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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.

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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 neuroprosthetic 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

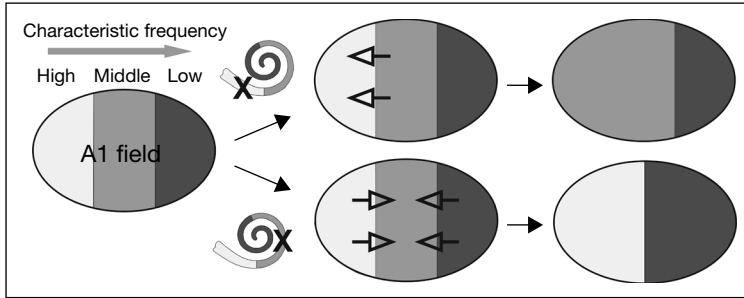


Fig. 1. Effects of restricted cochlear damage on the cortical representations. Damage in the high-frequency region of the cochlea leads to cortical remapping of the middle-frequency representation with the effect of expanded middle frequencies at the level of the cortex. Damage in the middle-frequency 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 inter-species 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 transneuronal 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.