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Brain Plasticity under Cochlear Implant Stimulation

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Abstract

The benefit of cochlear implantation crucially depends on the ability of the brain to learn to classify neural activity evoked by the cochlear implant. Brain plasticity is a complex property with massive developmental changes after birth. The present paper reviews the experimental work on auditory plasticity and focuses on the plasticity required for adaptation to cochlear implant stimulation. It reviews the data on developmental sensitive periods in auditory plasticity of hearing, hearing-impaired and deaf, cochlear-implanted, animals. Based on the analysis of the above findings in animals and comparable data from humans, a cochlear implantation within the first 2 years of age is recommended.

Electrical stimulation of the auditory nerve by cochlear implants evokes a pattern of activity which differs from that evoked by acoustical stimulation in the normal ear. In the normal ear, acoustic stimulation evokes a traveling wave that progresses from the base of the cochlea to the apex, tilting the cilia of the hair cells along the cochlea, generating a receptor potential that leads to activation of the primary fibers through a synapse. This whole sequence involves stochastic processes (e.g. in transmitter release) and nonlinear transformations from the cochlear amplifier [for review, see 1]. All these processes are bypassed in electrical stimulation of the cochlea in deaf individuals. The action potentials of the electrically stimulated auditory nerve fibers are strongly synchronized to the stimulus [for reviews see 2 and the paper by Shepherd and McCreery, this vol, pp 186–205]. The dynamic range of electrical activation of populations of auditory nerve

fibers (defined as the range of stimulus intensities over which the firing rate is modulated) is larger than that of a single nerve fiber because of their differences in thresholds. However, the dynamic range with electrical stimulation is much less than that of the normal activation of auditory nerve fibers through excitation of inner hair cells. This is why it is necessary to compress the auditory signal from the normal range of 40–80 dB of acoustic stimulation to a range of 3–10 dB before it is converted to electrical impulses for stimulation of the auditory nerve. The spread of excitation within the auditory nerve is much larger with electrical stimulation than with normal acoustic stimulation [3]. Last but not least, randomness in the temporal firing pattern with electrical stimulation is much less than it is in the normally activated auditory nerve partially due to the loss of spontaneous activity in 'deaf' auditory nerve fibers [4]. Electrical stimulation at a high rate such as used in modern cochlear implants might induce a slight increase in randomness of the firing patterns because of refractory periods and subthreshold electrical stimulation [5, 6].

Since the activation of the auditory nerve through cochlear implantation is different from the normal sound-elicited discharge pattern, individuals with cochlear implants must learn to interpret this new input.

The ability to use an auditory neuroposthetic device is further challenged if the brain has never learned to process auditory information, as it is the case in congenitally deaf children whose auditory development has not been shaped by hearing experience.

Brain Plasticity and Its Mechanisms

Neural plasticity is the ability of the nervous system to modify its organization and function based on changing external or internal demands. The mechanisms of neural plasticity have been investigated for many decades. As early as at the beginning of the last century, Cajal [7] and later Hebb [8] presented the hypothesis that the coupling between neurons (i.e. the synapse) is responsible for learning by changing its efficacy. In the 1970s, scientists for the first time observed an increase in synaptic efficacy that lasted for a long time (long-term potentiation) [9, 10]. It is assumed that this process is the neural basis for the first steps in the process of brain plasticity.

Plasticity in the Adult Hearing Auditory System

The central auditory system is plastic at several of its hierarchical levels. Changes in properties of cortical cells with training or learning of specific tasks have been presented in studies published during the early 1980s [11, 12]. The

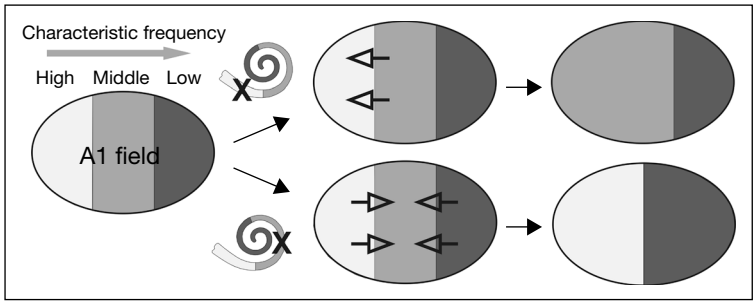

Fig. 1. Effects of restricted cochlear damage on the cortical representations. Damage in the high-frequency region of the cochlea leads to cortical remapping of the middle-frequency representation with the effect of expanded middle frequencies at the level of the cortex. Damage in the middle-frequency region of the cochlea leads to expansion of the high-frequency and low-frequency regions at the level of the auditory cortex.

first report on an 'active' cortical reorganization showed that change (partial deprivation) of the afferent input caused by mechanical destruction of a portion of the cochlea involving a limited frequency range could cause reorganization of the auditory cerebral cortex involving altered frequency representation (injury-induced plasticity) [13]. Frequencies corresponding to the border region between damaged and healthy cochlear tissue became represented in the cortical region previously used for frequencies now in the damaged region of the cochlea – effectively expanding the functional cochlear region into the damaged region (fig. 1). The decrease in the sensitivity of the altered region to the new stimulus indicated that the reorganization was a result of expression of neural plasticity and not acute changes of receptive fields caused by loss of inhibitory drive [14, 15]. The finding of plastic reorganization of cortical tuning curves obtained in studies in guinea pigs was confirmed in other species and in experiments using different methods [e.g. 16–19].

In the auditory system, the nucleus basalis plays an important role in promoting expression of neural plasticity in the auditory cortex. Weinberger and colleagues have shown that perceptual learning in animals involves changes in the threshold curves of cortical neurons (learning-induced plasticity) [16, 20–22], and that similar changes can be evoked by electrical stimulation of the nucleus basalis paired with sensory stimuli [e.g. 23, 24]. Temporal features of cortical units can also be affected by stimulation of the nucleus basalis when paired with sensory stimuli [25].

In a series of experiments, Suga and Ma [26] presented evidence that cortical plasticity plays a central role in inducing expression of neural plasticity in subcortical structures.

As mentioned above, there are two types of expression of neural plasticity, namely learning-induced plasticity and injury-induced plasticity. Learning-induced expression of neural plasticity requires activation of neuromodulatory systems and injury-induced plastic changes are caused by the absence of afferent drive and partial disinhibition of portions of the neural representation maps. The distinction between learning-induced plasticity and injury-induced plasticity, and whether the basal nucleus system has a function in both of them, is currently debated [27–29].

Only limited information regarding the plasticity of higher-order auditory systems is available. Some studies in the cat have indicated that the plasticity in the higher-order auditory cortices is greater than in the primary auditory cortex [30]. Lack of detailed information on the organization of the higher-order auditory fields hampers understanding of the changes that occur in these cortical areas during learning.

Plasticity in the Developing Auditory System

The capacity for reorganization of the brain is more extensive during development than in adult life. Postnatal cortical development involves many processes such as reductions in cell number [31; for review see 32], increases followed by decreases in complexity of dendritic morphology [33], increases followed by decreases in synaptic densities [34–37] and changes in projection patterns [for review, see 38]. Animal studies of the auditory system have shown that partial destruction of the cochlear partition leads to expanded representations of those portions of the cochlea that are functional (especially those neighboring to the destroyed portion of the cochlea). This expansion of response areas is larger in young kittens than in adult cats [39]. Passive listening to a pure tone leads to expansions of the representation of the tone frequency at the level of the auditory cortex in juvenile animals [18], an effect which has not been described for adults.

While newborn babies demonstrate some forms of voice recognition [40, 41; cortical imaging studies: 42, 43, auditory streaming: 44], phonetic specialization to the mother tongue takes place later in life [45, 46]. During the first 8 months of life, the ability to differentiate phonemes from foreign languages is gradually lost (sensitive developmental period for phonetics) [for review, see 47]. Several other sensitive periods exist for language [48]. These processes are especially relevant to the ability to learn to recognize features of speech in prelingually deaf cochlear implant users. The absence of sensory (auditory) experience during sensitive periods leads to a functionally less competent auditory system [e.g. 49; for review, see 50–53]. Similar findings have been

presented for the visual system, where it has recently been shown that interspecies face recognition in humans and monkeys is facilitated by passive watching of pictures in early infancy (up to 9 months), an ability that is otherwise lost at approximately 9 months of age [54].

Neural Plasticity with Cochlear Implants

The use of cochlear implants for recognition of speech and other sounds represents a special challenge for the brain and requires expression of neural plasticity to an extent that surpasses the changes that normally occur in an adult hearing person. After cochlear implantation, most of the representations of sounds in the nervous system have to be rebuilt to fit the characteristics of the new coding of auditory input. The outcome of cochlear implantation thus depends on two groups of factors:

Peripheral Factors. The excitation pattern in the auditory nerve depends on the processing of the sounds that occurs in the cochlear implant processor, the electrode type, its position and extent within the cochlea, pattern of degeneration in the auditory nerve, status of myelination of the auditory nerve.

Central Factors. These include the status of the central auditory system ('auditory experienced' in the case of postlingual deafness or 'naïve' in the case of congenital deafness), its plasticity (young subject vs. older subject) and subjective cognitive factors that determine how effectively the subject adapts to the new type of sensory input. These factors determine how quickly a person who has received a cochlear implant will learn to understand speech.

Effect of Hearing Loss on the Auditory Nervous System

In general, input deprivation in the nervous system causes functional and structural changes through expression of neural plasticity [55]. Many studies have shown that hearing loss and deafness cause changes in the auditory nervous system [for recent review, see 56]. The effect depends on the degree of hearing loss (or sound deprivation) and its duration.

Destruction of the inner ear or severance of the auditory nerve in animals has been used in studies of the effect of sound deprivation on the development of the nervous system [57, 58]. If the intervention that deprives the central auditory system of all sensory inputs is performed before hearing onset in animals born with a not yet functional cochlea, it simulates neonatal deafness and results in a naïve auditory system. However, in addition to deprivation of sensory inputs cochlear ablation leads also to denervation effects, and destruction of the

auditory nerve fibers may prevent the influences of neurotrophic factors in the cochlear nucleus.

In several laboratories, total deafness was induced by application of ototoxic substances locally or systemically [59, 60].

Another option to investigate effects of deafness on the central auditory system is to selectively breed species with a high natural occurrence of congenital deafness such as Dalmatians [61] and congenitally deaf cats [62–64]. The advantage of congenitally deaf cats is their similarity to prelingually deaf humans, especially with regards to the slow degeneration of spiral ganglion cells. The disadvantages are the small litters in these animals, and the fact that only 50–75% of the litters of deaf parents are completely deaf.

Morphological Subcortical Changes

Studies in gerbils and mice have shown that cochlear ablation leads to the loss of neurons in the cochlear nucleus if ablation was performed before hearing onset [65, 66], similar to that of activity blockage in the auditory nerve in gerbils [67]. Reduction in cell numbers in the cochlear nucleus has not been reported in any other animal models with hearing loss or in congenitally deaf humans [68; for review, see 56]. Other studies of animal models of deafness have shown physiological and anatomical transneural changes in auditory brainstem nuclei [61, 69, 70]. In cats, chronic stimulation via a cochlear implant reverses the reduction in the response area, provided that the total stimulation time exceeds approximately 700 h [for review, see 56]. Auditory midbrain nuclei of neonatally-deafened animals have fewer synapses and a smaller volume of the inferior colliculus [71, 72]. In the cochlear nucleus of congenitally deaf cats, there are fewer total terminal ramifications, smaller density of synaptic vesicles, and larger presynaptic and postsynaptic areas compared with hearing animals [e.g. 73; for humans, see 74]. These deficits in the cochlear nucleus are at least partially reversible through chronic electrical stimulation of the auditory nerve via a cochlear implant [75].

Functional Subcortical Changes

Pinna orientation reflexes could be elicited by electrical stimulation of the auditory nerve using a cochlear implant in both neonatally deafened and congenitally deaf cats [76–78]. The threshold of electrically evoked brainstem responses is higher in neonatally deafened cats compared with hearing cats [72, 79] while this was not observed in congenitally deaf cats [49]. Temporal jitter of

the responses from neurons in the inferior colliculus is increased in neonatally deafened animals [80], and that could contribute to the observed increase in the detectability thresholds of electrically evoked auditory brainstem responses (EABR). The thresholds of the EABR in congenitally deaf cats are not significantly different from those of hearing cats with cochlear implants [49], perhaps because the congenitally deaf cats do not express the extensive degeneration of the spiral ganglion cells found in neonatally deafened cats [72]. Other characteristics of cells in the inferior colliculus, such as the internuclear projection pattern and the nucleotopic projections, were present in congenitally deaf cats [81].

Chronic Cochlear Implantation and Effects on Subcortical Nuclei

Chronic electrical stimulation through a cochlear implant applying a sequence of pulses at a constant repetition rate over several hours per day can affect the properties of subcortical nuclei. For example, the bandwidth of the electrical spatial tuning curves increases significantly after chronic electrical stimulation through a single electrode [79]. Specifically, the representation of the chronically stimulated cochlear region in the inferior colliculus expands and inhibitory responses from neurons in the inferior colliculus increase after chronic electrical stimulation [76]. Therefore, the downregulation of inhibition in the afferent auditory system after auditory deprivation [82, 83] may be counteracted by chronic electrostimulation.

The shortest latency of the responses from neurons in the inferior colliculus decreased slightly but significantly in neonatally deafened cats after chronic stimulation by a cochlear implant, and the onset latency became shorter than in hearing cats in response to stimulation by a cochlear implant [76; for humans, compare 84]. Also, the occurrence of long-latency responses increased in the inferior colliculus of the chronically stimulated group, and that is assumed to be caused by increased descending input from the cerebral cortex. When the stimulation consisted of sequences of pulses presented at a low rate for several hours a day, no change in temporal properties of units in the inferior colliculus was observed. However, when the stimuli were amplitude- and frequency-modulated pulse trains with a frequency of 300 Hz, the temporal response properties in the inferior colliculus changed significantly [85, 86]. The maximum frequency of the stimulation that these neurons could follow increased from approximately 200 to 600 pulses per second, a sign of expression of neural plasticity in the auditory midbrain regarding the temporal properties of responses.

A study that compared the responses from subcortical structures using chronic electrical stimulation in adult deafened cats with those of neonatally deafened animals did not support the theory of a sensitive period for expansion of spatial representation of frequency tuning or changes in thresholds [87].

Chronic Cochlear Implantation and Effects on the Auditory Cortex

The gross morphology of the primary auditory cortex in naïve, unstimulated congenitally deaf cats and neonatally deafened cats appears to be largely preserved over time. However, cells in the primary field (A1), show a slightly (but significantly) increased spontaneous activity compared to those in hearing animals [88]. The primary auditory cortex remains responsive to cochlear implant stimulation of the auditory nerve even in adult, congenitally deaf or neonatally deafened animals [89, 90]. The range of latencies of unit responses is not significantly different between deaf and hearing animals. Latency-intensity functions and rate-intensity functions are similar [89]. A tendency towards steeper amplitude-intensity functions for local field potentials has, however, been observed in congenitally deaf cats [49]. All this may seem surprising because the cortical specificity of some areas in normal-hearing animals is lost after sound deprivation and cross-modal interaction may occur [91].

A rudimentary cochleotopic gradient in the primary auditory cortex is present even in congenitally deaf cats [90]. Similarly, the nucleotopic organization of the projection between the thalamus and the primary auditory cortex is preserved in pharmacologically deafened animals [92], but the rudimentary cochleotopy was considerably smeared in long-term deafened animals [93]. It is unknown if this is caused by auditory nerve degeneration in this particular animal model of deafness.

However, some functional deficits have been identified in the primary auditory cortex of deaf animals. The threshold of cells in the primary auditory cortex is lower in neonatally and congenitally deaf cats than in acutely deafened hearing animals [93, 49], representing a 'hypersensitivity' of the auditory system to auditory inputs. Auditory brainstem responses obtained in the same congenitally deaf cats showed no signs of hypersensitivity, indicating that the physiological abnormalities that caused the hypersensitivity are located at the thalamocortical level [49]. A downregulation of inhibition in the auditory cortex has been noted in congenitally deaf cats causing changes in long-latency (rebound) responses in the auditory cortex [49].

Studies of activity in the specific layers of the primary auditory cortex in congenitally deaf cats stimulated through a cochlear implant [94] revealed that

the cortical modules in the primary auditory cortex do not activate synchronously, which is regarded to be essential for proper functioning of the cortical columns [95, 96]. The decreased synaptic activity in the cortex in deaf animals is likely to be caused by the desynchronization of neurons in the cortical columns [94]. The reductions seen in the activity of the infragranular layers which send projections to the thalamus and other subcortical nuclei indicate a decrease in activity in descending projections from the higher auditory cortex [for review, see 97]. This projection is essential for the so-called 'cognitive modulation' of activity in primary auditory cortex, which further controls the relay of activity from the thalamus to the higher-order areas [compare 98]. Further, the thalamocorticothalamic loops play a role in short-term memory in the auditory system, and allow the association of stimuli coming successively into the auditory system, and this function is compromised in congenitally deaf cats.

Processing in the auditory cerebral cortex plays an important role in cognitive functions related to hearing. Biologically meaningful auditory stimuli are expected to cause great changes in the function of the auditory cortex through expression of neural plasticity. In studies of the effect of auditory experience in implanted cats using biologically meaningful stimuli delivered via portable single-channel speech processors, several forms of reorganization of the primary auditory cortex were demonstrated.

The animals were congenitally deaf, and implanted with a single electrode in the cochlea at the age of 2–6 months (as a comparison, hearing cats are born deaf, gain their hearing function around postnatal day 10, and become sexually mature between 4 and 6 months of age). The cochlear implant processors that were used in these experiments were similar to single-channel Vienna-type speech processors (using the compressed analogue coding strategy). All ambient and self-produced sounds above 65 dB SPL within the range of 125–8,000 Hz were coded in the electrical stimulation of the cochleae of these animals. Automatic gain control was used to limit the output to a dynamic range of 10 dB. The processors were fitted to the animals individually within a few days after implantation using the threshold of the pinna orientation reflex to set the gain. The animals were allowed to move freely on a daily basis. The animals were conditioned to respond to a pure tone using food rewards to make them aware of the newly-gained auditory input and to promote the use of audition for control of behavior. The animals learned the auditory task within 3–20 conditioning sessions [77] and they responded to ambient sounds generated during feeding and care. Animals were stimulated for 1–5 months, and after that their auditory cortices were investigated using electrophysiological recordings in acute experiments after which they were sacrificed and their brains prepared for morphologic studies.

The active cortical area expanded substantially and significantly, up to a factor of approximately 5 (sic), in direct proportion with the duration of auditory experience (fig. 2) [50, 77]. The morphology of the local field potentials recorded in the most activated region of the auditory cortex became more similar to that of normal hearing animals, the long-latency responses increased in

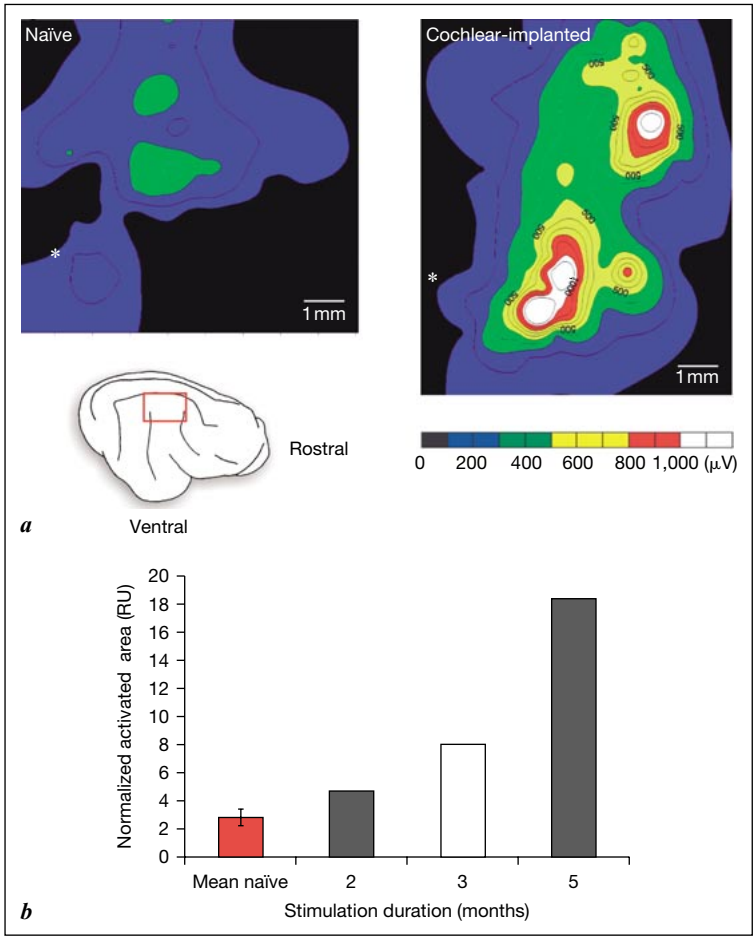

Fig. 2. Expansion of the activated cortical area after chronic electrical stimulation with a cochlear implant. Cortical maps were obtained on anaesthetized animals with monopolar electrical pulsatile stimulation (200 μs/phase, 10 dB over the lowest cortical threshold) and recordings with glass microelectrodes at approximately 150 recording positions within the A1 cortex (inset of the brain with the marked recorded area). ***a*** Data obtained from congenitally deaf cats. Left: naïve animal (not chronically stimulated). Right: Animal implanted at 3 months and stimulated for 5 months. ***b*** Bar chart with the mean normalized cortical activated area in adult naïve congenitally deaf animals (n = 5), a congenitally deaf cat implanted at 3 months and stimulated for 2 months, a neonatally deafened cat implanted at 3 months and stimulated for 3 months, and a congenitally deaf cat implanted at 3 months and stimulated for 5 months. Data show that the results on chronically stimulated animals are consistent between neonatally deafened and congenitally deaf cats, and that the active cortical areas expand with increasing stimulation duration [compare 78]. RU = Relative units.

amplitude. Single- and multi-unit recordings revealed more complex response patterns with variable rate-intensity functions [50], demonstrating that the same unit responded differently to different stimuli, and that the response to the same stimulus differed among the cells from which recordings were made [77]. These results, which were different from those observed in deaf animals, were interpreted to indicate the development of feature detectors in the primary auditory cortex of these chronically-stimulated congenitally deaf cats. The most extensive changes in the gross synaptic activity occurred in the supragranular layers II and III [77], which are known for their high capacity for plastic reorganization [99]. However, the activity in infragranular layers also increased, leading to a normalized pattern of activity within entire cortical columns.

This functional maturation only occurred in the animals that were implanted and chronically stimulated early in life. The later the animals were implanted the smaller were the effects of chronic electrical stimulation on several plasticity measures (i.e. from the age of 2.5 to 6 months after birth, thus adulthood; fig. 3), demonstrating a sensitive developmental period [50, 78]. The older the animals were at the time of implantation, the smaller were the expansions of cortical areas that occurred after chronic electrical stimulation, and the morphology of the field potentials in terms of longer-latency waves matured less completely. Latencies of middle-latency responses did not normalize after chronic electrical stimulation in animals that were implanted late during development or in adulthood.

In summary, most of the signs of plastic reorganization that occurred after cochlear implant stimulation became less pronounced the later in life the stimulation was begun. This is in agreement with many other studies of neurophysiological changes caused by expression of neural plasticity induced during the sensitive period for speech comprehension in prelingually deaf children [100; see also the paper by Sharma and Dorman, this vol, pp 66–88]. As a sensitive period in the midbrain has not yet been found with cochlear implant stimulation [101, 102], it appears likely that this phenomenon is of thalamocortical origin.

The results of the studies discussed above provide information about the optimal age for implantation of prelingually deaf children. Studies have indicated that the developmental sensitive period overlaps with the time during which neural circuits are functionally established, further coinciding with the time where there is a rapid increase in gross synaptic currents [synaptic currents, cat auditory cortex: 49; rapid synaptogenesis, cat visual cortex: 35, 103; synaptogenesis, human visual and auditory cortex: 37] and also with the increase in dendritic branching that occur during normal development [human visual and auditory cortex: 33]. The increase in gross synaptic currents during development is the process most extensively affected by deafness [for study in cats, see 49]. There is also a temporal

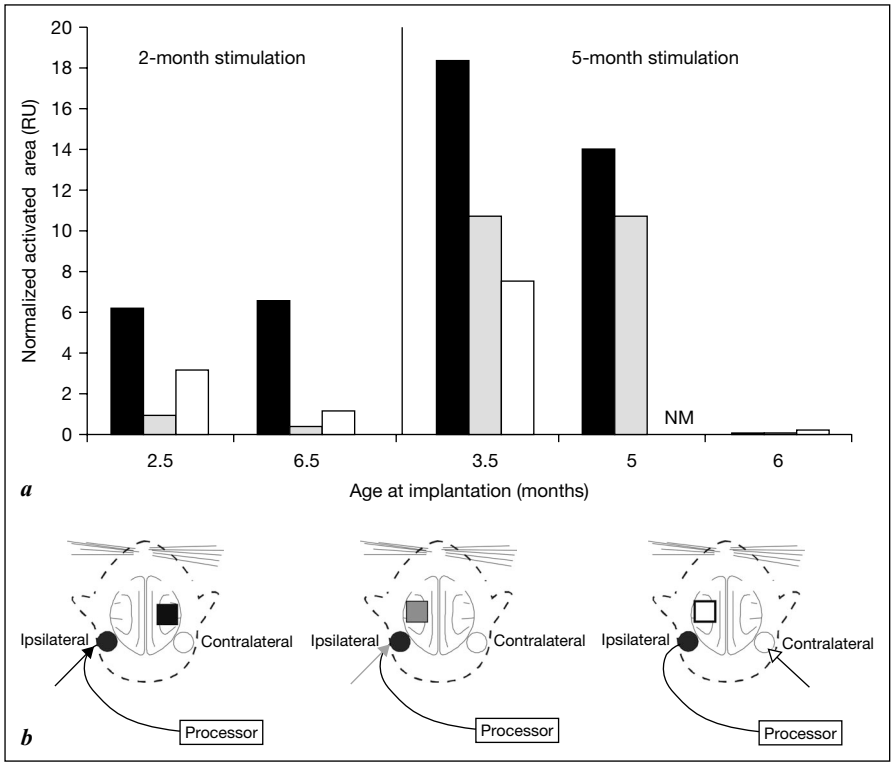

Fig. 3. ***a*** Effect of increasing age at implantation on the capacity for plastic reorganization. Bars show the activated areas determined at the cortex contralateral to the chronically stimulated ear with stimulation of this ('trained') ear (black), areas determined at the cortex ipsilateral to the 'trained ear' with stimulation of this ear (grey), and areas determined at the cortex ipsilateral to the 'trained ear' with stimulation of the other ('untrained') ear (white). With increasing age at implantation, the activated cortical area decreases, demonstrating a sensitive developmental period. The same effect was shown on latencies of the largest middle-latency wave (Pa) of the field potential. ***b*** Drawing indicating the stimulation and recording site. Arrows point to the ear that was stimulated to obtain the map, boxes show the position of the cortical recordings. The chronically stimulated ear is marked by the black circle connected to the sound processor. NM = Not measured; RU = relative units. For details, compare Kral et al. [78].

overlap between the time of decrease in synaptic densities that follows and the decrease in gross synaptic currents as shown in experiments in cats [35, 49, 78, 103]. The time course of the normal synaptogenesis in the human auditory cortex is well known: it continues from birth up to 4 years [33, 37]. This phase is the most sensitive to auditory deprivation, at least in functional measures [for study in cats, see 49]. Therefore, and in agreement with electrophysiology in

cochlear-implanted children [104–107], it is advisable to perform cochlear implantation before the age of 4 years in the congenitally deaf children. However, since the most rapid increase in synaptogenesis takes place within the first 1–2 years of age, by extrapolation from the cat functional data it may be suggested that the best benefit from cochlear implantation can be expected when implantation of congenitally deaf children is done at 1–2 years of age.

Cross-Modal Reorganization in Deafness

Congenital or perinatal deprivation leaves large portions of the central auditory system without an appropriate sensory stimulus. Do the nuclei of the afferent auditory system, when deprived of adequate inputs, take over new functions? At present, such reorganization in the subcortical lemniscal structures has not been demonstrated. Subcortical cross-modal reorganizations have only been demonstrated after destruction of a part of the normal auditory pathways (e.g. aspiration of inferior colliculus leads to cross-modal reorganization of thalamic inputs) [108–111; for review, see 112]. With such manipulations, natural inputs to other structures are destroyed. This leaves unoccupied synaptic space for inputs from other sensory systems, and axons may be redirected to new, atypical targets.

In this respect, the cortex differs from the subcortical auditory system [113]. While cross-modal interaction does not occur normally in the primary auditory cortex (A1) in adults, it occurs naturally in the secondary cortices that receive input from dorsal thalamus [compare also 114, 115].

In congenitally deaf individuals, visually-presented sign language activates the auditory cortex [116, 117]. A cross-modal reorganization was also demonstrated for nonlanguage (moving) visual stimuli [118], showing that the parts of the cortex devoted to auditory stimuli also process nonlinguistic visual inputs. This is in line with the evidence of superior visual performance of congenitally deaf individuals that has been reported in several studies which have been comprehensively reviewed by Bavelier and Neville [91]. Also, spontaneous glucose metabolism in the higher-order auditory cortical areas in prelingually deaf children increases with age, and is negatively proportional to speech comprehension after cochlear implantation, which has been interpreted as a sign of cross-modal reorganization [119].

The only study, which would indicate partial cross-modal reorganization of the primary auditory cortex, is that of Finney et al. [118]. These authors reported that a ‘few voxels’ of fMRI images in the right (but none in the left) primary auditory cortex were activated by moving visual stimuli in congenitally deaf adults. All other active voxels were located outside the primary auditory

cortex in the higher-order auditory areas [see also 117]. This latter finding corresponds to findings with visual stimulation in hearing humans, where the absence of activation of the primary auditory cortex by visual speech-relevant stimuli has been reported [120]. In neither awake nor anaesthetized congenitally deaf cats could activation be elicited with visual flashes or phase-reversal gratings of different spatial frequencies and orientations [88, 121].

Interestingly, congenitally deaf individuals with cochlear implants and electrical stimulation of the auditory nerve have shown significantly less activation of higher-order cortical areas than postlingually deafened individuals [122, 123]. Based on these data, and the reduction in synaptic activity in infragranular layers of congenitally deaf cats [49, 94], we propose that the primary auditory cortex de-couples functionally from the higher-order auditory cortex as a result of congenital deafness. The higher-order auditory cortex may then undergo cross-modal reorganization.

The results discussed above have relevance for decisions regarding cochlear implants in congenitally deaf children. One question that has often been asked is whether the caretakers of children with cochlear implants should keep signing with these children, or if this would be counterproductive for learning and maintaining a language through spoken words using the cochlear implant? Arguments for both alternatives have been made. Signs accompanying spoken language might facilitate learning by appropriately activating the semantic networks in the brain, thereby facilitating the coupling of the activity in the auditory system with the associative language networks already established in the brain. On the other hand, signing might prevent the reassignment of higher-order auditory cortex to the auditory modality, and thus it may be counterproductive in learning spoken language. The final decision between these alternatives can only be made after further data and clinical evidence have been gathered. Until then, abandoning signing may be considered in order to prevent its possible adverse effects.

Conclusions

Expression of neural plasticity is important for achieving the benefit from cochlear implants. The data presented here and in the paper by Sharma and Dorman [this vol, pp 66–88] demonstrate the extensive ability of the auditory system to process input from cochlear implants. Changes are localized in the afferent auditory system and in the cerebral cortex. The cortical reorganizations may direct the subcortical changes. Since functional development of the auditory nervous system requires auditory experience, congenital (prelingual) deafness results in a functionally incompetent (naïve) auditory cerebral cortex.

Early auditory input is important for restoring the ability of the naïve auditory cortex and subcortical auditory structures to adequately process sensory input. It is important that sensory input is established early in life while synaptic properties are immature and the synaptic densities are high in the cerebral cortex and other sensory structures in the brain because that provides a higher 'range' of possible plastic reorganizations of synaptic transmission and wiring pattern than what is available later in life. In prelingually deaf individuals, higher-order auditory areas can take over new functions, and over time cross-modal reorganization may occur. A sensitive period for recovery from deafness of approximately 4 years of age has been identified and research indicates that it would be advantageous to perform cochlear implantation before the end of the 2nd year of life, but at the latest within the 4th year of life in prelingually deaf individuals. When bilateral implantation is done, the second ear should be implanted before the end of the sensitive period, but simultaneous bilateral implantations appear to be the optimal procedure.

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