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REVIEW

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# Role of prefrontal cortex in a network for arbitrary visuomotor mapping

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**Abstract** In arbitrary visuomotor mapping, an object instructs a particular action or target of action, but does so in a particular way. In other forms of visuomotor control, the object is either the target of action (termed *standard* mapping) or its location provides the information needed for targeting (termed *transformational* mapping). By contrast, in *arbitrary* mapping, the object's location bears no systematic spatial relationship with the action. Neuropsychological and neurophysiological investigation has, in large part, identified the neural network that underlies the rapid acquisition and performance of arbitrary visuomotor mappings. This network consists of parts of the premotor (PM) and prefrontal (PF) cortex, the hippocampal system (HS), and the basal ganglia (BG). Here, we propose specialized contributions of the network's different components to its overall function. To do so, we invoke the concept of distributed information-processing architectures, or modules, which may involve a variety of neural structures. According to this view, recurrent neural networks involving cortex, basal ganglia, and thalamus operate largely in parallel. Each of these interacting networks can be termed a cortical-BG module. A large number of these modules include PM neurons, and they can be termed PM cortical-BG modules. A comparable number include PF neurons, termed PF cortical-BG modules. We propose that PM and PF cortical-BG modules compute specific object-to-action mappings, in which the network learns the action associated with a given input. These mappings serve as specific solutions to arbitrary visuomotor mapping problems. However, they are also exemplars of more abstract rules, such as the knowledge that nonspatial visual information (e.g., color) can guide the choice of action. We propose that PF cortical-BG modules subserve abstract rules of this kind, along with other problem-solving strategies. This view should not be taken to imply that the PF network lacks the capacity to compute specific mappings, but rather that it has higher-order mapping functions in addition to its lower-order ones. Furthermore, it seems likely that PF provides PM with pertinent sensory information. The hippocampal system appears to play a role parallel to that of both neocortical-BG networks discussed here. However, in accord with several models, it operates mainly in the intermediate term, pending the consolidation of the relevant information in those neocortical-BG networks.

**Key words** Conditional motor learning · Frontal cortex · Premotor cortex · Basal ganglia · Hippocampus

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## Introduction

Imagine a door knob located just above waist level and slightly to your right. When you reach toward the door knob, you automatically transform the relevant visuospatial information into a motor program that directs the forelimb toward the target of reach, in this case the door knob. This action is based on what has been termed *standard* visuomotor mapping, through which the central nervous system transforms the targets of action into motor coordinates (Wise et al. 1996a, 1997). Often, this class of visuomotor guidance involves the movement of the hand to a visible target.

Contrasting forms of visuomotor guidance depend on *nonstandard* mapping (Wise et al. 1996a), which comes in at least two categories. In one, termed *transformational* mapping, an algorithm relates visuospatial information to the direction of movement. For example, one might be required to direct a movement at a 90° clockwise deviation from the visual stimulus. The transform is generally, but not necessarily, the same for all stimulus

locations. In the other class of nonstandard visuomotor mapping, which is the topic of this paper, the relationship between the visual stimulus and the movement is arbitrary. The location of a visual stimulus does not indicate the direction of movement to be made, nor is there any algorithm that relates stimulus location to movement direction. Instead, the central nervous system maps the relevant visual information onto an action or set of actions. The system that performs this function appears to have highly general capabilities within its information-processing domain: any visual input that can be detected and discriminated from any other can apparently be mapped onto any movement within a learned motor repertoire.

In a typical *arbitrary* mapping task, nonspatial aspects of a visual stimulus, such as color, instruct a movement direction or target. Returning to our door-knob example, imagine now that you are in a strange building in which amber rooms require that the door knobs be twisted clockwise, but red rooms require a twist in the counter-clockwise direction. And to open a door, you only get one chance to choose which action to perform. You would reach toward the door knob using a standard mapping mechanism, but would have to compute an arbitrary visuomotor mapping to open the doors. Although our door-knob dilemma is contrived, arbitrary visuomotor mapping has *bona fide* applications in everyday life. Most signal-guided behavior, including almost all language-guided behavior, depends on arbitrary mapping abilities. This includes such behaviors as stopping at a red light or at the sound of the word "stop."

Much of the neural network that underlies arbitrary visuomotor mapping has been identified in macaque monkeys and rats. In this article, we review evidence implicating parts of the prefrontal cortex (PF), premotor cortex (PM), basal ganglia (BG), and hippocampal system (HS) in arbitrary visuomotor mapping. We will show, partly based on preliminary results from our own laboratories, that damage to any one of those four structures causes a deficit in some aspect of arbitrary visuomotor mapping. Thus, we will make reference to a distributed PF-PM-BG-HS network. In addition, we will review evidence that each of these structures contains neurons that systematically alter the pattern and level of their discharge modulations during the learning of such mappings. We will neglect the brain-imaging literature (see, for example, Passingham et al. 1998), which is discussed elsewhere in this volume (Passingham et al. 2000).

Our thesis does not imply that arbitrary visuomotor mapping encompasses the main function of the PF-PM-BG-HS network or that mapping visual inputs onto spatially directed motor outputs has any special prominence over other forms of associative learning. Visual-to-visual mappings, mappings involving other sensory modalities, and those involving reinforcement depend on many of the same structures. Nor does this network operate in a vacuum. The arbitrary visuomotor mapping functions of PF, PM, BG, and HS depend on interactions with the visual cortex and a motor-control network, at a minimum. Nevertheless, arbitrary visuomotor mapping tasks serve as a valuable laboratory tool, one that incorporates clearly observed responses with the rigorous sensory and motor control needed for behavioral neurophysiology. As such, it may serve as a paradigm for progress in understanding the general mechanisms underlying associative learning and memory. Finally, we note that in this article there is no attempt to distinguish between visuomotor and visuospatial mapping.

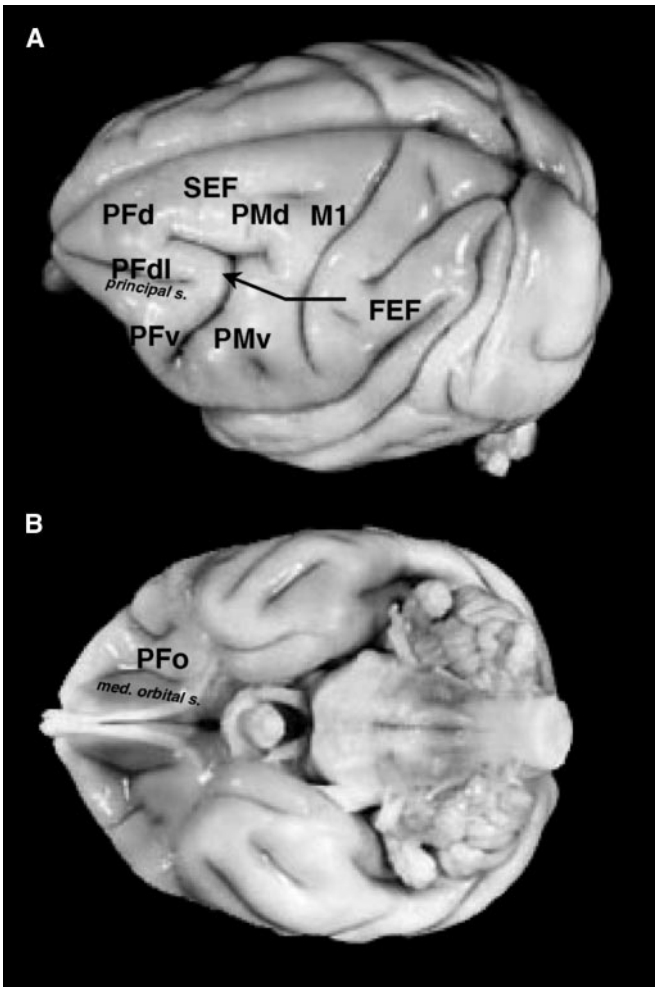


**Fig. 1A, B** Two surface views of the cerebral cortex of a macaque monkey. **A** Dorsolateral view of the left hemisphere. Rostral is to the left, dorsal is up. **B** Ventral view, rostral is to the left. Photographs from Noe et al. (1999). *PF* Prefrontal cortex, *PM* premotor cortex, *SEF* supplementary eye field, *FEF* frontal eye field, *M1* primary motor cortex, *d* dorsal, *dl* dorsolateral, *v* ventral, *o* orbital, *s* sulcus, *med* medial

## Terminology

Figure 1 shows the nomenclature we will use in referring to the various parts of the frontal cortex and the approximate locations of those regions. For example, the general region on the lateral convexity of the hemisphere ventral

to the principal sulcus will simply be termed PFv, for ventral prefrontal cortex. Similarly, the orbital prefrontal cortex will be designated PFo. When we want to refer to more than one region, we will use a notation such as PFv+o, which is meant to include both the orbital and ventral prefrontal cortex.

## Neuropsychology

Interruption of the basal ganglia outputs at the level of the thalamus (Canavan et al. 1989) and damage to the hippocampal system (Rupniak and Gaffan 1987; Murray and Wise 1996) cause profound impairments in arbitrary visuomotor mapping in monkeys. Canavan et al. (1989) found that monkeys with radiofrequency lesions centered in the ventral anterior nucleus of the thalamus could not retrieve or relearn preoperatively learned (i.e., familiar) visuomotor mappings. Because the monkeys could not relearn the familiar mappings postoperatively, it seems relatively unlikely that they could master novel ones, although that proposition remains to be tested experimentally. Hippocampal-system lesions that include the hippocampal formation as well as the underlying parahippocampal cortex, or in some experiments consist of fornix transection, have little effect on preoperatively learned visuomotor mappings, but severely disrupt the ability to acquire novel mappings. Frontal cortex lesions have effects on both previously learned and postoperatively acquired mappings (Murray and Wise 1997; Petrides 1997).

The hippocampal data have been reviewed recently (Wise and Murray 1999), and there is little to add to what is stated above for BG, at least for primates. Accordingly, we will focus the present discussion on the effects of frontal cortex damage in primates. We will then review some of the relevant literature derived from studies of rats.

### Clinical studies

In clinical studies, patients with large excisions of either left or right prefrontal cortex, often including portions of PM, were found to be significantly impaired in learning a visuomotor mapping task in which different colored lights instructed different hand postures (Petrides 1985). More recently, Vriezen and Moscovitch (1990) suggested that this impairment was due to deficits in the application of strategies, which would presumably be taxed by the noncorrection trial-and-error training method that was used, as opposed to deficits in visuomotor mapping *per se*. To address this possibility, Petrides (1997) trained subjects with similar excisions on the same task, but unlike the original study, he first showed the subjects the correct stimulus-response pairings. During learning, he offered subjects immediate correction after errors. As in the earlier study, the patients with excisions of the left or right frontal lobe were impaired in learning the arbitrary visuomotor mapping task. These findings support the view that the impairment reflects a failure to compute the mapping between stimulus and action. As is often the case in clinical studies, it is not possible to state with confidence whether the lesions involved PF, PM, or some combination.

### Premotor cortex in primates

In monkeys, Petrides and, separately, Passingham and his colleagues have examined the effects of frontal cortex ablations on the acquisition and retention of arbitrary visuomotor problems, respectively. Petrides (1982) found that monkeys with ablations including the dorsal aspect of PM were severely impaired relative to control monkeys in learning to emit different responses in the presence of two different visual cues. In his experiment, the monkeys were required to grasp a rod in the presence of object A and to touch a button in the presence of object B. Normal monkeys learned this problem in about 300 trials. The operated monkeys were unable to learn this task within the training limit of roughly 1000 trials, although the same monkeys could learn a visual discrimination problem at a normal rate. The latter observation rules out the possibility that the impairment was due to visual deficits *per se*. Halsband and Passingham (1982) found that monkeys with bilateral removals of PM, but not those with ablations of the frontal eye field, were severely deficient in the retention and relearning of a preoperatively learned visuomotor mapping problem. By contrast, the monkeys with PM lesions were able to learn new movements and to learn color discriminations as rapidly as control subjects. Taken together, these findings strongly suggest that the deficit after PM lesions was specific to mapping visual cues onto an appropriate action.

### Prefrontal cortex in primates

Gaffan and Harrison (1989) showed that ablations of the dorsolateral prefrontal cortex (PFdl in Fig. 1) caused mild impairments in learning novel visuomotor mappings. Other studies have found either a mild deficit (Petrides 1982) or no deficit (Petrides 1987) on visuomotor conditional tasks after lesions that included some of PFdl. There is also evidence that interactions of inferior temporal cortex (IT) with PF are important for arbitrary visuomotor mapping, which would be expected on anatomical grounds. The two general regions of temporal cortex that are most important in processing visual information about objects – area TE on the middle temporal gyrus and the perirhinal cortex on the inferior temporal gyrus (Meunier et al. 1993; Buckley et al. 1997; Buckley and Gaffan 1997, 1998a, 1998b; Murray and Bussey 1999) – both project to frontal cortex with axons that terminate in PFv+o (Pandya and Kuypers 1969; Webster et al. 1994; Carmichael and Price 1996). Gaffan and Harrison (1988)

made lesions of IT and PF in different hemispheres, combined with transection of the corpus callosum. They found that disconnecting IT from PF in this way caused a deficit in the acquisition of arbitrary visuomotor mappings. Interruption of the uncinate fascicle, the fiber bundle which connects much of IT with PF, also caused a mild deficit on this task (Eacott and Gaffan 1992).

Given the foregoing data, we found it surprising that there was no direct evidence in primates showing that bilateral ablations of ventral or orbital portions of prefrontal cortex caused deficits on arbitrary visuomotor mappings. To test the prediction that such effects should be observed, we used the same experimental design as in an earlier study that examined the role of the amygdala and hippocampus in arbitrary mapping (Murray and Wise 1996). The results of this experiment have been reported only in abstract form (Murray and Wise 1997). In brief, rhesus monkeys were seated in a primate chair in front of a video monitor and were required to move a joystick in a specific direction, according to an arbitrary visual instruction stimulus (IS) that appeared on the monitor screen. The joystick was constrained to move in only three directions in the horizontal plane. The monkeys were required to learn several new problems within their daily sessions and were always required to learn three arbitrary visuomotor mappings concurrently (e.g., if stimulus A, move the joystick to the left; if stimulus B, to the right; if stimulus C, pull the joystick). A correct response led to delivery of juice or applesauce reward and termination of the trial. An incorrect response led only to a blank intertrial interval followed by up to two additional presentations of the trial for correction. Just as for the original trial, a correct response on a correction trial led to delivery of reinforcement and termination of the trial. Each monkey was given 50 trials (not counting the correction trials) to learn a set of three arbitrary visuomotor mappings, after which it was presented with a new set of problems, and so on, until the monkey had completed eight such sets (for a total of 24 mapping problems) per day. After a long training period, we found that only one of the first two monkeys studied (Murray and Wise 1997) was able to solve the visuomotor mapping problems rapidly (Fig. 2, preoperative data), and we will therefore present data for that subject only. We are currently studying additional monkeys, but the results from that one subject were sufficiently striking to warrant mention here.

With the exception of the first trial, all learning trials could be divided into two main types: trials on which the IS was the same as that on the previous trials, termed *repeat trials*, and trials on which the IS differed from that on the previous trial, termed *change trials*. From our initial study (Murray and Wise 1996), we knew that monkeys used at least two strategies in performing this task. On repeat trials, they exhibited a high level of performance even before much learning had occurred, indicating that they were simply remembering the stimulus and response from the previous trial and emitting the correct response again. Because the monkeys almost always got

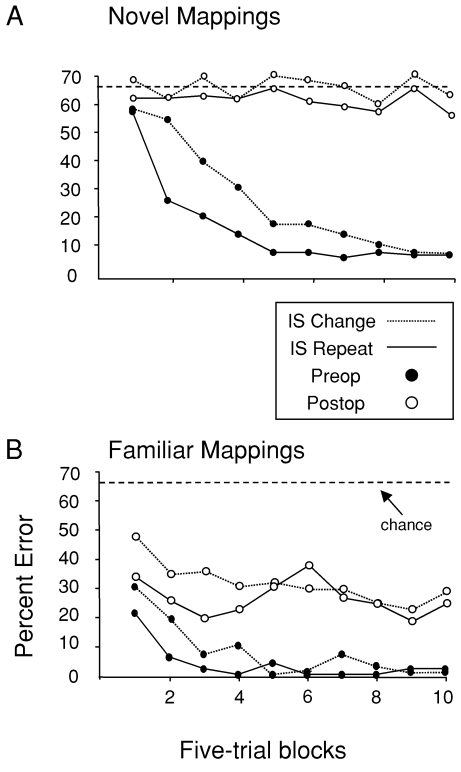


**Fig. 2** Effect of bilateral prefrontal (PFv+o) ablation on learning novel mappings (**A**) and retrieval of familiar mappings (**B**). Data from one monkey. Each curve shows the average learning rate for the monkey, pre- (*Preop*) and post-operatively (*Postop*), for repeat and change trials. Data are means for performance over 5 days of testing for novel mappings, 3 days for familiar mappings. *IS Change* Those trials in which the instruction stimulus changed from the previous trial, *IS Repeat* those trials in which the instruction stimulus was the same as in the previous trial

a trial correct, either on the original presentation or on one of the two correction presentations, and because roughly one-third of the trials were repeat trials, use of this *Repeat-Stay* strategy proved beneficial to the monkey's overall performance. In addition, on change trials, it turned out that monkeys avoided the previously emitted response in favor of one of the two remaining possibilities. Application of this *Change-Shift* strategy effectively reduced the three-choice problem to a two-choice problem. On change trials, then, initial performance was roughly 50% in experienced monkeys. Together, we refer to these two aspects of the monkey's performance as the Repeat-Stay/Change-Shift strategy (Wise and Murray 1999). We note that this strategy is related to, but different from, a Win-Stay/Lose-Shift strategy. According to the Win-Stay/Lose-Shift strategy, a new response is selected only after an error, i.e., after failure to obtain reward on the previous trial. By contrast, in the Change-Shift strategy, the change in response is driven not by a failure to obtain reward but, rather, by the knowledge that a different stimulus requires a different response.

After the monkey had learned the task, PFv was ablated from just below the principal sulcus (see Fig. 1A) ventrally to the junction with orbital prefrontal cortex,

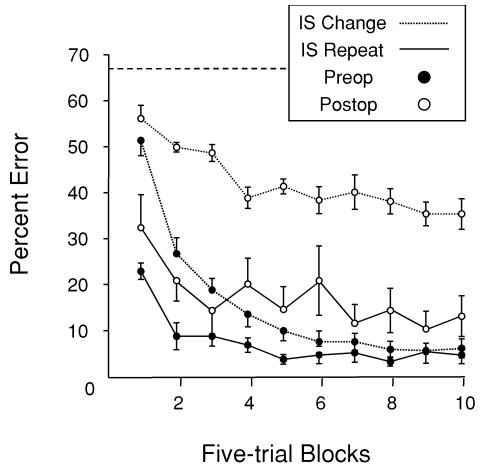


**Fig. 3** Effect of bilateral removal of hippocampal formation plus underlying parahippocampal cortex (*n*=4) on learning novel mappings. The task was the same as that used for the monkey with a bilateral prefrontal (PFv+o) lesion, illustrated in Fig. 2. Curves show means (±SEM; abbreviations as in Fig. 2). Data from Murray and Wise (1996)

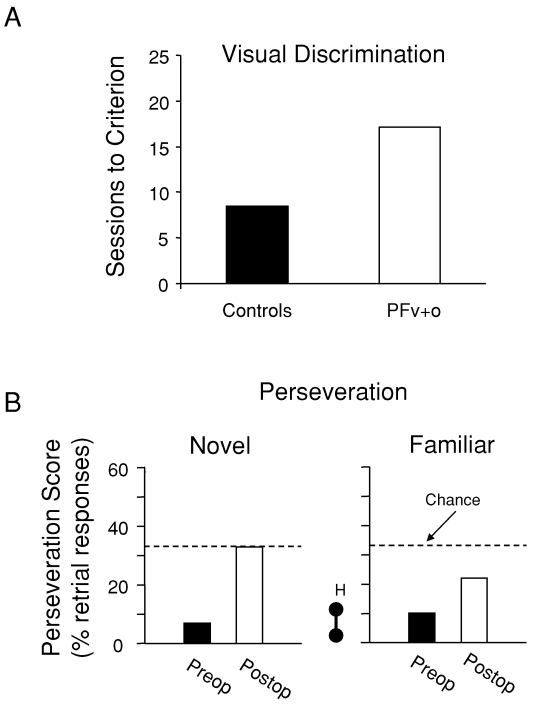


**Fig. 4** **A** Visual discrimination learning. The number of sessions to criterion (90% correct) on a set of two-choice visual-discrimination problems. Monkeys were trained on 20 problems concurrently at the rate of 20 trials (one per problem) per daily session. Control monkeys (*n*=13) versus one with bilateral prefrontal (*PFv+o*) removal (the same monkey on which Fig. 2 is based). **B** Perseveration scores for the same monkey. The *left panel* shows perseveration, defined as the immediate repetition of a previously unreinforced response, during novel mapping problems. The *right panel* shows comparable data for familiar mapping problems. Between the two panels, for comparison, are perseveration scores from the four monkeys with "hippocampal" (*H*) ablations (see Fig. 3). *Preop* Pre-operatively, *Postop* post-operatively

and PFo was removed from its lateral junction with PFv to the medial orbital sulcus (see Fig. 1B). After this single-stage, bilateral removal of PFv+o, the monkey was no longer capable of learning new mappings within sessions or of applying the Repeat-Stay/Change-Shift strategy (Fig. 2A). The monkey showed no place (or response) preference, i.e., it distributed its correct and incorrect responses roughly equally among the three response choices. For comparison, Fig. 3 shows previously published data for monkeys with removals of the HS. These animals were severely impaired in learning new mappings, but exhibited slow postoperative learning within the 50-trial training blocks on change trials and were virtually normal in their ability to perform the same task according to familiar (i.e., preoperatively learned) mappings (Wise and Murray 1999). By contrast, the monkey with a bilateral PFv+o lesion showed no evidence of learning within the 50-trial blocks (Fig. 2A) and was substantially impaired in performance for familiar mappings (Fig. 2B). However, performance of arbitrary visuomotor mappings for familiar stimuli was clearly above chance levels, so the prior experience or, alternatively, the accumulated experience across sessions, did benefit performance. We focus the remainder of this section on the dramatic deficit in learning novel, arbitrary visuomotor mappings that follows the bilateral PFv+o lesion.

Several accounts of the deficit appear plausible. First, the mapping deficit could have been due to an inability to discriminate the stimuli from each other. Such a deficit in what is often termed perceptual learning could be due to the postulated role of PFv in top-down attention and a loss of the mechanism for biasing specific feature or object representations in IT. To test that possibility, the monkey with a PFv+o lesion was trained postoperatively on a visual discrimination task. Figure 4A shows that, in accord with previous results after PF lesions (Passingham 1972; Gaffan et al. 1993), the monkey had a mild deficit, but was clearly able to reach criterion performance (>90% correct). Because the monkey required approximately twice the number of sessions to learn as did the unoperated control monkeys, we cannot rule out the possibility that a deficit in learning to discriminate visual stimuli contributed to the deficit in visuomotor mapping. However, the fact that the monkey seemed virtually unable to learn the visuomotor mappings suggests that sensory deficits alone do not explain the impairment. Clearly, a more detailed examination of this question is indicated, and we can reject the "sensory" interpretation of the deficit only provisionally.

The deficit could conceivably have resulted from response perseveration, which has been reported to follow PF lesions. Figure 4B shows the results from one analysis of perseveration: the repetition of a previously unreinforced response on correction presentations. Data from the HS-lesion group are also shown in Fig. 4B, between the two graphs. Preoperatively and after HS ablations, there was minimal perseveration. Instead, the monkey showed a Lose-Shift strategy, in which the repetition of

an unreinforced response was relatively unlikely (see also Chen and Wise 1996). After PFv+o lesions, relative to before surgery, the monkey was more likely to repeat a previously emitted incorrect response (unfilled bars in Fig. 4B), but appeared to be no more likely to do so than to emit any alternative response. We also searched for, and failed to find, any tendency to repeat incorrectly a previously rewarded response on change trials. Thus, these types of perseveration cannot account for the profound deficits in learning the arbitrary mappings.

Another possible cause of the deficits involves a failure of working memory. A detailed discussion of this issue is beyond the scope of the present paper and was not the focus of the experiment described here. Taking only the present results into account, we cannot rule out an interpretation in terms of working memory. However, the recent results of Rushworth et al. (1997a) show that the PFv, at least, is not necessary for the short-term storage of nonspatial visual information. In their study, monkeys with removals of PFv were able to store visual stimuli for up to 8 s, as measured in a delayed matching-to-sample task using familiar stimuli. We also note that not all the deficits that followed a PFv lesion in their monkeys could be accounted for in terms of working-memory dysfunction. The findings of Rushworth et al. thus falsify the widely promoted hypothesis that the sole specialized function of PF, as a whole, is the mediation of working memory. Furthermore, in the present experiment, demands for storage or manipulation of stimulus information were minimal. The instruction stimulus was present on the video screen throughout the time that the choice of response was made and the response was executed. Accordingly, we are inclined to dismiss the possibility that arbitrary mapping deficits after PFv+o lesions reflect problems with working memory.

We are thus left with two interpretations of the deficit, which are not mutually exclusive. First, PFv+o may compute and store the arbitrary mappings, as well as the strategies and rules that facilitate the network's acquisition of those mappings. Second, the deficit may be due to the disruption of routes by which information is transferred from IT to PM. These interpretations will be discussed in more detail in the section entitled Conclusions and interpretations, below.

## A comparable network in rats

The rat frontal cortex consists of several distinct regions, and it appears that at least some play a role in arbitrary visuomotor mapping. As in monkeys, BG and HS appear to do so as well.

Passingham et al. (1988) trained rats preoperatively to pull open a black door, and to push open a white door, in order to gain food reward. In a second experiment, rats were trained either to lift up or to push down a lever, depending on the ambient lighting conditions. Lesions of the medial agranular cortex, termed AGm by some researchers (Donoghue and Wise 1982) or Fr2 by others (Zilles 1985), disrupted the postoperative performance of both of these arbitrary visuomotor tasks. Lesions of approximately the same area caused disruption in the acquisition of a similar visuomotor mapping task (Winocur and Eskes 1998). In that task, the rat faced two levers and instruction lights were placed both to the left and right of center in an operant chamber. When the lights to the left of center were illuminated, they served as an instruction that depressing the left lever was appropriate on that trial and vice versa. However, because the location of a correct response was related to the location of the instruction stimulus, the mapping was not arbitrary in the sense used here. If taken as an example of visuomotor mapping more generally, these data would extend those of Passingham et al., which suggested a role for AGm in the retrieval and retention of familiar (i.e., preoperatively learned) mappings, to indicate a role in acquisition of novel mappings as well. More recently, Quirk et al. (1999) found that AGm lesions slowed the acquisition of a different arbitrary visuomotor mapping task, one in which the frequency at which a light flashes maps onto the direction of response. Rats learned a rule of the type "if lights flash slowly, then go left; if lights flash rapidly, then go right." For convenience, we term this a frequency-motor mapping task. Lesions of the agranular insular cortex (AGi) also impaired acquisition of this task and did so without causing deficits on a visual discrimination problem or on familiar (i.e., preoperatively trained) frequency-motor mappings. Thus, parts of what is often termed prefrontal cortex in rats, AGi and AGm, appear to be important for the acquisition of arbitrary visuomotor mappings.

Other experiments have examined the involvement of rat frontal and cingulate cortex in learning novel visuomotor mappings. Medial frontal cortex lesions, including the prelimbic cortex and the anterior cingulate cortex rostral to the genu of the corpus callosum, had no effect on acquisition of frequency-motor mapping (Bussey 1996) or on acquisition of another arbitrary visuomotor mapping task. In the latter, a nose-poke to targets on the left or right of a computer screen was instructed by a shape presented in the center (Bussey et al. 1997). Surprisingly, excitotoxic lesions of the anterior cingulate cortex caudal to the genu actually facilitated this type of learning, at least in the early stages of learning (Bussey et al. 1996), as did cholinergic denervation of cingulate cortex via lesion of the vertical limb of the diagonal band of Broca (Muir et al. 1996). By contrast, posterior cingulate cortex lesions led to impairments in acquisition, but only in the latest stages of learning, on both of the arbitrary mapping tasks described above (Bussey et al. 1996, 1997). A similar result, for frequency-motor mapping, has been reported to follow lesions of the infralimbic cortex (Quirk et al. 1999).

Taken together, the available data suggest an involvement of parts of the rat frontal cortex in arbitrary visuomotor mapping, with differential involvement of various frontal regions in acquisition and retention/retrieval. However, a general statement about these areas is under-

**Table 1** Summary of results from ablation studies (in monkeys) that examined the neural basis of arbitrary visuomotor mapping. *BG output* Basal ganglia output to cortex through thalamus, *HS* hippocampal system, *PFv+o* ventral and orbital prefrontal cortex, *PFdl* dorsolateral prefrontal cortex, *PM* premotor cortex

| Site of lesion | Higher-order rules and strategies | Lower-order rules, specific mappings, and exemplars | |
|---|---|---|---|
| | | Familiar mappings (retention, relearning) | Fast novel mappings (learning) |
| PFv+o | lost | partially preserved or relearned across sessions | lost |
| PFdl | ? | preserved | partially disrupted |
| PM | ? | lost | lost |
| BG output | ? | lost | ?, presumably lost |
| HS | preserved | preserved | severely disrupted |

mined by the difficulty in identifying homologous frontal areas in rats and monkeys (Preuss 1995).

Lesions in the BG can also affect visuomotor mapping in rats. Dorsal striatal lesions yield deficits on the visuomotor mapping task used by Winocur and Eskes (1998), which, as pointed out above, does not necessarily involve an arbitrary mapping. However, dopamine depletions in a similar region did have disruptive effects on a genuinely arbitrary visuomotor mapping task (Robbins et al. 1990). Reading et al. (1991), using selective excitotoxic lesions, found that damage to the lateral, but not the medial striatum impaired performance on the frequency-motor mapping task. Lesions of the nucleus accumbens also impaired acquisition of this task, but Reading et al. attributed that effect to an attentional deficit. More recently, Quirk et al. (1999) have reinvestigated the involvement of the BG in arbitrary visuomotor mapping. Using the frequency-motor mapping task, they found that lesions of neither the dorsolateral nor ventrolateral striatum caused a deficit. However, lesions of the core (but not the shell) of the nucleus accumbens did lead to impairment (Quirk et al. 1999).

As for the HS, both Winocur (1997) and Sziklas et al. (1998) have reported data from hippocampectomized rats that are consistent with a role in visuomotor mapping. Other studies of rats with hippocampal (Marston et al. 1993) or fornix lesions (Bussey et al., 2000), however, have failed to find an effect on acquisition of visuomotor mapping. We cannot resolve this discrepancy at the present time. However, as emphasized above, in two-choice mapping tasks, animals can perform exceptionally well by employing strategies such as the Repeat-Stay/Change-Shift strategy. Only when the task requires three or more responses can acquisition of the stimulus-response mapping be dissociated from the use of such a strategy. It is therefore conceivable that, in some of the above studies, negative results were obtained because the rats adopted such a strategy. Indeed, this possibility applies to all of the studies carried out so far in rats, which invariably used two stimuli mapped onto two responses. Reconciliation of the foregoing discrepancies may thus require further investigation, including the use of three-choice arbitrary mapping tasks (Wise and Murray 1999) and an explicit evaluation of learning strategy (Parker and Gaffan 1997; Collins et al. 1998; Wise and Murray 1999).

## Summary of the neuropsychological data

The data reviewed thus far indicate that a distributed network including PF, PM, BG, and HS underlies arbitrary visuomotor mapping in primates. A summary of the cited results is provided in Table 1. A similar network appears to underlie arbitrary visuomotor mapping in rats, with the qualification that the identification of PF and PM remains uncertain in rodents.

Other brain structures in monkeys appear to contribute little, if anything, to the computations underlying arbitrary visuomotor mapping. For example, lesions of the medial premotor cortex in monkeys, including supplementary motor and anterior cingulate areas, have little or no effect on the retention and retrieval of arbitrary visuomotor mappings (Chen et al. 1995; Thaler et al. 1995). There is a report that lesions to the dorsal prefrontal cortex (PFd in Fig. 1) result in similarly negative results (Passingham 1987). Parts of the posterior parietal cortex also appear to contribute little to the retention of familiar mappings (Rushworth et al. 1997b). As for subcortical structures, notwithstanding some clinical evidence suggesting involvement of cerebellum in arbitrary mappings of various kinds in humans (Bracke-Tolkmitt et al. 1989; Canavan et al. 1994; Tucker et al. 1996; Drepper et al. 1999), lesions of the deep cerebellar nuclei in monkeys do not appear to cause deficits in learning visuomotor mappings (Nixon and Passingham 1999). Complete bilateral ablation of the amygdala likewise has no effect on the rapid acquisition of arbitrary mappings (Murray and Wise 1996).

In rats, damage to brain regions outside the PF-PM-BG-HS network also yield few, if any, deficits in arbitrary visuomotor mapping. Burns et al. (1999), for example, report no effect on visuomotor mapping of excitotoxic lesions of the amygdala. Y. Chudasama, T. Bussey, and J. Muir (unpublished results) found no effect on visuomotor mapping of excitotoxic lesions of the mediodorsal nucleus of the thalamus, the anterior group of thalamic nuclei, or the prelimbic cortex. As noted above, Bussey et al. (1997) reported similar sparing after excitotoxic lesions of medial frontal or anterior cingulate cortex. In addition, Bussey et al. (2000) found no effect on visuomotor mapping of combined excitotoxic lesions of the perirhinal and postrhinal cortex. This sparing may be due to the stimuli being discriminable on the basis of

simple features such as luminance, thus failing to require access to the complex visual representations in perirhinal cortex (Murray and Bussey 1999).

In summary, we conclude that parts of PF, PM, BG, and HS underlie both the acquisition and retention of arbitrary visuomotor mappings and probably form the bulk of the network that subserves these mappings. As we will discuss in the next section, each of the four brain regions implicated by the ablation studies contains neurons that show dramatic and systematic changes in activity as monkeys learn visuomotor mappings.

## Neurophysiology

### Premotor areas

The first systematic study of the neural correlates of learning arbitrary mappings was that of Mitz et al. (1991) in PM. The experimental design was much like that described above for the ablation study involving PFv+o, with the exception that an *instructed delay period* of one to several seconds was inserted between the stimulus presentation and the choice of response. As in the lesion study, the monkey selected one of three possible joystick movements based on nonspatial information in a visual instruction stimulus. A fourth possible response was to refrain from moving the joystick (no go). Mitz et al. found that more than half of the sample of neurons in PM showed a systematic change in activity as the monkeys learned novel, arbitrary mappings. In that early study, most changes consisted of increases in discharge rate as the monkeys learned. Averaged over the entire population of PM neurons, the time-course of activity increases corresponded very closely with the animals' improvement in performance. Changes during learning were later confirmed with a very different experimental design (Germain and Lamarre 1993), in a study that emphasized the relative lack of such learning-dependent changes in the primary motor cortex (M1 in Fig. 1).

However, the complexity of limb movement in the study by Mitz et al. (1991) led to potential problems in interpreting the results. For example, it was conceivable that the monkey performed the joystick movement differently once the mapping had been learned. Perhaps such a change in the movement could account for the evolution of PM activity during learning. In addition, the monkeys' eye positions were not controlled, which led to possible interpretations of the data in terms of either the retinocentric or craniocentric location of the visual stimuli. This variable could also change systematically as the monkeys mastered the arbitrary mappings. For example, early in the process of learning, the monkeys may have scrutinized the stimulus carefully with foveal vision and done so for a protracted period of time. Later, when the mapping had been mastered, a brief glance could have been sufficient, given that the instruction could be rapidly recognized and "prospectively coded" into action (Gaffan 1977).

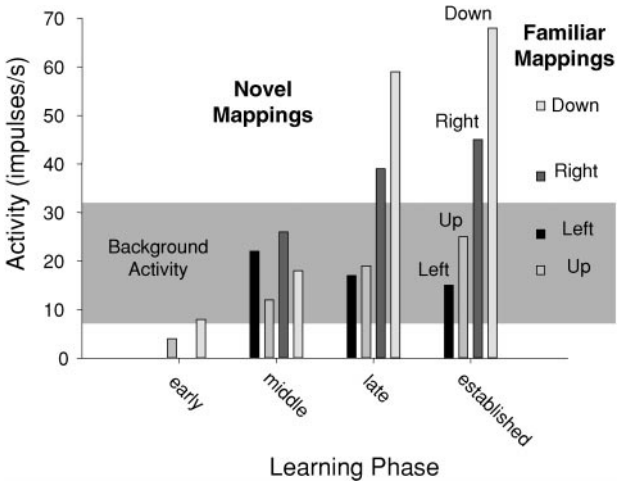


**Fig. 5** Development of directional selectivity during learning, from one neuron in the supplementary eye field (SEF). Learning is divided into four phases (*early, middle, late, established*). The cell's activity (measured in the period in which the instruction stimulus was presented) is plotted separately for stimuli (trials) instructing each of the four possible response directions (*up, down, left, right*). All data are from correctly executed trials. The *rightmost column* shows the activity of the same cell during performance of arbitrary visuomotor mappings according to four familiar instruction stimuli. The *shaded area* shows the background activity level ±SD for the familiar-mapping trials. Adapted from Chen and Wise (1996)

Accordingly, Chen and Wise (1995) redesigned the experiment to address those problems. Instead of moving a joystick, the monkeys responded to the visual stimulus by shifting gaze to one of four potential eye-movement targets. This change in task design helped rule out the possibility that any changes in neural activity during learning were related to variations in the way the movement was being performed, because the responses were highly stereotyped saccades. To avoid the problems resulting from the stimulus tracking across or lying on different parts of the retina, the monkeys were required to maintain central fixation before, during, and after the presentation of the visual instruction stimulus. Because eye movements were studied, the recordings were made in the supplementary eye field (SEF in Fig. 1), which is treated here as an oculomotor part of PM.

Each trial unfolded as follows: after a brief presentation of the instruction stimulus, the fixation point remained on the screen and four potential targets appeared in the cardinal directions from screen center. When the fixation point disappeared a few seconds later, the monkey was required to make a saccadic eye movement to one (and only one) of the four targets within about half a second and to maintain fixation of that target for about the same amount of time. We intermixed familiar and novel instruction stimuli in the same stimulus set.

Figure 5 shows the evolution of activity in one SEF neuron as the monkey learned four novel visuomotor mappings, one each for upward, leftward, rightward, and

downward saccade targets. The activity was measured in the period that the instruction stimulus was presented. The cell showed its greatest discharge rate for visuomotor mappings to the downward target. Significant activity, compared with that in a reference period, was also seen for mappings to the rightward target. No significant neuronal activity was observed for mappings to the leftward or upward targets. Thus, we can say that the cell had a preferred direction of down and to the right, mainly down. The most important feature of the data shown in Fig. 5 is that, for novel problems, the cell's activity evolved during learning, only becoming significantly different from background levels of activity during the later stages of learning.

It is important to emphasize that the data shown in Fig. 5 were taken exclusively from trials on which the monkey executed the correct response. Incorrect responses have been eliminated. The reason for the selection of "correct" trials is that, for any given direction of saccade, the monkey made the same response to the identical stimulus. This makes the physiological data much easier to interpret, since it rules out variation in motor or sensory factors as the cause of change in activity modulation. Because the stimulus changed on every trial, and remained present for only 0.5 s, we can be confident that the monkey not only attended to the stimulus in a general sense, but also attended to some of its nonspatial information at that time. Presumably, the monkey attended to some subset of features that distinguished the stimuli from each other, although in these complex, multi-dimensional stimuli we do not know which of the many stimulus features the monkey used. Nevertheless, we can be confident that, for each saccade direction, the stimulus was the same in all spatial coordinate frames and that it was attended on every correctly executed trial.

But there are other variables that could confound interpretation of the neurophysiological result. As the monkey learned, a variety of general factors changed in correlation with learning. For example, as the monkey mastered a novel visuomotor mapping, the reward frequency (rewards per minute) increased. It is reasonable to infer, and impossible to exclude, the possibility that reward expectation paralleled that increase. Furthermore, the monkeys may have changed their general level of motivation or arousal as they became more familiar with the initially novel mapping. However, none of these general factors can account for the evolution of activity illustrated in Fig. 5. The same changes in reward frequency, motivation, and arousal occurred for the visuomotor mappings to the upward and leftward targets as for the downward and rightward targets, but the neuronal activity did not increase significantly for the former. About half of the cells have sufficient directional selectivity to rule out general factors common to all mapping directions. Thus, the systematic change in discharge rate shown in Fig. 5 can be attributed to learning the arbitrary visuomotor mapping.

Figure 6 shows learning-related activity changes for a population of SEF cells. The panels on the left are aligned to the onset of the visual stimulus. Those on the right are aligned to the time that the monkey's saccade brought gaze into a window around the target. In each row, activity during a "background" reference period was subtracted from that in each of several successive time bins, averaged over the entire population for each of three phases of within-session learning. The row labeled "familiar" came from intermixed trials in which the monkey performed the task according to the familiar mappings. Early in learning (top row), there was little increase in activity over background levels for most of the trial. Note, however, that there was a significant burst of activity as the time of reinforcement approached, after target acquisition. Later in learning (second and third rows), the cells' activity increased throughout the trial to include significant stimulus-period, delay-period, presaccadic, and postsaccadic activity. By the end of the learning blocks (third row), activity levels typically exceeded that for the familiar stimuli, a phenomenon also seen for the single cell illustrated in Fig. 5.

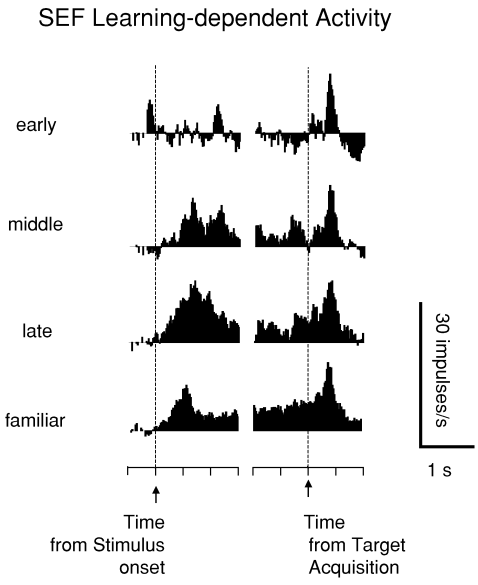


**Fig. 6** Population histograms for a subpopulation of neurons in the supplementary eye field (*SEF*). The *left column* shows the neuronal-activity data aligned on the onset of the visual instruction stimuli. The *right column* shows data from the same neurons aligned on the acquisition of the eye-movement target. The *top three rows* show average activity for three phases of learning. The *bottom row* shows the average activity for performance according to familiar mappings. Note the development of activity during learning. Adapted from Chen and Wise (1995)

As illustrated in Fig. 7, three main types of learning-related activity were observed. The SEF population featured in Fig. 6 was termed learning-dependent activity (increasing), because the cells' modulation increased as the monkeys learned the arbitrary mapping (Fig. 7A). These cells had activity at the end of the learning block that was generally similar to that observed when familiar stimuli instructed the same action. Another kind of activity was only observed during the learning of novel map-

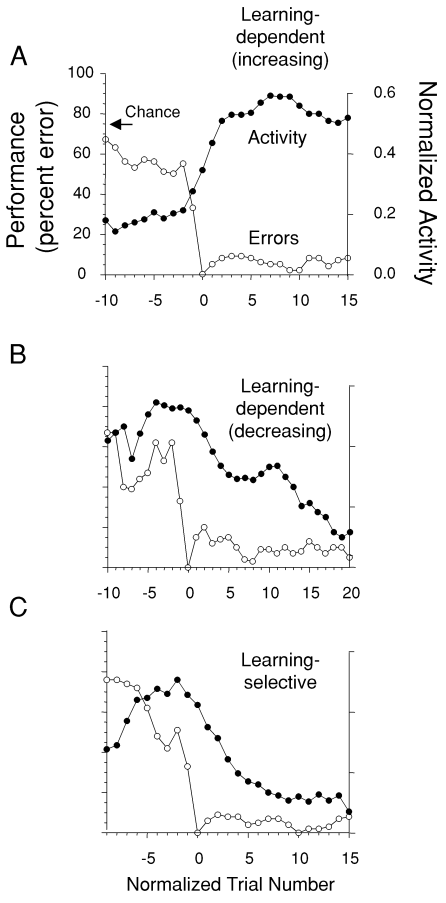


**Fig. 7A–C** Three subpopulations of supplementary eye field (SEF) cells, showing their evolution of activity during learning in relation to the rate of learning. **A** Learning-dependent activity, with increasing discharge rates (see also Fig. 6). *Unfilled circles* show mean error rate (moving average of three trials), as the monkey learns new mappings, aligned on the first occurrence of three consecutive correct responses. *Filled circles* show the three-point moving average of the subpopulation's activity, aligned on the same trial as the corresponding behavioral data point. **B** Learning-dependent activity, with net decreasing discharge rates. **C** Learning-selective activity. Adapted from Chen and Wise (1995)

pings and not for performance according to the familiar mappings. Accordingly, we termed this pattern of activity "learning-selective" (Fig. 7C). The third pattern of activity (Fig. 7B) was classed as learning-dependent (decreasing) by Chen and Wise (1995) because the cells showed a significant task relationship for the familiar mapping problems, which was the basis for their definition of learning dependency. In general, however, this pattern appeared more similar to learning-selective activity (Fig. 7C). These three patterns appeared to be completely intermixed within the SEF. The majority (55%) of SEF neurons showed either learning-dependent or learning-selective activity. From a population of 101 SEF neurons, 37% were classed as learning dependent (like those in Fig. 7A and B) and 18% as learning selective (like those in Fig. 7C).

## Prefrontal cortex

Watanabe (1990) reported changes in the activity of PFdl neurons during an arbitrary stimulus-stimulus mapping task, but reported on the activity of only three cells during learning. No systematic work had been done on learning-related neurons until very recently. For PFv and PFdl (see Fig. 1), Asaad et al. (1998) studied the changes in the directional selectivity of PF neurons as monkeys learned arbitrary mappings in an oculomotor paradigm similar to that described above for the SEF study. They found a systematic shift in the development of directional selectivity as the monkeys mastered the arbitrary mappings. Changes in activity during learning have also been reported by Tremblay and Schultz (1996) in PFo and by Li et al. (1997) in PFv. Asaad et al. (1998) confirmed a finding for PF that was originally made for SEF: activity for novel mappings, once learned, exceeded that for familiar ones (see Figs. 5 and 6). In their analysis, Asaad et al. were able to estimate the relative sensitivity of PF neurons to three different factors: the instruction stimulus, the direction of a saccade, and the mapping. First, they taught the monkey two mappings, e.g., stimulus A instructed a saccade to the left (A-left) and stimulus B instructed a saccade to the right (B-right). Then they reversed the mappings (to A-right and B-left). For many PF neurons, Asaad et al. recorded activity as the monkey performed the task according to both the original and the reversed mappings. They found that some PF neurons were selective for the stimulus, especially relatively early in a trial. An example would be a cell with activity that was greater for A-left and A-right than for B. That percentage decreased from 45% in the stimulus period, to 32% in the delay periods, to 21% in the presaccadic period. A smaller percentage of PF neurons was selective for saccade direction. An example would be a cell with greater activity for A-left and B-left than for right. That percentage increased from 14% during the stimulus period, to 21% and 34% in the delay and presaccadic periods, respectively. However, a large population of PF neurons reflected the specific mapping. In a typical example, a PF neuron had activity for one combination of stimulus and response, e.g., B-left, that was greater than for any other combination. The percentage of cells showing this property ranged from 41% to 47% in the various periods of the trial.

## Hippocampus

Cahusac et al. (1993) reported changes in activity levels during the learning of arbitrary visuomotor mappings. They found neurons that corresponded to both the learning-selective and learning-dependent activity changes reported for SEF. Learning-selective activity appeared to be more prominent than learning-dependent activity, 45% to 22%, and most of the latter took the form of increasing activity during learning. The changes in activity observed in hippocampus were relatively weak. This ob-

servation may reflect differences in the experimental design, of course. However, it is tempting to interpret the small hippocampal activity changes as a characteristic of a sparsely coded network like the hippocampus. Because the hippocampus represents so many different kinds of information, any given type is likely to be distributed over several neurons, which comprise only a relatively small percentage of the overall hippocampal network. By contrast, premotor areas like SEF represent only a limited kind of information, much of it having to do with eye movements and the sensory signals that guide such movements. The robust activity changes seen in SEF during learning may be representative of a densely coded network. This view corresponds with a role for the hippocampus in many information-processing domains, compared with a role for each individual neocortical area in relatively few domains.

### Basal ganglia

Tremblay et al. (1998) studied neuronal activity in the striatum that was associated with arbitrary visuomotor learning. They compared activity for novel mappings with activity in the same neurons during familiar mappings. About one-third of the striatal neurons they studied had firing rates that differed between the novel and familiar mappings, despite the similarity of the response and stimulus material. In addition, they noted a much higher incidence of learning-related changes immediately after the instruction stimulus relative to that observed after other task events (such as the movement). Tremblay et al. also concluded that, compared with PM, SEF, and PFo (Tremblay and Schultz 1996), the striatum had fewer neurons that showed learning-related activity evolution.

## Conclusions and interpretations

It seems unlikely that all parts of the PF-PM-BG-HS network make the same contribution to arbitrary visuomotor mapping. In discussing potential specializations within the network, we will make use of the concept of distributed information-processing architectures spanning several neural structures, especially as applied to the frontal cortex and basal ganglia (Houk and Wise 1995). In this view, recurrent neural networks include the neocortex, basal ganglia, and thalamus, and each cortical area participates in a large number of such cortical-BG modules, operating largely in parallel.

We propose that several interacting capabilities, supported by cortical-BG modules, contribute to arbitrary visuomotor learning. The central ability, of course, consists of acquiring the specific mappings. However, underlying and speeding that process is the ability to learn higher-order rules (defined below), to learn and apply strategies for problem solving and to transfer processed information from cortical-BG modules in one area to those in another. We further propose, in accord with several other models, that HS stores mappings, rules, and strategies over the intermediate term pending their consolidation into frontal cortical-BG modules. Our conclusions and interpretations are summarized in Table 2.

### Higher-order rules

In the section entitled Prefrontal cortex in primates, we suggested two interpretations of the deficit in arbitrary visuomotor mapping that followed bilateral ablation of PFv+o. The first involved disruption of rules and strategies; the second invoked the concept of a disconnection. The latter interpretation is taken up below in the section titled Disconnection. We distinguish between higher-order rules and lower-order rules (Wise et al. 1996b). Lower-order rules are equivalent to exemplars and specific mappings, for example, when a red square maps onto a leftward joystick movement. A higher-order rule deals with the same kinds of information as a lower-order rule, but at a more abstract level. For arbitrary visuomotor mappings, one important higher-order rule is that colors and shapes instruct a particular action or target of action. The disruption of higher-order rules, which we suppose to be encoded in PF cortical-BG modules, could have contributed to the deficit observed after PFv+o lesions. Of course, a role for PF in learning higher-order rules does not preclude a role in learning lower-order rules (i.e., exemplars) as well. However, once PFv+o is removed, its contribution to both would be eliminated.

Failure to learn or apply the higher-order rule that nonspatial visual information guides action could have devastating effects on arbitrary visuomotor learning, but only on the assumption that higher-order rules are necessary for learning lower-order ones. That assumption is doubtful, however. Each exemplar could be learned, one by one, without ever encoding the general rule that nonspatial visual information always provided the critical signal. Accordingly, this factor alone does not explain the severe deficit that follows PFv+o lesions (Fig. 2A). Nevertheless, the ability to learn and apply higher-order rules may increase the speed and efficiency of learning.

### Strategy

A strategy can be considered to be a plan or method for solving a problem, and evidence obtained in monkeys implicates PF in the learning and implementation of strategies (Parker and Gaffan 1997; Collins et al. 1998). The Repeat-Stay/Change-Shift strategy is particularly effective in a three-choice visuomotor mapping task because, as noted above, it reduces a three-choice problem to a two-choice problem for change trials and solves the problem completely for repeat trials. Despite their marked deficit in new learning, monkeys with HS lesions continued to apply the Repeat-Stay/Change-Shift

**Table 2** Summary of conclusions and interpretations (*italic text*) regarding the effects of brain damage on arbitrary mapping abilities in monkeys. *BG* Basal ganglia, *M1/BG* cortical-BG modules of the primary motor cortex, *PM/BG* premotor cortex cortical-BG modules, *PF/BG* prefrontal cortex cortical-BG modules, *HS* hippocampal system, *PFv+o* ventral and orbital prefrontal cortex, *PFdl* dorsolateral prefrontal cortex, *BG output* basal ganglia output through thalamus

| Ability after lesion | Higher-order rules and strategies | Lower-order rules, specific mappings, and exemplars | |
|---|---|---|---|
| | | Familiar mappings (retention, relearning) | Fast novel mappings (learning) |
| Relatively spared | **After HS lesion** *due to preserved PF/BG* | **After HS, PFv+o, or PFdl lesion**[a] *due to preserved PM/BG and PF/BG*[b] | |
| Lost or almost lost | **After PFv+o lesion** *due to lost PF/BG* | **After PM lesion** *due to: i) lost PM/BG, ii) disconnection of PF from motor output*[c]<br>**After BG-output lesion** *due to lost PM/BG and/or PF/BG* | **After PFv+o lesion** *due to: i) lost PF/BG for strategy and/or rules*[d], *ii) disconnection of PM/BG from visual input*[e]<br>**After PM lesion** *due to lost PM/BG and/or lost motor input to PF*[f]<br>**After HS lesion** *due to lost intermediate-term, fast-mapping network*[g] |

[a] Partial retention or relearning across sessions after PFv+o ablations (see Fig. 2B)
[b] For PFv+o and PFdl lesions, those PF cortical-BG modules not removed by the ablation
[c] PF/BG→PM/BG→M1/BG
[d] Lower-order rules as well as higher-order rules
[e] IT→PF/BG→PM/BG
[f] PM/BG→PF/BG
[g] Slow encoding into long-term mapping network preserved (Fig. 3), but HS needs PF/BG and/or PM/BG to effectuate learned actions, hence the deficits after PM or PFv+o lesions

strategy (Fig. 3). However, a different result followed PFv+o removals. That lesion eliminated the strategy as well as learning (Fig. 2A), at least within the 50-trial blocks we examined. This finding indicates that PFv+o is necessary for implementation of the Repeat-Stay/Change-Shift strategy, and we attribute the loss of this ability to the elimination of cortical-BG modules that include neurons in this region.

Although PFv+o lesions abolished the Repeat-Stay/Change-Shift strategy, it seems unlikely that this factor alone accounts for the dramatic deficit observed in Fig. 2A. In a three-choice task, perfect application of the Repeat-Stay/Change-Shift strategy decreases the initial error rate, when faced with a set of novel mapping problems, from 67% to 33% (0% on the repeat trials and 50% on the change trials, which occur twice as often). After the PFv+o removals, the percentage of errors on initial choices was, therefore, increased to ~ 67%. Still, that does not explain why the visuomotor mappings that were reinforced were not learned at all over the 50-trial block. As with higher-order rules, the ability to learn and to apply problem-solving strategies may contribute to the speed and efficiency with which arbitrary visuomotor mappings can be learned.

## Disconnection

PFv+o may support arbitrary visuomotor mapping through either or both of two mechanisms. One mechanism could involve computing and storing the mappings within its cortical-BG modules. However, this mechanism cannot account for all the evidence, because PF is insufficient to support learning in the absence of PMd. This finding points to a possible second mechanism, namely, that fast, novel visuomotor mappings may depend on PFv+o providing a route by which visual information reaches PMd. More specifically, it seems likely that the PFv+o lesion interrupted the flow of information from nonspatial visual areas (particularly IT, including perirhinal cortex) to PM cortical-BG modules. PFv+o receives most of the frontal lobe's input from IT, which does not project directly to PM (Pandya and Kuypers 1969; Webster et al. 1994; Carmichael and Price 1996). Thus, a lesion of PFv+o could effectively disrupt the transmission of information between IT and PM. This disconnection could involve corticocortical pathways, projections through the basal ganglia, or both. By cutting off the route of nonspatial visual information to PM and the parts of the basal ganglia interconnected with PM, the ability of PM cortical-BG modules either to acquire or execute mappings would be undermined. Taken together, the direct effects of PFv+o lesions (including the loss of rules and strategies) and the disconnection could account for the devastating deficit in fast, new learning that we observed after PFv+o removal.

Similarly, the ability of PF cortical-BG networks to encode specific mappings and to produce motor outputs could have been compromised by lesions of PM. Such

lesions could deprive PF networks of information about the movements that are being prepared and executed on each trial. The lack of such information, especially at the time of the occurrence or absence of reward, could prevent the encoding of exemplars into PF cortical-BG modules as well as the extraction of higher-order rules based on those exemplars. In addition, PM lesions could disrupt the flow of information from PF cortical-BG modules to the motor output structures of the caudal frontal lobe.

### Long- versus intermediate-term memory

It appears that HS supports specific mappings or exemplars in the intermediate term, pending consolidation of that information into a long-term memory store involving both PM and PF *cortical-BG* modules. We suggest that HS also supports, in parallel, higher-order rules and strategies in the intermediate term pending their consolidation into PF *cortical-BG* modules.

Lesions of HS (Rupniak and Gaffan 1987; Gaffan and Harrison 1989; Murray and Wise 1996), PFdl (Gaffan and Harrison 1989) and PFv+o (described above) cause a deficit in learning novel mappings, but have much less dramatic effects on familiar (i.e., preoperatively learned) mappings. The relative sparing of preoperatively learned mappings could arise in either of two ways. First, preserved performance might be due to repeated presentation of the same stimulus-response mappings over several days. [For the data presented here (Fig. 2A), novel stimuli were presented on one day only, but familiar stimuli reappeared across days.] Preliminary data suggest that this interpretation may apply to the effects of PFv+o lesions (T. Bussey, S.P. Wise and E.A. Murray, unpublished observations). However, there is a second possibility, one that would lead to an even more dramatic preservation of familiar mappings. If the networks storing exemplars in the long term were preserved, then excellent performance on familiar-mapping problems should emerge quickly after surgery, without requiring days of repeated experience with specific mappings. The HS-lesion data support this interpretation (E.A. Murray and S.P. Wise, unpublished observations). In accord with several models of hippocampal function, we suppose that HS functions as the intermediate-term storage network, whereas frontal cortical-BG modules store the same information in the long term.

## Generality and advantages of arbitrary mapping

How general is the capability of this distributed neural network, and is it specific to mapping visual inputs onto action? There is reason to believe that at least part of the network is involved in mapping functions of a more general nature. An interaction of IT with PF supports other types of mapping, for example, when a visual stimulus maps onto another visual stimulus (also known as visual paired-associate learning or arbitrary visuovisual mapping). Transection of the uncinate fascicle causes a dramatic impairment in that task (Eacott and Gaffan 1992; Gutnikov et al. 1997). Using a crossed-lesion disconnection approach, Parker and Gaffan (1998) have also pointed to IT/PF interactions as important in arbitrary mapping. In their study, food rewards mapped onto visual stimuli. Specifically, the arrival or nonarrival of a food-pellet reward served as an instruction cue, signaling which one of two visual stimuli was correct on that trial. These data thus support a more general role for these parts of the network in arbitrary mappings involving visual information, one not restricted to arbitrary visuomotor mapping.

In contrast to its role in arbitrary mapping, IT/PF interaction does not appear to be necessary for other tasks involving visual information, such as visual discrimination and configural learning (Eacott and Gaffan 1992; Gutnikov et al. 1997; Parker and Gaffan 1998). These problems could be solved by an arbitrary mapping mechanism, but they are probably not. We think that discrimination learning is more akin to standard mapping than to arbitrary mapping. Solving the discrimination problem only requires "approach" to a visible target of relatively high affective valence. Some configural learning tasks could have a similar solution. For example, a typical configural discrimination problem might involve AB+ or CD+ versus BC– or AD–, where + indicates a rewarded configural stimulus and – an unrewarded one. This problem could be solved by approaching AB and CD, but avoiding BC and AD. When sample and choice stimuli occur at different times or are in different spatial locations, animals could be biased toward solving the problems through arbitrary mapping (Holland 1991). However, if the features are always temporally and spatially contiguous, as they were in the monkey experiments (e.g., Gutnikov et al. 1997), animals may be biased toward learning these by approaching configurations with high affective valence. Thus, the lack of deficits observed after PF/IT disconnections in either discrimination or configural learning tasks does not rule out the possibility that these structures underlie arbitrary mapping of visual information in some general sense.

Could an arbitrary mapping ability, assuming it is highly general and arbitrary, have some bearing on the search for precursors to human language? Both Lieberman (1991) and Bickerton (1992) have emphasized that, in an attempt to understand the evolution of language, some attention should be paid to capabilities that could be "co-opted" by the language system once it evolved. This view should not be construed as antithetical to current conceptualizations of a language module specific to humans; it holds only that the nervous system would not dispense with an information-processing capacity that could be marshaled in the service of language, merely because it evolved before language. In visuomotor mapping, the relationship between visual stimuli and the actions that they map upon is arbitrary, and so is the relationship of words to the information they represent.

A characteristic of "arbitrariness" in vocal communication is shared by human language and nonhuman primate vocalization (Hockett 1960). Furthermore, "fast mapping" is a key concept in the psycholinguistics of word learning and the learning of other information as well (Markson and Bloom 1997). Of course, both arbitrary-mapping ability and vocalizations in monkeys lack many of the other essential features of language, to say nothing of syntax. Nevertheless, it is of some interest that the regions involved in subserving arbitrary mapping in monkeys (PM/PF anterior to orofacial M1 cortex, BG and HS) are all thought to have an important role in language (Heit et al. 1988; Pickett et al. 1998). The neocortical components of this network are closer, in anatomical terms, to human language areas (e.g., Broca's area) than to the medial motor and auditory areas usually put forward as precursors to human language areas (Sutton and Jürgens 1988). Like human language areas, they are situated on the lateral convexity of the frontal lobe, generally rostral to the orofacial and forelimb representations of the primary motor cortex.

Even if the ability to acquire arbitrary mappings was a precursor to one aspect of language, it would do macaque monkeys no good. The ability of monkeys to acquire arbitrary visuomotor mappings is, in itself, an adaptive advantage. Arbitrary visuomotor mapping allows the ability to select any action within an already learned behavioral repertoire in response to any environmental context that can be detected and discriminated from any other. This rapid, arbitrary mapping provides nothing less that the ability to learn, in the short term, the behavioral significance of stimuli, places, and events, enabling monkeys to respond flexibly to challenging and changeable circumstances.

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