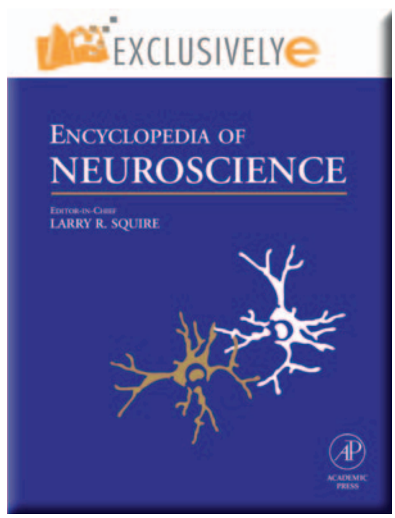

Miller E K and Wallis J D (2009) Executive Function and Higher-Order Cognition: Definition and Neural Substrates. In: Squire LR (ed.) Encyclopedia of Neuroscience, volume 4, pp. 99-104. Oxford: Academic Press.

Executive Function and Higher-Order Cognition: Definition and Neural Substrates

E K Miller, Massachusetts Institute of Technology, Cambridge, MA, USA
J D Wallis, University of California at Berkeley, Berkeley, CA, USA

Cognitive, or executive, control refers to the ability to coordinate thought and action and direct it toward obtaining goals. It is needed to overcome local considerations, plan and orchestrate complex sequences of behavior, and prioritize goals and subgoals. Simply stated, you do not need executive control to grab a beer, but you will need it to finish college.

Executive control contrasts with automatic forms of brain processing. Many of our behaviors are direct reactions to our immediate environment that do not tax executive control. If someone throws a baseball toward our face, we reflexively duck out of the way. We have not necessarily willed this behavior; it seems as if our body reacts and then our mind 'catches up' and realizes what has happened. Evolution has wired many of these reflexive, automatic processes into our nervous systems. However, others can be acquired through practice because learning mechanisms gradually and thoroughly stamp in highly familiar behaviors.

For example, consider a daily walk to work. If the route is highly familiar and if traffic is light, our mind can wander. Before we know it, we may have gone a considerable distance and negotiated street crossings and turns with little awareness of having done so. In these cases, the control of our behavior occurs in a 'bottom-up' fashion: it is determined largely by the nature of the sensory stimuli and their strong associations with certain behavioral responses. In neural terms, they are dependent on the correct sensory conditions triggering activity in well-established neural pathways.

Suppose, however, that during our walk to work something unexpected happens or we encounter difficulty. For example, we might encounter a busy street that we need to cross. Then, the executive system takes over and we need to 'take charge' of our actions. We pay attention to the people and cars around us to anticipate and accommodate their actions, or we may decide to take an alternate route. Now, straightforward stimulus–response associations are insufficient to govern our behavior. We must use knowledge of our current objective (arriving at work on time and intact) and results from previous experiences to weigh the alternatives and consequences. During this 'controlled mode,' we also engage the basic sensory, memory, and motor processes that mediate automatic behavior. Only now, the environment is not simply triggering these processes. Instead, we use our current goals to shape and control these processes in a 'top-down' fashion.

Figure 1 summarizes these ideas by illustrating a widely accepted view of the architecture of cognition. At the lower level are the automatic processes, which include sensory analysis, memories, details of motor acts, and well-learned skills. The system is in automatic mode when processing flows through the lower level, from input to output, along established pathways without any hindrance or modification. However, at any given instant the executive system can step in and modify this flow should it detect that the automatic processes are no longer sufficient to obtain our goals. In understanding the neuronal mechanisms that underlie this process, the prefrontal cortex (PFC), the brain area directly behind our forehead, seems especially critical.

The Prefrontal Cortex

PFC has dramatically expanded in size and complexity across evolution, and its development correlates with the complexity of the behavioral repertoire exhibited by an organism. It has reached its pinnacle in humans, in which it accounts for approximately 30% of the total cortical area. It consists of a collection of cortical areas that differ from one another in terms of the size, density, and distribution of their neurons. Figure 2 shows the major PFC divisions of the monkey PFC, although anatomists have subdivided these further, describing at least 18 distinct areas. The subdivisions have partly unique, but overlapping, patterns of connections with the rest of the brain, which suggests some regional differences in function. As in much of the neocortex, however, there are local connections between different PFC areas that can result in an intermixing and synthesis of the disparate information needed for cognitive control.

PFC is anatomically in a good position for a central role in executive control. Collectively, the various PFC areas have interconnections with brain areas processing external information, including all sensory systems and cortical and subcortical motor system structures, as well as internal information from limbic and midbrain structures involved in affect, memory, and reward. Indeed, neuronal activity in PFC reflects the multimodal nature of its inputs. PFC neurons

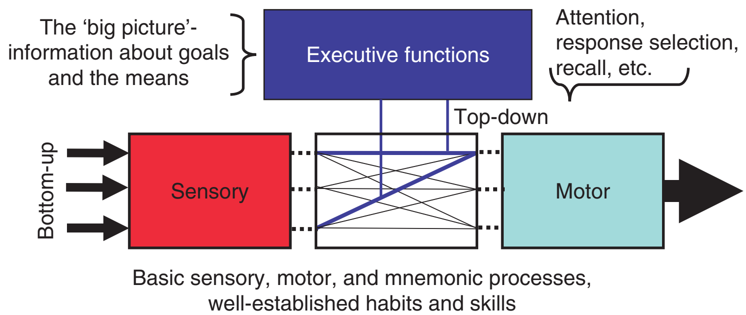

Figure 1 Two levels of cognitive processes. Specialized functions that acquire information about goals and means (top) select and coordinate among innate and well-established routines (bottom). Inputs from the environment are 'bottom-up,' whereas signals based on knowledge about goals and task demands are 'top-down.' Active processing lines are shown in blue.

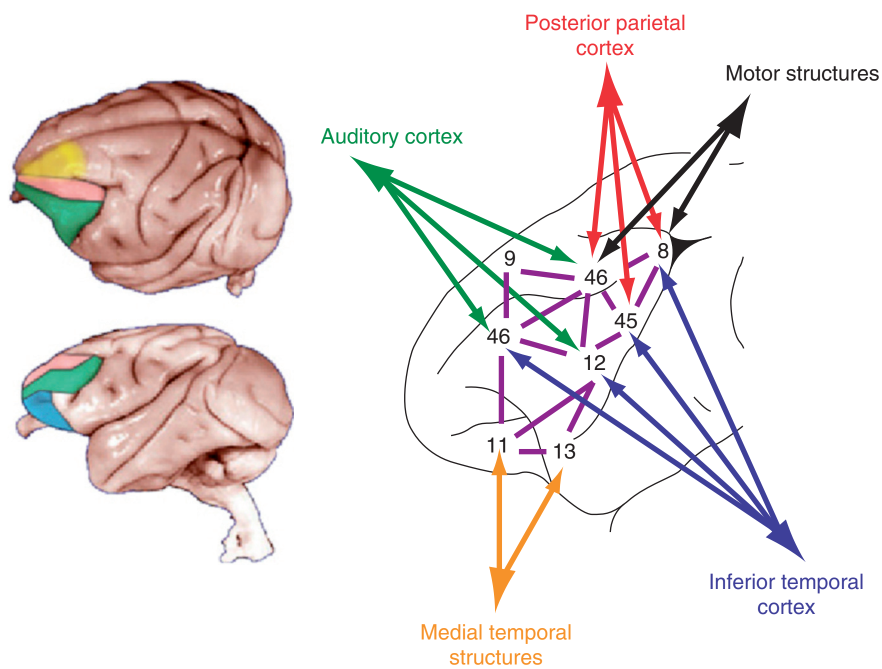

Figure 2 The monkey prefrontal cortical areas with some connections. (Left) Dorsal is yellow, dorsolateral is red, ventrolateral is green, and orbital is blue. The medial PFC is not pictured. (Right) Some extrinsic and intrinsic connections. Not all connections are illustrated; this figure is meant to convey how the PFC can synthesize and integrate diverse inputs from other brain structures.

encode visual, auditory, tactile, olfactory, and gustatory cues, as well as recalled memories and behavioral responses such as voluntary limb and eye movements. In short, the functional and morphological anatomy of PFC is consistent with its role in synthesizing diverse information about the external and internal world in order to produce goal-directed behavior.

PFC Contributions to Executive Control

PFC damage does not result in simple deficits; there is relatively little overt impairment, at least with superficial examination. Patients with PFC damage have intact sensory capabilities, they can remember events and facts, and they appear remarkably normal in casual conversation. However, despite the superficial appearance of normality, PFC damage devastates a person's life. Patients have trouble staying employed, married, or even completing simple daily errands. Furthermore, they often seem to act without any apparent consideration to future consequences. Careful testing of PFC patients has revealed a number of underlying cognitive deficits that might explain their impairments.

Inhibition

PFC damage often produces 'stimulus-bound' behavior. Patients engage in whatever habitual behaviors happen to be triggered by cues in the immediate environment. For example, when they see a glass of water, they may drink it regardless of whose glass it is. Because other learning and memory systems are intact, they can learn to respond to specific cues in specific ways. However, they then become stuck in that behavioral rut, producing the same response to the cue even when it is no longer appropriate – a phenomenon called 'perseveration.'

Planning

After PFC damage, the basic units of behavior remain intact. What is lacking is the ability to organize them toward a goal. For example, one patient, when making coffee, first stirred and then added milk. Another example is a patient who had been an excellent cook until she had a large tumor removed from her frontal lobes. Her basic skills remained but she seemed unable to organize them. She would move haphazardly from preparing one part of the meal to another so that some parts of the meal would burn, whereas others had hardly been started.

Evaluating Consequences

Goal-directed behavior depends on our capacity to evaluate the consequences of our actions so that we can choose an optimal plan. Evidence that certain types of PFC damage impair this process comes from a gambling task. The subject has to choose cards from four different decks. Some cards win the subject some money, but others cause the subject to lose money. Unbeknownst to the subject, cards from two of the decks will occasionally win large amounts of money but are also occasionally associated with very large losses. Thus, consistently choosing from these decks will lead to a net loss. In contrast, if the subject chooses from the other two decks, he or she will win smaller amounts, but the losses are also smaller, so that overall the subject will obtain a net profit. Control subjects quickly learn to limit their choices to the profitable decks, whereas patients with PFC damage, particularly of the orbital region, continually choose from the decks associated with large rewards and larger losses until they lose all their money.

This led to the hypothesis that the orbital PFC is responsible for labeling cues or situations with an affective significance or 'somatic marker.' It associates memories of past, affect-laden events with a representation of the state of the autonomic nervous system that the event evoked. Similar events in the future can then evoke a 'gut feeling' of the appropriate course of action by recall of the somatic marker. This is particularly helpful in very complex situations in which it is difficult to evaluate rationally and deliberatively all the pros and cons of a choice.

Further evidence that PFC neurons participate in this process comes from studies showing that a large proportion of them encode information about expected rewards. For example, some neurons encode the delivery of a reward, whereas others respond when a reward does not occur as expected. After training, many PFC neurons will show responses to visual cues that signal whether a reward will or will not be forthcoming and reflect the identity, size, and preference of an expected reward.

Working Memory

The importance of a short-term memory buffer for cognition is apparent to anyone who has tried to do math in their head; intermediate answers and operations must be buffered in a way that allows them to be kept 'in mind.' The pattern of deficits following PFC damage might be sequelae of an underlying deficit in working memory. Patients may have difficulty planning or appear disinhibited because without working memory, goal-relevant information is lost over all but the briefest delays and thus their behavior takes its cue from the immediate environment.

This hypothesis stems from observations that PFC damage in monkeys impairs a spatial delayed-response task that requires them to remember the location of a stimulus or behavioral response over a brief delay of several seconds. In addition, there are many studies illustrating that PFC neurons sustain their activity over several seconds to bridge short delays imposed between a cue and a response – observations that Fuster, Niki, and colleagues first made in the 1970s. Goldman-Rakic and colleagues used a more controlled version of the task using an oculomotor response to a visual target presented in the periphery of the visual field. They demonstrated that dorsolateral PFC neurons have precise tuning for memories of particular visual field locations.

In humans, a similar task, called the 'two-back' task, is sensitive to PFC damage or dysfunction. Subjects observe a sequence of sample stimuli and must respond if a current sample stimulus matches one seen two samples ago. Because this involves matching to a specific stimulus, it may rely on working memory rather than other, more passive, forms of immediate memory, such as those that automatically detect repetition.

PFC activity sustains brief memories of a wide range of behaviorally relevant cues: objects, colors, the frequency of a vibration to the hand, and forthcoming movements. Similar activity is also evident in the sensory and motor systems. This is not surprising; sustained activity is evident in many brain structures and must play a role in many neural processes from sensory afterimages to holding a motor state. However, specificity and robustness are what separates more 'cognitive' short-term memory processes, such as working memory processes, from such lower level processes. Working memory selectively retains task-relevant information, rather than just any stimulus, and does so over potential distractions. PFC neurons have this ability. For example, when monkeys are required to sustain the memory of a sample object across a delay period filled with visual distractors that require attention and processing, sustained activity within the PFC can still maintain a memory of the sample object. By contrast, sustained activity in visual cortical areas seems more labile; it is disrupted by the presence of distractors.

Learning and Using Rules

The PFC is important when we need top-down processing – that is, when our internal states or intentions guide behavior. It is critical in situations in which the mapping between sensory inputs, thoughts, and actions is weak relative to other existing ones or when the mapping is rapidly changing. In such circumstances, we often rely on previously constructed models of regularities in our environment and our expectancies of future events – the so-called 'rules of the game.'

Conditional learning tasks are a laboratory test of rule learning. They require learning of associative relationships that are arbitrary and extend beyond the simple one-to-one mappings that underlie reflexive reactions. Whether or not a given response is the correct response to a given cue constantly changes because it depends on additional information. For example, reaching for a beer can be rewarding, but only if one considers other information. If the beer belongs to another patron, the result could be disastrous. Monkeys with PFC damage are impaired at a variety of conditional learning tasks. When monkeys learn associations between, for example, three visual cues and three directional movements of a joystick, simply moving the joystick is not enough to produce reward. Rather, the specific movement direction is dependent on the specific cue. One means 'up,' the other 'down,' etc. Following PFC damage, monkeys have difficulty acquiring this task. Furthermore, PFC neurons encode multiple aspects of conditional tasks, including the sensory cues, the motor responses, and the specific associations between the cues and responses (Figure 2).

PFC is also essential in enabling the control of behavior by abstract, high-level rules. Consider, for example, dining in a restaurant. We are not born knowing how to act in this situation. Instead, after several experiences in restaurants we begin to abstract the common features of importance. For example, we learn the important sensory information deserving our attention (e.g., the wine list), typical events, appropriate actions, and expected consequences (e.g., paying the bill). The rules underlying ordering a meal in a restaurant are essentially networks of predictive relationships between immediate cues, internal and external context, and actions and consequences long divorced from the details of the individual restaurants in which we have dined. We can then use these abstract rules to order a meal in any subsequent restaurant, even those in which we have never dined before. Several investigators have argued that the encoding of rule information is a cardinal function of the PFC.

One task that directly tests this ability is the Wisconsin Card Sorting Test (WCST). The patient is required to sort a deck of cards on which there are a number of colored shapes. The patient has to determine by trial and error the correct property by which to sort the cards. For example, if the 'color' rule were in effect, the subject would have to sort the cards according to the color of the shapes. Unbeknownst to the subject, the experimenter can switch which is the correct rule, and the subject needs to detect this and modify his or her behavior accordingly. Patients with PFC damage, particularly lateral PFC, have difficulty doing this. Using more focal, experimentally induced lesions in monkeys, experimenters have confirmed that lateral PFC is the most important PFC region for rule or strategy implementation. Furthermore, studies show that single PFC neurons are capable of encoding abstract rules. For example, monkeys saw two pictures appear successively separated by a delay. At the start of the trial, a cue instructed the monkeys to release a lever if the two pictures were either the same or different. Thus, to solve the task the monkeys had to maintain in working memory both the picture and the currently relevant abstract rule (same or different) during the delay. Many PFC neurons, more than one-third, encoded the abstract rule.

What function does the ability to abstract a rule serve? Abstraction is a type of generalization that permits a shortcut in learning, allowing us to apply what we have learned in similar situations to novel circumstances. Without the ability to abstract the general principles behind related situations, we would have to learn the correct behavior on each new occasion by trial and error. The problem with such trial-and-error learning is that errors necessarily occur. This is a less efficient way of dealing with novelty since errors frequently lead to lost opportunities for reward. Consistent with these ideas, PFC seems to be most important when subjects must deal with novel situations.

Neurobiological Models of Executive Control

Note that the pattern of deficits following PFC damage seems to reflect a selective loss of the higher level functions from the bipartite cognitive architecture pictured in Figure 1. Well-established automatic routines on the lower level are intact and available to be triggered by the appropriate sensory cues. However, without the higher level functions specialized to acquire and represent goals and means, the system would be at the mercy of the environment, ruled by whatever sensory inputs happen to flow into the system and by whatever thoughts, emotions, and actions are strongly associated with these inputs. Thus, behavior would seem impulsive and disinhibited and reactions inappropriate because they would be emitted reflexively without any consideration of the future. Furthermore, without the influence of predicted goals to continually drive task-appropriate processes, individuals would be distractible and would easily go 'off track' when there are temporal gaps between sensory inputs or between those inputs and the individual's responses. The system might be capable of learning to react to cues, but this learning would be inflexible. Without the ability to predict goals and means, the system would be stuck in a behavioral rut, always reacting to a cue with whatever behavior it was first associated.

This architecture is also apparent in neurobiological models of executive control. Network models of Dehaene and Changeux include an executive layer of 'rule-coding' units, thought to correspond to the PFC, that controls the flow of information between the input and output layers (Figure 3(a)). Arthur Shimamura proposed a dynamic filtering model of PFC function in which patterns of information sustained by the PFC select and reroute the flow of activity in posterior association cortex (Figure 3(b)). Miller and Cohen proposed that the cardinal PFC function is to acquire and actively maintain patterns of activity that represent goals and the means to achieve them (rules) in terms of a map of the cortical pathways needed to perform the task (hence 'rulemaps') (Figure 3(c)). Under this model, activation of a PFC rulemap sets up bias signals that propagate throughout much of the rest of the cortex, affecting sensory systems as well as systems responsible for response execution, memory retrieval, emotional evaluation, etc. The aggregate effect is to guide the flow of neural activity along pathways that establish the proper mappings between inputs, internal states, and outputs to best perform the task. In short, rule information is acquired by the PFC, which provides support to related information

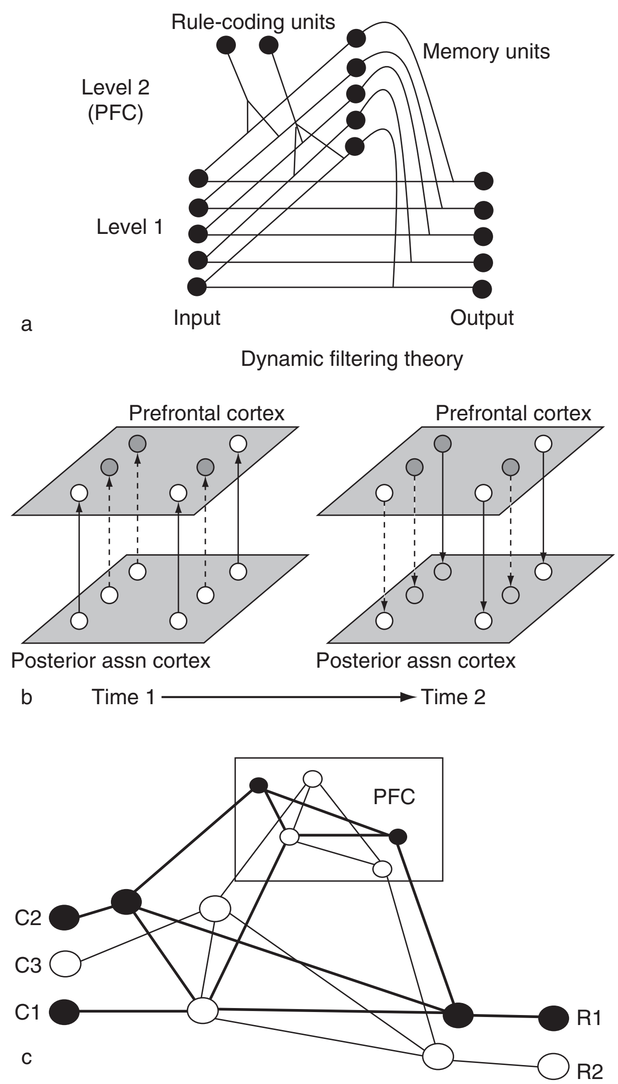

Figure 3 Models of PFC function. (a) The models of Changeux and Dehaene include an executive level (level 2, thought to correspond to the PFC) with rule-coding units and working memory units that gate the flow of activity along lower level input–output lines. (b) Shimamura's dynamic filtering model. At time 1, a region in PFC is activated by feed-forward (i.e., bottom-up) projections from posterior cortex. This activity, along with influences such as task demands, sets up a pattern of activation in PFC (light circles, activation; dark circles, inhibition). At time 2, posterior cortex is modulated by PFC via feedback (i.e., top-down) projections that enable both selection of task-relevant and inhibition of task-irrelevant neural activity. Figure provided by Arthur Shimamura. (c) In the Miller and Cohen model, a task model is formed in the PFC when reward signals link together neurons activated by the events that led to reward. A subset of cues can then activate the entire representation. Bias signals resulting from the maintenance of this pattern guide the flow of activity along neural pathways that establish the task-relevant mappings between representations of inputs (C1, C2, C3), internal states, and outputs (R1, R2) in posterior cortex. Thick lines and solid circles denote active processing lines. Reproduced from Miller EK and Cohen JD (2001) An integrative theory of prefrontal function. *Annual Review of Neuroscience* 24: 167–202.

in posterior brain systems, effectively acting as a global controller or 'traffic cop.'

A key issue is to understand how PFC acquires these high-level representations. One possibility is that they develop through the action of reinforcement signals on multimodal PFC circuitry. During learning, when a behavior meets with success, reward signals augment the unique pattern of PFC activity evoked by that situation, action, and consequence by strengthening connections between the neurons activated by those events. These representations might begin quite modestly, but with time and repeated iterations of the process, the PFC representation can 'bootstrap' into further elaboration as combinations of events and contingencies between them and the requisite actions are learned. Midbrain dopaminergic neurons have ideal properties for the reinforcement signal. Early in learning, rewards activate dopamine neurons, but later in learning the cues that predict those rewards activate dopamine neurons rather than the rewards. Furthermore, there is an inhibition of the firing rate of the dopamine neurons when an expected reward does not occur. This 'reward prediction error' signal is ideal for instructing when and what the system should learn and consequently enables the organism to acquire the representations necessary to achieve reward.

The resulting pattern of PFC activity reflects the task's contingencies and in neural terms amounts to a 'map' of the pathways between inputs, internal states, and outputs needed to perform the task successfully. The ability to construct this map arises from the intermingling of diverse information that takes place within PFC. Although the PFC may be critically involved in acquisition of this information, other parts of the brain may be responsible for its consolidation in long-term memory. The PFC, however, would retain the requisite links to retrieve the appropriate pattern and bring it online to guide behavior.

Summary

Executive control refers to the ability to take charge of one's actions and direct them toward unseen aims. Virtually all theories of cognition posit that executive control requires making predictions about available goals and what means might achieve them. This knowledge can then be used to select and coordinate among a myriad of lower level, automatic sensory, memory, and motor functions.

The PFC, a brain structure that reaches its greatest complexity in the primate brain, seems to play a central role in executive control. It has access to all major forebrain systems, as well as the means to influence them. Individuals with PFC damage seem capable only of emitting habitual or innate reactions to the immediate environment without any consideration or anticipation of future consequences and unseen goals. Neurophysiological studies indicate that PFC neurons seem to mediate the mechanisms essential for a cognitive control system: They are multimodal, they acquire and signal the formal demands of tasks, and they can sustain their activity to keep task-relevant information online and available during behavior.

Different theories of PFC function emphasize different contributions to cognitive control: maintenance and/or manipulation of information in working memory, the assignment of affective tags on events and choices, and the acquisition and online representation of task rules. These theories are not mutually exclusive; each may reflect different facets of a system that is necessarily multivariate because of its role in guiding many different behaviors and interfacing with many other brain systems. However, in the healthy individual, the different processes work in harmony and enable the organism to behave flexibly and cope efficiently with novel situations, which are hallmark features of PFC function.

See also: Cognitive Control and Development; Cognitive Deficits in Schizophrenia; Congenital Muscular Dystrophy; Executive Function and Higher-Order Cognition: Neuroimaging; Executive Function and Higher-Order Cognition: Computational Models; Frontal Lobe Syndrome; Prefrontal Cortex: Structure and Anatomy; Short Term and Working Memory.

Further Reading

Damasio AR (1994) *Descartes' Error: Emotion, Reason, and the Human Brain.* New York: Putman.

Fuster JM (1995) *Memory in the Cerebral Cortex.* Cambridge, MA: MIT Press.

Miller EK and Cohen JD (2001) An integrative theory of prefrontal function. *Annual Review of Neuroscience* 24: 167–202.

Schultz W and Dickinson A (2000) Neuronal coding of prediction errors. *Annual Review of Neuroscience* 23: 473–500.