Commentary

Learning and receptive field plasticity

Charles D. Gilbert

The Rockefeller University, 1230 York Avenue, New York, NY 10021

The cerebral cortex has long been known to play a central role in the storage and retrieval of long-term memories. Therefore it would be expected that mechanisms of cortical plasticity underlying information storage should be found in the cortex of adult animals, and they should be manifest as an alteration in the functional specificity of cells, in the functional architecture of cortex, and in the strength of connections between cortical cells. The prevalent thinking attributed this plasticity to cortical areas involved in processing of the most complex stimuli, perhaps associating multiple sensory modalities, such as the temporal and frontal lobes. Historically, for example, lesions in the temporal lobe were recognized to lead to an inability to recognize faces, so it would follow that object recognition based on visual cues would be based there, far from the primary visual cortex, which is located in the occipital lobe. Primary sensory cortices were thought to be much more stable in their properties. The pioneering work of Hubel and Wiesel on plasticity during early postnatal development showed that at least some properties, and some connections, were mutable early in life, but were fixed after a "critical period" which lasted for only the first few months after birth. This background may have contributed to the idea that early stages in sensory processing should be fixed and stereotyped, that primary sensory cortices should represent "preprocessors" whose properties should be independent of sensory experience.

In counterpoint to this way of thinking is a long history of work on perceptual learning showing that the discrimination of simple attributes, such as tones or textures or position in depth, can improve as a result of training (for review, see ref. 1). The specificity of the learning in these tasks to the trained frequency or position in space or orientation is suggestive of the involvement of early stages in cortical sensory processing. At these early stages the sensory cortex has the highest resolution maps for these attributes. Primary visual cortex, for example, has a map of visual space projected on its surface, and has columns of cells responding to particular line orientations systematically organized in cycles of progressive clockwise and counterclockwise shifts as one moves across the cortical surface. Primary auditory cortex has the frequency spectrum mapped out in a series of isofrequency bands, with a progressive shift toward higher or lower frequencies as one moves in directions orthogonal to the bands. The match in specificity of perceptual learning and the specificity of cortical maps opens the possibility that the substrate of perceptual learning is based in primary sensory cortex, and that a substantial mutability of receptive field properties is possible in adult sensory cortex. The particular advantage of studying learning of simple attributes in early sensory stages is that elaborating the mechanisms of learning becomes a much more approachable job. In these areas most is known about the functional properties of cells and the topographic maps of particular functional attributes; hence it is possible to follow functional changes associated with the learning. The relationship between connectivity, functional architecture, and receptive field properties is best characterized in these areas, so it is possible to trace functional alteration to changes in the weights of specific, identified connections.

Various forms of learning have been explored, some of which involve traditional associative conditioning and some of which are implicit learning, resulting from repeated exposure to a stimulus but not requiring an association or reward. Learning involving a stimulus and reward, or classical conditioning, begins with the conditioned stimulus and is followed by the unconditioned stimulus, such as a food reward or an aversive stimulus. The original evidence for the change in auditory responses with reward came from the observation of increased auditory-evoked potentials when a sound stimulus was associated with a food reward (2). 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 (3). The mechanism by which the presence of the unconditioned or reward stimulus can influence the cortical responses to the conditioned stimulus is addressed by the paper by Bakin and Weinberger in this issue of the *Proceedings* (4). 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.

The paper by Bakin and Weinberger (4) explores the potential role of a basal forebrain nucleus, nucleus basalis (NB), in the alteration of auditory receptive fields associated with learning. They found that stimulation of NB 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 (5). 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 memory seen in Alzheimer disease.

The results presented here add to a growing body of evidence that plasticity is a universal property extending to all cortical areas, and that cortical plasticity may play a role in many different forms of learning. A number of experiments in cortical areas representing different sensory modalities have shown that lesions of the sensory periphery or of the central nervous system leads to a remapping of the topography of the cortical areas receiving input from these structures. In the somatosensory system, animals trained to detect differences in the frequency of tactile vibration stimulation, restricted to one segment of one finger, improve over a number of weeks. The change in cortex depends on the active involvement of the animal in making the discrimination, and is associated with cortical recruitment, an increase in the cortical representation of the stimulated digit (6). Analogous experiments were done in the auditory system, where it was indicated that for animals trained to discriminate small differences in the pitch of a tone, the area of cortex representing that tone enlarged (7). Further experiments will reveal the extent to which the cortical changes

Commentary: Gilbert

Proc. Natl. Acad. Sci. USA 93 (1996)   10547

show specificity that correlates with the specificity of the perceptual improvement.

In the visual system there is also evidence that sensory experience in the adult can lead to substantial alterations of receptive fields. When a receptive field is located in an occluder surrounded by a pattern of moving lines of dynamic random dots, the field expands to fill the occluder, increasing in diameter severalfold (8, 9). This expansion is associated with the increase in the effective connection strength between cortical cells, which has been postulated to involve the plexus of long range horizontal connections formed by cortical pyramidal cells (10). These short-term changes have also been observed in visual area V4, and in both cases may play a role in the phenomenon of perceptual fill-in (11, 12). The short-term changes described here, and longer-term changes in cortical topography observed after retinal lesions (13–17), point toward a capability for pronounced functional changes in adult visual cortex. Changes in visual cortical topography have been shown to be cortical in origin, as opposed to originating from subcortical stages in the visual pathway (16, 18, 19). Under circumstances of normal visual experience, this mutability of visual cortical topography may be invoked in perceptual learning (1). The specificity of perceptual learning for the trained position in visual space and for stimulus orientation suggests the involvement of primary visual cortex, which has the finest resolution of topographic and columnar organization. Much of the work on perceptual learning shows that improvements occur after performing a discrimination repeatedly, without reward or error feedback, and thus would not be expected to invoke the kinds of reinforcement mechanisms seen in associative learning as demonstrated by Bakin and Weinberger (4).

The contribution of Bakin and Weinberger (4) shows the extent to which learning is amenable to a mechanistic analysis. One can associate learning with specific changes in the tuning characteristics of individual cells, and with the interactions between cortical and subcortical structures. The results suggest a specific pharmacology of learning and will lead to studies of the associated signal transduction cascade that will ultimately allow one to characterize the mechanism of learning from changes at the molecular level to changes in circuits and neuronal ensembles to changes at the cognitive level.

1. Gilbert, C. D. (1994) *Proc. Natl. Acad. Sci. USA* **91**, 1195–1197.
2. Durup, G. & Fessard, A. (1935) *Ann. Psychol.* **36**, 266–281.
3. Bakin, J. S. & Weinberger, N. M. (1990) *Brain Res.* **536**, 271–286.
4. Bakin, J. S. & Weinberger, N. M. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 11219–11224.
5. Weinberger, N. M., Ashe, J. H., Metherate, R., McKenna, T. M., Diamond, D. M. & Bakin, J. (1990) *Concepts Neurosci.* **1**, 91–132.
6. Recanzone, G. H., Schreiner, C. E. & Merzenich, M. M. (1993) *J. Neurosci.* **13**, 87–103.
7. Recanzone, G. H., Merzenich, M. M. & Schreiner, C. E. (1992) *J. Neurophysiol.* **67**, 1071–1091.
8. Pettet M. W. & Gilbert, C. D. (1992) *Proc. Natl. Acad. Sci. USA* **89**, 8366–8370.
9. Gilbert, C. D., Das, A., Ito, M., Kapadia, M. K. & Westheimer, G. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 615–622.
10. Das, A. & Gilbert, C. D. (1995) *J. Neurophysiol.* **74**, 779–792.
11. DeWeerd, P., Gattas, R., Desimone, R., Ungerleider, L. G. (1996) *Nature (London)* **377**, 731–734.
12. Ramachandran, V. S. & Gregory, T. L. (1991) *Nature (London)* **350**, 699–702.
13. Gilbert, C. D., Hirsch, J. A. & Wiesel, T. N. (1990) *Cold Spring Harbor Symp. Quant. Biol.* **55**, 663–677.
14. Kaas, J. H., Krubitzer, L. A., Chino, Y. M., Langston, A. L., Polley, E. H. & Blair, N. (1990) *Science* **248**, 229–231.
15. Heinen, S. J. & Skavenski, A. A. (1991) *Exp. Brain Res.* **83**, 670–674.
16. Gilbert, C. D. & Wiesel, T. N. (1992) *Nature (London)* **356**, 150–152.
17. Chino, Y. M., Kaas, J. H., Smith, E. L., III, Langston, A. L. & Cheng, H. (1992) *Vision Res.* **32**, 789–796.
18. Darian-Smith, C. & Gilbert, C. D. (1994) *Nature (London)* **368**, 737–740.
19. Darian-Smith, C. & Gilbert, C. D. (1995) *J. Neurosci.* **15**, 1631–1647.