

All That Glitters . . . Dissociating Attention and Outcome Expectancy From Prediction Errors Signals

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Roesch MR, Calu DJ, Esber GR, Schoenbaum G. All That Glitters . . . Dissociating Attention and Outcome Expectancy From Prediction Errors Signals *J Neurophysiol* : 587–595. . First published June 16, 2010; doi:10.1152/jn.00173.2010. Initially reported in dopamine neurons, neural correlates of prediction errors have now been shown in a variety of areas, including orbitofrontal cortex, ventral striatum, and amygdala. Yet changes in neural activity to an outcome or cues that precede it can reflect other processes. We review the recent literature and show that although activity in dopamine neurons appears to signal prediction errors, similar activity in orbitofrontal cortex, basolateral amygdala, and ventral striatum does not. Instead, increased firing in basolateral amygdala to unexpected outcomes likely reflects attention, whereas activity in orbitofrontal cortex and ventral striatum is unaffected by prior expectations and may provide information on outcome expectancy. These results have important implications for how these areas interact to facilitate learning and guide behavior.

INTRODUCTION

When an animal's expectations about its environment are violated, it is critical for the animal to somehow update its expectations to predict the changing circumstances. Classical learning theory postulates that learning to predict unexpected events is driven by errors in reward prediction (Pearce and Hall 1980; Rescorla and Wagner 1972; Sutton 1988). Correlates of reward prediction errors have been reported in the primate midbrain dopamine system, where evidence for them is compelling (Mirenowicz and Schultz 1994; Montague et al. 1996).

More recently, however, neural correlates of prediction errors have been reported in a variety of areas outside of the midbrain, including prefrontal cortex, orbitofrontal cortex, ventral striatum, amygdala, habenula, and putamen (Bayer and Glimcher 2005; Belova et al. 2007; D'Ardenne et al. 2008; Knutson et al. 2003; Matsumoto and Hikosaka 2007; McClure et al. 2003; Nobre et al. 1999; Roesch et al. 2007; Satoh et al. 2003; Schultz and Dickinson 2000; Tobler et al. 2005, 2006; Yacubian et al. 2006). Many of these areas have traditionally been implicated in value and associative encoding—signaling of outcome expectancies—rather than error reporting and the data implicating them in signaling errors are often sparse and incomplete. In addition, a number of alternative interpretations exist that may account for observed increases or decreases in neural activity associated with reward delivery. Such alternatives, which might better capture the nature of these signals, include not only variations in event processing (e.g., salience

or attention), but also outcome expectancy or prediction. As a result, it remains unclear what critical function these new areas might play in error encoding versus attention and associative learning.

Resolving this question is becoming increasingly critical to understanding how these corticolimbic regions interact in both guiding behavior and facilitating learning. Here we will compare changes in activity in response to changes in reward in ventral tegmental area (VTA), amygdala (ABL), orbitofrontal cortex (OFC), and ventral striatum (VS). These data suggest that activity in response to unexpected outcomes in VTA and ABL reflects encoding of prediction errors and event processing or attention, respectively, whereas output from OFC and VS—evident in single units—provides information bearing on outcome expectancy.

Dissociating attention and outcome expectancy from prediction errors

According to the influential Rescorla–Wagner model (Rescorla and Wagner 1972), prediction errors are calculated from the difference between the outcome predicted by all the cues available on that trial ($\sum V$) and the outcome that is actually received (λ). If the outcome is underpredicted, so that the value of λ is greater than that of $\sum V$, the error will be positive and excitatory learning will accrue to those stimuli that happened to be present. Conversely, if the outcome is overpredicted, the error will be negative and inhibitory learning will take place. Thus the magnitude and sign of the resulting change in learning (ΔV) is directly determined by prediction error according to the following equation

$$\Delta V = \alpha\beta(\lambda - \sum V) \quad (1)$$

where α and β are constants referring to the salience of the cue and the reinforcer, respectively. This basic idea is also captured in temporal difference reinforcement learning (TDRL) models, which extends the idea to apply to cues and other events and the value that they acquire through learning, allowing one to compute successive predictions of future reward within a trial rather than computing a single trial-based prediction as in Rescorla–Wagner.

Outcome-related neural activity in a large and growing number of brain areas has been shown to change in response to unexpected outcomes (Bayer and Glimcher 2005; Belova et al. 2007; D'Ardenne et al. 2008; Knutson et al. 2003; Matsumoto and Hikosaka 2007; McClure et al. 2003; Nobre et al. 1999; Roesch et al. 2007; Satoh et al. 2003; Schultz and Dickinson 2000; Tobler et al. 2005, 2006; Yacubian et al. 2006). These correlates are typically cited as evidence that these regions

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encode some version of a prediction error—i.e., the difference between expected and actual outcomes ($\lambda - \sum V$). Yet these errors are not the only theoretically important factor thought to drive learning. Attention and even signaling of the outcome expectancies themselves are critical for this process. Distinguishing among these alternative signals is a critical question facing neurophysiologists looking to assign functions to different brain areas based on these correlates.

Fortunately, in theory, signaling of prediction errors should be dissociable from signaling of attention and outcome expectancy. For example, Rescorla–Wagner (Rescorla and Wagner 1972) and TDRL (Sutton 1988) models predict bidirectional encoding of prediction errors to drive learning. In contrast, theoretical models of attention (Mackintosh 1975; Pearce and Hall 1980) posit that changes in event processing should result from a signal that is unidirectional, increasing following both unexpected reward delivery and omission. Finally, representations that encode outcome expectancy should be dissociable from error and attention-related encoding, in that such prediction signals should be small whereas the outcome is surprising (i.e., poorly predicted) and increase as the outcome becomes better predicted.

Dopamine neurons signal bidirectional prediction errors

Dopamine neurons of the midbrain have been widely reported to signal errors in reward, and more recently punishment, prediction (Bayer and Glimcher 2005; D'Ardenne et al. 2008; Fiorillo et al. 2003; Hollerman and Schultz 1998; Matsumoto and Hikosaka 2009; Mirenovic and Schultz 1994; Montague et al. 1996; Morris et al. 2006; Pan et al. 2005; Roesch et al. 2007; Tobler et al. 2003; Ungless et al. 2004; Waelti et al. 2001). Although this idea is not without critics, particularly regarding the precise timing of the phasic response (Redgrave et al. 1999) and the classification of these neurons as dopaminergic (Margolis et al. 2006), the evidence supporting this proposal is strong, deriving from multiple labs, species, and tasks. These studies demonstrate that a large proportion of the dopamine neurons exhibit bidirectional changes in activity in response to rewards that are better or worse than expected. Thus putative dopamine neurons fire to an unpredicted reward and firing declines when the reward becomes predicted and is suppressed when the predicted reward is not delivered. This is illustrated by the single-unit example in Fig. 1. Notably, although theoretical, signed prediction errors do not necessarily have to be represented in the form of bidirectional phasic activity within the same neuron, the occurrence of such a firing pattern does rule out other competing interpretations such as encoding of salience, attention, or motivation. Moreover, the fact that firing in dopamine neurons is negatively correlated with the ability to predict the outcome excludes the possibility that such activity may be encoding outcome expectancy.

Although much of this evidence has come from primates, recently similar results have been reported in other species. For example, imaging results indicate that blood oxygenation level dependent (BOLD) response in the human VTA is high when rewards occur unexpectedly and is suppressed when expected rewards are omitted, consistent with signaling of a bidirectional prediction error (D'Ardenne et al. 2008).

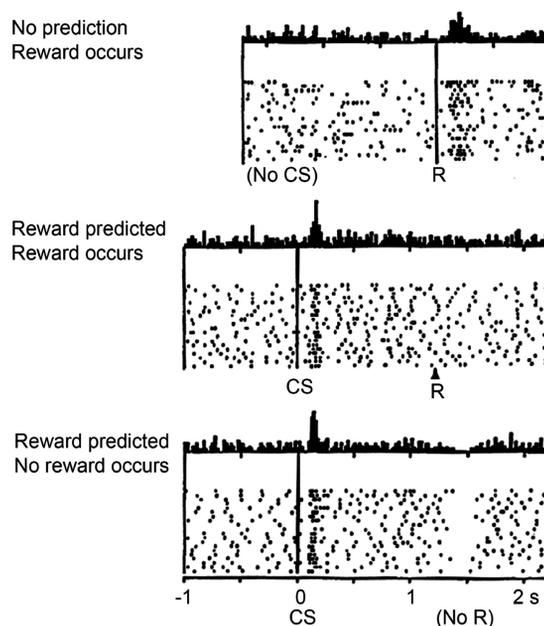


FIG. 1. Changes in firing in response to positive and negative reward prediction errors (PEs) in a primate dopamine neuron. Figure shows spiking activity in a putative dopamine neuron recorded in the midbrain of a monkey performing a simple task in which a conditioned stimulus (CS) is used to signal reward. Data are displayed in a raster format in which each tick mark represents an action potential and each row a trial. Average activity per trial is summarized in a perievent time histogram at the top of each panel. *Top panel* shows activity to an unpredicted reward (+PE). *Middle panel* shows activity to the reward when it is fully predicted by the CS (no PE). *Bottom panel* shows activity on trials in which the CS is presented but the reward is omitted (−PE). As described in the text, the neuron exhibits a bidirectional correlate of the reward prediction error, firing to unexpected but not expected reward and suppressing firing on omission of an expected reward. The neuron also fires to the CS; in theory such activity is thought to reflect the error induced by unexpected presentation of the valuable CS. This feature distinguishes a TDRL (temporal difference reinforcement learning) signal from the simple error signal postulated by Rescorla and Wagner (1972). (Figure adapted from Schultz et al. 1997.)

Similarly, Hyland and colleagues have reported signaling of reward prediction errors in a simple Pavlovian conditioning and extinction task (Pan et al. 2005). Putative dopamine neurons recorded in rat VTA initially fired to the reward. With learning, this reward-evoked response declined and the same neurons developed responses to the preceding cue. During extinction, activity was suppressed on reward omission. Parallel modeling revealed that the changes in activity closely paralleled theoretical error signals.

Prediction error signaling has also been reported in VTA dopamine neurons in rats performing a more complicated choice task, in which reward was unexpectedly delivered or omitted by altering the timing or number of rewards delivered (Roesch et al. 2007). This task is illustrated in Fig. 2, along with a heat plot showing population activity on the subset of trials in which reward was delivered unexpectedly. Dopamine activity increased when a new reward was instituted and then declined as the rats learned to expect that reward. Activity in these same neurons was suppressed later, when the expected reward was omitted.

In addition, activity was also high for delayed reward, consistent with recent reports in primates (Fiorillo et al. 2008; Kobayashi and Schultz 2008). Furthermore, the same dopamine neurons that fired to unpredictable reward also developed

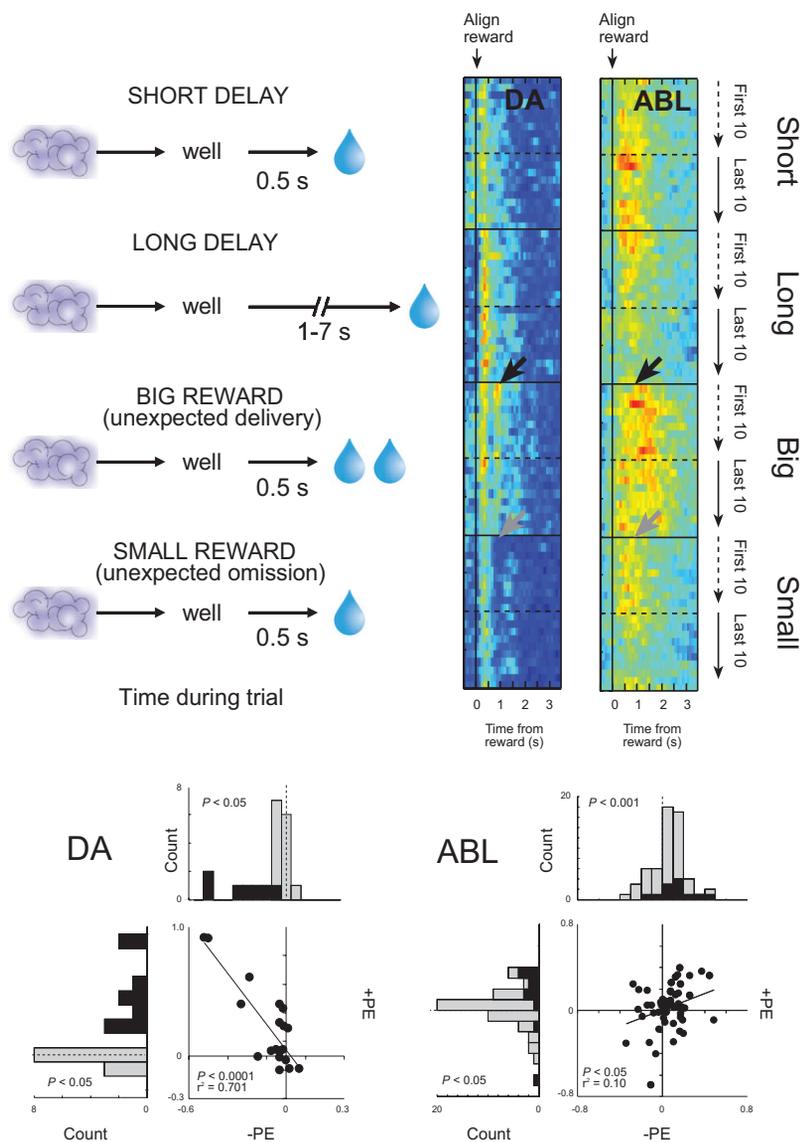


FIG. 2. Changes in firing in response to positive and negative reward prediction errors (PEs) in rat dopamine (DA) and basolateral amygdala (ABL) neurons. Rats were trained on a simple choice task in which odors predicted different rewards. During recording, the rats learned to adjust their behavior to reflect changes in the timing or size of reward. As illustrated in the *left panel*, this resulted in delivery of unexpected rewards (+PE) and omission of expected rewards (-PE). Activity in reward-responsive DA and ABL neurons is illustrated in the heat plots to the *right*, which show average firing synchronized to reward in the first and last 10 trials of each block, and in the scatter/histograms below, which plot changes in firing for each neuron in response to +PEs and -PEs. As described in the text, neurons in both regions fired more to an unexpected reward (+PE, black arrow). However, only the DA neurons also suppressed firing on reward omission; ABL neurons instead increased firing (-PE, gray arrows). This is inconsistent with the bidirectional error signal postulated by Rescorla and Wagner (1972) or TDRL and instead is more like the unsigned error signal used in attentional theories, such as Pearce and Hall (1980). (Figure adapted from Roesch et al. 2007, 2010.)

phasic responses to preceding cues with learning and this activity was higher when the cues predicted the more valuable reward. These features of dopamine firing are entirely consistent with prediction error encoding (Bayer and Glimcher 2005; D'Ardenne et al. 2008; Fiorillo et al. 2003; Hollerman and Schultz 1998; Matsumoto and Hikosaka 2009; Mirenowicz and Schultz 1994; Montague et al. 1996; Morris et al. 2006; Pan et al. 2005; Roesch et al. 2007; Tobler et al. 2003; Waelti et al. 2001).

Amygdala neurons signal shifts in attention

Although the amygdala has often been viewed as critical for learning to predict aversive outcomes (Davis 2000; LeDoux 2000), the last two decades have revealed a more general involvement in associative learning (Gallagher 2000; Murray 2007). Although the mainstream view holds that amygdala is important for acquiring and storing associative information (LeDoux 2000; Murray 2007), there have been hints in the literature that amygdala may also support other functions related to associative learning and error signaling. For exam-

ple, damage to central nucleus disrupts orienting and increments in attentional processing after changes in expected outcomes (Gallagher et al. 1990; Holland and Gallagher 1993, 1999) (see *Box 1*) and functional magnetic resonance imaging studies have correlated activity in the amygdala with the detection of monetary losses (Breiter et al. 2001; Yacubian et al. 2006). These findings suggest a role for amygdala in error signaling or detection.

Consistent with this idea, Salzman and colleagues (Belova et al. 2007) recently reported that amygdala neurons in monkeys are responsive to unexpected outcomes. However, this study showed minimal evidence of negative prediction error encoding or transfer of positive prediction errors to conditioned stimuli in amygdala neurons and many neurons fired similarly to unexpected rewards and punishments. This pattern of firing does not meet the criteria for a Rescorla-Wagner or TDRL prediction error signal. Instead, these authors suggested it might reflect changes in motivational salience or attention.

Similar firing patterns are also evident in rat basolateral amygdala (ABL), during performance of the same choice task

used to isolate prediction error signaling in rat dopamine neurons (Roesch et al. 2010). These data are presented alongside data from the dopamine neurons in Fig. 2. As in monkeys, many ABL neurons in rats increased firing when reward was delivered unexpectedly. However, such activity differed markedly in its temporal specificity from what was observed in VTA. This is evident in Fig. 2, where the increased firing in ABL occurs somewhat later and is much broader than that in dopamine neurons.

Moreover, activity in these ABL neurons was not inhibited by omission of an expected reward. Instead, activity was actually stronger during reward omission and those neurons that fired most strongly for unexpected reward delivery also fired most strongly after reward omission. Activity in ABL also differed from that in VTA in its onset dynamics. Whereas firing in VTA dopamine neurons was strongest on the first encounter with an unexpected reward and then declined, activity in the ABL neurons continued to increase over several trials after a shift in reward. These differences and the overall pattern of firing in the ABL neurons are inconsistent with signaling of a signed prediction error as envisioned by Rescorla–Wagner and TDRL, at least at the level of individual single units. Further, the gradual increase in activity suggests that this signal cannot be related to saliency or novelty; instead, such activity in ABL appears to reflect an unsigned error signal. Theories of associative learning have traditionally used unsigned errors to drive changes in stimulus processing or attention, operationalized as a learning rate parameter (Mackintosh 1975; Pearce and Hall 1980). According to this idea, the attention that a cue receives is equal to the weighted average of the unsigned error generated across the past few trials, such that attention on trial n (α_n) reflects attention on the prior trial (α_{n-1}) plus the absolute value of the summed error in reward prediction—reflecting surprise or uncertainty—on the preceding trial, according to the extended version of the Pearce–Hall model (Pearce et al. 1982). Thus

$$\alpha_n = \gamma |\lambda_{n-1} - \sum V_{n-1}| + (1 - \gamma)\alpha_{n-1} \quad (2)$$

where $(\lambda_{n-1} - \sum V_{n-1})$ is defined as the difference between the value of the reward predicted by all cues in the environment ($\sum V_{n-1}$) and the value of the reward that was actually received (λ_{n-1}) and γ is a weighting factor ranging between 0 and 1. This quantity—termed attention (α)—is multiplied by constants representing the intrinsic saliency (e.g., intensity) of the cue (S) and the reward (λ) to calculate the teaching signal (ΔV) that drives learning

$$\Delta V = \alpha S \lambda \quad (3)$$

Models incorporating attention as a critical factor in learning have been able to explain a number of important learning phenomena that cannot be readily accommodated by theories based on simple reward prediction errors (Hall and Pearce 1979; Kay and Pearce 1984; Swan and Pearce 1988; Wilson et al. 1992).

Interestingly changes in firing by neurons in amygdala in both rats and primates were evident only at the time of reward delivery. Such a signal could be providing trial-by-trial unsigned errors to alter the attentional resources devoted to the cues, in the manner anticipated by Pearce and Hall (1980). This could occur locally within ABL and may be evident in the rapid onset of cue-selective activity that characterizes firing in

ABL in a variety of tasks (Quirk et al. 1995; Schoenbaum et al. 1999; Tye et al. 2008) or it may occur in downstream targets. Potential targets would include OFC or VS, which show ABL-dependent associative encoding (Ambroggi et al. 2008; Schoenbaum et al. 2003), and regions such as basal forebrain or perhaps even in the midbrain dopamine neurons, which are reported to show cue-evoked activity related to cue saliency (Lin and Nicolelis 2008; Matsumoto and Hikosaka 2009).

However, an alternative possibility is that these signals are involved in modulating the processing of the rewarding event itself. Although this interpretation lies outside the scope of the Pearce–Hall model, which is concerned with attentional changes to cues rather than outcomes, recent evidence shows that processing of a reinforcer may also be enhanced when expectations about its occurrence are violated (Hall et al. 2005). Notably these ideas are not mutually exclusive. In other words, signaling of unsigned prediction errors by ABL may be related to variations in cue and reward processing. Indeed it is worth noting that ideas about errors and attention are generally not mutually exclusive; although these ideas are often presented as contrasting proposals, they can combine—and have been combined—in more general theories of learning (Lepelley 2004). To some extent, results such as those described here are consistent with these more integrative models (see *Box 2*).

Presumably, VTA signaling of prediction errors and ABL signaling of attentional factors would interact at some level. For example, error signaling by the dopamine system may initiate changes in activity related to attentional factors in ABL, enhancing representations of cues and/or outcomes when the latter are unexpected. Such an interaction is supported by the finding that activity related to unexpected reward in VTA preceded changes in reward-related activity in ABL by several trials. The time course of activity in these two areas is intuitively consistent, given that recognition of an error between expected and actual outcomes should presumably precede changes in attention. It is also possible that activity in ABL may feed back directly onto midbrain areas to regulate prediction error signaling. Thus once attention is being paid to unexpected rewards, prediction error signals are less necessary. Of course, a third possibility is that ABL and VTA do not influence each other directly, but rather interact via independent effects on downstream areas that encode representations of value critical in optimizing long-term behavior.

If single-unit activity in ABL contributes to attentional changes, then the role of the ABL in a variety of learning processes may need to be reconceptualized or at least modified to include this function. ABL appears to be critical for properly encoding associative information; associative encoding in downstream areas requires input from ABL (Ambroggi et al. 2008; Schoenbaum et al. 2003). This has been interpreted as reflecting an initial role in acquiring the simple associative representations (Pickens et al. 2003). However, an alternative account—not mutually exclusive—is that ABL may also augment the allocation of attentional resources to directly drive acquisition of the same associative information in other areas. As noted earlier, the signal in ABL, identified here, may serve to augment or amplify the associability of cue representations in downstream regions, so that these cues are more associable or salient on subsequent trials. Such interactions may be evident in neural activity reflecting uncertainty, which has been

reported in ABL and in prefrontal regions that receive input from ABL (Herry et al. 2007; Kepecs et al. 2008).

A role in attentional function for ABL would also affect our understanding of how this region is involved in neuropsychiatric disorders. For example, amygdala has long been implicated in anxiety disorders such as posttraumatic stress disorder (Davis 2000). Although this involvement may reflect abnormal storage of information in ABL, it might also reflect altered attentional signaling, affecting storage of information not in ABL but in other brain regions. This would be consistent with accounts of amygdala function in fear that have emphasized vigilance (Davis and Whalen 2001). Similarly, schizophrenia, which has been proposed to reflect the spurious attribution of salience to cues (Kapur 2003), could reflect altered signaling in ABL (Taylor et al. 2005), perhaps under the influence of aberrant dopaminergic error signaling.

Orbitofrontal cortex and ventral striatum signal state values

Two other areas that are often cited as signaling errors are the OFC and VS (Abler et al. 2006; D'Ardenne et al. 2008; Hare et al. 2008; Knutson and Gibbs 2007; McClure et al. 2003; O'Doherty et al. 2003; Rolls et al. 2008; Tobler et al. 2006); human brain imaging studies in particular have often shown that the BOLD signal in these regions is elevated in response to unexpected rewards. Yet it is unclear whether such BOLD correlates, when they are reported, reflect functional output (spiking activity) in these regions. This is because few single-unit studies in these areas have looked for neural correlates of reward prediction errors in tasks known to isolate errors in the dopamine system. Three recent reports on neural activity in OFC and VS in the same task used previously to assess signals in dopamine and ABL neurons directly address this question (Roesch et al. 2006, 2009; Takahashi et al. 2009). In this setting, the number of OFC or VS cells showing stronger firing during unexpected versus expected reward delivery was no more than would be expected by chance and roughly the same number of VS or OFC fired less during unexpected than that during expected reward delivery. One caveat is that reversal tasks are not always the most sensitive ones for identifying reward prediction errors because errors in reward prediction occur for only small numbers of trials, immediately after the reversal, and thus do not always provide as much data as would ideally be hoped for. Nevertheless, these findings suggest that spiking activity at the time of reward delivery in VS and OFC reflects neither attention nor reward prediction errors.

To the extent that output should be evident in spiking activity, then these results suggest that prediction errors encoded by the BOLD signal in imaging studies are not present in the output of OFC or VS. However, such a signal could reflect internal processing or input to these areas. Notably, both the midbrain dopamine system and amygdala project strongly to both VS and OFC; thus there is a ready source of input to explain these signals (Groenewegen et al. 1990; Haber et al. 1995; McDonald 1991a,b; Wright et al. 1996). As noted earlier, such inputs might serve to drive associative encoding in these areas. Similar suggestions have been made in a number of the aforementioned imaging studies, particularly regarding BOLD error correlates.

If OFC and VS do not provide error or attentional signals, then what is the function of these areas in the context of associative learning? Cells in both OFC and VS have been reported to fire in anticipation of expected rewards (Carelli 2002; Cromwell and Schultz 2003; Feierstein et al. 2006; Gottfried et al. 2003; Hassani et al. 2001; Hollander and Carelli 2005; Nicola et al. 2004; O'Doherty et al. 2002; Padoa-Schioppa and Assad 2006; Roesch and Olson 2004; Roesch et al. 2006, 2009; Tremblay and Schultz 1999), suggesting that VS and OFC might be involved in signaling cue-generated outcome expectancies ($\sum V$). A role in outcome expectancy signaling had been proposed previously for VS in the so-called Actor-Critic models (Joel et al. 2002), which have gained support from imaging studies (O'Doherty et al. 2004). According to this hypothesis, VS is proposed to act as a Critic, signaling the value of the current state. This signal can then be used to generate error signals as well as to calculate both action and choice values in downstream areas, such as the dorsal striatum, which then function as the Actor (Lau and Glimcher 2008).

OFC might perform a similar function as a Critic in some situations. OFC plays a critical role in learning driven by reward prediction errors (Takahashi et al. 2009). Specifically, OFC must be online when errors are generated for changes in behavior to be observed later during testing. Interestingly, this role for OFC appears to depend on connections with VTA. These data are consistent with the proposal that OFC is providing information about the prevailing expectation of reinforcement.

Importantly, OFC and VS may be signaling outcome expectancies based on different types of information. OFC has been implicated in signaling information about specific outcomes (Burke et al. 2008; Gallagher et al. 1999; Izquierdo et al. 2004; McDannald et al. 2005; Ostlund and Balleine 2007), whereas VS is more clearly implicated in signaling information about the general affective or emotional value that a particular outcome shares with other outcomes (de Borchgrave et al. 2002; Hall et al. 2001). Interestingly, different regions of VS (core vs. shell) may contribute differently to this valuation (Corbit et al. 2001).

Here we suggest that the respective roles of OFC and VS in signaling different types of associative information may also extend to any involvement in error signaling. According to such a proposal, OFC would serve as an outcome-specific critic, whereas VS would serve as a general-affect critic, each providing VTA with different components of outcome expectancy ($\sum V$) from which to construct prediction errors ($\lambda - \sum V$). These roles should be dissociable using task designs that independently manipulate the value and identity of expected rewards. Indeed, outcome-specific unblocking, in which reward identity is manipulated to drive learning, has been shown to be critically dependent on OFC function (Burke et al. 2008).

Conclusions

When an animal's expectations about its environment are violated, it is critical for the animal to somehow update its expectations to predict the changing circumstances. Classical learning theory postulates that learning to predict unexpected events is driven by discrepancies between actual and expected outcomes. These discrepancies are thought to directly drive learning (Mackintosh 1975; Pearce and Hall 1980; Rescorla and Wagner 1972; Sutton 1988) and also contribute to changes

in attention or processing of cues (and perhaps rewards) that also facilitate learning.

Several compelling lines of evidence for correlates of reward prediction errors have been reported in the primate midbrain dopamine system (Mirenowicz and Schultz 1994; Montague et al. 1996). However, ever increasing lines of evidence are accumulating that other areas contribute to this process (Bayer and Glimcher 2005; Belova et al. 2007; D'Ardenne et al. 2008; Knutson et al. 2003; Matsumoto and Hikosaka 2007; McClure et al. 2003; Nobre et al. 1999; Roesch et al. 2006, 2007, 2009, 2010 [some of the most recently published study is included here, as Supplemental material, for review]; Satoh et al. 2003; Schultz and Dickinson 2000; Takahashi et al. 2009; Tobler et al. 2005, 2006; Yacubian et al. 2006).¹ A comparison of these data suggests a model in which output from VTA and ABL signal prediction errors ($\lambda - \sum V$) and event processing or attention, respectively, whereas output from OFC and VS provides information bearing on outcome expectancy ($\sum V$).

Although such a model is attractive, it leaves many critical issues unanswered. They include questions regarding 1) how the error signals from VTA and the attentional signals in ABL interact, 2) what the roles of different parts of amygdala are in supporting attention and error encoding, and 3) how these signals instantiate or stamp in associative representations in downstream regions such as VS and OFC. Additional work is also necessary to differentiate the functions of OFC and VS (and perhaps other areas) in guiding behavior versus providing information to facilitate learning.

Box 1: role of the central nucleus of amygdala in attention

Behavioral and lesion studies of the amygdala have indeed implicated this area in attentional function. Despite emerging evidence that ABL may be important for signaling attention, the central nucleus of the amygdala has been the primary focus in studies of incremental attentional function (Holland and Gallagher 1999). For example, the central nucleus is critical for modulation of conditioned orienting responses during learning. Although stimulation of the central nucleus has been found to generate alerting behavior (Stock et al. 1981), rats with neurotoxic lesions of the central nucleus fail to acquire orienting responses to stimuli paired with food (Gallagher et al. 1990). Further investigation of this area reveals that central nucleus functions enhance associations when reward expectancies are violated. This has been demonstrated with the use of traditional blocking and modified unblocking tasks. In these tasks, a rat is trained that a cue predicts reward. Subsequently this cue is presented along with a second cue, followed by the same reward. Normally the second cue fails to acquire any associative strength, since the first cue is fully predictive of the outcome, and thus rats will respond at low levels to the new cue when it is presented alone during testing. However, if the amount (or other features) of reward is changed when the second cue is introduced, learning for this second cue is facilitated or unblocked. Importantly, increased conditioned responding for the new cue after unblocking is observed whether the amount of reward is increased or decreased. Although there are multiple explanations for learning in response to increased reward, the most parsimonious explanation

of excitatory learning in response to decreased reward is an up-regulation of attention.

Unblocking in response to decreased reward is critically dependent on the amygdala (Holland and Gallagher 1993). Rats with damage to the central nucleus of amygdala fail to develop conditioned responding to the new cue. This effect is observed only in response to decreases in reward value; rats with central nucleus lesions perform normally when reward value is increased. The specific deficit seen in lesioned rats is striking, especially when taking into account theoretical predictions from Rescorla–Wagner and Pearce–Hall learning models. Both models predict excitatory learning to unexpected increases in reward value. Thus unimpaired conditioned responding after central nucleus lesions in this context could reflect the contribution of multiple systems. Unexpectedly increasing reward value would result in positive reward prediction errors, which alone can support increases in conditioned responding, without the influence of attentional modulation provided by the central nucleus. However, only the Pearce–Hall model can readily account for excitatory learning in response to a surprising decrease in reward value. This is because unexpected downshifts in reward value would result in negative prediction errors, which the Rescorla–Wagner model predicts will contribute to inhibitory learning and decreases in conditioned responding.

Box 2: integration of attention and prediction errors

Traditional learning theories are often classified according to whether they ascribe the amount of learning accrued on a trial to the degree of processing received by the reinforcer (Rescorla and Wagner 1972) or by the predictor (Mackintosh 1975; Pearce and Hall 1980). Although each of these approaches has proven fruitful in advancing our understanding of the processes involved in associative learning, their inability to account single-handedly for all conditioning phenomena has recently spurred the search for more holistic models (Lepelley 2004). Thus far, such attempts have been dominated by the recognition that variations in both cue and reinforcer processing take place during conditioning and that each of these factors contributes to how much is learned on future trials.

The hybrid model described by LePelley (2004), for example, extends and integrates the rules in the Rescorla–Wagner (Rescorla and Wagner 1972), the Pearce–Hall (Pearce and Hall 1980), and the Mackintosh (Mackintosh 1975) models in such a way that it is able to accommodate empirical phenomena that previously were the preserve of its constituent theories. In a nutshell, this model posits that the increment of excitatory associative strength gained by a cue A (ΔV_A) on reinforced trials is given by

$$\Delta V_A = \alpha_A \sigma_A \beta_E (1 - V_A + \bar{V}_A) \left| \lambda - (\sum V - \sum \bar{V}) \right|$$

and the amount of inhibitory associative strength ($\Delta \bar{V}_A$) on extinction trials is given by

$$\Delta \bar{V}_A = \alpha_A \sigma_A \beta_I (1 - \bar{V}_A + V_A) \left| \lambda - (\sum V - \sum \bar{V}) \right|$$

where V_A and $\sum V$ denote, respectively, the conditioned excitation accrued by the target cue and all stimuli present and \bar{V}_A and $\sum \bar{V}$, their conditioned inhibition. It is assumed that excitatory learning is engaged if the summed error term

¹ The online version of this article contains supplemental data.

$[\lambda - (\sum V - \sum \bar{V})]$ is positive and that inhibitory learning is recruited if this error is negative. Thus the first issue of note is that conditioned excitation and inhibition are construed in this model as two separate quantities rather than two ends of a continuum in accord with the Rescorla–Wagner model (Rescorla and Wagner 1972). In the preceding equations, the absolute value of the summed error term $[\lambda - (\sum V - \sum \bar{V})]$ is multiplied by some cue-specific error term [e.g., $(1 - V_A + \bar{V}_A)$], in keeping with Rescorla's findings that the error generated by the individual predictors contributes—along with the summed error term—to determining the size of the increment in learning (Rescorla 2000, 2001). This product is then multiplied itself by a number of learning-rate parameters. The parameters β_E and β_I represent the salience of a present or absent reinforcer, respectively; α , in turn, denotes the amount of selective attention devoted to the cue in accord with Mackintosh (1975), increasing as the cue proves to be the best predictor available and decreasing as it shows to be no better a predictor than other cues present. Finally, σ denotes the attention commanded by the cue based on its predictive accuracy in accord with Pearce–Hall (Pearce and Hall 1980), its value being high when the cue is novel or its consequences are surprising and low when its consequences are accurately predicted. One interesting prediction of the model is that, overall, the attention paid to a cue ($\alpha \times \sigma$) should be maximal when the cue is both relevant (high α) and an imperfect predictor of its consequences (high σ).

Whatever the merits of this particular instantiation, hybrid theories pointedly underlie the fact that learning is multiply determined. Some of the factors involved have long been identified, but the nature of their interaction remains an open question—one that should inform and be informed by the study of interacting brain systems in behaving animals.

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