Cochlear Implantation in Adults With Prelingual Deafness. Part II. Underlying Constraints That Affect Audiological Outcomes

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Objectives/Hypothesis: To discuss the underlying physiological and anatomical constraints on audiological performance of late-implanted prelingually deafened adult cochlear implant patients. Study Design: Retrospective review. Methods: Published literature on the topic of auditory pathway responses to prolonged congenital deafness was reviewed. In particular, the authors sought to identify the anatomical and physiological changes that take place in both the peripheral and central auditory pathways in response to prolonged deafness, as well as how they are altered by chronic electrical stimulation. Results: The currently available evidence suggests that the colonization of the auditory cortex by other sensory modalities is the main limiting factor in postimplantation performance, not the pathological degenerative changes of the auditory nerve, cochlear nucleus, or auditory midbrain. Conclusion: The reviewed evidence, although circumstantial, suggests that emphasizing aurally based educational programs before (with hearing aids) and after cochlear implantation could reduce the cortical colonization phenomenon and potentially improve postimplantation audiological performance of patients with long-term prelingual deafness. Key Words: Auditory plasticity, cochlear Implants, critical period, long-term deafness.

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INTRODUCTION

Most studies that have investigated cochlear implant (CI) use by prelingually deafened adults have focused on the results of clinical tests using behavioral measures of speech perception and spoken word recognition. Few studies have dealt with the underlying sources of performance limitation and the nature of the variability in outcome measures frequently observed in this group of patients. With only a small number of prelingually deafened CI users available for testing, an alternative approach, based on considerations of known physiological and histological responses of the auditory system to prolonged deafness, may be more helpful in explaining the results we observed. Such an approach has been facilitated by a recent surge of interest and the available information in the areas of auditory plasticity and electrical hearing, due in large part to recent advances in laboratory technologies that allowed researchers to electrically stimulate the deafened auditory nerve of experimental animals.

In the present study, we examine and review the anatomical, physiological, and cognitive changes in both the peripheral and the central auditory pathways in response to prolonged congenital deafness and chronic electrical stimulation. Our objectives are threefold. First, we examine the likely anatomical and physiological correlates of the sensitive period observed in CI patients. Second, we identify the possible limiting factors that contribute to the poor performances of many prelingually deafened adult CI users. Third, we use this information to guide us in selecting appropriate candidacy criteria for future cochlear implantation in this population of patients.

MATERIALS AND METHODS

Published literature on the topic of auditory pathway responses to prolonged congenital deafness was reviewed. In particular, we sought to identify the anatomical and physiological changes that take place in both the peripheral and central auditory pathways in response to prolonged deafness, as well as how they are altered by chronic electrical stimulation.
RESULTS AND DISCUSSION

Peripheral Auditory System

For CI patients, their sensorineural hearing loss is a result of degeneration of or damage to the sensitive transducer hair cells in the cochlea. Because the sensory hair cells do not regenerate, the resulting hearing loss is permanent, and the cessation of afferent inputs to the auditory system leads to a series of predictable pathological changes along the entire auditory pathway.

Studies using animal models have shown that damage to the sensory hair cells leads to extensive degeneration and loss of the dendritic processes of the spiral ganglion cells (SGCs). This process is followed by demyelination or complete degeneration of the remaining peripheral processes and cell bodies of the SGCs. With a long period of profound deafness, the ongoing degeneration of the auditory nerve fibers eventually results in only a small number of surviving SGCs. Such laboratory findings in animals were supported by a human temporal bone study, in which the total SGC loss was found to be significantly correlated with the duration of total deafness.

Based on these findings, several researchers have suggested that the favorable outcomes achieved by congenitally deaf patients implanted in early childhood can be explained by preservation of the peripheral auditory system. However, all histopathological evidence to date has not supported such a hypothesis. Fayad et al. reported no correlation between auditory performance of their CI patients with postmortem SGC counts. A more recent study even reported an apparent negative correlation between residual SGC count and the patient’s hearing performance during life. Taken together, the results of these studies suggest that the atrophic and degenerative changes of the peripheral auditory pathway alone cannot adequately explain the audiological outcomes of the CI patients and that the central auditory pathways may play a more important role in the speech and language outcomes of these patients.

The robustness in the peripheral auditory system appears to be due, at least in part, to the redundancy and overcapacity of the auditory nerve fibers when compared with the limited spatial channels of the CI. Previous studies have shown that the closely spaced electrodes may stimulate overlapping populations of neurons, resulting in only a small number of percepts along the electrode array that can be clearly discriminated. Therefore, the loss of some auditory neurons may not be the limiting factor in influencing CI users’ audiological performance. Several studies have also shown that chronic electrical stimulation of the cochlea could provide neurotrophic support for the spiral ganglion cells, thereby improving the SGC survival rate by 50 to 70% compared with the nonstimulated ear.

The physiological correlates of the clinical findings can be found by examining the electrophysiological measurements of long-term deafened animals. Shepherd and Javel reported that auditory nerves with severe neural loss (<5% SGC survival) were able to generate electrically evoked auditory brainstem response with normal morphology, albeit with elevated thresholds and decreased response amplitudes. Single-fiber recording further confirmed that these neurons were capable of generating and propagating action potentials. However, differences were noted between the diseased and the normal ears. Auditory nerves with significant disease were found to have reduced spontaneous activity, reduced temporal resolution, and increased latencies and thresholds. Such changes probably reflect the degenerative process of the auditory nerve, including the loss of the peripheral dendritic processes, demyelination of the SGCs, and the reduced SGC count. Theoretically, such changes can be expected to reduce the neuronal responsiveness to electrical stimulation and increase the CI’s power consumption. Exactly how these changes affect the clinical outcome measures obtained from CI patients remains unknown.

Cochlear Nucleus and Auditory Midbrain

The cochlear nucleus (CN) and auditory midbrain differ from the peripheral auditory pathway in a significant fashion. Whereas the degeneration of SGCs in the absence of afferent hair cell stimulation is an ongoing process, cell death of CN occurs only during a short critical period before the onset of hearing. Cochlear ablation studies using animal models have demonstrated the existence of an abrupt, well-defined critical period (lasting 2 d–2 wk depending on the specific species) within which cessation of afferent inputs results in significant cell loss in the anteroventral cochlear nucleus (AVCN). Beyond the critical period, neurons in all areas of the CN lose their susceptibility to the deafferentation-induced neuron death. Thus, given that hearing in humans is developed early in gestation, the CN critical period ends long before birth.

Such findings have significant clinical implications for prelingually deafened patients. For many common causes that lead to prelingual deafness, such as aminoglycoside ototoxicity, meningitis, and several forms of genetic hearing loss, the susceptibility of the inner hair cells only begins after the onset of auditory functions. Consequently, such pathological conditions result in only minimal neuronal cell loss within the CN.

The basic development of the ascending pathway beyond the CN has also been shown to be independent of the afferent inputs. By labeling the afferent brainstem projections with tracers, Friauf and Kandler showed that connections to the inferior colliculus from the cochlear nuclei and nuclei of the superior olivary complexes and the lateral lemnisci are all present at birth. There were no significant changes in the quantity of labeled neurons or the basic labeling pattern during successive development. The evidence strongly suggests that internuclear connections from auditory brainstem to the inferior colliculi appear to be established prenatally. Furthermore, some of these connections appear to be maintained over time, even without normal afferent input. Studies of animals with long-term deafness have shown that the mammalian inferior colliculus was able to maintain a rudimentary cochleatoptic organization even in the absence of any afferent stimulation.
Although neuronal cell loss of the auditory brainstem is minimal if the sensorineural hearing loss occurs after the onset of hearing, other significant structural and functional changes have been observed in the studies of deafened animals. Histological studies have reported significant reduction in the overall soma area of neurons in the CN and medial nucleus of the trapezoid body, the superior olivary complex, the lateral lemniscus, and the inferior colliculus. The volume loss has been attributed mostly to loss of supporting neuropil, with minor contribution from shrinkage of neurons. Although the loss of neuropil appears to be permanent, neuronal shrinkage has been found to be partially reversible following chronic intracochlear electrical stimulation.

Ultrastructural examinations of the auditory brainstem of animals with long-term deafness also revealed significant abnormality and reorganization in the neuronal synaptic morphological appearance. Observed changes include attenuation in terminal branching, a reduction in synaptic vesicle density, thickening of the presynaptic and postsynaptic densities, and enlargement of synapse size. These changes can be viewed as compensatory responses to diminished afferent input and transmitter release. However, the structural complexity of the neural pathway remains unchanged, and much of the deafness-related synaptic changes in AVCN could be prevented with chronic electrical stimulation. Thus, the reorganization of the central auditory pathway during auditory deprivation appears to extend well beyond the onset of hearing. Some of the associated deleterious effects appear to be reversible with reintroduction of afferent stimulation with cochlear implants.

The anatomical and morphological alterations caused by prolonged deafness are reflected in the results of several physiological studies. The response threshold of the ventral CN to electrical stimulation was significantly elevated in deafened cochleas. Also adversely affected were the synchrony of excitatory postsynaptic potentials of AVCN neurons and the response latency and temporal jitter of the inferior colliculus neurons. It is likely that such changes significantly decrease the temporal resolution of the inferior colliculus neurons. However, the reduction of temporal resolution was improved with chronic electrical stimulation of the auditory nerve, presumably as a result of stimulation-induced neural growth and synaptic remodeling.

Taken together, the evidence reviewed to date suggests that prolonged deafness produces significant changes in the anatomy and physiology of the auditory brainstem. It appears that temporal processing is particularly affected by the deafness-induced synaptic changes, as supported by the results of several psychophysical studies involving congenitally deaf adult CI patients. However, many of the underlying physiological changes appear to be partially reversible with re-establishment of afferent input with a CI. Thus, the results suggest that changes at the level of the auditory brainstem are likely to be responsible for some of the limitations of the CI patients in speech perception, but no evidence to date suggests the existence of a definitive developmental critical period due to deafness-induced changes in the CN or the auditory midbrain.

**Auditory Cortex**

Unlike the peripheral auditory system and the auditory midbrain, the basic anatomical structure of the human auditory cortex is immature at birth. Prolonged auditory deprivation during the ensuing maturation process has been shown to produce significant long-lasting effects on the eventual speech perception capability of the patients. In addition, language and speech perception are complex information processing activities that involve more than simple detection and discrimination of auditory signals: The development of secondary cortical centers with interhemispheric and intrahemispheric projections are necessary for the processing and understanding of speech. To understand how such complex development is affected by prolonged auditory deprivation, we first review the maturation stages of the different axonal systems of the human auditory cortex and the ways auditory deprivation affects these developmental processes. Second, we consider the impact of communication mode and educational experience on the cortical remodeling process and how such information may shed light on the limitations and variabilities of the outcome measures we observed in the long-term prelingually deafened CI patients.

Three developmental stages of the human auditory cortex have been identified, with full maturation not achieved until approximately 12 years of age. Each stage of cortical development is characterized by the maturation of a different axonal system. During the perinatal period, only the most superficial layer (layer 1) of the auditory cortex contains any mature neurons. The axons of these neurons are not connected to projections from the auditory midbrain and therefore are thought to carry no information on external auditory stimuli. Between 4.5 months and 5 years of age, axons of thalamocortical afferents begin projecting into cortical layers 4, 5, and 6, carrying inputs from the lower auditory pathway. This represents the beginning of cortical processing of auditory stimuli. Interhemispheric and intrahemispheric connections begin developing in layers 2 and 3 between 5 and 12 years of age. These commissural and association corticocortical axons interconnect various speech and language processing centers, allowing more complex processing of speech signals.

Little is known about how profound bilateral hearing loss at different stages of development affects the morphological appearance of the auditory cortex. Our current knowledge is based mostly on indirect findings obtained from electrophysiological and imaging experiments. Animal studies have shown that in response to electrical stimulation of the auditory nerve, the basic response properties of the adult primary auditory cortex of congenitally deaf white cats are similar to those reported in normal hearing animals. In addition, the cortex of the congenitally deaf white cats appears to retain at least some rudimentary level of cochleotopic organization. Thus, the results suggest that prolonged congenital deafness does not completely inhibit the development of the ascending thalamocortical afferents, and the basic connections from
the auditory periphery to the primary auditory cortex could develop without the presence of auditory input. However, more recent studies have indicated significant functional deficits of the congenitally deaf white cat auditory cortex if the duration of the auditory deprivation exceeds a sensitive period of 6 months. In particular, it has been found that the synaptic currents of the infragranular output layers are substantially attenuated if auditory experience is not restored by cochlear implantation within the sensitive period. The naive auditory cortex also exhibited deficiency of synaptic activities at long latencies (>30 ms), suggesting that the deficiency was probably due to immaturity of the higher-order cortical connections. Because the commissural and association corticocortical and corticothalamic axons are the last to mature, it is not surprising that they are the most susceptible to the effects of early auditory deprivation. In contrast, when the congenitally deaf white cats are implanted early in life, the deaf kittens were able to develop high-amplitude cortical field potentials, expansion of activated auditory cortical areas, and long latency responses that are suggestive of higher-order intracortical information processing.

The results of the animal studies are consistent with the reported findings of human imaging experiments. Using positron emission tomography (PET) imaging technique, Truj et al. and Naito et al. have shown that the primary auditory cortex of prelingually deafened adults remains responsive to intracochlear electrical stimulation. However, speech activation of the secondary auditory cortex was much less than that found in either normal-hearing or postlingually deaf subjects. Thus, the results suggest that, although the auditory pathways to the primary auditory cortex remain functional for a long period after prelingual auditory deprivation, the perceived sensation may not be interpreted as meaningful sound by some users, most likely because of their inability to process the incoming signals in the appropriate higher-order speech and language centers.

It is imperative to note that under prolonged auditory deprivation, the original intended targets of the corticocortical projections (i.e., the secondary auditory and association areas) do not atrophy or degenerate. Instead, the inherent cortical plasticity allows for cross-modal reorganization and colonization by other sensory modalities. The auditory association area (the supratemporal gyrus), but not the primary auditory cortex, has been shown to be responsive to manual sign language used by congenitally deaf adults. Thus, the auditory language area may become "rewired" to process visually evoked signals, whereas the dormant primary auditory cortex remains reserved for auditory processing. For example, after the patient in the study of Nishimura et al. received a CI, it was found that spoken words activated the primary auditory cortex but not the adjacent language areas, and the patient was unable to understand the spoken words. In addition, Lee et al. showed that the extent of the cross-modal colonization of the auditory association cortex was directly proportional to the duration of deafness, and both factors were inversely correlated with the postimplantation speech perception performance. Taken together, the evidence suggests that an alternative communication modality such as manual sign language could "occupy" the underused secondary auditory cortical centers of prelingually deafened patients, impeding any potential future improvement of speech perception after cochlear implantation.

The findings suggest that the use of auditory-verbal therapy and oral-aural rehabilitation should be advocated as the preferred educational method for prelingually deafened patients, especially if they intend to obtain a CI as a treatment option for their hearing loss. We think that by providing even minimal aided auditory input to the auditory cortex, together with reducing interference from other competing sensory modalities (e.g., American Sign Language or variants of manually coded English), it may be possible to decrease the cortical colonization phenomenon and preserve the auditory pathways to the cortical auditory language centers. Indeed, several clinical outcome studies have supported this hypothesis. Improvements in open-set spoken word recognition, language development, and speech communication abilities of oral children receiving cochlear implants were significantly more rapid than in children who used total communication (i.e., combination of sign and oral languages). It also appears that the recent improvements noted in the speech perceptual performance of the long-term prelingually deafened patients are probably the result of patient selection criteria, because the vast majority of the better-performing patients were oral communicators. Therefore, communication mode should be considered an important candidacy criterion for planning future cochlear implantation in patients with long-term prelingual deafness.

Another important consideration is the nature of the sensitive period in human cortical maturation. Extensive experimental data on congenitally deaf white cats have shown a sensitive period of approximately 5 to 6 months, within which the amount of excitable cortical tissue increases with increasing duration of intracochlear electrical stimulation. It is widely assumed that a similar sensitive period exists in humans, but the lack of experimental data has hampered our understanding of the exact nature and duration of the human cortical plasticity after prolonged deafness. Aside from the clinical outcome data, the most revealing findings to date are based on studies of cortical auditory evoked potential of prelingually deafened CI patients who were implanted at different ages. Ponton et al. first noted that the latency delay of the P1 cortical auditory evoked potential could be used as a measure of cortical auditory maturation. They found that for implanted children, maturational delays for P1 latency approximated the period of auditory deprivation before implantation. With the reintroduction of stimulation by the CI, the maturation of the P1 latency resumes and it appears to grow at the same rate as in normal-hearing children. However, longitudinal and cross-sectional data indicate that even after many years of implant use, the evoked potentials of adult prelingual CI users with long-term deafness still remain different from their normal-hearing counterparts: The P1 peak latency remains prolonged and P1 amplitude remains larger in CI users. The results suggest that age-related changes in
the P1 peak occur only over a finite period and that the underlying cortical plasticity ends by 12 years of age. More recently, Sharma et al.\textsuperscript{42} reported similar findings in their analysis of cortical potentials obtained from 104 congenitally deaf CI patients and concluded that the human auditory system is maximally plastic in the absence of auditory stimulation for approximately 3.5 years. The plasticity gradually declines with increasing duration of deafness, and it is significantly reduced after age 7 years.

The neurophysiological findings reviewed in the present study are consistent with the clinical outcome data that we summarized in Part I of the present series.\textsuperscript{48} The postimplantation audiometric performance of prelingually deaf patients is inversely related to their duration of deafness, and the patients with the longest period of auditory deprivation (10 y or longer) typically reach their performance plateaus within a short period of time (<1 y). These findings are probably the direct consequences of the loss of plasticity in the higher-order secondary auditory cortex, reducing the patients’ ability to acquire the cognitive skills necessary to process complex speech signals. The present findings are in sharp contrast to the previous conclusion that prelingually deaf patients may require longer time periods to achieve their maximal audiological potentials.\textsuperscript{42}

At present, the cortical colonization phenomenon that we observed in the higher-order auditory cortex is nonreversible once a patient reaches adulthood. However, active research is under way to find ways to modify some of the factors that govern cortical plasticity, especially after the sensitive period of cortical development has elapsed. One recent development deserves mention. Chondroitin sulfate proteoglycans, components of perineuronal nets that are thought to inhibit axonal sprouting and synaptic rearrangement, have been implicated recently as a main contributing factor to the end of the sensitive period.\textsuperscript{49} It has been shown that it is possible to reestablish the cortical plasticity by dissolving the perineuronal net around the neuronal cell bodies and dendrites. By identifying the molecular correlates of the neural plasticity, it may be possible to reverse the “cortical colonization” phenomenon of the auditory cortex through therapeutic pharmacological interventions.

CONCLUSION

It appears that the deafness-induced changes along the entire auditory pathway, including the degeneration of the auditory nerve, the alteration of synaptic structures in the midbrain, and the failure to establish appropriate intracortical projections in the auditory cortex, all contribute to the gradual deterioration of auditory performance with increasing duration of auditory deprivation. However, only the cortical colonization and reorganization phenomenon of the secondary auditory cortical areas by other sensory modalities exhibit a sensitive period with characteristics and time course that are similar to the clinical outcome measures observed in prelingually deaf CI patients with long-term deafness. Thus, the ultimate limitation on the speech perception performance for this group of patients depends on the integrity of their connections between the primary auditory cortex and the secondary speech processing centers. Clearly, early implantation and restoration of auditory input through electrical stimulation are the treatments of choice in promoting such connections. The adoption of universal newborn hearing screening is an important step toward that goal. However, for patients with prolonged deafness, the alternative is to provide aurally based therapy before (with hearing aids) and after implantation. The evidence presented in the present report suggests that educational programs that stress oral communication as the preferred educational modality could potentially reduce the cortical colonization of the central speech and language processing centers. Indeed, the advantages of oral communication over total communication have been documented extensively in the recent clinical outcome studies of prelingually deafened patients.\textsuperscript{40,41} Consequently, the use of oral communication should be an important candidacy criterion in cochlear implantation of patients with long-term prelingual deafness. At this time, the audiological prognosis for many prelingually deafened patients with long-term profound deafness remains poor. However, with the continuing advances in neuropharmacology, it is possible that one day we may be able to restore the cortical plasticity with pharmacological intervention, even after the expiration of the sensitive period.

BIBLIOGRAPHY


