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Review

What's to lose and what's to learn: Development under auditory deprivation, cochlear implants and limits of cortical plasticity

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ABSTRACT

Sensory and environmental manipulations affect the development of sensory systems. Higher-order auditory representations (auditory categories or "objects") evolve with experience and via top–down influences modify representations in early auditory areas. During development of a functional auditory system, the capacity for bottom–up reorganizations is successively less well expressed due to a molecular change in synaptic properties. It is, however, complemented by top–down influences that direct and modulate the residual (adult) capacity for circuit reorganization. In a deprived condition, this developmental step is substantially affected. As higher-order representations cannot be established in absence of auditory experience, the developmental decrease in capacity for "bottom–up regulated" reorganizations (as repeatedly demonstrated in also in deprived sensory systems) cannot be complemented by an increasing influence of top–down modulations. In consequence, the ability to learn is compromised in sensory deprivation, resulting in a sensitive period for recovery.

Contents

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Cortical functions seem to be more dynamic than previously thought. Even receptive fields of neurons in primary auditory cortex, previously imagined a constant "filter" property of the neurons (although subject to long-term plasticity), can rapidly change depending on the behavioral task in non-anaesthetized animals (Fritz et al., 2003). If ferrets are trained to detect a pure tone within a complex series of sounds ("TORC" stimuli), a facilitation of cortical responses specific to the target tone is observed in primary auditory cortex (Fritz et al., 2003). This facilitation is irrespective of the location of the target stimulus within the receptive field and is observed already after a single presentation of the TORC stimulus including the target tone. In other words, this plasticity is rapid and specific to the target. Long-term training of two groups of rats to respond to different parameters of the same complex acoustic stimulus leads to highly task-specific plasticity in field A1 (Polley et al., 2006). Thus, both these studies demonstrated that cortical reorganization is specific to the task and must be goal-directed. Nonspecific modulatory systems (e.g. projections from nucleus basalis or ventral tegmental area) have a strong influence on cortical activity and receptive field plasticity (Bakin and Weinberger, 1996; Kilgard and Merzenich, 1998; Bao et al., 2001). However, due to their nonspecific, rather general, influence they do not appear able to moderate the highly specific and rapid changes in receptive fields described above.

Higher-order cortical areas (e.g. secondary and association areas) have projections to these nonspecific modulatory systems, and also feedback projections to the primary sensory areas. Visual perception has been suggested a two step process: first, a "gist" of the visual scene (and thus the perceptual task) has to be identified – "vision at the glance", followed by processing of the details of the visual scene – "vision with scrutiny" (Hochstein and Ahissar, 2002). Due to increasing size of cortical receptive fields in the way up the cortical hierarchy, the theory has implicated different cortical areas involved during these steps: first, higher-order areas have to decode the gist of the scene to secondly guide lower-order areas in processing the details of the visual scene. Such "reversed hierarchy theory" suggests the progression of the input processing from top to bottom.

Some theories and data are in accord with the notion that the primary cortical areas represent features of those auditory objects (or events) that the brain is currently processing (Nelken et al., 2003). Feature categorization possibly takes place in higher-order areas, although effects of categorization have also been demonstrated in early areas (Ohl et al., 2001). Such effects would, in our interpretation, represent a top–down cognitive modulation of early sensory areas. This top–down modulation may explain how changes in characteristics of receptive fields can be specifically directed depending on the requirements of a given behavioral task (Polley et al., 2006). In the auditory pathway corticofugal influences (Fig. 1) have been recognized as an important factor in plastic reorganization of subcortical structures (Suga et al., 2002; Sakai and Suga, 2002; Ma and Suga, 2003; Zhang and Suga, 2005; for somatosensory rapid plasticity and top–down effects see Krupa et al., 1999). Cortical top–down influences during conditioning (activity associated with reward timing, traditionally regarded as a higher-order function) have been observed in infragranular layers of field V1 recently (Shuler and Bear, 2006).

Top–down modulations, even beyond attention at a more elementary level of processing, may thus play an important role in the processing of sensory inputs and in perceptual learning in the subcortical and cortical auditory system. Abundant cortical top–down projections target cortical and subcortical structures (Fig. 1). Top–down modulation is of perceptual importance, as the automatic filling in of "gaps" in the phonetic stream, the phonemic restoration effect, demonstrates (Warren, 1970). The site of similar effects has been demonstrated in higher-order auditory areas using functional brain imaging (Davis and Johnsrude, 2003). In this respect, higher-order areas could influence the processing in the primary areas and by that the "gating" of information on the way up the cortical "hierarchy". Bottom–up and top–down cooperation is thus of cardinal importance for perception and learning. Visual (and also auditory) cortical areas are so heavily interconnected that under physiological circumstances they behave as a functional unit. When sensory input can be categorized to "sensory objects" in higher-order areas, it will have immediate top–down effects on primary areas. This can modulate feature representations in primary areas, explain the rapid changes in receptive fields observed in different behavioral contexts (see above) and explain why effects of auditory categorization can be observed in the primary areas. During category learning the top–down influence can rearrange or enhance the representation of features distinctive for the given category (Kouramäki et al., 2007). It has indeed been shown that during category learning, higher-order areas are increasingly sensitive to such distinctive features (Sigala and Logothetis, 2002).

Here we want to argue that this process is also important during development and that developmental sensitive periods are possibly influenced by such an interaction.

1. Plasticity and development

Several seemingly opposing findings can be explained by top–down and bottom–up modulation of plasticity. Experiments in which young and adult animals were set into an acoustically enriched environment yielded differential results depending on the behavioral task. Provided that the acoustically augmented environment was giving the animal behaviorally relevant information, the responses (measured by local field potential amplitude and firing rate) massively increased, both in juvenile and in adult animals (Engineer et al., 2004). On the other hand, if the enriched acoustical environment did not provide any information for adult animals, it led to habituation of responses at the level of the primary auditory cortex despite considerable spectro-temporal complexity of the environmental stimuli (Norena et al., 2006).

During development the brain has to bootstrap its complex structure from an initial naïve state based on genetic make–up and experience. From the visual system, we know that although some of the feature detection abilities in field V1 are present before eye opening (like retinotopy, ocular dominance or orientation preference, Crair et al., 1998), there are also features that need experience for maturation to occur (e.g. directional selectivity, Li et al., 2006). Although species differences have to be taken into account, it appears that at

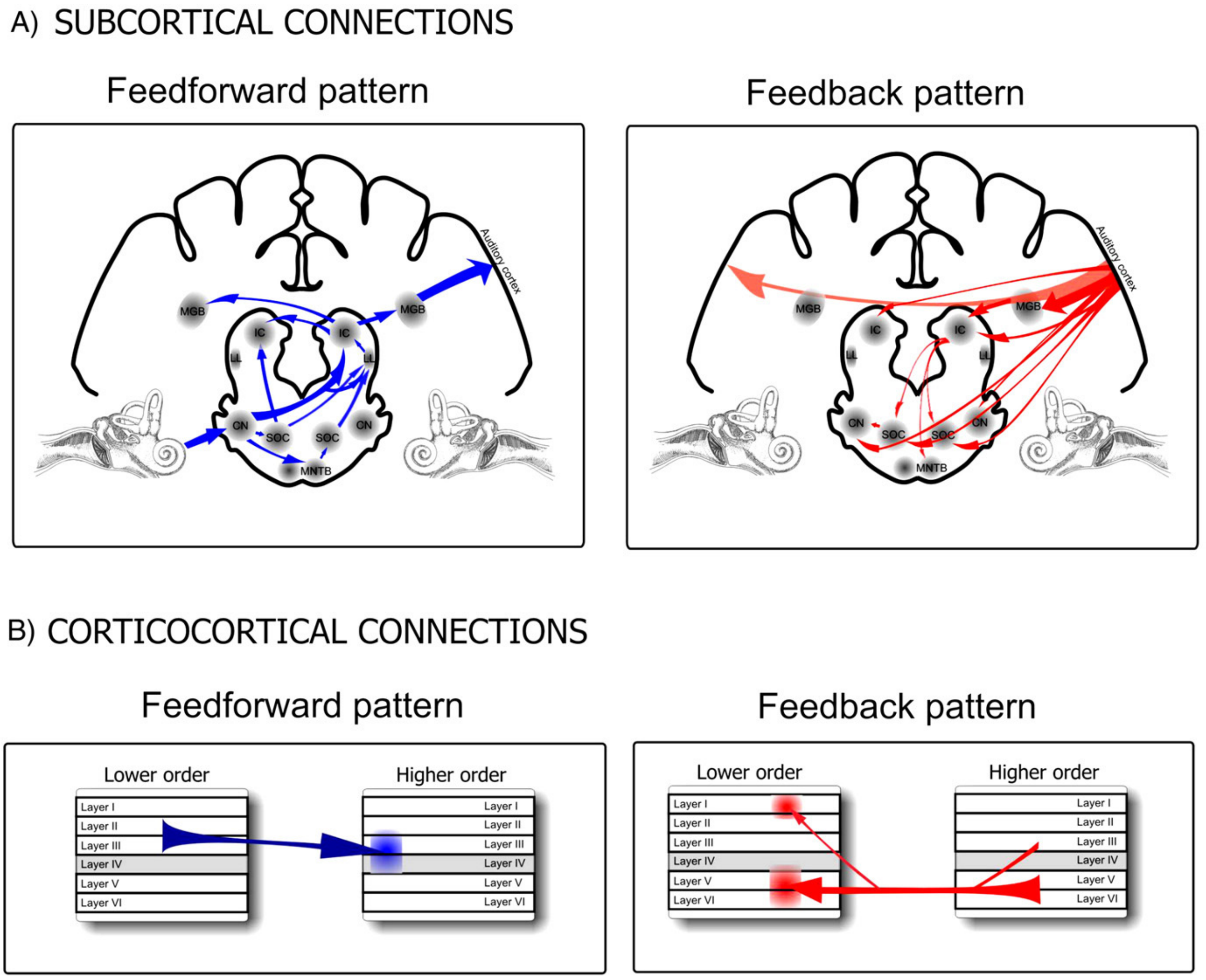

Fig. 1 – Schematic illustration of most important afferent and efferent projections of the auditory cortex. (A) Subcortical afferent and efferent projections. The efferent system is very extensive and targets all major relay sites of the subcortical auditory system. (B) Pattern of feedforward and feedback projections common to the sensory systems. Feedforward and feedback projection patterns are layer-specific.

least certain properties in the primary visual cortex do not need visual experience for development. In other words, the primary sensory cortex makes assumptions on the sensory input it is going to receive and based on its genetic make–up develops (prior to sensory experience) such neuronal networks that are effective in processing the expected input. This conclusion is supported by investigations in the primary auditory cortex of animals that were either deafened perinatally or were congenitally deaf.

The tonotopic gradient was, despite complete lack of auditory experience, rudimentary preserved in adult congenitally deaf cats (Hartmann et al., 1997). Also, when rate–intensity and latency–intensity functions were compared between adult hearing and neonatally deafened cats, only minor differences could be identified (Raggio and Schreiner, 1999). Last but not least, rudimentary binaural sensitivity has also been demonstrated in field A1 of adult congenitally deaf cats (Tillein et al., 2006). This shows that certain feature sensitivity must be based on genetically predetermined mechanisms.

However, spontaneous activity plays an important role in this process in the visual system (Cang et al., 2005): the precise cortical retinotopic maps in mice require peripheral spontaneous activity (but not patterned visual input), whereas some rudimentary retinotopy in a deprived condition is possibly also the result of central spontaneous activity. In the retina, waves of spontaneous activity were found propagating along the receptors (Wong, 1999). Using correlational rules, this pattern of activity can lead to development of retinotopic organization in the central visual system (Cang et al., 2005). Considerable spontaneous activity characterized by bursting patterns long before hearing onset could be demonstrated in the avian auditory system (Lippe, 1994) and in the central auditory system of marsupials (Gummer and Mark, 1994) and bats (Rübsamen and Schafer, 1990). To what extent this very early spontaneous bursting activity in the auditory system influences central development is not clear, but provided it is correlated at neighboring fibers of the auditory nerve it could constitute a basis for a cochleotopic organization.

If some feature representations are preserved in the congenitally deaf, how can one explain the extent of the long-term problems in mastering certain auditory tasks by prelingually deaf subjects cochlear-implanted in adulthood (Dawson et al., 1992)? And why does the ability to learn speech comprehension continually decrease with increasing implantation age in cochlear-implanted prelingually deaf children, demonstrating a sensitive period of 4–5 years (e.g. Fryauf-Bertschy et al., 1997)?

It is known that in congenitally deaf cats, the extent of plastic reorganizations in auditory cortex following cochlear implant stimulation decreases with increasing implantation age (Kral et al., 2001, 2002), demonstrating a neurophysiological correlate of a developmental sensitive period. Also in hearing animals, corresponding sensitive periods have been concomitantly shown (Zhang et al., 2002; Nakahara et al., 2004).

One mechanism participating in sensitive periods represent developmental changes in excitatory postsynaptic potentials, whose durations decrease with increasing age (Aramakis et al., 2000). The reasons for this phenomenon are manifold, but a changing proportion of AMPA and NMDA receptors, as well as a change in composition of NMDA channels (Quinlan et al., 1999; review in van Zundert et al., 2004) are the most important ones. Longer postsynaptic potentials during early development endow the cortex with an initial higher level of synaptic plasticity, which is decreasing with increasing age. Additionally to maturation of excitatory synaptic transmission, developmental increase in inhibition (Gao et al., 2000) as well as changes in intrinsic circuitry within the primary cortex contribute to this decrease, too. Massive changes in dendritic branching (Conel, 1939–1967) as well as corresponding changes in synaptogenesis have been identified in primary auditory cortex of hearing subjects (Huttenlocher and Dabholkar, 1997).

In humans, the peak in synaptic density (as well as in complexity of dendritic branching patterns) has been observed between the 2nd and 4th year of life, with subsequent (slow but extensive) decreases. There is a correlation between the sensitive period for language learning in cochlear-implanted prelingually deaf subjects (4–5 years) and the onset of synapse elimination in hearing subjects (in deaf subjects synaptic densities are unknown), suggesting that synapse elimination takes part in initiating the closure of a sensitive period. Despite of growth and elimination of synapses during sensory learning in primary areas, the overall number of synapses remains constant in adult primary cortex (primary somatosensory cortex: Trachtenberg et al., 2002). This indicates the operation of a limiting factor that prevents excessive changes in number of synapses in adult primary sensory cortex and also limits the ability to extensively remodel cortical microcircuitry in adults. During development new functional synapses appear without compensation by loss of other synapses, and this process is modulated by experience (Winfield, 1981; Kral et al., 2005). Thus, the opportunity to massively reorganize the inborn circuitry is considerably larger during development and can be achieved by a bottom–up mechanism alone.

Provided that synaptogenesis and synapse elimination are dependent on activity (Changeux and Danchin, 1976), in case of congenital deafness these processes will not establish the essential synapses, do not properly redistribute them on the dendritic tree (for visual system, see Bourgeois and Rakic, 1996) or eliminate the inappropriate ones. This results in a naïve auditory cortex that is not capable to process incoming activity appropriately (Kral et al., 2000, 2006). The starting point for later learning is altered.

2. Top–down influence in plasticity

During development, experience-dependent representations in higher-order cortical areas first have to emerge conditional upon the action of bottom–up mechanisms. Genetically predetermined feature detectors and increased capacity for plastic reorganization are important preconditions that allow adaptation during the time when cortical high-level representations are immature. At that time, even a passive stimulus presentation can reorganize the feature maps within primary sensory areas. In primary auditory cortex, passive stimulation suffices to reorganize feature maps, leading to enhanced representation of, e.g., a constantly present warble tone (Stanton and Harrison, 1996). More sophisticated methodology in recent years confirmed and extended these results (Zhang et al., 2002; Nakahara et al., 2004), and demonstrated the true extent of the reorganizations that can be achieved. Nonetheless, this type of “passive” plasticity shows a critical period (Zhang et al., 2002; Nakahara et al., 2004). After a certain developmental period has passed, passive stimulus presentation alone does not lead to overrepresentation of the stimulus features.

In adult animals, a paradigm where a wide frequency range (4–20 kHz) was enhanced in the environment was even shown to lead to a massively decreased responsiveness to the enhanced frequencies (Norena et al., 2006). This was not a consequence of peripheral adaptation or increase in hearing threshold. Additionally, the enhanced acoustic environment consisted of continuously changing stimuli within its frequency range. Interestingly, the neurons in the region of primary auditory cortex that normally responded to 4–20 kHz were now either responding normally to those frequencies (<15% of the neurons), or responded to frequencies above or below the enhanced frequency range with low thresholds. The responses to the frequencies outside the enhanced range had longer latencies and sustained responses, characteristic of those mediated by intracortical horizontal fibers (Norena et al., 2006). The classical interpretation of this finding is given by a bottom–up process: The continuous but dynamic stimulus may exhaust the available transmitter pools to such a low steady-state level (Dobrunz and Stevens, 1997) that this would allow a competitive mechanism to take over the synaptic control of the pyramidal cells by the horizontal fibers originating from cells outside the depressed frequency region. The fact that still about 10–15% of the neurons in the depressed region show normal responses in terms of thresholds and frequency-tuning curves suggests that some thalamo-cortical synapses are less vulnerable to this depletion process than others (Norena et al., 2006).

A possible alternative interpretation of this result is that it is the consequence of a top–down modulation of the activity in the primary areas. Such a mechanism could be conveyed by feedback projections from higher-order auditory fields; in fact, suppressive feedback feedback effects have been demonstrated in primary visual cortex (Dong et al., 2004). Here a comparison to the same paradigm applied during development would clarify the proper alternative: the bottom–up process would yield a stronger habituation of the stimulated region in juvenile animals, the top–down theory would propose the absence of the habituation effect in juvenile animals due to immaturity of top–down influences.

In our interpretation, the transition of juvenile to adult plasticity occurs when sensory categories develop. Then reorganization in primary areas as a result of learning switches from dominance by a bottom–up process to increased contribution from a cognitive top–down modulation.

The maturity of cortical properties is delayed both in congenital auditory deprivation (Kral et al., 2005) as well as during exposure of normal hearing animals to continuous masking wideband noise (Chang and Merzenich, 2003). However, in congenital deprivation after a certain delay (~2 months in cats), the maturation proceeds, albeit that the developmental sequence is altered compared to hearing controls (Kral et al., 2005) and the ability for adaptation in the cortex ceases (Kral et al., 2002). As (supposedly) auditory categories cannot develop in deafness, the decreased plasticity in the auditory cortex cannot be compensated and directed by top–down modulatory influences. This developmental decrease in synaptic plasticity together with the absence of top–down mechanisms leads to a decrease in general ability to learn. A drop in the degree of reorganization of cortical activity has indeed been demonstrated in an active learning paradigm (classical conditioning) in congenitally deaf cats (Kral et al., 2002). Thus supervised learning does not help and passive learning is not sufficient for adaptive cortical changes in late implantation (late onset of hearing).

3. Corticocortical interaction in congenital deafness

Several neurophysiological findings provide additional support for the view that sensory deprivation reduces the ability for appropriate plastic adaptation (learning). When activity in primary auditory cortex of congenitally deaf cats was analyzed in a layer-specific manner (Fig. 2), reductions in activity within deep cortical layers were demonstrated (Kral et al., 2000). These reductions were attributed to a delay in the activation and maturation of supragranular layers, disorganization of cortical microcircuitry and reduction of the descending modulatory activity from higher-order cortical areas. Top–down (feedback) projections from higher-order cortical areas target mainly infragranular layers (Rouiller et al., 1991; review in de Ribaupierre, 1997). Reductions in activity in these layers consequently demonstrate that descending modulation of activity in field A1 originating from higher-order auditory fields is compromised (in addition to less strong and desynchronized intrinsic input from supragranular layers of the same column; Fig. 3). This deficit is reversible with chronic electrostimulation after early cochlear implantation (Fig. 2; Klinke et al., 1999; Kral et al., 2006).

Layer-specific processing in the sensory cortex is known to be of crucial importance for the sensory cortex: it is well known that a desynchronization of activity between supra- and infragranular layers affects the processing mode of pyramidal cells in layer V (Larkum et al., 1999; Llinas et al., 2002). In the adult auditory cortex, all layers receive some thalamic input, however, the strongest input targets layer IV and deep layer III (Niimi and Naito, 1974; Mitani and Shimokouchi, 1985; Mitani et al., 1985; Prieto et al., 1994). The thalamic input to infragranular layers causes strong synaptic activity there, but it is not essential for vertical activation of the cortical column (Sherman and Guillery, 1996; Benardo, 1997; Rockland, 1998; Thomson and Bannister, 2003; McLaughlin and Juliano, 2005). Projections from infragranular layers to layer IV and supragranular layers are weaker and are modulatory (as opposed to driving, review in Callaway, 2004). Thalamic input activity proceeds from middle cortical layers IV and III mainly to supragranular layers III and II and from there to infragranular layers (Mitani et al., 1985; Kral et al., 2000; barrel cortex: Lubke et al., 2000; visual cortex: Dantzker and Callaway, 2000). Neurons in layer IV mainly project within the cortical column, however, also horizontal collaterals to neighboring columns exist (Lubke et al., 2000; review in Callaway, 2004). Major projection from the primary auditory cortex to secondary auditory areas comes from neurons in layer III, with lesser but significant contribution of other layers (Winguth and Winer, 1986).

Deep cortical layers morphologically develop before superficial layers (Gleeson and Walsh, 2000). The vertical propagation of synaptic activity from layer IV into layers II/III is functional (even with well-tuned receptive fields) just after neurons ceased to migrate into supragranular layers (day 8 postnatally in rat barrel cortex, Bureau et al., 2004). Horizontal connections in layers II/III mature later (Nelson and Katz, 1995; human: Burkhalter et al., 1993). All available data thus demonstrate that the vertical spread of activity within the cortical column matures before the horizontal collaterals become fully functional. Early in postnatal development, the strongest evoked activity can be observed in the subplate, then in layer IV and supragranular layers, less in infragranular layers in cats (Friauf and Shatz, 1991). Similarly, in vivo investigations of the feline primary auditory cortex demonstrate that large activity is concentrated in supragranular layers II, III and layer IV during the first postnatal weeks (Kral et al., 2005). Pyramidal cells of layers II/III project to higher-order (secondary) auditory cortex (Rouiller et al., 1991). Infragranular layers, on the other hand, receive feedback (top–down) projections from higher-order auditory cortex (Rouiller et al., 1991, for review on auditory cortex see de Ribaupierre, 1997; visual cortex: Dong et al., 2004; Raizada and Grossberg, 2003). Infragranular layers are hypothesized to modulate activity within the cortical column: on the input side they integrate thalamic input and top–down activity from higher-order areas, their output modulates layer IV and supragranular layers (Raizada and Grossberg, 2003; Callaway, 2004). High-amplitude activity in infragranular layers in the auditory cortex appears later in development than in supragranular layer (Kral et al., 2005), indicating that top–down modulations can be incorporated into processing within primary auditory areas only late in development.

In human anatomical studies, axonal development (neurofilament staining) was shown to be slower in supragranular than infragranular layers (Moore and Guan, 2001). Although it

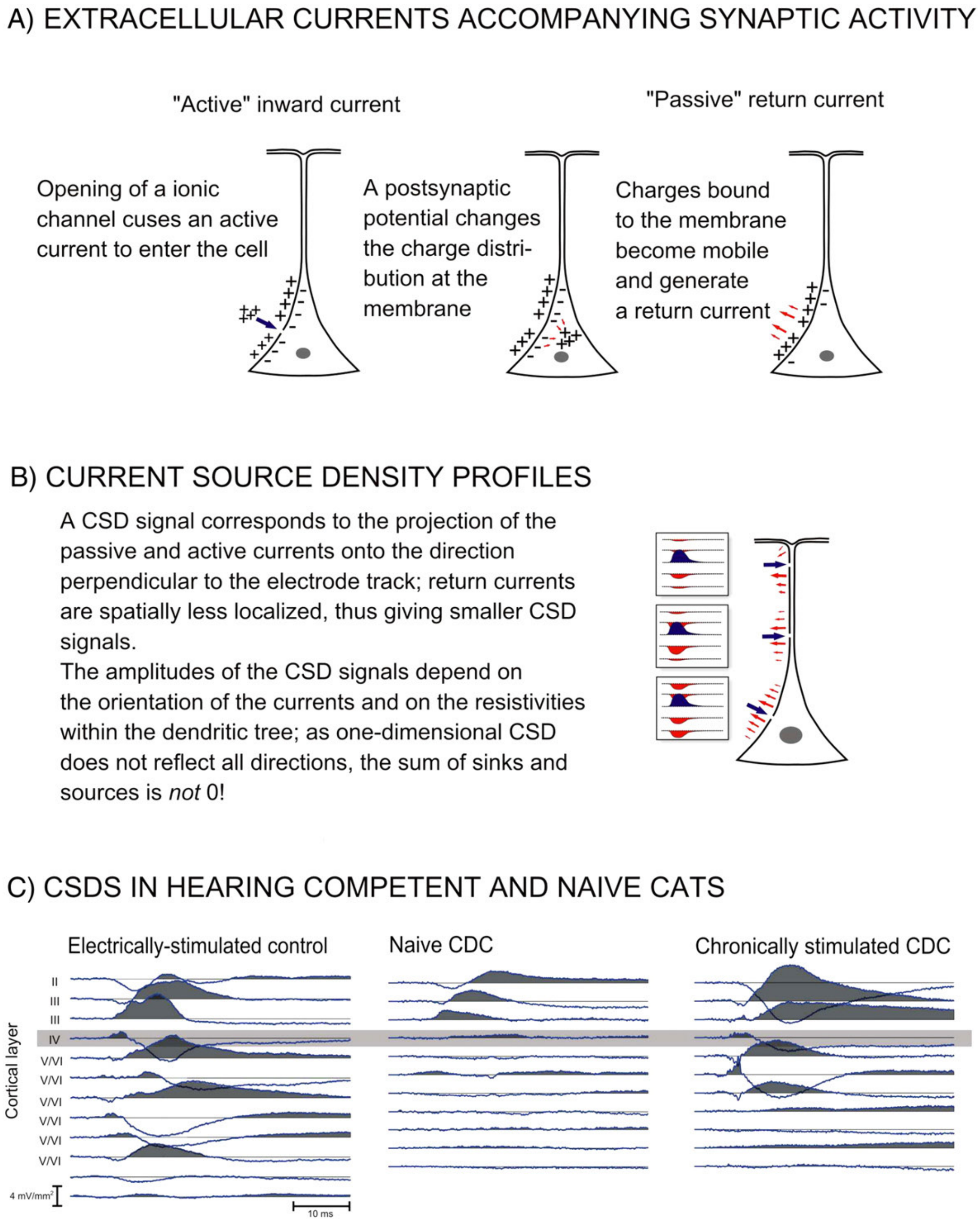

Fig. 2 – **The current source density method relies on computation of transmembrane currents from extracellularly recorded local field potentials. (A) Transmembrane currents related to opening of a sodium channel. "Active" and "passive" currents result from ionic movements either through an open ionic channel or as a result of detachment of ions attracted to the neuronal membrane. (B) Current source density events related to the above changes. The CSD method does not resolve the function of individual synapses if recorded with conventional extracellular electrodes. Instead, activities of a large number of functionally similar synapses are necessary to generate the CSD signals. (C) Results of a series of studies on the auditory cortex of naïve congenitally deaf cats demonstrate most extensive deficits in activity of infragranular layers. After chronic electrical stimulation through a cochlear implant and a portable signal processor with biologically meaningful stimuli lead to restoration of the deficit in infragranular layers.**

remains unclear what is the functional impact of immature neurofilament on signal conduction, immature axons could lead to late and asynchronous activation of target structures due to differences in conduction times. Consequently, immature axons of neurons in supragranular layers, even if strongly activated, can most probably only weakly activate infragranular

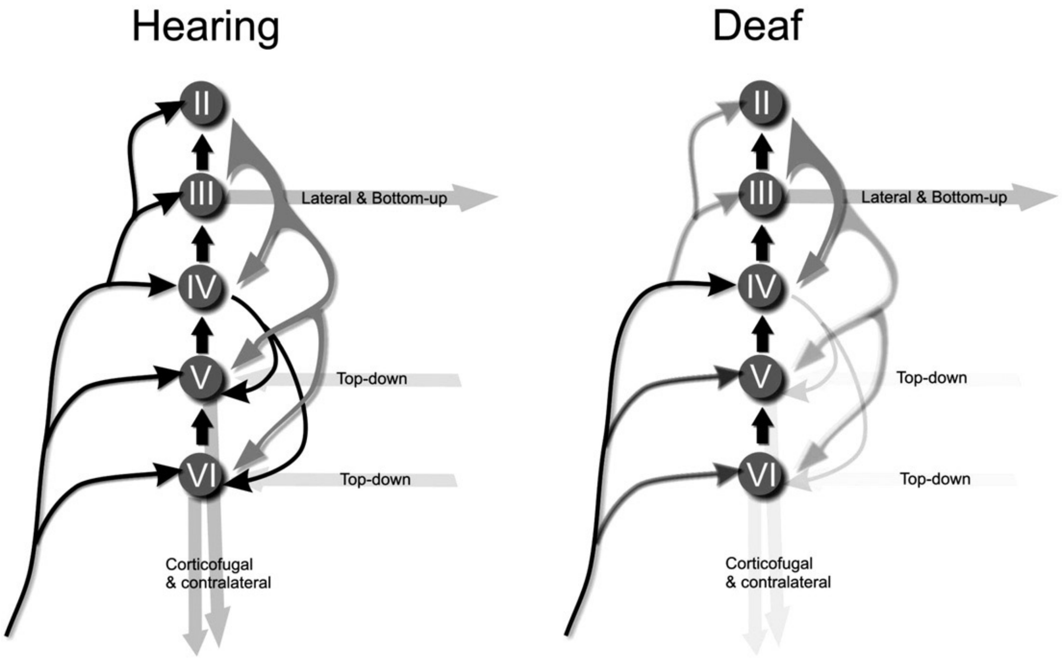

Fig. 3 – Schematic illustration of the deficits in the primary auditory cortex of congenitally deaf cats. Most prominent deficits are found in the direct thalamic activation of supragranular layers, in intrinsic and descending (top–down) activation of infragranular layers and consequently also in the recruitment of thalamo-cortico-thalamic loops with peripheral stimulation.

layers and spread of activity into secondary sensory cortex. The faster axonal development in deep cortical layers follows the general line of morphological development of the cortex (from deep to superficial, for review see Gleeson and Walsh, 2000) and might be crucial for establishing functional thalamocorticothalamic loops. Unfortunately, the differentiation of thalamocortical axons penetrating through infragranular layers into layer IV is difficult using neurofilament staining: thalamocortical axons are less abundant and consequently are not likely to contribute significantly to the result.

Visual deprivation is likely to dominantly affect the feedback projections in the primate visual cortex (Batardiere et al., 1998). It was repeatedly demonstrated that *feedforward* connections are established early (in primates during prenatal development) and that they preceded the development of feedback projections (Burkhalter, 1993; Barone et al., 1995, 1996b; Coogan and Van Essen, 1996). The maturation of *feedback* connections in the visual cortex, on the other hand, is protracted into the first months of postnatal life, likely making their establishment dependent on sensory experience (Price et al., 2006). Information on the corresponding aspects in auditory development is not yet available. Comparisons between different cortical sensory systems and different species are complicated, but can be approximated by using the date of thalamic innervation as a reference (for review and a model, see e.g. Clancy et al., 2001).

Deprivation affects corticocortical development differentially: Development of inhibition is delayed in visual cortex of visually deprived rats (Morales et al., 2002; Dong et al., 2004), particularly in layers IV and III. These data strongly indicate facilitated feed-forward transmission of information in deprived sensory cortex. However, in the deprived state this pathway is not fed with input, and consequently higher-order areas cannot be activated via lemniscal thalamic input, despite of a facilitated feedforward information transmission.

Lower cortical thresholds for cochlear implant stimulation in congenital deafness indicate that a similar mechanism might operate in the primary auditory cortex (Kral et al., 2005). In the primary auditory cortex, indirect signs of a delay in development of inhibitory activity in deep layer III and layer IV were also found (Hubka et al., 2004; Kral et al., 2005), together with concomitant changes in excitatory transmission after deprivation (Kral et al., 2005; Kotak et al., 2005).

With increasing age, the target structures of facilitated feedforward transmission (the secondary auditory cortex) undergo cross modal reorganization (Naito et al., 1997; Nishimura et al., 1999; Petitto et al., 2000; Finney et al., 2001, 2003) and possibly will not be available for processing the auditory input any more.

Analysis of the cortical connectivity after visual deprivation have revealed a more extensive deficit in *feedback* connections than in feedforward connections (Dong et al., 2004; Barone et al., 1996a). Complementing later development of feedback projections when compared to feedforward, these data further support a developmental change from a mainly feedforward interaction to a combined feedforward–feedback interaction between cortical areas. Also non-specific modulatory system mature postnatally in altricial animals (Robertson et al., 1991; Harper and Wallace, 1995). Developmental changes of the non-specific modulatory system (e.g. the cholinergic system originating in basal nucleus) could contribute to the developmental change in feedforward and feedback projections.

Case reports support the concept that dysfunctions in the deprived visual systems increase with the complexity of visual task: elementary functions of the visual system were preserved despite early deprivation, but more complex functions like recognition of visual objects were significantly compromised (Fine et al., 2003). This finding implicates more extensive deficits in higher-order cortical areas and in their top-down modulation of primary areas then in the processing of primary areas themselves.

The neural mechanism of the top–down influence could be in modulating the synchrony in firing between different neuronal populations in primary sensory areas (Engel et al., 2001). In cat primary auditory cortex, neural synchrony within a column decreased in the first 3 months of age, whereas that across columns did increase (Eggermont, 1992). Around 3 months after birth in cats, activity in infragranular layers increases (Kral et al., 2005), making top–down influences one possible component modulating the synchrony within and between different columns (review in Kral et al., 2006).

4. Top–down influences in congenital deafness: imaging

Further evidence of top–down influence comes from functional studies in the deprived human auditory system. Electroencephalographic data revealed a developmental delay in the morphology of acoustically evoked potentials as well as in latencies of individual evoked potential components in prelingually deaf children (Ponton et al., 1996; Ponton and Eggermont, 2001). This delay could not be compensated by auditory experience with cochlear implants if implantation took place after the 4th year of life. However, electrical hearing induced a maturation from the time point of implantation, leading to the theory that latency of evoked potentials express the “time in sound” of the child (Ponton et al., 1996; Ponton and Eggermont, 2001). Implantation of younger children (<4 years) suggests some compensation of the developmental delay (Sharma et al., 2002). These findings support the concept of a sensitive period for recovery in the auditory system within the first 4 years of life. Interestingly, in prelingually deaf children implanted after the age of 6, the evoked potentials did show some maturation of the P1 wave, but they never developed the N1 wave (Ponton and Eggermont, 2001). Invasive recordings from human auditory cortex demonstrate that wave P1 is generated both in early (primary) auditory areas and in higher-order auditory cortex, whereas wave N1 is predominantly generated in higher-order areas (Liegeois-Chauvel et al., 1994). Our interpretation of the missing wave N1 in late-implanted children is that it indicates an improper activation of higher-order areas. Similar findings have been reported in positron emission tomography of prelingually deaf cochlear implanted children (Nishimura et al., 2000), where activation of higher-order auditory areas was discernible only after some time of cochlear implant use, and this recruitment of higher-order auditory cortex was not achieved in late-implanted children. These findings fit well into the concept of developmental patterning in bottom–up connections during development, which is a precondition for activation and patterning of top–down interactions.

5. Conclusions

The here reviewed data strongly indicate that auditory experience is important for proper activation of higher-order auditory areas. This explains why studies on the primary auditory cortex of congenitally deaf animals showed a decrease of activation in infragranular layers. These layers are the targets of descending (feedback, top–down) modulation of activity from higher-order areas. Lack of activation in higher-order areas would thus explain this finding.

During development, the central auditory system can either learn or lose: under proper stimulation it can to learn to organize sensory input into categories (auditory objects) according to the environmental conditions and behavioral needs of the organism. 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.

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