Adult Cortical Dynamics

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Gilbert, Charles D. Adult Cortical Dynamics. Physiol. Rev. 78: 467–485, 1998.—There are many influences on our perception of local features. What we see is not strictly a reflection of the physical characteristics of a scene but instead is highly dependent on the processes by which our brain attempts to interpret the scene. As a result, our percepts are shaped by the context within which local features are presented, by our previous visual experiences, operating over a wide range of time scales, and by our expectation of what is before us. The substrate for these influences is likely to be found in the lateral interactions operating within individual areas of the cerebral cortex and in the feedback from higher to lower order cortical areas. Even at early stages in the visual pathway, cells are far more flexible in their functional properties than previously thought. It had long been assumed that cells in primary visual cortex had fixed properties, passing along the product of a stereotyped operation to the next stage in the visual pathway. Any plasticity dependent on visual experience was thought to be restricted to a period early in the life of the animal, the critical period. Furthermore, the assembly of contours and surfaces into unified percepts was assumed to take place at high levels in the visual pathway, whereas the receptive fields of cells in primary visual cortex represented very small windows on the visual scene. These concepts of spatial integration and plasticity have been radically modified in the past few years. The emerging view is that even at the earliest stages in the cortical processing of visual information, cells are highly mutable in their functional properties and are capable of integrating information over a much larger part of visual space than originally believed.

I. INTRODUCTION

A growing body of evidence points toward a new view of cortical function in the adult brain. Rather than being fixed in its properties, with memory being a specialized property of a limited set of cortical areas, all areas of cortex are capable of change on a wide range of time scales. These changes can be induced by context, experience, and attention. The central concept of cortical function that is undergoing a profound change is that of the receptive field. The receptive field was originally characterized by Charles Sherrington in 1906 (194) as “the whole collection of points of skin surface from which the scratch-reflex can be elicited may conveniently be termed the receptive field of that reflex.” With the advent of refined electrophysiological techniques for recording from individual nerve fibers, it was possible to talk in terms of the receptive fields of individual neurons. This was initially done in the visual system by H. Keffer Hartline (86), who in 1938 defined the receptive field as “the region of retina which must be illuminated to obtain a response in any given fiber.” He also pointed out that the receptive field size was subject to the state of light adaptation. Subsequently, a more nuanced definition came from Stephen Kuffler (122), who in effect set the stage for the more complex receptive field properties that are the subject of this review. In 1953, he pointed out that “not only the areas from which responses can actually be set up by retinal illumination may be included in a definition of the receptive field but also all areas which show a functional connection, by an inhibitory or excitatory effect on a ganglion cell. This may well involve areas which are somewhat remote from a ganglion cell and by themselves do not set up discharges” (122). This already subsumes the properties thought of in more recent studies as belonging to the “nonclassical receptive field” and in fact makes the distinction between classical and nonclassical receptive fields somewhat fuzzy (see sect. ii). Not anticipated in...
these earlier definitions, however, are the newer findings on dependence of receptive field properties on experience and attention. Another seminal contribution to the concept of receptive field came from the work of David Hubel and Torsten Wiesel in 1962 (94), who emphasize the importance of stimulus configuration on a cell. They realized that for cortical simple cells “the most effective stimulus configurations, dictated by the spatial arrangements of excitatory and inhibitory regions, were long narrow rectangles of light (slits), straight-line borders between areas of different brightness (edges), and dark rectangular bars against a light background. For maximum response the shape, position and orientation of these stimuli were critical” (94). What is now being revealed is that even within primary visual cortex, cells can be selective for even more complex stimulus features.

In this review, we emphasize the dynamic nature of receptive field properties. The modifiability of receptive field properties can be termed plasticity or dynamics, but the different manifestations of cortical dynamics can involve very different mechanisms. For example, altering a cell’s response by changing the context surrounding the receptive field does not necessarily involve a change in synaptic strengths. Instead, a given input can have a very different effect depending on the other inputs that are concurrently active, and the combined effect of two inputs acting together could be very different than the sum of their individual effects. Such nonlinear behavior could be achieved by membrane properties such as voltage-dependent sodium conductances, for example. On the other hand, alteration in a cell’s response to the same input, as a result of a previous period of conditioning, can involve an alteration in synaptic weights. The precise mechanism by which a particular pathway is altered depends partly on the time course over which the change takes place. A rapid facilitation of a pathway can be accomplished by a direct facilitation of excitatory connections or by a depression of inhibitory connections. Facilitation taking place over longer time periods can involve axonal sprouting and synaptic proliferation.

II. CONTEXTUAL INFLUENCES

The functional characteristics of cells in sensory pathways, or receptive field properties, have been traditionally viewed as being very limited in spatial extent and tuned to simple stimulus attributes. It is increasingly evident, however, that even at early stages cells are sensitive to the more global characteristics of the sensory environment. A cell’s response to a local feature is heavily influenced by the context within which that feature is presented. In the visual system, these contextual influences play a central role in the process of integration of information from different parts of a scene. The visual system must assemble percepts of global shapes from information about local attributes, such as surface brightness, color, shading, texture, depth, and contour orientation. Attempts by the visual system to integrate information over space is seen in completion illusions such as illusory contours and perceptual fill-in, in grouping operations such as contour saliency and pop-out, in perceptual constancies, and in the segmentation of surfaces and contours into distinct objects. The process intervening between the perception of simple, physical attributes and the recognition of complex objects is referred to as “intermediate level vision.” A growing body of evidence now reveals that what may be considered an intermediate perceptual process actually involves very early events in the cortical processing of visual information, including the primary visual cortex. These findings come as quite a surprise in view of the traditional notions of receptive field structure, cortical functional architecture, and cortical connectivity. Although the receptive fields of cells may seem quite small when mapped with simple visual stimuli such as short line segments of a particular orientation, the way in which a cell responds to such a stimulus is dependent on the context within which that stimulus is presented. The perceptual consequences of context dependency are likely to be related to the process of linkage of boundary contours and fill-in of surfaces. The association of contours and surfaces belonging to a single object also requires the dissociation of these features from their background or from the contours and surfaces belonging to other objects. This is referred to as segmentation.

The context dependency required for these processes is seen even in striate cortex. Although the traditional view of cellular function revolves around the characterization of the receptive field, there is a changing view on how the receptive field is defined, and this plays a central role in understanding the cellular basis of visual spatial integration and contextual influences. The characterization of receptive field properties is highly dependent on the nature of the visual stimulus used. When one uses a very simple stimulus, such as a single short line segment of the appropriate orientation, one can activate the cell to suprathreshold levels over a very limited area, sometimes referred to as the “classical receptive field.” If, in addition to the line lying within the classical receptive field, one places additional stimuli outside the receptive field, the response of the cell changes. Peripheral influences on responses within the receptive field were originally found in the retina (140), with influences coming from positions as far as 90° from the receptive field center. It has therefore been important when studying modulation from outside cortical receptive fields to differentiate influences originating from cortical neurons, which are more likely to play a role in form integration, from those arising in the retina (109). The distinction between the classical and nonclassical receptive field for cortical cells was first
made by Maffei and Fiorentini (135). Modulatory influences from outside the receptive field were characterized in a number of studies, both in primary visual cortex and in extrastriate cortex (5, 79, 119, 154, 159, 200).

The term nonclassical receptive field has been applied somewhat loosely, since there is no clear boundary between classical and nonclassical receptive field properties. It has long been known, for example, that there are inhibitory regions surrounding the excitatory core of the receptive field (94). These regions are the underpinning of properties such as end inhibition and side-band inhibition and have been suggested to play a role in a range of functions such as disparity sensitivity and depth perception, perception of local curvature, surface segmentation, and so on. One gradually gets into a domain of less “classical” properties when one talks about facilitatory influences, selectivity for complex stimuli that cannot be predicted from responses to a simple stimulus placed in different visual field positions, and influences that extend far from the receptive field core.

The nonclassical receptive field can be made manifest in the facilitatory effects of a line placed outside the receptive field which, by itself, would not cause the cell to respond, but when presented in conjunction with a line segment placed within the receptive field can boost the cell’s response severalfold. This shows a dependency on the relative position and orientation of the two lines, similar to that observed in psychophysical experiments that demonstrate the influence of colinear lines on the perceived brightness of target lines (44, 109, 164, 165). When a series of randomly placed and oriented lines surround the receptive field, this will inhibit the cell’s response, but the response can be disinhibited by colinear, isoriented lines placed outside the receptive field. As a consequence, cells respond not just when the local contour is of the appropriate orientation, but when the line segments within the global image have the appropriate geometry (102, 109). The influence of the receptive field surround provides a plausible cellular basis for contour saliency, since contours made up of similarly oriented, colinear line segments are more readily visible than ones constructed of lines with large orientation differences (56, 82, 206, 220). This is reflected in the response of cells: even though one puts the same stimulus within the receptive field, the cell will only respond when the local stimulus is embedded within a global pattern of linked components, obeying the same geometric constraints as perceptual saliency.

The process of contour linkage is also seen in illusory contours, where one sees completed figures (such as the Kanizsa triangle, Ref. 107) despite the fact that only segments of the figure are present. Cells in area V2 have been shown to respond to “illusory contours” even though the inducing elements of the figure are located outside of the classical receptive field (161, 209).

In addition to the linkage and segmentation of contours, the process of surface fill-in may find its basis in processes occurring as early as area V1. When one masks a portion of the visual field and keeps the boundary of the mask stationary on the retina, the color or pattern of the surrounding area fills into the masked area (29, 121, 160, 169, 227). Perceptual fill-in has been studied with the use of “artificial scotomata,” a gray area within a pattern of moving lines or twinkling dots (169) and with textured fields within a region of a contrasting texture. Cells in V1 have been shown to respond when their receptive fields are placed within an artificial scotoma (37, 74, 162, 208). This response entails a dynamic alteration of receptive field structure, so it is dealt with in greater detail in section V.

The cellular mechanisms of perceptual fill-in have been explored outside of area V1 as well. Cells in area V3, over a period of seconds, begin to respond to an artificial scotoma, even when the classical receptive field is contained within the blank area. The time course of this response corresponds to that of the psychophysical measurements of fill-in (41), and the gradual build up of the response was referred to as “climbing activity.” The responses of cells to this pattern were not observed in V1 by DeWeerd et al. (41), although, as discussed above, it was seen in the earlier studies (37, 162). The time course of receptive field expansion in V1 has not yet been measured, so it is not yet possible to determine its relationship to that of perceptual fill-in. In dealing with these phenomena, there is a potential for confusion between the meaning of receptive field expansion as measured by simple stimuli and a cell’s response to complex patterns outside the classical receptive field. The two phenomena may represent a continuum. Initially, there are subthreshold, modulatory influences from outside the receptive field, possibly mediated by intrinsic long-range horizontal connections (see below), which cannot be seen with a single line stimulus, but can be seen by the conjunction of stimuli inside and outside the receptive field. As these influences are facilitated, either by direct potentiation of the horizontal connections or by unmasking via adapting out inhibition, they can be elevated to a suprathreshold influence. To a degree, the suprathreshold effects may require multiple stimuli, e.g., the pattern of lines used in an artificial scotoma. If the lateral influences are elevated sufficiently, one can see suprathreshold activation even with a simple stimulus, such as a single line. This would then be characterized as receptive field expansion.

Line segments outside the receptive field can influence the orientation tuning of a cell to a line segment placed within the receptive field (79). This effect has been related to perceptual orientation contrast effects, such as the tilt illusion (71, 221). In addition to the perception of contours, the influence of lines of contrasting orientations on the responses of cells in primary visual cortex may play a role in the perception and segmentation of regions of contrasting textures. When a cell’s receptive field is
located within an area containing one pattern of oriented lines, which is surrounded by a contrasting pattern, for example, lines of another orientation, its response is facilitated relative to that seen when the field has a uniform texture (119). Some cells in monkey V1 have been described which, when activated by a grating of the optimal orientation within the receptive field, are disinhibited and sometimes facilitated by a large grating of the orthogonal orientation in the receptive field surround (195). The presence of a texture boundary in the visual field can activate some cells even when the texture boundary is located well outside the classical receptive field (123). Cells were capable of responding to patterns with a central area up to $10^\circ$ in diameter, an area roughly an order of magnitude larger than their classical receptive fields (229). In these studies, the response of the cell to the texture contrast is seen not in its initial burst, but in the subsequent tonic response. This delay was interpreted as suggesting an involvement of a feedback from higher order cortical areas, but alternative mechanisms involving lateral interactions within primary visual cortex have also been suggested.

These experiments might represent a more general case of perceptual fill-in, where the central area is filled with a texture rather than a uniform gray. The time course of the response did not depend on the diameter of the central area, however, which is different from the process of perceptual fill-in (160). The classical view of receptive fields from those of retinal ganglion cells to those in primary visual cortex is that cells are primarily activated by contrast boundaries within the visual environment rather than by areas of uniform illumination. Our visual system is capable, however, of interpolating the boundary information to see continuous surfaces of uniform brightness. In a sense, this is the more common occurrence of perceptual fill-in. This leads, however, to brightness contrast effects, where the same surface can look black when surrounded by brighter surfaces or gray or even white when surrounded by dark surfaces. Some aspects of these contrast effects are retinal in origin and can be explained by properties such as the center surround organization of retinal ganglion cells. There are other aspects of brightness modulation, however, that might originate in the cortex. Cells in area V1 have been shown to be sensitive to modulation of the brightness of surfaces placed well outside their receptive fields (185). These long-range effects are not seen in the lateral geniculate nucleus and, therefore, cannot be accounted for by the traditional center-surround organization of retinal ganglion cells.

Lateral interactions across visual space are needed not only for perceptual fill-in but also for perceptual constancies such as color constancy. To make color appearance relatively independent of the wavelength of the illuminating light, one compares the wavelength distribution of reflected light across the scene, interpreting those surfaces that reflect relatively more long wavelength light as "red" and so on (104, 126, 211, 214). Cells showing the property of color constancy, e.g., sensitivity to color as opposed to wavelength, have been reported in cortical area V4 (228). It is plausible that this property may be generated by horizontal connections within V4. As mentioned above, brightness appearance shows the same sort of dependency on context, and context can have quite complex influences on brightness perception. The form of objects and depth relationships between surfaces can profoundly affect brightness appearance, indicating a possible role of surface segmentation and feedback influences on early visual processing (1).

The assembly of the elements of a scene into object boundaries and completed surfaces depends on the depth relationships between occluding surfaces and intersecting contours. It has been suggested that the visual system first parses a scene into surfaces, as an intermediate stage between the perception of local attributes such as contrast, orientation and curvature, and the identification of objects. Intermediate level vision depends on a number of cues, including depth, and the higher level segmentation of a scene will influence one’s perception of local features. The relative depth of objects, as measured by binocular disparity, determines whether one links components of an object, as one does with illusory contours (153). The linkage of features depends on an initial representation of a scene in terms of surfaces with which the features are associated (87). Surface segmentation, the division of the scene into object vs. background, has been shown to play an important role in the perception of motion (197). The responses of cells in the middle temporal area (MT) are dependent on such higher level segmentation operations: when parsing the direction of movement of elements of a complex pattern, the cells have to differentiate between foreground and background, suggesting a possible influence of a calculation done in higher order cortical areas on the response properties of these cells (47). Linking occluded surfaces based on depth cues influences the direction of perceived motion and the responses of cells in MT (46). The interaction between the processes of surface segmentation and analysis of local attributes suggests an important role for top-down influences in early visual processing.

III. ANATOMIC BASIS OF CONTEXTUAL EFFECTS

Contextual effects may operate by a combination of mechanisms, including lateral interactions within cortical areas mediated by long-range horizontal connections and feedback connections from higher to lower order cortical areas. The long-range influences from different visual field locations may be mediated, at least in part, by long-range horizontal connections that are intrinsic to all cortical
areas. The existence of these connections in adult animals is reminiscent of the exuberance of connections seen during development. It is known that connections are initially very widespread and that they become pruned to reach the adult pattern. In the adult, connections are also more widespread than would seem appropriate for the functional properties of the target cells, providing input from much larger parts of the visual field than expected from the cells’ classical receptive fields. The resolution of this apparent contradiction is that responses can be modulated from positions well outside the classical receptive field, as discussed in section II. In addition, the synaptic weights of different sets of synapses within a large axonal field can be differentially adjusted so that the function that a cell expresses at any given time represents a subset of its potential functional range.

The observation that ascending and horizontal connections are so widespread has been a common and often puzzling aspect of connectivity in the central nervous system. There are many examples of inconsistencies between the cortical circuitry, receptive field size, and topographical order. In the cortex, this divergence of connectivity begins with the thalamocortical afferents. Across an ocular dominance column in area V1, there is a highly ordered shift in receptive field position (19, 97). Because individual geniculocortical afferents can cover the full width of the column, sometimes spanning two columns, and the dendritic fields of cells in the afferent layer extend over one-half a column width, each cell has access to all the afferents innervating that column (20, 65, 113, 134). Despite this, however, the receptive field sizes of the cells receiving geniculate input are comparable to those of single geniculocortical afferents, and there is a strikingly orderly mapping of receptive field position within the column. A comparable example is seen in the somatosensory system with the projection of muscle afferent fibers to the cuneate nucleus. Here, there is overlap of ~300 afferent fibers at any one point, but the receptive field sizes of cuneate cells are at least an order of magnitude smaller than would be predicted by such convergence (215). The only way a cell can have a receptive field of such a restricted diameter is to select input from only a few afferents, or for local inhibitory processes within the target structure to restrict receptive field size. In any event, the end result is that not all inputs to a cell are equipotent, and only a subset has the capacity to activate it. The nonactivating inputs may either be entirely silent, weak, or modulatory. Another intriguing possibility is that different inputs may be functional at different times. This kind of plasticity is suggested by experiments, described below, involving permanent modification of sensory input.

A prime example of the exuberance of connectivity in cortex is the plexus of long range horizontal connections formed by the axons of pyramidal cells within V1 (76, 77, 138, 180, 181; for review, see Ref. 72). It has been suggested that spatial integration may be mediated by these connections. They were initially explored with anatomic techniques, and their functional nature has been explored further by combining optical recording with electrophysiology. When they were initially discovered, they seemed to violate the principles of receptive field structure and cortical topography. The horizontal connections extend for distances over 6 mm parallel to the cortical surface. Their functional implications can be understood in terms of the topographic order of visual cortex; the distances traversed by the horizontal connections relate cells with widely separated receptive fields, since a distance of ~1.5 mm separates cells with nonoverlapping receptive fields, taking into account magnification factor, receptive field size, and scatter (96). Consequently, the cellular targets of horizontal connections effectively integrate input over an area of cortex that represents an extent of visual field roughly an order of magnitude in area larger than the cells’ own receptive fields. This finding was in marked contrast to the belief that all the connections in the cortex are vertical, between cells of overlapping receptive fields and similar orientation preference, with relatively little lateral transfer of information, and raised a seeming contradiction in the definition of the receptive field, in that it suggested that cells should be sensitive to stimuli lying outside of the receptive field. The resolution for this seeming contradiction lies in the distinction outlined above between the classical and nonclassical receptive field.

Another key feature of the long-range horizontal connections is a distinct clustering pattern seen in the axon collaterals. This clustering was found to be related to the columnar functional architecture of cortex, with connections running between columns of similar orientation specificity, as revealed by cross-correlation analysis (202, 203) and by combining labeling of the horizontal connections with labeling of the orientation columns with 2-deoxyglucose autoradiography or by optical imaging (78, 218). The fact that these connections relate cells of similar orientation but widely separated receptive fields suggests that they may represent the mechanism of contour integration and saliency described above.

These studies have confirmed the earlier findings of the relationship of intrinsic horizontal connections with cortical orientation columns. One way of visualizing the functional nature of the horizontal connections is to measure the area of cortical activation resulting either from a point stimulus, known as the cortical point spread, or from a short oriented line segment. The area of activation with a point stimulus shows a central area of spiking activity surrounded by a much larger area of subthreshold activation, with the area of spiking activity representing only 5% of total activated area measured optically (37, 81). The orientation specificity of the larger area supports the idea that lateral interactions run between columns of similar orientation specificity (37). Optical recordings also
reveal how multiple visual stimuli interact with each other. Stimuli placed outside the classical receptive field show predominantly iso-orientation suppression of responses to stimuli lying within the receptive field (81). These findings may reveal the mechanisms underlying the modulatory effects arising from outside the classical receptive field. The functional specificity of the horizontal connections was supported by combined optical recording and slice experiments, which showed that both the excitatory and inhibitory long range interactions run between columns of similar orientation specificity (218), confirming the rules of connectivity revealed by cross-correlation analysis and 2-deoxyglucose autoradiography. The existing framework of horizontal connections can mediate increases in effective connectivity between cortical neurons whose receptive fields are caused to expand within a cortical scotoma (36). Thus these connections can be boosted in strength from a subthreshold, modulatory role under some conditions to a suprathreshold, driving role under others. The mechanism underlying the alteration in effective connectivity is not known, but it could involve a potentiation of excitatory connections, or a reduction in inhibitory inputs that would then unmask the long-range excitatory inputs (226).

It has been variously argued that the contextual effects involve lateral interactions at lower levels or feedback interactions from higher order cortical areas. It has been found, for example, that grouping operations are lost in animals with V2 lesions and that this area may therefore be involved in figure-ground segregation (143). Facilitation produced by linked contours observed in area V1 might be mediated, then, by feedback from area V2, by the horizontal connections within V1, or by both. The characteristics of the lateral interactions of V1, however, suggest that they are well suited to mediate these effects. An alternative hypothesis is that the feedback connections modulate the surround interactions that are specified by horizontal connections, with a joint role of the two. A manifestation of this interaction is the modulation of contextual influences in area V1 by visuospatial attention (101). Additional evidence for a gating of the influence of horizontal connections within V1 by feedback connections from area V2 is seen in the differential effect on the receptive field center and surround in area V1 after silencing of area V2 (100). This idea might further explain why there would be a difference between the explicit receptive field properties seen by summation within the receptive field and the nonclassical interactions from outside the receptive field. The latter would allow the nonclassical properties to be more dynamic, set up by feedforward interactions mediated by horizontal connections but gated by attentional mechanisms mediated by feedback connections. This highly interactive nature of the feedback and horizontal connections would make interpretation of ablation or inactivation studies quite problematic, since a grouping operation performed by local interactions within a given cortical area would only operate as long as the feedback influences were intact.

The mechanisms involved in the context-dependent changes do not necessarily entail plasticity in the classical sense of the word, which usually implies a change in “synaptic weights” or formation of new connections. Rather, there are a host of nonlinear interactions between converging inputs to a cell such that a given input can have very different effects depending on the state of activity of other inputs. The horizontal connections, for example, can be potentiated by other depolarizing inputs due to voltage-dependent sodium conductances (91). Nonetheless, even these mechanisms can produce changes in the response of a cell to a local feature when presented within different contexts. As described in section IV, however, more profound changes, involving alterations in local circuitry, can be produced by changes in sensory experience over an extended period of time.

IV. LESION-INDUCED PLASTICITY OF SENSORY AND MOTOR MAPS

The idea that neural activity can alter the functional properties of cells and the patterns of connections in the brain is well established. Most of the evidence in support of this comes from studies of sensory deprivation in early postnatal development, and it has only been in the last few years that the capacity for plasticity in the adult brain has been appreciated. The idea of a critical period, a restricted period of plasticity early in postnatal development, led to the expectation that all connections and functional properties, at least in primary sensory cortex, would be fixed after the end of this period. In the primary visual cortex, it was established that the balance of input from the two eyes, a property termed ocular dominance, can be altered by limiting visual input to one eye for a few days (95). The mechanism underlying this plasticity is sprouting and retraction of the collateral fields of thalamocortical afferents (98). It is now evident that although certain properties, such as ocular dominance, are fixed in adulthood, a large range of other properties in different sensory systems is mutable throughout life. This is reflected in experience-dependent alterations in receptive field properties, cortical functional architecture, and intrinsic cortical connectivity.

The initial evidence for such plasticity came from studies in the somatosensory system, which, like the visual system, has a map of the sensory surface on the cortical surface. Amputation of a finger leads to an alteration of this map, such that the area of cortex originally receiving input from the amputated finger changes its representation to the adjacent fingers. This is seen with various means of peripheral lesions, including deafferentation as well as amputation (22, 23, 106, 114, 145–147, 171–173, 204, 205). If one finger is amputated, the area...
of cortex originally representing that finger becomes re-mapped, where it instead represents the adjacent fingers. Experiments in the motor system give a similar result. For example, if the facial nerve is cut, the area of motor cortex originally driving the vibrissal musculature comes to drive the forelimb or eye musculature instead (42, 188–190). In the auditory system, one sees a similar phe-nomenon with partial destruction of the cochlea; the tonotopic map of the cortex changes, with a shrinkage in the representation of some frequencies and an expansion of others (168, 179).

In the visual system, this form of reorganization has been demonstrated with focal retinal lesions. In some ex-periments, the lesions were placed in homologous posi-tions in the two eyes to remove visual input from a re-stricted area of striate cortex (75, 88), and in others, a lesion was placed in one eye, and the other eye was re-moved (105). By recording from identical cortical sites, using the vasculature as reference, one can follow the effect of the lesion from minutes to many months after the lesioning procedure. In striate cortex, the zone receiv-ing input from the lesioned part of the retina is initially silenced, but over a period of a few months, it recovers visually driven activity. This area is sometimes referred to as a “cortical scotoma.” The receptive fields of cells in the cortical scotoma shift from representing the lesioned part of the retina to representing the retinal area surround-ing the lesion, effectively remapping the cortical to-pography, with a shrinkage of the representation of the retinal lesion and an expansion of that of the surrounding part of the retina. The reorganization has been observed even with monocular lesions (184, 191). The extent of the reorganization can be quite substantial, with changes spanning nearly a centimeter of cortex. The reorganiza-tion may have some beneficial effects, in that the gray patch one initially sees in the part of the visual field covered by the lesion disappears, such that contours passing through the retinal scotoma will appear complete, albeit somewhat distorted (28). This form of perceptual fill-in in a retinal scotoma has also been found to occur in the blind spot, such that cells with receptive fields in the homologous part of the retina contralateral to the blind spot will respond to binocular stimulation, as long as the stimulus covering the blind spot extends beyond it (57).

Other manipulations involving changes in visual input also lead to alterations of visual cortical maps. When mon-keys were fitted with prisms to reverse the visual field, after a few months some cells in the primary visual cortex were reported to have receptive fields in the ipsilateral as well as the contralateral visual fields, at the same eccen-tricities (198).

More central lesions of the visual pathway have also shown a considerable potential for plasticity. When area MT, which plays a role in the perception of movement and in visuospatial behavior such as smooth pursuit eye movements, is lesioned, the capability to execute such movements is initially lost. After as little as 1 wk, however, this capability returns (155), presumably as a result of the takeover of the function of lesioned cortex by the regions, either within MT or in other parietal areas, that are left intact.

In all of these systems, the underlying mechanism has been a focus of speculation and experimentation, es-specially with respect to the site at which the reorganiza-tion is taking place and the connections that are responsi-ble. Experiments in which reorganization was observed in primary somatosensory cortex led to the suggestion that the changes were intrinsic to the cortex. Earlier work by Wall and colleagues (39, 40, 210), however, found reor-ganization at antecedent stages in the somatosensory pathway, in spinal cord and nucleus gracilis. Moreover, the potential for reorganization at early levels in the somatosensory pathway has been reinforced by the finding that afferent terminals sprout within the spinal cord and nucleus gracilis after peripheral nerve damage (24, 43, 61, 62, 124, 125, 137, 142, 225). In addition to the evidence of reorganization in the spinal cord, reorganization has been observed in the thalamus (69, 178, 219). It has also been suggested that some of the changes seen in the cortex could be accounted for by alterations in the peripheral innervation, such that axons originally targeting the ampu-tated digits shift toward the remaining stump (136). Changes at the earlier stages in the somatosensory path-way would then change maps at all subsequent stages in the pathway, including the cortex. Because of the extent of reorganization, investigators observing cortical changes proposed that thalamocortical arbors within the cortex represented the neural substrate of reorganization (22, 145, 188). Direct evidence for changes originating in the cortex in this system has been limited. It had also been assumed, because of the extent of reorganization seen initially (~2 mm), that the reorganization was medi-ated by thalamocortical connections, but subsequent ex-periments, involving more extensive deafferentation and longer survivals, revealed reorganization extending >10 mm (167).

This issue was examined in some detail in the visual system. There, the extent of reorganization, ~6–8 mm, is much larger than the lateral spread of thalamocortical afferents, ~2 mm (20, 55, 65, 66, 76, 77, 99). Along the visual pathway, before the cortex, there is no appreciable lateral spread of connectivity as there is in the somatosen-sory system (for example, the sensory afferents to the spinal cord). The substrate for the reorganization was explored by recording at various stages along the visual pathway. Although a small amount of reorganization may occur in the lateral geniculate nucleus (51, 52), even when the cortex has completely reorganized, there is still a large area of lateral geniculate nucleus that remains silent, indicating that most of the reorganization must be intrinsic.
to the cortex (35, 80). Moreover, the thalamic afferents cannot account for the reorganization. The extent of reorganization, ~6–8 mm in diameter, could not be explained by the lateral spread of thalamic afferents, which spread ~1.5–2 mm laterally in cortex, unless they increased their projection pattern into the center of the reorganized region. Not only are they too restricted in their extent normally, but they do not sprout into the cortical scotoma, as would be required if they were to be responsible for the reorganization (35, 80).

The most likely source of the reorganization is the plexus of long-range horizontal connections. They normally extend 6–8 mm, which is the same distance over which the cortical reorganization has been observed, and are capable of providing cells in the scotoma with input from parts of the visual field surrounding that covered by the retinal lesion. An additional feature of these connections, as described above, is that they link cells of similar orientation preference. The idea that the horizontal connections are responsible for the reorganization is supported by the finding that after recovery, the pattern of orientation columns is quite similar to that seen before the lesion, despite the fact that the receptive fields of the cells in this region shift considerably in visual space (36). Given that the horizontal connections run between columns of similar specificity, the involvement of a preexisting framework of horizontal connections in the reorganization would cause the reorganized cortex to recover its original pattern of orientation columns. Although it remains to be seen whether feedback projections from higher order cortical areas also participate in the reorganization, the most likely candidate at present appears to be the long-range horizontal connections. Feedback projections do provide widespread arbors in striate cortex; those from V2 do not extend as far as the intrinsic horizontal connections, although other sources of feedback to V1 may ramify more widely, such as those from V4 and the temporal lobe (182, 183). For the receptive fields of cells in the scotoma to shift, the horizontal connections must be strengthened from the modulatory role discussed above to a suprathreshold, driving influence. The way they do this is by sprouting axon collaterals and synaptogenesis, whereby existing clusters within the existing framework of horizontal connections are reinforced by adding collaterals and synaptic boutons (34). The change observed here does not entail an increase in the extent of the horizontal arbor, but an increase in the density of collateral arborization within the existing clusters of axon collaterals. To see sprouting in the adult brain as a result of alteration in visual experience is quite a contrast to the implication of a critical period, in which certain properties and certain connections are expected to be fixed after the first few years of life. Clearly, even in adulthood, brain plasticity results from a continuing process of experience-dependent synaptogenesis.

The association of sprouting with topographic reorganization has also been seen in the spinal cord after sensory deafferentation (61). In the motor cortex, sprouting has been induced by cerebellar lesions and by stimulating thalamic afferents (115, 116).

The plasticity of cortical maps has been proposed to play a central role in the cause and potential remediation of a number of clinical disorders. The reorganization of somatosensory maps may explain, for example, the phenomenon of phantom limb sensations. A representation of the skin of the amputated limb is found on the skin of the limb stump or on the cheek, which can be explained by expansion of the representation of the cortical areas adjoining those originally receiving input from the amputated limb (170). The extent of reorganization, measured with functional magnetic resonance imaging, appeared to correlate with the severity of phantom limb pain (60). The mechanisms governing reorganization of cortical maps have also been implicated in language deficiencies seen in language-based learning impairments, such as dyslexia.

An important principle proposed for the reorganization is that inputs that are activated synchronously tend to be localized at nearby cortical sites and that, in general, temporal patterns of activation govern map organization (4, 158, 212). On the basis of that principle, changing the temporal characteristics of processed speech used in computer games enabled children with language deficits to improve markedly in their language comprehension (144, 199). Although the actual mechanism underlying these improvements is not established, it seems plausible that some form of use-dependent plasticity plays a role in the improvement. In general, the plasticity seen in a number of cortical areas and in a number of modalities might have application toward improving function in individuals with developmental disorders and in facilitating recovery after damage of the central nervous system, such as that occurring with stroke.

**V. SHORT-TERM PLASTICITY**

The experiments described above demonstrate changes occurring over weeks and months. Similar experiments also show extensive changes that can take place over much shorter periods of time, within minutes and perhaps seconds. Inactivation of peripheral sensory nerves, by either anesthetic injection or damage, can lead to cortical map alterations over periods of minutes (22, 23, 204). In the motor cortex, within a period of hours after transection of the facial nerve that innervates the vibrissae, stimulating the original vibrissal representation of the motor cortex evokes forelimb muscle activation (42). Digit amputation in the flying fox leads to an expansion of the sensory receptive fields of cortical cells originally representing the digit alone to one that represents the arm and wing, and this occurs within 15 min (23). As in the experiments on long-term changes, a persistent
question is whether the changes are intrinsic to the cortex or they reflect changes at antecedent levels of sensory processing. In rats chronically implanted with electrodes in the thalamus, immediate changes in receptive field maps were observed after injection of anesthetic in the face (156). Even under conditions of normal sensory stimulation, the receptive fields of these thalamic neurons have been shown to receive input from more whiskers than previously thought, and the receptive fields tend to shift to different sets of whiskers over a few tens of milliseconds during the response period (157). This is reminiscent of findings in the visual system, where different components of a receptive field may have different latencies, such that a spatiotemporal plot of the receptive field shows some shift during the response period. Including these types of changes under the rubric of “dynamic changes” may be stretching the term a bit and is clearly different from an alteration in response to the same stimulus after a period of conditioning, as described below.

In the visual cortex, within minutes after making retinal lesions, cortical receptive fields located near the boundary of the lesion expand in size by an order of magnitude. There is also a measure of remapping of cortical topography, with a fill-in of the cortical scotoma extending for a couple of millimeters (80). This was also seen after monocular retinal lesions followed by enucleation of the contralateral eye. Immediately after the enucleation procedure, the area of cortex initially silenced to stimulation of the lesioned area of retina recovers input from the surrounding retinal area (25). Both studies showed shifts in topographic representation over a cortical distance of ~2 mm, as compared with a reorganization of 6–10 mm seen in the longer term recoveries.

The fact that the plasticity of receptive fields and of cortical topography could occur very quickly after retinal lesions, and that some of the lesions involve only the destruction of the photoreceptor layer (and therefore does not involve any physical deafferentation of the cortex itself), led to further experiments demonstrating plasticity resulting from patterned visual stimulation. In these experiments, the effects of retinal lesions were mimicked with the use of an artificial scotoma, a masked area of the visual field with patterned stimulation in the area surrounding the mask. As described above in the section on contextual influences, the artificial scotoma has been used to study the phenomenon of perceptual fill-in. The changes in responsiveness over time of cells whose receptive fields are placed within an artificial scotoma go beyond mere contextual effects and reveal a capability for receptive fields to be modified by previous conditioning with a visual stimulus. When a cell’s receptive field is placed within an artificial scotoma, the field expands beyond its original limits (37, 74, 162, 208). It has been suggested that the change is primarily one of responsiveness (38). The different ways in which changes in receptive field properties within an artificial scotoma have been characterized may reflect a semantic difference on how receptive field dimensions are defined. Further experiments have shown, however, that there is a genuine increase in receptive field area, even when one normalizes for peak response, with cells responding to parts of the visual field where stimuli elicited no prior response (74). In addition to perceptual fill-in, the consequences of the expansion may be manifest as a distortion of spatial perception, such that objects lying near the boundary of the artificial scotoma appear to be pulled in toward its center (108). This effect occurs much more rapidly than perceptual fill-in, suggesting that receptive field plasticity may be observed within as little as 1 s.

Receptive fields have also been shown to be modulated by eye position. This form of modulation was originally proposed as a way of stabilizing the image in a “world centered” coordinate system, as opposed to one based strictly on retinotopic position. By modulating retinotopic fields by eye position, one could in principle encode information about the position of a stimulus in extrapersonal space. This kind of modulation, which has been referred to as a “gain field,” was found initially in area 7a of the parietal cortex, and subsequently in other areas of parietal cortex and in the frontal lobes (6, 7, 21, 68). Neurons in parietal cortex will also respond differentially depending on whether an intended eye movement will bring a stimulus into the cell’s receptive field, and receptive fields appear to shift before the execution of an eye movement (45). The influence of eye position on responses as far back in the visual pathway as area V1 is still under debate. Gain field effects have been reported in cat V1 (224). It has even been suggested that fields in primate V1 may shift to a small extent with changes in fixation (152). This was interpreted as a support of models incorporating shifting fields to achieve binocular fusion or as a response to changing the focus of attention (8). The ability to shift fields with eye movements has, however, been disputed by others (83).

Changes in receptive field properties, such as orientation preference and ocular dominance, have been induced by simultaneous visual stimulation and infusion of glutamate, to increase the activity level of the postsynaptic cells during presentation of a particular visual stimulus. The stimulus selectivity of the cell then became shifted toward the stimulus used during conditioning (64). Receptive field expansion has also been documented by simultaneously placing stimuli inside and outside the receptive field. With the association of a stimulus within the receptive field, which causes it to fire, with a stimulus presented simultaneously outside the receptive field, the field is caused to expand in the direction of the extra-receptive field stimulus (50). Both of these experiments are thought to work via Hebbian mechanisms of strengthening inputs to a cell, via synchronous pre- and postsynap-
tic activation. In this way, inputs from other parts of the visual field, such as those mediated by the long-range horizontal connections, while initially subthreshold and incapable of driving a cell, become strengthened. The strengthening is sufficient to allow a stimulus that had previously been outside the receptive field to activate the cell, thus constituting a receptive field expansion. Similar kinds of approaches of associating conditioning with test stimuli, with the conditioning stimulus being a sensory stimulus or excitation induced by electrical or chemical means, have been used to alter receptive field specificities. In auditory cortex, pairing tones with electrical current-induced excitation causes a sustained increase in the response of cells to the tone used in conditioning (32).

The ability to induce changes in receptive field properties after conditioning with various stimuli may have implications for the mechanisms underlying the context-dependent changes in functional specificity. Although the contextual effects have not been shown to result from changes in synaptic weights, the possibility exists that they may operate via the same mechanisms generating experience-dependent effects. The main difference between the two models is in the sequence of stimulus presentation; the contextual stimuli are presented at the same time as the target stimuli, but with the experience-dependent changes, the conditioning and test stimuli are presented asynchronously.

The mechanisms of short-term plasticity are likely to involve changes in the effectiveness of existing connections, rather than formation of new connections, as has been demonstrated in long-term plasticity. Without going into a detailed discussion of the synaptic mechanisms of plasticity, the primary mechanism that has been suggested in a number of systems is a Hebbian one, strengthening connections between synchronously active cells. Although the ability to alter synaptic weights (long-term potentiation and long-term depression) has been studied most extensively in the hippocampus, the neocortex also shows such plasticity, even in mature animals (9, 18, 63, 92, 93, 117, 118). Such a mechanism has been demonstrated specifically for the long-range horizontal connections in visual cortex (92) and has also been shown in motor cortex (89). In both instances, the potentiation is most readily observed when the inhibition present in the pathway is minimized. Because the long-range horizontal connections contact inhibitory interneurons as well as other excitatory neurons, the strength of the connection can be modulated by reducing inhibition. It has been shown that the kinds of changes in the map of primary motor cortex after nerve transection can be mimicked by pharmacological blockage of cortical inhibition (103). The link between synaptic plasticity observed in cortical slices and the changes in receptive fields resulting from an artificial scotoma has not been established. One problem with applying a Hebbian role in the plasticity associated with an artificial scotoma is that the postsynaptic cells are silenced, rather than hyperactivated. One can get around this problem by adding a “sliding threshold” rule to the implementation of synaptic plasticity, such that the relationship between the amount of presynaptic activity and the amount of strengthening varies with the amount of overall cortical activity (17, 117). It has also been suggested that the expansion of visual receptive fields of cells in area V1 within an artificial scotoma can be modeled by a reduction of location inhibition (226), although this would require a long-lasting adaptation of inhibition, well after the conditioning stimulus has been turned off. One can imagine that pathways may be strengthened via a cascade of effects, reducing inhibition which then allows for stronger facilitation which then leads, over longer periods, to consolidation via synaptogenesis and growth of axon collaterals.

VI. PERCEPTUAL LEARNING

Much of the interest that has been generated by studies of cortical plasticity comes from its potential relevance to learning. The profound changes in cortical functional architecture that follow retinal lesions may represent the mechanisms of recovery after lesions of the central nervous system, but they may also reveal adaptive mechanisms associated with normal processes such as perceptual learning. Because what one traditionally associates with memory is localized to the temporal lobe, it would be something of a surprise if primary sensory cortices would be involved as well. One should bear in mind, however, that there are many different categories of memory, including declarative and nondeclarative, with different brain locations responsible for the different types (196). Although one normally associates memory in the visual system with object recognition, and with areas that are at advanced stages of visual processing such as those found in the inferior temporal lobe, there are forms of implicit learning that suggest the involvement of much earlier stages of processing, even in the primary visual cortex. This simpler form of learning is known as perceptual learning. It involves an improvement in the ability to discriminate simple sensory attributes, such as pitch, texture, visual acuity, and so on. It is entirely plausible that the long-term plasticity associated with peripheral or with central nervous system lesions did not evolve as a way of recovering function after injury, although it is certainly useful for that, but as a mechanism evoked throughout the normal functioning of sensory and motor systems, as evidenced by perceptual learning.

Perceptual learning has been studied for over 100 years (see Refs. 70, 73), with improvement demonstrated with practice in visual acuity, pitch, orientation and direction of movement, and depth. Recent studies on its specificity have suggested the involvement of primary sensory
cortex. The basic finding in these studies is that repeated performance of a simple discrimination task, such as whether one line is located to the right or the left of a reference line, leads to an improvement in the performance threshold. For example, in vernier acuity, which is the ability to detect an offset in the alignment of two lines, a typical starting threshold is 10 s of arc. After repeatedly being presented with targets at varying offsets and making such a discrimination, the performance might improve to 5 s of arc (141). A similar improvement is seen in stereoacuity, the ability to discriminate the relative depth of two points placed at different distances from the observer, as measured by the interocular disparities of the two points (54). Although some of the studies provide the subject with error feedback, feedback is not generally required to see improvement.

Various studies have shown that practice of this sort can lead to improvement in discriminating position in depth, direction of movement, line orientation, and so on. Hyperacuity, defined as a spatial threshold that is smaller than the grain of the sensory mosaic (often by an order of magnitude or more), shows improvement with training. One way of demonstrating hyperacuity is to ask an observer to judge an offset in the positions of two points or lines. Poggio et al. (163) found learning in hyperacuity occurring within a few minutes of practice on such a task. Stereoacuity shows a considerable improvement with practice (223). For a patterned stimulus, such as a compound sinusoidal grating, one can improve in the ability to discriminate the spatial phase or offset of the components of the grating (58, 59). Texture discrimination shows improvement, as evidenced by the ability to determine, within a set period of time, the orientation of an array of oriented lines in a background array of differently oriented lines (110). Finally, motion discrimination, the ability to see differences in the direction of motion, also shows improvement with repeated trials (13, 14).

Insight into the physiological mechanisms of perceptual learning comes from the specificity of the learning and the lack of transfer to similar tasks. Such specificity implies that the substrate of the learning may be found at early stages in visual processing. Improvement in grating waveform discrimination is specific for the orientation of the trained pattern (59). Training in a texture discrimination task, where the foreground and background textures are composed of lines of different orientations, does not transfer to a similar task when the orientation of the background lines is changed (110). Training subjects on a hyperacuity task with lines of one orientation does not transfer to doing the task with lines of the orthogonal orientation (30, 53). Similarly, training on an orientation discrimination task does not transfer to the orthogonal orientation (193).

Training is also specific for visual field position. In several studies, subjects were trained with visual stimuli placed in one quadrant of the visual field, and the training effect did not transfer to other visual field quadrants (16, 110). This specificity has been shown to be highly localized, where improvement in depth discrimination does not transfer to the same task shifted a few degrees away (223), where improvement in orientation discrimination does not transfer to positions a few degrees away (193), and where improvement in a line localization task is restricted to an area a few degrees in diameter (30, 186). A few degrees of transfer have been observed in motion discrimination, although the transfer drops off quickly with increasing separation between the training and test targets, particularly when there is little overlap (14). These findings lead to the speculation that primary visual cortex may be involved in the improvement, since this area has the sharpest orientation selectivity, the smallest receptive fields, and the most highly ordered visuotopic maps.

The dynamic changes in visual perception resulting from context and from experience do not operate independently, but rather show a close interdependence. The visuotopic extent of lateral interactions can be increased by training, as observed by the facilitation in the visibility of a target line by a colinear line (164, 165). This observation, as with the receptive field plasticity seen with real and artificial scotomata, may involve a potentiation in the strength of the long-range horizontal connections.

The localization of learning has also been addressed by the ability to show interocular transfer. Although some studies have shown specificity to the trained eye (16, 110, 163), others show that training in one eye transferred to the other eye (14, 15, 111, 192). It has been suggested that the ability to show interocular transfer differs between faster and slower forms of perceptual learning (111). Lack of transfer would certainly speak to the involvement of early stages in visual processing, since input from the two eyes is integrated at the single-cell level in primary visual cortex. It is difficult to imagine, however, that learning could be both orientation and eye specific, since it has generally been found that monocular cells in the striate cortex lack orientation specificity (97, 130).

Other aspects of the specificity of the task add some complexity to the story, and the kinds of changes one might expect in any given cortical area might be somewhat involved. Although transfer has been shown between vernier (hyperacuity) and standard spatial resolution tasks (15), other studies have shown a lack of transfer between different tasks involving the same part of the visual field, even when they are composed of lines of the same orientation (30). Learning effects appear to depend on the configuration of the stimulus used in training, including the context surrounding the feature being discriminated. When stereoacuity is done in the presence of an array of surrounding dots, the learning in stereoacuity of a central dot is specific for the separation between the
central dot and the surrounding array that is used during training (27). Hyperacuity learning done with lines as the conditioning stimulus does not transfer to a hyperacuity task composed of dots (163). This implies that the underlying cellular changes are specific for the visual or behavioral context. If the improvement does involve the primary visual cortex, one might see it manifest as a change in the contextual influences described above, perhaps involving the lateral interactions within V1, or feedback connections from areas where cells might show specificity for more complex forms and configurations.

An alternative model to the involvement of primary sensory cortex comes from experiments on the effect of attention in higher cortical areas. Although receptive fields in area V4, for example, are larger, and would be expected to carry less specificity about spatial position, it is possible to effectively reduce receptive field size by attention (148). Even if one normally associates higher visual cortical areas, such as inferotemporal cortex, with storage of more complex percepts, training can give cells there a specificity for very simple features. Conceivably, therefore, one might confer greater specificity to cells at higher levels by training.

The time course over which learning takes place differs between studies. Some improvement in discrimination has been observed over a few tens of trials within a single session (163), whereas other learning phenomena develop over days and weeks (108, 141). One interesting feature of perceptual learning studies is that learning is often most clearly seen between sessions, perhaps allowing for a period of rapid eye movement sleep that might be required for consolidation of the memory (111, 112, 193).

The cortical changes accompanying perceptual learning have been studied in the somatosensory and auditory systems by Merzenich and colleagues (174). Animals trained to discriminate small differences in the frequency of a vibrating surface while using a specific digit showed an increase in the size of the cortical representation of that digit, or “cortical recruitment,” within primary somatosensory cortex, S1 (174). The improvement is better when the animals are actively involved in the task, making a discrimination, than when their fingers are passively stimulated while they are attending to an unrelated auditory stimulus. In addition to the changes in the somatotopic representation, the temporal characteristics of the responses changed, with responses becoming more closely locked to the time course of the stimulus, leading to more synchrony in the firing (175). It has been proposed that these kinds of changes might occur in individuals who become accomplished at skills involving manual dexterity. With the use of magnetic resonance imaging techniques in humans, it was found that the cortical representation of the digits of the left hand of string players is larger than nonplayers (49).

The original evidence for the change in auditory responses with training came from the observation of increased auditory evoked potentials when a sound stimulus was associated with a food reward (48). Associating a simple tone of a defined frequency with an aversive (foot shock) stimulus causes cells in primary auditory cortex to increase their response to tones of that frequency, even for cells whose pretraining best frequency is different from the conditioning frequency (11, 217). The mechanism by which the presence of the unconditioned or reward stimulus can influence the cortical responses to the conditioned stimulus is likely to involve the basal forebrain (12). The basal forebrain has long been thought to play a central role in informing the cortex of the presence of a reward or aversive stimulus. It receives input from the amygdala and the medial temporal lobe system of associative memory. Stimulation of a basal forebrain nucleus, the nucleus basalis, during the presentation of a tone of a specific frequency causes cells in primary auditory cortex to increase their responses to that tone in a manner similar to that observed when a tone is paired with an aversive stimulus. These results support a model of cortical information storage involving the combination of specific sensory stimulation and release of the neurotransmitter acetylcholine, which is released by the cortical input from the basal forebrain (217). The cholinergic system has been implicated in the mechanism of cortical plasticity both in development and in adulthood and has been suggested to play a role in the dysfunction of memory seen in Alzheimer’s disease.

With the use of a model similar to that used in the somatosensory system, animals trained to discriminate small differences in pitch around a particular frequency show a perceptual improvement specific for that frequency. The cortical map changes accordingly, with an increase in the area of primary auditory cortex representing that frequency (176). The interaction between cells in auditory cortex can be facilitated by conditioning (activating one neuron by its preferred stimulus while a second neuron is active), but the ability to alter effective connectivity is limited to circumstances where the animal is attending to the stimulus (3). Thus the ability to induce alterations in cortical circuits depends not only on the synchrony of activity of neurons, but also on behavioral contingencies.

Changes have also been seen in motor cortex. Animals trained on a motor task involving skilled manipulation of small objects showed changes in area M1 of the motor cortex. The representation of the evoked movement digit representations expanded and the evoked movement wrist/forearm representations contracted. The opposite changes occurred for animals trained on a task involving the forearm. Also, movement combinations used in the trained task became represented in the same cortical area, whereas before training they would have been represented by distant cortical sites (158).
Whether cortical recruitment will consistently be associated with perceptual learning is an open question. In the visual system, where the training shows dependency on context, it is unlikely that cortical recruitment would represent the exclusive mechanism, since the different tasks would still involve the same cortical area. If there is recruitment, it might be transitory, lasting only while the animal is performing the task, or it might involve more subtle changes in contextual influences, without an increase in the number of cells participating in the task. Recruitment can aid in making a discrimination by “probability summation,” where there is an improvement in signal-to-noise ratio by averaging the activity of many independently functioning units (which also requires that the variability in firing between different units operates independently). Alternatively, the improvement could be mediated by sharpening of the tuning of a cell for the trained attribute, again with specificity for context, perhaps by modulating the long-range horizontal connections (31).

Although studies of the physiological basis of perceptual learning in the visual system are only just beginning, particularly with respect to earlier stages of visual processing, there is evidence for cortical changes at later stages in the visual pathway associated with learning. Improvement in the discrimination of direction of motion of a random dot field has been shown to be associated with a change in the response characteristics of individual cells in area MT (230). Clearly in inferotemporal cortex, where it has long been thought that the representations of complex forms are stored, the functional specificities of cells reflect the images on which animals have been trained (120, 187). There is an extensive neurological and physiological literature pointing toward the role of inferotemporal cortex (IT) in storing the representation of complex objects, from faces to a range of objects for which a detailed categorization is required (for review, see Ref. 33). The more recent work attempts to manipulate the specificity of cells in IT, imposing selectivities for novel objects, which allows one to explore how a given image is represented by neuronal ensembles, and to see how a set of cells with given stimulus selectivities handle novel objects or novel views of objects (132). One can also explore the mechanisms of memory storage and associations at the level of interactions between different cortical areas; the importance of feedback signals to IT from the perirhinal and entorhinal cortices for associating one visual image with another was shown in lesion studies (90). The discovery of a functional architecture for object representation in inferotemporal cortex opens the possibility for studying systematically the distribution of activity underlying recognition of a particular object, and for delineating a syntax of object representation in the brain (67, 213).

The ability to store various forms of visual information, reflective of the ongoing experiences the animal receives, is a universal property of cortex. The nature of the information stored may vary from one cortical area to another, with discrimination of simple attributes stored in primary sensory areas and more complex attributes stored at the highest levels in sensory pathways. The mechanisms involved in learning may be common to all these areas, in terms of the synaptic changes involved, the classes of connections participating in the changes, and the interaction between connectivity and functional architecture required to represent learned information. Thus the work done on implicit learning in early sensory processing is likely to reveal mechanisms involved in representing even the most complex information.

VII. ATTENTION AND EXPECTATION

Up to this point, the influences on cortical plasticity that have been discussed are of a feedforward nature, involving influences of the context and experience of sensory input. In addition to these influences, attention to spatial position and higher order representations of form may be fed back toward cortical areas processing the incoming sensory input. It is clear from psychophysical studies that discrimination of simple attributes is influenced by attention to stimulus position and that interpretation of form is influenced by anticipation of stimulus configuration. Moreover, a fundamental feature of the anatomy of cortical pathways is a feedback of information from higher order cortical areas to areas that are closer to the input from the periphery. It is likely, therefore, that one would influence the response properties of cells at early stages in sensory pathways by attention. There is evidence for such influences from studies of visual areas V4 and MT, and newer evidence points toward attentional influences extending as far back as primary visual cortex.

In psychophysical experiments, discrimination thresholds of very simple attributes such as stereoaucity, line length estimation, and orientation are strongly influenced by attention (128, 129). This is seen when the observer attends to a particular position in visual space as opposed to being uncertain as to which of a number of possible positions in which the stimulus may appear. Similar influence of positional certainty was seen with respect to line orientation discrimination thresholds. There is also an influence of temporal certainty, knowing when a test object will appear will decrease the threshold of the discrimination relative to being uncertain as to the time of occurrence (222).

Some of the initial experiments on attention were done in area V4, but attentional effects are now being reported at earlier stages in the visual pathway, even in primary visual cortex. In V4, receptive fields are relatively large, and responses to stimuli placed in different parts of the receptive field are modulated by attention to cued stimuli placed in those locations (148). Even for stimuli that are irrelevant to the attentional task, attention to a
particular position in the visual field will increase a cell’s response to an oriented bar over the attended portion of the receptive field of a cell (26). The response selectivity of cells in V4 can also be modulated by attention, showing, for example, a sharpening of orientation tuning during an orientation matching task (84, 85). In an orientation match-to-sample task where the sample is either a visual or a tactile cue, the sample orientation frequently affected the response of the cell to oriented visual stimuli (139). The activity of V4 cells can be doubled when the color of a test stimulus matches that of a cued stimulus (150), and activity is heightened for stimuli that pop out of a field of background stimuli and suppressed for stimuli that are part of the background (151).

In many visual areas, including V1, focal attention to a stimulus can enhance a cell’s peak response (85), particularly when the stimulus is in the presence of multiple competing stimuli (149). In area V2, a cell’s nonpreferred stimulus will suppress its response to a preferred stimulus, but attention to the preferred stimulus will reduce the inhibitory effect of the nonpreferred stimulus, and attention to the nonpreferred stimulus will increase its inhibitory effect (177). The various influences on receptive field properties described above interact with attentional mechanisms; attention can have a stronger effect on contextual influences than on the target stimuli themselves, and the difference between focal and diffuse attention on the perception of target attributes can be greatly reduced by learning (102). These effects are reflected in the activity of neurons in V1 (101). In addition to the effect of learning on attention, the manifestation of perceptual learning, as described above, is gated by attentional mechanisms (2). A further testimony to the dynamic nature of cortical receptive field properties is the observation that the contextual interactions observed at the level of individual receptive fields in area V1 are themselves task dependent, influenced by the perceptual discrimination the animal is currently performing (31).

In area MT, where cells are highly sensitive for movement of objects in a particular direction, cells will continue to respond when an object moves behind an occluder, as if the cell is signaling the “awareness” of the presence of the object, even though for a period the retina receives no physical stimulus (10). When two stimuli are moving in opposite directions within an MT receptive field, the cell responds much more when the animal attends to the stimulus moving in the cell’s optimal direction than to the stimulus moving in the opposite direction, even though the sensory input under both circumstances is identical (201).

Another example of changing cellular responses that parallel changing perceptions for an unchanging image is binocular rivalry. Here, the two eyes see dissimilar images, and the resulting percept shifts from components seen by one eye to those seen by the other. Despite the fact that there is no difference in the incoming sensory information, neurons in area MT change their activity during motion rivalry, and neurons in V1, V2, and V4 alternate activity during viewing of rival gratings of orthogonal orientations (127, 131, 133).

One model of pattern recognition incorporates the idea that feed-forward and feedback mechanisms influence cells at all stages in the visual pathway and that the pathways selected for information transfer in an ascending direction are influenced by the product of calculations made in a descending direction (207). Similar models suggest that higher order cortical areas make abstractions that, via the feedback connections, are fit to the more concrete data represented in the lower order areas, in effect a process of checking hypotheses. The lower areas in turn send information concerning the errors between the data and the abstractions. These ideas generally give to the lower areas a role of a high-resolution buffer that can be modified or written to by the higher areas.

VIII. CONCLUSIONS

In contrast to the classical idea that the response properties of cells at early levels of visual processing in the adult are fixed and that these cells deal only with local features, it now appears that they are highly dynamic and perform considerable spatial integration. There are numerous influences that play a role in sculpting the functional properties of cells and the functional architecture of cortex, including the context within which a feature is presented, the history of previous visual stimulation, operating over a range of time scales, and attention or expectation. These findings suggest the need for new ways of thinking of receptive fields: rather than being fixed in specificity and restricted in area, fields must be thought of as adaptive filters, modified by context, experience, and expectation and sensitive to the global geometric characteristics of visual scenes. The mechanisms underlying this plasticity include feed-forward processes or lateral interactions, such as those mediated by the long-range intrinsic horizontal connections within each cortical area, and the feedback connections from higher to lower order stages in the visual pathway. Finally, one must emphasize that all of these influences are interdependent, with, for example, expectation influencing contextual interactions and learning effects and learning affecting attentional effects and context. It is therefore important to consider all of these influences together in exploring how any one of them may alter receptive field properties and cortical functional architecture. The impending revolution in our view of cortical processing is that early stages are not preprocessors for the integrative functions of higher level areas, with fixed properties. Rather, they are dynamic buffers with properties set for performing a given perceptual task and are as subject to the current context, to internal represen-
tations, and to top-down influences as they are to inputs reflecting external physical reality.

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