The problem of selective attention is one of the oldest in psychology. William James wrote at the turn of the century, "Everyone knows what attention is. It is the taking possession by the mind in clear and vivid form of one out of what seem several simultaneous objects or trains of thought." This chapter deals with three aspects of attention: (1) the selection of sensory objects, (2) the control of voluntary trains of thought or actions, and (3) the maintenance of the alert state required for attentive processing.

We have chosen to stress those aspects of attention that are closest to the study of neuroscience. Until recently, researchers studying human information processing and neuroscientists have differed in their approaches to attention. The former approach tended to describe attention either in terms of a bottleneck that prevented limited-capacity central systems from overload or as a resource that could be allocated to various processing systems as if they were economic entities. On the other hand, neuroscience, on the basis of animal experiments, emphasized several separate neural mechanisms that might be involved in orienting and maintaining alertness. These two approaches are now being integrated within a cognitive neuroscience of attention. For example, studies of visual search have included a modern neuroscience view of the multi-channel visual system, incorporating separate mechanisms for dealing with color, form, and motion with the cognitive idea of a separate visual attention system needed to integrate information from these channels.

An impressive aspect of current developments in this field is the convergence of evidence from studies using various methods. These studies include performance studies of reaction time, dual-task performance studies, recording from scalp electrodes, and studies of lesions in humans and animals, as well as those using various methods for imaging and recording from restricted brain areas, including individual cells.

Current progress in the anatomy of the attention system can be attributed to two important methodological developments. First, the use of microelectrodes with alert animals has made it possible to gather evidence of increased activity in specific cell populations under conditions of selective attention. Second, anatomical (e.g., computerized tomography or magnetic resonance imaging) and physiological (e.g., positron emission tomography, functional magnetic resonance imaging) methods of studying parts of the brain have facilitated investigations of the localization of cognitive function in normal people. In addition, the use of localizing methods has been coupled with methods for tracing the time course of brain activity in the human subject. This combination provides a convenient way to trace the rapid time-dynamic changes that occur in the course of human information processing.

These methods have been applied with special vigor to three general aspects of attention. The first aspect concerns orienting to sensory events, the part of attention for which human and animal investigations are most closely related. The second is the area of executive control that relates attention to semantic memory (Chapter 56) and language (Chapter 57). The third area is arousal or maintaining the alert state, which is closely related to material presented earlier on sleep.

**ORIENTING TO AND SELECTING FROM COMPETING STIMULI**

**Orienting Aligns Attention with a Source of Signals**

Most everyday scenes are cluttered, containing numerous objects that stimulate our senses at the same time. For instance, in a busy market the hubbub of many superimposed sounds reaches our ears, while
our eyes receive input from innumerable stimuli. We cannot respond to all these objects at once; we cannot pick up every item at one stall in the market simultaneously, nor can we visit every stall at the same time. We also cannot fully perceive all the stimuli reaching our senses at once. For instance, when choosing fruit at a market, we typically inspect the details of each potential purchase one at a time, rather than attempting to judge every fruit simultaneously. Mechanisms of attention address the need for selection that is imposed by the occurrence of multiple concurrent stimuli. These mechanisms allow us to pick out particular stimuli, to control our responses, and to receive fuller perceptual processing.

Covert Orienting Is the Ability to Concentrate Our Attention on a Particular Stimulus without Moving Any Part of Our Bodies

In Chapter 36 we discussed the control of overt orienting in vision through head and eye movements. Orienting can also be achieved by purely internal means, with no external realignments. We can concentrate on particular visual, auditory, or tactile stimuli, without moving our eyes, head, or body around. These abilities are referred to as covert orienting and have been extensively examined with a behavioral technique known as spatial cueing (see Fig. 54.1). Covert orienting can be an automatic response to a sensory event (exogenous orienting) or voluntary control (endogenous orienting).

Spatial Cueing Has Been Used Extensively to Investigate Covert Orienting

In one version of spatial cueing, the subject’s task is to detect the onset of a flash of light, which can appear on the left or on the right, by pressing a single button as fast as possible, without moving the eyes. The critical manipulation is that before the target appears, the experimenter “cues” the person’s attention to one side or another—for instance, with a peripheral flash on that side or by an instruction such as a central arrow that indicates the side where the target is most likely to appear. Typically, the person will be faster to respond to targets on the cued side than on the uncued side even though the eyes do not move from the center. Since no shift of receptors toward the cued side is permitted, the benefit for the cued side is usually attributed to some covert shift in attention toward that side. A common metaphor is that of a mental “spotlight” with limited extent that can be shifted internally, analogous to external shifts of the fovea.

Does the faster target detection on the cued side reflect a genuine effect of covert attention on perception? Subjects might show benefits if they were simply less cautious in responding to the cued side (i.e., prepared to press the button on the basis of less evidence from that side, lowering their “criterion,” to use the technical term). The question of whether covert attention affects sensory perception, and if so at what level, is of long standing and has been addressed in a number of ways with the cueing technique. Instead of using a simple detection task, the subject can be required to make some choice discrimination—for example, to press one of several buttons as fast as possible in response to, say, the shape of the target when it arrives. With such techniques, both the speed and the accuracy of a wide range of discriminations at the cued location can be enhanced. If the effect of the cue were simply to induce a less cautious response to the cued location, faster but less accurate performance should be observed there. In an alternative behavioral method, near-threshold stimuli are presented for discrimination in the absence of time constraints, so that sophisticated signal-detection analyses can be applied to the data. Several such studies have found that perceptual sensitivity is indeed affected by covert spatial orienting.4

One Can Measure Underlying Neural Activity during Covert Spatial Orienting

One of the beauties of the spatial-cueing method is that its simplicity allows spatial orienting to be studied with many converging methods in many different species. For instance, event-related potentials (ERPs) can be measured noninvasively in humans by averaging voltage fluctuations from scalp electrodes in response to particular stimuli over many trials (see Fig. 54.2 and Box 54.1). The same stimuli are presented while the experimenter manipulates whether the subject is cued to attend to them covertly. Several such studies have found that early components of the sensory ERP (those occurring starting around 80 ms after the stimulus onset) can be modulated by covert attention toward or away from the stimulus. Researchers have used the ERP method to show that cueing affects extra striate visual cortex after about 100 ms of input, as shown in Fig. 54.3. The most straightforward interpretation of such findings is that covert attention modulates sensory processing, amplifying the signal for attended stimuli and/or attenuating the signal for unattended stimuli.

Endogenous covert orienting is isolated by using cues that predict the likely target locus (see Fig. 54.1B) but do not appear directly at it (e.g., a central arrow that correctly points to the target side on 80% of trials). Here the aim is to get subjects to shift their covert attention voluntarily toward the side where the target
FIGURE 54.1  (A) Exogenous cue. At left, a cue pulls attention covertly to its location, where the subsequent target is presented and is given priority. (B) Endogenous cue. An arrow cue may inform the person where to place attention. Targets at the cued location will be given priority (valid trial), while those at uncued locations will be responded to slowly (invalid trials).
attentional rather than sensory. For example, a benefit in target detection at the location of an uninformative cue might, in principle, be caused by some sensory interaction between the cue and the subsequent target—for example, an energy summation when the targets appear at the same place as the preceding cue. Such sensory effects can be ruled out by comparison with further conditions. For instance, concurrent peripheral cues on both sides should produce energy summations with a subsequent target comparable to those with single cues, yet they should not produce any shift of attention toward only one side. Such methodological issues are less problematic in studies of endogenous covert orienting, because the stimulus events can be held constant while only the location where subjects expect to see the targets is varied.

The endogenous effects of such expectations should last as long as the subject’s expectancy. In contrast, whereas the exogenous effects of uninformative peripheral cues (e.g., a sudden flash that does not predict target location) usually emerge very rapidly (commencing as soon as the cue appears), the benefit in target detection at the cued location is typically short-lived. Indeed, about 300 ms after an uninformative visual cue, this benefit usually reverses to become a disadvantage for target detection at the cued location. This paradoxical effect has been termed inhibition of return, reflecting the hypothesis that covert exogenous attention is first drawn to the location of the uninformative peripheral event and then moves elsewhere with a bias against returning. The phenomenon is not observed with informative peripheral cues—though it may still apply, but be “hidden” under the beneficial effect of continued endogenous attention to the expected target location. Such differences between the effects of informative and uninformative cues suggest that endogenous and exogenous covert orienting may rely on distinct neural mechanisms. For instance, the superior colliculus may be involved only in exogenous covert orienting.

The studies reviewed so far indicate how covert orienting can be measured in normal human subjects and can influence performance by giving the selected signal priority during performance. They also suggest a distinction between endogenous selection under voluntary control and exogenous selection when a sudden event captures attention.

### Damage to Specific Areas Disrupts Covert Orienting

Suppose there were indeed two distinct “spotlights” of covert attention, one exogenous and one endogenous, with different neural substrates for each. Then, in principle, lesions in one substrate should be able to
Scientists have been measuring brain waves for more than 50 years, ever since Hans Berger showed that electrical activity from the brain could be measured by placing conducting material on the scalp and amplifying the resultant electrical signal so that it could be written out by a pen recorder. His instrument, the electroencephalograph (EEG), has been a standard tool for diagnosing brain damage in the years since.

The EEG did not become suitable for cognitive studies, however, until G. D. Dawson developed a method of averaging the EEG signal following a stimulus. The concept is simple. The stimulus is presented many times to the same subject. At each electrode, the electrical activity is recorded at fixed intervals following the stimulus—say, every 4 ms. The electrical values at each interval are taken from many trials and averaged together so that electrical activity not caused by the stimulus averages to zero and the resultant signal shows only the activity produced by the stimulus. Usually 10 to 100 presentations of the stimulus suffice to produce a reliable potential that reflects characteristics of both the individual brain and the particular stimulus. The waveform can be described by giving the direction (positive or negative) and the delay to the appearance of each of the bumps in the wave (see Fig. 54.2).

To improve the chances of finding an electrical signal from the areas where brain activity has been found with PET or other neuroimaging methods is a complex task. First, a large number of electrodes are used to achieve as thorough a sample of electrical activity from the surface as possible. Second, each electrode's activity is compared to the average activity of all other electrodes. Finally, a subtractive strategy similar to that used in PET studies helps to isolate the effects of a particular mental operation.

For example, one study (Fig. 54.2) measured event-related potentials in tasks similar to those used in PET. One task involves the presentation of visual words. Each trial starts with a fixation cross that serves as a warning signal. During the entire procedure, the subject's eye position is monitored through a TV camera to make sure that the eyes have not wandered from the fixation point. After half a second a word replaces the cross and remains present for another half to one second. Half a second after it is taken away, a prompt tells the subject to press a key to give his or her response. Brain waves are recorded just before the warning signal and continue to be recorded throughout the trial. Later the event-related potentials for a given condition (e.g., words or nonsense strings) are averaged for each subject, and grand averages over all subjects are computed.

Disrupt exogenous but not endogenous covert orienting, while lesions in the other substrate would have the reverse effect. A widely accepted double dissociation of this kind has not yet been demonstrated, although researchers have suggested that parietal lesions impair primarily exogenous, not endogenous, covert orienting in humans, while frontal lesions may do the reverse. Perhaps we should not expect to find a complete dissociation between exogenous and endogenous mechanisms, because these seem most likely to interact as components in a complex network, as do the superior colliculus and frontal eye fields in overt orienting.

Despite this failure to demonstrate a clear double dissociation as yet, evidence indicates that particular lesions can impair only certain aspects of covert orienting. For instance, inhibition of return after uninformative peripheral cues is absent in patients suffering from progressive supranuclear palsy (PSP), but is present in a variety of control groups with cortical lesions. PSP is a progressive degenerative disease, which, judging by postmortem studies, seems to affect primarily the midbrain. This site for the disease coincides with the suggested collicular substrate for exogenous covert orienting and thus for inhibition of return. On the other hand, whereas cell abnormalities are found only in the midbrain of PSP patients at postmortem, positron emission tomography (PET) reveals a diffuse hypometabolism throughout the frontal cortex in vivo, so that linking the effects of PSP on covert orienting to a specific anatomical location is difficult. Within distributed networks, distant areas may interact so that damage to one region can have effects on function elsewhere. For this reason, arguments based on the lesion method need support from converging methods.

Patient Studies Link the Parietal Cortex, Midbrain, and Thalamus to the Component Processes “Disengage–Move–Reengage”

Unilateral parietal lesions have long been associated with clinical deficits of attention (such as the neglect syndrome; see Chapter 56). When the effect of these lesions is analyzed with the spatial-cueing techniques,
FIGURE 54.3 Recordings of scalp electrical activity show larger event-related potentials (see Box 54.1) to targets after cues to the same visual field (valid trials, solid line) than to targets in the field opposite the cue (invalid trials, dashed line). These effects occur within 80–100 ms after presentation of the target. Components of the electrical activity are given a letter (N or P) to indicate positive or negative electrical activity and a time (e.g., P110 = a positive wave that peaks at about 110 ms after the stimulus). LVF, left visual field; RVF, right visual field.

A characteristic deficit in the behavioral markers of covert orienting is found.64 Like normal individuals, patients with unilateral parietal damage show an advantage in visual detection at the cued location, regardless of whether the cue falls on the ipsilesional or contralesional side. This result suggests that the patients can shift their attention covertly to engage it on a new location in either direction. Their abnormality arises specifically on trials where they are cued in the ipsilesional direction and then presented with a target further toward the contralesional side. Responses are then disproportionately slow, and the target is sometimes missed completely. This pattern of results may be due to a specific deficit in disengaging attention from an ipsilesional location once a cue has been perceived there. The “disengage deficit” has been replicated several times across different patients with unilateral parietal damage and the experimental deficit has been successfully correlated with the extent of their everyday attentional difficulties.65

Other groups of patients show other specific abnormalities in spatial cueing. We have already pointed out the PSP patients’ lack of inhibition of return. This group shows another abnormality: the usual advantage in target detection for peripherally cued over uncued locations is slow to emerge. This deficit has been attributed to a slowness in “moving” attention to the cued location, rather than to any difficulty in disengaging or engaging attention once there. Finally, patients with unilateral thalamic damage are slow to detect contralesional targets, regardless of where the cue falls. This deficit can be considered a difficulty in “engaging” attention on contralesional targets.

Thus, a model of covert spatial orienting has three components: disengage–move–reengage. Patient studies suggest that these components are localized to the parietal cortex, midbrain, and thalamus, respectively. This model has had considerable influence, but is not without its critics. As it stands, the model says little about potential differences between exogenous and endogenous mechanisms. The success in precisely localizing the three components has also been questioned. For instance, which region of the parietal lobe is critical for the disengage deficit and whether only parietal lesions can produce it remain uncertain. In addition, the hypothesis of three quite distinct components has been debated.10 For instance, if the disengage operation were truly separate from the move operation, why would the disengage deficit of unilateral parietal patients show up only when they must “move” in a contralesional direction after disengaging?

Despite these potential criticisms, the initial patient studies with cueing techniques provide hope that covert attention can be broken down into component operations, each with a specific function and substrate. The substrates themselves could be localized more certainly by combining different methods, such as relating
Covert Orienting Mechanisms Exist in Other Sensory Modalities

Up to now, we have concentrated on visual covert orienting, but similar mechanisms exist in other modalities, and evidence of strong cross-modal links, as for overt orienting, is emerging. Researchers have found that auditory endogenous attention toward one side tends to be accompanied by visual covert orienting to that side. Subjects in these experiments heard different spoken messages from left and right sides simultaneously. When they had to repeat the words from only one side, their visual sensitivity (for the shape of briefly flashed characters) was greater on that side even though they did not move their eyes. Evidence for audiovisual links in exogenous covert orienting comes from observations that patients with unilateral parietal damage show the characteristic disengage deficit even when an uninformative sound is the spatial cue for a subsequent visual target. Covert orienting has also been present with the spatial-cueing technique in purely auditory experiments and purely tactile experiments, thereby allowing the links between the modalities to be explored in full.

The studies described here show how aspects of orienting can be related to the functions of regional brain areas through studies of lesioned patients and by use of neuroimaging methods in healthy individuals.

Covert Orienting Allows for Attending to Locations and Objects

Overt orienting is clearly a spatially selective operation. Although covert attention has a spatial dimension, it also allows us to select a particular object rather than just a region of space. Thus, covert orienting is a part of the process of searching a visual scene for an object.

A number of behavioral results involving vision demonstrate that covert attention does indeed tend to select separate objects, rather than only predetermined regions of the retinal image. In one experiment, subjects were presented with two distinct objects but in the same two-dimensional space: one object was a box and the other a line that crossed the box. These objects were presented briefly (to rule out eye movements) and followed by a nonsense pattern (to make judgments about them difficult). Subjects had to make decisions about one or two attributes in each display without time pressure. When judging two attributes, the subject might have to compare attributes from the same object (e.g., was the box tall, and where was the gap in it?) or one attribute from each object (e.g., was the box tall, and was the line across it dotted or dashed?).
Results showed that subjects could make two judgments about the same object as accurately as one judgment, but could not judge two attributes from separate objects as well as one attribute. The basic result has now been replicated many times and applies for all the visual qualities that have been examined (color, size, shape, movement, position, and so on), even though these dimensions are thought to be processed in separate visual regions of the brain (see Chapter 52). The implication is that covert attention selects all the properties of an individual object. Somehow a selection for the properties of the relevant object must spread across the diverse neural areas in which each of these properties is coded. Certainly, these results are difficult to explain in a purely spatial model of covert attention, since the two objects were superimposed in roughly the same place, and the attributes that had to be judged were no closer when both were in a single object than when they were in different objects.

The idea that covert attention may operate on segmented objects that the visual system has separated from other parts of the retinal image rather than on fixed positions does not apply only to complex judgments; it has also emerged from spatial-cueing experiments. Peripheral cues in exogenous cueing studies have often taken the form of brightening an outline box (see Fig. 54.1). Attention might be applied to this box itself, rather than to its position alone. In experiments in which the outline boxes were moved after the peripheral brightening, attention was found to track the cued box. In other experiments, the performance of unilateral parietal patients was examined in a covert orienting study with two rotating boxes. Again, it was found that attention may track a moving object. This ability to update the position of an attended object would clearly be adaptive, given that most of our visual environments are dynamic.

Although many studies suggest that visual attention tends to select objects, spatial-cueing effects cannot all be object-based. For instance, when subjects are cued to expect targets in one region of an entire empty display, there is no object for the system to lock onto, and yet covert-orienting effects are still found. Clearly, covert visual attention is both space-based and object-based, although these two are often presented as mutually exclusive alternatives. Both components have been measured behaviorally within the same task (see Fig. 54.1). Researchers have spatially cued normal people to expect a visual target at one end of an object (an elongated rectangle). Visual detection was slower when the target subsequently appeared at the other end of the same object than when it appeared at the cued end, demonstrating the time costs of a purely spatial shift. However, the delay was even greater when the target appeared in another object, the same distance away, thus demonstrating the additional time cost of a between-object shift. Patients with parietal lesions to the right or left hemisphere showed the characteristic spatial disengage deficit in this task, as measured for shifts within an object; that is, they were slower to detect targets on the contralesional side after a cue on the ipsilesional side. In addition, the patients with left-hemisphere damage were found to show an object-based disengage deficit; they were exceptionally slow in detecting a contralesional target when they had been previously cued to the wrong object. The possibility that the left hemisphere may be specialized for between-object shifts of covert attention would be consistent with the proposal (see Chapter 58) that this hemisphere may be specialized for categorical representations of space (e.g., same versus different object) rather than for metric representations (e.g., 10 degrees apart).

**In Visual Search There Is Competition between Targets**

So far we have considered orienting in a simple field with few objects, but important new principles emerge when we consider multiple objects appearing within the same receptive field of a cell (see Fig. 54.5). The two basic phenomena that define the problem of visual search can be illustrated in a simple example. Consider the arrays shown in Fig. 54.5. In a typical search experiment, subjects are asked to report letters in one color (e.g., black letters) and to disregard those in the other color (e.g., white letters). The array is then briefly flashed before the subjects, without any opportunity for eye movements, and the subjects give their report. The display mimics our usual cluttered visual environment. It contains one or more objects that are relevant to current behavior, along with others that are irrelevant.

The first striking point about these experiments with multiple targets is that as long as the distinction between targets and nontargets is based on a simple feature such as black versus white, the difficulty of visual search is a function only of the number of targets. When the targets and distractors differ in a single feature (e.g., a black letter among white letters), the target pops out and responses are independent of the number of distractors.

When subjects have to report features of the targets, or when the distractors share many features with the targets, subjects do not perform as well, because their attention is divided instead of being focused on one feature. When subjects are required to identify simple properties of each object such as size, brightness, orien-
tation, or spatial position, the result is much the same as when they have to identify more complex properties such as shape. One exception is when subjects can rely on detection of a large change in brightness or energy.

A second point is that as long as exposure to the stimulus is brief and the experiment measures the accuracy with which the stimulus is identified, perception of the stimulus input, rather than subsequent short-term storage and response, seems to be the major limitation on performance. For example, interference from processing two objects is abolished if the objects are shown one after the other, with an interval of perhaps a second between them, even though the two responses called for must still be remembered and made together at the end of the trial.

Third, interference is independent of eye movements. Even though the gaze is fixed, it is easier to identify one object in the periphery than two.

An enduring issue is the underlying reason for between-object competition. It has often been argued that full visual analysis of every object in a scene would be impossibly complex. Competition reflects the fact that there is a limit on the capacity for visual identification. Equally strong, however, is the view that competition concerns the control of response systems. Certainly, some response activation often occurs from objects a person has been told to ignore, so that unwanted information is not entirely filtered out. Very probably, competition between objects occurs at multiple levels within sensory input and motor output.

The Neural Basis for Competition Depends on Receptive Fields

If the nervous system had an unlimited capacity to process information in parallel throughout the visual field, competition between objects would presumably be necessary only at the motor output stage, where the number of effectors limits the ability to respond to multiple objects simultaneously. However, there do appear to be important limits on the parallel processing of visual information, and we will consider the nature of these limits and the role of attention in biasing the competition between objects within the visual system before discussing the role of attention in controlling motor output.

Receptive fields can be viewed as a critical visual-processing resource for which objects must compete (see Chapter 28 for explicit definition and discussion of receptive field organization in vision), especially in areas such as V4 and inferior temporal (IT) cortex, where the receptive fields are so large that the neurons typically receive inputs from multiple objects at any given moment. As ever more objects are added to a receptive field in these areas, the information available about any one of them must certainly decrease. This is illustrated in Fig. 54.6 (left), which shows the responses that a typical V4 neuron might give to colored squares. This neuron is selective for color, producing a large response to a red square (50 spikes/s), a small response to a blue square (10 spikes/s), and an intermediate response to a violet square (30 spikes/s). When a neuron in one of these areas is simultaneously presented with a stimulus that normally elicits a large response and a stimulus that normally elicits a small response, the result is usually an intermediate response. For example, the neuron in Fig. 54.6 produces a response of 30 spikes/s to the simultaneous presentation of a red stimulus and a blue stimulus. If this cell's computational role is to signal the presence of red, then this intermediate response might be a useful signal that half of the objects within the receptive field are red. However, the neuron's response is ambiguous, because the same firing rate is produced for a single violet square and for the combination of a red square and a blue square.

This ambiguity may be reduced by linking objects and their features to specific retinal locations. For example, if a neuron has a small receptive field, it is likely to contain only a single object and can unambiguously

VII. BEHAVIORAL AND COGNITIVE NEUROSCIENCE
signal that the feature for which it is sensitive is present at a specific location. However, if all visual neurons had small receptive fields, it might be very difficult to recognize that a given stimulus is the same object no matter where in the visual field it is presented. This potential difficulty may explain why neurons in high-level visual areas tend to have large receptive fields.²⁷

Although the coding of spatial location in the dorsal stream has been emphasized,²⁸ it is important to note that ventral-stream areas such as area V4 and IT cortex also code stimulus location, albeit coarsely. Specifically, although the receptive fields in these areas are large, they are not infinitely large and they are not homogeneous. Thus, it is possible at least in principle to localize an object on the basis of the pattern of responses across many ventral-stream neurons, just as an object’s color can be determined very precisely from the pattern of activation it elicits in photoreceptors that are broadly tuned to red, green, and blue (see Chapter 28). However, this sort of coarse coding tends to break down when multiple objects are presented simultaneously, placing limits on the effectiveness of processing the entire visual field in parallel.

Figure 54.6 (right) illustrates the role that attention appears to play in resolving the ambiguities that occur when two or more objects compete for a neuron’s receptive field. Specifically, it has been proposed that an attended object will gain control of a neuron such that the neuron’s output reflects only the features of the attended object and not the features of the ignored objects.²⁹,³⁰ For example, if the red and blue squares are presented simultaneously inside the receptive field of the neuron illustrated in Fig. 54.6, but only the red square is attended, then the neuron’s output will be the same as if only the red square were present inside the receptive field (i.e., 50 spikes/s). Similarly, if the
blue square is attended, the neuron’s output will be the same as if only the blue square were present inside the receptive field (i.e., 10 spikes/s). In this manner, the competition between the red and blue squares is biased in favor of the attended square, allowing the neuron’s output to unambiguously signal the color of that square.

This proposed role of attention in regulating competition between stimuli leads to an interesting prediction: If attention serves to regulate competition between objects for access to the receptive field, then attention should have little or no effect when competition is eliminated by presenting only one object inside the receptive field. This is illustrated in the bottom two panels of Fig. 54.6 (right), which show the predicted effects of attention when the red square is inside the receptive field and the blue square is outside. In this situation, the red and blue squares do not compete for control of the neuron, and so the neuron’s response to the one item inside the receptive field—the red square—should be unaffected by attention. This prediction may seem surprising, but it has now been verified in two separate experiments, as will be described in the next section.

Top-Down Control Is Required to Coordinate Selection in Multiple Systems

Several investigators have proposed that the selection of objects by attention is based on a top-down “attentional template” that specifies the characteristics of the objects that are relevant for the current task. For example, if you are searching for a friend who is wearing a red cap and is sitting somewhere on the left side of a crowded movie theater, your attentional template might specify “red” and “left.” The attentional template is then used to coordinate selective processing across the multiple visual areas that are responsible for coding different features, allowing inputs that are red and on the left to have a competitive advantage for the control of perception and action. The concept of an attentional template may also help us to understand the relationship between spatial selection and object selection, because an object’s spatial location can be considered one of its features. Indeed, there appear to be similarities between space-based and object-based attention in addition to the differences described earlier in this chapter.

Visual Selection Based on Spatial Location

The proposal that attention regulates competition between objects for access to neural receptive fields (Fig. 54.6) has been supported by experiments in which neural activity in monkeys was recorded while they attended to one of two locations. In one study of cells in area V4 and in IT cortex, the monkeys performed a discrimination task on target stimuli at one location in the visual field, ignoring simultaneously presented distractors at a second location. The target location for a given trial block was indicated to the monkey by special instruction trials at the beginning of each block, and the monkey was required to remember which location to attend throughout the remainder of the block; that is, spatial attention was controlled in a purely top-down manner on the basis of information held in working memory (see Chapter 59). When the attended-location target and the ignored-location distractor were both within the receptive field of the cell being recorded [as in the top two panels of Fig. 54.6 (right)], the neuron’s response was determined primarily by the target stimulus and not by the distractor stimulus. In other words, the neurons responded as though their receptive fields had “shrunk” around the target. However, when either the target or the distractor was placed outside the receptive field [as in the bottom two panels of Fig. 54.6 (right)], so that they were no longer in competition for control over the neuron being recorded, attention no longer had any effect on the neuron’s response. Thus, attention appears to provide a top-down bias over the competition that occurs when multiple stimuli fall within a receptive field.

Although attention-related modulations of neuronal responses may be observed even when only a single stimulus is placed inside the receptive field, every study that has ever compared configurations with one versus two stimuli inside the receptive field has found larger attention-related modulations when two stimuli were presented inside the receptive field. In addition, attention-related modulations appear to be more easily obtained in areas with larger receptive fields, such as area V4, area MT, and IT cortex. For example, with one exception, experiments with monkeys have failed to find consistent effects of spatial attention on neural activity in area V1, where the receptive fields are too small to contain both an attended stimulus and an ignored stimulus. Neurophysiological studies in human subjects have similarly failed to observe attentional modulations of responses in area V1, although substantial modulations have been observed in higher level areas where the receptive fields are presumably larger. Receptive fields are also small in area V2, and one study of V2 neurons found attentional modulations only in neurons whose receptive fields were large enough to contain both an attended and an ignored stimulus. By the stage of inferotemporal cortex, receptive fields are so large that it is almost impossible to place one stimulus inside and another outside the receptive field, leading to attentional modulations in
almost every neuron. These results suggest that target selection is a multistage process, working over small spatial ranges in a small subset of neurons at early stages of the visual system and operating over the entire visual field in the majority of neurons at late stages.

To summarize, spatial attention can strongly modulate neural responses in visual cortex, but these effects are found primarily when multiple stimuli compete for access to a given neuron. Because receptive field sizes increase as information travels anteriorly through the visual system, the probability of multiple stimuli appearing inside a given receptive field also increases at the more anterior areas, which should lead to an increase in the proportion of neurons that are influenced by attention in these areas (although this has never been directly quantified). It might seem strange that the effects of attention are limited to a subset of visual areas and to a subset of the neurons within an area for a given stimulus array. However, it would be inefficient for the visual system to code only a single object at any given moment and suppress the information from the rest of the visual input. Indeed, with the exception of certain neurological patients, most people report that they see the entire visual world rather than a single object at a time, even when attention is strongly focused. This aspect of experience may be the result of the many neurons within the visual system that are not influenced by attention at a given moment.

**Mechanisms of Spatial Biasing**

Although the synaptic mechanisms mediating the gating of V4 and IT responses are not known, anatomy dictates that they fall into one of two classes. In the first class, spatial bias signals control which specific subset of a given cell’s inputs causes the cell to fire, whereas in the second class, the bias signals control which specific cells in a population are allowed to fire. In other words, attention-related modulation of neural activity can be achieved by gating the inputs to individual neurons or by gating entire neurons.

If the gating of V4 and IT responses occurs as a result of an external signal that biases competition in favor of the attended location, some evidence of this signal should be discernible. A possible signal of this nature has been observed in a recent study of spatial attention in areas V1, V2, and V4. In this study, V2 and V4 cells showed a sustained elevation of their baseline (prestimulus) firing rates when the monkey’s attention was directed inside rather than outside their receptive fields. The elevation in firing rate can be seen by comparing the firing rates when attention is directed to location 1 with those when attention is directed to location 4 in Fig. 54.7.

![Possible attended locations](image)

**FIGURE 54.7** (Top) Location of attention within the receptive field; (bottom) the typical prestimulus firing rates in area V4 as a function of the position of attention relative to the receptive field of the cell being recorded. Baseline firing rates are highest when attention is directed to the center of the receptive field and decline as attention is directed progressively farther away. This effect may reflect the attentional template that indicates which location is to be attended.

The elevation in tonic neural activity observed when the monkey attended inside the receptive field could reflect the attentional template that specifies which location is to be attended. First, this elevation was present at the beginning of each trial, before any stimuli had appeared, which is consistent with it being a control signal rather than a sensory response. Second, because the only information about where to attend was given to the animal minutes earlier, the elevation of baseline activity must reflect top-down information about the to-be-attended location that is held in working memory. Third, this elevation of baseline neural activity was absent in area V1, where attention was found to have no effects whatsoever. These factors suggest that the elevation of baseline activity reflects an attentional template, although it is not yet known how this signal
ultimately influences stimulus-elicited neuronal responses.

Receptive fields in area V4 are moderately large, and the attentional template must have a higher resolution than the diameter of a V4 receptive field to be effective (after all, the animals are able to attend to a target outside the receptive field while ignoring a distractor that is also inside the receptive field). Consistent with this proposal, the attention-related elevation of baseline firing activity appeared to have high spatial resolution. Specifically, when attention was shifted to different regions within the same receptive field, the baseline firing rate varied according to the distance between the attended location and the center of the receptive field (see Fig. 54.7). Thus, visual cortex appears to contain tonic attention-related signals that have a spatial resolution finer than the diameter of V4 receptive fields.

Summary

Orienting to places in the visual field is the aspect of attention that has been studied most extensively in cognitive neuroscience. Much orienting is done overtly by eye movements, but it is also possible to attend to things within a single fixation by covert orienting of attention. When many objects appear together in the visual field, they are in competition for the processing within each cell’s receptive field. Recordings from cells in the object pathway indicate how this competition is influenced by attention, which serves to shrink the effective receptive field of the cell around the attended object.

EXECUTIVE CONTROL OF BEHAVIOR

All normal people have a strong subjective feeling of intentional or voluntary control of their behavior. Asking people about goals or intention is probably the single most effective way to obtain information that is predictive of their behavior during problem solving. The importance of intention and goals is illustrated by observations of patients with frontal lesions or mental disorders that cause disruption in either their central control over behavior or the subjective feelings of such control.

This section first reviews efforts to develop a cognitive model of executive control and consider how experimental methods can be used to explore conditions under which executive control will operate. We then examine neuroimaging studies that incorporate these cognitive methods to explore the anatomy and circuitry of executive control. Finally, we consider evidence from lesion and developmental studies to further define which areas are involved in executive control.

A Cognitive Model Specifies the Conditions for Executive Attention

Norman and Shallice have created one representative model of executive control that assumes multiple, insoluble subsystems of cognitive processing (Fig. 54.8). These multiple subsystems interact to coordinate goals and actions and are controlled by two qualitatively different mechanisms. The first level of control operates via contention scheduling. The contention-scheduling mechanism corresponds to routine selection—for example, the selection that might be involved in selecting a red stimulus among other visual items, as in the visual search task described previously. When the situation is novel or highly competitive (i.e., requires executive control), a “supervisory system” intervenes and provides additional inhibition or activation to the appropriate schema for the situation (see Fig. 54.8). The supervisory system has access to the overall representation of the environment and the goals of the person, unlike the contention-scheduling mechanism, which involves only competition among subsystems.

Norman and Shallice argued that the supervisory system is necessary for five types of behaviors or situations in which the routine or automatic processes of the contention-scheduling mechanisms are inadequate and the executive control of the supervisory system is required:

1. Situations involving planning or decision-making
2. Situations involving error correction
3. Situations in which the response is novel and not well learned
4. Situations judged to be difficult or dangerous
5. Situations that require overcoming habitual responses

In the following sections, we discuss some evidence of brain systems involved in situations calling for executive control.

Executive Attention Works by Means of Inhibitory Control

In the Norman–Shallice model, contention scheduling works via local inhibition of competing schemas. In the last section visual-subprocessing systems were viewed as selectors of stimuli that were competing locally for receptive fields, which are a critical resource. In addition, it was suggested that the competition be-
tween stimuli can be biased by a top-down mechanism that selects objects that are important to the current behavior or goal. Like the supervisory system mechanism of the Norman–Shallice model, competition for control of behavior appears to be resolved at local sites by the relative amplification (involving both increases in the selected objects and decreases in the competition) of the selected competitor.

As in Visual Search, Multiple Targets Interfere with Executive Control

To understand the mechanisms of supervisory control, we must have reliable experimental techniques for causing executive control to be employed. A well-established principle of cognitive psychology is that interference will occur whenever two tasks require access to the same underlying systems. Interference between tasks that use quite separate input and output pathways has been taken as a method for measuring central attentional control.

In an early series of experiments, subjects were presented with two separate streams of information, one to each ear, and were required to rivet their attention to one stream by saying each word heard on the ear aloud as quickly as possible. This task is called shadowing and requires very intense attention to the message being repeated. Most information from the nonshadowed ear is lost. In a basic experiment, Treisman and Geffen asked subjects to tap a key whenever they heard the word "tap." When the word was presented in the attended ear, subjects tapped the key close to 100% of the time, but when the word was presented in the unattended ear, they almost never did. On the other hand, significant events presented to the unattended ear or presented visually during shadowing can still activate the memory trace of a previously presented item (priming) or produce a skin response indicating emotional arousal.

When the subjects were not required to shadow one of the two messages and were instead required to monitor a number of channels to detect a target, the number of channels information was coming from did not make a difference. For example, subjects could attend to a tone coming to the left or right ear and at the same time monitor for visual and tactile signals. Subjects appeared to have a nearly unlimited capacity to monitor various sensory channels as long as no targets were actually presented. This contrasted sharply with the results obtained with shadowing. Work by Duncan reconciled the shadowing and monitoring studies. He showed that attention could be summed to one of several input channels with very great effectiveness, but when a target occurred on one channel, processing of targets on any other channel dropped dramatically. In other words, major interference was found between items selected for focal attention (targets).

PET Studies Localize the Functional Anatomy of the Executive Network

Tasks requiring supervisory control are severely affected by lesions of the frontal lobes. Because these tasks are quite complex with many components and because the frontal lobes constitute a large part of the brain, neuroimaging methods have been used in an attempt to localize supervisory functions.

Neuroimaging allows examination of brain metabolism during task performance. Many studies involving the detection of targets or the resolution of conflict between targets have found that activation occurs in a midline frontal area called the anterior cingulate. Although this area alone is probably not responsible
for executive attention, it is important to consider the efforts to link executive control to anatomical areas. We turn to a consideration of two tasks that have been used to accomplish such linking: the generate-uses task and the Stroop task.

In the generate-uses task, subjects are asked to name a use for a visually or aurally presented noun as quickly as possible (e.g., hammer → pound). In the control condition, subjects read the word name aloud. Blocks of 40 trials, during which blood flow is averaged, are presented. A subtractive strategy is then used in which the blood flow found in the read-aloud task is subtracted from the blood flow in the generate-uses task. The assumption is that this strategy subtracts away the stimulus and response process common to the two tasks and leaves intact the additional activation involved in generating an association. The subtraction of repeat from generate reveals three areas of activation: the anterior cingulate and two left lateral areas, one in a frontal area anterior to Broca’s area and one in Wernicke’s area. The lateral areas were near classical language areas, so that it seems more likely that the midline anterior cingulate area is involved in attention to the task.

Subjects are then given the same list in a new order and asked to generate the same use. Practice on the same list reduces the mental effort needed to perform the task, and reaction times drop markedly. As the task becomes more automatic, the Normal and Salличе model would suggest that a “schema” formed after practice would trigger when the stimulus was presented. The supervisory system would then not be necessary. Raichle et al. had subjects perform the generate-uses task while undergoing PET scans and found the expected activation of the anterior cingulate. In addition, Raichle also had subjects practice the same list repeatedly, generating the same appropriate use for each word until the list was thoroughly learned. After the extended practice, subjects again were scanned. This time, the anterior cingulate and the left lateral activation were gone; instead, there was increased activation in the anterior insula, which now displayed activation similar to that found when a word was read aloud. Following their practice, Raichle et al. had subjects generate a use for a new, unpracticed list. Again, the anterior cingulate and left lateral areas were active. Thus, the anterior cingulate is active when the supervisory system is necessary for appropriate behavior, as in the Norman–Salличе model, and the anterior cingulate is inactive when the supervisory system should be inactive and the contention-scheduling mechanisms active. Because both the cingulate and the lateral cortex behaved in the same way with practice, whether they are both part of the supervisory attention system cannot be determined. However, the lateral cortex seems to be rather specific to language tasks, so it may merely be increased in activation when attention is directed to language.

The Stroop tasks involve naming the color of ink in a word that can be congruent (matching the color of the ink in which it is printed; e.g., the word red in red ink), neutral (non-color-related; e.g., the word lot in red ink), or incongruent (a mismatch of the word with the color of ink in which the word is printed; e.g., the word red in blue ink). One analysis of the components of the Stroop task can be outlined as follows: (a) remember the instructions for vocalizing the ink color, (b) attend to the visually presented stimulus, (c) determine the ink color of the word, (d) inhibit the naming of the word, and (e) make the appropriate response (being careful not to name the color word presented). Anterior cingulate activation while carrying out such activities is confirmed by four separate Stroop (or Stroop-like) studies (see Fig. 54.9).

As described earlier, the Norman–Salличе model suggests five situations in which the supervisory system is necessary for appropriate behavior or successful execution of a task or goal. The first of these situations involves internally planned, or voluntary actions. Using PET, Passingham and his colleagues have shown statistically significant increased activation in the anterior cingulate in voluntary, planned arm and hand movement compared to resting, learned sequence movements and fixed-sequence movements. Two other situations in which the Norman–Salличе model holds the supervisory system to be necessary are those that require overcoming habitual responses and those where responses are not well learned or contain novel sequences of actions. The generate-use and Stroop tasks fit this profile. Another situation in which the Norman–Salличе model necessitates a supervisory system involvement is in error correction or detection (troubleshooting). Studies involving error detection are considered in the next section.

**ERPs Can Be Used to Investigate the Time Course of Attention**

To perform a supervisory function, a brain area must influence widely distributed parts of the brain where computations related to the task are performed. Anatomical studies suggest that the anterior cingulate, like many brain regions, has close contact with many other cortical areas. One interesting feature of the cingulate is that connections to parietal and prefrontal cortex alternate in a columnar organization. The cingulate has particularly strong anatomical connections to lateral frontal areas involved in word recog-
nition and posterior parietal areas involved in orienting.

Researchers made efforts to trace the dynamics of these interactions by using ERPs (Fig. 54.10 and Box 54.1). Determining the generator of electrical activity from a scalp distribution of such activity can be a difficult task. However, when the generator is identified by PET or fMRI studies, researchers can more easily evaluate whether the scalp distribution could come from that generator (see Heinze et al. [38].

FIGURE 54.9 In the Stroop task subjects are asked to name the ink color in which a word is written. In the incompatible condition the words are different ink colors (e.g., the word red in blue ink). In a neutral condition, words are unrelated to color, and in a compatible condition they are the same color as the name of the word. PET experiments have been done in which blood flow in the relatively easy neutral or compatible condition is subtracted from blood flow in the more difficult compatible condition. As shown in the diagram, areas of the left and right cingulate gyrus show stronger activation in the incompatible condition. This has supported the idea that this brain area is related to the resolving of conflict and thus a part of an executive attention network.

FIGURE 54.10 Subjects are asked to attend to stimuli in one visual field. PET studies (large circle) show activation of the fusiform gyrus opposite to the attended visual field. ERP studies show that the best-fitting dipole generators (at different times) cluster around the PET activation area. The ERP's generators at 110–130 ms are thought to be most closely related to the attention effect. After Heinze et al. [38].
for an example of this methodology). The algorithms for relating a generator to the scalp distribution work best when fewer generators are involved. In more complex tasks, it is necessary to use a control condition that allows a subtraction, thus reducing the number of generators active at any time. For example, by subtracting reading aloud from the generate-uses task, researchers can remove sensory and motor sources, allowing a better chance of localizing the sources unique to generating the association.

Making an error gives rise to a negative scalp potential. This negative potential was investigated in an effort to isolate the brain areas generating it. When human subjects were aware of making an error in speeded tasks, recordings of scalp ERPs showed a very strong negativity in a localized area over the mid frontal scalp. Further analysis using the BESA algorithm showed that this error negativity most likely came from the anterior cingulate. Errors can be either slips—incorrect execution of a motor program—or mistakes—selection of an inappropriate intention. The finding that error negativity comes from one of the brain areas involved in the generate-uses task supports the idea of a supervisory system concerned both with response selection and with monitoring the correctness of a response.

Event-related potentials have been used to study the generate-uses task described previously and have provided evidence of an anterior cingulate activation starting about 170 ms after visual presentation of a word. This activation was presumably related to some kind of focal attention. The cingulate activation continued and was joined after 50 ms by a left frontal activation.

This experiment took a further step in replicating the PET results. Subjects generated uses for the same list several times. The left frontal and cingulate activations tended to disappear after practice, but the activations were restored when a new list was presented or when subjects were required to generate a new use for the practiced words (Fig. 54.11). This finding from ERPs fits well with similar results obtained with PET and thus supports the general approach of combining the two methods.

Executive Attention Works by Altering Neuronal Activity in Other Areas of the Brain

These PET and ERP experiments suggest that the anterior cingulate, together with related areas involved in executive attention, is active during tasks that require some thought. Such activity is reduced or disappears as tasks become routine—for example in reading words aloud or after practice generating the same use.

What is the cingulate activation actually doing? According to one analysis, the cingulate is involved in producing the local amplification in neural activity that accompanies top-down selection of items. It is easiest to understand this function in the domain of processing words. It is well known from cognitive studies that a target word is processed more efficiently after presentation of a word that retrieves related information; for example, subjects can pronounce or classify the word “doctor” more rapidly after receiving the related prime “nurse.” A portion of this improvement occurs automatically because the prime word activates a pathway shared with the target. However, another portion of the activation is top-down because the attention to the prime leads the subject to expect a particular type of target. Under some conditions, the prime is not attended so that its influence on the target must be primarily bottom-up. Some conditions where the prime will be unattended are when it is followed by a visual
mask that prevents subjects from being aware of the identity of the prime; they thus cannot pay attention to its meaning. Also, if the prime does not predict the type of target (low validity), there is little incentive to attend. If the prime is of high validity or subjects are instructed to attend to the prime or to use the prime to think of another category (e.g., animal prime means to expect body parts), top-down or attentional effects dominate. When an ambiguous target is used (e.g., palm can be a tree or body part), top-down priming effects tend to be limited to only one meaning but masked primes that are processed automatically tend to activate both meanings. Executive attention in usually thought to be responsible for the top-down effects by providing a boost to items associated with the expectations indicated by the prime.

Anatomically, these effects may involve the cingulate in contact with areas of the left lateral and posterior cortices that seem to be involved in understanding the meaning of a given target word. Indeed, the time courses of activation of the cingulate (170 ms) and the left lateral frontal (220 ms) cortex during the generative uses task support the view that attention interacts with the semantic activation pattern.66

In addition, cingulate activation may be involved in the voluntarily reactivation of brain areas that can also be driven automatically from input. For example, feature analysis of visual targets appears to involve right lateralized posterior parts of the brain. When subjects are instructed to examine a feature voluntarily, similar electrode sites are activated, but much later. By increasing activation of the brain area that performs a specific computation, one can change the time course of the organization of the component operations.

Frontal Structures Are Important in Executive Function

Lesions of the frontal lobe often produce disorganized or incoherent behavior.56,57,69 The dysexecutive syndrome that follows closed head injury, stroke, or degenerative disorders of frontal structures is characterized by the loss of the ability to plan coherently, to solve problems, or to organize the routines of daily life. Patients suffering from this syndrome have difficulty with problem-solving tasks such as the Tower of Hanoi, in which planning ahead is an important component.

There has been some controversy about the importance of cingulate involvement in the loss of executive function. Large lesions of the frontal midline produced by strokes can have devastating effects on human behavior. Damasio,70 who has studied many of these patients, suggests:

Before leaving the subject of human brain lesions, I would like to propose there is a particular region in the human brain where the systems concerned with emotion, attention and working memory interact so intimately that they constitute the source for the energy for both external action and internal action, thought, animation, and reasoning. This fountain head region, is the anterior cingulate cortex, another piece of the limbic puzzle.

This observation comes from patients who show akinetic mutism after strokes in the general area of the cingulate. These patients can orient to events but initiate little in the way of spontaneous behavior. One woman studied by Damasio recovered and when Damasio asked her what was going on during the time she suffered from the brain injury and why she didn’t initiate any behavior, she said, “Well, nothing ever came to mind.” The fact that there can be recovery after a brief period of akinetic mutism suggests considerable distribution of executive function both within the cingulate and in other structures related to it. Considerable work with cats and monkeys that have lesions of the cingulate71,72 produced results similar to those of Damasio’s studies. Both cats and monkeys with extensive anterior cingulate lesions show the same failure to initiate voluntary behavior or movement.

In contrast to the profound effects of massive cingulate trauma, more discrete cingulate lesions that have been induced to treat patients with pain or anxiety give little evidence of the gross loss of conscious control reported in the studies cited above.73 Perhaps this lack of evidence relates to the various subareas of the cingulate that might be involved in different aspects of attention. As shown in Fig. 54.10, even a single task seems to activate different regions of the cingulate in different studies. What is not yet known is whether these are merely errors introduced by different laboratories, subjects, and exact procedure or whether they indicate that parts of the cingulate are differentially influenced by task demands. It is also likely that the cingulate works in close connection with the supplementary motor area and basal ganglia, which may also play a role in executive attention.

Summary

A higher level executive attention system appears to be involved when processing requires careful planning, mediating conflict, or handling novel stimuli. Our understanding of the brain networks involved in this higher form of executive attention is not far advanced. Many tasks that involve conflict, response selection, and/or response monitoring appear to activate
the frontal midline, sometimes in conjunction with more lateral frontal cortical areas and the basal ganglia. In generating the use of words, medial and lateral frontal areas show activity within the first 200 ms after input. The midfrontal activity suggests that attention is used in generating and selecting word meanings. As the act of generation becomes automated with practice on the same list and requires little or no attention, the midfrontal activity drops away. Lesions of the frontal areas often produce disorganization of behavior, and large-scale lesions of the frontal midline can produce a complete loss of the initiation of spontaneous behavior.

ATTENTIONAL STATE

At the beginning of this chapter, we described two aspects of attention. The first aspect involves selection and cognitive control, and the second involves the maintenance of an attentive or alert state. Both of these attentional functions depend on input from the monoaminergic transmitter systems. Many basic properties of these systems are described in Chapter 8. As was discussed in Chapter 46, these systems are important in the diurnal rhythm and in the distinction between sleep and wakefulness.

In this section, we focus on the noradrenergic locus ceruleus (NE-LC) system. The other widely projecting modulatory systems (see below) may also have important roles in the regulation of attentional state and alertness, but to date the most evidence in this regard is available for the NE-LC system.

Monoamines Affect Cortical Function

Neurons located in the brainstem are the origin of most of the monoaminergic systems: acetylcholine (ACh), norepinephrine (NE), dopamine (DA), and 5-hydroxytryptamine (5HT). In addition, important modulatory systems that employ ACh or histamine originate in the basal forebrain and hypothalamus, respectively. The anatomy of these systems has been described in Chapter 49. One important attribute of all of these systems is their very widespread projection anatomy. Indeed, these systems project more globally throughout the CNS than is typical of other brain systems (e.g., thalamocortical systems). These systems behave as modulators in that they modulate the responsivity of target (postsynaptic) neurons. Classical neurotransmitters typically simply excite or inhibit neuronal activity. Good examples of nonmodulatory, or “classical,” neurotransmitters are glutamate [Glu; especially when acting at non-NMDA (N-methyl-D-aspartate) ionotropic receptors] and γ-aminobutyric acid (GABA; especially when acting at GABA_A receptors). In contrast, a neuromodulator may have little effect on its own but act principally by altering the response of neurons to other inputs (often mediated by classical transmitters). A variety of modulatory effects have been found both for these monoamines and for other transmitters acting at certain receptors (see Chapter 9).

NE Modulates Glu and GABA Responses

The cerebellum has been used as a model system for studying the effects of NE on neurons because (i) LC neurons send NE projections into the cerebellum, and (ii) the anatomy and physiological properties of the cerebellum are well understood (see Chapter 35). Several groups have described modulatory effects of NE on the activity of the principal output neuron of the cerebellar cortex—the Purkinje cell (described in Chapter 35). Moises and colleagues (1981) have found that NE, either directly applied from a micropipette or from stimulation of the LC afferents to the cerebellum, increases responses of Purkinje neurons to both excitatory and inhibitory inputs. In both cases, NE acts to increase the Glu- or GABA-evoked response relative to the basal activity of the cell. NE modulation of neuronal responsiveness is found in many target areas, including the cerebral cortex. The obvious implications for signal processing have led to the proposal that NE may enhance the signal-to-noise ratio—or signal-processing capacity—of neurons. It is interesting that the relative augmentation of Glu and GABA responses in the cerebellum and cerebral cortex is mediated by distinct NE receptors, with β-adrenoceptors implicated in the augmentation of GABA responses and α-adrenoceptors linked to the augmentation of Glu responses.

Neurons That Use Neuromodulators as Chemical Transmitters Have Specific Patterns of Activity

The specific patterns of activity of neurons that use neuromodulators presumably reflect times that they release their neuromodulator chemicals onto postsynaptic neurons in the thalamus, in the cerebral cortex, and elsewhere. Most important in this regard is the relationship between behavior and the modulatory influence of these systems; this relationship has been studied by recording impulse activity of the various modulatory source neurons in unanesthetized behav-
ing animals. These and other relevant findings are discussed in this part of the chapter.

**Noradrenergic LC Neurons Modulate Activity**

Tonic LC activity varies with behavioral state. Aston-Jones and colleagues\(^{79}\) found that spontaneous LC impulse activity is fastest during waking, slower during slow-wave sleep, and virtually silent during paradoxical sleep (PS). A subpopulation of LC neurons with similar activity has been reported in cat\(^{80}\) and in unanesthetized monkeys.\(^{81-84}\) Noradrenergic LC neurons are more difficult to study in some species (e.g., cat, rabbit) because the NE neurons are interdigitated with non-NE neurons within the LC nucleus. For this reason, rats and monkeys, whose noradrenergic LC nucleus is more homogeneous, are the species of choice in such studies.

Neurons of the LC also are strongly activated in association with orienting responses. In both rat\(^{85}\) and monkey,\(^{81-83}\) the highest phasic discharge rates observed for LC neurons are consistently associated with spontaneous or evoked behavioral orienting responses. LC activity associated with orienting behavior is most intense when ongoing preprogrammed behavior (e.g., sleep, grooming, or consumption) is suddenly disrupted and the animal orients. Thus, “spontaneous” bursts of LC activity, termination of preprogrammed low-vigilance behaviors, and increased attentiveness are closely connected (see below).

LC neurons exhibit polymodal sensory responsiveness. In addition to fluctuations in tonic activity, LC neurons in unanesthetized rats and monkeys are responsive to a variety of environmental stimuli.\(^{79,81,85}\) In rats, LC neurons exhibit phasic short-latency (15–50 ms) activation following unconditioned auditory, visual, somatosensory, or olfactory stimuli. Responses are most consistently evoked by intense, conspicuous stimuli.

A particularly salient characteristic of NE-LC neurons is that stimuli effective in eliciting LC responses also disrupt ongoing behavior and elicit a behavioral orienting response in both rats and monkeys. The largest responses are elicited by stimuli that cause an abrupt transition from sleep to waking, with associated behavioral orientation. Also, LC responses to stimuli that do not interrupt grooming or drinking are reduced, whereas stimuli that disrupt such activity and generate orienting behavior elicit strong LC responses.\(^{85}\) Thus, in rats, as in monkeys, sensory-evoked LC impulse activity is strongly correlated with behavioral responses, and in both species LC responses are associated with behavioral disruption and reorientation.

**Monkey LC Neurons Can Be Selectively Activated by Meaningful Stimuli**

LC neurons in behaving monkeys readily become conditioned to respond to low-intensity stimuli when the stimuli are made meaningful by serving as CS + (target) cues in operant tasks.\(^{85,86,87}\) In experiments, monkeys performed a visual discrimination task. First, they viewed a video monitor that presented a central fixation point that the animal was required to look at to ensure attentiveness to the task. After successful visual fixation of this point, a vertical or horizontal bar was presented at the center of gaze. One was chosen to be target (CS+) and the other was non-target (CS−). Monkeys had to release a lever after CS+ stimuli to receive a drop of juice, but to continue depressing the lever after CS− stimuli. As seen in Fig. 54.12, CS+ stimuli consistently activated all LC neurons examined. These same stimuli presented before conditioning, or similar intensity unconditioned stimuli, elicited no response from LC cells. Interestingly, these responses were selective for CS+ stimuli, as other task stimuli (including CS− stimuli) did not activate LC neurons. These cells also were not activated during lever release outside of the task, indicating that these LC responses were not primarily motor in nature. The latencies of LC responses to target cues were relatively short (~100 ms onset for an overlearned contingency) and preceded behavioral responses by ~200 ms. Moreover, the latencies of response for LC neurons and lever releases were significantly correlated over a number of trials, so that shorter LC responses were associated with shorter behavioral responses to the same cues. These findings indicate that LC target responses could facilitate behavioral responses to target cues.

These responses of LC neurons to target stimuli were not driven strictly by sensory attributes, as either vertical or horizontal bars could evoke responses, depending on which was conditioned to be the target stimulus. Recordings during reversal training further confirmed that these LC responses were independent of sensory attributes.\(^{87}\) In reversal training, the former CS+ cue is conditioned to be CS−, and the former CS− stimulus is conditioned to become CS+. As shown in Fig. 54.12, such reversal of cue meaning causes LC cells to reverse responsiveness; the cells become selectively activated by the new target cue and lose responsiveness to the old target (new nontarget cue). These data indicate that phasic LC activation in this task is specifically related to the meaning of the stimuli, not to their physical attributes.

The results of experiments with conditioned stimuli show a close relationship between phasic activation of LC neurons and behavioral responding to meaningful
sensory cues. These results extend those found earlier in unconditioned animals in which conspicuous stimuli that evoked behavioral orienting responses were most effective in activating LC cells. These findings indicate that LC responses can readily be conditioned to salient stimuli, an important factor in understanding the role of this system in attentional processing.

**Tonic LC Activity Varies with Attentional State**

Very low LC activity is accompanied by drowsiness (as noted earlier in the chapter) and cessation of task performance, whereas levels of tonic LC activity during alert task performance vary between "intermediate" and "elevated" discharge rates. The difference between these tonic rates is small, in the range of 1-2 spikes/s. However, similar changes in tonic activity have functional effects (e.g., EEG activation).

These different levels of tonic LC discharge in the intermediate to elevated range are closely associated with differences in behavioral performance on the visual discrimination task. During periods of elevated tonic LC activity, monkeys foveate the central fixation point (required to initiate each trial; described earlier) less frequently, and exhibit more eye movements unrelated to the task. This behavior suggests that at these times monkeys are less focused on the task and are more distracted by nontask stimuli. Consistent with this interpretation, periods of elevated tonic LC activity are consistently accompanied by an increased number of false alarms or errors (erroneous lever responses for nontarget stimuli; Fig. 54.13). In addition, responses to CS+ stimuli (described above) are much reduced in magnitude during periods of elevated tonic LC discharge. Analyses of behavioral performance have revealed that during periods of elevated LC activity the discriminability of stimuli decreases and the animal's tendency to respond behaviorally to any stimulus increases. Researchers speculate that during elevated LC activity the animal may be less focused on task stimuli (making it more difficult to discriminate target
vated LC activity corresponds to less focused, labile attention and poorer task performance with many errors.

**The Locus Ceruleus May Regulate Attentional State**

When taken together, the cellular properties of the LC-NE system have several functional implications. The broad efferent trajectory of the LC system throughout the CNS (Chapter 8) implies that it has a global function. It is also important to note that LC-NE neurons are physiologically homogeneous, and the properties described here are typical of perhaps all LC neurons. Thus, robust LC activity in many circumstances may result in globally synchronized release of NE onto target neurons located throughout the neuraxis. Areas associated with attentional functioning may receive relatively high NE-LC input. Postsynaptically, NE biases target cells to promote responses to strong inputs while reducing spontaneous or low-level activity. These findings, combined with the specific conditions of LC activation in behaving animals, can be integrated to produce a picture of overall LC function.\cite{36, 39, 92} In this view, very low LC activity causes relatively low responsibility of many neurons throughout the brain that are innervated by the LC, precluding strong engagement with the sensory environment. This facilitates internally driven vegetative programs such as sleep\cite{29} (Chapter 46). Conversely, high tonic LC activity produces tonically elevated neuronal responsiveness in many CNS regions, resulting in extensive interaction with the sensory environment instantiated as scanning or labile attentiveness. Such a mode of attentiveness is not conducive to focused attention, but rather would be associated with a short attention span and low threshold for distraction by exogenous stimuli. This state may be adaptively suited to behavior in a dangerous or uncertain environment. Intermediate levels of LC tonic activity coupled with selective, phasic LC responsiveness to meaningful stimuli may facilitate performance on tasks that require focused selective attention (such as the visual discrimination task described here). The low tonic NE release would prevent overly high neuronal responsibility and behavioral distractibility, while the phasic LC activation would promote processing selectively for stimuli that are salient or meaningful within the current behavioral context. (Note that phasic activation of LC neurons by CS+ stimuli is much reduced during periods of elevated tonic discharge, as described earlier). This mode of LC activity may thereby produce an attentional state that facilitates focused or selective attention and behavioral performance in accordance with an executive process.

**FIGURE 54.13** Tonic activity of monkey LC neurons is correlated with rates of false alarm errors. (A) Upper trace shows discharge frequency of a typical LC neuron during the visual discrimination task. Lower trace shows corresponding occurrences of false alarm errors (bar releases to nontarget stimuli). Note that more false alarms occur during the epochs of elevated LC discharge (e.g., marked II) than during the epochs of intermediate activity (marked I and III). (B) PSTH of activity of this same LC neuron in response to target stimuli during this session. Epochs for data accumulated into each of the PSTHs in I, II, and III are marked in (A). Note that target responses of LC neurons occur only during epochs of intermediate tonic activity (I and III). From nontarget stimuli (lower response criterion). That is, intermediate levels of LC activity with phasic activation by CS+ stimuli are closely correlated with stable focused attention and good task performance with few errors, whereas elevated LC activity corresponds to less focused, labile attention and poorer task performance with many errors.
for planning, described in the preceding pages of this chapter.

Summary

Attentional state varies from sleep to waking and, within the waking state, from low to high levels of alertness. These states relate to widespread effects of neuromodulatory systems originating in the brainstem and influencing the activity of cortical neurons. The norepinephrine system arising in the locus coeruleus is the best understood of these systems. Experiments show that strong activation of this system can lead to premature responding, whereas low levels of activation can produce sleepiness and cause targets to be missed. Target stimuli tend to modify this system, inducing higher levels of activation and increasing alertness.

References


