

Anterior Cingulate Cortex, Selection for Action, and Error Processing

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Introduction

The concepts of “attention to action” (Norman & Shallice, 1986) and “selection for action” (Allport, 1987) refer to how particular cognitive intentions and sensory inputs are selected and coupled with the effector system for the control of action production. A central role in this process has been attributed to the anterior cingulate cortex (ACC) (Posner, Petersen, Fox, & Raichle, 1988; see also Mesalun, 1981; Posner & Dehaene, 1994; Posner & DiGirolamo, 1998; Posner & Petersen, 1990). According to this view, the ACC contributes to executive or strategic aspects of motor control by allowing only particular sources of information access to the output system. More specifically, the ACC appears to be involved in selecting actions or action plans that are consistent with task goals, that is, to transform intentions into actions. This proposition has been supported by converging evidence from a broad array of empirical techniques, including functional neuroimaging, neuroanatomical, neurophysiological, intracranial stimulation, and lesion studies in humans and animals (Bush, Luu, & Posner, 2000; Devinsky, Morrell, & Vogt, 1995; Dum & Strick, 1993; Goldberg, 1992; Paus, 2001; Picard & Strick, 1996). This research has indicated that a caudal/dorsal area of the ACC appears to be involved in the cognitive control of motor behavior.

Consistent with this role, the ACC is also thought to be involved in error processing (Holroyd & Coles, 2002; cf. Botvinick, Braver, Barch, Carter, & Cohen, 2001). This position holds that the ACC is sensitive to incorrect or inappropriate behaviors, and suggests that one aspect of the ACC control function involves bringing erroneous behaviors in line with desired goals. The motivation for this proposal is due primarily to observations of the error-related negativity (ERN), a component of the event-related brain potential (ERP) associated with error commission, which appears to be generated in the ACC. In this chapter, we review these ERN studies and discuss what insights they have provided into ACC function. We begin by describing the initial investigations that demonstrated that ERN is produced by an error processing system. Then, we review studies that suggested that the ERN is generated in the ACC and, thus, that the ACC is involved in error

processing. We next present a recent theory that holds that the ERN is produced by the impact of reinforcement learning signals conveyed by the mesencephalic dopamine system on the ACC, and that the ACC uses that information to improve performance on the task at hand. Lastly, we provide empirical support for this theory.

The ERN and Error Processing

The ERN is a negative deflection in the ERP that peaks about 80 ms after subjects make an incorrect response in speeded response-time tasks (Figure 1a). Although a similar component can be seen in the reports of several studies appearing in the eighties (e.g., McCarthy, 1984; Renault, Ragot, & Lesevre, 1980), a paper by Falkenstein and his colleagues in Dortmund (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990) seems to have acted as a stimulus for a recent surge of interest in brain potentials associated with errors. The report from Dortmund was followed by observations from laboratories at Illinois (Gehring, Goss, Coles, Meyer, & Donchin, 1993) and Oregon (Dehaene, Posner, & Tucker, 1994). One thing that intrigued these early investigators was that the onset of this negative potential preceded the overt erroneous response, suggesting that the cognitive system “knew” about the error as it was being made.

These early reports were followed by studies of the influence of various factors on the amplitude and latency of the component, and of the relationship between the component and remedial actions that appeared to be consequences of erroneous behavior (see Falkenstein, Hohnsbein, & Hoormann, 1995; Gehring, Coles, Meyer, & Donchin, 1995). The amplitude of the ERN increases with the importance of errors (Falkenstein et al., 1995; Gehring et al., 1993) defined by speed versus accuracy instructions, and with the degree of error, defined by the number of movement parameters that differ between incorrect and correct responses (Bernstein, Scheffers, & Coles, 1995; Falkenstein et al., 1995). The ERN is present when errors cannot be corrected by a second motor response, as in a Go/NoGo task (Scheffers, Coles, Bernstein, Gehring, & Donchin, 1996), and it decreases as the quality of performance declines with fatigue (Scheffers, Humphrey, Stanny, Kramer, & Coles, 1999) or with degraded stimuli (Scheffers & Coles, 2000). Finally, the amplitude of the ERN appears to be

related to remedial actions that compensate for the fact that an error is or has been made. These remedial actions include error correction, error force, and an increase in reaction time on trials following an error (Gehring et al., 1993).

A second line of research was stimulated by the observation that a similar brain response occurs when subjects receive feedback indicating that they have just made an erroneous response. Miltner, Braun, and Coles (1997) observed ERN-like activity in a time-estimation task when subjects received feedback that their previous time estimate was incorrect (see also Badgaiyan & Posner, 1998). This phenomenon has been called the “feedback ERN” to distinguish it from its counterpart, the “response ERN” (Figure 1b). Importantly, the discovery of the feedback ERN seemed to indicate that ERN production does not depend directly on motor processes associated with error commission (such as remedial actions that follow the error), but rather on processes that can occur subsequent to the error, such as the detection of the error or learning from the error. Also important was the observation that the feedback ERN was produced independently of whether the feedback was delivered in the auditory, somatosensory, or visual modalities (Miltner et al., 1997). In like fashion, subsequent research demonstrated that the response ERN was produced by errors committed not only with the hands, but also with the feet (Holroyd, Dien, & Coles, 1998), the eyes (Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001; Van ‘t Ent & Apkarian, 1999), and the voice (Masaki, Tanaka, Takasawa, & Yamazaki, 2001), as well as by slow (but correct) responses in tasks in which speed is of the essence (Johnson, Otten, Boeck, & Coles, 1997; Luu, Flaisch, & Tucker, 2000). These findings indicate that the system that produces the ERN is involved in a “generic” form of error processing that is sensitive to error information regardless of its type or source.

Taken together, these results motivated the theory that the ERN is elicited either by a process of error detection or by a process that is engaged following the detection of the error (Falkenstein et al., 1991; Gehring et al., 1993). As articulated by Coles, Scheffers, and Holroyd (2001), the theory proposes that error-detection

involves a comparison between two response representations: (a) a representation of the response that is being executed, derived from efference copy; and (b) a representation of the response that should be executed, derived from further stimulus processing, and application of the appropriate stimulus–response mapping rule. (In most cases, the ERN has been investigated in situations where errors occur as the result of impulsive action, such that further processing of the stimulus can lead to a representation of the correct response.) When the comparison process detects a mismatch between these two representations, or when error feedback is provided, an error-signal is generated. The signal provides an input to the remedial action system whose function is to deal with the fact that an error is being made, or has been made.

The ERN and the ACC

Coincident with the effort to understand the function of the system that produces the ERN was a search to identify where in the brain the ERN is produced. Early studies suggested that the ERN was generated in the ACC. This inference was based on the component's frontal-central scalp distribution, which suggested that the ERN was generated by "a system involving the anterior cingulate cortex and supplementary motor areas" (Gehring et al., 1993, p. 389), but also on the results of primate studies that reported that neurons in the ACC were activated by errors (e.g., Gemba, Sasaki, & Brooks, 1986) and by the absence of expected rewards (Niki & Watanabe, 1979). A recent study has further indicated that some ACC neurons are sensitive to both error responses and error feedback (Ito, Stuphorn, Brown, & Schall, in press). Source localization studies of the ERN were also consistent with this hypothesis, with dipole modeling of the difference in activity between correct and incorrect responses yielding a single source located in the inferior ACC (Dehaene, et al., 1994). Follow-up studies showed ACC sources irrespective of whether the errors were made with hands or feet (Holroyd et al., 1998), and studies using MEG yielded similar results (e.g. Miltner, et al., in press). Analyses of the feedback ERN also showed an ACC source, irrespective of whether the feedback was presented in the

visual, the auditory, or the somatosensory modality (Miltner et al., 1997; see also Gehring & Willoughby, 2002).

Imaging studies using rapid event-related fMRI confirmed the dipole models, reporting activation in the ACC (BA 24/32) in response to errors (Carter et al., 1998). A number of studies have indicated that the rostral-caudal extent of the ACC is activated more to errors than to correct responses (e.g., Kiehl, Liddle, & Hopfinger, 2000; Menon, Adleman, White, Glover, & Reiss, 2001; Ullsperger & Von Cramon, 2001). Initial investigations aimed at identifying the locus of feedback-related error activity were less successful (e.g., Van Veen, Holroyd, Cohen, Stenger, & Carter, 2002), but recent imaging studies have found that a dorsal region of the ACC is activated by error feedback (Ullsperger & Von Cramon, 2003) and by unexpected decreases in rewards (e.g., Bush et al., 2002). Furthermore, a recent study showed that a single area in caudal and dorsal ACC is activated by both error responses and by error feedback (Holroyd, Nieuwenhuis, et al, 2003). These results indicate that this region of the ACC comprises part of a generic error processing system that is sensitive to both internal and external sources of error information, and are consistent with the hypothesis that this brain region produces both the response ERN and the feedback ERN.

The suggestion that the ACC produces the ERN was corroborated by findings in patients with focal brain lesions. Stemmer, Segalowitz, Witzke, and Schoenle (in press) studied patients with a ruptured aneurysm of the anterior communicating artery, resulting in damage to the ACC and adjacent regions. They reported that these patients, although showing error rates comparable to normal control subjects, did not produce ERNs following error responses. A similar result was obtained by Swick and Turken (2002), who studied a patient with a rostral-to-middorsal ACC lesion. Gehring and Knight (2000) showed that patients with lateral prefrontal damage produced an ERN following incorrect trials, but also following correct trials. In contrast, Ullsperger and colleagues found a reduced ERN in people with lateral prefrontal lesions (Ullsperger, Von Cramon, &

Müller, 2002). Although these two results are in disagreement, they both suggest an interaction between the ACC and the prefrontal cortex in error processing.

Finally, involvement of the ACC in ERN production has been suggested by studies of clinical populations. Key among these populations are people with obsessive-compulsive disorder and people with Gilles de la Tourette syndrome, who have been shown to produce abnormally large ERNs (Gehring, Himle, & Nisenson, 2000; Hajcak & Simons, 2002; Johannes, Wieringa, Müller-Vahl, Dengler, & Münte, 2002). These disorders disrupt high-level error processing and motor control functions, and are believed to affect a neural network involving the ACC and the basal ganglia (Devinsky et al., 1995; Wise & Rapoport, 1991).

Reinforcement Learning Theory of the ERN

Although these studies established a role for the ACC in error processing and in the production of the ERN, they were less specific about the details of that role. In contrast, a recent theory has formalized these ideas in a computational model that makes explicit the functional significance and neural implementation of the error processing system that gives rise to the ERN (Holroyd & Coles, 2002; for a contrasting view see Botvinick et al., 2001; Yeung, Botvinick & Cohen, 2003). The theory is based on previous research that indicates that the basal ganglia monitor ongoing events and continuously predict whether the outcomes of those events will end favorably or unfavorably (Barto, 1995; Houk, Adams, & Barto, 1995; Montague, Dayan, & Sejnowski, 1996). According to this position, when the basal ganglia revise their predictions for the worse (indicating that ongoing events are “worse than expected”), they produce a negative error signal. Conversely, when the basal ganglia revise their predictions for the better (indicating that ongoing events are “better than expected”), they produce a positive error signal. These negative and positive error signals are conveyed from the basal ganglia as phasic decreases and increases, respectively, of the tonic activity of the mesencephalic dopamine system. In turn, the dopamine system conveys the signals back to the basal ganglia, where they are

used to improve the predictions, and to frontal cortex (for reviews of this phasic activity, see Schultz, 1998, 2002).

The ERN theory builds on this theoretical framework by proposing that the ACC uses these dopamine signals to improve performance on the task at hand according to principles of reinforcement learning (Holroyd & Coles, 2002; see also Sutton & Barto, 1998). According to the theory (Figure 2), the ACC receives motor command information from multiple neural sources (called “controllers”), including dorsolateral prefrontal cortex, orbitofrontal cortex, the amygdala, and other areas. Because the commands from the different systems can sometimes conflict, the function of the ACC is to give control over the motor system to the controller that is best suited to carry out the task. Thus, consistent with its putative role in selection for action, the ACC acts as a “control filter” that decides which high-level executive commands gain control over the motor system. The theory also holds that the dopamine signals modulate and reinforce ACC activity such that the filtering function is optimized, a position that is consistent with the established role played by dopamine in reinforcement learning (for reviews see Schultz 1998, 2002), and with dopaminergic modulation of ACC activity (e.g., Crino, Morrison, & Hof, 1993; Porrino, 1993; Richardson & Gratton, 1998; Vogt, Vogt, Nimchinsky, & Hof, 1997; Wilkinson et al., 1998). According to the theory, furthermore, the impact of the dopamine signals on the apical dendrites of motor neurons in the ACC modulates the amplitude of the ERN, such that phasic decreases in dopamine activity (indicating that ongoing events are worse than expected) are associated with large ERNs, and phasic increases in dopamine (indicating that ongoing events are better than expected) are associated with small ERNs. Thus, response ERNs and feedback ERNs are elicited, respectively, by unpredicted error responses and error feedback.

This “reinforcement learning theory of the ERN” (RL-ERN theory) has inspired several empirical studies of the feedback ERN (reviewed by Nieuwenhuis, Holroyd, Mol, & Coles, 2003). All of these studies have employed a pseudo trial-and-error learning paradigm in which, on each trial, subjects select one of several

response options and are then told the outcome of their choice by means of a feedback stimulus. The first of these studies tested a fundamental prediction of the theory, which is that the ERN should occur following the first indication that ongoing events are worse than expected. Thus, if a negative feedback stimulus is not predicted by prior events, then presentation of the feedback stimulus should elicit the ERN. On the other hand, if the subject has learned a set of stimulus-response mappings and the feedback merely confirms the application of an inappropriate mapping, then the ERN should occur at the time of the error response and not at the time of feedback presentation. According to the theory, on trials when the system detects the error at the time of the response, there is a negative prediction error and a large ERN. Therefore, when the feedback is presented the system has already detected the error, and there is no change in prediction and no ERN associated with the feedback. These predictions were confirmed in two recent experiments involving a probabilistic learning task: The response ERN was elicited on trials in which the feedback was fixed and the stimulus-response mappings could be learned, and the feedback ERN was elicited on trials in which the feedback was random and the stimulus-response mappings could not be learned (Holroyd & Coles, 2002; Nieuwenhuis et al., 2002). Furthermore, in an event-related fMRI study that adopted a similar task design, a caudal and dorsal area of the ACC was activated following error responses on trials with fixed mappings and following error feedback on trials with random mappings, consistent with the ERN results (Holroyd, Nieuwenhuis, et al., 2003).

These studies also demonstrated that the changes in the predictions are not all-or-none: The relative size of the response ERN and feedback ERN is highly sensitive to the degree to which a response is predictive of the value of the feedback (Nieuwenhuis et al., 2002), and even when the feedback is delivered at random, the amplitude of the feedback ERN tracks the size of the prediction error on a trial-by-trial basis (Holroyd & Coles, 2002). Furthermore, in a study in which the global probability of rewards and punishments was varied by condition, it was found that the amplitude of the feedback ERN was largest when the unfavorable outcomes

were infrequent (and therefore less likely to be predicted) compared to when the unfavorable outcomes were frequent (and therefore more likely to be predicted) (Holroyd, Nieuwenhuis, Yeung, & Cohen, in press).

Other recent studies have investigated how the monitoring system determines whether an outcome is good or bad. In one such study, feedback stimuli conveyed information along two different dimensions: a "gain/loss" dimension indicating whether the subject's choice led to a gain or loss of money, and a "correct/error" dimension indicating whether the subject's choice was better or worse than the alternative choice that the subject could have made (Nieuwenhuis, Yeung, Holroyd, Schurger, & Cohen, 2003). The results demonstrated that the feedback ERN was sensitive to both the gain/loss information and the correct/error information conveyed by the feedback, depending on which dimension of the feedback was made most salient to the subjects. Results from another study are consistent with this view (Gehring & Willoughby, 2002). These findings support the notion that the ERN is sensitive to any performance-related feedback information indicating favorable or unfavorable outcomes.

In these studies, the feedback indicated explicitly whether an outcome was favorable or unfavorable (such as a red square of color indicating monetary loss and a green square of color indicating monetary gain). However, the question arises as to how the monitoring system determines the favorableness of an outcome when that information is not made explicit by the feedback. To address this question, Holroyd, Larsen, & Cohen (in press) varied the range of possible outcomes by condition. On each trial of a "win" condition, subjects either won nothing, won a small reward, or won a large reward, and on each trial of a "lose" condition, subjects either lost nothing, lost a small reward, or lost a large reward. It was found that winning nothing in the win condition elicited a large ERN whereas losing nothing in the lose condition did not elicit an ERN, even though these two outcomes were identical (no change in total reward); and that small losses in the lose condition and small wins in the win condition elicited ERNs of comparable amplitude, even though these outcomes were different (wins versus losses). These results indicate that the monitoring system determines

whether an outcome is good or bad relative to the range of outcomes possible: For example, a \$500 reward is good when the alternative is nothing, but a \$500 is bad when the alternative is \$1000 (but see also Mars, Bruijn, Hulstijn, Miltner, & Coles, 2003). The results also dovetail with those of Yeung and Sanfey (2003), who showed that ERN amplitudes elicited by large losses in the context of large gains and losses are about the same size as ERN amplitudes elicited by small losses in the context of small gains and losses.

In all of these studies, the feedback stimuli indicated only the outcome of each trial (e.g., win vs. loss), but not what should be done to improve performance at the task (e.g., press the left button). According to the RL-ERN theory, the error information carried by the mesencephalic dopamine system describes only whether an event was favorable or unfavorable, but not how that information should be used.¹ By default, then, the theory holds that a different neural system processes error information that indicates what a subject should do to improve performance. To investigate this issue, Mars et al. (2003) conducted a reinforcement learning experiment that included two conditions, one in which the feedback indicated only the outcome, and a second in which the feedback also indicated how performance should be improved. They found that the feedback ERN was smaller in the second condition, consistent with the position that the associated error information was processed by a different neural system.

Other studies have investigated the neural basis of the theory - in particular, whether the mesencephalic dopamine system contributes to ERN production. Although the results of these studies must be viewed as only suggestive, many of the findings are consistent with the theory and provide some preliminary support for it. For example, ERN amplitude is increased by administration of d-amphetamine, which releases dopamine and inhibits its reuptake, suggesting that dopamine affects the mechanism that produces the ERN (De Bruijn, Hulstijn, Verkes, Ruigt, & Sabbe, 2003). Conversely, alcohol consumption reduces ERN amplitude (Ridderinkhof et al., 2002), possibly because dopamine receptors may contribute to the reinforcing aspects of alcohol addiction (Holroyd & Yeung, 2003). Although Parkinson's disease disrupts the

mesencephalic dopamine system, evidence of abnormal ERNs in people with mild to moderate Parkinson's disease has been mixed (Falkenstein et al., 2001; Holroyd, Praamstra, Plat, & Coles, 2002). On the other hand, ERN amplitude is smaller in older adults, perhaps because of age-related changes of the dopamine system (Nieuwenhuis et al., 2002). Moreover, dopamine dysfunction is thought to be an important factor underlying schizophrenia (e.g., Dolan et al., 1995; for review see Davis, Kahn, Ko, & Davidson, 1991; Harrison, 2000), and people with schizophrenia evidence abnormal ERNs (Bates, Kiehl, Laurens, & Liddle, 2002; Kopp & Rist, 1999; Mathalon et al., 2002). Also suggestive is the finding of abnormally large ERNs in people with Gilles de la Tourette syndrome (Johannes et al., 2003), because hyperactivity of the midbrain dopamine system has been proposed to be the main neurochemical abnormality underlying this disorder (Devinsky, 1983; Singer, Butler, Tune, Seifert, & Coyle, 1982).

Conclusion

In a recent review of the ACC, Paus (2001, p. 423) concluded that “the ACC is a prime example of a brain structure in which a regulatory network, composed of cells from the modulatory brainstem nuclei, interacts with an executive network, composed of local-circuit neurons.... By virtue of their action on ACC neurons, neuromodulators such as dopamine ... are in a powerful position to regulate the interaction between cognition and motor control in relation to changes in emotional and motivational states.” In this view, the selection for action process mediated by the ACC is fine-tuned by the reward-related functions associated with midbrain dopamine. Research into the ERN has provided insight into how such a process might occur. In particular, the RL-ERN theory has specified how the ERN may provide a window into this control mechanism. The principles underlying the theory are computationally robust and, in other domains, have been used to teach autonomous systems how to operate in uncertain and variable environments (Sutton & Barto, 1998), including how and where to deploy attention (Ballard, 1991; Whitehead & Lin, 1995). These successes afford the hope that the same principles can be used to understand the contribution of the ACC to attention and action selection.

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Acknowledgements

This research was supported in part by postdoctoral fellowship MH63550 from the National Institute of Mental Health (C.B.) and by the Netherlands Organization for Scientific Research (S.N.).

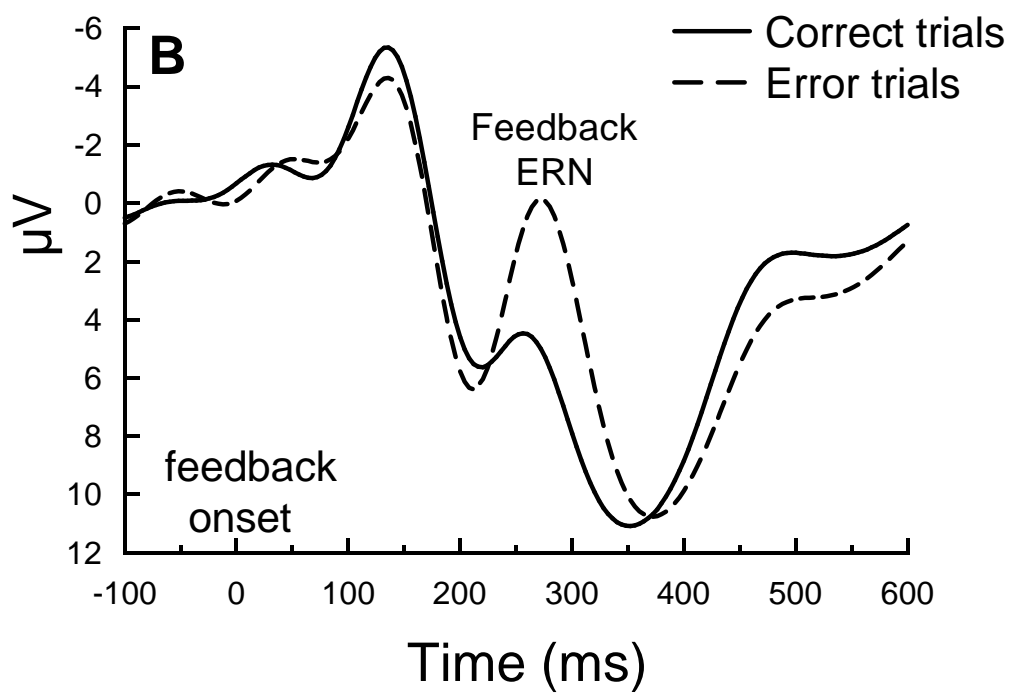
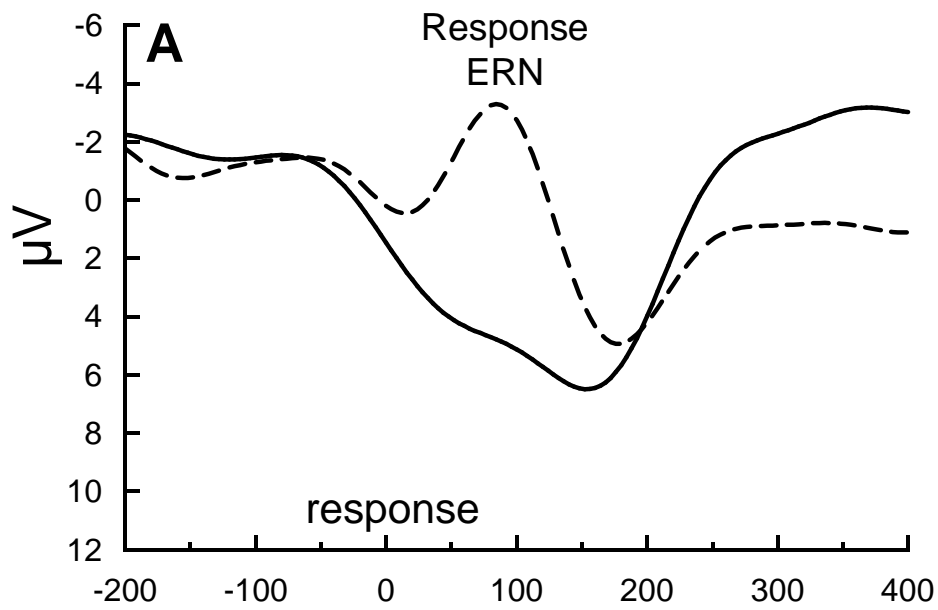
Footnote

1. The midbrain dopamine system is sometimes said to convey a “scalar” signal (one piece of information: good vs. bad), as opposed to a “vector” signal (many pieces of information: good vs. bad and how the behavior should be modified).

Figures

Figure 1. The error-related negativity (ERN). a. The response ERN. b. The feedback ERN. Negative is plotted up by convention. Adapted from Nieuwenhuis et al. (2002).

Figure 2. Reinforcement learning theory of the ERN. Multiple controllers in the brain process sensory input and produce motor commands. These commands are filtered by a control area in the anterior cingulate cortex, such that a subset of appropriate, non-conflicting commands are passed to the motor system. Simultaneously, a monitor located in the basal ganglia processes sensory information from the external environment, feedback information (such as rewards and punishments), and efference copies of the response in progress. The monitor produces error signals that are conveyed by the mesencephalic dopamine system to other parts of the brain, including anterior cingulate cortex, where they reinforce processes that contribute to optimal task performance. The amplitude of the ERN is determined by the impact of the error signals on the control area in the anterior cingulate cortex.



Controllers
(amygdala,
dorsolateral prefrontal cortex,
orbitofrontal cortex,
etc.)

