Auditory development and the role of experience

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The human ear is functionally mature shortly after birth, but the central auditory system continues to develop for at least the first decade of life. Current interest focuses on the relation between the very late developing aspects of hearing and other aspects of cognition and behaviour. While active neural input to the brain is essential during the very early stages of development, auditory experience is now thought to be a powerful influence on central function throughout an individual's lifespan. Studies of sound localization and hearing with two ears have shown the capacity of the auditory system to adapt to altered environmental cues, even into adulthood. This environmental influence may either be harmful, as during conductive deafness, or beneficial, as evidenced by the positive outcomes of auditory training.

Hearing in humans begins around the 22nd week of gestation (see Moore and Jeffery1). At this stage, behavioural responses to sounds are produced only by intense airborne stimulation, since the fetus is in a highly sound-attenuated environment, the outer and middle ears are fluid-filled2, and the cochlea and central auditory pathway are structurally and functionally immature. Following birth, sensitivity to sound is rapidly acquired, and many simple aspects of hearing achieve maturity during the first year. However, some aspects, such as sound localization and temporal processing, that seem to require more extensive processing in the central auditory system, do not achieve mature performance for many years, even into adolescence.

Many factors contribute to the relatively slow development of hearing: the environment, poor sound conduction, and incomplete neural development. Of these, it is neural development that has received the most attention, that has seen the most significant advancement in understanding, over the last 10 years, and that will form the focus of this review. I will present a synthesis of recent findings and thinking on the role that experience plays in shaping auditory function. The two volumes of the Springer Handbook of Auditory Research dealing with development3 and plasticity4 of hearing are more general accounts. Here, I will define ‘experience’ broadly to include the effects of both sensorineural and conductive hearing loss, as well as exposure to...
‘passive’ auditory environments and ‘active’ auditory training and learning. While early auditory experience is still considered especially critical for normal development, a major change of thought in the last 10 years has been the recognition of a life-time dependency on auditory input, and the ability of the mature system to respond to clinical or experimental manipulation of that input.

**Development of the auditory nervous system**

The neural basis of hearing begins in the cochlear hair cells, where transduction channels in the tips of stereocilia pass K⁺ and other cations in response to mechanical displacement of the organ of Corti (see reviews by Richardson and by Ashmore, this volume). The electrical driving force behind the transduction current, the endocochlear potential of the scala media, begins to function only a short period before the onset of functional hearing. At the same time, the cochlear partition is maturing structurally, in a basal-to-apical direction. Paradoxically, the earliest neural responses recorded from the central auditory system are evoked by low frequency sounds (e.g. Aitkin and Moore). This appears to result from an immaturity of cochlear mechanics, such that the peak of the travelling wave along the cochlear partition produced by a given frequency occurs more basally than in the case in adults. Other significant neural developments in the cochlea include changes in the size and shape of the hair cells, and the acquisition of mature synaptic function. These latter developments impair initial auditory function by limiting, respectively, the highest stimulus frequency at which auditory neurones can phase lock, and the maximum rate of firing of single auditory nerve fibres. In short, there are known structural and functional restrictions on the ability of the cochlea to function at all before a certain age, and to function in an adult-like way for some further period. It is not completely clear how long these developmental processes take in humans, but peripheral auditory function appears to mature by the end of the first few postnatal months (Fig. 1A).

Developmental changes of function in the central auditory system, by contrast, appear to continue for several years. Neurones throughout the system show mature responses to single tones relatively soon after cochlear function begins and, indeed, the capacity for neural function may precede that of cochlear function (see Romand). However, hearing of some more complex sounds, such as temporally separated pairs, and performance on higher demand listening tasks (e.g. sound localization) may remain immature well into the second decade of life (see Ponton et al). One important, and increasingly recognised, issue in the interpretation of
behavioural studies of hearing is the extent to which performance reflects sensory and non-sensory factors. Cognitive influences (e.g. attention) may be developing in parallel with sensation and, without appropriate experimental control, give a misleading impression of immature function in the auditory system. On the other hand, a strict distinction between sensory and non-sensory influences on perception, even at relatively low levels of the brain, has recently been called into question by neuro-imaging studies of the human visual cortex. Nevertheless, physiological studies in anaesthetised animals and in awake humans of neural responses to dichotic (i.e. binaurally discordant) or rapidly presented sounds suggest that much of the immaturity of hearing seen after birth does have a sensory basis, in the conventional sense.

The protracted immaturity of the human central auditory system (Fig. 1B) could be caused by several known factors. Both morphological and physiological studies indicate that development beyond the second to third year is a property of the higher, thalamocortical auditory system. 

**Fig. 1** Development of human central auditory physiology. Auditory evoked potentials recorded from (A) the auditory nerve (wave N1 of the compound action potential) were, in terms of response latency (shown here, relative to adult values) and amplitude to tone stimuli, mature by the sixth postnatal month (0.5-year-old [y.o.]). The difference in latency between waves V and I of the auditory brainstem response (V–I) is a measure of conduction time from the cochlea to the midbrain. A substantial reduction in this conduction time occurred between a group tested at birth (0 y.o.) and a group tested at 6–24 months. Extrapolation of the V–I data yielded a final maturation age of 15–24 months, with responses to lower frequency tones developing more rapidly. In the auditory cortex (B), the N1 and P1 responses (see text) to click stimuli underwent substantial development into the second decade of life. Again, the measure is response latency, referenced to values for adult listeners. Adapted from Ponton et al.
While cortical cyto-architecture develops early, myelination of the thalamic fibres innervating the auditory cortex begins around one year of age and progresses until the fourth year. Expression of cortical neurofilament protein, forming the basis of the axonal cytoskeleton, continues to change through to the age of 5–10 years. Conduction pathways are, therefore, immature for a protracted period of postnatal life and this will, of course, affect neural functions, such as auditory temporal processes. However, recent auditory evoked potential studies suggest that human thalamocortical function, as measured by the long-latency (40–200 ms) P1 - N1 - P2 response sequence, continues to develop ‘well into adolescence’ according to Ponton et al. Although the later components of these compound responses are notoriously difficult to localize, the P1 response is thought to originate predominantly from the lateral portion of Heschl’s gyrus and, therefore, represents a relatively

![Diagram of auditory experience](image)

**Fig. 2** Auditory experience may be thought of as neural activity generated in the cochlea and transmitted to the brain. Removal of auditory (VIIIth) nerve activity early in life abolishes glutamate (Glu) neurotransmission and causes some auditory brain stem neurones to die and some to survive. In the chicken cochlear nucleus (CN), the cellular processes underlying this experience-dependent regulation have been worked out in some detail. In the synapse, de-activation of metabotropic glutamate receptors (mGluRs) signals an increase in intracellular calcium levels via the AMPAR type of glutamate receptors. Neurones destined to die undergo other rapid responses to the de-activation, including ribosomal disaggregation and a decrease in amino acid incorporation. If input is restored within 1–2 days, the neurones can return to normal. Neurones that do not die nevertheless undergo a number of responses including soma shrinkage and an increase, followed by a decrease, of oxidative metabolism and mitochondrial density. Recently, an increased phosphorylation of a transcription factor (CREB) has been demonstrated. This may lead to compensation for the activity deprivation and thence to neurone survival. Again, if input is restored, the neurones can return to normal. Adapted from Garden et al and Zirpel et al.
'low' level of auditory processing. Nevertheless, the P1 and N1 responses do not reach maturity until 14–15 years of age. The very late development of these responses, which involve a decrease in both amplitude and latency, may be related to decreasing synaptic density and dendritic elaboration in the auditory cortex. However, insufficient anatomical data are available in the 5–15-year-old age range to form more definite conclusions.

The nature of auditory experience

We generally think of auditory experience as the sounds we hear. But neuroscientists think in terms of neural activity generated in the cochlea and transmitted to the brain (Fig. 2). Environmental sound (e.g. speech) will modulate and increase auditory nerve activity, conductive hearing loss (e.g. otosclerosis, otitis media) will decrease and desynchronize nerve activity, and sensorineural loss will reduce and broaden, or abolish nerve activity from damaged parts of the cochlea. The brain is affected by these input fluctuations in two ways. The first is, of course, that it will pass the information to, and through, the various centres of the auditory system for processing, and on into the cortex for understanding, integration and action (see Palmer and Summerfield, this volume). The second is that it will change the way in which the brain processes future input. These latter changes may be either beneficial, as occurs during developmental shaping of speech processing circuits, or detrimental, as when lack of stimulation produced by (untreated) deafness leads to neurodegeneration. In the following sections, I discuss in more detail recent thinking about these two contrasting roles of auditory experience in shaping the function of the auditory brain.

Bad auditory experience

The notion of ‘critical’ or ‘sensitive’ periods of development is well over 100 years old, but it is one that has undergone substantial recent revision. In hearing, there has been much progress in defining and characterizing a very early period during which clinical, surgical or chemical de-afferentation, resulting in total abolition of nerve activity, leads to wide-spread neurodegeneration in brain centres normally receiving direct input from the deaf ear (Fig. 2). In the cochlear nucleus of rodents, 50-70% of neurones have been found to die following cochlear removal before postnatal day (P) 10, where hearing begins at about P12. This apoptotic neurone death is but the end stage of a complex cascade of intracellular events that is triggered within minutes.
of activity withdrawal. However, just before the time at which hearing normally begins, the short-term dependence of auditory neurones on afferent activity abruptly stops. Thereafter, total deafening leads to shrinkage of neurones, probably due to membrane responses to axon retraction, but little or no death of target neurones, at least over a time course of months to years. One rationale for early cochlear implantation has been the need to provide trophic support for central auditory neurones in the absence of afferent activity. The early cessation of extreme sensitivity to de-afferentation suggests the importance of providing that support very early in development, and a reduced urgency for support thereafter.

Sensitive periods for some other aspects of auditory system plasticity have been more difficult to establish, especially where the change in auditory experience has consisted of a conductive hearing loss or a modification of the auditory environment. In addition, there has been a general realisation in neuroscience over the last decade that some aspects of the brain's susceptibility to experience-dependent plasticity are maintained throughout life. This will come as no surprise to those familiar with the well-known capacity in the elderly for recovery from stroke. However, there has been a great increase recently in the power of methods available for observing and measuring the plasticity. The new technology includes functional magnetic resonance imaging (fMRI) in

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**Fig. 3** Unilateral or asymmetric conductive hearing loss, as seen in middle ear disease in children and otosclerosis in adults, can lead to poor binaural hearing. In the laboratory, these diseases are modelled using ear plugs in experimental animals to control for variability and to investigate mechanisms. Ferrets receiving several months of unilateral ear plugging had reduced binaural unmasking for several more months after the plug was removed (A; adapted from Moore et al27). Sound localization abilities (B; from King et al28) show adaptation to the plug during plugging (as shown in the figure) but, surprisingly, there is no lasting impairment after plug removal. The latter result suggests that, in this case, altered experience leads to the formation of a parallel neural representation ('map') of space, rather than to re-ordering of an existing map.
humans (see Griffiths, this volume), and direct, optical imaging of the living brains of animals23.

The plasticity of binaural and spatial hearing has been studied behaviourally, using psycho-acoustic methods, and physiologically24. Although binaural hearing may be adversely affected by unilateral or asymmetric hearing loss, there is no clear evidence, in mammals, for an elevated susceptibility of the developing binaural system to abnormal experience. Clinically, both otosclerosis in adults and otitis media with effusion (O.M.E) in children perturb binaural hearing. More surprisingly, poor auditory function at any age may persist beyond the time of the peripheral pathology25,26. These effects have also been demonstrated in the laboratory. For example, prolonged ear plugging can lead to poor sound localization and binaural unmasking, a measure of the detection of sounds in noisy environments (Fig. 3)24,27. When the plug is inserted, some adaptation (recovery of function) may occur but, following removal of the plug, performance may remain impaired. These results suggest that impoverished auditory experience produces a protracted difficulty in detecting sounds in noisy environments. This difficulty may contribute to the early language processing problems that have been reported28 in some children with severe, recurrent O.M.E.

Good auditory experience

The adaptive plasticity of the brain appears capable both of mediating recovery of auditory function after hearing loss and of improving function following auditory training. Children who have had recurrent O.M.E, and who have persistent, impaired binaural hearing, gradually recover normal binaural function29,30. Adult human listeners who have the normal cues for sound localization distorted gradually ‘adapt’ to the new cues and regain normally accurate localization31,32. Most interestingly, ferrets that have had their auditory spatial localization disrupted by unilateral ear plugging gradually improve their localization if left in the home cage33. If, however, they are given additional training in sound localization, the improvement occurs more rapidly. Each of these cases provides compelling evidence for an experience-dependent improvement in spatial hearing following earlier maladjustment. That the improvement is at least partly mediated by auditory system neural plasticity is suggested by animal experiments showing that a neural ‘map’ of auditory space in the midbrain is shifted by manipulating the input from the ears in a way that is predictable from the localization behaviour. In the barn owl, for example, recent experiments34 have shown frequency-specific changes in the tuning of midbrain neurones to the binaural cues underlying sound localization following several months of
wearing an acoustic device that alters the time and level cues independently. Other experiments on the plasticity of spatial hearing mechanisms in mammals suggest that neurones in both the midbrain and the auditory cortex are influenced by prior auditory experience.

Enhanced auditory experience has recently been shown to be a useful therapeutic tool. For many years, it has been known that subjects in psycho-acoustic and other sensory tasks improve their performance with practice. When those practice effects have been applied to training listening skills in children with language impairments, dramatic results have been reported; (but see review by Bailey and Snowling, this volume). While the therapeutic effectiveness of this approach appears to be impressive, it is unclear whether the technique works through auditory perceptual learning or, more indirectly, through building up attention and other more general sensorimotor skills. Perceptual learning is thought to be highly specific to the trained stimulus, at least for some types of task. A recent study that trained adults in the time and level cues for sound localization has shown that the long-term, intensive training that is often considered necessary to obtain robust improvements is specific both for the stimulus frequency used during training and the type of cue trained. These findings suggest that sensory training will only be practically effective if the trained stimuli closely resemble the skill that the training is designed for. In the case of language training, this seems to indicate the use of appropriate linguistic stimuli rather than simpler signals of the type usually used in auditory research.

Deprivation followed by enhancement of ‘auditory’ experience in profoundly deaf people fitted with cochlear implants is thought to lead to the same cycle, and mechanisms, of neurodegeneration and recovery found in other examples of adaptive plasticity. Traditionally, the focus of interest in implantation has centred on the design of the speech processor and how that interfaces with remaining neural elements in the cochlea. It is now more widely recognised that both the problem (deafness) and the solution (implantation) are also dependent on the central auditory system. For example, recent studies have shown that activation of the auditory cortex in congenitally deaf cats is substantially enhanced by long-term electrical stimulation of the cochlea. Animals deafened and stimulated at later ages seem not to respond as well to implantation, but it is unclear to what extent that limitation is due to more peripheral effects of the deafening.

Neuro-imaging techniques are beginning to capture the changes in brain activation in humans that accompany impaired or enhanced auditory experience. Unilateral, congenital deafness leads to changes in the symmetry of auditory cortex fMRI activation produced by stimulation of the functional ear. Experience of cochlear implantation in adults following post-lingual deafness modifies activation of the auditory and temporal cortices. Individuals with impaired auditory and/or linguistic function...
have correlated perturbations of sound processing in the auditory cortex\textsuperscript{45,46}. Audiovisual training, matching simple non-linguistic sound sequences to patterns of rectangles on a computer screen, has been found to improve both reading skills and an electrophysiological indicator of cortical function (the ‘mismatch negativity’) in dyslexic children\textsuperscript{47}. While these efforts to study the ‘mechanisms’ of auditory system plasticity are exciting, the results need to be interpreted with considerable caution. As noted above, it is not always clear just what aspect of the life experience of the affected individuals has led to the impaired, or enhanced, function. It is also uncertain how the changes in observed activation relate specifically to auditory function. From the viewpoint of auditory experience, it is also sometimes unclear what the direction of causation is when relating patterns of activation to hearing. Nevertheless, careful improvements in experimental design, and continually evolving technology, including data from two or three techniques (e.g. fMRI and auditory evoked potentials) for a single listener, hold the promise of significant advances in understanding the neural basis of auditory system plasticity over the coming few years.

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