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NEURONAL CODING OF PREDICTION ERRORS

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■ **Abstract** Associative learning enables animals to anticipate the occurrence of important outcomes. Learning occurs when the actual outcome differs from the predicted outcome, resulting in a prediction error. Neurons in several brain structures appear to code prediction errors in relation to rewards, punishments, external stimuli, and behavioral reactions. In one form, dopamine neurons, norepinephrine neurons, and nucleus basalis neurons broadcast prediction errors as global reinforcement or teaching signals to large postsynaptic structures. In other cases, error signals are coded by selected neurons in the cerebellum, superior colliculus, frontal eye fields, parietal cortex, striatum, and visual system, where they influence specific subgroups of neurons. Prediction errors can be used in postsynaptic structures for the immediate selection of behavior or for synaptic changes underlying behavioral learning. The coding of prediction errors may represent a basic mode of brain function that may also contribute to the processing of sensory information and the short-term control of behavior.

INTRODUCTION

Consider the situation of a visitor to a foreign country looking for an ice tea at a vending machine. Not surprisingly, all symbols are incomprehensible to him. A tentative press of one of the buttons produces a can of orange juice. Trying again, he presses another button and, much to his surprise, receives the desired ice tea. Thus, the iced tea has arrived as unpredicted outcome. During the next few days he may press more wrong buttons at this vending machine, but ultimately he succeeds in reliably receiving iced tea, indicating that the symbols on this particular button have now become reliable predictors of iced tea. The learning curve for button-pressing for iced tea has reached an asymptote. As this example shows, learning results in the acquisition of reliable predictions about future outcomes.

Now, assume that the visitor failed to notice that the symbols indicating iced tea are different from those indicating cold coffee and that these buttons are close together. While predicting that his press will deliver iced tea, he presses the wrong

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button and receives cold coffee. This difference between the actual outcome (cold coffee) and the predicted outcome (iced tea) is referred to as a prediction error, an error that will make him choose more carefully in the future. In order to generalize the mechanisms underlying erroneous behavior, differences between outcome and prediction are referred to as errors in the prediction of outcome. As this example shows, prediction errors lead to the acquisition or modification of behavioral responses until the outcome can be reliably anticipated. When everything happens just as predicted and the prediction error is nil, no further behavioral changes will occur.

In this chapter, we discuss whether various brain structures process prediction errors that could control the modification of behavior in an attempt to understand the neuronal mechanisms underlying behavioral learning. Our discussion is limited to error-driven learning and does not include other forms, such as perceptual learning or certain forms of declarative learning in which the role of prediction errors is less obvious.

ROLE OF PREDICTION ERRORS IN LEARNING

The form of learning based on prediction errors enables behavior to adapt to the predictive and causal structure of the environment. The ability to learn about signals for motivationally significant events, usually termed reinforcers, can have a major influence on biological fitness by facilitating the impact of attractive and appetitive events and by mitigating the effects of aversive or noxious events. In many cases, the reactions elicited by a signal are controlled solely by the predictive relationship between the signal and the reinforcer. This form of predictive learning is manifest in Pavlovian or classical conditioning. In instrumental conditioning, by contrast, signals come to control new or altered reactions through experience with the causal relationship between the reaction and the reinforcer. Thus, our hypothetical visitor exhibited instrumental conditioning when he learned to operate the foreign vending machine, with the button symbol acting as the predictive signal, the press as the instrumental response, and the iced tea as the reinforcer. Whereas Pavlovian conditioning allows anticipation of biologically important events, instrumental conditioning enables a person to control the occurrence of these events. Thus, the predictive and causal learning manifested in these two forms of conditioning is a central process of adaptive and intelligent behavior.

Unpredictability of Reinforcement

Associative learning theory assumes that both types of learning consist of the formation of associations between representations of the signal or behavioral reaction and the reinforcer (Dickinson 1980). Moreover, the theory assumes that the associations are established when the signal or reaction is closely and regularly followed by the reinforcer (Mackintosh 1975), with each pairing of the signal or

reaction with the reinforcer bringing about an increment in the strength of the association. However, this simple contiguity-based learning rule does not sufficiently explain the formation of associations, which are prone to occur even when the signal is redundant as a predictor of the reinforcer and, therefore, relatively uninformative. This point can be illustrated by a blocking procedure involving four stimuli: A, B, X, Y.

	Stage 1	Stage 2	Test
Experimental:	A → reinforcer	AX → reinforcer	X
Control:	B → nothing	BY → reinforcer	Y

In stage 1, stimulus A is paired with the reinforcer and stimulus B is presented alone, so that stimulus A, but not B, becomes established as a predictor of the reinforcer. In stage 2, the pretrained stimuli A and B are presented in compound with two further stimuli, A with X and B with Y. Each of these compounds is then paired with the reinforcer for a number of trials.

According to simple associative rules, stimuli X and Y should be established as equivalent predictors of the reinforcer, as both received the same number of reinforcer pairings during Stage 2. This is not the case, however, because the reinforcer is differently predicted in AX than in BY trials. In BY trials, the reinforcer is not predicted by stimulus B, and stimulus Y becomes the key predictor of the reinforcer. By contrast, in AX trials, the reinforcer is already fully predicted by stimulus A, and stimulus X supplies no additional information and is redundant. Thus, stimulus Y is clearly more informative about the reinforcer than is stimulus X. Accordingly, the final test reveals that stimulus Y has acquired a much better prediction for the reinforcer than X. It appears as if learning about the predictive relationship between stimulus A and the reinforcer in the first stage blocks learning about stimulus X in the second stage.

Numerous studies demonstrate that learning in both humans (e.g. Martin & Levey 1991) and animals (e.g. Kamin 1969) is sensitive to the prediction of the reinforcer. On the basis of this blocking effect, Kamin (1969) suggested that the simple pairing of a stimulus and reinforcer is not sufficient for learning, that the occurrence of the reinforcer has to be surprising or unpredicted for the stimulus to be established as a predictor of the reinforcer. In this way, associative learning discriminates against redundant stimuli, which are relatively uniformative predictors of reinforcement.

Prediction Error and Behavioral Learning

The degree to which a reinforcer is unpredicted can be formalized in terms of a prediction error ($\lambda - \Sigma V$), with λ the strength of associations with the reinforcer that is required to predict fully the occurrence of the reinforcer, and ΣV the combined associative strength of all signals present on a learning episode. Thus, the predictor error ($\lambda - \Sigma V$) represents the extent to which the reinforcer occurs

surprisingly or unpredictably. If none of the signals have been trained, as is the case on the initial BY episode, ΣV is zero and the resulting prediction error is λ, representing the fact that the reinforcer is completely unpredicted. By contrast, when $\Sigma V = \lambda$, representing the fact that the reinforcer is fully predicted, the prediction error is zero. This is the case in the initial AX episodes when stimulus A has been pretrained to predict the reinforcer.

The notion of a prediction error relates intuitively to the very essence of learning. In general terms, learning can be viewed as the acquisition of predictions of outcomes (reward, punishment, behavioral reactions, external stimuli, internal states). Outcomes whose magnitude or frequency is different than predicted modify behavior in a direction that reduces the discrepancy between the outcome and its prediction. Changes in predictions and behavior continue until the outcome occurs as predicted and the prediction error is nil. No learning, and hence no change in predictions, occurs when the outcome is perfectly predicted. As is paradigmatically shown by the blocking phenomenon, this idea restricts learning to stimuli that signal surprising or altered outcomes and precludes learning about redundant stimuli preceding outcomes already predicted by other stimuli.

Although the concept of prediction error has been particularly well characterized with Pavlovian conditioning, it also applies to instrumental learning, in which the behavioral reaction is performed in the expectation of a predicted outcome, and the error occurs when the actual outcome differs from what had been predicted. Whatever the particular form of learning, these learning systems generate predictions of an event, process this event, and then compute the error between the event and its prediction, which is then used to modify both subsequent predictions and performance. Depending on the nature of the predicted outcome, prediction errors can concern a large range of events. These include positive reinforcers (rewards), negative reinforcers (punishments), external signals including attention-inducing stimuli, and behavioral goals and targets.

Associative learning theory deploys the concept of prediction error in two distinct ways. In the first, learning about a stimulus or response is determined directly by the prediction error, whereas according to the second, the prediction error has an indirect effect on learning by controlling the attention allocated to the predictive stimuli.

Direct Learning with Prediction Errors The rule of Rescorla & Wagner (1972) is an example of the first class of learning process. This rule assumes that the increment in the associative strength of a signal, ΔV, on a learning episode is directly determined by the prediction error

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

In this equation, α and β are learning constants that determine the rate of learning and reflect properties of the stimulus and reinforcer, respectively, such as their salience. During learning, reinforcement is incompletely predicted, the error term is positive when reinforcement occurs, and associative strength increases. After

learning, reinforcement is fully predicted, the error term is nil on correct behavior, and associative strength remains unchanged. When reinforcement is omitted because of changed contingencies, the error is negative and associative strength is reduced. During each learning episode, the increment in associative strength on trial *n* is added to the current associative strength of the signal to yield a cumulative change in the predictive status of that signal:

$$V_{n+1} = V_n + \Delta V_n. \qquad 2.$$

Under this rule, the selective learning seen in the blocking effect follows directly from the properties of the prediction error. As the error $(\lambda - \Sigma V)$ is zero, or at least of a small magnitude on AX episodes, little associative strength accrues to signal X. By contrast, the error on the initial AY episode has a larger value, thereby producing increments on the associative strength of signal Y.

In summary, the $(\lambda - \Sigma V)$ term represents an error in the prediction of reinforcement and determines the rate of learning. Learning occurs when the error term is positive and the stimulus does not fully predict the reinforcer. Nothing is learned when the prediction error is nil and the stimulus fully predicts the reinforcer. Forgetting or extinction occurs when the error term is negative and the reinforcer is less than predicted.

Learning Via Attention Induced by Prediction Errors Associability or attentional theories argue that prediction errors do not have a direct impact on associative strength but rather affect the attention that is allocated to stimuli and thereby indirectly modulate later changes in associative strength (Mackintosh 1975, Pearce & Hall 1980). The underlying assumption is that the more attention is allocated to a stimulus, the more readily it is associated with a reinforcer.

According to Pearce & Hall (1980), for example, a stimulus commands greater attention when it has been present during a previous learning episode whose outcome was unpredicted and less attention when the outcome of the episode was fully predicted. In other words, a subject assigns greater attention to a signal that has occurred in uncertain environments in the recent past, thereby facilitating learning about the predictive structure of such environments, and assigns less attention to a signal that perfectly predicts the outcome of an episode. These attentional changes are modeled by equating the changes in the associability parameter, α, of the signal with the absolute value of the prediction error on an episode:

$$\Delta\alpha = | \lambda - \Sigma V |, \qquad 3.$$

where | indicates absolute value. These changes in associability are cumulated successively across learning episodes so that the associability on episode *n* is a function of the associability on the preceding $n-1$ episode plus the change in associability on this episode (Kaye & Pearce 1984),

$$\alpha_n = g\Delta\alpha_{n-1} + (1 - g)\,\alpha_{n-1}, \quad 4.$$

where g is a parameter (bounded by 0 and 1) that determines the relative weight given to the associability of the signal on the preceding episode (αn_{-1}) and to the change in associability on that episode ($\Delta\alpha n_{-1}$). The associability of the stimulus, α, is then deployed to control the change in excitatory associative strength on episodes in which the stimulus is paired with the reinforcer, and in inhibitory associative strengths when the stimulus is paired with the omission of a predicted reinforcer. Thus, the prediction error plays no direct role in changes of associative strength, which are simply a function of the signal's associability, α, and the magnitude of the reinforcer, λ.

Attentional theory protects against redundant learning by ensuring that the associability of a signal is low when the reinforcer is fully predicted. Thus, in the blocking procedure, less attention is allocated to stimulus X than to Y. The reinforcer is predicted by stimulus A in initial AX trials, thus making the prediction error small. The resulting decreased attention to signal X reduces the associability of signal X and, consequently, the amount of learning about this stimulus. By contrast, the prediction error is large on initial BY trials because the reinforcer is not predicted by stimulus B, thereby ensuring that attention is elicited by signal Y, which in turn facilitates the subsequent growth of its associative strength. Although the role of the prediction error in the Rescorla-Wagner (1972) rule differs from that ascribed by attentional theories, behavioral analysis reveals that selective learning, such as that exhibited in the blocking effect, appears to involve both types of learning processes (Dickinson et al 1976).

Learning Mechanisms Based on Prediction Errors Associationism has the virtue of explaining behavioral learning in terms of processes that are in principle compatible with neuronal functioning. Konorski (1948) and Hebb (1949) attempted to explain predictive learning in terms of strengthening of synapses by conjoint pre- and postsynaptic activity. Subsequent neuronal network models have developed this neurobiological theory of learning by arguing that the synaptic connection weights between model neurons are controlled by the prediction error in the form of the Delta learning rule (Widrow & Hoff 1960), which is based on the LMS (least mean square) error procedure of process control (Kalman 1960, Widrow & Sterns 1985). Extensions of the Delta rule have been deployed as learning algorithms for complex connnectionist networks (Rumelhart et al 1986).

The Delta rule can be implemented by an assembly of neural units that computes the prediction error. Starting from the analysis of conditioning in aplysia by Hawkins & Kandel (1984), McLaren (1989) proposed that the prediction error could be computed by the negative feedback assembly shown in Figure 1. Changes in the weight of the connection between the signal and response units, $\Delta\omega$, are controlled by the activity in the signal unit, A_s, and the activity in a facilitatory unit, F. The facilitatory unit receives two inputs: direct excitation from the reinforcer or outcome unit, A_r, and negative feedback from the response unit

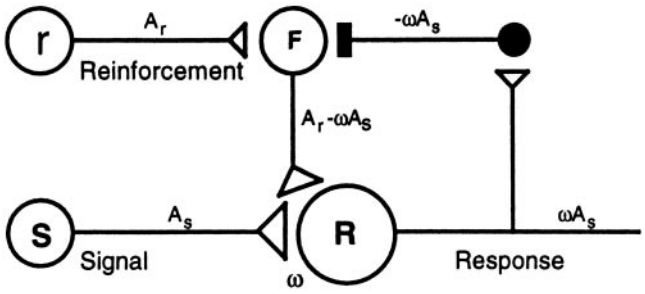

Figure 1 Schematic representation of an assembly for computing and delivering prediction error. The prediction error ($A_r - \omega A_s$) is computed in the facilitatory unit *F* as the difference between the primary reinforcement *r* and the output of the predictive response unit *R*. The prediction error serves to change the efficacy of the synaptic connection between the input signal unit *S* and the response unit *R*. A_s, activity of the signal unit; A_r, activity of the reinforcer unit; and ω, weight of connection between the signal and response units (after McLaren 1989).

via an inhibitory unit. As the activity in the response unit is a product of the activity in the signal unit and the weight of the connection, this feedback will be $-\omega A_s$ when inverted by the inhibitory unit. Consequently, at the time of reinforcement, the facilitatory unit carries the prediction error ($A_r - \omega A_s$), which is formally equivalent to the prediction error ($\lambda - \Sigma V$) described by associative learning rules (Sutton & Barto 1981). The change in connection weight between signal and response units, $\Delta\omega$, is analogous to changing the associative strength (V). It is a function of the conjoint activity in the signal and facilitatory units,

$$\Delta\omega = \eta\ (A_r - \omega A_s)\ \ A_s, \qquad 5.$$

with η the learning rate parameter. During initial learning when the signal is paired with the reinforcer, the synaptic weight is low, so the output of the response unit, ωA_s, is less than the input to the reinforcement unit, A_r. As a consequence, the facilitatory unit is active in response to the reinforcer, which in conjunction with the signal unit activity increases the connection weight across successive learning episodes until ωA_s equals A_r and the facilitatory unit is no longer active in response to the reinforcer. Under these circumstances, the presentation of the signal produces activity in the response unit that perfectly predicts the input to the assembly caused by the reinforcer. Correspondingly, if reinforcement is omitted, the error term is negative and synaptic weights are reduced appropriately.

The assembly by McLaren (1989), shown in Figure 1, deploys the prediction error in the direct manner implicated by the Rescorla & Wagner (1972) rule at the behavioral level, with the error term directly controlling the connection weight between the signal and response units. By contrast, the implementaion of the attentional theory of Pearce & Hall (1980) in a neural assembly would deploy the prediction error to control the attentional processing of the signal rather than

the connection weight between the signal and response units. Although implementation of this rule would be more complex than that shown in Figure 1 (Schmajuk 1997), the general principle of modulating connection weights by negative feedback through a facilitatory unit can also be employed.

CHARACTERISTICS OF NEURONAL PREDICTION ERROR SIGNALS

Whatever the relative merits of the predictive and attentional accounts of the deployment of an error term on learning, both theories have common neurobiological implications: Are there neuronal systems whose electrophysiological profile encodes prediction errors by reflecting the unpredictability of outcomes? In other words, are there systems that respond differentially to predicted and unpredicted outcomes and to the unexpected omission of a predicted outcome? As neurophysiological experiments investigate brain functions over time, we consider predominantly phasic predictions evoked by temporally explicit events rather than the more tonic outome predictions based on associations with the experimental context. The following sections evaluate various candidate neuronal systems by the formal criteria of learning theories and assess the kinds of events processed in the form of prediction errors, namely rewards, punishments, external signals including attention-inducing stimuli, and behavioral goals and targets.

Dopamine Neurons

Dopamine neurons show homogeneous, short latency responses to two classes of events, certain attention-inducing stimuli and reward-related stimuli. Attention-inducing stimuli, such as novel or particularly intense stimuli, elicit an activation-depression sequence. These stimuli are also motivating by eliciting behavioral orienting reactions and approach behavior, and they can be rewarding (Fujita 1987). Reward-related stimuli, such as primary liquid and food rewards, and visual and auditory stimuli predicting such rewards elicit pure activations (Romo & Schultz 1990, Schultz & Romo 1990, Ljungberg et al 1992). Events that physically resemble reward-predicting stimuli induce smaller, generalizing activations followed by depressions (Mirenowicz & Schultz 1996). Innocuous aversive stimuli are relatively ineffective in eliciting short latency activations (Mirenowicz & Schultz 1996), which suggests that dopamine responses reflect rewarding components of motivating stimuli rather than attentional components.

The dopamine neurons code an error in the prediction of reward (Figure 2). This can be observed when reward predictions change in learning situations (Ljungberg et al 1992, Schultz et al 1993, Mirenowicz & Schultz 1994, Hollerman & Schultz 1998). Primary rewards are unpredictable during initial behavioral reactions and reliably elicit neuronal activations. With continuing experience, reward becomes predicted by conditioned stimuli, and the activations elicited by

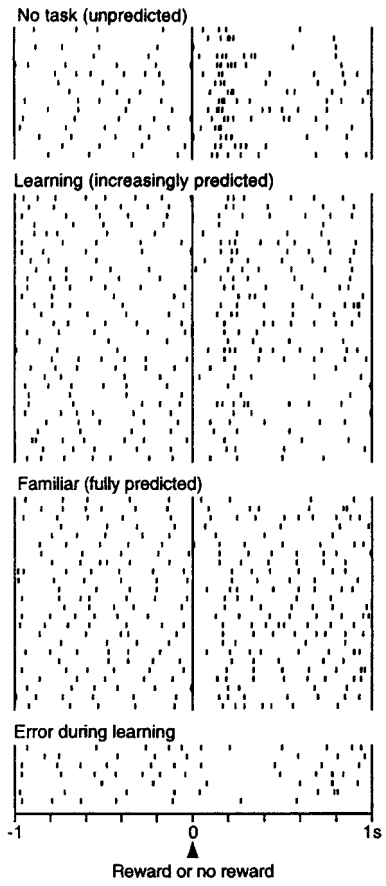

Figure 2 Coding of reward-prediction error during learning by a single dopamine neuron. No task: The temporally unpredicted occurrence of reward outside of any task induces reliable neuronal activation. Learning: The presentation of a novel picture pair in a two-picture discrimination task leads to uncertain behavioral performance with unpredictable occurrence of reward and dopamine response. (*Top* to *bottom*) Response decreases with increasing picture acquisition (only correct trials shown). Familiar: Presentation of known pictures in same task leads to predictable occurrence of reward and no dopamine response. Error during learning: Error performance with novel pictures leads to omission of reward. Note that the reward probability is >0.5 in two-choice discrimination. (*Dots*) Neuronal impulses, each line showing one trial, with the chronological sequence in each panel being from *top* to *bottom.* Rewards were small quantities of apple juice delivered to the mouth of a monkey. (From Hollerman & Schultz 1998.)

reward decrease, whereas the conditioned, reward-predicting stimuli now induce activations. If, however, a predicted reward fails to occur because the animal makes an incorrect response, dopamine neurons are depressed at the time the reward would have occurred.

The depression in the activity of the dopamine neuron at the expected time of the omitted reward shows that this activity encodes not only the simple expected occurrence of the reward but also the specific predicted time of the reward. This temporal sensitivity is also illustrated by the neural response to a shift in the time of reward. Introducing a temporal delay in reward delivery leads to a depression at the original time of reward, and an activation occurs at the new, unpredicted time of reward (Hollerman & Schultz 1998). A reward occurring earlier than predicted induces an activation, but no depression occurs at the original time of reward, as if the precocious reward has cancelled the reward prediction. However, the more general reward prediction within a given experimental context does not

seem to determine dopamine responses, as responses to free liquid outside of any task persist during the course of several months in the same laboratory environment, as long as the time of the liquid is unpredictable (Mirenowicz & Schultz 1994).

In summary, the reward responses depend on the difference between the occurrence and the prediction of reward (dopamine response = reward occurred − reward predicted). This represents an error in the prediction of reward analogous to the effective error term in associative learning ($\lambda - \Sigma V$) (Equation 1). The responses show the characteristics required by the facilitatory unit in the learning assembly from McLaren (1989) (Figure 1) by encoding the error term ($A_r - \omega A_s$) (Equation 5). The dopamine response and the acquisition of responses to reward-predicting stimuli also closely resemble the characteristics of the reinforcement signal of temporal-difference models of learning (Montague et al 1996, Schultz et al 1997, Schultz 1998), the development of which was independent of the biological results from dopamine neurons and which constitute efficient learning algorithms (Sutton & Barto 1981, Barto 1995). The transfer of the highly adaptive teaching signal from the primary reinforcer backward in time to the predictive stimulus results in a more specific influence on the involved synapses, as predictions occur closer in time to the stimuli and behavioral reactions to be conditioned, as compared with reinforcement at trial end.

The observation that omitted rewards induce opposite changes in dopamine neurons compared with unpredicted rewards suggests a form of error coding that is compatible with the idea that the error term directly controls learning about the prediction or, in other words, the connection between the signal and response units in the learning assembly (Figure 1). By contrast, this opponent response is more difficult to reconcile with an attentional account of learning that relates associability changes to the absolute (rectified) value of prediction errors (Equation 3). According to attentional theory, omitted rewards should induce neuronal changes in the same direction as do unpredicted rewards, which is not observed with dopamine neurons. The directional response, and the low efficacy of attention-inducing aversive stimuli, makes it unlikely that the dopamine reward response serves as a general attentional teaching signal. On the other hand, the dopamine responses to novel or intense stimuli might be compatible with an attentional account of learning. A further evaluation of these attentional responses for learning would require more formal assessments in terms of prediction errors.

Norepinephrine Neurons

Most norepinephrine neurons in locus coeruleus in rats, cats, and monkeys show homogeneous, biphasic activating-depressant responses to visual, auditory, and somatosensory stimuli eliciting orienting reactions (Foote et al 1980, Aston-Jones & Bloom 1981, Rasmussen et al 1986). Responses are often transient and appear to reflect changes in stimulus occurrence or meaning. Activations may occur only for a few trials with repeated presentations of food objects (Vankov et al 1995) or with conditioned auditory stimuli associated with liquid reward, aversive air

puff, or electric foot shock (Rasmussen et al 1986, Sara & Segal 1991, Aston-Jones et al 1994). Responses reappear transiently whenever reinforcement contingencies change during acquisition, reversal, or extinction (Sara & Segal 1991). Norepinephrine neurons rapidly acquire responses to new target stimuli during reversal and lose responses to previous targets before behavioral reversal is completed (Aston-Jones et al 1997). Particularly effective are infrequent events to which animals pay attention, such as visual stimuli in an oddball discrimination task (Aston-Jones et al 1994). Norepinephrine neurons respond in a rather homogeneous manner to free liquid delivered outside of any task (Foote et al 1980). Within a task, responses occur to the reward-predicting stimulus but are lost to the primary reward (Aston-Jones et al 1994). These neurons discriminate well between arousing or motivating and neutral events. These data suggest that norepinephrine responses are driven by the arousing and attention-grabbing components of a large variety of stimuli.

In relation to prediction errors, it appears that norepinephrine neurons respond to unpredicted but not predicted rewards (Foote et al 1980, Aston-Jones et al 1994), probably as part of their responses to attention-inducing stimuli. Whether a similar relationship to event unpredictability might apply to aversive and other attention-inducing events remains to be tested. In conclusion, norepinephrine neurons may code an error in the prediction of attention-inducing events, although assessment of the full extent of error coding would require further tests, including event omission.

Nucleus Basalis Meynert

Primate basal forebrain neurons are phasically activated by a variety of behavioral events, including conditioned, reward-predicting stimuli and primary rewards. Many activations depend on memory and associations with reinforcement in discrimination and delayed-response tasks. Activations (*a*) reflect the familiarity of stimuli (Wilson & Rolls 1990a), (*b*) become more important with stimuli and movements occurring closer to the time of reward (Richardson & DeLong 1990), (*c*) differentiate well between visual stimuli on the basis of appetitive and aversive associations (Wilson & Rolls 1990b), and (*d*) change within a few trials during reversal (Wilson & Rolls 1990c). Neurons respond frequently to fully predicted rewards in well-established behavioral tasks and to predicted visual and auditory stimuli (Richardson & DeLong 1986, 1990; Mitchell et al 1987), although responses to unpredicted rewards were more abundant in some studies (Richardson & DeLong 1990) than in others (Wilson & Rolls 1990a–c).

In relation to prediction errors, it appears that some nucleus basalis neurons respond particularly well to unpredicted rewards (Richardson & DeLong 1990), although more elaborate assessment would require further experimentation.

Cerebellar Climbing Fibers

Probably the first error-driven teaching signal in the brain was postulated to involve the divergent projection of climbing fibers from the inferior olive to Purkinje neurons in the cerebellar cortex (Marr 1969), and many models of cere-

bellar function are based on this concept (Ito 1989, Kawato & Gomi 1992, Llinas & Welsh 1993, Houk et al 1996).

Movement Climbing fiber inputs to Purkinje neurons are particularly activated when loads for wrist movements or gains between arm movements and visual feedback are changed, and monkeys adapt their behavior to the new situation (Gilbert & Thach 1977, Ojakangas & Ebner 1992). Climbing fiber input activity also shows changes in probability in relation to magnitudes of errors in reaching visual targets (Kitazawa et al 1998). Most of these changes consist of increased climbing fiber activity, irrespective of the direction of error, rather than activations or depressions related to errors in opposing directions. In a model of predictive tracking of moving targets by the eyes, climbing fibers carry prediction errors between eye and target positions (Kettner et al 1997). These data suggest that climbing fiber activity is compatible in several instances with a role for a prediction error in motor performance.

Aversive Conditioning A second argument for a role of climbing fibers in learning is derived from the study of aversive classical conditioning. A fraction of climbing fibers is activated by aversive air puffs to the cornea. These responses are lost when the air puff becomes predicted after Pavlovian eyelid conditioning using an auditory stimulus (Sears & Steinmetz 1991). After conditioning, neurons in the cerebellar interpositus nucleus respond to the conditioned stimulus (McCormick & Thompson 1984, Berthier & Moore 1990). Lesions of this nucleus or injections of the GABA antagonist picrotoxin into the inferior olive prevents the loss of inferior olive air puff responses after conditioning (Thompson & Gluck 1991, Kim et al 1998). The remaining response to the unconditioned stimulus is associated with the failure of these animals to undergo behavioral blocking (Kim et al 1998). These data indicate that monosynaptic or polysynaptic inhibition from interpositus to inferior olive suppresses neuronal responses to the unconditioned aversive stimulus after conditioning. This mechanism would allow inferior olive neurons to be depressed when a predicted aversive event is omitted. Taken together, climbing fibers are activated by unpredicted aversive events; they do not respond to fully predicted aversive events, and they might be depressed by omitted aversive events. This suggests that the responses of climbing fibers are sensitive to event unpredictability, which would allow them to report a full error in the prediction of aversive events.

Relation to Prediction Error The increased climbing fiber activity with motor performance errors may be related to error magnitude but possibly not error direction. Climbing fibers responding to aversive events may code a punishment prediction error, as they (*a*) are activated by unpredicted aversive events, (*b*) do not respond to fully predicted aversive events, and (*c*) are possibly depressed by omitted aversive events. Thus, climbing fibers may report errors in motor performance in analogy to the Delta rule (Equation 5) (Kawato & Gomi 1992) and

signal errors in the prediction of aversive events analogous to the Rescorla-Wagner rule (Equation 1) (Thompson & Gluck 1991). They may serve the function of the facilitatory unit (*F*) in the learning assembly shown in Figure 1, modifying the efficacy of the parallel fiber–Purkinje cell synapses.

Superior Colliculus

Neurons in the intermediate layer of superior colliculus are activated in association with a predicted visual stimulus brought into their receptive fields by a future saccadic eye movement. However, the same stimulus would not elicit a response in a fixation task, nor is saccadic eye movement alone associated with neuronal discharges (Mays & Sparks 1980, Walker et al 1995). These neurons appear to code the difference between the current and future eye position and not specific retinal target positions. Similarly, activity in neurons of the deep layer of superior colliculus change their activity during ocular fixation when eye position does not match target position (Figure 3) (Krauzlis et al 1997). Neuronal activity increases with mismatches in one direction and decreases with deviations in the opposite direction. Activity changes are particularly strong with small mismatches and occur even when the fixation error is so small that animals do not perform corrective saccades ($<$0.2–0.5°), which suggests that the activity changes do not reflect corrective eye movements. Activity changes occur also with fixation errors

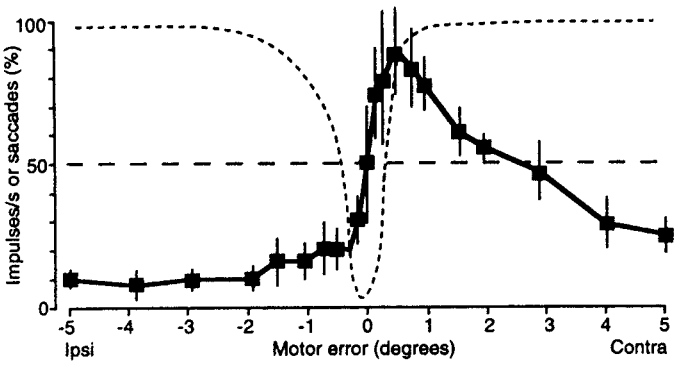

Figure 3 Coding of mismatches between eye and target position in superior colliculus. (*Solid line*) Impulse activity of a single neuron during ocular fixation as a function of mismatch between eye position and fixation target. Motor errors were induced by target steps. Error bars indicate a standard deviation of $+1$ (average of 12 trials). (*Horizontal dashed line*) Average firing rate without target steps; (*dotted line*) percentage of trials in which target steps elicited corrective saccades. Note that the steepest change of neuronal activity occurs with mismatches that were too small to be corrected by the monkey, indicating a lack of simple relationship to eye movement. [Reproduced with permission of the American Association for the Advancement of Science (from Krauzlis et al 1997).]

to extinguished targets, thus reflecting an oculomotor error rather than a visual mismatch.

In relation of prediction errors, it appears that intermediate and deep-layer neurons code errors in current eye positions relative to future eye positions and targets. This oculomotor prediction error would be best described by the Delta error between target and actual state (Equation 5).

Frontal Cortex

Anterior Cingulate Cortex Probably the earliest descriptions of neuronal error signals concern the anterior cingulate cortex. While monkeys erroneously perform movements around a lever outside of the permitted time window indicated by a trigger signal, particular transcortical mass potentials occur in anterior cingulate cortex (area 24) but not in medial or lateral premotor cortex of area 6 (Gemba et al 1986). These potentials may reflect the uncertainty about the appropriateness of the behavioral reaction. In humans, error-related negative brain potentials occur, with behavioral errors, in the area of anterior cingulate (Falkenstein et al 1991). With sudden changes of highly predicted target positions in well-learned movement sequences, blood flow is increased in anterior cingulate (Berns et al 1997). Some of these changes may reflect ongoing comparisons between actual and predicted states of behavior (Carter et al 1998). These data suggest that the anterior cingulate cortex is involved in the processing of error signals, although it is unclear how directional information about errors is coded. Most error coding appears to concern various aspects of behavioral performance rather than motivational outcomes.

Dorsolateral Prefrontal Cortex Some dorsolateral prefrontal neurons in behaving monkeys are only activated when predicted rewards are omitted by the experimenter or following erroneous task performance (Niki & Watanabe 1979), thus specifically coding negative reward-prediction errors. Conversely, during task performance, other neurons in this area respond to predicted reward but not to unpredicted reward, thus coding the absence of reward-prediction errors and being potentially related to the reinforcement of fully established task performance (Watanabe 1989). Some dorsolateral prefrontal neurons show activations with behavioral errors but not with delayed reward (Watanabe 1989). Their error coding may relate not to reward prediction but to task performance. Thus, error coding in dorsolateral prefrontal cortex may concern both reward-prediction errors and behavioral performance errors, albeit in different neuronal populations.

Orbitofrontal Cortex The erroneous spatial or temporal prediction of targets increases the blood flow in human orbitofrontal cortex, which may reflect a sensory prediction error, modification of a planned behavioral reaction, or emotions associated with these procedures (Nobre et al 1999). Some neurons in this area are activated only by rewards occurring at unpredicted times either within or

outside of any task (L Tremblay & W Schultz, manuscript in preparation). A second relationship to reward prediction is found during learning when reward predictions change with novel instruction stimuli and neurons modify their reward expectation-related activity in parallel with behavioral indicators of adapted reward expectation (L Tremblay & W Schultz, manuscript in preparation). Thus, activity in some orbitofrontal neurons reflects reward unpredictability, although the assessment of full reward-prediction error coding would require a test of the response to reward omission.

Frontal Eye Fields Neurons in frontal eye fields show predictive visual responses that code the difference between current and future eye position in a manner similar to that of neurons in the intermediate layer of superior colliculus (Umeno & Goldberg 1997).

Relation to Prediction Error Activity in anterior cingulate, dorsolateral prefrontal, and orbitofrontal cortex is increased when target stimuli appear at locations different from that predicted, when subjects make behavioral errors, or when rewards are omitted. Some neurons in the frontal eye field appear to code the difference between current and future eye position in a manner similar to that of neurons in superior colliculus. Although the forms of available data make comparisons with formal learning rules difficult, the selective activations with prediction errors concerning external signals, motor behavior, or rewards would be in general compatible with the Delta rule (Equation 5) or the Rescorla-Wagner rule (Equation 1).

Visual Cortex

Using a modeling approach, Rao & Ballard (1999) explored the idea that coding of prediction errors may contribute importantly to the functions of primary and higher-order visual cortex. On the anatomical basis of the long-known, heavy reciprocal connections between visual cortical areas, they suggest that each stage of visual cortex may compute the discrepancy between the information about the actual visual scene coming from lower-level visual areas and predictions arriving from higher-level visual areas that have evolved from previously experienced visual objects. The prediction error would be coded by the classical end-stopping hypercomplex neurons of visual cortex, which are sensitive to the length of a previously experienced bar stimulus. Only this prediction error would be propagated to the next higher level of visual cortex. Reiteration of this process across successive levels of cortex would lead to highly complex visual analysis. The model refers to error coding in the retina, where the surround creates a prediction of the center image, thus enhancing the discrimination of intensities within expected narrower ranges (Srinivasan et al 1982). These theories should provoke a number of interesting experiments for validating and assessing the role of pre-

dictive coding relative to other mechanisms, such as lateral inhibition and feedforward processing.

Striatum

Many tonically active striatal neurons respond with depressions to primary rewards (Apicella et al 1991) and reward-predicting stimuli (Aosaki et al 1994). When rewards occur unpredictably, responses are more frequent outside of behavioral tasks than during Pavlovian or operant tasks, where rewards are predicted by external stimuli (Apicella et al 1997). However, with omitted rewards, these neurons do not appear to show any response, not even opposite ones (P Apicella, personal communication), which suggests a relationship to reward unpredictability without coding of a full reward-prediction error. During learning, some slowly firing medium spiny striatal neurons show a change similar to that of orbitofrontal neurons. They rapidly modify reward expectation-related activity with novel, reward-predicting stimuli in parallel with behavioral indicators of adapted reward expectation (Figure 4) (Tremblay et al 1998).

In relation to prediction errors, tonically active neurons in the striatum appear to be sensitive to reward unpredictability but not to reward omission. The assessment of possible reward-prediction error coding in the larger group of slowly firing striatal neurons would require further tests, including the omission of reward.

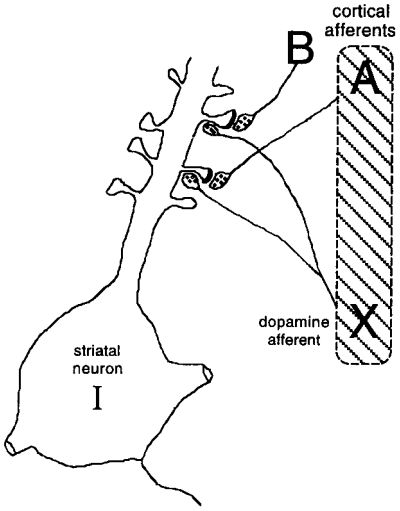

Figure 4 Basic design of possible influence of dopamine prediction error signal on neurotransmission in the striatum. Synaptic inputs from a single dopamine axon *X* and two cortical axons *A* and *B* contact a typical medium spiny striatal neuron *I*. Corticostriatal transmission can be modified by dopamine input *X* contacting indiscriminately the stems of dendritic spines that are also contacted by specific cortical inputs *A* and *B*. In this example, cortical input *A*, but not *B*, is active at the same time as dopamine neuron *X* (*shaded area*), e.g. following a reward-related event. This could lead to a modification of the $A \rightarrow I$ transmission, but leave the $B \rightarrow I$ transmission unaltered, according to the learning rule $\Delta\omega = \varepsilon rio$ (ω, synaptic weight; ε, learning constant; *r*, reinforcer prediction error; *i*, input activation; *o*, output activation). A similar synaptic organization exists with dopamine projections to cerebral cortex (Goldman-Rakic et al 1989). [Anatomical drawing based on anatomical data (Freund et al 1984) and modified from Smith & Bolam (1990).]

Functions of Neuronal Prediction Error Signals

Whatever the various forms and contents of prediction errors coded in different structures, the use of these messages for neuronal functioning depends on a number of additional neurobiological criteria. First, the nature of the anatomical projections from neurons encoding the prediction error determines whether the error signal is broadcast as a kind of global message to large populations of neurons or whether it only influences highly selected groups of neurons. In both cases, the error message would exert a selective influence on those neurons that were active in relation to the stimuli and behavioral reactions leading to the prediction error. In addition, the ways in which the neurons carrying error signals act on postsynaptic neurons determine how these signals are used. They could control the immediate behavioral response to the eliciting stimulus or, alternatively, induce long-lasting storage of changed predictions and behavioral reactions. In order to demonstrate such a learning function, it is necessary to show long-lasting modifications of neuronal functions, such as changes in postsynaptic responses to environmental events or modifications in the efficacy of teaching signals.

Global Alert or Reinforcement

Some of the neuronal systems we have described consist of relatively small numbers of neurons that show a largely homogeneous response to stimuli and behavioral reactions and project in a divergent and widespread mannner to much larger numbers of postsynaptic neurons. This is true of the dopamine neurons, which code positive and negative errors in the prediction of rewards, and of the norepinephrine neurons in the brainstem and the cholinergic neurons in nucleus basalis, which respond to unpredicted, attention-inducing stimuli and rewards.

Nature of Divergent Anatomical Projections Each dopamine cell body in substantia nigra or ventral tegmental area sends an axon to several hundred neurons in the striatum or frontal cortex (Percheron et al 1989) and has about 500,000 dopamine-releasing varicosities in the striatum. The dopamine innervation reaches nearly every neuron in the striatum as well as a considerable proportion of specific neurons in superficial and deep layers of frontal cortex (Berger et al 1988, Williams & Goldman-Rakic 1993). The anatomical projections of norepinephrine neurons from locus coeruleus and neighboring cell groups are probably even more divergent and widespread, with axons from single neurons projecting to cerebellar cortex and mainly deep layers of many areas of cerebral cortex (Morrison & Foote 1986, Lewis & Morrison 1989). A widespread projection exists also for the acetylcholine neurons in nucleus basalis to cerebral cortex and hippocampus (Lewis 1991). These projections often terminate at the same dendrites or even at the same dendritic spines that are also contacted by other inputs carrying specific and diverse behavior-related activity. This dendritic convergence is known for striatal and cortical dopamine terminals (Freund et al 1984, Gold-

man-Rakic et al 1989) and may also exist with cortical norepinephrine terminals (Aoki et al 1998) (Figure 4).

Taken together, the anatomical organization of these projections allows the prediction error to be broadcast as a global message to postsynaptic structures. The homogeneous reward and attention error messages of dopamine and norepinephrine neurons may influence in a selective manner the efficacy of concurrently active inputs to postsynaptic neurons while leaving inactive synaptic connections unchanged (Figure 4) (for further details, see Schultz 1998).

Immediate Influence on Neuronal Processing and Behavior The prediction error message may provide a gating or enabling signal for neurotransmission at the time of the erroneously predicted event but not lead to storage of new predictions or behavioral reactions. With competing synaptic inputs, neuronal activities occurring simultaneously with the error signal would be preferentially processed. This mechanism would result in biasing, prioritizing, or selection of certain inputs over others, depending on the temporal coincidence with the error signal (Schultz 1998). Behaviorally, the subject would show an orienting response toward the error-generating event. The attention induced by the error would increase the associability of the stimulus.

The immediate effects of prediction errors would be primarily determined by the influences of impulse-dependent synaptic transmission on postsynaptic membranes. Phasic dopamine signals to the striatum mainly affect D1 receptors (Schultz 1998), enhancing or reducing simultaneous cortically evoked excitations (Cepeda et al 1993, Hernandez-Lopez et al 1997). In the cortex, D1 activation increases the efficacy of local inputs (Yang & Seaman 1996). At the systems level, this process may lead to a focusing effect whereby all cortical inputs are reduced and only the strongest activities pass through the striatum to external and internal pallidum (Yim & Mogenson 1982, Toan & Schultz 1985). As a consequence, the dopamine error signal could produce a rapid switch of attentional and behavioral processing to surprising external events (Redgrave et al 1999). Signals from norepinephrine neurons reduce excitations by local neurons (Law-Tho et al 1993), increase the signal-to-noise ratio of responses in cerebellar Purkinje cells (Freedman et al 1977), and potentiate excitatory and inhibitory influences in cerebral cortex (Waterhouse & Woodward 1980, Sessler et al 1995).

Taken together, these data suggest that the global error messages can be used for dynamically and instantaneously selecting which external stimuli and behavioral reactions are processed within the limited channel capacity of neuronal transmission. This function is analogous to the role of the prediction error in controlling attentional processes within associative learning theories (Mackintosh 1975, Pearce & Hall 1980).

Influence on Neuronal Plasticity and Learning Neuronal error signals may induce or facilitate long-lasting changes of synaptic transmission at immediate postsynaptic sites or at neurons further downstream. Dopamine neurotransmission

is involved in long-term depression in the striatum via D1 and D2 receptors (Calabresi et al 1992) and the frontal cortex (Otani et al 1998), induction of long-term potentiation in the striatum (Wickens et al 1996), and enhancement of long-term potentiation in hippocampus via D1 receptors (Otmakhova & Lisman 1996). In a generally comparable manner, norepinephrine induces or facilitates the induction of various forms of long-term depression and potentiation in the hippocampus via alpha and beta receptors (Dahl & Sarvey 1989, Katsuki et al 1997). These data accord with an earlier theory that suggests that the widespread norepinephrine projection to cerebellar Purkinje cells may modify the synaptic efficacy of parallel fiber inputs and thus contribute to motor learning (Gilbert 1975).

Taken together, these data suggest that the error messages carried by dopamine and norepinephrine neurons may influence the efficacy of synaptic transmission in a global manner. The potential effects of error signals on synaptic plasticity would comply with a three-factor learning rule (Figure 4). The presence of a neuronal error input would modify neuronal transmission at synapses with Hebbian-type plasticity based on coincident pre- and postsynaptic activity. Only those synapses would be modified that are activated by stimuli or behavioral reactions associated with the prediction error, whereas synapses not involved would remain unchanged. Synaptic transmission would be changed every time an error signal arrives. By contrast, synapses would be stabilized and not undergo further changes when the neuronal error signal is zero, because the occurrence of the behavioral outome is fully predicted. Moreover, a directional error signal, such as is exhibited by dopamine neurons, supports not only increments in synaptic transmission under the influence of a positive error signal but may also mediate decrements under the influence of a negative error signal in the form of a depression of the baseline rate of activity. By contrast, unidirectional error signals, possibly emitted by attention-coding mechanisms, may require additional mechanisms in order to result reasonably rapidly in appropriate synaptic changes. In sum, the mechanisms governing the use of neuronal error signals for synaptic modifications match closely the use of prediction errors for behavioral modifications derived from animal learning theory.

A variation of this learning mechanism may involve changes in the efficacy of teaching signals. The responses of dopamine and norepinephrine neurons shift during learning episodes from the primary reward to the stimulus predicting the reward (Ljungberg et al 1992, Sara & Segal 1991, Aston-Jones et al 1994). This transfer may mediate the behavioral phenomenon of conditioned reinforcement, as predictors of primary reinforcers acquire reinforcing properties themselves. Thus, predictive learning could involve two consecutive steps (Schultz 1998). In the first step, the reinforcement signal is transferred from the primary reinforcer to the predictive stimulus. In the second step, the error signal elicited by the predictive stimulus then serves as an effective teaching signal at target plastic synapses. The efficacy of these synapses would be selectively modified on the basis of coincident stimulus- and behavior-related activity, as with an error in the prediction of primary reinforcement. In this way, chains or sequences of predic-

tive stimuli can be acquired that allow progressively earlier anticipation of the primary reward. Modeling studies have demonstrated that conditioned reinforcement signals are more efficient for acquiring sequences than are primary reinforcers occurring only after the behavioral reaction (Sutton & Barto 1981, Friston et al 1994, Suri & Schultz 1998). The transfer of the prediction error to conditioned reinforcers may constitute a mechanism for behavioral learning even in the absence of synaptic plasticity in target areas. In this case, only the shift to predictive coding would occur during learning, and the advance information provided by this earlier signal would make behavioral reactions more frequent, rapid, and precise on the basis of the immediate influences on the neuronal processing described above (Lovibond 1983).

Anatomically Selective Error Correction and Prediction Learning

Some error coding systems consist of selected, distributed groups of neurons that show heterogeneous, selective relationships to specific physical aspects of stimuli or parameters of behavioral reactions and project in an anatomically highly specific and selective manner to postsynaptic neurons. Examples of these systems are found in the superior colliculus, in the frontal cortex, and with cerebellar climbing fibers, where positive and negative errors in the prediction of rewards, punishments, external signals, behavioral states, and targets are coded, and in the orbitofrontal cortex and striatum, where neurons respond to the unpredicted appearance of rewards and movement targets. These error signals may induce long-term potentiation or long-term depression at modifiable synapses, which are found in several structures, such as hippocampus, visual cortex, prefrontal cortex, motor cortex, cerebellum, and striatum (Artola & Singer 1987, Iriki et al 1989, Ito 1989, Hirsch & Crepel 1990, Calabresi et al 1992). The effects of error signals may in some cases comply with a three-factor learning rule, as seen with the cerebellar climbing fibers influencing the efficacy of parallel fiber synapses on Purkinje cells (Eccles et al 1967, Ito 1989).

Prediction errors have been classically used for modifying the behavior of agents in models of negative feedback control (Widrow & Sterns 1985). These control processes are primarily concerned with immediate corrections of errors and do not necessarily lead to the emergence and storage of modified predictions. However, it is difficult to judge from the available data whether neuronal systems would serve error-correcting functions without storing altered predictions or behavioral reactions. Modified predictions may be stored for only a few seconds while specific behavioral tasks are efficiently performed, or they may result in more long-lasting changes compatible with the common notion of learning.

Examples for short-term storage and use of predictions are found with a predictive model of visual cortex, which proposes that prediction errors are used for establishing visual receptive field properties in different stages of cortical processing (Rao & Ballard 1999). The prediction error is computed between visual

input signals and predictions arriving from the next higher stage of visual cortex. This error signal is continuously fed back to the higher stage for updating the predictions. The computation of errors between current and future eye positions and between eye and target positions in neurons of the superior colliculus, frontal eye fields, and parietal cortex (Duhamel et al 1992, Walker et al 1995, Krauzlis et al 1997, Umeno & Goldberg 1997) might evolve by propagation among these closely interconnected structures and serve for the continuous, predictive coding of eye positions. The resulting command signals could then be employed by oculomotor neurons for moving the eyes to targets without continuously computing complete target positions in retinal or supraretinal coordinates (Umeno & Goldberg 1997).

The error signal of cerebellar climbing fibers may be used for inducing long-lasting changes in the efficacy of simultaneously active parallel fiber inputs to Purkinje cells, in particular long-term depression (Ito 1989). Each climbing fiber contacts 10–15 Purkinje cells with hundreds of synapses (Eccles et al 1967). Evidence that climbing fiber activity acts as a teaching signal for behavioral learning comes from the observation that alteration of this activity influences the amount of associative aversive conditioning that occurs in the blocking procedure (Kim et al 1998). The activation of cerebellar climbing fibers by behavioral errors would reduce the efficacy of parallel fiber inputs and decrease simple spike activity in Purkinje cells. This mechanism could explain the adaptation of the vestibulo-ocular reflex (Ito 1989), although an alternative learning mechanism may involve nonsimultaneous climbing fiber activity (Raymond & Lisberger 1998). Decreased simple spike activity was observed during adaptation of wrist movements to load changes (Gilbert & Thach 1977), but not with gain changes between visual cursor and hand movement (Ojakangas & Ebner 1992). On a shorter time base, a model of cerebellar function in predictive eye movements uses climbing fiber prediction errors for continuously updating predictions of target motion and thus optimizing smooth pursuit eye tracking (Kettner et al 1997). Thus, climbing fiber error messages could modify the efficacy of movement- or punishment-related parallel fiber inputs to Purkinje cells.

Neurons in the dorsolateral prefrontal, orbitofrontal, and anterior cingulate cortex are activated in relation to errors in the prediction of reward (Niki & Watanabe 1979, Watanabe 1989; L Tremblay & W Schultz, manuscript in preparation) and behavioral performance (Gemba et al 1986, Falkenstein et al 1991, Watanabe 1989, Carter et al 1998, Nobre et al 1999). These error signals might be elaborated in conjunction with neurons in the striatum that code rewards relative to their unpredictability (Apicella et al 1997) and neurons in the amygdala signaling reward-predicting stimuli (Nishijo et al 1988). The error signals are conceivably propagated to specific neurons concerned with immediate changes in behavior and the updating of predictions. Neurons in the cingulate motor area of monkeys are activated during movement changes following reductions of predicted reward (Shima & Tanji 1998). This activity does not occur when behavior fails to change following reward reduction, which suggests a relationship to the

consequences of the reward-prediction error. Rapid updating of neuronal reward predictions over the course of a few minutes occurs during learning in the striatum (Tremblay et al 1998) and orbitofrontal cortex (L Tremblay & W Schultz, manuscript in preparation). These mechanisms in fronto-striatal systems may serve for behavioral adaptations by which subjects remain able to predict and obtain desired reward objects in changing environmental situations. They are compatible with the general function of these structures in the control of goal-directed behavior.

Coding of Prediction Errors as Basic Mode of Brain Function

Predictions provide two main advantages for behavior. First, they reflect stored information and thus bridge the time gap between the occurrence of an event and the later use of the information about this event. Based on past experience, they provide advance information and allow subjects to prepare behavioral reactions and judge the respective values of behavioral alternatives. Humans and animals switch as frequently as possible to predictive modes for optimizing behavioral reactions, for example when tracking regularly moving targets with the eyes (Kowler & Steinman 1979). Second, predictions serve as references for evaluating current outcomes. Are outcomes better, similar, or worse than predicted? Such comparisons result in prediction errors that can be used for changing predictions or behavioral reactions until the prediction error disappears. This forms the basis for associative learning theories that postulate that learning depends crucially on prediction errors and reaches its asymptote once everything occurs as predicted (Rescorla & Wagner 1972, Mackintosh 1975, Pearce & Hall 1980).

The use of prediction errors for changing predictions or behavioral reactions occurs over a large time range. Some of the described neuronal systems may contribute to learning by signaling errors in reference to predictions that were set up several hours or days earlier, such as dopamine neurons. By contrast, other systems process predictions that are established only during the course of a few seconds or minutes. Such prediction errors might be more appropriate for the immediate control of behavior than for long-term learning. They are seen with neurons in the frontal eye fields, parietal cortex, and superior colliculus, which signal differences between current and future eye positions (Duhamel et al 1992, Walker et al 1995, Umeno & Goldberg 1997), with neurons in superior colliculus reacting to mismatches between eye and target positions (Krauzlis et al 1997), and with cerebellar climbing fibers activated with hand-target mismatches (Kitazawa et al 1998). Rapid changes of predictions are seen with neurons in the striatum during learning (Tremblay et al 1998).

Prediction errors may not only serve for adaptive changes of behavior but could constitute a mode of on-going neuronal processing. Rather than processing the full and often redundant amount of incoming or outgoing information, neurons may simply compute the differences between the predicted and current input or output, thereby making neuronal processing more efficient (MacKay 1956). Pre-

diction errors might be put to use in primary sensory systems, where neurons in the retina compute the difference between actual visual stimulus components and those predicted from the visual surround (Srinivasan et al 1982). A related idea forms the basis for a model of visual cortex explaining the properties of end-stopping neurons (Rao & Ballard 1999). Neurons in the cerebellar cortex of fish may compute the difference between actual and predicted sensory input and signal preferentially inputs that are unpredicted (Bell et al 1997).

It thus appears that prediction errors contribute importantly to several aspects of brain function. Basic brain mechanisms establish predictions, compare current input with predictions from previous experience, and emit a prediction error signal once a mismatch is detected. The prediction error signal then acts as a strong impulse for changes of synaptic transmission that lead to subsequent changes in predictions and behavioral reactions. The process is then reiterated until behavioral outcomes match the predictions and the prediction error becomes nil. In the absence of a prediction error, there would be no signal for modifying synapses, and synaptic transmission would remain unchanged and stable. Thus, the computation and use of prediction errors may contribute to the self-organization of goal-directed behavior.

The computation of prediction errors appears to be a basic capacity of neuronal processing on different time scales and for a variety of purposes. Behavioral learning is an important function supported by the general capacity for computing and deploying prediction errors in the control of synaptic efficacy. Understanding the ways in which prediction errors are computed, specifying their use in neuronal learning rules (Raymond & Lisberger 1998), and determining their other potential neuronal functions are immediate and important goals for neuroscience.

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