a common neural process, or "central motivational state,"[8,13] should mediate the

doi: 10.1111/j.1749-6632.2011.06270.x

effects of various motivational manipulations on choice.[14] Indeed, some recent findings appear to support this prediction. For example, lesions of the basolateral amygdala (BLA) were reported to abolish both the effect of changes in reward value, induced by outcome devaluation, and in stimulus-based decisions, assessed by Pavlovian-instrumental transfer, on choice.[15,16] Furthermore, as the BLA maintains both extensive inputs from structures sensitive to sensory and visceral information[17] and has been consistently found to be involved in reward-related processes,[18,19] it appears to be the kind of neural structure anticipated by incentive theory to mediate motivational influences on performance.[20]

The role of the orbitofrontal cortex in incentive learning

Nevertheless, although evidence from manipulations of the BLA supports this prediction from incentive theory, considerable evidence from other sources has been accumulating that counters this view. For example, early studies assessing the effects of neural manipulations of incentive learning found, as with lesions of the BLA, that lesions of the prelimbic prefrontal cortex (PL) abolished the sensitivity of rats to the effects of outcome devaluation on choice between goal-directed actions.[1] Given the effects of amygdala lesions and this effect of PL lesions, it would seem to be a clear prediction that the latter should also abolish the effects of Pavlovian cues on choice in a test of outcome-specific Pavlovian-instrumental transfer. This prediction was assessed by Corbit and Balleine[21] and, importantly, although they were able to replicate the deficit in outcome devaluation after PL lesions, they found no effect of these lesions on Pavlovian-instrumental transfer,[21] suggesting that the neural processes subserving the effect of changes in reward value on choice differ from those involved in stimulus-based decisions.

Studies assessing the role of cortical regions other than the PL in incentive learning have bolstered this claim, chief among which has been the orbitofrontal cortex (OFC). The OFC is a complex structure in humans and other mammals. It has several subregions that have distinct connectivity including a medial region and, in humans and primates, a lateral region that appear to mediate quite distinct functions.[22,23] The same appears to be true in rodents; however, until very recently,[24,25] few studies assessing the function of the medial region have been reported. Generally, the lateral OFC in rats (subdivided anatomically into ventral, lateral, and dorsolateral subregions[26]) has been argued to play a critical role in incentive learning, particularly in evaluating the relative value of outcomes and in altering performance when those values change.[27] Evidence from electrophysiological studies suggests that neurons in the OFC are sensitive to the value of outcome-related stimuli and alter responding when the value of the predicted outcome changes.[28] Furthermore, lesions to the OFC attenuate the effect of outcome devaluation on conditioned responding elicited by Pavlovian cues that predict that outcome.[29]

However, the involvement of the OFC in the choice between goal-directed actions in instrumental conditioning is not so clear.[30] In one study,[31] half of the rats were given excitotoxic or sham lesions of the OFC (the remainder were given no treatment) before initial training sessions in which rats were made hungry and then trained to predict the delivery of food pellets and of sucrose solution from two distinct auditory stimuli (i.e., A1-pellet and A2-sucrose). They were then trained to press two freely available levers, one earning the food pellets and the other the sucrose solution (i.e., R1 $\rightarrow$ pellet; R2 $\rightarrow$ sucrose). After this training, rats given pretraining lesions received no treatment, whereas the remainder were given either excitotoxic or sham lesions of the OFC. All rats were then given two choice tests conducted in extinction: the first, a test of changes in predicted value, allowed the rats to choose between the two levers in the presence of each of the two auditory stimuli (A1: R1 vs. R2; and A2: R1 vs. R2); the second, a test of changes in experienced value, allowed them to choose between R1 and R2 after one of the two outcomes (O1 or O2) had been devalued. Although incentive theory predicts that any effect of the lesions on sensitivity to changes in either predicted or experienced reward should affect both incentive learning effects, posttraining lesions of the OFC abolished sensitivity to changes in predictive value on choice in the Pavlovian-instrumental transfer test, whereas neither pre- nor posttraining lesions had any influence on the effect of changes in experienced value after outcome devaluation. This effect of posttraining lesions was likely due to compensation following small pretraining lesions that spared the ventral OFC. In a recent study, we gave rats large pretraining lesions that produced cell loss in both

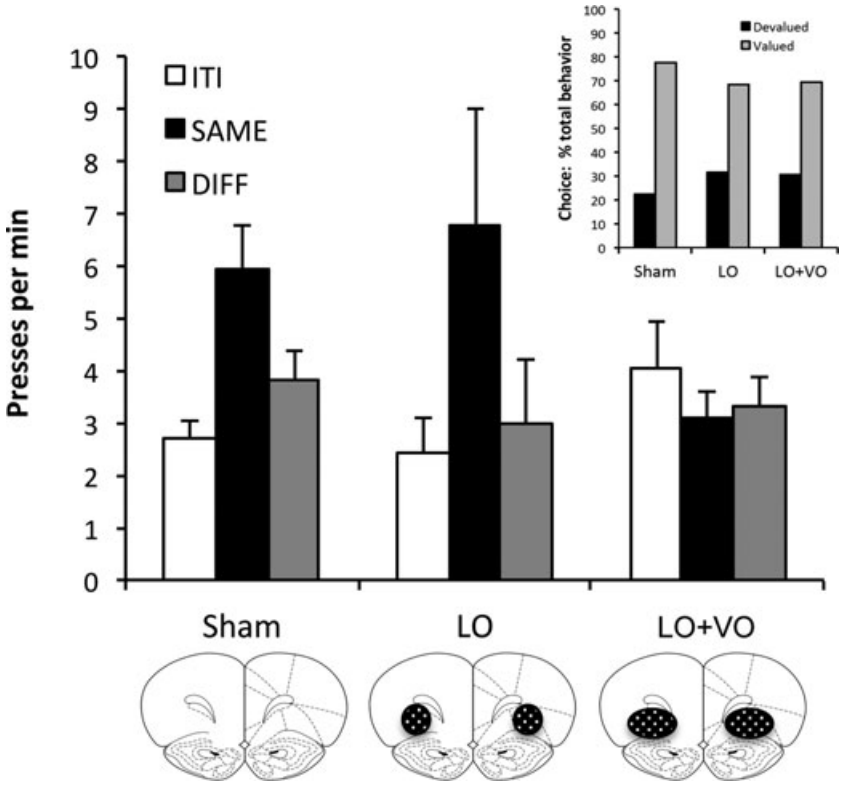

Figure 1. **Effect of large pretraining lesions of the OFC on outcome-specific Pavlovian-instrumental transfer. Previous studies have found an effect of lesions of the lateral OFC (LO) on Pavlovian-instrumental transfer, but only when made posttraining. Although pretraining lesions of LO were without effect (left panels), we have recently found that large pretraining lesions encompassing both lateral and ventral OFC (LO + VO) are effective in abolishing specific transfer (right panel). Note too that, although these more complete pretraining lesions abolished transfer, they did not have any effect on the rats' sensitivity to the effects of outcome devaluation on instrumental choice performance (inset).**

the lateral OFC (LO) and the ventral OFC (VO) (i.e., in LO + VO) and then gave them Pavlovian and instrumental conditioning as described above. In contrast to the smaller lesions, this larger pretraining lesion abolished outcome-specific transfer (see Fig. 1). However, these large pretraining lesions had no effect on sensitivity to outcome devaluation (see Fig. 1, inset).

This result stands in direct contrast to the effects of pretraining PL lesions: whereas pretraining PL lesions abolished sensitivity to the effects of changes in reward value on choice, they left stimulus-guided decisions intact. In contrast, pretraining lesions of the OFC affected sensitivity to outcome-related stimuli on choice but left sensitivity to effect of changes in reward value intact. Hence, these results suggest a double dissociation between the role of the PL and OFC in reward-guided and stimulus-guided decision making and, importantly, suggest that these incentive processes are not mediated by the same neural mechanism.

Reward-guided versus stimulus-guided decisions

The distinct effects of lesions of prefrontal and orbitofrontal cortices on the way changes in experienced and predicted value affect choice are important but are far from the only data to suggest that these incentive processes differ. At a purely behavioral level, Rescorla's[32] finding that outcome devaluation has no effect on outcome-selective Pavlovian-instrumental transfer presents severe difficulties for any claim that these effects rely on a common incentive process; in this case, changing the experienced value of an outcome did not alter the ability of cues associated with that outcome from affecting choice (see also Refs. 33–35 for evidence of similar behavioral dissociations). However, perhaps the

most telling evidence comes from a study by Corbit *et al.*[36] designed to investigate the role of core and shell subregions of the nucleus accumbens on instrumental conditioning. Prior to training, groups of rats were given excitotoxic lesions of either the core or shell region. After recovery, they were made hungry and first exposed to pairings of two auditory stimuli with food pellet and sucrose outcomes and then trained to press two freely available levers to gain access to these outcomes. After this training, two choice tests were conducted in extinction: the first, a test of changes in stimulus-based decisions, allowed the rats to choose between the two levers in the presence of each of the two stimuli, and the second, a test of changes in reward value, allowed them to choose between actions after either the pellet or sucrose outcome had been devalued. Although incentive theory predicts that any effect of the lesions on sensitivity to changes in either predicted or experienced reward should affect both processes, lesions of the core abolished the influence of outcome devaluation but not of the Pavlovian cues on choice, replicating the effects of PL lesions,[21] whereas lesions of shell abolished the effects of the Pavlovian cues but not of outcome devaluation on choice, replicating the effects of OFC lesions.[31] Together, these effects of accumbens lesions provide clear within-experiment support for the double dissociation found across studies using cortical lesions and demonstrate that the neural bases of reward-guided decisions are independent of those sub serving the effect of stimulus guided decisions on choice.

OFC involvement in stimulus-guided decision making

What, then, are we to make of the effects of BLA lesions on outcome devaluation and Pavlovian-instrumental transfer? It is important to note that the BLA maintains strong but distinct connections with the accumbens shell and the core; indeed, BLA–shell and BLA–core projections have been reported to be anatomically segregated, with the former arising largely in the posterior and the latter the anterior BLA.[37] Furthermore, in a recent study, Shiflett and Balleine[38] confirmed that these connections between the BLA with the core and shell of the accumbens are functionally segregated using asymmetrical lesions. Thus, a unilateral lesion of the BLA, coupled with a unilateral lesion of the contralateral accumbens core, abolished the influence of outcome devaluation but not of the Pavlovian cues on choice, replicating the effects both of bilateral core lesions and of PL lesions. Conversely, a unilateral lesion of the BLA coupled with a unilateral lesion of the contralateral accumbens shell abolished the effects of the Pavlovian cues but not of outcome devaluation on choice, replicating the effect of bilateral shell lesions and of OFC lesions.

Although these effects of BLA–accumbens disconnection are consistent with the conclusion that it is direct connections between these structures that mediate these effects on choice, it is possible that an indirect connection involving frontal cortex is responsible. Indeed, a rich connection between the BLA and OFC has been reported, raising the possibility that the shell involvement in predicted reward, rather than being direct, is driven by the BLA via a BLA $\rightarrow$ OFC $\rightarrow$ shell pathway.[39] We have recently started to assess this suggestion using a double-labeling tract-tracing approach in which we infused the retrograde tracer Fluoro-Gold (FG) into the accumbens shell and examined the degree of c-Fos–related immunoreactivity (as a measure of cellular activity) induced by the Pavlovian-instrumental transfer test in retrograde-labeled neurons in the OFC. If this pathway plays a critical role in the effect of predicted value on choice, we anticipated observing considerable FG + c-Fos double-labeled neurons in the OFC. The results of this assessment are presented in Figure 2. We found clear evidence of both FG- and c-FOS–labeled neurons and, indeed, a similar number of labeled neurons in both the ventral and lateral OFC. We also found a similar number of double-labeled neurons. As such, there is clearly a role for the OFC efferents to the accumbens shell in the influence of Pavlovian cues on choice. Nevertheless, as only 15% or so of neurons activated by c-Fos were double labeled, it is possible that this pathway plays only a limited role, and further experiments are underway to examine more fully the functional role of the BLA and OFC inputs to the accumbens shell.

The other alternative, based on evidence that OFC–BLA connections are reciprocal,[39,40] is that at least some of the activated neurons in the OFC that do not project to the shell, project instead to posterior BLA and control aspects of BLA function relevant to the influence of stimulus guided decisions on choice. In fact, there are several lines of evidence to support this suggestion: first, like

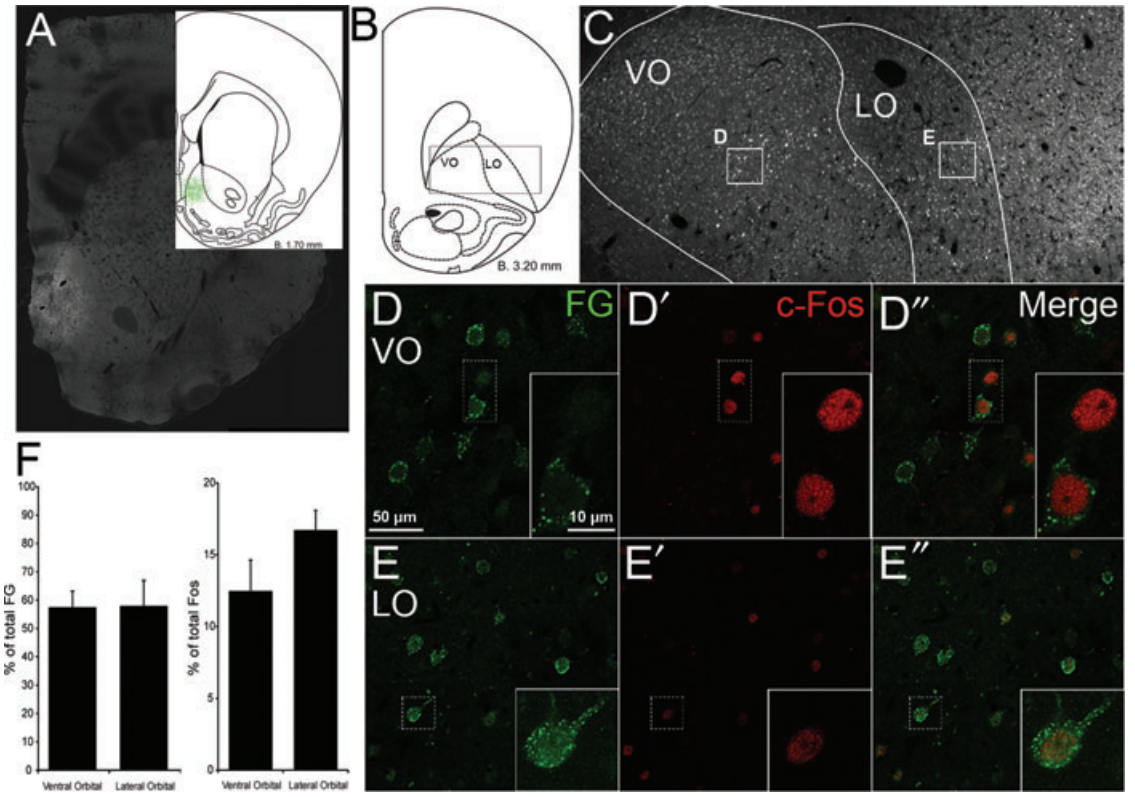

Figure 2. **Activation of OFC projections to the nucleus accumbens shell during Pavlovian-instrumental transfer. (A) Photomicrograph of a nucleus accumbens shell after Fluoro-Gold (FG) injection, with a schematic diagram showing stereotaxic location. (B) Schematic diagram (from Ref. 54) showing location of the ventral orbital cortex (VO) and the lateral orbital cortex (LO). (C) Photomicrograh of FG-positive neurons in VO and LO. (D, E) Colocolization of FG-positive neurons (green) with c-Fos–positive neurons (red) in VO and LO. (F) Total counts in the LO and VO for double-labeled neurons, (left) as a percentage of total FG-positive neurons, (right) as a percentage of total c-Fos–positive neurons.**

the BLA,[20] the OFC is strongly involved in appetitive Pavlovian conditioning, particularly in the formation of uncondition stimulus (US)–specific associations.[41] Thus, during the course of conditioning, as conditioned stimuli (CS) begin to elicit US-specific conditioned responses (CRs), OFC neurons also begin to fire differentially in anticipation of those USs.[28] Furthermore, lesions of the OFC abolish these US-specific CRs[42] as well as the US specificity of Pavlovian contingency degradation induced by either context blocking[31] or transreinforcer blocking.[43] It is also interesting to note that many other functions ascribed to the OFC appear, at their core, to depend on sensory-specific, stimulus–outcome predictions (e.g., van Duuren *et al.*[44] and olfactory predictions of chosen value; also Padoa-Schioppa[45] and neuronal signals of "offer value"—meaning the value of potential or predicted choices among many others). One example of this is the commonly reported involvement of the OFC in reversal learning. Although this involvement is often characterized in terms of the role of the OFC in behavioral flexibility or in response inhibition, the reversal situations that tap OFC function generally require subjects rapidly to acquire and adjust to changes in US-specific, stimulus–outcome associations.[27,46–48]

Nevertheless, differences in the role of the OFC and the BLA in stimulus-guided decisions have also been reported. For example, although lesions of the OFC abolish Pavlovian-instrumental transfer and Pavlovian contingency degradation, they appear to do so by reducing the animals' discrimination of one CS from another based on the specific US it predicts.[30,31] These lesions abolish the outcome specificity of these effects and not the

animals' sensitivity to changes in the predictive status of Pavlovian cues with respect to appetitive events generally. In contrast, BLA lesions completely eradicate specific transfer and render the Pavlovian CS insensitive to contingency degradation in a manner that suggests the animals' are no longer sensitive to prediction error.[16,49] These deficits appear to suggest that the OFC is controlling at least some aspects of amygdala function through an OFC → BLA connection—potentially the outcome specificity of BLA-dependent stimulus–outcome associations.

There are, however, data that stand discordant with this suggestion. For example, during reversal learning, changes in neural activity associated with the reversed contingency occur first in the BLA, then in the OFC,[50] and, as shown by Stalnaker *et al.*,[51] the degree of change in neural activity in the OFC during reversal is actually inversely related to the rate of reversal learning. It is possible, therefore, that the BLA first encodes stimulus–outcome information that, through the BLA → OFC connection, allows it to control OFC-related functions, such as reversal. Consistent with this claim, lesions of the BLA reduce the outcome specificity of OFC unit activity to CSs.[52] Furthermore, Stalnaker *et al.*[53] were also able to show that, whereas lesions of the OFC produced a deficit in reversal, lesions of the BLA were able to correct this deficit.

Nevertheless, it remains possible that this corrective effect was induced by normalizing the influence of converging projections from the BLA and OFC onto some third structure. The question for future experiments, therefore, is whether *functional* interactions involving the BLA and OFC emerge from their direct reciprocal connections or through their joint regulation of activity in a common projection region. In the case of the influence of stimulus-guided decisions on choice, one candidate structure is the accumbens shell, where OFC and BLA efferents appear to converge.

Conclusion

Although the OFC has been implicated in a wide variety of functions, particularly in aspects of goal-directed action and decision making, it is becoming somewhat clearer in the course of recent research that much of the rodent OFC, particularly the ventral and lateral OFC, is engaged in the Pavlovian control of action through its control over the representation of predicted reward values and not, as some have suggested, in the assignment, representation, or imputation of experienced reward values. The role of predicted value in decision making is not trivial by any means. Among the most important ways in which environmental events influence actions is through the predictive relations that they maintain with primary rewards. Nevertheless, there is an important distinction to be made between different regions of the OFC, and its role in assigning predicted values may be limited to its ventral and lateral regions, whereas the medial OFC could well be involved in experienced reward or in the calculation of values as they relate to relative reward more directly. There is almost no evidence on which to decide this issue in rodents and only little in humans. Along with the description of the functional circuits within which the OFC sits, specifying the regional division of functions within the OFC is a major question for future research.

Acknowledgments

Preparation of this paper was supported by Grants from the Australian Research Council, # FL0992409, the NH&MRC, #633267, and the NIMH, #56446.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Balleine, B.W. & A. Dickinson. 1998. Goal-directed instrumental action: contingency and incentive learning and their cortical substrates. *Neuropharmacology* **37:** 407–419.
2. Walton, M.E., S.W. Kennerley, D.M. Bannerman, *et al*. 2006. Weighing up the benefits of work: behavioral and neural analyses of effort-related decision making. *Neural Netw.* **19:** 1302–1314.
3. Cardinal, R.N., D.R. Pennicott, C.L. Sugathapala, *et al.* 2001. Impulsive choice induced in rats by lesions of the nucleus accumbens core. *Science* **292:** 2499–2501.
4. Dickinson, A. & B.W. Balleine. 1994. Motivational control of goal-directed action. *Anim. Learn. Behav.* **22:** 1–18.
5. Dickinson, A. & B.W. Balleine. 2002. In *Learning, Motivation & Emotion. Vol. 3 of Steven's Handbook of Experimental Psychology*, *Third Ed.* C.R. Gallistel, Ed.: 497–533. John Wiley & Sons. New York.
6. Balleine, B.W., N.D. Daw & J. O'Doherty. 2008. In *Neuroeconomics: Decision making and the brain.* P. Glimcher, C. Camerer, E. Fehr, & R. Poldrack, Eds.: Ch. 24, 367–387. Academic Press. New York.
7. Bolles, R.C. 1972. Reinforcement, expectancy, and learning. *Psychol. Rev.* **79:** 394–409.
8. Bindra, D. 1968. A neuropsychological interpretation of the effects of drive and incentive motivation on general activity and instrumental behavior. *Psychol. Rev.* **75:** 1–22.

9. Rescorla, R.A. & R.L. Solomon. 1967. Two-process learning theory: relationships between Pavlovian conditioning and instrumental learning. *Psychol. Rev.* **74:** 151–182.
10. Trapold, M.A. & J.B. Overmier. 1972. In *Classical Conditioning: II. Current Research and Theory*. A.A. Black & W.F. Prokasy, Eds.: 427–452. Appleton-Century-Crofts. New York.
11. Balleine, B.W. 2001. In *Handbook of Contemporary Learning Theories*. R. Mowrer & S. Klein, Eds.: 307–366. LEA. Georgia.
12. Bindra, D. 1974. A motivational view of learning, performance, and behavior modification. *Psych. Rev.* **81:** 199–213.
13. Bindra, D. 1969. A unified interpretation of emotion and motivation. *Ann. N.Y. Acad. Sci.* **159:** 1071–1083.
14. Glickman, S.E. & B.B. Schiff. 1967. A biological theory of reinforcement. *Psychol. Rev.* **74:** 81–109.
15. Balleine, B.W., A.S. Killcross & A. Dickinson. 2003. The effect of lesions of the basolateral amygdala on instrumental conditioning. *J. Neurosci.* **23:** 666–675.
16. Corbit, L.H. & B.W. Balleine. 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.
17. Sah, P., E.S. Faber, M. Lopez De Armentia & J. Power. 2003. The amygdaloid complex: anatomy and physiology. *Physiol. Rev.* **83:** 803–834.
18. Hatfield, T., J.S. Han, M. Conley, *et al*. 1996. Neurotoxic lesions of basolateral, but not central, amygdala interfere with Pavlovian second-order conditioning and reinforcer devaluation effects. *J. Neurosci.* **16:** 5256–5265.
19. Blundell, P., G. Hall & S. Killcross. 2001. Lesions of the basolateral amygdala disrupt selective aspects of reinforcer representation in rats. *J Neurosci.* **21:** 9018–9026.
20. Balleine, B.W. & S. Killcross. 2006. Parallel incentive processing: an integrated view of amygdala function. *Trends Neurosci.* **29:** 272–279.
21. Corbit, L.H. & B.W. Balleine. 2003. The role of prelimbic cortex in instrumental conditioning. *Behav. Brain Res.* **146:** 145–157.
22. Rudebeck, P. H. *et al*. 2008. Frontal cortex subregions play distinct roles in choices between actions and stimuli. *J. Neurosci.* **28:** 13775–13785.
23. Rushworth, M.F., M.P. Noonan, E.D. Boorman, *et al*. 2011. Frontal cortex and reward-guided learning and decision-making. *Neuron* **70:** 1054–1069.
24. Mar, A.C., A.L. Walker, D.E. Theobald, *et al*. 2011. Dissociable effects of lesions to orbitofrontal cortex subregions on impulsive choice in the rat. *J. Neurosci.* **31:** 6398–6404.
25. Gourley, S.L. *et al*. 2010. Dissociable regulation of instrumental action within mouse prefrontal cortex. *Eur. J. Neurosci.***32:** 1726–1734.
26. Ongür, D. & J.L. Price. 2000. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cerebral Cortex* **10:** 206–219.
27. Schoenbaum, G., M.R. Roesch, T.A. Stalnaker & Y.K. Takahashi. 2009. A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. *Nat. Rev. Neurosci.* **10:** 885–892.
28. Schoenbaum, G., A.A. Chiba & M. Gallagher. 1998. Orbitofrontal cortex and basolateral amygdala encode expected outcomes during learning. *Nat. Neurosci.* **1:** 155–159.
29. Gallagher, M., R.W. McMahan & G. Schoenbaum. 1999. Orbitofrontal cortex and representation of incentive value in associative learning. *J. Neurosci.* **19:** 6610–6614.
30. Ostlund, S. & B.W. Balleine. 2007. The contribution of orbitofrontal cortex to action selection. *Ann. N.Y. Acad. Sci.* **1121:** 174–192.
31. Ostlund, S.B. & B.W. Balleine. 2007. Orbitofrontal cortex mediates outcome encoding in Pavlovian but not instrumental conditioning. *J. Neurosci.* **27:** 4819–4825.
32. Rescorla, R.A. 1994. Transfer of instrumental control mediated by a devalued outcome. *Anim. Learn. Behav.* **22:** 27–33.
33. Corbit, L.H. & B.W. Balleine. 2003. Instrumental and Pavlovian incentive processes have dissociable effects on components of a heterogeneous instrumental chain. *J. Exp. Psychol. Anim. Behav. Process* **29:** 99–106.
34. Holland, P.C. 2004. Relations between Pavlovian–instrumental transfer and reinforcer devaluation. *J. Exp. Psychol. Anim. Behav. Process* **30:** 104–117.
35. Ostlund, S.B. & B.W. Balleine. 2007. Selective reinstatement of instrumental performance depends on the discriminative stimulus properties of the mediating outcome. *Learn. Behav.* **35:** 43–52.
36. Corbit, L.H., J.L. Muir & B.W. Balleine. 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.
37. Alheid, G.F. 2003. Extended amygdala and basal forebrain. *Ann. N.Y. Acad. Sci.* **985:** 185–205.
38. Shiflett, M.W. & B.W. Balleine. 2010. At the limbic-motor interface: disconnection of basolateral amygdala from nucleus accumbens core and shell reveals dissociable components of incentive motivation. *Eur. J. Neurosci.* **32:** 1735–1743.
39. Krettek, J.E. & J.L. Price. 1977. Projections from the amygdaloid complex to the cerebral cortex and thalamus in the rat and cat. *J. Compar. Neurol.* **172:** 687–722.
40. McDonald, A.J. 1991. Organization of amygdaloid projections to the prefrontal cortex and associated striatum in the rat. *Neurosci.* **44:** 1–14.
41. Pickens, C.L., M.P. Saddoris, M. Gallagher & P. C. Holland. 2005. Orbitofrontal lesions impair use of cue-outcome associations in a devaluation task. *Behav.Neurosci.***119:** 317–322.
42. Schoenbaum, G., B. Setlow, S.L. Nugent, *et al.* 2003. Lesions of orbitofrontal cortex and basolateral amygdala complex disrupt acquisition of odor-guided discriminations and reversals. *Learn. Memory* **10:** 129–140.
43. Burke, K.A., T.M. Franz, D.N. Miller & G. Schoenbaum. 2008. The role of the orbitofrontal cortex in the pursuit of happiness and more specific rewards. *Nature* **454:** 340–344.
44. van Duuren, E. *et al.* 2009. Single-cell and population coding of expected reward probability in the orbitofrontal cortex of the rat. *J. Neurosci.* **29:** 8965–8976.
45. Padoa-Schioppa, C. 2009. Range-adapting representation of economic value in the orbitofrontal cortex. *J. Neurosci.* **29:** 14004–14014.
46. Schoenbaum, G., A.A. Chiba & M. Gallagher. 2000. Changes in functional connectivity in orbitofrontal cortex and basolateral amygdala during learning and reversal training. *J. Neurosci.* **20:** 5179–5189.
47. Rolls, E.T. 2000. The orbitofrontal cortex and reward. *Cerebral Cortex* **10:** 284–294.

48. Chudasama, Y. & T.W. Robbins. 2003. Dissociable contributions of the orbitofrontal and infralimbic cortex to pavlovian autoshaping and discrimination reversal learning: further evidence for the functional heterogeneity of the rodent frontal cortex. *J. Neurosci.* **23:** 8771–8780.
49. Ostlund, S.B. & B.W. Balleine. 2008. Differential involvement of the basolateral amygdala and mediodorsal thalamus in instrumental action selection. *J. Neurosci.* **28:** 4398–4405.
50. Paton, J.J., M.A. Belova, S.E. Morrison & C.D. Salzman. 2006. The primate amygdala represents the positive and negative value of visual stimuli during learning. *Nature* **439:** 865–870.
51. Stalnaker, T.A., M.R. Roesch, T.M. Franz, *et al.* 2006. Abnormal associative encoding in orbitofrontal neurons in cocaine-experienced rats during decision-making. *Eur.J. Neurosci.* **24:** 2643–2653.
52. Schoenbaum, G., B. Setlow, M.P. Saddoris & M. Gallagher. 2003. Encoding predicted outcome and acquired value in orbitofrontal cortex during cue sampling depends upon input from basolateral amygdala. *Neuron* **39:** 855–867
53. Stalnaker, T.A., T.M. Franz, T. Singh & G. Schoenbaum. 2007. Basolateral amygdala lesions abolish orbitofrontal-dependent reversal impairments. *Neuron* **54:** 51–58.
54. Paxinos, G. & C. Watson. 1998. *The Rat Brain in Stereotaxic Coordinates*. Academic Press. New York.