Physiol Rev 94: 35–79, 2014
doi:10.1152/physrev.00041.2012

NEUROPHYSIOLOGY OF PERFORMANCE MONITORING AND ADAPTIVE BEHAVIOR

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Ullsperger M, Danielmeier C, Jocham G. Neurophysiology of Performance Monitoring and Adaptive Behavior. *Physiol Rev* 94: 35–79, 2014; doi:10.1152/physrev.00041.2012.—Successful goal-directed behavior requires not only correct action selection, planning, and execution but also the ability to flexibly adapt behavior when performance problems occur or the environment changes. A prerequisite for determining the necessity, type, and magnitude of adjustments is to continuously monitor the course and outcome of one's actions. Feedback-control loops correcting deviations from intended states constitute a basic functional principle of adaptation at all levels of the nervous system. Here, we review the neurophysiology of evaluating action course and outcome with respect to their valence, i.e., reward and punishment, and initiating short- and long-term adaptations, learning, and decisions. Based on studies in humans and other mammals, we outline the physiological principles of performance monitoring and subsequent cognitive, motivational, autonomic, and behavioral adaptation and link them to the underlying neuroanatomy, neurochemistry, psychological theories, and computational models. We provide an overview of invasive and noninvasive systemic measures, such as electrophysiological, neuroimaging, and lesion data. We describe how a wide network of brain areas encompassing frontal cortices, basal ganglia, thalamus, and monoaminergic brain stem nuclei detects and evaluates deviations of actual from predicted states indicating changed action costs or outcomes. This information is used to learn and update stimulus and action values, guide action selection, and recruit adaptive mechanisms that compensate errors and optimize goal achievement.

I. INTRODUCTION

Errare humanum est, sed in errore perseverare diabolicum . . . Seneca the Younger

When humans perform goal-directed actions, they strive to achieve their goal accurately, quickly, with minimal effort, without interfering with other concurrently pursued goals and while keeping available sufficient flexibility and attentional resources to respond appropriately to sudden changes of the environment. A number of challenges render it nearly impossible to meet all these criteria equally well for most actions. Often actions are performed despite substantial uncertainty or lack of information about particular context parameters; context, expected value, and risks of the action may change unexpectedly. Humans may pursue several partly incompatible goals at the same time. Moreover, challenges to homeostasis, such as mental and muscular fatigue, sleep deprivation, stress, disease, etc., influence action performance and require adjustments. Therefore, it is essential for successful goal-directed behavior to continuously monitor the context, course, and outcome of actions and to derive appropriate cognitive, affective, and autonomic regulations resulting in behavioral adaptations that keep action performance as near to the optimum as possible. Here, we will review the current knowledge and theories on the physiological and anatomical implementation of performance monitoring and how the monitoring results are transferred into appropriate adaptation.

Optimization of performance can be understood in the framework of a simple feedback loop **(FIGURE 1)**. Once a goal has been identified on the basis of the organism's needs, an appropriate action is selected. The executed action leads to outcomes that are reflected in changes in the state of the organism and the environment. Before, during,

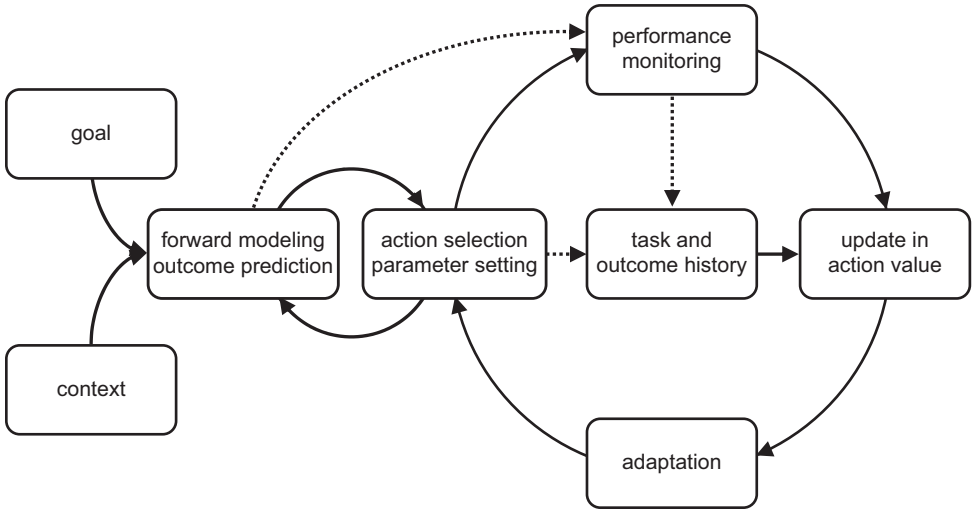


FIGURE 1. Processes involved in goal-directed behavior and cognitive control. Flexible adaptations can be viewed as a feedback loop in which weighted differences between expected and real action outcomes are used to trigger appropriate adjustments and to improve outcome prediction. During an action, events indicating unexpected difficulties or decreased likelihood to succeed can also trigger adaptation.

and after the action, sequences of events reflecting these outcomes are predicted through learning and forward modeling processes (141, 190, 584). Performance monitoring systems search for deviations of the observed outcomes from the predicted sequence of events. When deviations from the expected outcome are detected, they are communicated to structures of the nervous system that can implement counteractive mechanisms, thereby correcting and optimizing ongoing and/or future actions. Such feedback loops are implemented at many levels of the nervous system, ranging from simple spinal reflexes (e.g., limb withdrawal from a noxious stimulus), via complex motor corrections (e.g., postural reflexes, online corrections of externally disturbed reaching movements) to the most complex cognitive and affective adaptations that may result in remedial actions, long-term learning, and even changes in goals. In this review, we mainly focus on the latter type of monitoring and adjustment processes which involve telencephalic including especially frontal structures and relate to the valuation of actions and their outcomes with respect to reward and punishment. In other words, the performance monitoring of complex goal-directed actions has, in contrast to more basic feedback control mechanisms, clearly an affective dimension that directly influences motivated behavior.

When action performance fails and its outcomes are worse than expected, an error has been made. In addition to their negative consequences, errors can provide valuable information about the necessity, direction, and magnitude of adaptations that aim at avoiding similar mistakes in the future and at action optimization. They can moreover trigger immediate remedial actions such that the goal could still be achieved. In experimental situations, errors are a useful means to challenge the performance monitoring system and to study adaptive behavior. Depending on context, errors detected by the performance monitoring system can induce a multitude of adjustments at various levels of information processing and various time scales.

In this review, we focus on the healthy human brain, but we also include results from research in animals and from clinical populations whenever appropriate. Starting with a brief historical perspective, we provide an overview of the electrophysiological and neuroimaging correlates of error detection and performance monitoring, thereby focusing on the role of the posterior mesial frontal cortex (pMFC; see sect. II). While invasive and noninvasive electrophysiological techniques have provided insights into the time course of performance monitoring and adaptation, research in this field has been advanced substantially by functional neuroimaging, which revealed the functional neuroanatomy of the involved brain networks. After having reviewed correlational studies, we discuss causal evidence for the performance monitoring network based on lesion and interventional data (see sect. III). With this background in mind, we review the most influential theoretical models of performance monitoring and recruitment of cognitive control (see sect. IV). Section V is dedicated to the adaptive processes initiated when performance problems occur. In this section we also discuss learning and decision making based on the results of monitoring in detail. Section VI gives an overview of the neurochemical underpinnings of performance monitoring and adaptive behavior. We close this review with general conclusions and open questions for future research.

II. CORRELATES OF PERFORMANCE MONITORING

A. Electrophysiology

Behaviorally the processes underlying performance monitoring cannot be observed directly; only indirect inference

can be drawn through the consequences of errors and other performance problems. In the 1960s, Rabbitt (429, 430) described typical behavioral changes after errors in speeded choice reaction time tasks: immediate error corrections by a second key press and response slowing after errors. Sometimes performance was also found to improve on trials after errors (316, 317), and error signaling (pressing a specific button whenever an error was encountered) was introduced to study conscious error detection (427, 431, 432).

Also in the 1960s, the first physiological evidence for a performance monitoring system in the human brain was reported by Bechtereva and colleagues (27–30), who by means of depth electrodes found increased neuronal activity in caudate and putamen specifically after errors but not after correct responses in psychological tests, which they interpreted as activity of "error detectors" of the brain.

1. Invasive electrophysiology

Single-unit recordings in the anterior cingulate cortex (ACC) of monkeys revealed that a subset of neurons specifically increased firing rate after errors and after omission of reinforcement on correct trials (380) (for anatomical details and nomenclatures used in this review, see **FIGURES 2** and **3**). A study on motor learning identified transcortical field potential changes in macaques' ACC area 24 at the ventral bank of the cingulate sulcus that were associated with erroneous and unrewarded movements (201). More recent experiments using a saccade countermanding task in which monkeys had to withhold prepotent prosaccades to a visual target upon occurrence of a rare stop signal extended these findings (271, 459, 500). This task allows the study of error-related activity on incorrectly executed saccades (errors of commission) and activity related to response conflict, which arises by competition between the impending prosaccade and the intention to withhold it. This response conflict (see sect. III*B* for a detailed discussion of this concept) was reflected by simultaneous activation of movement and fixation neurons in the frontal eye fields and superior colliculus. It was shown that neurons in the dorsal bank of the anterior cingulate sulcus (in the rostral cingulate motor area, CMAr) responded to errors (271). Half of these neurons were also responsive to omission of re-

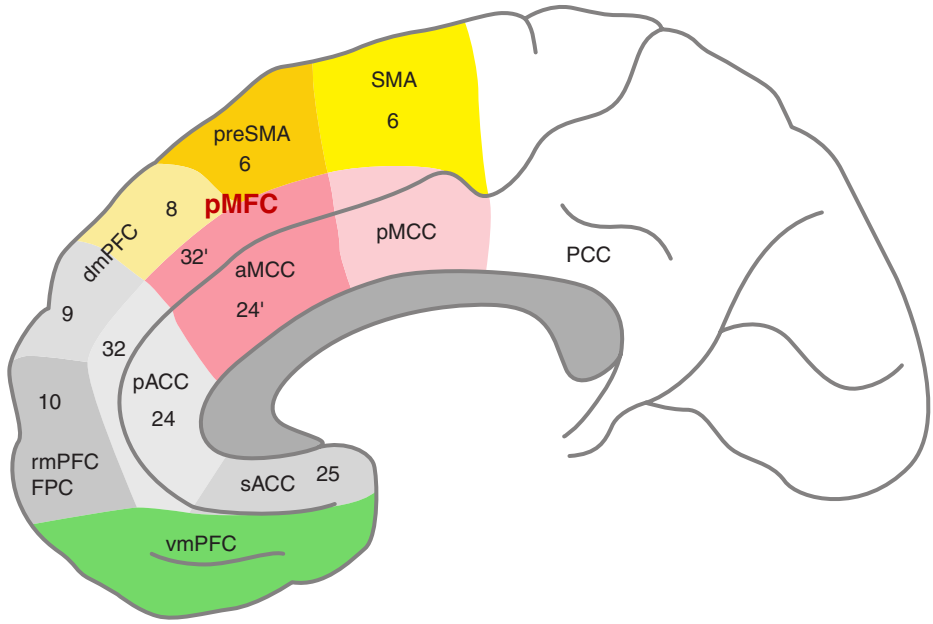


FIGURE 2. Subregions of the medial frontal wall. Based on cytoarchitectonical and functional criteria, the medial frontal cortex can be divided into cingulate and isocortical areas. The cingulate cortex has been divided into anterior, middle, and posterior portions, which are further subdivided into the subcallosal and pregenual anterior cingulate cortices (sACC and pACC, respectively), the anterior and posterior midcingulate cortices (aMCC and pMCC, respectively), and the posterior cingulate cortex (PCC) (556). Another terminology of the regions around the dorsal section of the cingulate sulcus has been suggested in an early meta-analysis attempting to link human cortical areas to their monkey's homologs (412, 413): the anterior and posterior parts of the rostral cingulate zone (RCZ), largely overlapping with the aMCC, are assumed to be the homolog of the monkey's rostral and ventral cingulate motor areas (CMAr, CMAv), respectively; and the caudal cingulate zone (CCZ) might correspond to the monkey's dorsal cingulate motor area (CMAd). The isocortical regions can be divided into ventromedial, rostromedial, and dorsomedial prefrontal cortex (vmPFC, rmPFC, dmPFC, respectively) and the presupplementary and supplementary motor areas (preSMA and SMA, respectively) (160). Hemodynamic signals in neuroimaging experiments often coactivate several neighboring regions such that the descriptive term posterior medial frontal cortex (pMFC) has been used to commonly refer to pre-SMA and aMCC, as well as adjacent SMA, posterior dmPFC, and pMCC (439). The numbers refer to cytoarchitectonic areas. FPC, frontopolar cortex.

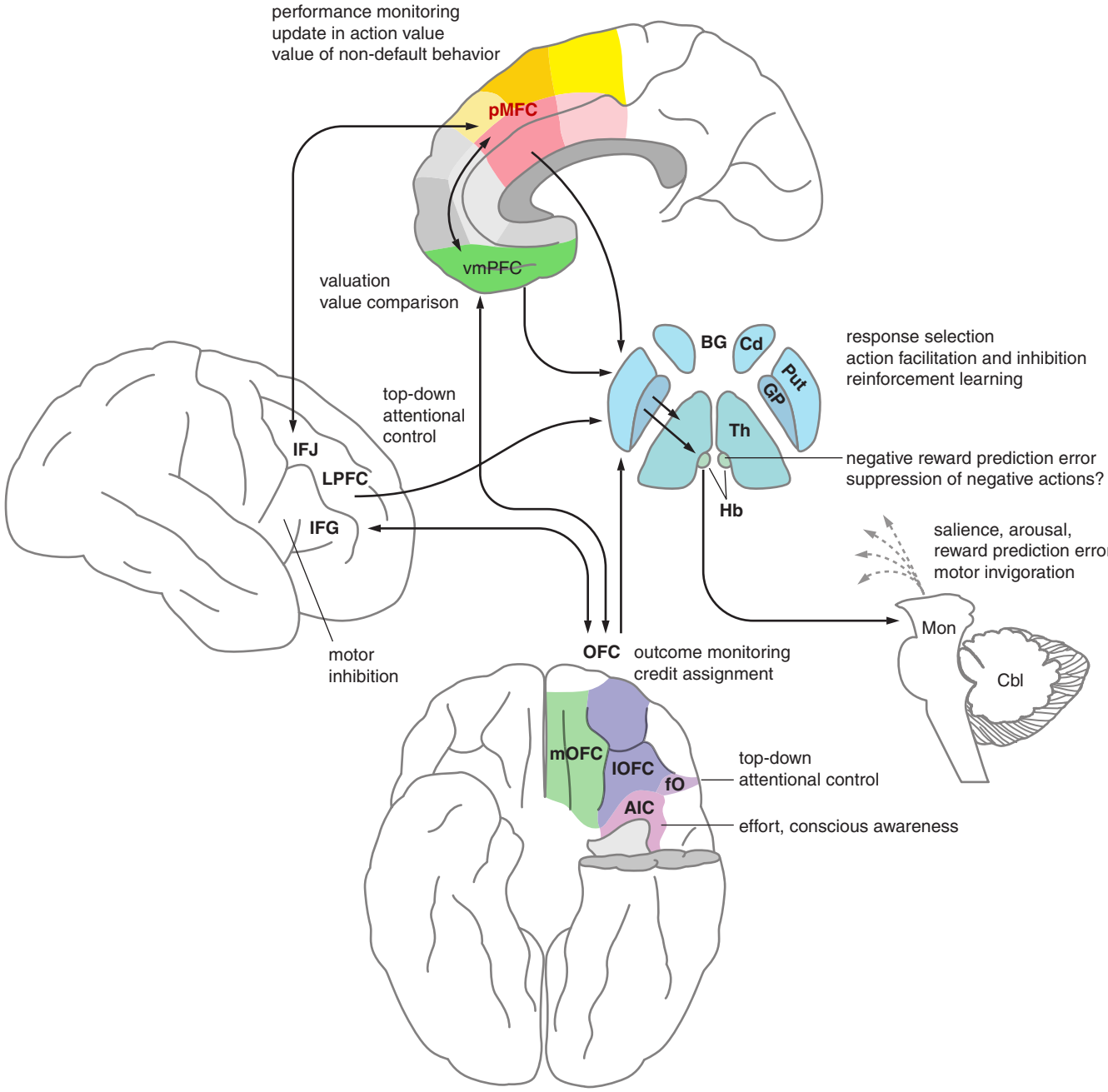


FIGURE 3. Important brain structures involved in performance monitoring and adaptive behavior, their function, and interaction. pMFC, posterior medial frontal cortex (see **FIGURE 2** for details); vmPFC, ventromedial prefrontal cortex; LPFC, lateral prefrontal cortex; IFJ, inferior frontal junction; IFG, inferior frontal gyrus; OFC, orbitofrontal cortex; m/lOFC, medial/lateral OFC; AIC, anterior insular cortex; fO, frontal operculum; BG, basal ganglia; Cd, caudate nucleus; Put, putamen; GP, globus pallidus; Th, thalamus; Hb, habenula; Mon, mesencephalic and pontine monoaminergic nuclei; Cbl, cerebellum.

wards. A different subset of ACC neurons specifically responded to earned and unexpected reward. Whereas none of the recorded ACC units showed activity related to response conflict, the supplementary eye fields contained distinct neuronal populations that were responsive to errors, reinforcement, or response conflict, respectively (500). In contrast, studies in humans undergoing cingulotomy for medically intractable psychiatric disorders reported neurons sensitive to response conflict in the anterior midcingulate cortex (aMCC), the putative homolog of the monkey's CMAr (127, 482).

A combined single-unit recording and inactivation study showed that the monkey's CMAr does not only respond to undesired action outcomes but is also involved in subsequent adaptive changes in action selection (485). In a modified response reversal task, the reward magnitude was gradually decreased on correct actions until the monkey

switched to the alternative action, which then became the rewarded response. Interestingly, 37% of CMAr neurons specifically increased firing *1*) after the reward was reduced and only *2*) before the monkey selected an alternative response on the subsequent trial. When the CMAr was reversibly inactivated by the injection of the $GABA_A$ agonist muscimol, the monkeys showed perseverance even when the reward was considerably reduced and spontaneous response switches in trial series with constant maximal reward. Nearly identical results were found in intraoperative single-unit from recordings the aMCC in humans undergoing surgical cingulotomy (580). Thus aMCC activity seems to translate changes in action outcomes into the need for adaptive behavior. This view is supported by findings that CMAr neurons encode action sequences and multiple feedbacks during exploration (423, 424). This activity ended as soon as enough information was accumulated to adapt behavior and exploit the gained knowledge. Action outcomes are informative with respect to the necessity of adaptation when they deviate from expectation, which can be expressed formally as reward prediction error (RPE). Several studies have demonstrated that CMAr neurons code RPEs (7, 288, 346, 455). Other variables needed for action valuation and assessing the need for ongoing and future adjustments also appear to be coded by anterior cingulate neurons, for example, reward expectancy and reward proximity (342, 484) as well as effort (111, 243, 244), often in an action-specific fashion. In addition to CMA, adjacent supplementary motor area (SMA) and pre-SMA also contain neurons that code evaluative signals such as expected outcome, actual outcome, RPE, and surprise (458).

While single-unit recordings in humans are performed rather rarely, more evidence on anatomical structures involved in performance monitoring has been collected using intracranial local field potentials (LFPs) reflecting postsynaptic activity. Error-related LFPs were reported in the ACC, aMCC, lateral frontal and mesial temporal cortices, and the amygdala of epilepsy patients (55, 56, 421) and in the dorsal ACC and supplementary eye fields of monkeys (154, 155). This suggests that performance monitoring signals are available throughout a distributed network rather than a single "error detector" region, but the electrophysiological responses to performance problems have been reported most consistently in the aMCC. A study using arrays of microelectrodes (566) in the human aMCC showed larger source currents with inhibited firing (in superficial layers) for errors compared with correct responses and for negative compared with positive feedback. Interestingly, source currents were also increased for novel stimuli and with increasing task difficulty. The authors suggest active inhibition in superficial cingulate layers based on these findings. The neuronal activity from deep layers where the efferents of the ACC arise was not recorded, however.

2. Event-related potentials

In the 1990s, performance monitoring research was significantly boosted by the discovery of error-related event-related brain potentials (ERPs) in the scalp-recorded EEG making the monitoring process observable by noninvasive techniques **(FIGURE 4)**. The error-related negativity (ERN) or error negativity (Ne) was discovered in response-locked ERPs on errors in speeded choice reaction time tasks (165, 198). It is a frontocentrally distributed negative deflection starting around the time of the response and reaching its peak between 50 and 100 ms later. When referenced to averaged mastoids, ERN amplitudes can reach up to 15 μV at the electrodes FCz and Cz. It is preceded by a positive deflection peaking 50 to 0 ms prior to the response and followed by another positive deflection which peaks 100–250 ms after the response. This sequence of frontocentral positive and negative deflections has raised the notion of an oscillation time-locked to the erroneous response in the theta band (5–7 Hz). This theta power increase is larger on errors than on correct trials and has been observed in averaged and single-trial data (79, 136, 328, 330, 379, 599, 600). The question whether the ERN might result from a power increase and/or phase-locking of theta oscillations is still under debate (592). The frontocentral positive deflection directly following the ERN (also called early error positivity, see below) is somewhat broader than the ERN which is in line with findings of an error-specific increase in delta power (1.5–3.5 Hz; Ref. 599). The ERN is independent of stimulus and effector modality, i.e., independent of whether visual, auditory, or tactile stimuli are presented (166, 213) and independent of whether manual, foot, eye-movement, or vocal responses are given (193, 194, 250, 340, 376, 539, 574). Electrical source analyses consistently suggest the ERN and its magnetoencephalography (MEG) equivalent to be generated in the posterior mesial frontal cortex (pMFC), specifically in the aMCC (137, 213, 250, 287, 355, 536). A recent MEG study (1) suggested additional involvement of the posterior cingulate cortex (PCC). In a study with simultaneous EEG and functional magnetic resonance imaging (fMRI), we found a trial-by-trial correlation of the ERN amplitude with the hemodynamic response in the aMCC (136). Moreover, studies in monkeys suggest a close link between error-related LFPs in the anterior cingulate cortex and the scalp-recorded ERN (154, 204). Taken together, source localization findings and invasive recordings in humans and monkeys provide overwhelming evidence that the ERN is generated in the pMFC with a focus in the aMCC. Further research is needed to elucidate the significance of the recently reported additional activity in PCC (1, 83). Various functional interpretations of the ERN will be discussed in section III.

Whereas in young healthy participants correct responses only sometimes elicit a clear response-locked negativity in the raw ERPs, a negativity similar to the ERN, usually of smaller amplitude, is often seen in older subjects and pa-

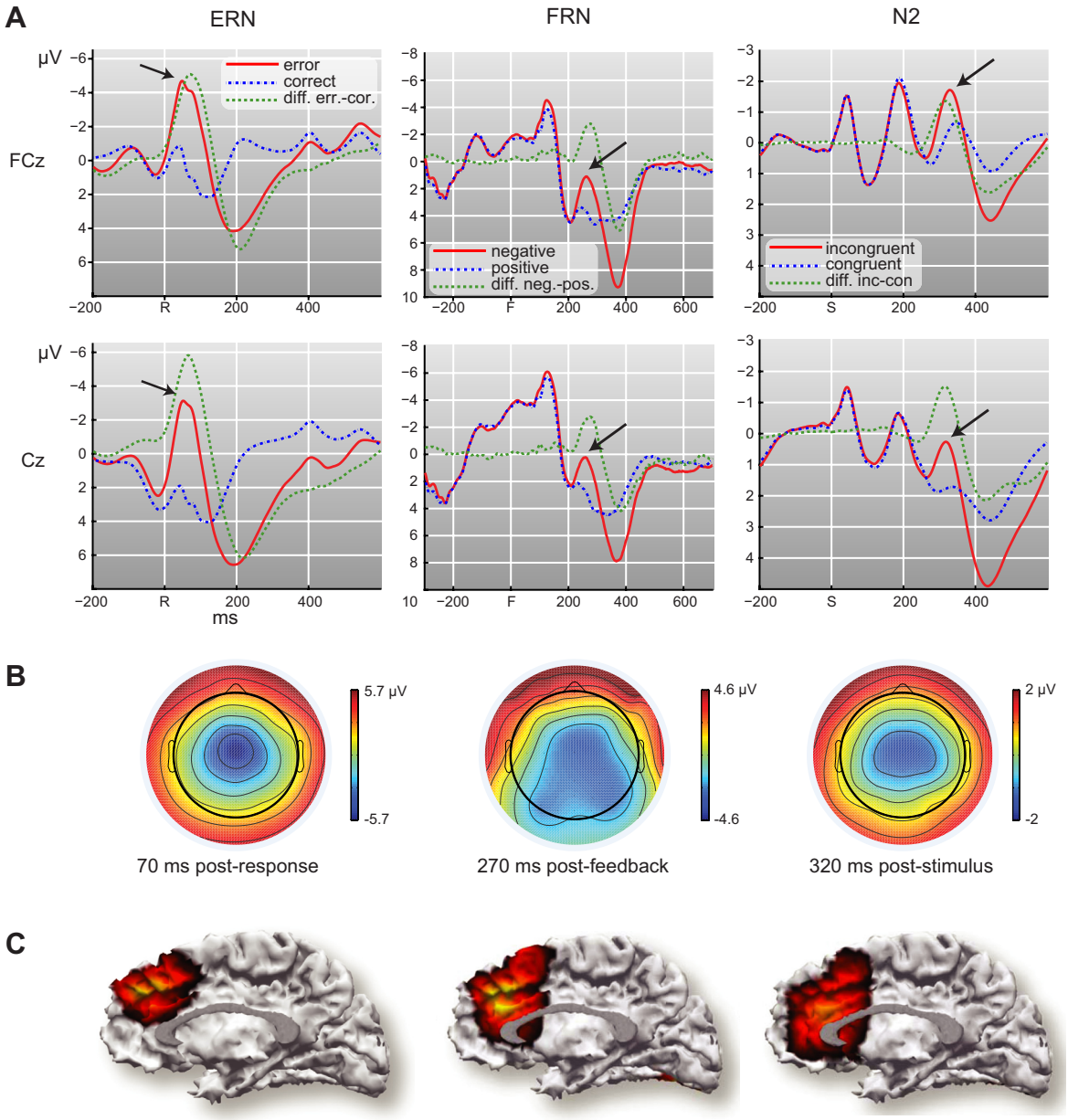


FIGURE 4. Event-related potentials associated with performance monitoring. *A*: prototypical ERPs in response to errors (ERN, response-locked), negative feedback (FRN, feedback-locked), or preresponse conflict (N2, stimulus-locked) at midline electrodes FCz and Cz. *B*: corresponding topographies of difference waves from *A*. *C*: source localizations ERN, FRN, and N2. R, response; F, feedback; S, stimulus. [From Gruendler et al. (213).]

tients, the so-called correct-related negativity (CRN) (181, 199, 538). In young participants it can be revealed by Laplacian transforms of the EEG data (553, 554) which filter out low spatial frequencies masking the focal CRN activity. Recent studies using blind source separation by temporal independent component analysis (ICA; Refs. 335, 336) strongly suggest that ERN and CRN stem from the same or largely overlapping generator structures (202, 441, 573). A temporospatial principal component analysis (PCA) revealed two temporospatial factors contributing to both ERN and CRN (156). In agreement with the ICA findings, a central factor was found that was sensitive to response correctness and task difficulty. A more frontal negative factor was present for all responses and was not modulated by accuracy and difficulty. It has been suggested that the CRN reflects partial error processing on correct trials with high uncertainty about the action outcome, for example, due to stimulus ambiguity (101, 401, 460). Notably, partial error execution observable by isometric muscular activity of the incorrect response hand is not a necessary prerequisite for the CRN (553). Rather, the amplitude of the response-related negativities CRN and ERN seems to reflect the objectively accumulated evidence in favor or against having made an error (574). It has been suggested

that both, ERN and CRN, signal the need for adjustments (22). This is consistent with the finding that the CRN amplitude is smaller on trials preceding errors and the resulting notion that it is involved in keeping up resources (effort) allocated to the task at hand (5, 219, 437). The above-mentioned finding that the CRN is larger and easier to detect in older subjects and some patient groups has not been explained unambiguously, yet. Perhaps several factors such as higher motivation (and thus higher effort invested in the task), higher uncertainty, as well as delay and increased jitter of other onging EEG activity with the potential to mask CRN activity contribute to this effect.

As shown in **FIGURE 4**, the ERN is followed by positive deflections specific to error trials, collectively referred to as error positivity (Pe) (165, 166). The frontocentral positive deflection following the ERN is sometimes called "early Pe"; a positive slow wave at parietal electrodes sustained from 300 to 500 ms post response is the classical Pe, sometimes called "late Pe" (546). Dipole localization studies suggest the early Pe to be generated by the same generators as the ERN, whereas parietal cortex and rostral ACC seem to contribute to the late Pe (232, 546). However, these results have to be interpreted with caution due to methodological limitations such as low electrode number and localization based on grand mean average activity. The functional significance of the Pe is still rather unclear. It appears to reflect the accumulated subjective evidence for an error associated with conscious perception of the error (398, 497, 526, 574). Furthermore, it seems to share features with the P300 observed on infrequent target stimuli in oddball tasks (12, 126, 438).

The ERN occurs in speeded reaction time tasks, in which stimuli usually convey the necessary information to unequivocally determine the correct response (given enough processing time). Therefore, errors can be detected without external feedback. In many situations, however, we select our actions under significant uncertainty. In such underdetermined situations, errors can only be detected based on external information about the action outcome provided by the sensory systems. Negative feedback provides evidence to the performance monitoring system that the action was not successful. In a time estimation task, in which participants had to press a button within a small, adaptive time window around 1 s after an imperative stimulus, only feedback can provide sufficient information whether the response was given at the correct time or not. Such time estimation tasks reliably elicit a negative ERP deflection with a frontocentral scalp distribution similar to the ERN (213, 252, 356), the feedback-related negativity (FRN; also called feedback-ERN or feedback negativity). This negative deflection is usually greater on negative than on positive feedback, occurs independently of feedback modality, and peaks approximately between 200 and 300 ms after the feedback. It was also found in gambling tasks and reinforcement learning tasks (200, 249). The FRN amplitude is higher on more unexpected outcomes and was suggested to scale with the RPE, i.e., the difference between predicted and obtained action outcome (84, 96, 249, 252, 255, 375). In contrast, other studies suggest that the FRN amplitude is only influenced by the valence of the outcome in a quasi-binary fashion and that the magnitude of the violation of outcome expectancy is reflected in the amplitude of the subsequent feedback-related P300 deflection (216, 251, 411, 598). Moreover, the FRN is modulated by task context such as the range of possible outcomes (254) and whether attention is directed to the utilitarian (gain/loss) or performance information (error/correct) contained in complex feedback (377). Interestingly, the FRN is also elicited when an unfavorable action outcome requiring behavioral adjustments cannot be attributed to the actor but results from external factors, e.g., technical malfunction (202). Interpreting FRN results requires attention to several caveats. Studies differ substantially in FRN quantification (e.g., difference waves vs. single-condition ERPs, theta-band filtering), baseline correction, and how they deal with the overlap with the subsequent P300 deflection. Moreover, the FRN occurs in the time range of the N2 family of ERPs (180) and may therefore be masked by other factors influencing the N2 (248). A recent systematic review of FRN studies synthesizes the above-mentioned findings and concludes that the FRN represents quantitative RPE, is elicited by outcomes as well as outcome-predicting stimuli, changes (along with behavior) with learning of stimulus-outcome contingencies, and is maximally engaged by volitional actions (563). A recent study comparing EEG activity elicited by real outcomes (reward/punishment) and by fictive outcomes (based on feedback indicating what would have happened had one decided differently) revealed a double dissociation (177). Real outcomes elicited a frontocentral FRN reflecting an RPE and a subsequent frontocentral P3a. In contrast, no FRN or P3a was found in the fictive condition; instead, an earlier occipitoparietal outcome correlate was found. About 400 ms after feedback, brain activity for both conditions converged into a common adaptive pathway, reflected in parietal P3b-like activity that was predictive of future choice behavior. The absence of the FRN for fictive feedback is surprising as even the observation of mistakes made by others elicits similar EEG activity (see further below). It may result from the fact that fictive feedback was given, when participants decided not to actively select a stimulus, which is in line with the notion that the FRN is maximal for volitional motor actions (563).

The initial assumption that ERN and FRN are functionally equivalent (249, 356) has found strong support by electrical source localization (213) and blind source separation using ICA (202), suggesting that the ERN and FRN stem from the same or at least highly overlapping generator structures in the pMFC.

In addition to own, self-generated errors, humans can also detect when other persons make mistakes, adjust their own behavior accordingly, and learn to avoid similar mistakes. The observation of mistakes committed by others elicits a frontocentrally distributed negative ERP deflection similar to the FRN to visual feedback (134, 302, 354, 544). Source localization of this observed-error-related negativity (oERN) again hints at the pMFC. It appears, however, that the observed error must entail a consequence to the observer along a reward-punishment axis to elicit the oERN, because the mere counting of errors in everyday behavior did not evoke ERN-like activity (130). A recent study in macaques revealed that neurons in the pre-SMA and cingulate sulcus increased activity on observed errors associated with omission of the reward delivery to both the observing and acting monkeys (601). Whereas a subset of these neurons did also respond to unexpected reward delivery when the monkey was acting, the overlap with pMFC neurons responding to own errors was negligible. Activity of neurons responsive to observed errors in the cingulate sulcus appeared furthermore to be associated with subsequent behavioral adjustments of the observing monkey.

The stimulus-locked N2 deflection comprises a family of ERP responses which, in part, are related to performance monitoring and cognitive control (180). Simultaneous activation of competing response tendencies is associated with increased frontocentral N2 amplitudes (306, 546). Particularly in the framework of the response conflict monitoring theory discussed further below, a functional equivalence of the stimulus-locked N2 on correct high-conflict actions and the response-locked ERN has been suggested (125, 593, 595). Frontocentral N2 modulations are also found during inhibition of preactivated motor responses in GoNogo and stop signal tasks (180). It has been argued that the N2 increase in GoNogo tasks can be explained by a conflict between executing and inhibiting a response (146, 158, 378). A comparison of scalp distribution and results of source localization suggested a large overlap between N2, FRN, and ERN (213). In addition to a pMFC source found for all three ERPs, an additional N2 source was found in the right inferior frontal cortex, which is in line with other findings suggesting an involvement of this area in motor inhibition (14, 15). Intracranial recordings also showed conflict-related theta-band activity coupled with frontocentral surface N2-like EEG activity (97).

Salient and surprising events such as novel stimuli are also associated with modulations of the stimulus-locked N2-P300 complex (110, 180, 420, 492). Recently, it has been shown that ERN sources estimated with ICA can explain a substantial part of novelty N2 activity, suggesting overlapping sources of brain activity related to errors and valence-free surprising action outcomes (573). In a number of studies the FRN appears to be more driven by unexpectedness of an outcome than by its valence (145, 173, 248), also suggesting that this ERP wave is to some extent susceptible to valence-free expectancy violation (i.e., surprise). This is in line with recordings from the aMCC homolog in monkeys showing neuronal activity coding valence-independent prediction errors (227, 346) and novelty of stimuli (347).

In sum, invasive recordings in rodents and primates have consistently demonstrated pMFC responses coding various pieces of information needed for action valuation and evaluation such as reward expectation, reward proximity, reward delivery, errors, surprise, effort, and observed errors. Thus pMFC neuronal activity appears to integrate multiple decision parameters using a common valuation currency (288). These information contents appear to also modulate scalp-recorded ERPs related to performance monitoring such as the ERN, FRN, oERN, N2, Pe, and P3. It appears, however, that a one-to-one matching of type of information and ERP is not possible, although these ERPs are modulated differentially.

B. Functional Neuroimaging

As a result of its high spatial resolution, functional neuroimaging has been particularly influential in performance monitoring research. In line with the electrophysiological findings, fMRI signal increases related to various evaluative signals have been found in the pMFC with great consistency (for reviews and meta-analyses, see Refs. 296, 374, 439, 534). For example, hemodynamic signals related to errors in speeded forced choice task (76, 196, 256, 290, 292, 536); to conflict between competing response tendencies (44, 76, 195, 291, 352, 536, 545); to decision uncertainty, outcome predictability, and volatility of the environment (33, 406, 407, 558, 559); to feedback and punishment (256, 297, 339, 361, 532, 565); to reward, reward anticipation, and reward prediction errors (282, 300, 301, 397); to the observation of errors committed by others (131, 478); to externally induced failure to achieve action goals (528); and to valence-free surprising action outcomes (573) have been reported. Furthermore, pMFC activity has been shown to correlate positively with effort and negatively with the subjective action value discounted by effort (121, 422). This fits with the finding that in two-choice decisions an inverse value difference signal was found in aMCC. The hemodynamic signal increases when the difference between the values of the choice options decreases, i.e., when value comparison becomes more difficult and time-consuming (24, 224).

Furthermore, appreciation and expression of negative emotions and acute pain, observation of others experiencing pain, and social exclusion are associated with signal increases in this region, too (152, 160, 318, 475, 555). These latter situations have in common with the performance monitoring signals that they are evaluative and may trigger adaptive actions (530). This notion has been addressed and

elaborated in a recent review demonstrating overlapping activation in aMCC to pain, negative effect, and cognitive control resulting in the adaptive control hypothesis (475). Briefly, this hypothesis suggests that the aMCC "represents a hub, where information about pain, and other, more abstract kinds of punishment and negative feedback could be linked to motor centers responsible for expressing emotion on the face (a communicative means of adaptation; note from the authors) and coordinating aversively motivated instrumental behaviours" (p. 156; Ref. 475). We will return to this hypothesis and reconcile it with other theories in section IV.

Cyto- and receptor architecture as well as connectivity data suggest that the pMFC is subdivided into different regions (31, 284, 404, 405, 556). It is conceivable that these different anatomical subregions, although often coactivated during performance monitoring, serve at least partly dissociable functions. On the basis of electrophysiological data, functional subregions differing with respect to the motor effects of stimulation have been identified in the pMFC of monkeys (413). In humans too, several studies have suggested that the different evaluative signals found in the pMFC are coded in distinct subregions, which has caused an ongoing debate. Although a somatotopy for motor actions has been described for the anterior and posterior rostral cingulate zone (413), the distribution of conflict-related fMRI signals appears to be unaffected by effector modality (19). Some studies, however, showed that response errors predominantly elicited aMCC responses, whereas response conflict on correct trials was more associated with increased activity in the more dorsal mesial area 8 and pre-SMA (53, 195, 534, 536) or, more generally, that pre-response performance problems are coded more dorsally than post-response performance problems (439). In contrast, a more recent analysis showed a somewhat different distribution along an anterior-posterior and inferior-superior axis (374). Other studies found localization differences of response conflict (more anterior) and degrees of freedom in choice of a volitional action (more posterior) within the pMFC (370) (see also Refs. 182, 565). Moreover, it has been suggested that the different subregions of the pMFC might play different roles in the initiated adaptations. Increased arousal and autonomic responses (115, 118, 408) as well as reactive, general cognitive adjustments appear associated with aMCC activity (294, 527). In contrast, proactive, task-specific adjustments may be associated with pre-SMA activity increases (242, 294, 527). Most of the above-mentioned studies were not designed to reveal subtle regional differences and suffered from spatial smoothing and the fact that group analyses ignore individual anatomical variations. Thus, at this point, we have to state that evidence for the suggested subregional dissociations is still too sparse and equivocal to extract a clear functional distribution within pMFC. Therefore, future research aiming at a functional parcellation of the pMFC needs to better take into account individual anatomy, use high-resolution imaging, and combine functional data with structural, e.g., tractographic data. Recent reports suggest that individual patterns of pMFC gyrification influence performance monitoring functions as well as their ERP and fMRI correlates (8, 267).

During performance monitoring, numerous other brain regions are usually coactivated with the pMFC. Most consistently, the anterior insula, parietal cortex, lateral prefrontal cortex, and subcortical regions such as the basal ganglia, thalamus, and midbrain are reported (296). Reward and reward prediction error-related signals are also found in many cortical and subcortical areas, as will be discussed further below.

With the use of separate and simultaneous EEG/fMRI recordings, correlations between the hemodynamic response in the aMCC and scalp-recorded ERN and FRN amplitude, respectively, have been found within and across participants (1, 73, 136, 266, 341). More negative single-trial ERN amplitudes were associated with stronger aMCC responses and increased reaction times on subsequent trials (136).

III. THE PERFORMANCE MONITORING NETWORK: CAUSAL EVIDENCE

Based on the above-discussed electrophysiological and imaging findings and anatomical studies on the connectivity of the pMFC, a basic network of brain structures typically involved in performance monitoring can be derived **(FIGURE 3)**. The causal involvement of the nodes in this performance monitoring network can be addressed in lesion studies in animals and in patients with circumscribed lesions resulting from stroke, tumor excision, traumatic brain injury, etc. Furthermore, stimulation of the network constituents using transcranial magnetic stimulation (TMS) or in patients undergoing deep brain stimulation (DBS) can reveal functional interactions.

A. Cortical Regions

As discussed above, correlative evidence suggests that the pMFC is essential for performance monitoring. Focal lesions of the pMFC, in particular of the aMCC, are rare, and resulting impairments may be transient and can disappear in chronic stages (99). The small number of patients and studies, the uncontrollable size of lesions often extending far beyond pMFC, and the limited amount of behavioral and neurophysiological variables that could be obtained from these patients render the results hard to interpret. Despite these difficulties, a series of studies in patients with unilateral focal lesions of the aMCC demonstrated impairments in post-error and conflict-driven adaptations, accom-

panied by reduced ERN amplitudes (142, 504–506). In contrast, in another patient group with large pMFC lesions, no impairments in error- and conflict-induced performance adjustments were found (171), except for slowed error corrections in a flanker task (360). This suggests that pMFC lesions interfere with the solution of response conflict, because fast error corrections result from concomitant activation and sequential execution of the incorrect and correct responses (496, 533). In line with this, TMS of the pre-supplementary motor area (pre-SMA) affects processing of competing response tendencies (512) and intracranial stimulation of the pre-SMA in monkeys replaced automatic incorrect responses by slower correct responses (270). Moreover, patients with pMFC lesions showed increased false alarm rates in a two-back task associated with higher subjective confidence in action selection (518). This seems to be in line with findings that macaques with sulcal anterior cingulate lesions show increased impulsivity and reduced impact of reinforcement history in choice behavior (289). In sum, the pMFC appears involved in and necessary for rapid online adjustments, evaluation of confidence with choice, and between-trial adjustments. Lesions of the pregenual and subcallosal ACC have been shown to result in strongly reduced ERN amplitudes (499) and difficulties in conflict-induced trial-by-trial adjustments (142). These conflict-driven sequential adaptations seem particularly impaired when stimuli had an emotional component such as face expression (333).

Different subregions of the lateral prefrontal cortex (LPFC) have been implicated in maintaining and updating task representation, goals, and contextual information (51, 139, 551), and in exerting top-down control in mutual interaction with the pMFC (291, 331). Its necessity for performance monitoring is strongly suggested by the fact that ERN generation is impaired in patients with LPFC lesions comprising the middle and inferior frontal gyri, anterior insula, and underlying white matter: the amplitudes of ERN and CRN did not differ from each other (199, 535, 538). Whereas post-error slowing appeared unaffected, in some patients error corrections were diminished (199), particularly when white matter tracts connecting LPFC, pMFC, and the striatum were affected (535). The importance of the fiber connections at the base of the middle and inferior frontal gyri is also reflected in a reduced ERN in patients with isolated lesions in that area (245).

Whereas patients with lesions of the posterior orbitofrontal cortex (OFC) extending into the subgenual ACC and the ventromedial prefrontal cortex (vmPFC) showed severe attenuation of the ERN and error corrections (520), more anterior OFC and frontopolar lesions did not interfere with performance and ERN generation in a flanker task (538). Nevertheless, vmPFC and OFC play a major role in motivated and adaptive behavior, particularly with respect to establishing stimulus-outcome associations, credit assignment, task and reinforcement history, and value-guided choice. These aspects will be discussed in section V*D* on monitoring-based learning processes.

B. Subcortical Circuitry

Cortico-striato-thalamic circuits are highly important for action selection and learning. They can thus be expected to be an essential part of the performance monitoring network. The basal ganglia are closely connected to the cortical areas involved in performance monitoring and adaptive behavior, such as pMFC, LPFC, vmPFC, and OFC. Particularly, spiraling connections from the striatum to the dopaminergic midbrain and back, as well as nonreciprocal cortico-thalamic projections appear important in connecting the different basal ganglia loops (215). Thus the subcortical circuitry discussed below is involved in performance monitoring by receiving and sending information about outcome predictions, aversive and appetitive outcomes, prediction errors, and adaptive signals from and to the relevant cortical areas.

The necessity of the basal ganglia in performance monitoring is demonstrated by the finding that focal and isolated damage in the striatum disrupts the generation of the ERN (535). Performance monitoring is also impaired in degenerative diseases of the basal ganglia. Parkinson's disease (PD) is characterized by a gradual loss of dopaminergic neurons that progressively affects dorsal and later ventral striatal function. PD patients quite consistently display reduced ERN amplitudes (162, 498, 579; but see Ref. 257), but no significant effects of medication on the ERN have been observed. Less is known about the FRN in PD, although behavioral studies show an imbalance of preference versus avoidance learning depending on whether the patients are medicated or not (187, 188). Generally, the FRN might be affected later in the course of disease progression than the ERN because the ventral striatum, relevant for reward processing, seems to be affected by dopamine depletion only at more severe stages of PD (104, 105).

Huntington's disease (HD) is an autosomal dominant neurogenetic disorder characterized by striatal degeneration. In HD patients, a consistent reduction of the ERN was found that was related to the genetic mutation and the reduction of gray matter volume in pMFC (37, 38).

Therapeutic high-frequency deep brain stimulation (DBS) opens up the opportunity to investigate the effect of stimulating subcortical brain regions. In a patient treated for intractable alcohol dependence, bilateral DBS in the nucleus accumbens over 12 mo reduced clinical symptoms significantly reflected in subpathological clinical scores at the end of the observation period. In addition, DBS nearly doubled the ERN amplitude in a flanker task (315). This effect was reversible when stimulation was temporarily turned off and

replicable over several measurements. Notably, behavioral performance remained unaffected. It suggests fast functional interactions of the ventral striatum and the medial frontal ERN generators.

Studies in non-human primates suggest that the aMCC receives inputs from the basal ganglia circuitry mostly via the ventral anterior (VA) and ventrolateral anterior (VLa) nuclei of the thalamus (226, 543), a region which also integrates cerebellar circuitries assumed to be involved in motor control (262). In addition to the VA/VLa nuclei the mediodorsal (MD) thalamus sends fibers to the pMFC (483, 557). Compared with healthy controls, patients with thalamic lesions show impaired conscious error detection, post-error slowing, post-error accuracy improvement, and smaller error-related ERPs (410, 471). A detailed analysis revealed a double dissociation within the thalamus: lesions affecting VA and VLa abolish the ERN while leaving the Pe nearly intact. In contrast lesions encompassing MD only slightly decrease the ERN amplitude and completely wipe out the Pe (299, 471). This suggests a differential involvement of thalamic nuclei in different stages of performance monitoring.

The subthalamic nucleus (STN) is an important modulatory part of the cortico-striato-thalamocortical circuits. It has been suggested to modulate cognitive control and decision making by providing a general NoGo signal unspecifically inhibiting motor response tendencies under situations of high response conflict and uncertainty (14, 183). Indeed, high-frequency DBS in the STN for PD results in more impulsive decisions (reflected in shorter reaction times in high-conflict conditions) in decision making and more errors of commission in simple motor Go/NoGo tasks, respectively (17, 80, 187). It has been suggested that evaluative signals stem from pMFC via a hyperdirect pathway and that STN then implements motor inhibition to slow down reactions on conflict-laden decisions (183), thereby allowing to accumulate additional information useful for more specific adaptation. This might also apply to errors; in section VC we present evidence for involvement of the STN in post-error slowing. However, DBS in STN seems to yield paradoxical effects dependent on the stage of decision making and response selection: fast impulsive errors appear disinhibited, but slow selective inhibition of incorrect responses is improved at later stages (590). The effect of DBS on impulsivity appears to also depend on the subtype of PD (591). In any event, the STN appears to use performance-monitoring signals to on-line modulate motor behavior. In line with this notion, depth recordings from STN revealed conflict- (80) and action-outcome-related signals that were related to motor adjustments on subsequent trials (62) and modulated by motivation (313).

The habenular complex (Hb) is another key subcortical structure for performance monitoring and adaptive behavior. It is part of a major top-down pathway from forebrain to midbrain modulating the activity of dopaminergic and serotonergic brain stem nuclei (230, 231, 241, 324). Neuroimaging in humans and invasive recording in animals showed that the Hb codes negative prediction errors (59, 259, 344, 454, 532). In animals, electrical stimulation of the lateral Hb strongly inhibits firing of dopaminergic neurons in the ventral tegmental area (VTA) and substantia nigra pars compacta (SNc) (88, 277, 344) and of serotonergic raphé neurons (567). Conversely, Hb lesions result in increased striatal and prefrontal DA turnover (327, 381). Thus the Hb seems to influence approach-avoidance decisions, impulsivity, and acute pain- and error-induced remedial actions; in particular, it has been suggested to regulate motor suppression induced by these diverse situations (241). Support for this hypothesis comes from the finding that electrical stimulation of the lateral habenula after rewarding saccades can delay subsequent saccadic eye movements (343). Similarly, in gerbils, stimulation of the lateral habenula and VTA, respectively, had opposite effects on the acquisition of avoidance behavior (487).

IV. PSYCHOLOGICAL AND NEUROBIOLOGICALLY INFORMED MODELS

A. Mismatch Theory

Early evidence on nearly immediate error corrections, post-error slowing, and post-error improvements in accuracy suggested a genuine error detection mechanism (10, 11, 428–430). The discovery of the ERN triggered the proposal of the mismatch theory of error detection. It assumes a comparator detecting a discrepancy (i.e., mismatch) between the representations of the executed and the correct actions, which then is reflected in the ERN and error-related aMCC activity (101, 165, 166, 198, 536). On the basis of behavioral observations, the early onset of the ERN which sometimes even precedes the erroneous motor response, and a single-case study showing a normal ERN in a patient with sensory deafferentation (6), it has been argued that the representation of the executed response cannot be derived from proprioceptive feedback but rather from a central efference copy of the motor program. The representation of the correct action directly results from ongoing, even after response elicitation continued perceptual processing and stimulus-response mapping according to the task rules. In line with this view, the ERN is often seen on premature erroneous responses executed before completion of stimulus-response mapping. Factors that affect the representations of either executed or correct action reduce the amplitude difference between ERN and CRN, reflecting disturbance of the comparison process (101, 460). On the basis of continuous flow of information accounts of stimulus-response mapping (208), it has been assumed that the action comparator issues its signal when the motor efference copy

arrives and uses whatever information about the correct response is available at this stage (101). The mismatch theory has been extended to explain the FRN occurring when external feedback information is available (356). Here, the mismatch between representations of the intended outcome, derived from reward prediction, reinforcement learning, and forward modeling, and the actually achieved outcome gives rise to the error signal driving the pMFC activity. Limitations of the mismatch theory are that it is, at least in its original form, not mathematically formalized and that it cannot explain pMFC activity and N2 modulations on correct actions involving response competition and/or higher effort.

B. Response Conflict Monitoring

A broader perspective on cognitive control suggests that not only erroneous actions but also difficulties during ongoing actions can initiate adjustments. This has been formalized in the response conflict monitoring theory (46), which suggests that the performance monitoring system monitors for response conflicts between concomitantly evolving response tendencies rather than for errors per se. Response conflict arises when action implementation simultaneously activates two or more incompatible response tendencies. This may occur when distractors or apparent regularities of the stimuli prime a prepotent but incorrect response. A strong correct response tendency may override incorrect response tendencies. In these cases, the highest overlap of the competing response tendencies occurs before the (correct) response, thus yielding preresponse conflict. If, however, a strong and prematurely executed incorrect response tendency results in an error, response conflict reaches its maximum after the response. Continuously incoming information from stimulus processing is translated into a rising correct(ive) response tendency which conflicts with the executed error. Thus errors in reaction time tasks are typically associated with postresponse conflict.

Computational models have allowed simulations and predictions for numerous task situations which have been compared with empirical evidence (46, 47, 595). Briefly, response conflict signals are assumed to recruit cognitive control processes and to initiate appropriate adjustments. Connectionist parallel distributed processing models of various stimulus-response compatibility tasks (159, 488, 489) form the basis of the response conflict monitoring theory. The models usually comprise three layers of units: an input layer with units representing stimulus features, a response layer consisting of a unit for each response, and an attentional layer with units corresponding to each feature of the stimulus set. The information flow is realized by bidirectional excitatory weights between layers. Competition is elicited by within-layer inhibitory links between the units. The measured response conflict depends on the relative activation levels of the competing response units and is computed by a multiplicative measure, the Hopfield energy (46, 260). A conflict monitoring feedback loop is assumed to reflect the contribution of the pMFC to performance monitoring and initiating adjustments of control. When a stimulus pattern is fed to the input units, activations flow via their connections to the response units. If a response unit crosses an arbitrary response threshold, the corresponding response will be produced by the model, allowing to predict reaction times. When one response unit is active and the others are inhibited, conflict is low or zero. When two or more response units are active, however, the response conflict is large. Adaptation is brought about by feeding back the conflict signal to the attentional layer where it drives attentional refocusing on task-relevant features and/or to the response unit where it modulates response threshold (46, 595). The response conflict model quite accurately predicts behavioral effects of conflict on current and subsequent trials (46, 125, 495, 496).

Numerous neuroimaging studies have demonstrated that the pMFC is engaged when response conflict occurs (20, 44, 53, 76, 77, 291, 348, 353, 439, 536, 545, 570, 604). Also ERP findings, such as the modulation of the stimulus-locked N2, ERN and lateralized readiness potentials by differential stimulus conditions, attentional and pathological states can be explained by conflict monitoring models for the according tasks (125, 495, 593, 595, 597). The N2 is assumed to be modulated by pre-response conflict, whereas the ERN reflects mostly post-response conflict. Strong post-response conflict signals may serve as a reliable basis for internal error detection, rendering a specialized error detection mechanism unnecessary (595). It was furthermore shown that conflict-related pMFC activity varies with the amount of conflict at the response level but not with conflicts at other levels such as stimulus identification (148, 353, 547).

The response conflict monitoring theory has repeatedly been challenged and is still under debate (63, 64, 72, 210, 211, 496, 594). Moreover, the theory cannot account for feedback-related activity in the pMFC that occurs in the absence of motor response activation.

It is noteworthy that invasive studies in monkeys did not find any neurons whose firing patterns coded response conflict (271, 373, but see Ref. 482 for single unit activity in human aMCC associated with response conflict). Perhaps the discrepancy between the ease at which conflict-related signals in pMFC can be measured at the mesoscopic (multicellular) level using EEG and fMRI and the difficulty to find single neurons coding response conflict could be explained by biophysical cortical network attractor models that have been applied successfully to sensory and value-based decision making in parietal and ventromedial prefrontal cortices (265, 278, 585, 586). A substantial number of pMFC neurons show activity specific to a particular action or action sequence from the available action set (423,

485). Simultaneous activation of intermingled neuronal ensembles coding the competing motor actions could result in a sum network activity that scales with the conflict measure (i.e., the Hopfield energy).

Despite the ongoing debates, the response conflict monitoring theory has been highly influential. It has great power to make predictions for speeded reaction time tasks involving interference, but it might need to be modified or extended to cover other domains of performance monitoring and cognitive control (45).

C. Reinforcement Learning Theory

The reinforcement learning (RL) theory of error processing and cognitive control (249) draws on physiological evidence from the field of reward-guided learning and decision making in primates. Recordings of single dopamine (DA) neurons in the monkey midbrain revealed that the firing pattern of these cells is consistent with a RPE. These neurons show phasic increases in firing when reward delivery occurs at an unexpected time, or when the reward is bigger than expected. In contrast, when an expected reward is omitted or when the obtained reward is less than expected, DA neurons respond with a transient depression of firing below baseline activity (26, 246, 345, 457).

A central assumption of the RL theory of error processing is that a similar dip in midbrain DA neuron firing occurs in humans upon commission of a response error, or very generally, when negative feedback is received. Indeed, RPE coding in midbrain DA neurons has recently been shown in a human intracranial recording study (602). Furthermore, it is assumed that this transient depression in firing translates into a reduction of extracellular DA levels in the PFC, in particular in the aMCC. This transient reduction in DA transmission is then thought to disinhibit apical dendrites of layer V pyramidal neurons, thereby giving rise to the ERN. The aMCC is assumed to act as a motor control filter which, influenced by the dopaminergic RPE signal, adjusts behavioral output according to the needs. Via the nigrostriatal and mesolimbic pathways the RPE signal is also conveyed to dorsal and ventral striatum, where it is used as a teaching signal to improve outcome prediction. Similarly as in previous models of RL (23, 263), the striatum is assumed to act as an adaptive critic making predictions on action outcomes and evaluating events as to whether they indicate better or worse outcomes than predicted. Via direct connections from the striosomes to substantia nigra and ventral tegmental area (203, 209, 215), this information is conveyed to mesencephalic DA neurons which, in turn, broadcast the new RPE signals to the basal ganglia and frontal cortices, thereby closing the loop of the RL model.

The theory has particular appeal since it has linked the field of executive control with reward-related learning and decision making and computational modeling. Recently, a number of studies have tested whether feedback-driven activity in pMFC reflects the unfavorable versus the favorable outcome itself or the prediction error per se. With the use of an axiomatic approach (71) and by separating the RPE term into the reward and its expectation, pMFC signals in fMRI and EEG/MEG responses in the time range of the FRN have been proven to reflect RPE (32, 177, 450, 508).

The theory has also helped to move the neurochemistry of behavior into the focus of researchers working on cognitive control. It also offers a number of testable predictions. However, many of these predictions are only amenable to testing using invasive methodology, and so far, not many rigorous tests have been performed. The first assumption is that response errors in a situation like a Flanker task elicit a similar pause in DA neuron firing like that seen after reward omissions in primates, which has yet to be tested. A further assumption is that there is a one-to-one relationship between decreased DA neuron firing activity and diminished DA transmission in projection areas. This is of particular importance given that both ERN and FRN are very fast and temporally precise in onset and offset. However, as we (283) and others (319, 469) have argued, the mesoprefrontal DA system does not possess this temporal precision. Whereas in the striatum, the primary mechanism for DA inactivation is rapid reuptake by the DA transporter, this mechanism accounts only for ~40% of DA clearance in the PFC (569). This is due to the very low expression of DA transporters in the PFC (472). Instead, DA inactivation in the PFC is primarily achieved by reuptake via the norepinephrine transporter, catabolism by catechol-*O*-methyltransferase and monoamine oxidase, and diffusion (66, 78, 569). As a consequence of this, extracellular levels of DA take several seconds to return to baseline after stimulation is terminated (322, 367). Moreover, the cellular effects of DA are even much more persistent. The depolarization of inhibitory interneurons and the increase in evoked pyramidal neuron firing outlast the stimulation for many minutes (205, 469). Despite this, after stimulation of the VTA in vivo, a rapid EPSP-IPSP sequence is observed. However, it has been suggested that the EPSP is driven by corelease of glutamate from mesoprefrontal neurons, whereas activation of GABA interneurons via D2 receptors underlies the following inhibitory postsynaptic potential (IPSP) (322). Again, this glutamate-mediated excitatory postsynaptic potential (EPSP) cannot explain the ERN, as the effect is "in the wrong direction." The RL theory of the ERN assumes that a pause in DA cell firing leads (via reduction in DA release) to disinhibition of prefrontal pyramidal neurons. However, a reduction of DA neuron firing would also reduce corelease of glutamate, thereby actually reducing excitatory drive of pyramidal neurons. Recent evidence suggesting that GABAergic VTA neurons projecting to the prefrontal cortex (75) and ventral striatum may play a role in coding RPE and aversive outcomes (95, 548) may hint to an

alternative interpretation of the interaction between VTA and aMCC. Simultaneous recordings of neuronal activity in midbrain and aMCC might be helpful to solve this conundrum.

In addition to these physiological constraints, the predictions of the theory are difficult to test in humans due to the lack of specificity of available experimental manipulations. For instance, a number of studies (reviewed in Ref. 283) have made use of pharmacological challenges, genetic polymorphisms, and clinical models. While they have generated important insights into the role of DA in cognitive control, the evidence either in favor of or against the theory is less conclusive, however. As mentioned above, this is mainly due to the nature of available interventions. For instance, after systemic administration of drugs, it is not possible to tell at what level(s) of the nervous system the observed effects were generated.

Despite these obvious limitations, the RL theory of error processing has nevertheless been of great value. It has stimulated a great deal of research, in particular addressing the neurochemistry of cognitive control. These studies have contributed significantly to our understanding of brain function underlying adaptive, goal-directed behavior. The theories discussed in section IV, *D* and *E*, build on similar learning principles and can be, although developed independently, seen as modifications and extensions of the RL theory.

D. Action Outcome Prediction in pMFC

In an attempt to reconcile the RL and conflict monitoring theories of pMFC function, the error-likelihood theory was developed (61). It states that the pMFC learns to predict error likelihood based on context features. The magnitude of the pMFC signal scaled by the learned error likelihood is used as an early warning signal recruiting cognitive control. Response conflict in this theory is only a special case of situations entailing high error likelihood. While in fMRI studies direct comparison with the response conflict monitoring theory seemed to suggest a superiority of the error-likelihood model in predicting the pMFC response and behavioral effects (54, 60, 276), the opposite result was found in an EEG study (596).

More recently, a predicted response-outcome model of pMFC function has been suggested (3). In this model, individual neurons are assumed to code the learned prediction of the probability and timing of the various possible outcomes of the action at hand. When an expected outcome occurs, the corresponding prediction signal is inhibited. Thus nonoccurrence of predicted outcomes results in maximal pMFC activity. The predicted response-outcome model is thus based on a generalized temporal difference error algorithm, with the important feature that it can predict multiple possible action-outcome relationships simultaneously. Outcomes are then evaluated with respect to their deviation from prediction, irrespective of their positive or negative valence. As a result, surprising outcomes are associated with greater pMFC signals and then recruit adaptive control. As reviewed above, surprise-related pMFC signals have been described at neuronal, EEG, and fMRI levels (173, 227, 276, 346, 455, 573, 601).

E. Action Value Updating

Based on RL and action outcome prediction models, a recently emerging view in the literature is that outcome-related activity in the pMFC is related to the extent that an outcome will be used to guide future decisions. As discussed above, it has been shown that aMCC activation is not exclusively seen after negative action outcomes. In contexts in which individuals can learn from both positive and negative outcomes, aMCC activation is seen after both types of feedback (565). Thus, whatever the valence of feedback, when it was useful to instruct future behavior, it elicited aMCC responses. Furthermore, it has recently been shown that the aMCC response to negative outcomes varies as a function of the reward environment. If a negative feedback is highly likely to indicate the need for a behavioral adjustment, a strong aMCC response is triggered (33, 282). In addition, even within the same reward environment, aMCC does not respond in a uniform fashion to negative outcomes. Responses are more pronounced when the subject has already experienced negative feedback on preceding trials, that is, when the outcome is more likely to indicate that behavior needs to be adjusted (282). In line with this, lesions of the sulcal part of primate ACC led to very characteristic deficits in response-based reversal learning. In particular, lesioned monkeys frequently reverted back to previously correct actions. This was due to the lesioned monkeys' choices being guided exclusively by the outcome of the immediately preceding trial. In contrast, control animals used the outcomes of several past trials to determine their choice. Thus lesions of the ACC caused an inability to construct an extended reinforcement history (289). The deficit seen after ACC lesions in updating values seems to be specific to action values. Updating of stimulus values in contrast is spared after ACC lesions and is instead impaired after damage to the orbitofrontal cortex, in both humans and non-human primates (70, 446). Thus action value updating, although conceptually similar to the predicted response-outcome model, additionally takes into account features of the environment and reward history and weights teaching signals accordingly.

A common theme of the models and theories discussed above is that the performance monitoring network and its key player pMFC determine the necessity, type, and magnitude of adaptations that serve goal achievement, the avoidance of negative consequences, and the optimization

of actions. The models differ with respect to the kind of information processing that underlies this function. While some models including the adaptive control hypothesis discussed in section II (475) emphasize that information about (potential) punishment is used, the action outcome and action value update models also cover situations in which subjectively positive or valence-free information is used to estimate the value of adaptation.

V. CONSEQUENCES OF PERFORMANCE MONITORING

Performance monitoring serves the correction, adaptation and optimization of actions. Thus the functional importance of neuronal correlates of performance monitoring can only be claimed, if these correlates are shown to be associated with physiological and/or behavioral consequences. A broad range of adaptations have been observed after errors and other performance problems, such as unexpectedly high response conflict, decision uncertainty, or task difficulty. These adaptations range from immediate compensatory mechanisms to long-term strategic changes in behavior and learning. Several psychological classifications for action control mechanisms have been suggested (52, 436), converging on the notion that there may be reactive control induced by unexpected events (e.g., performance problems) and proactive, anticipatory control preparing the individual to optimally perform a task. All adjustments induced by unexpected performance problems are per definition reactive, but they may also entail further proactive adaptations allowing to anticipate increased need for control in similar situations and to recruit these control mechanisms or to circumvent (preempt) situations of increased demands by strategic changes in behavior (436). It has been suggested that subregions of the pMFC as well as the lateral prefrontal cortex play major roles in the selection of reactive or proactive modes of cognitive control (52, 242, 294, 527).

Here, we will review the performance-monitoring-driven adaptations with respect to their temporal occurrence from immediate via trial-by-trial to long-term adjustments. Some fast adaptations are very general and goal unspecific and may provide the conditions for longer-lasting goal- and task-specific adjustments. For example, performance problems trigger not only cognitive and affective effects but also recruit autonomic responses providing the somatic basis for behavioral adaptations.

A. Autonomic Concomitants of Performance Problems

Mental and physical effort during goal-directed behavior is associated with changes in the autonomic nervous system (ANS). For instance, increased task difficulty or conflict goes along with increases in heart rate (HR) in the Stroop interference task (50). Autonomic reactions prepare the individual to adapt attentionally and physically to changes in the environment, enabling the organism to execute fast fight or flight reactions.

Failures in performance have been shown to trigger specific ANS reactions: error commission leads to an immediate HR deceleration (120, 122, 174, 217, 541, 574) that is followed by a reacceleration ~4.5 s after the erroneous response (574). HR slowing has also been observed after negative feedback, i.e., disadvantageous choices, in a gambling task (119).

Additionally, pupil dilations have been reported after errors (118, 574). Error-related pupil dilation correlates with activity in the pMFC and the anterior inferior insula (118), two brain areas that are usually active during error commission.

Furthermore, skin conductance changes in response to errors. Whereas there was almost no skin conductance response (SCR) modulation after correct responses, large SCRs were elicited after errors in interference tasks (218, 303). SCRs were also increased after punishment in a gambling task (119), suggesting that SCR changes are comparable after self-inflicted errors and after punishment.

Error commission activates the pMFC (specifically the aMCC) and the anterior insular cortex (AIC) (e.g., Refs. 296, 439, 534, 573). Both brain areas have also been associated with ANS responses (117). It has been shown that *1*) pMFC activity correlates with SCRs (114, 191, 371), *2*) direct electrical stimulation of the pMFC leads to changes in SCR (337), and *3*) lesions in this brain area lead to attenuated SCRs (515). PMFC activity also correlates with pupil diameter (118) and HR (116, 293, 561). As reviewed by Critchley et al. (115), there are direct and indirect connections between the pMFC and autonomic brain stem nuclei that influence the HR.

A recent meta-analysis revealed that activity in the ventral AIC is correlated with autonomic responses as well (369). AIC activity has been associated with pupil dilation (118), HR (116, 369), and SCR (369, 371) changes. Direct insula stimulations in humans led to changes in cardiac responses (396). Craig (112, 113) suggested that the AIC is involved in interoception, i.e., in the subjective perception of bodily responses, thus linking AIC to somatic awareness. Furthermore, it has been assumed that AIC is part of a "salience network," comprising AIC, pMFC, and the frontal operculum/orbitofrontal cortex (470). The assumption that most errors are salient events could explain the substantial overlap between error-related activity and the salience network. This assumption is supported by the finding that consciously perceived (or salient) errors are associated with

stronger AIC activity than unnoticed (presumably less salient) errors (234, 238, 296).

1. Autonomic responses related to conscious error perception

It has been demonstrated that HR deceleration, pupil dilation, and SCR are more pronounced after consciously perceived (reportable or aware) errors than after unperceived errors (388, 574). On the one hand, fMRI studies on conscious error perception (error awareness) have shown that activity in the pMFC (237) and AIC (234, 237, 238, 296) is stronger after perceived than after unperceived errors (299). On the other hand, pMFC and AIC are associated with autonomic responses (see above). Together, these findings suggest a link between conscious error perception and autonomic responses.

Whether activity in the pMFC correlates with error awareness is still under discussion (572). While earlier studies on error awareness did not find activity differences in the pMFC between perceived and unnoticed errors (234, 296), recent fMRI studies reported stronger pMFC activity for perceived errors compared with unperceived errors (237, 238). Similarly, mixed results have also been reported for the ERN: several studies found larger ERN amplitudes for aware than for unaware errors (239, 332, 460, 477, 497, 574); however, other studies did not find any awareness-related ERN modulation (157, 376, 388, 476). In contrast, the error positivity (Pe) is a reliable marker for error awareness (157, 298, 368, 376, 574) with more positive deflections after perceived errors compared with unnoticed errors.

It has been proposed that the emergence of error awareness involves the accumulation of evidence that an error has been committed (526, 572). This evidence accumulation model assumes that information from different sources is gathered: the presence of response conflict, proprioceptive feedback or sensory input about goal achievement, and autonomic responses might contribute to the conscious perception of an error. The ERN and the Pe could be the electrophysiological correlates of this information. For instance, the ERN has been associated with the level of response conflict (125, 595) (see sect. III). Because autonomic responses might also contribute to error awareness, the observation that ANS modulations are more pronounced after consciously perceived errors than after unnoticed errors seems plausible. ANS reactions can represent autonomic post-error adjustments that show some commonalities with behavioral post-error adjustments (see sect. VC). These might also be modulated by error awareness, but the current evidence for such a relationship is still sparse and mixed, with some support for the notion that post-error slowing is more likely after consciously perceived errors (124).

However, it is still an open question whether a salient event, like an error, triggers an autonomic reaction, which then contributes to error awareness, or whether, alternatively, an error that is perceived consciously leads to autonomic reactions subsequently. Thus the question is whether the autonomic reaction precedes or follows the conscious perception of a salient event. In the future, this question could be addressed with lesion studies.

2. Errors and the orienting response

It has recently been shown that surprising events, which are usually highly salient, also activate large parts of the performance monitoring network, including pMFC and AIC (573). Because of several commonalities between surprising or novel events and errors, it has been suggested that both event types elicit an orienting response (384). Both novel events (18) and errors lead to reaction time slowing on the subsequent trial (384, 573). This is known as post-novelty slowing and post-error slowing, respectively. Common to both event types is that they are usually rather infrequent events. Novel and surprising events generally elicit an orienting response (491), and this has also been suggested for infrequent errors (384).

An orienting response elicited by infrequent errors could explain both the ANS responses associated with errors and the motor inhibition following errors. Pupil dilation and SCRs have been described as part of an orienting response to novel or surprising stimuli (491). Thus pupil dilation and SCRs follow both novel events and errors. Moreover, motor slowing after the occurrence of a novel event is an integral component of the orienting response (491). Therefore, it has been suggested that post-novelty slowing and post-error slowing might be comparable processes, as both might be due to an orienting response (384; see sect. VC).

B. Immediate Adjustments

When an error occurs, it may make sense to immediately counteract or correct it, such that the action goal is still achieved. An early finding was that skilled typists executed errors more often with light keystrokes than correct responses, suggesting that errors were counteracted by pulling back (426). Such online within-trial control inhibiting the execution of errors is supported by reduced electromyographic (EMG) burst activity and a longer latency between EMG onset and motor response in errors compared with correct actions (4). Counteracting errors may also be reflected in reduced force production. The relationship between error force and pMFC activity is unclear: higher force was found to be associated with increased (306) or decreased (198) ERN amplitude.

In speeded choice reaction time tasks, participants often correct their errors by rapidly pressing the correct button

even if they were not explicitly instructed to do so (103, 430). Correction times, i.e., the latency between error and corrective response, can be extremely short, sometimes far below 100 ms. This has given rise to the question whether corrective responses can always be interpreted as such, i.e., as intentional actions implemented to correct an error. Usually error corrections occur in tasks involving the competition of two response tendencies, an incorrect one induced by salient but misleading stimulus features and a correct one driven by processing the relevant stimulus feature according to the task rules. In such tasks, reaction times for errors are often shorter than for correct trials. Thus the majority of errors result from premature responses based on the quickly building-up distractor-driven response activation reaching the motor threshold earlier than the slower correct response activation. It has, therefore, been argued that immediate error corrections may reflect delayed correct responses that are executed after the premature error (425, 533). Compared with uncorrected errors, corrected errors are associated with higher pMFC activity as reflected in greater ERN amplitudes (163, 164, 198) and larger hemodynamic signals (176). Moreover, corrected errors elicit ERNs with shorter latencies than uncorrected errors (175). Faster error correction is associated with shorter ERN latency and greater ERN amplitude (175, 440). These findings are compatible with the response conflict monitoring account of the ERN (595): the faster the corrective action relative to the error, the higher and earlier the conflict between erroneous and corrective response tendencies. Thus error correction modulates the activity of the performance monitoring system, but it is questionable whether performance monitoring is a necessary prerequisite for fast action sequences of erroneous and correct responses that post hoc appear like intentional corrections. Hence, error corrections are a rather insensitive measure of error processing; error signaling may be much better suited to reveal error monitoring deficits in clinical populations (471, 533).

C. Trial-by-Trial Adjustments

When an error has been committed, it would be advantageous to implement mechanisms that lead to improved performance in the following trials, that is, to avoid further errors. Following erroneous responses, three types of behavioral adjustments have been observed in post-error trials (124): post-error slowing (PES), post-error improvement in accuracy (PIA), and post-error reduction of interference (PERI). Two or more of these post-error adjustments can co-occur in a given task, but preliminary evidence suggests that the different types of adjustments are independent from each other (124). For instance, PES and PIA have been observed together (123, 140), but they do not seem to be correlated necessarily (74, 124). Moreover, PES is not related to PERI (294). However, all of these adjustments are measured in the trial directly following the error, and therefore, they seem to occur more or less simultaneously. Below, we will discuss each of these behavioral adjustments and point out similarities between post-error and post-conflict adaptations.

Various attentional and motor adjustments have been observed in post-error periods in the cortex. In task-related visual areas, adjustments are twofold: an activity increase can be observed in extrastriate task-relevant visual areas (e.g., in color-processing areas, if color is relevant to solve the task) (123, 294), whereas activity in task-irrelevant visual areas decreases in post-error trials (e.g., in motion processing areas, if motion is a distracting feature of the stimuli). These attentional adjustments are correlated with the preceding error-related activity in the pMFC (123), suggesting that pMFC activity during the error trial triggers these visual adjustments in the following trial. Error-related pMFC activity also predicts an activity decrease in motor areas in post-error trials, which, in turn, is related to PES (123, 294). **FIGURE 5** presents the relation between error-related pMFC activity and subsequent adjustments in motor and perceptual cortices underlying post-error adjustments in the framework of a feedback-control loop.

In line with the described attentional adjustments, a recent EEG study also found interactions between mediofrontal and occipital brain areas after errors (98). In time-frequency analyses, these interactions were observed in the theta band. Subjects with stronger mediofrontal-occipital interactions were more likely to show improved performance in post-error trials (PIA) (79, 98).

1. PES

PES is an increased reaction time in correct trials following errors compared with correct trials following other correct trials (317, 430). It is still under debate why PES occurs. It has been suggested that PES reflects the implementation of cognitive control, or that it represents the slowing associated with an orienting response (for a review, see Ref. 124). Perhaps common to both accounts is that PES is associated with motor inhibitions. After describing the characteristics of PES, these accounts will be discussed further.

A couple of factors influence the strengths of PES in a given task. First, it has been shown that PES depends on trial timing. The shorter the interval between erroneous response and the next stimulus (response-stimulus interval), the more PES can be observed (124, 275). How long exactly the interval can maximally last so that errors still generate PES might depend on the nature or complexity of the task. This assumption still needs to be investigated more systematically.

Second, PES depends on the frequency of errors. Several recent experiments (264, 384, 386) have shown that PES can predominantly be observed in those experimental conditions where subjects commit fewer errors. If error fre-

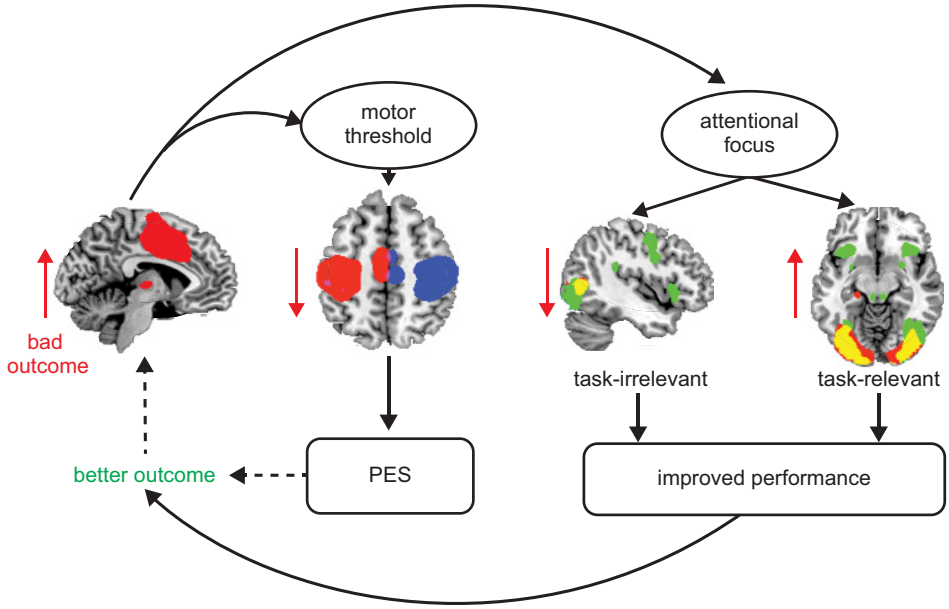


FIGURE 5. Error-driven motor and attentional adjustments. A bad action outcome, like an error in an interference task, leads to increased pMFC activity that triggers adjustments in both motor threshold and attentional focus. Increases in motor threshold are reflected in decreased motor activity in post-error trials, which in turn is correlated with post-error slowing (PES). Adjustments in attentional focus are twofold: activity in task-irrelevant (distracter-encoding, here motion-sensitive) extrastriate visual areas decreases, whereas activity in task-relevant (here color-sensitive) visual areas increases in post-error trials. Attentional adjustments serve to improve future performance, but it is still under debate whether PES contributes to better action outcomes. [Based on data from Danielmeier et al. (123).]

quency is increased, PES is reduced or absent. In task conditions where errors outnumber correct responses, that is, if errors are rather frequent, individuals show post-correct slowing instead of post-error slowing (384–386). This observation led to the assumption that PES reflects an orienting response to infrequent or surprising events (384). The assumption that surprising events and infrequent errors are both associated with an orienting response is supported by fMRI findings showing that both event types activate neural networks that overlap in large parts (573). In a modified oddball task, the frequency of surprising/novel events was matched to the individual's error frequency. Brain areas activated by both novels and errors comprised the aMCC, anterior insula, pre-SMA, lateral prefrontal cortex, thalamus, and other subcortical structures. Independent component analysis of EEG data using the same task revealed that the error-related component also explained substantial parts of the novelty-related N2b component (573). Together, fMRI and EEG results provide converging evidence that there is a common process to novel stimuli and errors, which is most likely an orienting response.

Third, individuals show more PES, if accuracy is stressed, compared with conditions where speed is stressed (529). However, accuracy manipulations are usually confounded with error frequency (529), that is, individuals who try hard to avoid mistakes usually commit fewer errors than individuals who perceive errors as being less serious. Moreover, different instructions regarding speed and accuracy will lead to different motor thresholds and presumably also to stronger motor threshold adjustments when accuracy has been stressed (147).

Furthermore, it has been shown that PES depends on the task context. Individuals also show PES when they observe errors of other humans or computers (387, 467). Interestingly, the size of PES after observed errors is larger when participants are in a cooperative task context, that is, they play together with the other individual (or computer), compared with when they are in a competitive task context, i.e., playing against the other individual (387). Nunez Castellar et al. (387) pointed out that the other individual's errors have a different meaning for the participant in the cooperative versus the competitive condition: whereas observed errors are negative events in the cooperative condition, they represent positive events in the competitive condition. The authors suggested that errors representing negative outcomes are more threatening and motivationally more significant than errors representing positive outcomes. Thus the context dependency of PES might also be explained by the motivational salience of errors.

Several suggestions have been made regarding the underlying mechanisms leading to PES (124). One potential explanation assumes that PES reflects the implementation of cognitive control processes (46, 197). As mentioned above, it has recently been suggested that PES reflects an orienting response elicited by surprising or infrequent events such as

errors (384). Additionally, inhibitory mechanisms in the motor system have been discussed for post-error periods (123, 434).

We suggest that PES reflects the inhibitory component of an orienting response. An increased latency of motor responses has been described by Sokolov (491) as part of the orienting response. Therefore, increased reaction times following errors, i.e., PES, can be interpreted as part of an orienting response elicited by the error (see sect. V*A*). This orienting response could elicit inhibitory processes in the motor system in post-error trials. Indeed, there is structural and functional evidence for this hypothesis.

We recently demonstrated that activity in the pMFC (and other brain areas related to performance monitoring) on error trials predicts the decrease of activity in motor areas in the post-error trial (123). The post-error activity in motor areas, in turn, correlated with the individual's PES, in that less motor activity is observed when an individual shows more PES. Another study (294) also reported decreased activity in motor areas in post-error trials and a negative correlation between motor activity in these trials and PES, in that less motor activity is observed when an individual shows more PES. The decreased motor activity following errors presumably reflected an increased response threshold, hence, motor inhibition. When Botvinick et al. (46) described the response conflict theory, they already modeled PES as increase in motor threshold. This is in line with the results of a recent study investigating the processes behind PES with a drift diffusion model. The model showed that the reaction time increase after errors can be attributed almost exclusively to an increase in boundary separation, that is an increase in response threshold (147). Results of these models are supported in an EEG experiment (338) showing that increased beta-band power is related to PES. Increased beta-band power indicates inhibitory processes, specifically motor inhibition (314, 503).

There is also structural evidence that PES is related to inhibitory brain networks. A diffusion-weighted imaging (DWI) study revealed the involvement of a right hemispheric network, consisting of preSMA, lateral inferior frontal cortex and subthalamic nucleus (STN), in PES (123). This network has previously been associated with processes of motor slowing or stopping (14, 502, 551); thus the DWI result provides a further link between PES and motor inhibition. A positive correlation between PES and white matter integrity in frontal parts of the brain has been replicated in another DWI study (178).

In several experiments, the individual size of PES was predicted by the individual's ERN amplitude (136, 198, 575, 576), by their midfrontal theta power increase in error trials (79), or by their BOLD response in pMFC (87, 196, 291, 296). These studies suggest that PES is triggered by pMFC activity after error commission. However, some studies reported correlations between PES and the Pe instead of the ERN (217, 376) and between PES and feedback-related P300 (386).

PES seems to be a general behavioral adaptation that does not correlate with (an improvement in) post-error accuracy in a number of studies (74, 124; but see Ref. 218). However, the response caution inherent to PES might nevertheless allow for task-related adjustments, and thereby facilitate performance improvements in an indirect manner.

In conclusion, PES seems to be an unspecific post-error behavioral adaptation that is directly or indirectly related to pMFC activity during the error and directly related to decreased motor activity in post-error trials. The size of the PES effect is influenced by *1*) the duration between erroneous response and the following stimulus, *2*) error frequency or perhaps how surprising an error is, and *3*) the motivational salience of an error.

2. PIA

It has often been argued that post-error adjustments, like PES, are necessary to enable individuals to improve their performance after an error (post-error improvement in accuracy, PIA). However, when comparing accuracy in post-error trials with that of post-correct trials, findings about post-error accuracy are not that unequivocal. While several studies indeed report improved accuracy after errors (123, 140, 316, 317, 334, 338), other studies do not find a difference between post-error and post-correct accuracy (217, 220), or report even a decrease in post-error accuracy (98, 175, 428), at least in some experimental conditions.

As mentioned above, PIA and PES do not always occur together and are not necessarily correlated (124). This finding suggests that PES and PIA are not due to the same underlying process. There is indeed evidence that both behavioral adjustments follow different time courses. A study that investigated the effects of different response-stimulus intervals (RSI) on PES and post-error accuracy found that PES is larger with short intervals between erroneous response and the following stimulus, and decreases with longer RSIs (275). In contrast, post-error accuracy was reduced with short RSIs (post-error accuracy lower than post-correct accuracy) and improved with longer RSIs (no difference between post-error and post-correct accuracy). However, it still needs to be tested, if improvement in accuracy would continue with even longer RSIs.

There is preliminary evidence that post-error accuracy is associated with error-related mediofrontal brain activity. It has been shown that both the ERN amplitude and the Pe amplitude correlate with subsequent accuracy (74, 513). Time-frequency analyses of EEG data revealed that participants who showed more theta band power over medio-

frontal electrodes during an error trial are more likely to improve their performance in the following trial (98). Furthermore, stronger interactions between mediofrontal and occipital areas predicted improved performance after errors. Therefore, error-related brain activity in the pMFC seems to influence subsequent performance and potentially triggers attentional changes in posterior brain regions. This would be consistent with the hypothesis that the pMFC signals the need for adjustments after an error has been committed. However, Higo et al. (240) suggested that top-down modulations in visual areas are regulated by the frontal operculum/anterior insula. Since pMFC and anterior insula are often coactivated, it remains to be shown which area is mainly responsible for top-down adjustments after errors.

3. PERI

Errors and post-error adjustments have often been observed in interference tasks. In these types of tasks, cognitive interference emerges from task-irrelevant information included in the stimuli. For instance, in a standard Simon task, stimuli are presented on the left or right side of the screen, where the identity of the stimuli (e.g., color) is relevant, but the spatial position of the stimuli is task-irrelevant. This distracting information can either be congruent or incongruent with the required response (e.g., left or right button press). Since individuals hardly ever manage to completely ignore the irrelevant dimension, it influences reaction times (RTs): RTs are shorter in congruent than in incongruent trials, known as interference effect. Ridderinkhof et al. (435) found that this interference effect is reduced after error trials compared with after correct trials. They described this as PERI. It is assumed that PERI reflects cognitive control processes that trigger improved interference resolution in post-error trials (294).

King et al. (294) demonstrated PERI-related modulations in task-relevant visual areas. They employed a face-gender version of the Simon task, where participants were asked to judge whether a face is female or male, i.e., face-gender was the relevant stimulus dimension. Stronger activity in the fusiform face area, the task-relevant visual area that encodes faces, was associated with a stronger PERI effect. Thus PERI and PES appear to be implemented in different neuronal networks: while PERI effects are correlated with activity in task-relevant areas, PES is correlated with motor activity. However, both adjustments seem to be driven by the pMFC.

4. Adjustments after high conflict

Adjustments do not only occur after errors, but also after correctly solved high-conflict trials. The aMCC (among other areas) has been associated with trial-to-trial adjustments after high-conflict trials (e.g., Refs. 291, 578). It has been observed that RTs in incongruent trials following congruent trials (cI) are longer than RTs in incongruent trials following incongruent trials (iI). This is known as conflict adaptation effect or Gratton effect (207). It is assumed that high-conflict situations, as in incongruent trials, lead to the implementation of cognitive control processes (46, but see Ref. 462). With more control present, conflict in a subsequent incongruent trial will be reduced, resulting in shorter RTs (501, 524, 581) and less pMFC activity (291) compared with situations after congruent trials where control is not enhanced. Recently, it has been demonstrated that neurons in the human pMFC encode the conflict history in an interference task and, thus, show conflict adaptation (482).

Kerns et al. (291) showed overlapping activity in the pMFC for incongruent trials and errors. The level of activity in this area predicted both adjustments in subsequent incongruent trials (reflected in shorter RTs in iI trials) as well as adjustments after error trials (reflected in more PES). Similar to adjustments in task-related visual areas after errors (123, 294), adjustments in the task-relevant visual area have been observed after high-conflict trials (149). According to the conflict monitoring theory (46, 595), commonalities between post-error and post-conflict adaptations are not surprising, because errors are trials with high post-response conflict, whereas correctly solved incongruent trials are characterized by high pre-response conflict. Thus both trial types are associated with high levels of conflict (i.e., simultaneous activation of correct and incorrect response tendency). Yeung et al. (595) suggested that pre- and post-response conflict is reflected in the electrophysiological signals N2 and ERN, respectively. Indeed, conflict adaptation effects have been shown in both N2 and ERN amplitudes (321, 581).

Usually, conflict adaptation effects are investigated in interference tasks using only congruent and incongruent trials. Recently, it has been suggested that there might be two overlapping processes in the trial affected by conflict from the previous trial (552) which are hard to disentangle if the present trial is again congruent or incongruent. On the one hand, high conflict in the previous trials triggers attentional focusing to the task-relevant dimension, which leads to reaction time advantages, especially if the present trial is incongruent. On the other hand, the response conflict model (47, 595) predicts more cautious responding after high conflict, which should result in longer reaction times. When post-conflict effects are measured in truly neutral (univalent) trials, the advantage of post-conflict focusing to the stimulus relevant dimension disappears, and one can observe post-conflict slowing resembling PES (552). Taken together, post-conflict processes seem to be the same after both correctly answered incongruent trials and errors. In both cases, individuals show a reaction time increase and attentional focusing to task-relevant aspects.

D. Learning and Decision Making

1. pMFC and associated brain regions

It seems clear to everyone that, in addition to the short-term adjustments reviewed above, one can learn from mistakes and change the choice of actions strategically. The RL, outcome prediction, and action value updating theories of performance monitoring (see sect. IV, *C–E*) have placed the findings on error detection in a learning context. As reviewed above, pMFC activity is related to reward prediction errors and may reflect a teaching signal for subsequent learning processes. In learning paradigms it has been shown that outcome-related pMFC activity changes during learning: in early phases, when feedback provides new information, feedback-related activity is largest, and it decreases with increasing learning success. The type of errors in these experiments changes from mistakes resulting from insufficient rule knowledge towards action slips on premature responses, which is reflected in increased response-related activity. This has been demonstrated in EEG, where FRN activity decreases and ERN activity increases as learning progresses (249, 253, 311), and fMRI (339). To rule out that these effects are only an epiphenomenon, it is important to show a relationship between the magnitude of performance monitoring signals and learning. Indeed, in an associative learning paradigm in which errors were followed by feedback indicating the correct choice, feedback-related activity in pMFC, anterior insula, and hippocampus predicted whether an error would be corrected on a later occurrence of the same target stimulus (233). In addition, anterior insular activity predicting learning success is sensitive to the magnitude of punishment associated with erroneous choices (236). Similarly, error-related pMFC activity in a Go/NoGo task was predictive for successful response inhibition at the next presentation of the same NoGo target (235). In the learning phase of a probabilistic selection task, feedback-related pMFC activity was even shown to predict decision performance in a delayed memory test (297). PMFC showed stronger functional connectivity with the hippocampus and ventral striatum during early learning when feedbacks were highly informative, compared with the asymptotic phase of learning when probabilistic misleading feedback should be ignored. Moreover, a genetic polymorphism associated with striatal dopamine D2 receptor density modulated the ability to learn from negative feedback and the associated neuronal response (279, 297). In the same probabilistic learning paradigm, participants who learned better to avoid actions with negative consequences than to prefer actions with positive outcomes ("negative learners") showed increased FRN amplitudes on negative feedback than "positive learners" who learned better to prefer positive actions than to avoid negative actions (189). Oscillatory activity at frontocentral electrodes was also shown to predict learning in a time-estimation task with informative feedback (correct, too fast, too slow): theta-band power correlated with learning after negative feedback (requiring subsequent adjustments) and beta-band power predicted learning after positive feedback (requiring to stay with the learned response interval) (540).

The above-discussed findings convincingly demonstrate that performance monitoring yields a teaching signal reflected in pMFC activity that can trigger learning, which is compatible with the reinforcement learning and action value update models. Whereas the reinforcement theory suggests that pMFC activity reflects the RPE (249), the action value model goes a step further in assuming that an adaptive signal guiding future decisions is formed by weighting the RPE with statistical parameters from reinforcement history that determine which impact a single action outcome should have (33, 282, 289). This reinforcement history statistics is reflected in the learning rate, which, in turn, can be modulated by volatility of the environment (33) or reliability of the feedback (282). In accordance with the action value updating account, hemodynamic as well as electrophysiological activity in pMFC has been shown to correlate with the reward prediction error and to be modulated by parameters reflecting reinforcement history (33, 177, 282, 508).

While even delayed feedback is tracked by medial frontal FRN activity (329), the delay may interfere with credit assignment and learning performance. This has been demonstrated in an artificial grammar learning task, in which, compared with immediate feedback, delayed feedback resulted in lower FRN amplitudes and reduced learning performance (395).

1. Orbitofrontal and ventromedial prefrontal cortices

After discussing the role of the pMFC-centered system classically associated with performance monitoring in learning and decision making, we will now turn to other cortical areas involved in valuation, outcome and history tracking, and credit assignment, namely, the orbitofrontal (OFC) and ventromedial prefrontal cortices (vmPFC). While at first glance similar functions in action outcome monitoring and decision making seem to be localized in aMCC and OFC (531), fMRI, lesion, and animal studies revealed important dissociations suggesting complementary functions (70, 288, 447, 565). In the following we will focus on the contribution of OFC and vmPFC to stimulus and action valuation based on external feedback and resulting learning and decision making processes.

A classic finding in neuropsychology is that lesions to the OFC in both humans and non-human primates cause deficits in situations where acquired response tendencies need to be flexibly changed. This is particularly evident in studies using reversal learning (172, 261, 272, 274, 285, 351, 442) or reinforcer devaluation (25, 414, 415), or during extinction of a previously acquired instrumental response (65, 442). The deficit has been interpreted as behavioral inflex-

ibility or perseveration. It was assumed that perseveration with a previously successful behavior results from the inability to inhibit a prepotent response (143, 442). However, this view appears no longer tenable. While OFC-lesioned animals indeed have difficulty reducing their choice of a reward after it has been devalued (by feeding to satiety or pairing with illness), they still show reduced consumption of that food (192, 274, 466), and they also retain the capacity to suppress a prepotent response (89). Moreover, more recent studies (discussed below) demonstrate that the aberrant behavior following OFC lesions is not perseverative in nature. Thus response inhibition seems to remain largely intact after OFC lesions. Rather, a large body of evidence points to a role for OFC in encoding value-related parameters. Activity of neurons in OFC reflects the value of available rewards and chosen rewards (399, 400, 516). In humans, the OFC responds to the valence of outcomes of different modalities (9, 40, 391, 444, 473). In both humans and nonhuman primates, OFC responses adapt to changes in the value of an outcome. Responses of OFC neurons to a food reward decreases after it has been devalued by feeding it to satiety (445). In humans, activity in the OFC correlates with the subjective pleasantness of food, and activity decreases as participants are fed to satiety on that food (which is accompanied by decreased desirability ratings) (312, 392).

Some studies reported aversive outcomes to be represented in lateral OFC (lOFC), whereas appetitive outcomes correlated with activity in medial OFC (mOFC), suggesting a functional mediolateral gradient (206, 390, 443). However, a number of studies do not concur with such an interpretation. It has been shown that the same OFC neurons often respond to both rewarding and aversive outcomes. The same was true for conditioned stimuli that predicted either rewarding or aversive outcomes (363). This strongly suggests that information about appetitive and aversive outcomes converges onto the same individual neurons in OFC. Furthermore, in human neuroimaging studies, it appears that vmPFC/mOFC generally represents expected subjective value, independent of whether the outcome is appetitive or aversive (24, 418, 419, 514). Most likely, increased activity in lOFC to negative outcomes reflects the fact that in most experimental situations negative feedback is most strongly linked to an updating of cue-outcome associations. Nevertheless, these findings highlight an important anatomical distinction. On the basis of both cortico-cortical and cortico-subcortical connections, an orbitofrontal and a ventromedial prefrontal network have been defined. The orbital network includes mainly central and lateral parts on the orbital surface. The ventromedial network comprises primarily medial OFC (such as area 14) and anterior ventromedial prefrontal areas 25, 32, and 10 (394). Given that those networks differ both in terms of the inputs they receive and in their target structures, it appears likely that they also have separate roles in behavioral control.

As stated above, activation of lOFC during negative feedback is often associated with updating of cue-outcome associations. Indeed, during reversal of cue-outcome associations, OFC neurons adapt their firing to the new reward contingencies (464). Accordingly, it had been suggested that the OFC flexibly encodes such cue-outcome associations. However, as has been discussed elsewhere (465), a number of findings disagree with such an interpretation. First, reversal of encoding occurs a lot quicker in the amygdala than in the OFC. Second, a higher number of cue-selective neurons reverse firing in the amygdala than in the OFC (~55% compared with only 25%). Third, there is no relationship between rapid reversal of cue-related firing and rapid behavioral change. In fact, the opposite has been shown, with animals that showed rapid changes of cue-related firing being slower at adapting behaviorally (464, 494). It has to be noted however that, in particular, the relative contribution of OFC and amygdala to changing environments is far more complex than simply one brain region "leading" the other. For instance, reversal of cue-outcome associations was in fact faster for neurons in the amygdala compared with the OFC. However, this was only the case for neurons that responded primarily to aversive conditioned stimuli. On the contrary, cells responsive primarily to reward-predicting stimuli reversed faster in the OFC than their counterparts in the amygdala (362).

An alternative account (465) suggests that OFC generally encodes outcome expectancies. OFC neurons respond to both reward delivery and reward-predicting cues, and the change in anticipatory firing is related to the expected subjective value of the outcome. Such a signal would constitute an ideal candidate input for prediction error calculation in midbrain dopamine neurons. The OFC signal would then provide input about the expected value, which then, compared with the actually obtained reward, yields the prediction error. Takahashi et al. (507) directly tested this. They performed unilateral OFC lesions and then recorded prediction error-related activity from VTA dopamine neurons in rats performing a reward-guided learning task. The lesions profoundly changed prediction error coding by dopamine neurons. However, the pattern of results did not simply reflect a mere loss of value-related information. Instead, computational modeling strongly suggested that the deficit was due to a loss of information about the state of the task in which the animal currently was (507).

The findings of Takahashi et al. (507) are in line with a recently emerging view on functional specialization within vmPFC/OFC. Again, it appears that lOFC and vmPFC/mOFC play different roles. However, rather than a dichotomy between appetitive and aversive values, those findings suggest that lOFC is involved in contingent learning of values, whereas vmPFC/mOFC is important in implementing a value comparison, i.e., a choice. Lesions of the macaque lOFC caused specific impairments in credit assignment, the

attribution of a reward to the particular choice that caused that reward (449, 564). After lesions, monkeys no longer attributed the reward to the correct choice. Instead, credit for reward was assigned to the recent choice and reinforcement history. For instance, if option B was selected following several choices of A, then a reward for a choice of B should increase the probability of reselecting option B. While this was true for control animals, the opposite effect occurred in lOFC-lesioned animals. If B was rewarded, then those animals were more likely to reselect A, and this effect was more pronounced the more frequently A had been chosen on past trials. In addition to this influence by recent choice history, lesioned animals' choices were also guided by recent rewards. If an animal selected options A and B on successive trials, then subjects were more likely to reselect B when they had received a reward for the previous choice of A. That is, the effect of the reward for a choice of A spread forward in time and was incorrectly assigned to the choice of B on the following trial (449, 564). This is an intriguing set of results that explains a number of different findings. First, it accounts for the often-reported finding that OFC lesions cause deficits in reversal learning while leaving initial discrimination intact. This study, however, showed that OFC lesions can lead to impairments even in initial learning when there is a mixed history of choices. Such a situation occurs in an environment with multiple options that are close together in value, or after a change of reward contingencies. Furthermore, they show that the deficit during reversals is not perseverative in nature. Instead, lesioned monkeys were actually more likely than controls to switch between options following a reversal. This pattern has also been found in humans with OFC lesions. In a probabilistic context, patients were also impaired at initial learning (517, 577), and they did not perform more perseverative errors following reversal than controls. However, they were more likely to switch behavior away from the correct choice after having received a reward for it (517), a pattern very reminiscent of the lOFC-lesioned monkeys. Again, it is likely this mixed sequence of choices causes the deficits; rewards are no longer attributed to any specific choice, but to the average of all options. In the study by Walton and colleagues (564), this "spread-of-effect" was also present to some extent in control animals, but it was overruled by the contingent learning system. It appears that the lOFC lesion unmasked the effects of a different, less specific learning system. This kind of learning might be subserved by the amygdala, which could explain the surprising finding that impairments in reversal learning induced by OFC lesions are abolished by additional lesions to the basolateral amygdala (493).

A possible mechanism how neurons in lOFC could contribute to contingent learning has recently been described. Neurons in lOFC encode information about both recent rewards and recent choices. They encode information about the identity of a reward (i.e., what type of juice) over a delay period (320). In other words, they have a working memory for reward. Furthermore, while neurons in this area typically do not encode information about responses near the time that the response is made, or in the time following the response (before a reward is delivered), it has recently been shown that they do represent the choice that was made at the time of outcome delivery (519). Such a reactivation of the specific choice that was made at exactly the time when the reward is received would be an ideal candidate mechanism to link an outcome to the specific choice that caused it.

The pattern of deficits obtained after lOFC lesions contrasts markedly with those seen following lesions to the vmPFC/mOFC. In macaques with lesions to mOFC, no impairments in credit assignment were found. Instead, these lesions impaired value-guided choice. The impairment was most obvious when choices had to be made between multiple alternatives that were close together in value (383). This view is further supported by several studies showing that damage to human vmPFC causes impairments in value-guided choice (69, 169, 170, 228). These data indicate that while lOFC is involved in contingent learning of option values, vmPFC/mOFC is more concerned with value comparison. In human fMRI studies, vmPFC often shows correlates of such a value comparison. Frequently, BOLD activity in this region reflects value difference, that is, a positive correlation with the value of the chosen option and a negative correlation with value of the non-chosen option (42, 43, 278). Such a signal is thought to reflect choice, as, by definition, it can only be found after a choice has been made. However, the exact value parameter encoded in vmPFC differs between fMRI studies. Not all find a correlate of value difference; instead, some find a correlation with overall value (the sum of the available options' values). However, those studies often involve only a valuation stage without an explicit value comparison. For instance, participants are presented with a food item and are asked how much money they would be willing to spend to obtain this item or how desirable they rate it (222, 223, 418). Nevertheless, there are also studies that involve an explicit choice and nevertheless find only a correlate of either overall value or chosen, but not unchosen value (224, 587, 588). Network models (568, 585, 586) of decision making might offer a clue to a better understanding. Those models suggest that a decision is realized within a cortical network by a mechanism that is based on mutual inhibition and reverberatory excitation. In these models, there are two pools of neurons whose firing rate represents the value of each option. The competition in the network then results in one of the pools ending up in a high-firing attractor state (the chosen option) and the other pool ending up in a low-firing attractor state (the unchosen option). This architecture offers a mechanistic explanation of how an input related to the options' value can be transformed into a choice. One of the resulting predictions of this model is that network activity initially represents overall value and then transitions

to a representation of value difference as the competition in the network is resolved (265). That is, both signals can be observed in the same brain area, but at different times. Two recent studies provided evidence that such a competition mechanism is implemented in the vmPFC (265, 278). The first showed that neural activity in vmPFC recorded with magnetoencephalography indeed followed these temporal dynamics (265). Another finding from this study however was that vmPFC only represented value difference on trials that required computation of an integrated value (such as multiplying reward probability and magnitude to obtain an estimate of expected value). On trials where both stimulus dimensions dictated the same choice, no value difference correlate could be found in vmPFC. The second study showed that both the dynamics of the vmPFC value difference signal and decision performance were related to vmPFC concentrations of GABA and glutamate, providing further evidence for a neural competition mechanism in vmPFC supporting choice (278) **(FIGURE 6)**. Again, however, GABA and glutamate were not predictive of overall decision accuracy. Instead, this was a function of the options value difference: neurotransmitters were most predictive on difficult trials with low value difference.

These findings seem to suggest that vmPFC might primarily be involved during difficult choices or when an abstract value computation is required. Other brain areas such as posterior parietal cortex (265) may have a stronger involvement in choices that can be made on a more automated basis (such as deciding between two food items). It has also been shown that the value parameter encoded in vmPFC depends on available decision time. Consistent with modeling predictions, vmPFC activity correlated with overall value at short decision times, but with value difference without time pressure. Again, at short decision times, choices appeared to be primarily governed by posterior parietal cortex (G. Jocham, I. Kröger, P. Furlong, L. Hunt, M. Kahn, and T. Behrens, unpublished observations).

An intriguing finding is that vmPFC even signals value in the absence of an overt choice. Lebreton et al. (323) showed that vmPFC activity encoded preferences over options even when subjects were performing a different task (rating the age of faces, houses or paintings). However, it could be argued that a choice is generated nevertheless, even when it need not be executed behaviorally. An elegant study provides evidence for this. Wunderlich et al. (587) asked participants to make choices between two options. However, only a few seconds later they were told which action to perform (button press or saccade) to select the options. They showed that a chosen value correlate emerged in vmPFC even before the action to obtain the chosen option was known (587), further supporting the view that value signals in the vmPFC are tied to a reference frame of choice. However, another study suggests that the frame of reference is attended versus unattended, not chosen versus non-chosen. The authors manipulated attention independent of choice and found that vmPFC reflected the value of the attended option, not the chosen option (326). However, this distinction may in fact be artificial. First, even in this study, instructing subjects to attend to one stimulus had a small but significant influence on choice. Without explicit manipulation, visual fixations are indeed closely linked to choice (307). Lesions to vmPFC also not only impair value-guided choice, they also change how decisions are made in multiattribute contexts. While healthy controls usually compare across options within one attribute, before, advancing to the next attribute, humans with vmPFC lesions do the exact opposite: they first compare across attributes within one option before advancing to the next option (169).

Collectively, these data suggest that the lOFC may play a role in contingent learning by assigning credit to the causative choice. VmPFC/mOFC on the other hand appears to be involved in generating a choice, and it may do so by guiding attention to specific stimulus attributes.

VI. NEUROCHEMISTRY OF PERFORMANCE MONITORING AND ADAPTIVE BEHAVIOR

In the following section, we focus on the roles of dopamine and serotonin in performance monitoring, reward-guided learning and decision making, and behavioral flexibility. We will restrict our discussion to these two neuromodulatory systems since these are the ones for which most data are available. The sparse evidence on other transmitter systems is reviewed in Reference 283.

A. Dopamine

A recent tradition of research, mostly inspired by Holroyd and Coles' RL theory (249), has focused on dopaminergic modulation of brain responses and behavioral adjustments to response conflict and commission of errors. The ERN has been found to be reduced after administration of haloperidol (2.5 and 3 mg), either paralleled by an increase in error rates (603) or without any concurrent behavioral alterations (132). A recent study showed an effect of the COMT Val^{158}Met polymorphism on error-related EEG responses and post-error slowing. In addition, both behavioral and EEG effects were modulated by sulpiride (200 mg) in a fashion that depended on COMT genotype (366). Modulation of error and conflict processing by drug challenges and genetic polymorphisms that act on dopamine (DA) systems has been the subject of recent reviews (283, 521, 522). As discussed in section IVC, there is ample evidence for a role of DA in performance monitoring, but the neurophysiological mechanisms of direct or indirect DA action upon the aMCC remain poorly understood.

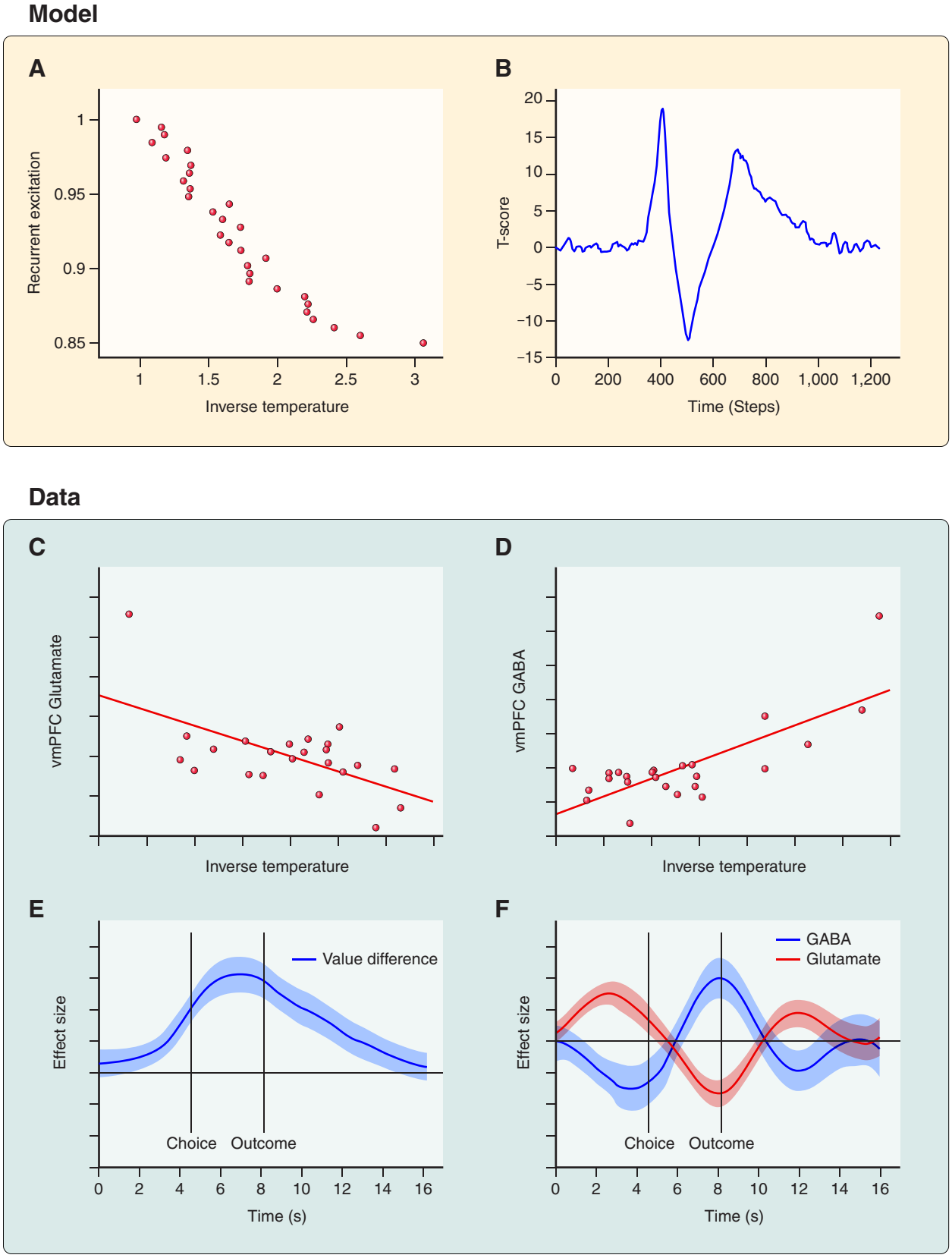
DA is indeed best known for its fundamental role in RL. A rich literature in animals has established that DA, particu-

larly in the striatum, is involved in instrumental learning from both appetitive and aversive outcomes (452, 453, 583). Evidence accrues that DA also contributes to RL in humans. A first study demonstrated modulation of RL and striatal prediction error coding by the DA precursor L-DOPA (100 mg with 25 mg of benserazide) and the DA D2 antagonist haloperidol (1 mg). Compared with L-DOPA, haloperidol attenuated subjects' learning to choose a reward-associated option, while it had no effect on avoiding an option that was associated with monetary loss. Likewise, the expression of appetitive (but not aversive) prediction errors in the striatum was decreased under haloperidol (409). Note that the observed differences were only found when comparing increased against decreased DA transmission, not when comparing against placebo. Depletion of striatal DA resulting from Parkinson's disease (PD) biases RL to increased learning from punishments compared with learning from rewards. Medication with L-DOPA reverses this bias (188, 365, 402). The opposite pattern was observed in patients suffering from Tourette's syndrome (TS). There is evidence for hyperdopaminergia in TS, and neuroleptic drugs are used as standard treatment (2). Unmedicated TS patients were biased to increased learning from rewards rather than punishments. Again, this pattern was reversed by neuroleptic treatment (402). In healthy individuals, L-DOPA (150 mg) increased an optimism bias by impairing learning from outcomes that were worse than expected, without an effect on outcomes that were better than expected (479). The overall pattern that emerges is that increased DA transmission improves learning from appetitive outcomes at the expense of aversively motivated learning. Modeling work suggests that these effects arise from differential effects on synaptic plasticity in the direct and indirect pathways of the striatum. According to this framework, phasic bursts of dopamine support reward learning by increasing plasticity in the direct pathway via D1 receptors while decreasing it in the indirect pathway via D2 receptors. The opposite is thought to occur during pauses in DA neuron firing, thus supporting plasticity in the indirect pathway, thereby promoting punishment learning (188). In agreement with this, it has been shown that a low-dose D2 receptor antagonism (presumably increasing phasic DA neuron firing by acting primarily on autoreceptors) increased behavioral performance that was based on learning from rewards. This was accompanied by increased prediction error coding in the ventral caudate (280). Genetic polymorphisms in the DARPP-32 gene, which relates to direct pathway function (as it is selectively expressed in D1 receptor expressing neurons), are related to increased learning from rewards, whereas polymorphisms relating to D2 receptor expression are related to the degree of learning from negative outcomes (185, 297). More direct evidence comes from highly selective optogenetic targeting. Direct optical stimulation (effectively bypassing the assumed dopaminergic effects on striatal projection neurons) of direct and indirect pathway neurons served as rewarding and punishing stimulus, respectively, in both a Pavlovian and instrumental sense (308). It appears at odds with this that in PD patients with problematic gambling or shopping, D2 agonists (pramipexole, ropinirole) increased learning from rewards and striatal prediction error coding (560). The low doses of DA agonists would be expected to primarily activate autoreceptors, thereby decreasing phasic activity. Likewise, another study found that never-medicated PD patients were better than controls at punishment learning but impaired at reward learning relative to controls and treatment with direct D2 agonists (pramipexole and ropinirole at mean doses of 4.0 to 4.5 and 5.5 mg, respectively) brought patients to the level of controls in reward learning but caused impaired punishment learning relative to controls (41). However, it has to be noted that in these studies, DA agonists were given chronically, rather than as a single dose. It is possible that this caused upregulation of D1 receptors, which could then mediate the observed effects (35). Indeed, administration of a single low dose of the D2 agonists pramipexole (0.5 mg) or cabergoline (1.25 mg) impaired learning from rewards (186, 417). The same effect was obtained from model simulations of reduced presynaptic DA activity (456). In addition to these differential influences on reward and punishment learning, it has also been found that DA depletion in PD increase choice perseveration (independent of reward history), which was reversed by treatment with L-DOPA (451). Notably, the same study found that learning rates did not differ between patients and controls, unless patients were split by disease severity, with more severely affected patients showing reduced learning rates (off medication).

It is noteworthy that in primates, not all midbrain DA neurons are excited by appetitive and inhibited by aversive events. Instead, a subgroup of putative DA neurons shows the opposite pattern. These two types of neurons show a different regional distribution: neurons that were excited by aversive events were predominantly found in the dorsolateral SNc, whereas those inhibited by aversive events were localized primarily in the ventromedial SNc and also in the VTA (345). It has been demonstrated that in PD, cell loss begins in the ventrolateral tier of the SNc (168). The above results raise the possibility that the differential degree to which reward and punishment learning are affected in PD might result from degeneration of appetitively coding cells in ventral SNc, with concomitant sparing of aversively coding cells in dorsolateral SNc.

While the effects of DA on RL are well documented, it becomes evident that DA is also involved in reward-guided decision making by acting on processes other than learning. It has been shown that in the sort of tasks often used in the studies cited above, at least some of the effects of DA are due to a direct effect on instrumental performance, independent of, or in addition to learning (486, 490), possibly through amplifying representations of learned value in

vmPFC (280). In a similar vein, DA also mediates the beneficial effect of reward on motor skill learning. In unmedicated TS patients, the effects of reward on motor skill learning are amplified, while medication with neuroleptics (mostly D2 antagonists) abolished it (403). It is also important to remember that DA has potent behaviorally activat-



ing properties; after all, the cardinal symptom of PD is difficulty in movement initiation. For example, it is well known from the rodent literature that amphetamine infusions into the nucleus accumbens potentiate responding for conditioned reinforcement in a DA-dependent manner (68, 510, 511). Rats with ventral striatal DA depletions prefer small rewards over large rewards when more effort is required for the large reward, even though the depletion leaves them physically capable of performing the effortful action (452, 453). Likewise, PD patients exert less physical effort for monetary reward and also show a blunted increase in skin conductance response to increasing monetary rewards (463). The representation of actions leading to reward, but not of actions leading to punishment, was amplified in the striatum and SNc/VTA of volunteers under the influence of L-DOPA (150 mg). This effect was independent of reward outcome per se (214). This response-invigorating action of DA has been computationally accounted for by the suggestion that tonic DA levels are related to the average reward rate per time. Because subjects are trying to maximize their reward per unit time, high rates of responding are beneficial in an environment with high average reward rates. In such environments, rewards would be lost by too low rates of responding (382). A related conceptualization of DA is that of incentive salience, which emphasizes that the same cue with a certain learned value may trigger different behaviors on different occasions. For example, a drug-associated cue may trigger relapse in a recovered addict despite being resisted on several previous occasions. That means, the same learned value may have opposing behavioral effects depending on the state in which the organism is. In Berridge's words, "... incentive salience is generated afresh by mesocorticolimbic circuits each time the stimulus is re-encountered..." (34). In humans, the expected pleasure to be obtained from an event was enhanced when that event was imagined in a state of elevated DA (using L-DOPA) compared with placebo (480). Reward-guided decisions are also governed by the temporal proximity of a reward, with animals and humans often preferring smaller, immediate rewards over larger, delayed rewards. This phenomenon, called temporal discounting, is also subject to variations in dopaminergic transmission (138, 286, 416).

At a higher cognitive level, DA also seems to be involved in the degree to which behavior is under model-based and model-free control, respectively. Model-based control refers to the subject exploiting explicit knowledge about a structure in the environment, whereas model-free control refers to simple trial-and-error learning that is blind to any such structure. Administration of L-DOPA (150 mg) to healthy volunteers increased model-based relative to model-free control over behavior (589). Furthermore, the COMT Val^{158}Met polymorphism, which is assumed to primarily affect prefrontal DA levels, has been shown to affect exploratory behavior that is guided by uncertainty (184) and to modulate the degree of influence of prior knowledge (through accurate or inaccurate instructions) on RL (144). It is also important to note that a vast literature implicates DA activity in the lateral prefrontal cortex in working memory (for reviews, see Refs. 13, 469). While a discussion of the neurobiology of working memory is clearly beyond the scope of this review, we would like to point out the intimate relationship between working memory and, e.g., RL (102).

DA is also involved in flexibly adjusting behavior to a changing world. L-DOPA administration to PD patients impairs reversal learning and attenuated reversal-related activity in the ventral (but not dorsal) striatum (105, 107). It has been suggested that this is due to "overdosing" of the ventral striatum, which, unlike the dorsal striatum (in particular the dorsolateral striatum) is not depleted of DA in early stages of the disease (295). On the other hand, selective dopaminergic lesions of the medial caudate nucleus in marmosets also impaired reversal learning (91), suggesting that both supra- and subnormal levels of DA are detrimental. PET measurements of baseline DA synthesis were found to be positively related to reward-based reversal learning (106). The D2 agonist bromocriptine (1.25 mg) impaired reversal learning (350); however, this effect seems to depend on baseline DA levels. Bromocriptine (1.25 mg) improved reward-based reversal learning in subjects with low baseline synthesis capacity, but impaired it in subjects with high baseline synthesis (106). Subjects carrying an allelic variant that is associated with reduced striatal D2 receptor density (DRD2/ANKK1-TaqIa) displayed subtle alterations in behavior and reversal-related brain activity. While they did not take more trials than noncarriers to adjust behavior after a reversal, they were less able to maintain the newly correct response. They also showed diminished recruitment of the ventral striatum and lateral orbitofrontal cortex upon reversals. Furthermore, the integration of action outcomes over several trials seen in the aMCC of noncarriers was conspicuously absent in those subjects (279). In addition, while DA depletion of the OFC (unlike in the caudate, see

FIGURE 6. Relationship between levels of GABA and glutamate in ventromedial prefrontal cortex (vmPFC) and decision making. Yellow background shows model predictions, and green background shows actual data. *A*: an increase in excitation relative to inhibition in the model leads to decreasing softmax inverse decision temperature (a measure of accuracy on difficult trials). *B*: modeled effect of increasing recurrent excitation on the dynamics of a cortical value comparison signal. Increased excitation leads to faster ramping up, followed by faster ramping down of the value difference signal. *C* and *D*: subjects with low levels of vmPFC glutamate (*C*) and high levels of vmPFC GABA are associated with good performance (high inverse temperature). *E*: activity in vmPFC reflects a value comparison (value difference between chosen and unchosen option), and this effect emerges around the time of choice. *F*: the ramping up (first temporal derivative) of the effect in *E* is related to local levels of GABA and glutamate. High levels of glutamate cause the value difference signal to ramp to peak quickly and decay again very fast, while GABA acts in the opposite direction. [Modified from Jocham et al. (278), with permission from Nature Publishing Group.]

above) does not impair reversal learning (94), it impairs the extinction of responding for conditioned reinforcement (562). However, there was no increase in perseverative responding (meaning that monkeys' responding was not biased towards the previously rewarded stimulus), which seems to suggest that after loss of OFC DA, behavior comes to be more under contextual, rather than stimulus control. DA also contributes to extinction of aversively motivated behavior. DA depletions of rat medial prefrontal cortex impair the extinction of conditioned fear (364), and in humans, a genetic variant leading to lower DA transporter availability (and hence increased striatal DA levels) expedited extinction of conditioned fear conjointly with increased signal related to an appetitive prediction error in the ventral striatum (433). In both cases, acquisition of conditioned fear was unchanged.

B. Serotonin

The brain serotonin (5-hydroxytryptamine, 5-HT) systems are highly multifarious. The projections originate from a number of different cell groups (B1 to B9), and 5-HT acts on at least 14 currently known receptor subtypes with manifold, often functionally opposing effects. Therefore, it is also not surprising that 5-HT is involved in an array of behaviors including behavioral inhibition, aggression, feeding, analgesia, anxiety, and depression, to name just a few. Within prefrontal cortex, $5HT_{1A}$ and $5HT_{2A}$ receptors seem to be key players, with other subtypes less abundantly expressed (81). Nevertheless, even when focusing only on those two subtypes, the cellular localization of these receptors gives rise to complex dynamics. On pyramidal cells, $5HT_{2A}$ receptors are mostly expressed on the apical dendrites where they amplify glutamate-mediated responses. $5HT_{1A}$ receptors to the contrary are mainly inhibitory, and they may reside mostly in the region around the axon hillock, which would place them in an ideal position to curb action potential generation. On top of this, pyramidal neurons are inhibited by GABAergic interneurons that are themselves modulated by $5HT_{1A}$, $5HT_{2A}$, and $5HT_3$ receptors (81).

It is a classic finding that forebrain 5-HT depletion affects behavioral flexibility, mostly as assessed by reversal learning. Selective neurotoxic lesions of the primate PFC with 5,7-dihydroxytryptamine (5,7-DHT) impaired reversal learning performance (90), an effect that could be reproduced by 5-HT (but not DA) depletions of the OFC (93). Furthermore, the deficit was not due to avoidance of the stimulus that was nonrewarding prior to reversal, but instead due to a failure to inhibit the previously correct choice. However, the effects of forebrain 5-HT on reversal learning are not trivial and seem to depend on a number of factors. For instance, brain region and the specific receptor family or subtype targeted makes a difference. Opposing effects on reversal learning have been described in rats after systemic administration of selective antagonists of $5HT_{2A}$ and $5HT_{2C}$ receptors. $5HT_{2A}$ receptor blockade impaired, whereas $5HT_{2C}$ receptor blockade improved reversal learning performance through increasing and decreasing, respectively, perseverative errors (48). In a follow-up study, the same authors showed that the improvement in reversal learning found after systemic administration of a $5HT_{2C}$ receptor antagonist could be reproduced by local injection of the compound into the OFC. In contrast, the deficit found after systemic blockade of $5HT_{2A}$ receptors could not be reproduced by direct injection into either OFC, medial PFC, or nucleus accumbens (49). Systemic $5HT_{2A}$ receptor antagonism also facilitated a different form of behavioral flexibility, namely, the ability to switch between a cue and response strategy in a cross-maze learning task, while blockade of $5HT_{2C}$ receptors had no effect (16). Furthermore, in primates, a double dissociation between the effects of both 5-HT and DA and OFC and striatum has been reported. 5-HT depletions of the OFC, but not of caudate nucleus impair reversal learning, whereas the reverse was found for DA depletion (92, 93). A correlational study measuring tissue levels of 5-HT and DA in OFC, putamen, and caudate found that neither 5-HT in OFC nor DA in the putamen had any significant effects on reversal learning alone, but their interaction explained 61% of behavioral variance (212). The effects of 5-HT on reversal learning are closely mirrored by those on impulsivity as measured by premature responding on the 5-choice serial reaction time test. Forebrain 5-HT depletion with 5,7-DHT increased premature responding without an effect on food motivation (225), and impulsivity was reduced and increased, respectively, after systemic administration of $5HT_{2A}$ and $5HT_{2C}$ antagonists (179, 582). 5-HT receptors where also shown to modulate the reversal learning deficit induced by subchronic administration of the noncompetitive glutamate NMDA receptor antagonist PCP. More specifically, the deficit was attenuated by antagonists of $5HT_{2C}$ and $5HT_7$ receptors, and by the $5HT_{1A}$ receptor agonist buspirone. However, the effects of buspirone were not fully abolished by the highly selective $5HT_{1A}$ receptor antagonist WAY-100635, which leaves the question to what extent the effects of buspirone were truly $5HT_{1A}$ mediated (349).

A more global approach to modulate 5-HT transmission is reuptake inhibition by interfering with the serotonin transporter. Low doses of selective serotonin reuptake inhibitors (SSRI) are thought of actually lowering extracellular levels of 5-HT in projection areas because activation of somatodendritic $5HT_{1A}$ autoreceptors rapidly silences the raphé 5-HT neurons (221, 269). In contrast, higher acute doses or chronic administration both increase 5-HT levels, the former because the terminal effects override the somatic effects, the latter because of autoreceptor desensitization (67, 229). In keeping with the reversal learning impairments seen after neurotoxic ablations with 5,7-DHT, chronic administration of the SSRI fluoxetine improved reversal learning in mice. Notably, however, in the same study, 5-HT depletion by synthesis inhibition with *para*-chlorophenylalanine (PCPA) had no effect on reversal learning (57). Another study found that genetic inactiva-

tion of the 5-HT transporter, while rendering rats less impulsive, had no effect on reversal learning performance (258). In humans, the SSRI citalopram (30 mg) impaired probabilistic learning both during initial acquisition and during reversal of stimulus-reward associations. It also made subjects more likely to switch away from the currently best option in responses to a probabilistically received negative outcome (82). It has to be noted, however, that there was also a marked increase in response times under citalopram. Using a probabilistic reversal learning task in rats, Bari et al. (21) showed impaired reversal learning after either an acute low dose of citalopram (1 mg/kg) or following global 5-HT depletion with 5,7-DHT, but improved performance following a high dose (10 mg/kg) or chronic administration. These opposing findings mirror the opposing effects of low and high (or chronic) doses of SSRI on extracellular 5-HT described above (21).

Unlike dopamine's well-described role in appetitive motivation and approach, 5-HT has a prominent role in aversively motivated behaviors (135). Behavioral, pharmacological, and anatomical evidence demonstrates close reciprocal interactions between DA and 5-HT (81, 549, 550), and it has been suggested that phasic 5-HT activity might support the learning of aversive values by encoding an aversive prediction error, thus being a mirror image of the mesencephalic DA systems (128). However, as discussed in detail in References 108 and 129, the relationship between 5-HT and aversive processing is complex, with an apparent paradox being that 5-HT covaries both positively and negatively with aversive events and aversively motivated behaviors. Furthermore, recordings of putative 5-HT neurons in the dorsal raphe nucleus of both rats (357) and primates (372) have thus far not revealed phasic responses when expected rewards were omitted. Likewise, in humans, 5-HT reuptake inhibition with citalopram (30 mg) had no effect on belief updating in response to undesirable information (479) or on the neural representation of punishing (and rewarding) actions (214). In a recent study by Seymour et al. (474), healthy human participants learned to choose between options that were associated both with a certain probability of reward but also with an independent probability of receiving a painful stimulus. Lowering central 5-HT levels with acute dietary tryptophan depletion (ATD) made subjects' choices less sensitive to rewards received on previous trials, whereas the effect of punishments was unchanged. However, independently of, and in addition to the effect of learning from previous rewards, 5-HT-depleted subjects were more likely to persevere with their previous choices (474). The latter finding is also consistent with the finding that with 5-HT depletion of primate OFC, while not causing a deficit in extinction from responding for conditioned reinforcement per se, responding during extinction was characterized by a higher degree of perseverance (responding with the previously rewarding stimulus). Notably, in this study, 5-HT depletion also impaired acquisition of conditioned reinforcement. In particular, while all animals displayed an initial bias towards the visually most salient stimulus, control animals overcame this bias during learning over days, whereas this bias even became progressively more pronounced over days in the depleted animals (562). Rhesus monkeys that are SS homozygotes for the 5-HTTPLR polymorphism (presumably associated with reduced expression of the 5-HT transporter and hence elevated 5-HT levels) are impaired at both reversal learning and extinction compared with heterozygotes and LL carriers (273). In humans, ATD increased participants' BOLD response to errors in the dorsomedial prefrontal cortex (161) in a reversal learning task, and it enhanced subjects' performance at predicting punishing outcomes without an effect on predicting rewards during an observational reversal-learning task (109). It should be noted that the behavioral changes described above in the study by Bari and colleagues do not exclusively point to altered aversive processing. While the acute low and high dose of citalopram impaired and enhanced reversal learning performance by increasing and decreasing, respectively, the occurrence of lose-shift behavior, they also found that chronic citalopram increased win-stay behavior, while leaving lose-shift behavior unchanged. Also, 5,7-DHT lesions decreased win-stay and only transiently elevated lose-shift behavior.

From the above findings, it appears that 5-HT is involved in the processing of both rewarding and aversive outcomes. This is in agreement with electrophysiological recordings performed in behaving animals. First, recordings from the primate dorsal raphé nucleus have shown that putative 5-HT neurons are tonically modulated by both the expected and received rewards, with the modulation being bidirectional; that is, some neurons were positively, others negatively modulated by expected and received reward (372). Also, as mentioned above, coding of experienced rewards did not depend on reward expectation, i.e., did not represent a prediction error. It has also been shown that the modulation in the pre-reward and reward-period of the experiment is correlated, such that neurons positively modulated by expected reward are also the ones that are positively modulated by obtained reward, and vice versa (58). A recent study by Inaba et al. (268) found that primate dorsal raphé neurons were modulated by a number of parameters. As the monkey progressed through successive states of a task, neurons encoded how far the monkey was from getting a reward, and whether the current task epoch was the onset of a new state or not. In addition, as described by the studies above, neurons also encoded reward expectation and reward outcome. Interestingly, some neurons were modulated in a threshold-crossing fashion, rather than parametrically by reward magnitude: some neurons did not increase their firing in receipt of one drop of liquid, but then showed the same increase for two and three drops; other neurons would not increase firing for either one or two, but only three drops of reward. While all of those parameters were encoded in the mean firing rates, information about the progress through successive states of the task was mostly contained in the temporal variation of the responses, as revealed through information theoretic analyses. In a contextual conditioning paradigm, rat dorsal raphé neurons predom-

inantly responded with a short-latency phasic excitation to a cue when it was given in a context in which the cue signaled absence of reward, i.e., the neurons predicted "lack of reward" (325).

In addition to its involvement in learning processes and affective control, 5-HT plays an important role in reward-guided decision making by affecting temporal discounting when delays have to be tolerated before a reward is delivered. A rich literature shows that 5-HT, most likely released from the dorsal raphe nucleus, is involved in tolerating longer delays to obtain larger rewards (39, 357–359, 468, 509). Finally, in a rat version of the Iowa Gambling task, tryptophan-depleted rats were impaired relative to controls at learning to choose the option with the long-term better payoff and instead continued choosing the long-term disadvantageous option. In a decision-making task, the same rats also maintained a preference for large rewards delivered with low probability over small but certain rewards (305).

Genetic polymorphisms in the 5-HT system have also been shown to affect the processing of errors. Fallgatter et al. (167) were the first to show that carriers of the S allele of the 5-HTTLPR had larger ERN amplitudes in a flanker task. However, this study did not yet take into account the fact that this polymorphism is in fact tri-allelic, and a later study taking this into account could not replicate this finding (393). Nevertheless, Holmes et al. (247), also taking care of the triallelic variant found that L carriers showed enhanced post-error adjustments, reflected in an increase in accuracy after errors, but a diminished ACC response to errors, compared with S-carriers. In fact, L-carriers showed a relative deactivation in response to errors. However, L-carriers showed increased conflict-related ACC activation (247). Furthermore, a polymorphism that is associated with increased expression of 5-HT_{1A} autoreceptors (and hence reduced 5-HT release) was shown to be related to both reduced ERN amplitude and reduced post-error slowing (36). In contrast to these genetic effects, acute administration of SSRI did not affect error-related brain potentials (132).

In sum, as can be expected by its complexity, the serotonin system modulates numerous functions serving performance monitoring and adaptive behavior. We are only at the beginning of understanding parts of 5-HT functions. Great efforts in future research at all levels of systemic neurosciences will be needed to create a comprehensive model reflecting the role(s) of 5-HT in behavioral adaptation and its interactions with other neurotransmitters such as DA.

VII. GENERAL CONCLUSIONS, OPEN QUESTIONS, AND DIRECTIONS FOR FUTURE RESEARCH

We have described the roles of several neuroanatomical and neurochemical systems and defined the different kinds of behavioral adjustments they are involved in **(FIGURE 3)**. We have highlighted the key role of the pMFC in performance monitoring and adaptive behavior. Its activity is related to events and action valuation parameters that have in common that they provide information on the necessity to adjust cognitive, affective, and autonomic functions in the service of behavioral adaptation. A crucial mechanism for post-error and post-conflict adjustments seems to be that the pMFC triggers attentional top-down adjustments in task-related extrastriate visual areas. Lateral prefrontal areas including the frontal operculum are thought to interact with pMFC to exert top-down control by maintenance and updating of relevant rules and task sets. OFC and vmPFC are crucially involved in learning the value of available options and making choices on the basis of them. While lOFC is of crucial importance for contingent learning by assigning outcomes to the choice that caused it (credit assignment), mOFC and vmPFC are directly involved in value comparison, i.e., in decision making on the basis of expected value. Finally, all of these cortical areas of course do not act in isolation; instead, they control behavior through complex interactions, with each other, but also with subcortical areas. Of the latter, cortico-striato-thalamocortical loops (including the STN) are important for action selection and learning. This might also extend to integrate cerebellar inputs, perhaps needed for forward modeling of sensorimotor events associated with an action and linking to more basic on-line motor correction mechanisms. This circuitry is completed by the habenular complex, which has been shown to control the firing of brain stem DA and 5-HT neurons. Specifically, during reward omissions, increased habenular activity curbs DA neuron firing. Increased striatal DA transmission promotes appetitively motivated learning at the expense of aversively motivated learning. However, DA also directly acts on value-guided performance and influences decision making in many ways, among them being effects on Pavlovian response vigor, incentive motivation, delay and effort discounting, or the balance between model-based and model-free control. Finally, DA is also pivotal for flexibly adjusting behavior to changing environments, and it is involved in error detection and post-error slowing. The role of 5-HT in error-related pMFC activation and post-error slowing is less clear. Like DA, 5-HT is also involved in RL, possibly by altering reward sensitivity and choice perseverance and changes in serotonin activity modify subjects' ability to respond flexibly to changes in the environment. Finally, 5-HT controls reward-guided choices by affecting temporal discounting. **FIGURE 3** highlights the main nodes of the brain network underlying performance monitoring and adaptive behavior and their putative roles.

Despite the enormous progress that has been made, many questions remain open for future research.

It appears well-established that the pMFC codes evaluative signals about the prospects, course, and outcome of actions

and integrates this information to signal the necessity, type, and magnitude of adjustments. This complex signal has been formalized mathematically in the recently proposed integrative theory, suggesting that pMFC codes the "expected value of control" (481). Future experiments have to test this theory and show whether it can integrate the full breadth of situations and tasks involving this region, ranging from simple, automatized reaction time tasks to pondering about possible options in complex decision making.

With respect to decision making, a recent review discusses several variants of how and what value information is conveyed to the pMFC from OFC and vmPFC (448). An interesting new direction of research suggests that the signal in pMFC correlates with the value of switching away from the current, default action (for a detailed discussion, see Ref. 448). In multiple-choice conditions, the pMFC appears to code the value of not continuing with the performed action (42), and in foraging tasks, it seems to reflect the value of searching for better alternatives to a currently performed action (304).

This notion of pMFC coding the value of non-default behavior needs to be reconciled with increased signals during response conflict in highly automatized, habitual actions during simple reaction time tasks and with the inverse value difference signal in perceptual decision making. These latter situations have in common that the evaluation of the imperative stimuli is already in progress. In contrast, general strategic decisions on leaving default behavior and implementing foraging/exploration can be made in the absence of imperative stimuli based on current beliefs about action values in preparation of new encounters with a specific task situation. A general, unifying theme seems to be that pMFC signal is related to the effort it takes *1*) to focus attention to task-relevant stimuli (e.g., in speeded reaction time task with distracters) and to diminish activity from distracter-encoding brain areas, *2*) to further and more thoroughly evaluate stimuli (e.g., in perceptual decision making), and *3*) to switch away from standard, previously more-or-less successfully employed actions to exploratory or other nonroutine behavior (e.g., in foraging tasks). The latter decisions appear to take place at a more abstract level beyond simple habitual stimulus-response mapping, but they might also occur during the simplest task situations (for example, participants might ask themselves whether it is worth completing a boring flanker task or whether they should break up an experiment in progress to do some more rewarding activity).

The neural computations underlying these functions and their measurable correlates in the pMFC are still poorly understood. A prominent theory holds that the pMFC monitors response conflict (see sect. IV*B*). What could the arrangement of inputs and local circuitry be that results in network dynamics mirroring a conflict signal? Recently, it has been suggested that conflict could be reflected in interneuron activity rather than in firing of great pyramidal cells (100), but mathematical simulations are still lacking. Moreover, single-unit recordings in nonhuman primates did not reveal any conflict-related activity in aMCC (yet). Furthermore, invasive recordings of conflict signals in humans (482, 566) could be interpreted as control-related rather than conflict-related. The model predicts reduced conflict signals on trials subsequent to high-conflict trials as a result of increased control (44, 46), but aMCC cells fired more on trials after high conflict (482).

A biophysical model of decision making in which decisions are realized through mutual inhibition and reverberatory excitation of two pools of cortical neurons representing the value of each option has been successfully used to predict activity in parietal and ventromedial prefrontal cortex (265, 278, 585, 586). Network activity (which is reflected in hemodynamic and magnetoencephalographic signals) initially represents overall value and then changes into a representation of value difference when competition of the two options is resolved. Could variants of this model also account for the inverse value difference signal in aMCC which, in fact, can be interpreted as a conflict signal?

The pMFC consists of several cortical regions that differ with respect to cytoarchitecture and connectivity. As discussed in section II*B*, several studies suggested that these regions also differ functionally in their contributions to performance monitoring and adaptive behavior. However, the findings are, in part, contradictory and inconclusive. Future work should focus on a more direct link between microanatomical features, connectivity, and function.

Once the performance monitoring system has identified a problem with an action and signals the need for adjustments, how is top-down control implemented? Evidence for an involvement of pMFC, lateral prefrontal cortex, and frontal operculum has been reported, but how exactly do these regions divide the labor? Are all of them involved in each situation requiring top-down control? How do they interact? A recent EEG study suggested that different error types (attentional lapses vs. failures of motor control) lead to different implementations of top-down control (542). This should be further explored in fMRI or combined EEG-fMRI studies (525). Among adjustments, is post-error slowing functionally relevant and, at least in some situations, helpful to achieve a goal within the next trials after an error, or is it just a "byproduct" or a secondary effect of an orienting response, which ideally would best be avoided?

In this review, we did not discuss the roles of the amygdala and the hippocampus in affective control, learning, deciding, novelty detection, and contextual and episodic control. An important goal of research is to integrate these structures and the network described here in an overarching model of adaptive behavior.

Similarly, links between the performance monitoring and valuation system discussed here and lower level feedback-loop mechanisms correcting the course of actions need to be established. First attempts have been made in continuous motor control tasks (309, 310). Particularly the vast sensorimotor integration literature needs to be related to valuation-based action control.

Finally, it is important to understand when and how performance monitoring fails. Failure to detect performance problems can lead to maladaptation and erroneous behavior at various levels. When the necessary effort is underestimated and insufficiently recruited, errors become more likely. EEG and fMRI studies on pre-error changes in performance-monitoring activity support this view (5, 150, 151, 219, 437). Apparent regularities in task history may also be interpreted by the performance monitoring system as informative and lead to overspecific adaptation entailing reduced flexibility and increased error proneness (150, 495); for instance, if a subject is required to solve task A for several consecutive trials, a sudden switch to task B is more likely to result in an error. This can be reflected in specific functional connectivity patterns (153), suggesting enhanced processing of distracting information that might have been misinterpreted as task-relevant. Errors and attentional lapses are additionally preceded by changes in brain activity into a mode reminiscent of resting state (151, 389, 571). A future goal is to reliably detect increased error proneness in monotonous attention-demanding tasks based on physiological measures and to develop interventions that help prevent mistakes. Moreover, physiological and pathophysiological mechanisms increasing error occurrence, such as stress, fatigue, and sleep deprivation (85, 86, 461) as well as various psychiatric diseases (133, 523), need to be understood to explain and perhaps prevent pathological behavior under these conditions.

ACKNOWLEDGMENTS

We thank Adrian G. Fischer for helpful comments on the manuscript.

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GRANTS

Research reported here was partly supported by German Research Foundation Grants UL196/1-1,2,3, UL196/2-1, and SFB 779/2-A12 (to M. Ullsperger) as well as JO-787/1-1 (to G. Jocham) and German Ministry of Education and Research Grant 01GW0722 (to M. Ullsperger).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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Physiol Rev 94:35-79, 2014. doi:10.1152/physrev.00041.2012