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Cochlear Implants and Brain Plasticity

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Abstract

Cochlear implants have been implanted in over 110,000 deaf adults and children worldwide and provide these patients with important auditory cues necessary for auditory awareness and speech perception via electrical stimulation of the auditory nerve (AN). In 1942 Woolsey & Walzl presented the first report of cortical responses to localised electrical stimulation of different sectors of the AN in normal hearing cats, and established the cochleotopic organization of the projections to primary auditory cortex. Subsequently, individual cortical neurons in normal hearing animals have been shown to have well characterized input-output functions for electrical stimulation and decreasing response latencies with increasing stimulus strength. However, the central auditory system is not immutable, and has a remarkable capacity for plastic change, even into adulthood, as a result of changes in afferent input. This capacity for change is likely to contribute to the ongoing clinical improvements observed in speech perception for cochlear implant users. This review examines the evidence for changes of the response properties of neurons in, and consequently the functional organization of, the central auditory system produced by chronic, behaviourally relevant, electrical stimulation of the AN in profoundly deaf humans and animals.

Keywords

Electrical Stimulation; Auditory Cortex; Plasticity; Cochleotopy; Reorganisation

Introduction

Worldwide, over 110,000 deaf adult and children benefit from direct electrical stimulation of their AN via a cochlear implant. Implant recipients exhibit a wide range of speech perception skills with a range of factors identified as affecting clinical performance (Blamey et al., 1996). The level of performance of pre-linguistically deaf adults generally remains well below that of post-linguistically deaf adults (Busby et al., 1999; Busby et al., 1993; Eddington et al., 1978). It is remarkable that the best patients can exhibit near-normal open-set speech perception, at least in a quiet environment, given the abnormal (and in many ways impoverished) input provided by these devices. The importance of auditory experience in the clinical performance of cochlear implant users has been consistently emphasized (Blamey et al., 1996; Gantz et al., 1993; Rubinstein et al., 1999). Clearly, changes within the auditory

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system underlie some of the improvements in speech perception seen in implant patients with device use, although it has not been established whether the improvements are mediated by changes in auditory cortex *per se*.

The capacity for plasticity in the response properties of neurons in, and consequently the functional organization of, cortical and sub-cortical sensory structures was generally believed to be maximal within 'critical periods' during early development (Hensch, 2004). It was believed that changes in experience during these early periods - when neuronal pathways and connections were being formed - but not later in life could drive changes in sensory processing mechanisms. However, the capacity for plasticity in adult sensory systems, given appropriate patterns of behaviourally significant input, has more recently become generally accepted (for review see Kaas et al., 2001) and confirmed in the auditory system (for reviews see Irvine, 2007; Weinberger, 2007).

The effects of restrictions in output from the cochlea, in both immature and adult animals, on the tonotopic organisation (for review see Irvine et al., 2005) and the temporal processing ability (Bao et al., 2004), of the thalamo-cortical auditory system have been well characterised. Less well studied are the effects of chronic, behaviourally relevant, electrical stimulation of the AN - similar to that used in cochlear implants - on cochleotopic organisation and temporal processing.

Complicating the interpretation of plasticity in the auditory cortex produced by such stimulation is that there are many changes consequent on a sensorineural hearing loss that almost invariably precede the chronic stimulation (for review see Shepherd et al., 2006). These changes include: significant reduction in spiral ganglion neurons; de-myelination of residual spiral ganglion neuron soma and possibly part of their central processes; shrinkage of the perikaryon of neurons throughout the auditory pathway; and reduced spontaneous activity throughout the auditory pathway. As many of the changes associated with sensorineural hearing loss are 'down-stream' from the cortex in the auditory pathway, they affect the input, and the organization of that input, into the auditory cortex. This problem of interpretation due to down-stream changes is equally true of changes associated with chronic stimulation.

It is also important to note that not all changes in neural responsiveness and organization are necessarily plastic in nature, as some changes can be explained as passive consequences of the altered input. For example, the frequency tuning of AN fibres, and consequently of neurons throughout the auditory pathway, is immediately altered after destruction of the outer hair cells (Dallos et al., 1978). It is also not always a simple matter to distinguish between plastic and non-plastic changes (Calford, 2002; Irvine et al., 2005). However, we will define plasticity as involving some form of active or dynamic modification of neural properties resulting from the altered input.

This paper will review the evidence of plastic changes in the central auditory system resulting from chronic electrical stimulation of the AN, with an emphasis on behaviourally relevant stimulation. First, evidence from animal studies focussing on the response properties of neurons in, and the functional organization of, the primary auditory cortex (AI) will be reviewed. Second, electrophysiological and functional imaging studies of the auditory cortex in cochlear implant patients will be reviewed. Finally, the relationship between the reported changes in the auditory cortex and psychophysical studies of both pitch and speech perception will be discussed.

Animal Studies

Basic Response Properties

Individual neurons within layer III/IV of AI of normal hearing (or acutely deafened) cats have well characterized input-output functions for electrical stimulation (Hartmann et al., 1997; Popelar et al., 1995; Raggio et al., 2003; Schreiner et al., 1996). Neurons exhibit either monotonic (~55%) or non-monotonic input-output functions, with dynamic ranges of approximately 10 dB, and minimum first spike latencies of around 8 ms. Cortical field potentials exhibit both a short- (< 80 ms) and long- (~ 150 ms) latency response (Hartmann et al., 1997; Popelar et al., 1995). The long-latency responses are thought to be mediated by corticothalamic loops, and are proposed to be essential for short-term memory and processing in higher-order auditory centres (Klinke et al., 1999).

A short period of profound deafness (~2 weeks) in an adult animal, results in a decrease in absolute threshold and an increase in dynamic range of neurons in AI (Raggio et al., 1999). Longer periods of deafness, including the early developmental period, result in little additional change to absolute threshold or dynamic range (Hartmann et al., 1997; Raggio et al., 1999). Cortical field potentials in congenitally deaf cats are reduced in size and exhibit only a middle-latency response, with no long-latency responses evident (Klinke et al., 1999; Klinke et al., 2001). There are no reports of changes in the temporal processing ability of AI neurons (i.e. changes in minimum latency, response jitter and maximum following rate). This is puzzling, given the occurrence of significant down-stream changes, including a decrease in the temporal processing ability of the inferior colliculus (IC), viz., increases in both the minimum latency and response jitter, and a decrease in the maximum following rate of individual neurons (Shepherd et al., 1999; Snyder et al., 1995). There are pronounced changes in current sinks (and therefore presumably synaptic currents) in different layers within AI, with a decrease in current sinks at long (>30ms) latencies in layers II, III and IV and a decrease in the deeper (infragranular) layers IV, V and VI at all latencies (Kral et al., 2000; Kral et al., 2001).

Evidence for cross-modal plasticity as a consequence of congenital deafness is equivocal. Although Rebillard et al. (1980) described invasion of AI by visual input, others have reported no evidence of visual responses in AI of congenitally deaf cats (Kral et al., 2003; Stewart et al., 1970).

Chronic, behaviourally relevant, electrical stimulation of the AN delivered from an early age results in significant changes in the response properties of neurons in AI compared to unstimulated deaf controls (Kral et al., 2006a). While there are no studies that have reported a systematic examination of stimulation-induced changes in single- or multi-unit threshold or dynamic range, cortical field potentials in stimulated animals are similar to those in normal-hearing animals (Klinke et al., 2001). That is, there is an increase in the amplitude of the field potentials compared to deaf controls, and the potentials comprise both middle- and long-latency components. Chronic stimulation also results in more sustained single- and multi-unit activity than in unstimulated deaf controls (Klinke et al., 1999). A preliminary report indicates that chronic stimulation results in a increase in first spike latency and an increase in the maximum following rate of neurons in AI compared to deaf controls (Fallon et al., 2007b). It is difficult to determine if these changes can be interpreted as indicative of an increase or decrease in temporal processing: the increase in first spike latency suggests a decrease in temporal processing, whereas the increase in maximum following rate indicates improved temporal processing. In contrast, chronic stimulation (albeit not behaviourally relevant) results in a significant down-stream increase in temporal processing (decreased minimum latency and response jitter and increased maximum following frequency) in the IC (Snyder et al., 1995; Vollmer et al., 2005; Vollmer et al., 1999). Interestingly, the temporal processing of electrical stimuli in the IC of chronically stimulated animals is superior to that in normal hearing animals.

Finally, chronic stimulation results in larger current source densities, resembling those in normal hearing animals (particularly in layers II & III Klinke et al., 1999), although these are diminished with increasing delays in the initiation of the chronic stimulation.

There is a critical period for the reintroduction of auditory input into the deafened auditory system, during which changes can be driven simply by 'passive' experience. During this period neural activity and developmental cues may interact to effect the production of a range of neurotrophic factors important for dendritic growth and synaptic formation (for review see Kral et al., 2006b).

These results suggest that chronic, behaviourally relevant, electrical stimulation of the AN allows an experience-dependent maturation of the basic response properties of individual neurons within AI, albeit not exactly as would have occurred in a normal hearing animal.

Cochleotopic Organisation

In normal hearing (and acutely deafened) animals, AI exhibits a functional cochleotopic organization to restricted electrical stimulation of the AN (Woolsey et al., 1942). This cochleotopic organization of AI along a predominantly caudal-rostral axis is the corollary of the well studied tonotopic organization to acoustic stimulation. In normal hearing cats, one millimetre of shift along the basilar membrane corresponds to an approximately 1.82-mm shift along the caudal-rostral axis (Raggio et al., 1999). Single biphasic pulses delivered at 6 dB above threshold result in the activation of a 2-mm wide dorso-ventral strip of AI (Raggio et al., 1999), which can be divided into dorsal and ventral zones, separated by a high threshold ridge. The area of cortex activated by a given stimulus changes during maturation, being largest one to two months after birth, and reaching adult-like levels around 4 months of age (Kral et al., 2005).

A short period of profound deafness (~2 weeks) in an adult animal, results in a degradation of the normal cochleotopic organization (Raggio et al., 1999). Specifically, for a given stimulus, there is an increase in the area of cortex activated, primarily in the caudal-rostral extent. That is, rather than a stimulus 6 dB above threshold activating a 2-mm wide dorso-lateral strip, it now activates a 3- to 4-mm wide strip. However, cochleotopicity, as defined by the relative cortical locations of minimum threshold for each cochlear stimulating electrode, is maintained (i.e. a shift of one millimetre along the basilar membrane corresponds to an approximately 1.82 mm shift along the caudal-rostral axis of AI). The combined result of these two changes is an increase in overlap between adjacent basilar membrane representations. The effects of longer periods of deafness, including the early developmental period, appear to be influenced by aetiology. Specifically, congenitally deaf cats are reported to maintain a rudimentary mapping of cochlea to cortical location (Hartmann et al., 1997; Klinke et al., 1999; Kral et al., 2001; Kral et al., 2002). Congenitally deaf cats also demonstrate a delay in the maturation of cortical activation area, with cortical activation being largest approximately two months later than in normal-hearing animals, but achieving near normal adult levels (Kral et al., 2005). In contrast, neonatal deafening results not only in a similar spread of cortical activation as short-term deafness (i.e. a 6 dB supra-threshold stimulus activates a 3- to 4-mm wide dorso-lateral strip), but also in a complete or near-complete loss of the orderly mapping of cochlea location to cortical location (Fallon et al., 2007a; Raggio et al., 1999). Using optical imaging techniques, Dinse et al. (2003; 1997a) also reported a disintegration of the normal map, with the emergence of isolated islands or patches of activity in response to stimulation of a given electrode. The loss of cochleotopy in AI is in contrast to the electrophysiological evidence from lower centres, most notably the IC, in which a near-normal cochleotopic organisation is maintained even after extended periods of deafness (Leake et al., 2000; Moore et al., 2002; Shepherd et al., 1999; Snyder et al., 1990).

Chronic, behaviourally relevant, electrical stimulation of a single sector of the AN delivered from an early age results in an expansion of the activated cortical area compared to unstimulated deaf controls (Klinke et al., 1999; Kral et al., 2001; Kral et al., 2002). The degree of expansion was related to the duration of electrical stimulation (Klinke et al., 2001; Kral et al., 2006a), with longer periods of electrical stimulation resulting in more cortical expansion, provided animals were implanted before approximately six months of age. There are few reports of the effects of chronic stimulation of multiple auditory nerve sectors on the cochlea-to-cortex mapping, but preliminary findings confirm an expansion in activated area superimposed on a relatively normal cochleotopy (Fallon et al., 2007a). The expansion in total activation area seen using electrophysiological techniques has also been reported in an optical imaging study (Dinse et al., 2003; Dinse et al., 1997a), but the expansion was of a very different sort. The large cortical territories activated by a single electrode were massively overlapping, such that there was “a profound reduction of representational selectivity”, in contrast to the near-normal cochleotopy seen by Fallon et al. (2007a). The electrophysiologically described effects of chronic stimulation on the organisation of AI are similar in some respects to the down-stream changes, particularly those at the level of the IC. Specifically, chronic stimulation (albeit not behaviourally relevant) of a single restricted sector of the cochlear results in an expanded representation of that area in both immature (Snyder et al., 1990) and mature (Moore et al., 2002) animals. However, competing inputs, achieved by non-simultaneous stimulation of two distinct sectors of the cochlea, were shown to maintain - or even sharpen - the selectivity of representations of those sectors in the IC (Leake et al., 2000). In contrast, simultaneous stimulation of two cochlear sectors resulted in a marked expansion, fusing the representation of the two sectors (Leake et al., 2000). The effects of different stimulation regimes on the cochleotopic organisation of IC may partly explain the different effects of chronic stimulation in AI reported in the electrophysiological and optical imaging studies, as they also used different stimulation regimes. In particular, Dinse et al (2003) used a stimulation strategy in which all electrodes were stimulated near-simultaneously. It is also possible that the different effects reflect differences in the laminar location of the activity recorded by the two techniques: the electrophysiological data are predominantly from the middle cortical layers, and thus reflect thalamo-cortical input, whereas the optical imaging recordings predominantly reflect activity in the superficial cortical layers.

These results suggest that chronic, behaviourally relevant, electrical stimulation of the AN, capable of resulting in significant changes to the cochleotopic organisation of the auditory midbrain, can also effect the cochleotopic organisation of AI (see Figure 1). All studies have reported an expansion in the total activation area, but there are conflicting reports on the underlying cochlear to cortical mapping (see Figure 1), which may relate to the precise nature of the stimulation.

Clinical Studies

Electrophysiology

Evidence from clinical studies of the P1 evoked cortical potential indicates that there is a sensitive period, ending around 3.5 years of age, during which the human central auditory pathway is maximally plastic (Eggermont et al., 2003; Ponton et al., 2001; Ponton et al., 1996; Sharma et al., 2002). Children who receive effective cochlear stimulation within this period develop electrically evoked cortical potentials with latencies (~ 100 ms) that reach those of aged-matched normal-hearing children within 6 months of the onset of stimulation (Sharma et al., 2005a). The recorded potentials suggest near-normal maturation of middle (IV & deep III) cortical layers, but there continues to be altered maturation or input to the superficial (II, upper III) layers (Ponton et al., 2001). In contrast, genetically deaf children implanted after 7 years of age exhibit incomplete maturation of their electrically evoked cortical potentials, including latencies that are always longer than aged-matched controls, leading to the suggestion

that the latency of this cortical evoked potential could be a useful diagnostic tool for determining the development of the auditory system (Sharma et al., 2006; Sharma et al., 2005b). It is worth noting the P1 response is generated by both auditory thalamic and cortical sources (Sharma et al., 2005a).

Imaging

Modern imaging techniques for measuring brain activity in humans have also provided evidence for plasticity of the central auditory pathway following a profound hearing loss (Berthezene et al., 1997; Giraud et al., 2001; Hari et al., 1988; Herzog et al., 1991; Ito, 1993; Ito et al., 1993; Lazeyras et al., 2002; Nishimura et al., 2000; Okazawa et al., 1996; Pelizzone et al., 1986). Collectively, these studies report low levels of auditory cortical activity among profoundly deaf subjects - the longer the duration of deafness, the lower the level of activity recorded. Additionally, it appears that the auditory cortex can be activated by other sensory modalities, although the 'take over' of auditory areas appears to be limited to secondary auditory areas (supratemporal gyrus / perisylvian region) normally used for auditory processing and language (Hickok et al., 1997; Nishimura et al., 1999; Petitto et al., 2000; Sadato et al., 2004). There is however, at least one report that has described the recruitment of primary auditory cortex in the profoundly deaf for processing purely visual stimuli (Finney et al., 2001), although the extent of the take-over was limited to a small region of only the right, but not the left, primary auditory cortex.

Following cochlear implantation, metabolic activity in primary auditory cortex is reported to increase to near normal levels, with greater activity on the side contralateral to the implant (Lazeyras et al., 2002), and the magnitude of the increase appears to be correlated with the performance of the implant patient (Green et al., 2005; Lee et al., 2007). Interestingly, the activity in 'higher-order' auditory centres of prelingual deaf patients is reported to decrease with cochlear implant experience (Lee et al., 2001), and to be lower in these patients than in postlingual deaf implant patients (Naito et al., 1997). Clearly, it is auditory experience that drives the functional specialisation in auditory association areas (Giraud et al., 2001).

Pitch and Speech Perception

Normal electrode pitch perception – the ability to discriminate between stimulation on different electrodes and to rank the percepts in a manner consistent with a normal cochleotopic organization - is highly correlated with speech perception (Henry et al., 2000). Postlingually deaf implant patients exhibit normal pitch percepts (Cohen et al., 2001; Fu et al., 2002; Pfingst et al., 2001), with some patients even able to perceive 'virtual electrodes', created by pairing stimulating electrodes, between physical electrodes (Busby et al., 2005). An interesting recent observation is that in patients with some residual hearing, it is possible to create a mismatch between cochlear location and the perceived pitch (Reiss et al., 2007). Specifically, it is possible to assign any portion of the acoustic frequency spectrum as the driving signal for a particular intra-cochlear electrode. For some patients, particularly those with short intra-cochlear electrode arrays, their implants are programmed to deliver electrical stimulation derived from acoustic signals up to two octaves below those that would normally excite that cochlear region. After some years of device use, the electrode pitch percepts of these patients come to match the programmed frequencies, rather than those predicted on the basis of cochlear-position, suggesting top-down influences on the regions giving rise to the percept from areas in which knowledge of the frequency composition of the language is stored.

A universal finding is that word recognition scores in postlingually deaf implant patients are inversely correlated with the duration of deafness, and the ratio of duration of deafness to age of implantation has a negative impact on clinical performance (Blamey et al., 1996; Gantz et al., 1993; Govaerts et al., 2002; Kirk et al., 2002; Rubinstein et al., 1999; Sarant et al., 2001).

The performance of postlingually deaf patients implanted later in life does not differ significantly from younger recipients (Leung et al., 2005; Tyler et al., 1996), emphasising the capacity of the adult auditory system to undergo change. Finally, patients with residual hearing typically have better speech perception scores than profoundly deaf patients (Gantz et al., 2005; Kiefer et al., 2005), reflecting - in part - their greater auditory processing experience.

Although prelingually deaf patients, implanted as young adults, improve with implant use, they typically exhibit poor levels of speech perception (Busby et al., 1999; Busby et al., 1993; Dowell, 2002; Eddington et al., 1978). Their temporal processing skills, as assessed by rate and gap detection tasks, are poor (Busby et al., 1999; Busby et al., 1993) and they do not exhibit normal electrode pitch percepts (Busby et al., 2000; Busby et al., 1992; Eddington et al., 1978; Tong et al., 1988). However, if implanted early, a majority of congenitally deaf children obtain open-set speech perception after 2–3 years of implant use at levels comparable to postlingually deaf adults (Dowell, 2002). As with postlingually deafened adults, auditory experience with cochlear implants is vital for good speech perception in children (Blamey et al., 2001; Dawson et al., 1992; Dowell, 2002; Fryauf-Bertschy et al., 1997; Osberger et al., 1991; Sarant et al., 2001; Waltzman et al., 1992). This is highlighted by children with a congenital hearing loss, who initially show poorer language development than children with an acquired hearing loss, but whose performance rapidly improves with device use (Dettman et al., 2007). Importantly, this improvement in communication skills begins to match that seen in normal development if the children receive a cochlear implant under 12 months of age (Dettman et al., 2007). Moreover, it is not surprising that family and educational environments emphasizing listening and speaking play a significant role in speech perception among paediatric cochlear implant subjects (Moog et al., 2003; Sarant et al., 2001).

A final interesting observation is that there is a positive correlation between low resting metabolic activity in the AI prior to cochlear implantation and post-implantation speech perception scores for the prelingual deaf (Lee et al., 2001; Lee et al., 2007). This suggests that while both the AI and other higher-order auditory centres are capable of plastic change, the best clinical outcomes for cochlear implant patients may in fact occur with the most immature auditory cortex, or the ‘cleanest sheet’.

Collectively, studies of clinical performance in adult implant subjects consistently emphasize the negative influence of duration of deafness and the positive influence of auditory experience on speech perception, and suggest that there is a critical period within which auditory cortical structures important for language development must receive appropriate input. However, it is important to emphasize that these factors only account for ~20% of the variance in the clinical data (Blamey et al., 1996); there remain other factors, as yet unidentified, that significantly contribute to clinical performance among implant subjects.

Conclusion

A growing body of functional imaging and psychophysical studies in humans and predominantly neurophysiological studies in animals is providing further evidence for plasticity in the central auditory pathway. It is clear that genetic cues are sufficient to generate a basic framework, with the development of at least a rudimentary pathway in the absence of any auditory experience, which is sufficient to provide both the temporal and spatial cues necessary for speech perception using a cochlear implant. However, auditory experience plays a key role in moulding the fine organisational structure of the central auditory system, and there is no doubt this plasticity contributes to the remarkable success of many cochlear implant subjects in achieving near-normal speech perception despite the abnormal (and in many ways impoverished) input provided by the prosthesis.

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Abbreviations

AI, primary auditory cortex; AN, auditory nerve; IC, inferior colliculus.

Figure 1.

Schematic representations of the cochleotopic organisation of the inferior colliculus (middle) and primary auditory cortex (right) in normal hearing animals (top row), congenitally deaf unstimulated animals (second row), neonatally deafened unstimulated animals (third row) and chronically-deaf chronically-stimulated animals (bottom row). The different results obtained with different recording techniques (optical imaging or electrophysiological) are illustrated.