DISCUSS THE IMPORTANCE OF PLASTICITY IN THE AUDITORY PATHWAY

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Introduction

Plasticity of the auditory pathway is central to both the healthy development of hearing and of language, and it is also very relevant when considering diseases which are known to affect hearing. Nearly nine million people are deaf or hard of hearing in the UK[1]. Some will have been born with a deficit, others will develop one, most commonly as part of the ageing process: over 70% of 70 year-olds in the UK have some kind of hearing loss[1]. The impact a deficit can have ranges from minor to profound, and it can affect how people interact with, and are perceived by, society. Understanding how plasticity affects the auditory pathway is playing an important role in improving the healthcare these people receive.

The scope of this topic exceeds what can readily be covered in this essay, so discussion will be limited to some key areas. The essay begins with a definition of plasticity and a brief reprise of the auditory pathway. The relevance of plasticity will then be discussed with respect to how hearing develops, how it can change in adulthood, what happens when it is disrupted, and what happens if it is restored. Many of the experiments cited are invasive, so necessarily come from animal models. However, the increasing use of non-invasive techniques, such as functional imaging studies, now allow the human auditory pathway to be studied *in vivo*.

Plasticity (or 'neuroplasticity') refers to, "alterations in the physiological and anatomical properties of neurones in the brain in association with sensory stimulation and deprivation[2]." In other words, the property of the central nervous system to modify itself as a result of sensory experience.

The auditory pathway (figure 1) comprises a cochlea, auditory processing centres contained within the brain (e.g. the primary auditory cortex, A1), and the neurones and relay nuclei connecting them. When sound waves reach the cochlea, inner hair cells (IHCs) on the basilar membrane transduce them into electrical impulses. The frequencies of the incoming waveform determine which parts of the basilar membrane, and therefore which IHCs, are stimulated: those at the base respond more to high frequencies, while those at the tip respond more to low frequencies. Thus, the frequencies of the waveform are mapped from high to low onto the basilar membrane in a so-called 'tonotopic map.' This topographic representation of frequency is replicated at successive levels of the auditory pathway, and the resultant maps are very relevant to our discussion because they are a common site of neuroplasticity. For example, the first region of the cerebral cortex to receive auditory input, the primary auditory cortex, is tonotopically organised (see figure 2). From here, increasingly complex feature detection takes place as information moves outwards to the secondary (A2) and tertiary (A3) auditory cortices, before reaching auditory association areas.

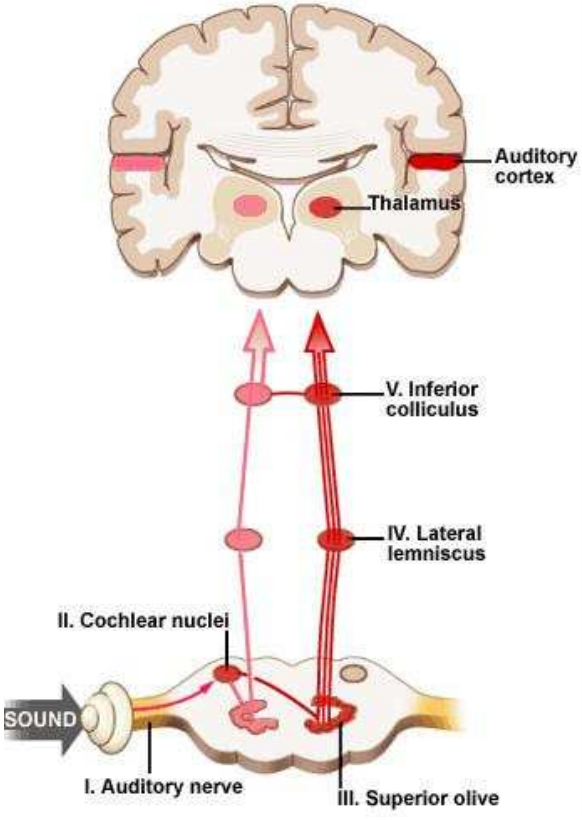

Figure 1. Overview of the ascending auditory pathway and its main relay centres. Both the contralateral and ipsilateral pathways are shown.

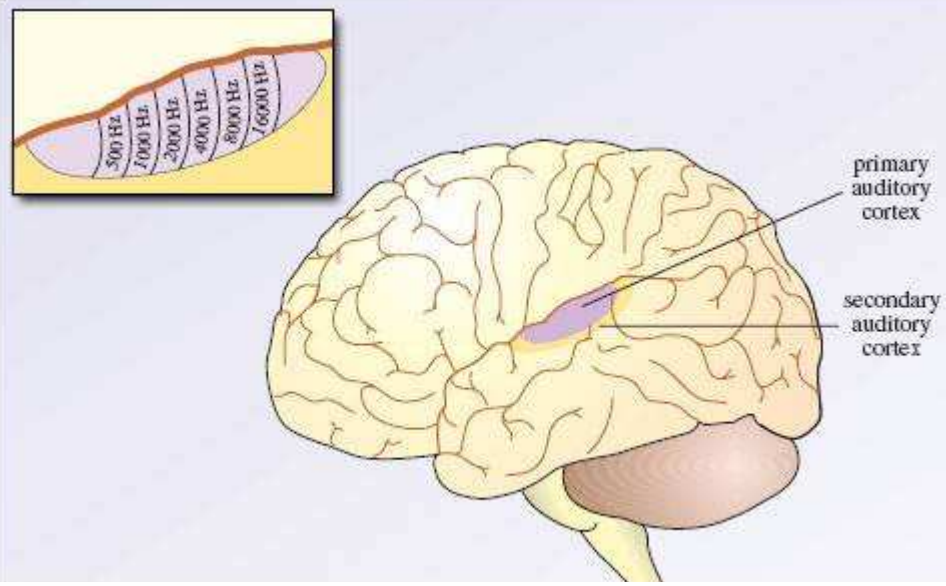

Figure 2. Location of the primary and secondary auditory cortices. The detail of A1 shows how the tonotopic map of the basilar membrane is preserved at this level of the auditory pathway.

Plasticity during normal development

Neuroplasticity is most pronounced during infancy, as neural architecture is being established[3]. Thus, early auditory input can have a profound effect on the functional organisation of the developing auditory pathway. For example, young rats exposed to pure-tone stimuli develop over-representation of training frequencies in their A1 tonotopic map at the expense of neighbouring frequencies[4] (see figure 3). The real-world importance of this tonotopic plasticity remains unclear, but it might allow frequency sensitivity to be adjusted to the environment in which a juvenile develops.

Plasticity is also important in developing sound localisation. Physical cues, namely the differences in sound level and arrival time between the two ears (binaural cues) and the spectral modifications produced by the pinnae (monaural cues), are processed to generate a map of auditory space, which is represented in the superior colliculus[5]. This map is highly plastic during development: the monaural occlusion of juvenile ferrets caused the map to undergo neural changes that preserved the alignment between representations of visual and auditory space[5]. This plasticity is crucial because it means the auditory pathway can accommodate the changes in head and pinna size that inevitably occur as part of growth. Without it, growth would increasingly derange sound localisation and we would lose the ability to detect where a sound was coming from as we got bigger.

Plasticity is not uniform throughout development. Instead, there are 'critical periods,' "temporal windows in postnatal development when experience profoundly influences the final organisation of neural connections[6]". During such periods, gross alterations of neural circuitry are possible, occurring at the level of axonal[7] and dendritic branching. The resultant circuitry is highly stable and seems to constrain the plasticity that is possible during adulthood[8]. Certain sensory inputs must be acquired during a critical period if normal development is to proceed. Full discussion of language acquisition is beyond the scope of this essay, but the learning of native speech sounds is a good example of plasticity and critical periods.

World languages collectively contain around 600 consonants and 200 vowels[9], but each language only employs about 40 phonemes[10] (the smallest segment of speech employed to form meaningful contrasts). Unlike adults, infants have the ability to discriminate virtually all phonemes[11], but this universality is not maintained: by 12 months, English-learning infants have difficulty distinguishing non-English phonemes[12]. At the same time, infants' ability to

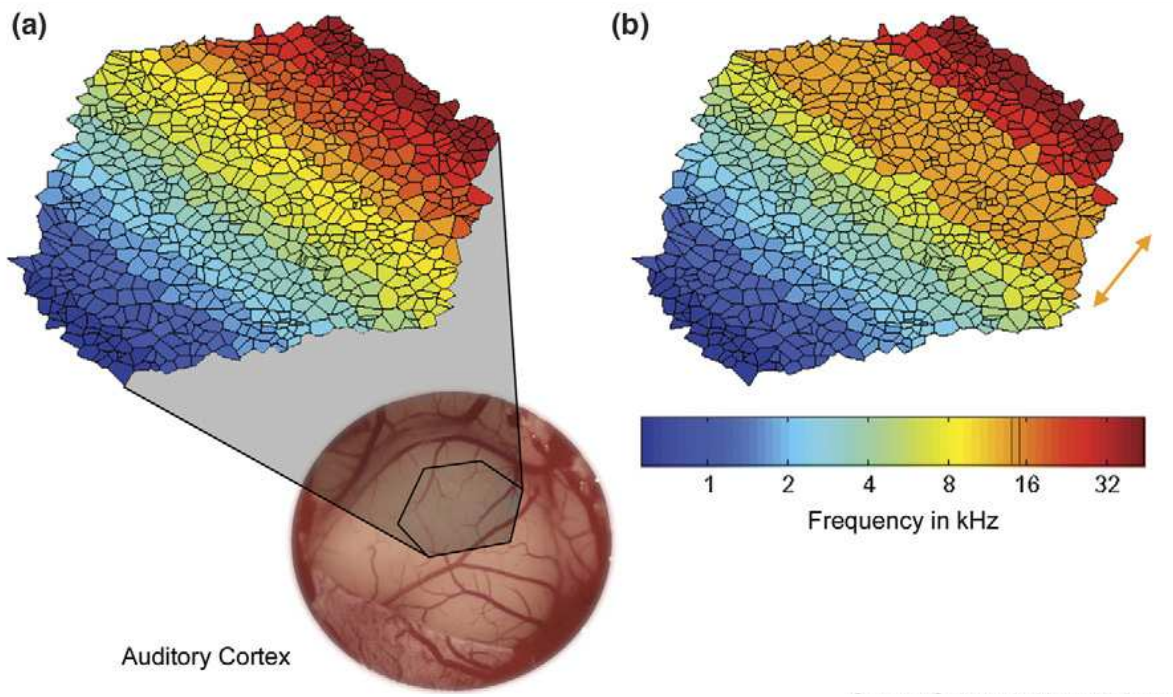

Figure 3. Effects of training on tonotopic representation in an area of A1. (a) Frequency map before training. The area occupied by each frequency band is roughly equal. (b) Frequency map after 15kHz pure-tone training. The region occupied by neurones selective for frequencies around 15 kHz is expanded. Frequencies just below and above 15 kHz are underrepresented. Reproduced from Dahmen and King[3]

discriminate native phonemes improves[13]. Thus, plasticity of the auditory pathway during this critical period optimises perception of our native language while constraining the subsequent learning of a second language. This has obvious educational implications, not least when languages are most effectively taught, but, as will be discussed, it also has implications for when cochlear implants are optimally implanted.

Plasticity in hearing adults

Contrary to previous thinking[14], we now know that neuroplasticity extends into adulthood, thanks in part to *in vivo* imaging[6] (see figure 4). Adult plasticity is more local than plasticity during development, and this is likely to limit the extent to which the adult brain can be reorganised[15]. It has been argued that the resulting stability "may be desirable... to achieve the efficiency and reliability of a mature neural system[3]". However, if sensory input is altered sufficiently, or if it possesses special behavioural relevance, surprising levels of plasticity can result, as illustrated by perceptual learning.

Perceptual learning describes how perceptual abilities can be improved by training, and it is thought to reflect neuroplasticity. The first to establish this in the adult auditory cortex were Recanzone *et al.*[16]. Monkeys trained on a tone discrimination task exhibited a redistribution within the A1 tonotopic map: areas representing training frequencies increased in size while areas representing non-training frequencies shrank. Furthermore, the size of the change correlated with performance: the bigger the redistribution, the better the monkey was at discriminating frequencies. In other words, this plasticity appeared to have *perceptual* consequences; the monkeys were, in some demonstrable sense, better able to 'hear' the sounds. Recanzone *et al.*[16] also showed that behavioural relevance helps determine the degree of neuroplasticity. If monkeys were played the same training tones but were simultaneously engaged in a tactile discrimination task, the tonotopic map of A1 did not alter.

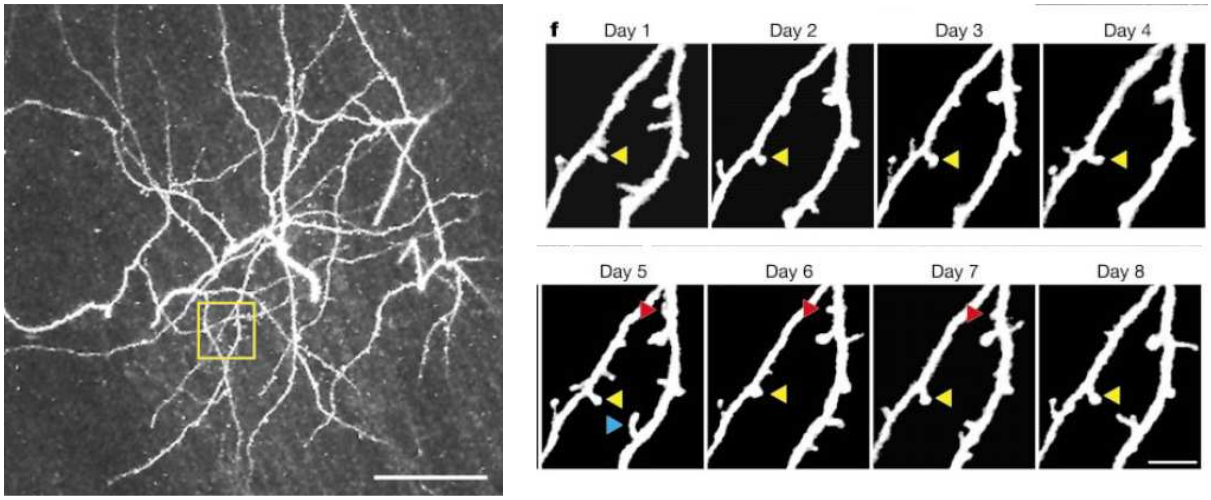

Figure 4. High resolution time-lapse images of a dendritic region (yellow box) in the mouse barrel map. Arrowheads demarcate transient, semi-stable and stable spine formation. Scale bar, 5µm. Reproduced from Trachtenberg *et al.*[6]

This is important because it shows that top-down inputs, such as attention, help determine whether neuroplasticity occurs.

Cortical redistribution may not be the only way plasticity can affect perceptual learning. Recent human studies using functional imaging have shown that improved speech segregation[17] and temporal discrimination[18] were accompanied by the auditory cortex becoming more responsive to the training stimuli rather than altering its tonotopic distribution. Taken collectively, these findings demonstrate that perceptual learning allows the auditory pathway to be shaped by the very experiences it gathers. The significance of this for day-to-day hearing is yet to be fully established, but its importance to auditory rehabilitation is discussed later.

Hearing loss and plasticity

When an ear is deafened, there is a cascade of changes in the auditory pathway. For example, animals in which IHCs were inactivated before the onset of hearing exhibited major changes in the auditory pathway: within days, 50-90% of cochlear nucleus neurones died[19] and there were substantial losses in the superior olivary complex[20]. Such degeneration has been linked to the loss of afferent activity in the auditory nerve[21], which may be clinically important given that electrical stimulation of the nerve has been shown to protect the developing auditory pathway from degeneration [22]. This is particularly relevant to tonotopic maps, which seem to initially develop without experience but which subsequently become plastic, requiring stimulation to be retained and refined[23].

The adult auditory pathway also exhibits neuroplasticity following hearing loss. If a specific region of an adult animal's cochlea is damaged, the resulting frequency-specific hearing loss causes the area of A1 representing it to reduce in size, while representations of the undamaged regions expand into it[24]. It has been suggested that this representational remapping could result in 'perceptual confusion'[2]. In humans, imaging studies have shown levels of auditory cortical activity decrease following a profound loss of hearing, and that the longer the duration of deafness, the lower the amount of activity recorded[25,26]. Furthermore, monaural deafness has been associated with increased activity in pathways emanating from the normal-hearing ear, suggesting that plasticity of spatial hearing mechanisms affords a degree of compensation[27].

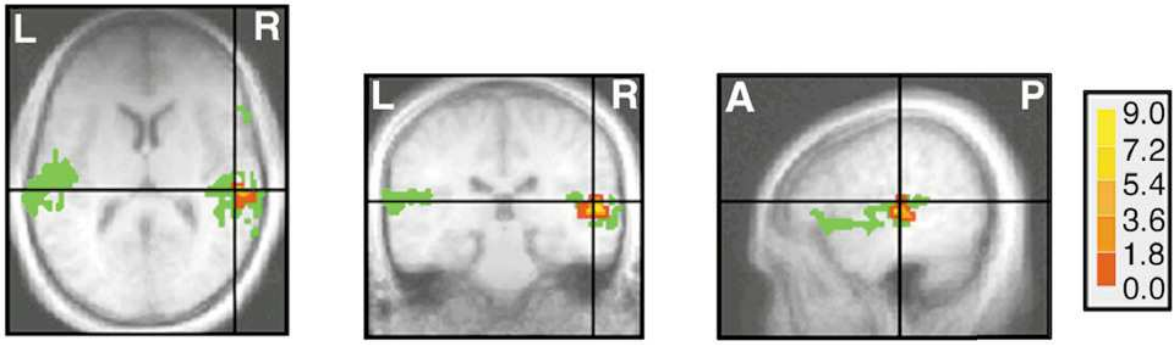

Figure 5. Visual stimuli activating the auditory cortex of deaf subjects. Anatomical scans (axial, coronal and sagittal) are shown averaged across all deaf and hearing subjects. Scale bar shows functional intensity value. Reproduced from Finney *et al*.[31]

Cross-modal plasticity

Cross-modal plasticity is a particular kind of plasticity that involves neural reorganisation *between* senses following sensory deprivation. In these instances, there is a reduction in the neural representation of the deprived sense which is mirrored by increased representation of intact senses[28]. This form of plasticity is important to the auditory pathway, particularly early in development. For example, individuals born blind show greater connectivity between their visual and auditory cortices[29], resulting in auditory processing being distributed between the two systems[30]. This increased representation is thought to underlie the enhanced auditory abilities of the blind, such as their improved identification of speech sounds[29].

Cross-modal plasticity is similarly important to the deaf. fMRI studies have shown that the auditory cortex of a congenitally deaf individual is partially taken over by visual representations[31] (see figure 5). However, some aspects of language processing are retained in A1: an fMRI study found that totally deaf subjects had activation in both their visual and auditory cortices when they observed sign language[32].

The reallocation of neural resources described here is greatest, and potentially irreversible, during early periods of development when high levels of neuroplasticity mean that more gross remapping can occur. This has major implications for the age at which cochlear implants (CIs) are optimally implanted.

Cochlear implants: plasticity and age at implantation

CIs are surgically implanted electronic prostheses that directly stimulate the auditory nerve[23]. They have provided hearing to more than 120,000 deaf people[23], but they do not work well in all patients. They are most successful in two groups: post-lingually deaf individuals and pre-lingually deaf individuals implanted at a young age[23]. Individuals with pre-lingual deafness implanted in later life enjoy improved sound awareness and lip-reading[23], but are usually incapable of understanding speech[33]. This dichotomy is thought to reflect the developing brain's greater plasticity, which in turn has a number of consequences.

First, it governs the extent to which the auditory pathway is shaped by cross-modal plasticity. If individuals with pre-lingual deafness are implanted early in life, the auditory input from the CI supports development of the auditory pathway and prevents significant cross-modal remapping, eventually enabling them to use the CI input to recognise speech[34]. In contrast, individuals implanted later have no auditory input to suppress substantial cross-modal plasticity, so benefit much less[23]. Second, up to 15 years of learning is required to establish

the complex pattern-recognition needed to perceive speech, especially if the input is distorted, as it is in CIs[35]. Pre-lingually deaf individuals implanted later in life have to acquire this pattern-recognition when neuroplasticity is lower and learning is consequently harder and less successful[23].

In order to avoid cross-modal plasticity irrevocably shaping the auditory pathway and to take advantage of the ease with which young children learn, it is important that people with pre-lingual deafness are implanted as young as is feasible. It is thought that there is a critical period ending around 3.5 years-of-age during which the auditory pathway is maximally sensitive[36], so ideally implants should be in place by this age, if not younger[37].

In comparison, no such urgency exists for post-lingually deaf people. By the time language has been acquired, the plasticity of the developing auditory pathway has diminished, so subsequent deafness only results in limited cross-modal change[38]. Furthermore, these individuals will have had their childhood to acquire the pattern recognition needed to recognise speech, so are better able to make use of the impoverished CI input[23]. Indeed, the performance of post-lingually deaf people implanted later in life is comparable to younger recipients[39], demonstrating the adult auditory pathway's capacity to undergo neuroplastic change[40].

Harnessing plasticity to improve auditory rehabilitation

Recent evidence suggests that plasticity induced by perceptual learning could improve rehabilitation of people with hearing aids[41] and CIs[42]. In the latter, auditory training using speech-based stimuli led to improvements in speech perception for all CI users, regardless of the age at implantation. Unfortunately, the sample size was small, but further support comes from studies showing that auditory training improves normal-hearing listeners' ability to recognise 'vocoded speech'[43,44,45]. While some argue that vocoded speech-perception in normal-listeners replicates CI performance quite well[46], it remains unclear whether it provides a good model for CI-users response to training[23]. Nevertheless, these studies suggest that 'harnessing plasticity' via perceptual learning may help CI-users to make better use of the input derived from their implants.

Discussion

The high level of neuroplasticity during early development can be viewed as a 'mixed blessing.' Among other things, it allows our auditory pathway to tune itself to our environment[4], compensate for our growth[5], even support learning of our native language[13]. Conversely, it means that early disruption has the potential to radically impair auditory pathway development[19,20] which, owing to critical periods, cannot be undone[8]. Luckily, the early implantation of CIs attests to how such plasticity may be turned to our advantage[23].

While greater stability of the adult pathway seems desirable[3], residual plasticity appears to underlie adults' perceptual learning[16,17,18], which is highly relevant to programmes aimed at maximising the benefits of hearing aids[41] and CIs[42,43,44,45]. Adult plasticity may also be a benefit when it follows unilateral deafness by affording a degree of compensation[27]. However, the representational remapping occurring after frequency-specific hearing loss[24] may be detrimental, with some suggesting it causes 'perceptual confusion'[2].

There are more examples of plasticity than could be discussed here, such as its possible role in tinnitus[47], or its importance to new hearing prostheses[23]. However, the examples cited have hopefully demonstrated that plasticity is relevant to every stage of the auditory pathway's development, from infancy into adulthood, in both health and disease.

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