Plasticity of Binaural Hearing and Some Possible Mechanisms following Late-Onset Deprivation

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Abstract

Evidence for binaural plasticity resulting from late-onset deprivation comes from behavioral adaptation in humans following experience of abnormal binaural cues, from physiologic changes in the organization of the cerebral cortex, and from anatomic rewiring of some of the pathways underlying binaural hearing in the brain stem. Some of this evidence is indirect, and the long-term functional consequences of these changes in the nervous system are unclear. Nevertheless, there are now sufficient data available on plasticity in mature nervous systems to warrant a substantially increased research effort in this field. Among the questions to be addressed are the site(s) of reorganization in the auditory system, the effects of different types of deprivation, and the neural mechanisms underlying the plasticity.

Key Words: Adaptation, brain stem, cochlear removal, cortex, earplugging

The possibility that late-onset deprivation may affect binaural processing is suggested by three lines of evidence. First, adult humans can, at least to some extent, adapt to altered binaural cues produced by real or artificial asymmetries of input between the two ears. Second, the physiologic responses of neurons in the higher levels of the central auditory system of animals remain plastic into adulthood and can be altered by lesions of the peripheral auditory system. Third, the bilateral balance of anatomic connections between auditory brainstem nuclei continues to change in adult animals following unilateral peripheral lesions in infancy or adolescence.

In this paper, I review the evidence for human binaural plasticity in the context of more general findings concerning mechanisms for adaptation and plasticity in the adult brain. Timing is a central issue in the ideas discussed here. Since most or all of the identified developmentally sensitive periods for sensory processing are over before sexual maturation occurs (Knudsen, 1988), I define “late-onset” as deprivation beginning during or after adolescence. Auditory stimulation produces behavioral, physiologic, and anatomic responses that almost invariably change with time. The rapidity of change has been used to distinguish short-acting “adaptation” (Hafter et al, 1988; Hudspeth, 1989) from longer-acting “plasticity” (Robertson and Irvine, 1989), although these terms have been applied, respectively, to longer- and shorter-acting change. In this paper I use the term plasticity to focus on changes occurring over a time scale of hours to years, rather than one of fractions of seconds to minutes.

PLASTICITY OF HUMAN BINAURAL HEARING

When a suprathreshold sound of equal sensation level (SL) in each ear is delivered to a listener via headphones, it might be expected that the fused sound image should be centered within the head; however, a number of studies of listeners with normal hearing (Fig. 1), or pathologic or induced hearing loss (Jerger and Harford, 1960; Wang and Dallós, 1972; Florentine, 1976; Durlach et al, 1981) have found that the level of a dichotically presented stimulus is set closer to equal sound pressure level (SPL) than to equal SL in order to achieve...
centering. The most obvious interpretation of these results is that the binaural mechanisms responsible for producing the fused image have somehow adapted to the altered cues associated with interaural asymmetry. Durlach and colleagues (1981) have labelled this phenomenon "long-term relearning" and they have suggested that, during normal development and adult asymmetric hearing loss, binaural hearing changes to maintain a correlation with visual and tactile perception and with sensorimotor feedback (Held, 1955).

It is unclear from most of these studies how "long-term" the changes in binaural processing actually are and to what extent the "relearning" occurs for binaural tasks other than simultaneous binaural balancing. Most of the clinical cases were of long duration with unknown or unspecified age at onset. However, Florentine (1976) measured the onset and decay of the change in midline centering with time by observing normal-hearing listeners who wore a unilateral earplug (Fig. 2). Note that in both this case and that of the unplugged normal-hearing listeners (see Fig. 1), centering data are compared with equal interaural loudness matches, obtained by successive or alternate interaural comparisons. In contrast to centering, loudness matches are not based on binaural interaction. They appear to follow interaural sensation levels closely (although not perfectly; see Fig. 1B) and they show no sign of systematic change with time following asymmetric hearing loss (see Fig. 2). Changes in centering, on the other hand, occur gradually over a period of hours to days (see Fig. 2) and are, therefore, an example of binaural plasticity.

In an attempt to find an example of interaural-time-based binaural plasticity in adult humans, my colleagues (Sarah Hogan and Mary Hutchings) and I have begun to examine the effects of unilateral earplugging on binaural unmasking. We have measured thresholds for 500-Hz tone bursts in a narrow band noise masker (N) centered at 500 Hz. The tone bursts (S) were either in-phase (N0S0) or out-of-phase (N0S90°) between the ears (Moore et al., 1991). Listeners were tested repeatedly before, during, and after earplugging for up to 1 week (Fig. 3). The results are preliminary, but suggest that earplugging produces an immediate and long-lasting reduction in binaural unmasking through an elevation in the (N0S0) threshold. This result is consistent with previous findings involving either unilaterally hearing-impaired subjects (Colburn, 1982) or an imposed mismatch of the level of the signal and masker presented to one ear (Durlach and Colburn, 1978). No evidence of plasticity is apparent in the results obtained to date, suggesting that binaural phase coding may not be subject to plastic change in the way that interaural level difference coding apparently is.

Figure 1 Comparison of interaural centering and interaural loudness matches in a group of normal adult human subjects. For each data point, the interaural level difference (ILD) required for centering or for equal loudness is plotted as a function of the interaural threshold difference (ITD) obtained from the same subject on the same day, and using the stimulus parameters indicated in the legends. The dashed lines show the linear regression expected for matching binaural balance to equal sensation levels (SPL). The other sloping lines show the actual linear regression obtained (with correlation coefficient, r; all stimulus conditions pooled) between ILD and ITD in each case. The horizontal lines through zero ILD show the predicted result of interaural matches based purely on sound pressure level (SPL). Stimuli in A were 4-kHz or 9-kHz (500 msec, slow rise/fall time) tones presented at SPLs of 20, 40, or 60 dB (re. the more sensitive ear). In B, stimuli were 4-kHz tones presented at 20 or 40 dB SL on 1 of 2 days (D1, D2). Thresholds and binaural balances were obtained using staircase procedures and, in the balancing tasks, two alternative forced choice (2 AFC) psychophysics. Note that the regression line of the data in A falls between equal SL and equal SPL. In contrast, that in B closely parallels equal SL. Further details in text. (Unpublished observations.)
Figure 2  Interaural centering and loudness matches for two normal adult human subjects before, and at three times (0 days = immediate) after the insertion of a unilateral earplug. The earplug produced a 20-to 30-dB attenuation, as indicated by the binaural imbalance in the loudness data. Stimuli were 30-msec tones (1 msec rise/fall) of the indicated frequency presented at 60 dB SPL in the more sensitive ear. Thresholds and binaural balances were obtained using adjustment procedures. Note the plasticity/adaptation of binaural centering, reflected as a decrease in the interaural SPL difference, occurring between 0 and 4 days after earplugging. (Adapted from Florentine, 1976.)

PHYSIOLOGIC PLASTICITY

Although adult humans have long been known to recover functionally, at least to some extent, from damage to the brain, there has recently been a dramatic increase in experimental interest concerning the effects of damage to the sensory periphery or other input pathways on the representation of sensory attributes in the central nervous system (CNS) of adult animals (see Kaas, 1991 for a review). This work is of interest here because it may explain how late-onset deprivation in the auditory system leads to changes in auditory perception. Indeed, following pioneering work in the somatosensory system (Devor and Wall, 1978; Kaas et al, 1983), recent experiments have examined the effects of cochlear lesions on the representation of sound frequency in the auditory cortex (Fig. 4; Robertson and Irvine, 1989; Irvine et al, 1992). In these experiments, small lesions were made in a limited region of one cochlea. The lesions initially produced elevated response thresholds to tones for auditory cortical neurons that normally represented the frequency range in the damaged part of the cochlea. Following 35 to 80 days of recovery, however, the previously high-threshold cortical region was found to contain neurons that responded with normal sensitivity to sound frequencies adjacent to those represented in the lesion. Since no regeneration has been found in the adult mammalian cochlea, these results sug-
suggest that CNS plasticity accounted for the recovery of neuron sensitivity in the auditory cortex.

In a separate series of experiments, Weinberger and colleagues (Diamond and Weinberger, 1989; Edeline and Weinberger, 1991) have shown that frequency-specific neuron response changes can occur in the medial geniculate body (MGB) and auditory cortex of adult animals during the acquisition of a conditioned association between an auditory tonal stimulus and a mild electric shock. Although these changes were rather short-lasting (< 1 hour in the MGB), they were based on relatively few conditioning trials and they demonstrated the potential of the mature central auditory system for dynamic experience-dependent change.

Despite the somewhat limited scope of the experimental evidence on plasticity in the central auditory system, comparison with the more extensive somatosensory literature (Merzenich et al, 1988, 1990; Kaas, 1991) suggests general aspects of changes in the adult brain contingent on sensory impairment and experience. In primates (presumably including humans), the changes begin immediately and may be progressive over several years. In extreme cases, they can result in a massive reorganization of the cortex (Pons et al, 1991). Changes can occur at both cortical and subcortical levels, but the weight of evidence suggests that the subcortical changes are less dramatic than those in the cortex (see, however, Irvine et al, 1992, for a dissenting view). In addition to peripheral lesions, the changes may be caused by natural or electrical stimulation of peripheral pathways, or by lesions or stimulation of brain tissue. Thus, in the auditory system, changes may occur as a result of conductive hearing loss or amplification (e.g., with hearing aids; see Silman et al, 1984), as well as sensorineural loss, and probably extend to sound attributes other than frequency. Since there is evidence that binaural processing and sound localization are organized in a topographically ordered manner within the brain (Imig and Adrian, 1977; Konishi et al, 1988; Overholt et al, 1992), these attributes are major contenders for neural reorganization following asymmetric hearing loss.

**ANATOMIC PLASTICITY**

Several sets of experiments have shown that cochlear removal in infancy leads to changes in the morphology of neurons in the brain stem and auditory cortex, and in the neural connections between central auditory nuclei (Rubel and Parks, 1988; Moore, 1992). Unilateral conductive hearing loss can also change the bilateral symmetry of projections deriving from the two ears (Moore et al, 1989) and the physiologic directional responses of midbrain neurons (King et al, 1988), indicating that auditory experience is important for the maintenance of appropriate binaural connections, at least in infancy.
Cochlear removal in adult animals has been shown to result in neuron shrinkage at several levels of the auditory system and in several different species (Powell and Erulkar, 1962; Hashisaki and Rubel, 1989; Moore, 1990b). As in infants, the neuron shrinkage is rapid and complete within 2 days (Hashisaki and Rubel, 1989). Unlike infants, cochlear nucleus (CN) neuron loss does not occur following removal in adults (Hashisaki and Rubel, 1989; Moore, 1990b), even after very long survival times (Moore, submitted). Conductive hearing loss and sound deprivation in adults do not lead to CN neuron shrinkage (Webster, 1983). It is unclear why neurons shrink following cochlear removal or what the functional consequences of the shrinkage are. A recent electron microscopic study (Deitch and Rubel, 1989) in the chicken nucleus laminaris (the avian homologue of the medial superior olivary nucleus) has suggested that neuron soma shrinkage may be secondary to or caused by dendritic atrophy following deafferentation.

Recently, we had the opportunity to examine binaural neural connections in some ferrets with relatively long-term cochlear removals (Fig. 5; Moore, submitted). One group had the right cochlea removed at postnatal day (P) 25 and a second group had the right cochlea removed at P90. For the removals at P25, the effects of the long survival period (1 year) between cochlear removal and examination of the brain were compared with earlier data (Moore and Kowalchuk, 1988) from animals having shorter survival following removal at P25. In this case (see Fig. 5B), there was a significant further change in the bilateral symmetry of projections between the CN and the inferior colliculus (IC), beyond the change already found after a 3-month survival period. For the removals at P90, the effects of 2.5 year survival were compared with earlier data, again obtained following a 3-month survival period. In this case (see Fig. 5B), the shorter survival period did not change the symmetry of CN-IC projections, but the much longer survival period did. Thus, the bilateral symmetry of auditory projections within the brain stem can continue to change in adolescence as the result of a cochlear removal performed in infancy, and cochlear removal in adolescence can induce changes in adult auditory brainstem connectivity.

It is important to note that, at least in infancy, the changes described here do not occur following bilateral hearing loss (Moore, 1990a). It maybe that it is the asymmetry between the ears that is of crucial importance in initiating these changes rather than hearing loss per se. The results of Silverman and Emmers (1993) support this hypothesis. Following long-term monaural amplification of bilaterally hearing-impaired adult humans, these authors found significant word-recognition decrements in the unaided ear, despite the lack of change in stimulation of that ear.

**MECHANISMS OF PLASTICITY**

We do not presently know how many other physiologic and anatomic changes in the mature auditory system can be induced by hearing loss or by variations in auditory experience. There is, however, mounting evidence from other neural systems that the morphology and functional connections of all neurons are constantly changing. For example, dendrites of individual neurons in the autonomic nervous system have been shown to appear, disappear, and change shape over a 3-month period in normal young adult mice (Purves et al, 1986). By implication, synaptic connections to these dendrites are also rearranged. In the adult primate somatosensory cortex, neurons have been recorded with chronically implanted microelectrodes (Merzenich et al, 1988). The region of skin providing input to the recorded neurons was found to change mark-
edly over time, apparently without systematic experimental intervention. In the mature visual cortex, deprivation of form vision through monocular eyelid suture has been found to change the expression of genes coding for neurotransmitters and calcium binding proteins involved in neural activity (Benson et al., 1991). The inference may be drawn from these studies that small changes in neuron morphology and function occur randomly and, under the influence of the pattern of activity in input pathways and the local extracellular milieu, the neuron is constantly resculptured to satisfy changing demands.

The therapeutic implications of adult neural plasticity are at once obvious and subtle. On the one hand, it would seem clear that restoration of central neural function after late-onset deafness is possible and obtainable using known methods of electrical or chemical stimulation. On the other hand, the consequences of providing misdirected or otherwise inappropriate stimulation might be to exacerbate the problem through the promotion of incorrect associations between the auditory world and the neural representation of that world. Important research questions stemming from these considerations would seem to be the following: To what extent and in which of its parts is the central auditory system of mature animals capable of reorganization? What are the necessary and sufficient stimuli for reorganization? Is it possible artificially and selectively to promote reorganization to the perceptual benefit of the client? Does age continue to play an important role in neural plasticity in adulthood, as it does during development? Is perceptual adaptation produced by the same mechanisms that are involved in neural responses to peripheral injury? Can the mechanisms of reorganization be up-regulated or down-regulated as indicated therapeutically? The answers to these questions may be as important for the future treatment of hearing problems as direct repair of the cochlea itself.

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REFERENCES


COMMENTARY

David Moore skillfully integrates diverse clinical and basic science data to convincingly demonstrate that asymmetric sound deprivation is followed by adaptive central changes in binaural hearing, even in adults. This conclusion challenges the generally held belief that the adult central nervous system is immutable.

The phenomena reviewed and documented are quite different from the recovery of function following cerebrovascular accidents or other traumatic brain insults. They are rather the sequellae of unilateral auditory deprivation, the causes of which vary from earplugging to removal of the cochlea, but involve no direct damage to the brain.

The changes that occur in the auditory forebrain (medial geniculate and auditory cortex) are comparable to those seen in forebrain somesthetic and visual centers following peripheral insults to those systems. Those in the auditory brain stem, however, are not. Further, the brain stem changes (at least) do not occur if...
the auditory deprivation is bilaterally symmetrical.

The long-term changes in the auditory brainstem that follow asymmetric peripheral losses are quite comparable to what happens in the vestibular system. A unilateral loss of the exquisitely balanced vestibular input (for instance, from a labyrinthectomy) results immediately in vertigo, nystagmus, whirling movements, and falling. These responses are followed (over a variable period ranging from days to months) by gradual loss of vertigo, recovery of balance, and loss of nystagmus.

Work with experimental animals demonstrates that similar recovery of function (adaptation) following unilateral vestibular deprivation is correlated with both structural and functional organizational changes in the vestibular brain stem. This central reorganization in turn permits appropriate responses to the new asymmetry of the vestibular input.

The parallels between vestibular system and auditory system adaptations to chronic asymmetric inputs are obvious and striking, but not unexpected. After all, the peripheral transducers of both systems (cochlea and vestibular apparatus) develop from the otocyst, and utilize hair cells as their mechanoreceptor/transducer cells. Although the vestibular and auditory brainstem pathways are separate, significant portions of each develop from the rhombic lip. The cochlea evolved from the phylogenetically older vestibular apparatus. With all the ontogenetic and phylogenetic similarities between the two systems, it is not surprising that the auditory system, like the vestibular system, undergoes adaptive changes to chronic asymmetric inputs.

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