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Auditory cortical plasticity: a comparison with other sensory systems

Josef P. Rauschecker

The auditory cortex has a crucial role in higher cognitive functions, including the perception of speech, music and auditory space. Cortical plasticity, as in other sensory systems, is used in the fine tuning of the auditory system for these higher functions. Auditory cortical plasticity can also be demonstrated after lesions of the cochlea and it appears to participate in generating tinnitus. Early musical training leads to an expansion in the representation of complex harmonic sounds in the auditory cortex. Similarly, the early phonetic environment has a strong influence on speech development and, presumably, on the cortical organization of speech. In auditory spatial perception, the spectral cues generated by the head and outer ears vary between individuals and have to be calibrated by learning, which most probably takes place at the cortical level. The neural mechanisms of plasticity are likely to be the same across all cortical regions. It should be useful, therefore, to relate some of the findings and hypotheses about auditory cortical plasticity to previous studies of other sensory systems.

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IT HAS LONG BEEN KNOWN that the mature state of the visual cortex is shaped by the interaction of genetic as well as environmental factors[1,2]. Studies on the role of visual experience in this process have been driven by two rather different, but not mutually exclusive, motives. A philosophically inspired debate has focused on the roles of nature versus nurture in perceptual development[3,4]. From a clinical, practical perspective it has been important to understand the role of childhood vision impairments, such as strabismus or cataract, in the etiology of amblyopia, a permanent central vision loss[5].

Studies of somatosensory plasticity have progressed even further. They have shown that the malleability of sensory cortices is not necessarily restricted to an early sensitive period, but continues (although perhaps to a lesser degree) throughout adulthood[6]. Thus, it has been argued by some that other forms of cortex-based learning might be governed by similar principles of synaptic modification[7,8]. As in the visual system, clinically relevant applications of this research are apparent, for example, in the remarkable cortical reorganization in individuals with peripheral injury, including amputation[9,10].

Research on the auditory system has been much slower to recognize the relevance of cortical self-organization and reorganization. Although there has been a number of studies of auditory plasticity at subcortical levels including the inferior colliculus (see, for example, Refs 11,12), comparatively little work has been done on plasticity of auditory cortex until recently[13]. Many important functions of the auditory system, however, can only be understood fully with cortical plasticity in mind. For example, even with an innate

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capacity for language[14], normal speech can hardly be acquired without auditory feedback and a capacity for learning[15]. Likewise, a system capable of localizing sound with extraordinary precision, using various sets of cues, cannot be achieved without resorting to tuning mechanisms that recalibrate the system continually, especially during the growth phase of the head and outer ears[16].

Spatial processing of sound and acoustic communication (speech perception in humans) epitomize two major cognitive functions of hearing. The present review will concentrate on auditory cortical plasticity from these two vantage points and, in surveying some of the existing literature, will make suggestions for further study. As it would be useful to compare auditory cortical plasticity with plasticity in other sensory systems, the review will discuss some examples of analogous cortical reorganization.

Cortical reorganization after peripheral lesions

Filling-in phenomena

The use of localized lesions of the cat retina as an experimental tool for the study of central visual plasticity was introduced some time ago (see Ref. 17 for a review) and has enjoyed a remarkable renaissance recently[18,19]. The universal outcome of these studies is that a small lesion in the periphery leads to a filling-in process in the cortical representation of the lesioned area. Receptive fields (the area of the retina or visual field that, when stimulated, produces a response in an individual cortical neuron) of neighboring neurons expand into the deafferented region. Perceptually, the lesion is not immediately apparent, in the same way that the normal visual blind spot goes undetected in everyday life.

In the somatosensory cortex, similar results have been obtained from peripheral deafferentation of the arms or fingers[9,20,21], which leads to massive reorganization in the somatosensory cortex of primates. Expansion from neighboring body-part representations is found, such that neurons in the area formerly representing the hand are now activated by touching areas of the face. This can explain the phantom sensations experienced by limb amputees, who often report feeling their phantom limb when touched in the face[22–24].

Similarly, small lesions of the cochlea, in a restricted region of the frequency axis of the basilar membrane, also lead to a missing frequency representation in auditory cortex[25]. The same region is now occupied by input from neighboring frequencies, which expand into the vacated space[26] (Fig. 1A). Two testable predictions can be made: (1) by analogy with vision, subjects might not be aware of the missing frequency range, unless specifically tested; (2) by analogy with touch, they might be expected to perceive phantom sensations that come from the deafferented frequency region. Evidence for the latter prediction is beginning to emerge from studies of tinnitus.

Tinnitus: an auditory phantom sensation?

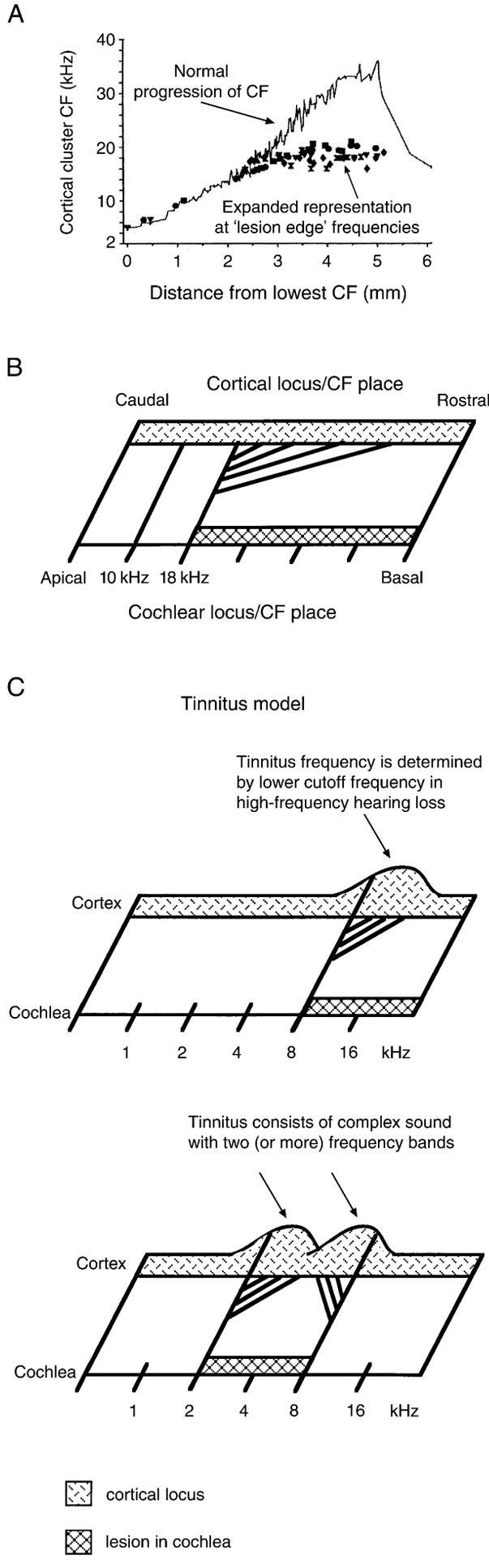
People with amputations often have the feeling that the amputated limb is still present, as a so-called phantom limb. This can include the perception of phantom pain in the amputated limb. Subjective tinnitus, the hearing of a disturbing tone or noise in the absence of a real sound source, is a similar experience and can indeed be thought of as an auditory phantom phenomenon[29]. According to this analogy, the process that leads to tinnitus begins with a sensorineural hearing loss in the auditory periphery. This could be a cochlear lesion from loud noise exposure or age-related hair-cell loss within a certain frequency range (usually high frequencies). While the loss of hair cells causes elevated thresholds in that frequency range, neighboring frequency bands can actually be enhanced because their central representation expands into the vacated frequency range (Fig. 1B,C). Recent human-brain-mapping studies using magnetoencephalography[27] and positron emission tomography[28] have provided evidence that cortical reorganization with a concomitant shifting of the frequency axis does indeed occur in tinnitus patients. Support for a central origin of tinnitus also comes from the fact that tinnitus persists in patients with acoustic neuroma even after transection of the auditory nerve[30,31]. Furthermore, studies using 2-deoxyglucose autoradiography in gerbils treated with salicylate (which is known to generate tinnitus) demonstrated reduced neuronal activity in the inferior colliculus but increased activation in areas of the auditory cortex[32].

'Productive' phenomena analogous to tinnitus or phantom limbs, with their disturbing subjective symptoms, have not been systematically explored in the visual system. It is well known, however, that patients with retinitis pigmentosa, which often starts with restricted lesions of the retina, complain about phosphenes (flashes or more prolonged light sensations, without an external visual stimulus) in specific parts of their visual field. Whether there is a systematic relationship between the locations of the lesions and the phosphenes in such patients remains to be investigated.

Cortical effects of sensory deprivation and training

The classic approach to studying developmental plasticity of the visual cortex has been to rear young animals in a restricted visual environment and measure the neurophysiologically and neuroanatomically determined changes that occur in comparison with normally reared animals[5,33]. Effects of auditory deprivation and restricted environments have been reported in early studies on the development of the inferior colliculus[11,12], but such work has not been extended to the auditory cortex. Part of the explanation could be that the control of the sensory environment is not as simple in the auditory system as in the visual system. Monaural deprivation can be accomplished by unilateral ear-plugging, but this creates only an interaural level difference of 20–30 dB. Ligation of the ear canal[11] is likely to be complicated by the fact that it can also lead to a sensorineural loss in the deprived ear.

In designing novel studies of the auditory cortex based on specific auditory experience or deprivation, using the visual system as a model, care must be taken in choosing the correct comparison. It is intuitively clear that ocular-dominance plasticity and binaural plasticity might be equivalent. The corresponding auditory analog to rearing in an orientation- or direction-selective visual environment, however, is less obvious. It has been argued that motion information in the visual domain is coded in the same way that frequency modulated (FM) sweeps are coded in the auditory domain[34,35]. Is rearing in a unidirectional visual environment, therefore, equivalent to rearing in an acoustic environment consisting of FM sweeps



in only one direction (up or down along the frequency axis)? Or is it equivalent to rearing in an acoustic environment where sound sources are moving in only one direction, as would be suggested by a more direct functional analogy[36]? If the latter were true, one might predict that the development of cortical areas involved in the processing of auditory motion[37,38] is influenced by early experience in the same way that areas involved in the processing of visual motion are[39].

In the somatosensory system, stimulation of specific finger regions has been shown to lead to an expansion of the corresponding areas of representation in the somatosensory cortex[40,41]. Similarly, training of monkeys at a particular tone frequency (the equivalent of place in the sensory periphery) leads to an expansion of the corresponding frequency representation in the auditory cortex[42]. In more practical terms, early musical training seems to be related closely to the development of absolute pitch and a concomitant expansion of auditory cortex in children[43,44] (Fig. 2). Experience-dependent plasticity for the perception of harmonic sounds is greatest before the age of eight or nine[44], which coincides with the critical period for development of absolute pitch (see Ref. 45 for a review). This corresponds well with findings on phonological development, which also demonstrate that non-native accents in a second language invariably develop if the latter is acquired after the age of eight[46].

Much of cortical plasticity is thought to be based on the rules of Hebbian learning[33,47]. Ocular dominance changes in the visual cortex have become one of the standard assays for the assessment of synaptic plasticity. However, the role of various neurotransmitters and neuromodulators, such as acetylcholine

Fig. 1. ***Cortical reorganization after peripheral deafferentation in the auditory system.*** **(A)** *Lesions of the cat cochlea in a restricted frequency range lead to an over-representation of neighboring frequencies (at the edge of the lesion) in the auditory cortex. The normal progression of characteristic frequency (CF) is found for the intact ear (solid line). For the lesioned ear, neurons respond to the same frequency range across several mm of cortical distance (filled symbols), which suggests that input from that frequency range has expanded into territory formerly driven by the deafferented frequency range. The same expanded representation of lesion-edge frequencies is not found at the level of the brainstem*[26]. Redrawn, with permission, from Ref. 26. **(B)** *Cartoon illustrating the expansion of lesion-edge frequencies in the auditory cortex after a restricted cochlear lesion* (redrawn, with permission, from Ref. 26). *The diagonal lines represent the mapping of the cochlea locus onto an area of the auditory cortex previously reserved for other frequencies to which the lesioned cochlea no longer responds.* **(C)** *Tinnitus as a phantom sensation based on similar mechanisms. Loss of hair cells in parts of the cochlea (by loud noise exposure or aging) leads to cortical reorganization. In high-frequency hearing loss (as shown in the upper diagram), the diagonal lines show how the area in the auditory cortex representing hair cells in the cochlea that respond to a frequency of 8 kHz expands. In middle-frequency hearing loss (lower diagram) the areas in the cortex representing the lesioned hair cells now represent hair cells that respond to the frequencies on either side of the lesion (diagonal lines). Thus, in both cases, neighboring frequency regions expand into the vacated space and become over-represented. In addition, these regions can lose intracortical inhibitory input from the deafferented cortex. Cortical neurons with input from frequency ranges next to the cut-off frequency thus display permanently elevated spontaneous activity levels. Recent brain mapping studies in human patients provide evidence for an expansion of auditory cortex around the tinnitus frequency*[27,28].

and noradrenaline, in visual cortical plasticity is still under debate. Recent attempts to extend these findings to auditory cortical plasticity might therefore be helpful in leading to a generalized understanding of cortical learning mechanisms[48–51].

Plasticity of auditory space perception

Experience-dependent adaptation of sound localization cues

It has often been argued that developmental plasticity exists largely because it permits the adaptation of brain systems to environmental factors that cannot be anticipated by genetic programming, or if they were would consume a great deal of genetic information. Adaptation to environmental factors could be coded more economically by epigenetic programs. Stereopsis during continuous head growth in infancy is the typical example of this continual adaptation taken from the visual system[52]. Interocular distance changes rapidly during the first years of life. If the disparity sensitivity of cortical neurons responsible for stereopsis were fixed from birth by genetic programs, they would be grossly mistuned later in life.

Similar arguments can be related to audition. Sound localization has classically been assumed to be a function of binaural interactions, such as interaural intensity and time- and phase-differences[53]. However, these cues are insufficient to discriminate between sounds originating from sources in front of or behind the head (known as the 'cone of confusion') or at different elevations[54]. Specific filtering of the sound by the head and outer ears (pinnae) creates a second set of cues that are based on unique location-specific attenuations ('head-related transfer functions' or HRTF) in the frequency domain[55,56]. Both binaural and spectral cues change constantly during development, and the neural circuitry for processing these cues has to be adjusted by developmental plasticity. The same arguments apply, although to a lesser extent, even during adulthood.

The sound localization mechanism based on spectral cues assumes a flat spectrum and compares the incoming sound with the acquired HRTF templates[54,57]. Familiarity with the spectrum of a sound, therefore, makes it easier to localize the elevation of a sound, and filtering a sound in specific ways can bias its perceived elevation[54]. Recent studies on guinea pigs have shown that there are large differences between the shape and size of external ears and, consequently, their HRTFs (Ref. 58; Fig. 3). These differences, which can also be found in humans[59], could not be anticipated by genetics. If monaural spectral cues are processed in the auditory cortex, as one might argue (see below), it would be most economical to adapt spectral coding of sound location by means of cortical plasticity. Some of the strongest evidence that the evaluation of monaural cues can change with experience comes from studies on blind humans, whose sound localization abilities are improved[60].

Representation of space in the auditory cortex

The way in which sound locations are normally represented in the auditory cortex is far from clear. Unlike midbrain structures, such as the inferior and superior colliculi, which contain maps of auditory space, auditory cortical areas do not seem to contain such global maps. Instead, there appears to be a clustering of preferred azimuth (position along the horizontal dimension)[61], and further evidence suggests the existence of spatial tuning columns, which can be modifiable by experience[62]. It is conceivable that HRTF templates that code for position in space are stored in piecewise repeating columnar matrices that combine spectral and binaural information based on modifiable synaptic connections.

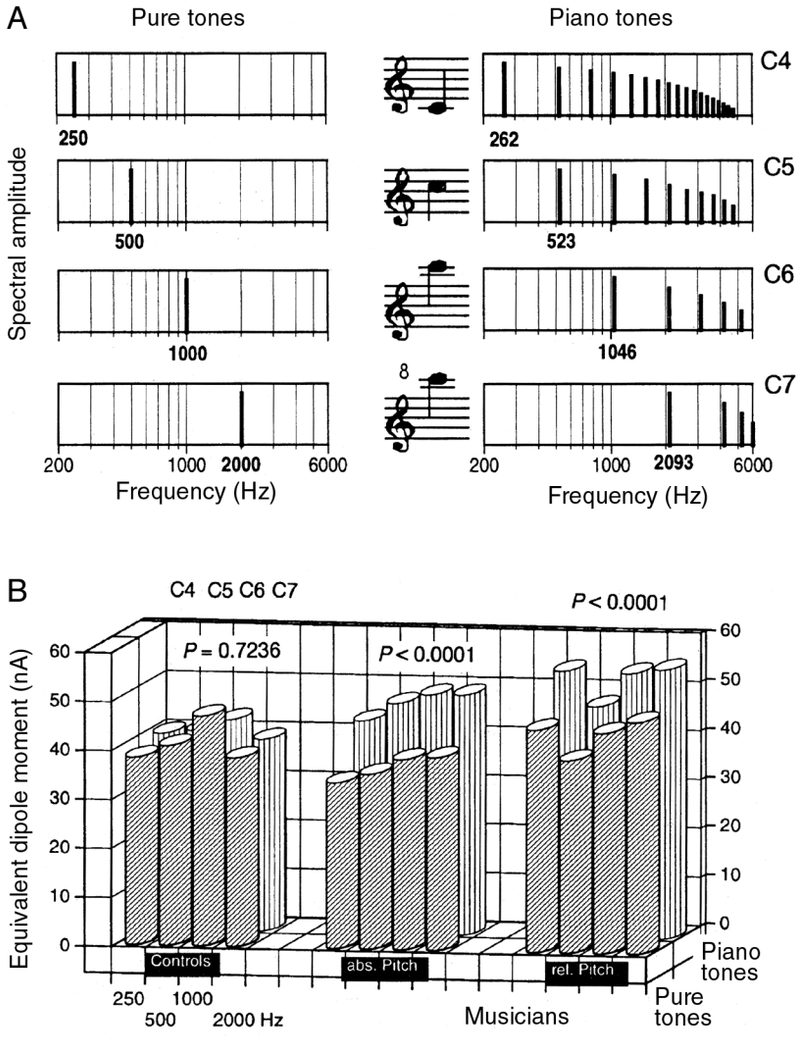


Fig. 2. ***Auditory cortical effects of early musical training.*** *The perception of complex harmonic sounds [piano tones,* **(A)***], which combine information from a wide spectrum of frequencies, is facilitated in individuals with absolute pitch and prior musical training[44]. (***B***) Concomitantly, the representation of such sounds in the auditory cortex, as assessed by magnetic source imaging, is expanded[44]. In control subjects pure tones (diagonal lines) and piano tones (vertical lines) lead to equally strong activation of the auditory cortex (as expressed by the equivalent dipole moment), whereas the activation of the auditory cortex by piano tones is significantly higher than that by pure tones in individuals with absolute as well as relative pitch. This is true regardless of the fundamental frequency of the tones (C^4–C^7).* Reproduced, with permission, from Ref. 44.

Neurophysiological studies of auditory spatial processing have recently focussed on the parietal cortex: the anterior ectosylvian cortex (AES) in the cat[62–64] and the posterior parietal cortex in humans[37,38,65]. These cortical regions had formerly been considered as predominantly visual or multimodal at best, but are now also known to contain unimodal auditory areas[66,67]. Further study of their normal function will be aided by the concurrent investigation of their plasticity.

Under normal circumstances, the motion of the head contributes to the localization of sounds of longer duration[57]. In cats that have been deprived of vision from birth, conspicuous scanning movements of head and pinnae in the vertical dimension are

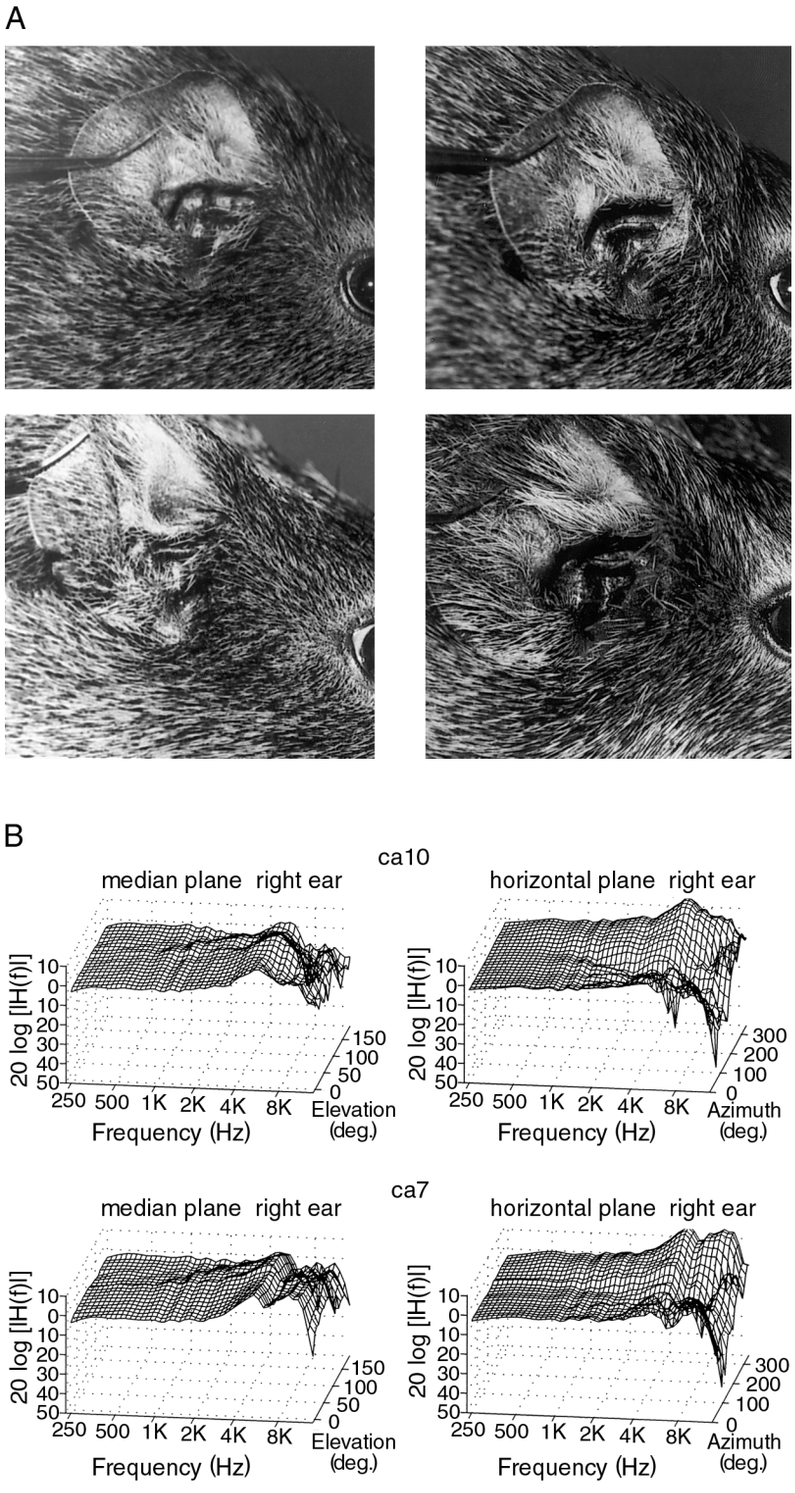


Fig. 3. ***Individual calibration of pinna cues for sound localization.*** *The individual variability in the geometry of the outer ear (pinna) and the resulting differences in head-related transfer functions (HRTFs) necessitate a calibration process that permits the individual to learn the relationship between HRTF and location of a sound source in space. Experience-dependent plasticity of the auditory cortex is assumed to play a role in this tuning process.* **(A)** *Examples of outer ears (pinnae) from four different guinea pigs illustrating the wide variability of shapes in different individuals[58].* **(B)** *Head-related transfer functions from two individuals (ca7 and ca10) illustrating how the differences in outer-ear geometry are translated into widely differing filter functions for both azimuth (right panels) and elevation (left panels)[58]. Graphs represent attenuation of sound as a function of frequency.* Courtesy of Susanne Sterbing and Klaus Hartung.

observed (P.T. Henning and J.P. Rauschecker, unpublished observations). These movements are triggered only by sound, are never found in sighted cats (even in the dark), but occur in blind cats regardless of ambient light conditions. One might conclude, therefore, that vertical auditory scanning is part of the compensatory plasticity mechanism in visually deprived cats[68] and that it provides an advantage for these animals in terms of improved perception of the elevation of a sound. The location of these adaptations in the brain is currently unknown, but it is reasonable to assume that cortical structures participate in them.

Auditory cortical plasticity in speech and language

Influence of early phonetic environment

Besides the localization of sounds, which can be achieved with astonishingly high precision, the decoding of acoustic signals for communication is the other main accomplishment of hearing. Its sophistication is perhaps even more remarkable than sound localization, especially when one considers a communication system like human speech. While the capacity for speech is obviously a genetic predisposition unique to humans[14,69], observations in deaf children show that learning and experience, that is, plasticity of specific brain structures and exposure to speech sounds, are required for the normal acquisition of spoken language.

The most obvious demonstration of the necessity of experiential factors in language acquisition comes from the observation that infants raised in different cultures or by different parents can acquire the language of their surrounding phonetic environment without impairment[15,70]. The inability of many Japanese speakers to distinguish or produce distinct sounds for ‘r’ or ‘l’ is thus not the result of a genetic disposition, of course, but is due to the absence of the distinguishing features in their early auditory environment[70]. Once acquired through early exposure, however, such a predisposition can only be reversed through intensive training[71].

Studies designed to show the influence of early auditory experience on speech development and phonetic perception have recently been performed by Kuhl *et al.*[72] Infants in different countries (Sweden, Russia and the USA) do not initially show a preference for phonemes unique to their own language. By about six months of age, however, they suddenly develop this preference. Work by Jusczyk *et al.* shows that language-specific preferences for prosodic cues, which are necessary for the segmentation of the speech stream into perceptual units, also develop between six and nine months of age[15,73].

At present, one can only conjecture how the changes in phonetic perceptual space (which are mirrored by changes in articulatory space) are accompanied by corresponding changes in brain representation. Considering that, in bilingual subjects, the distance between the representations of the first and second language areas is only a few millimeters[74,75], the changes of phonetic space within each area must occur on a minute scale of tens or hundreds of micrometers. It is noteworthy that this change is of the same order of magnitude as that of ‘minicolumns’ in the visual or other sensory cortices (50–100 μm)[76]. At the neuronal level, one might imagine that neurons are tuned to specific combinations of spectral and temporal information mapped across the cortical surface[66,67,77] (Fig. 4). Auditory cortical plasticity would enable the formation of such combinations under the influence of an early phonetic environment.

Auditory experience and language impairments

Fast temporal transients are particularly crucial for phonetic discrimination in human speech. Therefore, distortions of the early auditory environment that affect the perception of these features should have severe consequences for later speech perception and language learning. Indeed, it has been demonstrated that children with language-based learning impairments have major deficits in the recognition of some rapidly successive phonetic elements and non-speech sound stimuli[81–83], which can be improved by training[81,82]. Similarly, language-impaired children have severe perceptual deficits for brief but not for long tones, when the tones are masked by noise[84].

Masking thresholds are also severely altered in children with a history of otitis media[85]. The question arises, therefore, whether this very common disease, which occurs repeatedly in nearly a third of all infants before the age of three[86], could be a major cause of such perceptual and, ultimately, language deficits. According to some studies, a 20 dB hearing loss accompanying otitis media results in significant distortions of speech, especially at high frequencies[87].

Impairments of speech discrimination in noisy environments, especially in the presence of multiple speakers, are also becoming increasingly apparent in the elderly population[88]. The solution of this 'cocktail-party' situation probably involves top-down processing (the influence of a higher center on a lower center in a hierarchical processing scheme) that includes the auditory cortex[89] (similar to the classic 'figure-ground discrimination' in the visual domain). One can easily imagine that an auditory cortex deprived of the proper input would lead to impairment in that function. Clearly, much more research needs to be devoted to this important topic.

Cochlear implants and auditory cortical plasticity

When the concept of cochlear implants was originally conceived, several decades ago, it was based on the idea that they should implement the coding principles of the peripheral auditory system[90]. Once a transducer could be built that could generate the same signal as would normally be carried by the auditory nerve fibers, the problem of mimicking the peripheral auditory code would be solved. Not only did it prove to be difficult, if not impossible, to mimic the auditory code, but it was even more difficult to make the higher auditory centers understand it. Eventually, central auditory plasticity helped to solve the problem[91]. The recent, and rather unexpected successes of cochlear implant research are largely founded on the premise that, presumably, the auditory cortex adapts even to a highly incomplete signal, but only if it has the opportunity to learn the appropriate associations. According to what has been stated in this review, the use of cochlear implants that exploit the heightened plasticity of the auditory cortex during early development, should be strongly encouraged in prelingually deaf children.

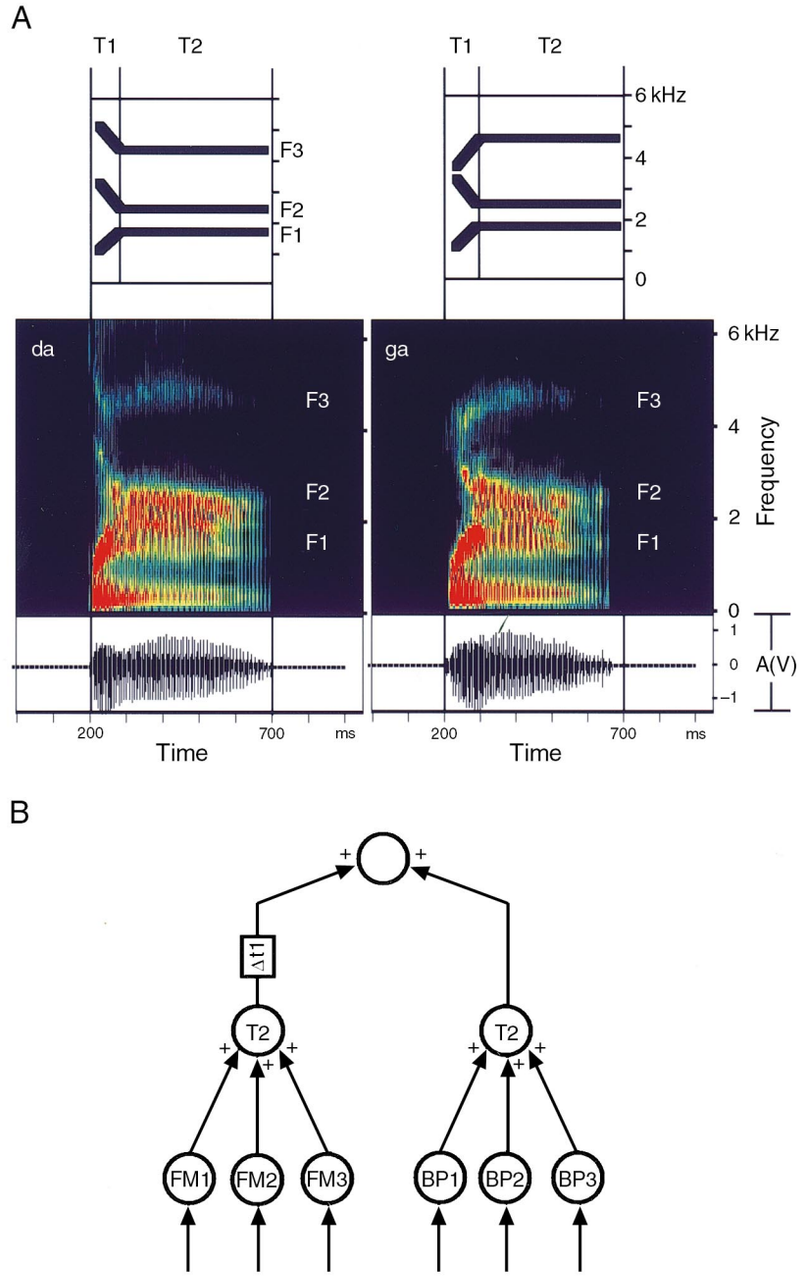


Fig. 4. ***Changing auditory representations during early development of speech.*** *The neural representation of phonemes in higher areas of the auditory pathway is thought to be in the form of neurons that combine spectral and temporal information in a specific, nonlinear fashion, mapped across the cortical surface[66,77,78]. The likelihood of such combinations being effective in triggering a neuronal response in cortical neurons might depend on exposure to a specific phonetic environment from as early as six months of age, as studies of speech development in humans have shown[72,73]. Unlike in nonhuman primates, where many of the call types show only limited modifiability[79], the phonetic environment should have a profound influence on the formation of combination-sensitive neurons in humans.* **(A)** *Pseudocolor spectrograms of two phonemes from human speech ('da' and 'ga') with amplitude–time signal underneath and schematic representation of formants F1, F2 and F3 above. The phonemes differ mainly in the initial time segment (T1) of the third formant, which is a descending frequency modulated (FM) sweep in 'da' and an ascending FM sweep in 'ga'.* **(B)** *Model of hierarchical neuronal network consisting of parallel inputs from FM and bandpass (BP) detectors, which could underlie phonological decoding[67]. Plasticity of synaptic connections within such a network could explain the dependence of speech perception on the early phonetic environment.* (A) reproduced, with permission, from Ref. 80.

Concluding remarks

The examples addressed in this brief review demonstrate how the study of auditory cortical plasticity might best be guided by functional principles. Only if we have a clear idea about the perceptual and cognitive functions supported by a particular cortical system can we begin to ask meaningful questions about parameters that might be influenced by early experience or other environmental factors. Sound localization and acoustic communication are the two main functions of the central auditory system. Both are computational tasks that require a great deal of information

processing within various parameter domains. We clearly need to improve our understanding of the way in which these different parameters are normally represented in various cortical areas, in order to understand their modifiability or plasticity. Conversely, studies of behavioral development and plasticity can provide important hints that might, in turn, direct us towards functional studies of normal auditory processing. Comparisons with other sensory systems can be helpful in this respect, but they are no substitute for considering the specific idiosyncrasies of the auditory system itself.

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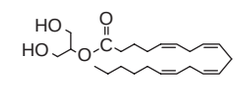
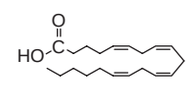
Erratum

Endocannabinoids: endogenous cannabinoid receptor ligands with neuromodulatory action, by V. Di Marzo, D. Melck, T. Bisogno and L. De Petrocellis, Vol. 21, pp. 521–528.

In Fig. 2 the incorrect structure was given for 2-arachidonoylglycerol, and in Fig. 3 the incorrect structure was given for arachidonic acid. The correct structures are shown below.



2-Arachidonoylglycerol



Arachidonic acid

We apologize to the authors and readers.

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