Much effort has recently been expended to investigate object processing in the prefrontal (PF) cortex. In this update, we summarize recent experimental findings from studies of human and nonhuman primates and discuss how they have contributed to our understanding of the functions of the prefrontal cortex.

In humans and macaque monkeys, the prefrontal cortex is composed of a number of highly interconnected frontal lobe areas (Petrides and Pandya 1999). At the coarsest level, researchers have differentiated (Fig. 1) between dorsolateral, ventrolateral, orbitofrontal, and anterior prefrontal cortex. Although it remains unclear what precise functions these regions implement, it is clear that these regions typically work in concert to enable goal-directed behavior. PF neurons participate in a variety of functions, including motor planning (Funahashi and others 1991) and the processing of auditory (Fuster and others 2000) and somatosensory (Romo and others 1999) stimuli. The PF cortex also contains many neurons that respond selectively to complex objects (Fuster 1973; Wilson and others 1993; Rao and others 1997; Scalaidhe and others 1997). Their activity—in terms of number of action potentials emitted—varies systematically during periods of sensory visual stimulation and during memory delays, depending on the identity of the presented object.

Coding for Objects by PF Neurons

This raises the question of how coding for objects in prefrontal regions differs from coding in inferior temporal (IT) regions that are more classically associated with the processing of object information. One major difference concerns spatial selectivity: IT neurons process information at the center of gaze—they have large bilateral receptive fields and invariably respond best to foveal stimulation (Op De Beeck and Vogels 2000). Prefrontal neurons, in contrast, provide a tiling of central visual space (Fig. 2) and process preferentially—but not exclusively—contralateral visual space. In addition, although the PF cortex contains some neurons that respond optimally to foveal stimulation, many neurons have receptive fields that do not include the fovea at all and respond best to peripherally presented objects (Rainer and others 1998a). Thus, the PF cortex contains a representation of visual space at, as well as surrounding, the current point of fixation. This is an integrated object and spatial representation, because PF neurons selective for a given object also represent that object’s location by virtue of their receptive fields. Thus, objects—or parts of visual scenes—could be selected by attention at the level of the PF cortex (Rainer and others 1998b), and feedback might propagate this signal to other structures that are more directly involved in object processing (Hasegawa and others 2000).

The PF cortex contains a representation of both the object currently at the center of gaze and the object that will be the target of the next saccadic eye-movement. Such a concurrent representation is consistent with the cross-temporal association functions that have been associated with the PF cortex (Fuster and others 2000). Separating relevant visual inputs in space could thus bridge temporal delays and facilitate integrated processing across time.

Working Memory

Both PF and IT neurons exhibit transient, stimulus-driven responses as well as sustained activity associated with
the active maintenance of object information (Postle and D’Esposito 1999; Rainer and others 1999; Ranganath and others 2000), but responses in these regions differ in a number of ways. First, prefrontal activity associated with maintenance of an object is robust in the face of distracting stimuli, whereas mnemonic activity in anterior IT is not (Miller and others 1996). Studies of retrieval of long-term associations have revealed other differences between IT and PF neurons. In IT, the pairing of two objects leads to the formation of pair-coding neurons, which respond similarly to the two paired objects after training (Naya and others 1996). Importantly, the responses tend to be similar right from the onset of the sensory visual response, implicating the pair-coding neurons in the long-term memory of the association between the objects. A different result was found in the PF cortex, where neural activity during the sensory visual response reflects the physical attributes of the objects and not their associative significance (Rainer and others 1999). Only during the delay did the PF activity “switch” to a prospective code, reflecting the anticipated target object (Fig. 3). Thus, the PF cortex processes sensory information early on, and the association is retrieved only later on during the delay so that it is available when the animal needs to make its choice. Although both IT and PF cells show prospective activity during the memory delay (Naya and others 1996), the PF cortex may be critical for initiating the recall of associative information. This notion of actively initiated retrieval receives support from a lesion study, in which recall of associative information from the opposite hemisphere could be supported by connection between the two PF cortices, even though visual areas were disconnected by severing the posterior corpus callosum (Hasegawa and others 1998). Together, these studies suggest complementary roles for frontal and temporal regions in object processing: Long-term associations between objects are stored in temporal cortical areas, whereas the frontal cortex is involved in selection, retrieval, and evaluation of this information to guide behavior. In this regard, different areas of PF cortex may play complementary roles in mnemonic processing (see below).

**Novelty and Memory**

Recent work has also implicated the frontal cortex in the processing of novel information (Knight and Nakada 1998). For example, the PF cortex may be necessary for the production of the von Restorff effect (von Restorff 1933). In this paradigm, the subject is given a group of homogenous items to remember, with interspersed items that are contextually novel (e.g., a red object interspersed among a series of blue objects). In intact humans and monkeys, memory for the novel item is better than for a homogenous item at the same serial position in the list. Interestingly, in monkeys, this advantage for contextually novel items was dependent on the connection between the perirhinal and the frontal cortex. Disconnection of these structures abolished the processing advantage of novel compared with homogenous items, indicating that the frontal-perirhinal interaction plays a critical role in conferring processing advantages to novel items (Parker and others 1998). Consistent with this finding, humans with lateral PF lesions exhibit attenuated orienting responses to contextually novel stimuli in all modalities (Knight and others 1995).

In addition to contextual novelty, PF activity is sensitive to perceptual novelty as well. For example, several studies have reported enhanced activity in PF cortex during processing of novel relative to familiar objects (Asaad and others 1998; Buckner and others 1998; Ranganath and others 2000; Koutstaal and others 2001). Similar reductions in neural responses to familiar objects have also been reported in IT cortex (Fahy and others 1993; Li and others 1993; Ringo 1996). Results from a recent study shed light on the potential significance of these repetition effects. In this study, fewer PF cells responded to familiar than to novel objects (Rainer...
Fig. 2. Receptive field structure of prefrontal neurons. The large central square represents $20^\circ \times 20^\circ$ of central vision; the center of gaze is represented by the cross. Visual space contralateral to the recording site is shown on the right, ipsilateral space on the left. Each white circle corresponds to the receptive field center of a single prefrontal neuron, and the structure of each receptive field is shown in the small panel connected by a line. Each small panel again represents $20^\circ \times 20^\circ$ of central vision, and the receptive field is shown in orange shading. Receptive fields are shown here for neurons communicating integrated object and spatial information ("what-and-where" neurons) during the memory period. Results during sensory visual stimulation are qualitatively similar. The number of neurons processing central, contralateral, and ipsilateral visual information is representative of the population. Adapted from Rainer and others 1998a.

Fig. 3. Dissociation between sensory and memory processing revealed using a pair-association task. Average population activity for prefrontal neurons in a pair-association task. The period of sensory visual stimulation lasted from 0 to 500 ms, the delay from 500 to 1000 ms. The orange curve represents differences in neural activity between physically similar sample objects (S1 and S2), associated with dissimilar choice objects (C1 and C2). Differences are relatively low early on and show an increasing trend throughout the delay, indicating that prefrontal neurons are activated at similar levels by physically similar objects early on, and this similarity in activation fades with time. By contrast, the blue curve represents differences in neural activity between physically dissimilar sample objects (S2 and S3), associated with similar choice objects (C2 and C3). Differences are large early on, indicating that prefrontal neurons reflect the physical dissimilarities of S2 and S3, but decrease as time progresses, reflecting the similarity of the associated choice objects C2 and C3. Adapted from Rainer and others 1999.
Fig. 4. Human prefrontal responses during encoding and recognition of objects. In this set of experiments, human brain activity was recorded while subjects learned objects (encoding trials) and were given different recognition tests on these objects (retrieval trials). During "general test" trials, participants were required to decide whether each object corresponded to a studied object. During "specific test" trials, participants were additionally prompted to recall specific perceptual attributes of studied objects. 

A, Event-related functional magnetic resonance imaging was used to identify regions that were reliably activated during encoding (blue) and retrieval trials (orange). Arrows point to overlapping regions in ventrolateral (VL) and dorsolateral (DL) prefrontal (PF) cortex that were active during both encoding and retrieval. In addition, the circled region of left anterior PF cortex was active during retrieval but not encoding trials. 

B, During retrieval trials, activation in left anterior PF cortex, but not other PF regions, was significantly greater when participants were prompted to recall specific attributes of studied objects. As shown in the graph, these modulations were observed for studied and novel objects. In parallel studies, electrophysiological measures of brain activity were recorded during similar tests. 

C, A topographic map showing that differences in brain potentials elicited during specific and general tests were largest over left frontal scalp sites. 

D, Left frontal brain potentials (i.e., the difference in potentials elicited during specific and general test trials) were modulated by the retrieval and evaluation of specific object information as early as 200 ms. Adapted from Ranganath and others 2000, Ranganath and Paller 1999, and Ranganath and Paller 2000.
and Miller 2000), but this smaller population was more narrowly tuned to the familiar objects, and the selectivity was more robust. Slight degradation of the novel objects dramatically disrupted the object-selectivity of prefrontal neurons, whereas this selectivity was maintained in the face of degradation for familiar objects. Together, these studies indicate that the PF cortex plays an important role in the processing of both novel and familiar objects, but that it may contain specialized mechanisms important for learning and consolidation of novel material.

Regional Differentiation within PF Cortex

As noted earlier, the PF cortex consists of multiple regions that exhibit distinct cytoarchitecture and anatomical connectivity. Furthermore, results from lesion studies of monkeys and neuroimaging studies of humans suggest that these regions may be functionally distinct as well. For example, lesions to the mid-dorsolateral PF cortex dramatically impair performance on tasks that require the active maintenance and manipulation of spatial (Passingham 1975; Mishkin and Manning 1978; Funahashi and others 1993) and, to a lesser extent, nonspatial information (Passingham 1975; Mishkin and Manning 1978; Petrides 1994). In contrast, lesions to the inferior convexity affect performance of spatial and nonspatial tasks, even when there is no requirement to maintain information across a delay (Rushworth and others 1997). Similar findings have also been reported in humans with large unilateral prefrontal lesions (Baldo and Shimamura 2000). Although it is unclear exactly what processes are implemented by dorsolateral and ventrolateral PF regions, results from functional neuroimaging studies of humans have also supported the idea that these regions are functionally distinct (D’Esposito and others 1998). One hypothesis guided by the extent imaging and lesion evidence is that the ventrolateral PF cortex acts to select and maintain incoming information, whereas the dorsolateral PF cortex acts to monitor and manipulate this information (Petrides 1996; D’Esposito and others 1998).

The effects of lesions to anterior portions of the PF cortex in monkeys or humans are unknown, but results from human neuroimaging studies suggest that its functions may be different from dorsolateral and ventrolateral PF regions. In one event-related functional magnetic resonance imaging (fMRI) study, regional PF activation was examined during learning and recognition of objects (Ranganath and others 2000). Responses to studied and unstudied objects at retrieval were compared between two tests with differing demands for the specificity of information to be retrieved. As shown in Figure 4, regions of dorsolateral and ventrolateral PF cortex were activated during both learning and recognition of objects, but activity in these regions was not reliably modulated by increasing the specificity of information to be retrieved (Fig. 4A). In contrast, the anterior PF cortex was reliably activated during retrieval only when subjects made recognition decisions (Fig. 4A), and activation in this region increased with demands to retrieve perceptually detailed information about studied objects (Fig. 4B). These modulations were observed for studied and unstudied objects, and results from parallel electrophysiological studies suggest that they occurred as early as 200 ms following stimulus onset (Ranganath and Paller 1999, 2000) (Fig. 4C–D). Collectively, these findings suggest that anterior PF activity reflected the evaluation of specific object information in comparison with information retrieved from memory. This process is critical for accurate episodic memory (Johnson and others 1993) and can be impaired in humans with PF lesions (Johnson and Raye 1998).

Summary

Recent findings have shed light on the role of the PF cortex in object processing. Specifically, PF coding is sensitive to the features of objects, including their spatial locations. Regions of the PF cortex may differentially participate in selection and manipulation of object information, coding of the affective significance of objects, and evaluation of these characteristics in comparison with information retrieved from memory. Thus, activity in these regions, in concert with posterior cortical regions, may enable transient attentional selection, online maintenance, and lasting learning of object information in the service of behavioral goals.

References