REVIEW

AUDITORY DEPRIVATION

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ABSTRACT

Prelingual deafness deprives the auditory cortices areas from the physiological stimulus which is mandatory for the normal anatomical and physiological development of the cortex.

In the absence of immediate intervention appropriate for auditory abilitation, the auditory cortex will lose its specific capacity to process the auditory informations. This phenomenon is known as auditory deprivation.

Due to the cerebral plasticity, conventional hearing aids or cochlear implants use allow the reorganisation of the cerebral auditory structures in order to regain their capacity to process correctly the sounds and the child to hear.

Age of implantation is determinant for the benefit obtained by deaf children with cochlear implants. As soon as the implantation occurs, the acoustic exposure of the hearing impaired children increases as well. Early exposure to sounds allows the deaf child to understand speech better and to develop language better. Prelingually deaf children, implanted by the age of two, develop speech and language skills similar to their normal hearing peers.

Keywords: congenital hearing loss, auditory deprivation, cochlear implant

Motto: If you "don't use it" you will certainly "lose some of it".

INTRODUCTION

Neural plasticity represents changing of structure, function and organisation in the brain. It is driven by one or several events/experiences. It is based on different mechanisms: recalibration of the nerve connections (strengthening or weakening), adding of new cell nervesand opening of the existing inactive synapses between neurons, but is dependent on stimuli to do so. The causes determining changes in the brain can be physiological or developmental and they are mediated by cognitive or sensory mechanisms.

Experience-related changes of brain function represent the biological base for learning and memory (Gilbert, Sigman, Crist 2001). In the auditory system plastic reorganization was first reported for primary sensory maps (Recanzone et al. 1993, Edeline 1999, Blake et al. 2002). Now it is known that cortical sensory maps are not static, but continuously changingin a use dependent manner (Tommerdahl et al., 2010, Dinse et al., 2002). Although this concept of plasticity seems to apply to any level of brain processing, neurophysiological evidence exists mostly for primary sensory areas. In this respect, neuromagnetic cortical responses suggest enhanced auditory object representation as result of neural plasticity.

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CONGENITALLY DEAF PATIENTS WITH COCHLEAR IMPLANTS

Cochlear implants are useful tools to provide auditory sensations in profoundly deaf patients (Rubinstein and Miller, 1999). Although the electrical stimulation only poor represent the cochlear place information (Hartmann et al., 1984), temporal information is reliably represented. This is obviously sufficient for frequency discrimination over lower frequencies and thus makes speech comprehension possible (Kral, 2000).

In congenitally deaf children, cochlear implants enable language development, but the outcome is critically dependent on the age of implantation. Congenitally deaf subjects implanted in adulthood showed a markedly poorer performance in speech discrimination than subjects implanted in childhood. As a consequence, screening programs of neonatal or early postnatal hearing status are being introduced in several countries (NIH Consensus Statement, 1993, 1995). According to present guidelines, the optimal implantation age is under 5 years in congenitally deaf subjects. Some authors suggest that implantations should be performed before the end of the 2nd year of life (Klinke et al., 2001), since cochlear implantation plays the role of an external trigger for language acquisition.

NEUROPLASTICITY

The plasticity of the cortex, known also as *cortical re-mapping* allows regaining of the designed function if stimulation occurs in the sensitive period of the cortical area – 2-3 years of life for the auditory cortex.

Like the language system, the auditory system also undergoes developmental changes during early postnatal life in both humans and animals. In the cat, functional cortical electrophysiological parameters in the primary auditory cortex mature during the first 5 months (Eggermont, 1996); in man during the first 12-15 years (Eggermont, 1988). As in the case with language, postnatal development of the auditory system is dependent on experience. Lack of activity in the auditory pathways is known as auditory deprivation and it is well demonstrated nowadays that the maturation process cannot proceed under congenital auditory deprivation.

Critical periods also appear to exist in the auditory system. Language development dependent on the auditory system is known to have a critical period (Skuse, 1993). Transient expression of acetylcholinesterase, seen in the rat visual and somatosensory cortices during their critical period, is also found in the auditory cortex with a similar time-course (Robertson, 1987; Robertson et al., 1991). The cholinergic system is known to be involved in learning effects in the auditory cortex (Juliano, 1998; Kilgard and Merzenich, 1998; Weinberger, 1998) and might play a role in the formation of thalamocortical connections. Lesion studies, in the cochlea as well as in the central nervous system, support the idea of a critical period in auditory development (Harrison et al., 1991; Wakita and Watanabe, 1997) as do the data from congenitally deaf individuals equipped with cochlear implants (Eddington et al., 1978; Fryauf-Bertschy et al., 1997). The deficits largely persist if initial stimulation takes place after this critical period. For example, binocular deprivation leads to a substantial reduction in visually responsive cells and loss of their orientation specificity in the primary visual cortex.

Cochlear implantation during this sensitive period determines normal hearing and language acquisition in prelingually deaf children without associated pathologies. After 3 years of age, treatment intervention cannot restore normal speech and language development, since cortical plasticity is limited.

There is a sensitive period of 3.5 years during which implantation occurs into a highly plastic central auditory system. Implantation after 7 years occurs into a re-organized central auditory system (Sharma et al., 2002).

Children implanted under ages 3-4 years show significantly better speech perception and language skills compared to children implanted after ages 6-7 years. (Kirk et al., 2002).

The higher-order auditory cortex (e.g. AII in cats) has greater physiological plasticity than the primary auditory cortex. In congenital auditory deprivation, the higher-order auditory cortex may be recruited for the processing of other sensory modalities. This view has been supported by the observation that performance of deaf patients in visual and cognitive tests is better in hearing subjects (Neville and Lawson, 1987 a,b; Marschark, 1998; Parasnis, 1998).

After 7 years of age, the auditory cortex is taken by other sensorial systems, especially by visual one and cochlear implantation is useless regarding speech and language acquisition. This is called *cortical re-organisation* and defines the end of the sensitive period of the auditory system development.

If this happens, auditory deprivation occurs. Auditory deprivation is a decrease in an ear's ability to understand speech clearly.

There are several theories on why auditory deprivation occurs. One thought is that the brain gradually loses some its ability to process sound information because of a lack of sound stimulation. When no action is taken in heard-of-hearing persons and the nerves of the hearing mechanisms are not used, they become deprived of stimulation and slowly become weakened or even atrophy occurs.

Not only the auditory nerves weaken over time, but the auditory cortex as well – they no longer receive and process hearing from the ear, which can lead to irreversible hearing loss/deafness.

The integrity of a sensory system depends on external stimulation. Deprivation studies, those in which the effect of withholding stimulus on the development of sensory neurons in a newborn animal is studied, conclusively showed that sensory stimulus is needed for the structural development of sensory neurons as well as their functional connectivity (Webster & Webster, 1977). Studies on children's development showed that appropriate sensory stimulation, especially between the ages of 0 to 2 years are critical for the proper development in later years.

With no auditory stimulation received for many years, cortical reorganisation occurs. This takeover of the auditory cortex by the visual system was demonstrated by magnetoencephalography technique and functional magnetic resonance – temporal lobe responds to visual stimuli (Finney et al., 2001) and it is defined as *cross-modal reorganisation*.

From clinical point of view, this irreversible cross-modal reorganisation is proven by very poor speech and language results in deaf children implanted after the age of 7. Aetiology of deafness does not influence the severity of cross-modal reorganisation and its severity has a high intervariability.

For these very well demonstrated reasons, newborn hearing screening and early cochlear implantation are mandatory. If early diagnostic and intervention is implemented, maturation of the auditory pathways follows the normal time-course and the child can learn to speak.

Although studies have shown that the central auditory system establishes functional neural connections in the absence of sound (Hartmann, Shepard, Heid, & Klinke, 1997; Klinke, Kral, Heid, Tillein, & Hartmann, 1999), auditory deprivation causes widespread degeneration in the central auditory system (e.g., Hardie, & Shepherd, 1999; Leake, Snyder, Hradek, & Rebscher, 1992; Moore, 1994; Ryugo, Pongstaporn, Hutchton, & Niparko 1999; Ryugo, Rosenbaum, Kim, Niparko, & Saada, 1998). These changes include reduction of cell density in the spiral ganglion, anteroventral cochlear nucleus and ventral cochlear nucleus; changes in neural projections between brainstem nuclei (Nordeen, Killackey, & Kitzes, 1983); reduced cortical synaptic activity in cortico-cortical and cortico-thalamic connections (Kral, Hartmann, Tillein, Heid, & Klinke, 2000); a reduced number of primary dendrites in cortical pyramidal cells; and take-over of auditory cortical areas by visual function (Lee et al., 2001; Finney, Fine, & Dobkins, 2001). In the absence of auditory stimulation, bilateral auditory deprivation induces decrease of the volume of the white matter, due to diminished myelinisation of the auditory pathways. This was demonstrated by PET evaluation which shows the hypometabolism in the temporal lobe; it is directly correlated with the length of the deafness.

Auditory experience is important for proper activation of higher-order auditory areas, where audition appears, as human sensation. This ipothesis is nowadays well demonstrated by animal studies which showed a decrease of activation in infragranular layers in the primary auditory cortex of congenitally deaf animals. These layers are the targets of descending feedback modulation of activity from higher-order areas. Lack of activation in higher-order areas would thus explain this finding.

Anatomical and physiological consequences of congenital auditory deprivation on the auditory cortex consist of:

- significant overall decrease in neuronal excitability by peripheral electrical cochlear stimulation;
- increase in synaptic current latency, particularly in layers III, V and VI;
- substantial decrease in synaptic activity at longer latencies and in infragranular layers.

These changes are caused by degeneration or failing maturation of cortico-cortical and cortico-thalamic connections (Kral, Hartmann, Tillein, Heid, Klinke 2000) and determines substantial deficits in the activity of a naive auditory cortex in response to stimulation of the auditory nerve.

It is reasonable to suppose that the degenerative effects described above, if found in humans, would reduce the effectiveness of a cochlear implant. On this view, the best time to implant a child would be before the effects of sensory deprivation alter the development and plasticity of the central auditory system. This view is supported by data from congenitally deaf white cats (CDCs), and both mice and rats fit with cochlear implants. Klinke, Hart-

mann, Heid, Tillein, and Kral (2001) and Kral, Hartmann, Tillein, Heid, and Klinke (2002) report that as the duration of intracochlear stimulation increases for CDCs, the amount of cortical tissue activated increases, provided that cochlear implantation takes place before 6 month of age. Kral et al. (2000) have shown that synaptic currents in young implanted CDCs are similar to those in hearing cats if stimulation is initiated early but not if stimulation is delayed until 6 month of age.

Experimental evidence for cross-modal remapping of the human auditory cortex has recently been presented. Higher-order auditory areas, but bot the primary auditory cortex, are incorporated in processing of visual stimuli in humans (Nishimura et al., 1999; Petitto et al., 2000). In prelingually deaf patients, the amount of activation of the higher-order auditory cortices by a cochlear implant decreases with increasing implantation age (Lee et al., 2000). Speech recognition by a cochlear implant correlates significantly with the activation in higher-order auditory cortices (Lee et al., 2001). Thus, cross-modal remapping of the higher-order auditory cortices may substantially interfere with the speech processing after cochlear implantation.

During development, the central auditory system can either learn or lose: if normal stimulation from periphery exists, it can learn to organize sensory input into categories (auditory objects). However, if a certain developmental period has passed without hearing experience, the representation of distinctive features degrades. In concert with lack of top-down modulation of plasticity by auditory high-level representations (auditory objects) and developmental reduction in synaptic plasticity, plasticity will become non-adaptive in congenitally deaf and the auditory cortex will lose the ability to learn.

Congenital deafness has a very high incidence among newborns. 1 to 3/1,000 of infants are born deaf and this incidence increase ten times (1-2%) in newborns at risk for hearing loss.

Recognised risk factors for hearing loss are:

- gestational age under 32 weeks and birth weight below 1,500 g;
- ICU ward admission for more than 5 days;
- mechanical assisted ventilation for more than 5 days;
- pulmonary hypertension and mechanical assisted ventilation for more than 5 days;
- systemic administration of aminoglycosides (Gentamycin, Tobramycin, Vancomycin, Amikacyn) for more than 7 days, without monitoring blood levels;
- association of aminoglycosides with loop diuretics;
- severe hyperbilirubinemia with prolonged phototherapy;
- severe perinatal asphyxia (APGAR score under 4 at 1 minute and under 6 at 5 minutes);
- postnatal infection complicated with viral or bacterial meningitis;
- family history of congenital or acquired hearing loss;
- genetic syndromes which include hearing impairment;
- craniofacial anomalies;
- intrauterine infections (especially with toxoplasma, rubella, cytomegalic or herpes virus, treponema pallidum or HIV);
- alcohol or drugs during pregnancy.

The prevalence of congenital deafness is 60 times greater than phenylketonuria, a disease which it is screened at birth in Romania. Efforts should be done in order to legislate universal newborn hearing screening since deafness it is an invisible handicap which is discovered late by parents in our country unfortunately – around 3-4 years of age. At this age, cross-modal reorganisation of the auditory cortex already started, with irreversible effects. 50% of the born-deaf infants are children with no risk for hearing loss and this is a powerful argument for universal hearing screening at birth and not for targeted newborn hearing screening.

Normal hearing is mandatory for proper speech, language, and cognitive skills development in children. For this reason, early identification of hearing impairment and appropriate bilateral intervention are the pillars of binaural hearing abilitation in children (Northern and Downs, 1991; Ross, 1980; Ross, Brackett, & Maxon, 1991).

Congenital deprivation has the most serious consequences and the resulting deficits may be irreversible:

- delayed acquisition of speech and language;
- limited academic results;
- severe decrease of quality of life;
- poor integration in the community;
- poor-paid jobs.

In people who are born deaf, neural plasticity has been observed in the superior temporal cortex, which is associated with auditory and speech processing. Deaf people are subject to cortex reorganisation consisting in sensory and cognitive changes. As mentioned above, auditory deprivation and lack of language experience lead to plastic changes of

the brain – auditory cortical areas are taken by other sensorial systems, visual mainly.

Different changes occur in left and right auditory cortical areas respectively due to their different functional role in audition. The temporal lobe holds the primary auditory cortex and is involved in primary auditory perception, such as hearing since the primary auditory cortex receives sensory information from the ears. It also consists of secondary auditory areas which process the information into meaningful units such as speech and words.

Congenitally deaf patients implanted in adulthood show deficits in temporal auditory processing such as gap detection and auditory counting abilities (Busby and Clark, 1999), which indicates a malfunction of the central auditory system. This is at least one of the causes of speech-processing difficulties experienced by congenitally deaf implanted as adults.

More than this, the left superior temporal cortex is important for the processing of semantics in both speech and vision in humans (Schacter, Daniel L.; Gilbert, Daniel T.; Wegner, Daniel M.). It is involved in the processing of language independent of modality.

The plastic changes in the left superior temporal lobe can be mediated by the mechanisms that support the development and the learning of sign language and not by „general visual processing effects". These changes seem to have linguistic origin and the effects are shaped by the sign language experience and not by auditory deprivation.

The right superior temporal lobe showed plasticity due to sensory deprivation and the use of sign language.

In conclusion, sensory and cognitive factors cause plasticity in anatomically and functionally distinguishable substrate.

CONCLUSION

The central auditory system in subjects with congenital auditory deprivation either cannot mature normally or degenerates because of the missing auditory experience. In congenital deafness, the excitability of the primary auditory cortex is decreased in the infragranular (output) layers. Indications of functional corticortical and corticothalamic loops (long-latency activity in the primary auditory cortex and synaptic activity in infragranular layers) are missing. When electrical stimulation of the auditory nerve by means of cochlear implantation stops early the auditory deprivation, the deficits can be overcome. But the magnitude of the benefit depends on the length of deafness. The more the hearing loss the greater the diminution of discrimination, and perhaps, the more permanent the effect!

Cochlear implantation during the sensitive period of the auditory system development ensures normal speech and language acquisition.

These data stress the need for a neonatal auditory screening program and an early rehabilitation of children with hearing loss.

The mode of processing activity in the auditory cortex changes during early postnatal development. A large spectrum of finely regulated molecular mechanisms participates in this change. Many of them are known for the visual cortex, but their coordinated action is still not understood. In the auditory cortex they still need to be identified. Knowledge of the molecular mechanisms of postnatal auditory plasticity could open new therapeutic possibilities in congenital deafness and other central auditory deficits.

Acknowledgement

Both authors have equal contribution to conceiving the scientific paper.

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