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Imaging Plasticity in Cochlear Implant Patients

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Key Words

Brain imaging · PET · MRI · Language · Cross-modal plasticity

Abstract

Auditory re-afferentation by cochlear implants (CI) offers a unique opportunity to study directly from within the auditory modality plastic changes taking place at organisational levels up to the supra- or polymodal level. These plastic changes resulting from deafness and chronic electrical stimulation can be studied using modern neuroimaging techniques. In this paper, we review the available techniques and the experimental approaches to human studies of plasticity, we discuss the different forms of plasticity that are associated with cochlear implantation and we point to the interest of imaging studies for providing a prognosis of functional outcome after implantation.

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Introduction

By restoring auditory input to the brain, cochlear implants (CIs) induce changes in cerebral function that affect neural structures ranging from cochlear nuclei [Lustig et al., 1994] to extra-auditory cortical territories [Giraud et al., 2001a, b], and that involve all levels of neural

organisation from intracellular components [Nagase et al., 2000] to large-scale cortical networks [Naito et al., 2000]. Depending on whether subjects have acquired auditory language prior to deafness or not, implantation corresponds to the discovery of a new sensory modality that minimally interferes with language, or to the restoration of a sense that is essential for communication. The use the brain makes of an implant and, in particular its integration as a communication tool, therefore can differ considerably according to the patient's individual history, and these differences are associated with different neural changes. By restoring or installing hearing, CIs also allow for investigations of the cerebral organisation resulting from deafness.

This paper reviews (i) the brain imaging techniques currently available for studies in implant patients, (ii) the experimental approaches that can be used and (iii) the different types of plasticity that auditory re-afferentation by implants induces and that can be studied in humans. Finally, (iv) we review the insights cochlear implantation has provided in the domain of human cortical plasticity.

Imaging Techniques in Implant Patients

Magnetic Resonance Imaging (MRI)

Functional magnetic resonance imaging (fMRI) is non-invasive and if optimised provides images of brain activity with a spatial resolution of less than 2 mm and a tempo-

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ral resolution in the subsecond range. This technique can be used for pre-surgical assessment of auditory pathway functionality up to the primary auditory cortex [Berthéze et al., 1997], and such measurements constitute a predictive factor for implantation outcome. These assessments are usually carried out using a non-magnetic electrode applied either transtympanically to the promontory or into the external auditory meatus [Hofmann et al., 1999]. The most recent stimulation setup uses the conversion of electrical signals into optical signals to drive an MRI-compatible current source [Obler et al., 1999].

Conventional CIs are not compatible with fMRI. This incompatibility is threefold: (1) high magnetic fields can damage electronic elements located within the skull and provoke local effects (heating, displacement of the device, etc.), (2) magnetisable elements induce artefacts in the images, and (3) stimulation by the implant during MRI is precluded. As MRI may be required for diagnostic purposes during a patient's life, implant companies are now developing MR-compatible devices that include no electronics in the implanted part. The safety of such devices in the MR scanner has been confirmed [Teissl et al., 1999; Weber et al., 1999]. However, recent studies conclude that even with such implants MRI should be used only for medical indications. Provided that post-implant structural MR scans are acquired safely, MRI could be used to study morphologic changes in the brain before and after implantation.

Preliminary reports also indicate the possibility of obtaining functional images with implants that have no implanted electronics [Eddington et al., 1999]. The magnitude of the currents induced during fMRI acquisition are in principle lower than the perceptual threshold of patients [Lazeyras et al., 2001], suggesting that fMRI can be performed without producing acoustic artefacts. fMRI is a promising future technique for examining implant patients, but currently remains technically demanding.

Positron and Single Photon Emission Tomography

Although inferior to fMRI in terms of temporospatial resolution, the most commonly used techniques for functional imaging in implant patients are positron emission tomography (PET) and single photon emission computed tomography (SPECT). These techniques are both safe for patients and implants and compatible with implant function during data acquisition. SPECT is less costly and easier to handle than PET, but the latter is quantitative and more specific and sensitive [Beverdorf et al., 1995]. It is therefore the technique of choice for studying plasticity in implant patients.

PET is used to measure the brain distribution of a radioactive tracer incorporated into a relevant biological ligand (water, glucose, etc.). The local concentration of a labelled ligand such as oxygen-15-labelled water changes as a function of local blood flow and metabolism that are driven by local synaptic activity. By computing and comparing the spatial distributions of activity during two physiological states, PET can detect changes in local ligand concentration and hence brain activity. The nature of the radioisotope-ligand complex determines the nature of the PET images acquired: images of brain metabolism are acquired with fluoro-deoxyglucose, and perfusion images with $H_2^{15}O$. Substances such as labelled water, with a rapid elimination (half-life 2.1 min), are preferable for the study of cerebral activation related to different categories of auditory stimuli because 10 min after an injection of $H_2^{15}O$, the amount of residual radioactivity is negligible and another scan can be taken after a new injection of tracer. Usually, a dozen successive scans with injections of approximately 9 mCi at a time are performed in 1.5 h. Under these conditions, duration of scanning and dose of radioactivity are compatible with the comfort and safety of the subject [Johnsrude et al., 2002].

As recently demonstrated in amputees [Capaday et al., 2000], neurotransmitter-specific ligands can be used for analyses of plasticity in the topographical distribution of synaptic receptors. For instance, changes in the distribution of GABA receptors after implantation, reflecting plasticity of cortical inhibitory mechanisms, could be assessed using ^{11}C -flumazenil.

Electro-/Magneto-Encephalography (EEG/MEG)

Although it is common to think of plasticity in terms of functional neuro-anatomical changes, the adaptation of the brain to new sensory conditions is also reflected in the time course of brain responses [Ponton et al., 1996]. The main disadvantage of PET is that it offers virtually no temporal resolution of relevance for functional studies. Stimulus-locked EEG averaging, i.e. auditory evoked potentials, provide a temporally accurate record of subcortical and cortical signals after an auditory stimulus. Recording of magnetic field changes by MEG is another available temporally resolving brain monitoring modality [Hari, 1997]. Reconstruction of the probable cortical sources of auditory evoked electrical/magnetic components is possible [Ponton et al., 2000] but localisation power remains far inferior to PET.

The time scale over which plastic changes are expected is an important criterion in the choice of an appropriate

technique. EEG/MEG are non-invasive and may therefore be used as often as required for correct sampling of plastic change. They are therefore preferred in follow-up studies requiring several successive assessments. PET is the best tool for identifying the neuro-anatomical substrate of plasticity. However, subjects are exposed to radioactivity and therefore the number of examinations is restricted (e.g., one per year), which may result in an undersampling of rapid cortical modifications. If more frequent sampling is preferred, the dose of radioactivity per session and therefore the number of observations have to be reduced.

Separate reviews in this volume report electrophysiological data in humans [Ponton et al., this vol.] and animals [Kral et al., this vol.]. The present paper concentrates on imaging findings in humans derived from PET studies.

Experimental Strategies for Functional Imaging Experiments

Plasticity refers to neural changes occurring over time and experience. Several experimental strategies have been used to study plasticity in CI patients.

The simplest strategy is the longitudinal approach where the same individual is examined repeatedly. As variability between subjects is higher than the variability within subjects across imaging sessions, follow-up studies are very good at detecting activation changes over time. However, changes in performance over time constitute the main confound of such studies. The effects associated with time not only reflect the neural changes that underlie an improvement of performance as a function of training with the implant, but also feedback effects resulting from increasing success in the task. A low-level task, e.g. a detection task, can help to maintain stable performance accuracy over sessions but does not ensure a constant reaction time. The effects detected in follow-up studies may also simply arise from habituation to the same protocol over sessions. Some confounds can be eliminated by studying differential changes that reflect plasticity-related effects while cancelling out global effects. For instance, non-specific habituation to the scanning procedure over sessions will affect all scanning sessions and conditions equally and should therefore be eliminated in comparisons between conditions.

The second experimental strategy is based on a cross-sectional approach where patients with varying characteristics are grouped according to the same timepoint rela-

tive to the neurobiological process under investigation. The effect of time is then studied by a comparison of groups at different time points. This approach is preferred when multiple sessions in the same subject are not possible, e.g., for studying changes that occur over a very long period of time. The main problem with this approach is that the subjects usually differ from each other in factors other than the factor of interest, i.e., time (duration of deafness or time elapsed since implantation). In particular, patients differ with respect to performance that is non-linearly related to time elapsed from implantation, but also with respect to other factors independent of time, e.g., number of electrodes, side of implantation, educational level, type of deafness, age at onset of deafness, etc.

A final approach consists in comparing brain responses in implant patients and control subjects, assuming that the differences in brain activation patterns reflect cortical reorganisation induced by deafness and subsequent implantation. As variations in brain activation are in general not interpretable unless performance is equated between subjects, this approach requires that both groups perform equally well during the scans. Ideally, performance should be identical both with respect to accuracy and reaction time. In reality, it is almost impossible to perfectly match groups with respect to both criteria. Accuracy is usually more demanding for patients than for controls and therefore reaction times are often longer. One solution is to train patients prior to scanning to obtain better homogeneity between patient and control groups, but such training may interfere with the natural evolution of plasticity. A correct match in performance to normal-hearing subjects can only be reached in some very good CI performers. This approach thus remains most useful in studies of postlingual deafness.

In summary, none of the approaches described is ideal, especially because they are all based on comparisons of brain activity patterns associated with heterogeneous performance (same patient over time, or different groups of subjects).

Analyses and Statistics

In follow-up studies, each subject constitutes his own control. With PET, simple contrasts of images sampled at different time points after implantation can reveal plastic changes. Direct contrasts, however, pick up only relative effects. For instance, a reduction of a deactivation appears identical to an increase in activation. A baseline condition can be helpful to distinguish between absolute

and relative effects. If several subjects with different individual characteristics (aetiology of deafness, duration of deafness pre-implantation, performance, etc.) are to be analysed, effects that are reproducible across subjects will selectively reveal time effects and eliminate interindividual variations.

Effects that are specific to CI patients relative to normal-hearing subjects can reveal cortical reorganisation resulting from deafness and subsequent implantation. In theory, inferences relevant to populations of such patients require experiments that are designed according to a random-effects model that requires a relatively large number of subjects per group [Friston et al., 1999]. In a random-effects model, the statistics are performed at the level of average parameter estimates for each condition thereby collapsing the variance associated with repetitions of a given condition across subjects in the sample. As it can be difficult to recruit many patients, a random-effects analysis may not always be possible. Alternative methods that permit the study of smaller groups of patients and avoid false positive results can be used. One method consists in using a fixed-effects analysis to detect any differences between the groups under study without generalisation to the patient population at large. Conservative statistical thresholds ($p < 0.05$, corrected for multiple comparisons or 0.001, uncorrected) are used and then the results are cross-checked with effects detected in single subjects at lower statistical thresholds (0.05, uncorrected). By considering only effects that are significant in the first analysis and detected in all of the patients and none of the controls at an identical threshold, this method safeguards against false positive findings (e.g., driven by 1 or a few subjects). It also protects against false negative results (weak but reproducible effects, e.g., effects coming from second-order contrasts, i.e. contrasts of contrasts) [Giraud et al., 2001a]. Another approach is to match each patient with 1 control subject, thereby creating pairs of single subjects, and to consider only effects that are systematically reproducible in each pair. A final approach consists in contrasting single patients against a population of normal subjects.

Interpreting Brain Activity Differences between Patients and Controls

Patient/control comparisons do not only raise issues of appropriate statistical analysis but also problems in the interpretation of results. In a recent paper [Giraud et al., 2001a], we distinguished three situations:

(1) Only one group activates a region. If a region is recruited by a given task in every control but none of the patients, the task can be performed without this region, provided that all patients were able to carry out the task. This would suggest that the activated region, albeit activated in controls, is not critical for the given task even in controls. This reasoning is not reversible between patient and control groups. If each patient activates a region that is *never* active in controls, then it has to be considered a *new* region that is specifically recruited by implant patients to carry out the task successfully.

(2) Patients and controls recruit the same regions under different task conditions, consistently in every subject of each group. This situation raises questions about the functional specialisation of the region. If a region is recruited in fewer experimental tasks in patients than in controls, we can conclude that it is more specialised in patients, but also that the region is not critical for those experimental tasks where it is activated in controls but not in patients. If a region is recruited in more experimental tasks in patients than in controls, we can only conclude that the region is less specialised in patients.

(3) A region is activated in one group more than in the other (statistically) but not consistently across all subjects of a group. In this case we conclude that the region contributes flexibly depending on task requirements and individual strategies and that it is not in general indispensable. This interpretation is equivalent for both patients and controls.

Imaging Plasticity in Humans: How Far Can We Get?

Brain imaging techniques are sensitive to differential changes in synaptic activity [see Poldrack, 2000, for review]. Therefore, they cannot (at least not directly) detect experience-dependent changes occurring at molecular and cellular levels, but can reveal those occurring at the level of cortical maps (e.g., spatial organisation of primary cortices) and at the systems level (e.g., plasticity in the organisation of the language system, or cross-modal plasticity). Recent fMRI studies performed in non-human primates at high magnetic field (4–9 T) suggest that cortical organisation can be imaged up to the columnar level [Menon et al., 1997; Duong et al., 2000]. Although these new methods may allow a study of organisational levels below that of cortical maps (e.g., intra-areal functional architecture), such high field studies have not yet been applied routinely to humans. The following paragraphs

are focussed on large-scale cortical changes associated with auditory deprivation and re-afferentation that occur at the cortical map and systems levels.

Deafness-Induced Plasticity

Sensory deprivation is known to cause plastic changes of brain function, especially during a critical period early in life [see Kral et al., 2001, this vol.]. Studying these effects directly requires stimulation of the deprived sensory modality. The sensory re-afferentation provided by CIs offers an opportunity to study the effects of preceding deafness on functional brain organisation.

Plasticity Associated with Prelingual Deafness

The absence of auditory input during the development of language is responsible for a number of differences that contrast patients with normal brain organisation and performance. These differences consist of:

(1) A takeover of the perisylvian region, that is normally dedicated to auditory and language processing, by other sensory modalities. In particular, sign language used by congenitally deaf adults activates not only visual areas but also bilateral supratemporal gyri [Nishimura et al., 1999; Petitto et al., 2000]. Unlike further connections to higher order auditory areas, connections from the cochlea to the primary auditory cortex develop irrespective of the presence of auditory input. Thus, cross-modal competition remains confined to secondary auditory and association areas and spares primary auditory regions [Nishimura et al., 2000]. The selective sparing of primary regions from takeover by other modalities can be deduced from the observation that the primary auditory cortex responds to noise and speech in prelingual CI adults [Herzog et al., 1991; Naito et al., 1997; Truy et al., 1995]. Persisting susceptibility of primary regions to potential auditory inputs allows prelingual patients to detect stimulation coming from an implant, but is insufficient for speech comprehension. The recruitment of auditory association areas by other cognitive processes, in particular by non-auditory language, is probably accompanied by an irreversible depression of connections from the primary auditory region. This idea is supported by a reduction of activation in secondary auditory and association language areas in response to speech in prelingual CI patients compared to normal and postlingual CI patients [Naito et al., 1997].

(2) An enhancement of visual performance associated with increased activation of areas related to vision. This is illustrated by experiments showing that congenitally deaf

people have shorter reaction times, larger evoked responses and recruit-specific visual areas (e.g., V5/V5a) more than normal-hearing subjects [Neville and Lawson, 1987a–c; Bavelier et al., 2000].

(3) A discrepancy between functional neuro-anatomical data and the sensation reported by patients in response to electrical stimulation of the auditory nerve. Despite relatively homogeneous results showing primary auditory cortex activation by implants, prelingual CI adults do not systematically experience electrical stimulation of the auditory nerve as an ‘auditory’ sensation. Auditory nerve stimulation can be associated with additional manifestations such as eye movements or somatosensory sensations [Ponton et al., 1993] probably due to excitation of other nerves located in the vicinity of the electrodes or perhaps due to the development of cross-modal connections. More surprisingly, some patients report no sensation despite significant cortical responses [Truy et al., 1995].

Plasticity Associated with Postlingual Deafness

A number of studies in humans and animals illustrate critical periods for both language and hearing development. If performed later, the efficiency of implantation for oral communication is compromised. In contrast to prelingual CI patients, those patients who lost hearing after the critical stages of language development show sound-induced responses after implantation that often extend to secondary auditory and association cortices, even very soon after implantation, i.e. before significant language rehabilitation [Naito et al., 1997; Okazawa et al., 1996].

We recently confirmed this observation. We studied the functional neuro-anatomy of the auditory system resulting from deafness in 4 postlingual CI patients. Early responses to sounds were obtained with PET in the 1st week after implant switch-on. All patients recruited primary and non-primary auditory cortices contralateral to the implant. The activation of non-primary auditory areas, however, was not specific and occurred in response to different sound categories (speech and noises) (fig. 1). This observation correlated with the inability of patients to distinguish speech from noises at that stage.

Non-specific cortical responses contralateral to auditory nerve stimulation are not very informative about deafness-induced plasticity, as similar responses persist after implantation in both pre- and postlingual CI patients [Naito et al., 1995]. Responses specifically associated with speech stimuli recorded very early after implantation reveal more about the impact of deafness on the organisation of the language system. Although secondary auditory

Fig. 1. In a postlingually deaf patient implanted on the left side, auditory cortex activation in response to speech and noise was contrasted with silent baseline (implant switch-on). The patient was scanned with PET 1 week after implant first switch-on and 1 year later. Activation of primary and non-primary auditory cortices is observed 1 week after implant switch-on. One year later, sound-related activation is focussed on the primary region. The non-primary regions have changed their functional specialisation during the 1st year post-implantation.

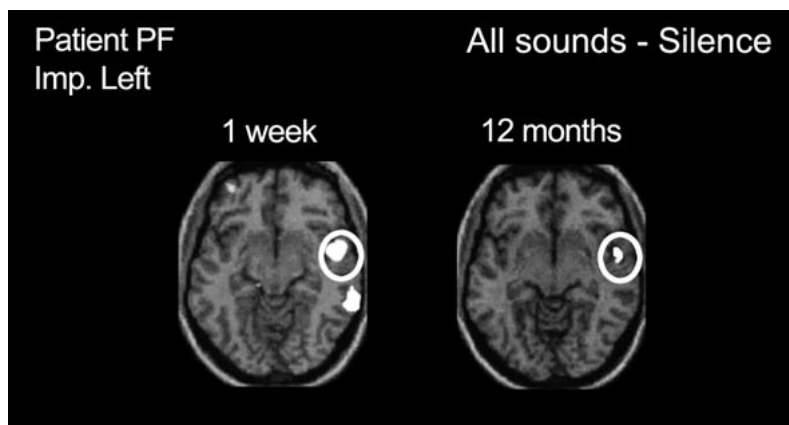
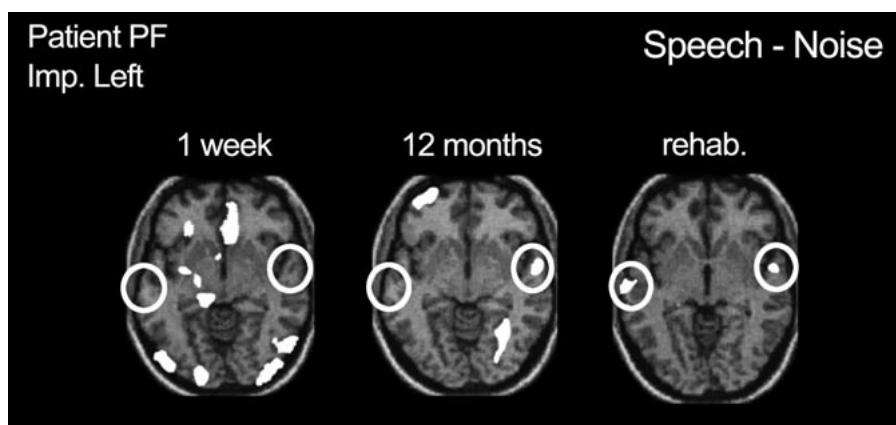


Fig. 2. Evolution of speech-related activation in the auditory cortex in the same patient as in figure 1. At 1 week, no brain region is specifically associated with speech. After 1 year, speech recruits the auditory cortex contralateral to implant. After complete rehabilitation, speech activates the classical superior temporal speech regions of the left hemisphere.



and association areas can be recruited by sounds even after a long period of deafness, their specificity is profoundly altered. Response patterns undergo major reorganisation in the months following implantation.

Plasticity Subsequent to Implantation

Recent imaging studies show that cortical reorganisation can be observed in adults after implantation [Suarez et al., 1999]. These studies were mostly conducted in implanted postlingually deaf adults, as prelingual deaf adults are no longer implanted and children cannot undergo scanning with radioactive tracers. We review here the principal findings in a hierarchical way, from the cortical map level to the cross-modal level.

Reorganisation of the Primary Auditory Cortex

Reorganisation of the primary auditory region has mostly been studied in animals. We recently sought to

assess the plastic changes occurring in this region during the 1st year post-implantation. We carried out a PET study where we compared the cerebral blood flow at rest and in response to speech and noises in 4 postlingual CI patients during the 1st week after the implant switch-on and after 1 year of daily practice with implant. We consistently observed less activation in the primary region in response to noises relative to a silent baseline condition after 1 year. At this time point we also noted a reduction of the number of activated clusters in the whole brain and activation was limited to the primary auditory region. These effects are shown in 1 patient (fig. 1). Similar reductions of activation have been observed during learning. They were associated with increase in strength of the connectivity between regions implicated in the learning process [Buechel et al., 1999]. Improvement of synaptic efficiency in association with reduction of attentional effort may account for these observations.

These results are not in contradiction with the enlargement of cortical regions stimulated by implants, with

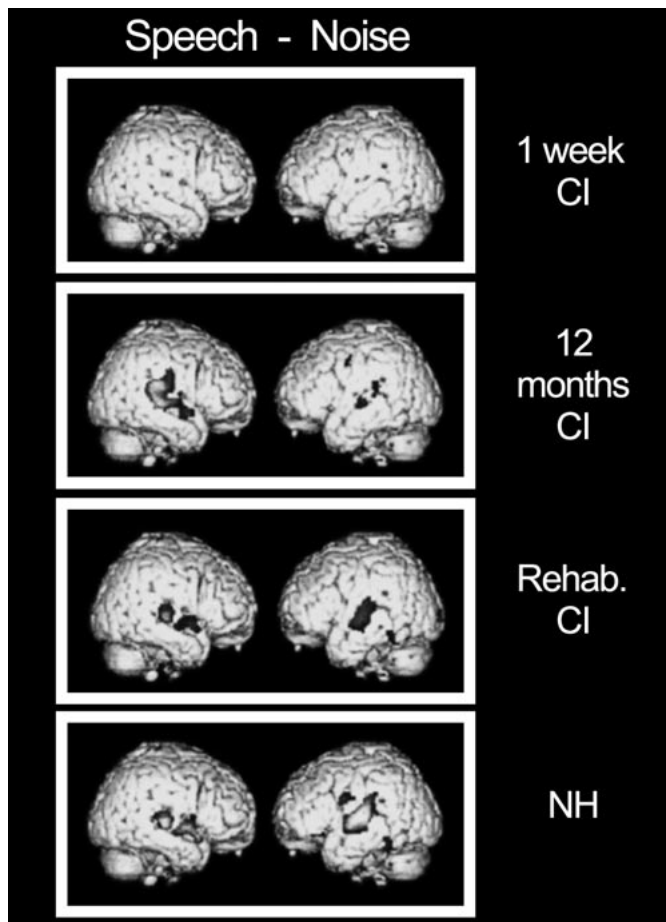


Fig. 3. Cerebral activation with PET in groups of 4 postlingual CI patients tested at different stages of the rehabilitation process. The same 4 patients were tested during the 1st week after the implant switch-on and a year later. A group of 6 other patients were tested, with an identical protocol, after complete rehabilitation (Rehab. CI). The response patterns can be compared with those obtained in a group of 6 normal-hearing subjects (NH). Several days of practice with implant speech does not produce specific cortical activation when contrasted with noises. After 1 year of practice, speech specifically involves perisylvian regions, mostly in the right hemisphere (2/4 patients were implanted on the left). In rehabilitated patients, the cortical pattern associated with speech is similar to normal, in particular with a restoration of the implication of the left hemisphere.

spreading into neighbouring regions, as observed in animals [Klinke et al., 1999]. Enlargements result from the absence of concurrent stimulation when using single-channel stimulation in congenitally deaf animals. With multichannel implants in postlingual CI patients, the situation is closer to physiological conditions. Competition for cortical space can occur within the primary auditory

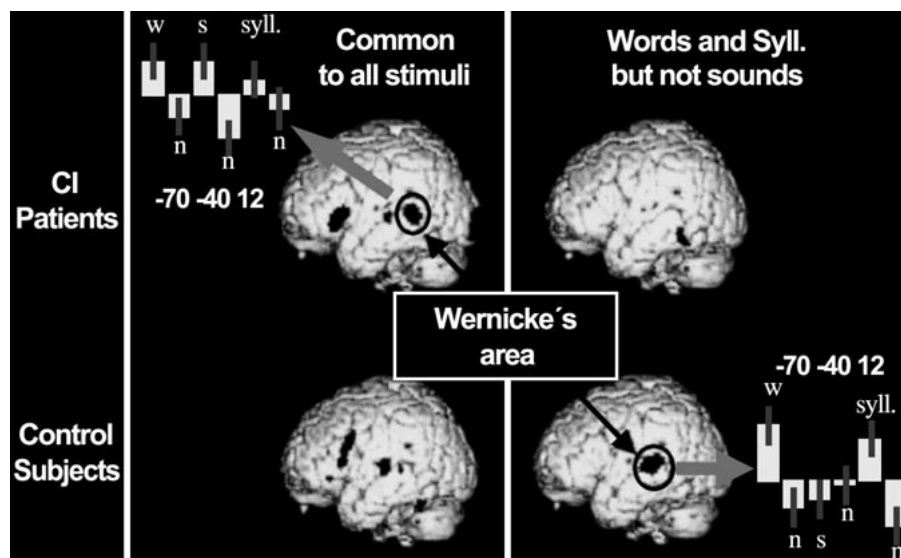
cortex due to concurrent stimulation from neighbouring electrodes. Regulation can also occur across auditory areas, as the activation produced by the implant extends to secondary and association areas. Differences in activation level of auditory association cortices arising from the implant coding strategy may additionally influence the regulation across cortical areas [Fujiki et al., 1998].

Reorganisation of the Speech Perception System

Many studies have described cerebral activation patterns in response to speech in postlingual CI patients. Very few of them, however, have shown response patterns specific to speech (relative to other sounds) and the evolution of these patterns over time after implantation. As mentioned above, we carried out a longitudinal study and observed that very soon after implantation words (contrasted with silence) were processed mostly by the contralateral association auditory cortex whatever the side of implant, and there was no specific response to words. After a year of practice with the implant, activation specific to words (words > noises) appeared in each of the 4 patients and progressively involved the classical left language regions. Yet, a clear left-sided activation in response to the same stimuli was observed only after rehabilitation, in patients with very good performance. Their activation pattern was very similar to that of normal-hearing subjects scanned under similar conditions, though more bilateral [unpublished data] (fig. 2, 3).

The usefulness of longitudinal studies to study plasticity in the speech perception system is limited by patients' speech performance after 1 year. In this context, the cross-sectional approach may be more appropriate. In a cross-sectional study involving post- and prelingual CI patients, Naito et al. [1997] did not observe a significant correlation between the relative increase in regional cerebral blood flow in left auditory association areas (BA 21/22) in response to speech and the duration of practice with an implant. This negative finding illustrates the fact that to investigate the full range of adaptive plasticity, experimental designs must go beyond mapping and address in detail the stimulus-response functions in areas where plastic changes are expected by contrasting specific experimental conditions. When contrasting meaningful sounds (words, syllables and environmental sounds) with noises, we recently observed in BA 21/22 in postlingual patients a significant correlation with duration of implant utilisation [Giraud et al., 2001b]. These observations converge to suggest that the speech perception system progressively learns to differentiate meaningful sounds from noises and that it probably does so by progressively reducing the

Fig. 4. Wernicke's area (circle) has a finer functional specialisation in normal-hearing subjects than in rehabilitated postlingual CI patients. This region is only recruited by speech in controls (w = words, syll. = syllables), but also responds to environmental sounds (s) in CI patients [adapted from Giraud et al., 2001a].



entry of irrelevant inputs evoked by meaningless noises into the language system.

In the same line of studies, we have further explored the functional response properties of language-specific cortical regions and their plasticity. We demonstrated that Wernicke's area had broader response properties in rehabilitated postlingual implant patients than in normal-hearing controls [Giraud et al., 2001a] (fig. 4). Several studies had previously shown that Wernicke's area was activated in post- and even prelingual CI patients in response to speech [Okazawa et al., 1996; Naito et al., 1997]. However, the specificity of the response was not clear. We found that Wernicke's area responded selectively to words and syllables but not to environmental sounds and noises in controls [Giraud and Price, 2001], whereas in patients there were also responses to non-verbal meaningful sounds (environmental sounds). This suggests that the functional response properties of Wernicke's area are modified in rehabilitated postlingual implant adults.

In sum, our studies suggest that deafness induces a loss of functional specialisation in auditory association areas. This process can be reversed by implantation. Some degree of specialisation is progressively reacquired, but even in long-term rehabilitated CI patients it remains less precise than in normal-hearing subjects. These findings confirm earlier observations on CIs that, unlike the obligatory recruitment of primary auditory cortex, recruitment of auditory association areas relies on experience and is dependent on the nature of the auditory input.

Reorganisation in Multimodal Systems: Semantics, Memory and Attention

Hard-wired reorganisation such as changes in functional specialisation of a given cortical region (remapping) depends largely on the nature of the afferent stimuli. This form of reorganisation can be distinguished from other forms of adaptation that are more flexible and depend on task requirement (comprehension, repetition, passive listening) rather than on stimulus characteristics. The latter form of adaptation to implants implicates supramodal brain regions such as the semantic system and regions involved in memory and executive functions.

Several imaging studies have suggested that sound processing requires the involvement of larger cortical networks in CI users than in normal-hearing subjects [Naito et al., 2000; Giraud et al., 2000]. Wong et al. [1999] showed in a PET study that processing strategies in postlingual CI patients differed from those in normal-hearing subjects. These strategies involved brain regions outside the speech network, in particular the semantic system. In a recent study, we confirmed decreased responses in semantic regions in patients compared to control subjects [Giraud et al., 2000]. We further sought to understand whether this indicated reduced semantics-related activation without changes in the response properties, or alterations of the nature of the processes taking place in semantic regions [Giraud et al., 2001a]. In normal-hearing subjects, we observed an activation of the left anterior inferior temporal region [Giraud and Price, 2001]. This activation was not consistently observed in CI patients.

Decreased levels of activation and larger interindividual variability in CI patients than controls were also observed in the temporoparietal junction (BA21/39). This multimodal semantic region [Mummery et al., 1998] was specifically recruited when subjects repeated words but not when they processed syllables or environmental sounds [Giraud and Price, 2001]. No change in functional specialisation was associated with decreased activation in inferotemporal and temporoparietal semantic regions. We concluded that the same semantic regions are implicated in patients and controls, but their recruitment is less systematic in CI patients.

Our study additionally demonstrated that semantic processing in postlingual CI patients implicates more brain regions than in controls. We observed that meaningful sounds (words and environmental sounds) not only engaged semantic regions but also the parahippocampal gyrus whereas meaningless sounds did not. In control subjects, no such activation was observed [Giraud et al., 2001a]. Activation of the parahippocampal region, that usually works as an interface between perception and encoding of stimuli [Buffalo et al., 1999; McDermott et al., 1999; Rombouts et al., 1999], suggests that mnemonic contributions to speech comprehension with an implant are important. This is not surprising since even very good implant performers compensate for acoustic ambiguities with an increased utilisation of contextual information [Wong et al., 1999], which requires more internal rehearsing and more elaborate mnemonic operations.

Attention is another cognitive faculty that helps patients to increase the accuracy of comprehension when facing incomplete and ambiguous auditory stimuli. We observed that postlingual rehabilitated patients recruited a set of regions classically involved in attention [Benedict et al., 1998; Coull and Nobre, 1998] in many auditory situations but also in the mere expectancy of auditory stimuli [Giraud et al., 2000]. Patients implanted on the left side showed a larger effect than patients implanted on the right side in the left lateral premotor and intraparietal regions when they were attending to speech. Activation of attentional regions reflects specific strategies to compensate for processing degraded speech signals with monaural stimulation [O'Leary et al., 1996].

We found further arguments for enhanced attentional top-down mechanisms in sound processing in CI patients. When listening to sentences, rehabilitated CI patients but not normal-hearing subjects recruited Heschl's gyrus. As the experimental condition (heard sentences) controlled for primary auditory processing by contrasting against a condition that involved listening to vowels, the recruit-

Post-lingual CI > controls

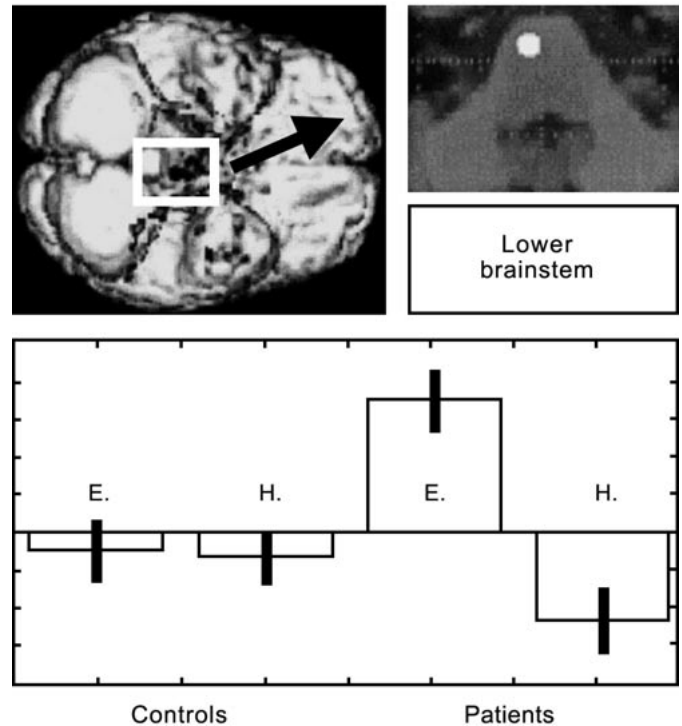
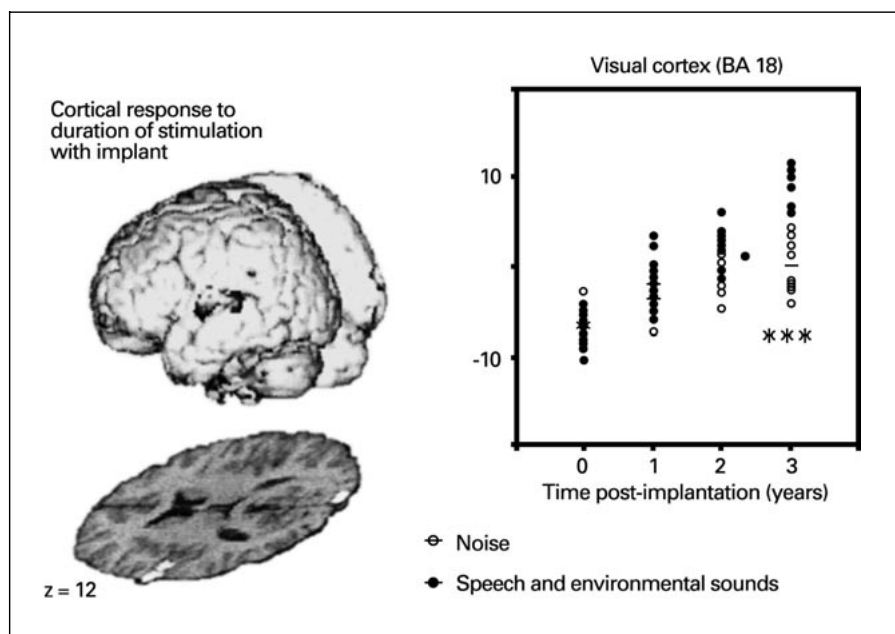


Fig. 5. Implication of the brainstem (compatible with the location of the superior olivary complex) when postlingual CI patients expected speech sounds to occur. The histograms indicate the estimated variations of blood flow relative to the mean of all conditions (H = hearing vowels; E = expecting vowels).

ment of Heschl's gyrus is likely to correspond to top-down modulation of early auditory processing that is evoked by task demand. Moreover, in a task where speech stimuli were expected, we observed a greater activity in the lower brainstem in postlingual implant patients than in controls (fig. 5). The location of the activation is compatible with that of the superior olivary complex. This structure contains efferent neurones involved in low-level attentional mechanisms [Giard et al., 1994] and in extraction of speech signals from background noise [Giraud et al., 1997]. This activation occurring without auditory stimulation is likely to reflect 'top-down' attentional control. As the olivocochlear neurones are no longer functional in CI patients, it is plausible to assume that top-down control should take place at the first stage where ascending auditory information can be modulated. These findings suggest that enhanced modulation via feedback loops also contributes to speech comprehension after cochlear implantation.

Fig. 6. In postlingual CI patients, the response of visual cortex to sounds evolves as a function of time post-implantation in a stimulus-specific manner. Visual cortical activation was observed together with activation of auditory and superior parietal cortices. The latter region could mediate interaction between auditory and visual cortices [adapted from Giraud et al., 2001b].



The conclusion of these studies is that patients resort to different neural strategies to access the meaning of sounds and to achieve performances that are similar to controls. They recruit the semantic system in a less specific and systematic way than controls but manage identical tasks by going through a series of concurrent steps involving non-specific cognitive networks such as those underlying attention and memory. The redistribution of cognitive resources in patients can be viewed as a form of cortical plasticity that does not entail alterations of functional neuro-anatomy.

Cross-Modal Reorganisation

We recently observed another form of post-implantation reorganisation that involves cortical regions beyond association areas and supramodal networks. Several PET imaging studies have systematically pointed to an involvement of visual cortex in response to sounds in the absence of any visual stimulus [Young et al., 1998; Giraud et al., 2000; Giraud et al., 2001a, b]. We found that visual cortex was already activated by sounds as early as several days after implant switch-on. Increased excitability of visual cortex by sounds could reflect dependence on vision during previous deafness (lip-reading). Surprisingly, however, rather than attenuating after auditory restoration, cortical visual responses to sounds evolved as a function of time from implantation (fig. 6). Moreover, the responses became increasingly selective to sounds that

were likely to convey a meaning (words, syllables and environmental sounds), and thus likely to require complementary visual processing. Specific activation of the visual cortical response to meaning evolved in parallel with the discrimination of noises from meaningful sounds in the association auditory cortex (BA 42/22). No such evolution of neuronal response properties was observed in the primary auditory cortex, which remained sensitive to any kind of sound over time (fig. 6). A similar dissociation of response properties between primary and association auditory cortices has previously been observed in CI patients [Fujiki et al., 1999].

Parallel refinement of neural response properties in visual and auditory association areas can result from cross-modal learning. Similarly located activation in early visual cortex (B18, V2) were observed in response to pure tones, after subjects had been trained to make specific audiovisual associations, i.e., learned that tones signalled visual events [McIntosh et al., 1998]. After such training, presentation of one stimulus alone raised the expectancy of the other and thus engaged the non-stimulated modality. In the absence of direct connections between auditory cortices and early visual cortical areas, cross-modal effects are likely to be mediated by higher-order cortical areas. We found by regression analysis that visual cortical activity correlated with that of superior parietal cortex. This region, classically involved in attention, could relay cross-modal effects.

After implantation, patients learn to match new and ambiguous sounds with their visual source. As the main goal of patients' everyday training is speech comprehension, we hypothesised that visual activation should somehow be related to the visual support to speech, lip-reading. We observed a positive correlation between lip-reading abilities and visual cortical recruitment; the patients with the larger cerebral blood flow increases in this region were also those with the better lip-reading performances. As this observation seemed to contradict the intuitive idea that after implantation patients should rely less on lip-reading, we studied the evolution of lip-reading performance after implantation in 20 postlingual implanted patients. We observed a U-shaped curve with an initial decrease of lip-reading performance just after implantation followed by a slight but significant improvement of performance that parallels the refinement of the response properties in visual cortex.

These findings corroborate previous behavioural data in prelingual patients [Tyler et al., 1997], suggesting that implantation promotes a mutual reinforcement of vision and hearing.

Predicting the Functional Outcome of Implantation

Aside from providing direct insights into the mechanisms of cortical plasticity, imaging techniques are expected to give valuable information relative to the outcome of implantation. A very large body of literature addresses this issue and it is beyond the scope of this review to summarise these studies. One line of research was to try to establish correlations between the level of electrical stimulation and the magnitude and extent of the cortical region activated. No conclusive result has been reached in this direction. However, a very recent study provides a new view on the topic. Lee et al. [2001] demonstrated that speech perception after implantation was better if auditory cortex had been hypometabolic before. Resting metabolic activity indicates to which extent deprived cortices have been taken over by competing synaptic inputs. This process is detrimental to reconnecting the auditory signals to large-scale neural circuits and therefore compromises the use of the auditory modality in language function. The study fits well with former findings that showed: (i) increased metabolic activity in the auditory cortices in cases of deafness of early onset and in the visual cortex of congenitally blind subjects [Catalan-Ahuma et al., 1993], and (ii) decreased metabolic activity in

auditory cortex in postlingual deafness of short duration [Ito et al., 1993].

Assessment of variable degrees of hypometabolism across cortical auditory regions could thus provide a differentiated picture of the potential of the auditory cortex to be recruited for oral communication. As it stands, hypometabolism in auditory regions seems to be a promising predictor of implantation outcome.

Conclusion

Brain plasticity is classically viewed as the competition of sensory afferents for cortical space. When occurring early in life, sensory deprivation is accompanied by a recruitment of deprived cortices in response to input from the intact senses [Bavelier et al., 2000; Roder et al., 1999; Weeks et al., 2000; Rettenbach et al., 1999]. Hence, in subjects deafened prior to language acquisition auditory cortex participates in processing sign language [Nishimura et al., 1999]. Cross-modal plasticity, however, is one of several aspects of brain plasticity associated with sensory deprivation. Brain imaging in cochlear implant patients has permitted identification and characterisation of other forms of brain plasticity associated with sensory deprivation and re-afferentation, and to delineate the large-scale neuronal networks in which plasticity can operate.

Cortical plasticity resulting from deafness generally spares primary auditory regions but affects post-processing cortices. The degree and nature of reorganisation in secondary and association auditory cortices is variable, depending on whether deafness occurred before or after critical stages in language development. In prelingual deaf subjects, hard-wired cross-modal connections preclude participation of these regions in oral communication. In postlingual deaf patients, cross-modal compensation is less important or involves reversible mechanisms permitting functional recovery.

Brain plasticity also occurs after implantation. As with deafness, the most important time-related changes are not observed in primary regions. Modifications of functional specialisation can be observed in auditory association cortices. Implantation additionally induces a flexible redistribution of supramodal cognitive resources. In the context of speech comprehension, this corresponds to a redistribution of the level of activity between brain regions involved in attention and memory and semantic processing.

Repeated use of a given cognitive strategy induces further cortical plasticity. Completing the information pro-

vided by an implant by cues gathered from other sensory modalities, in particular from vision, is a common strategy that progressively gives rise to stable cross-modal effects. The dynamics of these cross-modal effects suggest that restoring auditory input provokes a mutual reinforcement of vision and hearing rather than a rapid return to segregation between the senses.

References

- Bavelier D, Tomann A, Hutton C, Mitchell T, Corina D, Liu G, Neville H: Visual attention to the periphery is enhanced in congenitally deaf individuals. *J Neurosci* 2000;20:1–6.
- Benedict RHB, Lockwood AH, Shucard JL, Shucard DW, Wack D, Murphy BW: Functional neuroimaging of attention in the auditory modality. *Neuroreport* 1998;9:121–126.
- Berthezène Y, Truy E, Morgon A, Giard MH, Hermier M, Franconi JM, Froment JC: Auditory cortex activation in deaf subjects during cochlear electrical stimulation: Evaluation by functional magnetic resonance imaging. *Invest Radiol* 1997;32:297–301.
- Beversdorf D, Metzger S, Nelson D, Alonso R, Kight J: Single-word auditory stimulation and regional cerebral blood flow as studied by SPECT. *Psychiatry Res* 1995;61:181–189.
- Buechel C, Coull JT, Friston KJ: The predictive value of changes in effective connectivity for human learning. *Science* 1999;283:1538–1541.
- Buffalo EA, Ramus SJ, Clark RE, Teng E, Squire LR, Zola SM: Dissociation between the effects of damage to perirhinal cortex and area TE. *Learn Mem* 1999;6:572–599.
- Capaday C, Richardson MP, Rothwell JC, Brooks DJ: Long-term changes of GABAergic function in the sensorimotor cortex of amputees: A combined magnetic stimulation and ¹¹C-flumazenil PET study. *Exp Brain Res* 2000;133:552–556.
- Catalan-Ahumada M, Deggouj N, De Volder A, Melin J, Michel C, Veraart C: High metabolic activity demonstrated by positron emission tomography in human auditory cortex in case of deafness of early onset. *Brain Res* 1993;623:287–292.
- Coull JT, Nobre AC: Where and when to pay attention: The neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. *J Neurosci* 1998;18:7426–7435.
- Duong TQ, Kim DS, Ugurbil K, Kim SG: Spatio-temporal dynamics of the BOLD fMRI signals: Toward mapping submillimeter cortical columns using the early negative response. *Magn Reson Med* 2000;44:231–242.
- Eddington DK, Melcher JR, Qin M, Stroka J, Weisskoff RM: Electrically-evoked cortical activity in cochlear implant subjects can be mapped using functional magnetic resonance imaging (abstract 160). *Abstr ARO* 1999.
- Friston KJ, Holmes AP, Worsley KJ: How many subjects constitute a study. *Neuroimage* 1999;10:1–5.
- Fujiki N, Naito Y, Hirano S, Kojima H, Kamoto Y, Nishizawa S, Konishi J, Honjo I: Influence of speech-coding strategy on cortical activity in cochlear implant users: A positron emission tomographic study. *Acta Otolaryngol* 1998;118:797–802.
- Fujiki N, Naito Y, Hirano S, Kojima H, Shiomi Y, Nishizawa S, Konishi J, Honjo I: Correlation between rCBF and speech perception in cochlear implant users. *Auris Nasus Larynx* 1999;26:229–236.
- Giard M-H, Collet L, Bouchet P, Pernier J: Auditory selective attention in the human cochlea. *Hear Res* 1994;33:353–356.
- Giraud A-L, Garnier S, Micheyl C, Lina G, Chays A, Chéry-Croze S: Auditory efferents involved in speech in noise intelligibility. *Neuroreport* 1997;7:1779–1783.
- Giraud AL, Price CJ: The constraints functional imaging places on classical models of auditory word processing. *J Cogn Neurosci* 2001;13:754–765.
- Giraud AL, Price CJ, Graham JM, Frackowiak RSJ: Functional plasticity of language-related brain areas after cochlear implantation. *Brain* 2001a;124:101–110.
- Giraud AL, Price CJ, Graham JM, Truy E, Frackowiak RSJ: Cross-modal plasticity underpins recovery of language function after cochlear implantation. *Neuron* 2001b;30:657–663.
- Giraud AL, Truy E, Frackowiak RSJ, Grégoire MC, Pujol JF, Collet L: Differential recruitment of the speech comprehension system in healthy subjects and rehabilitated cochlear implant patients. *Brain* 2000;123:1391–1402.
- Hari R: Neuromagnetic approach to human auditory cortical functions, with emphasis on subjects with cochlear implants. *Adv Otorhinolaryngol* 1997;52:15–18.
- Herzog H, Lamprecht A, Kuhn A, Roden W, Vosteen KH, Feinendegen LE: Cortical activation in profoundly deaf patients during cochlear implant stimulation demonstrated by H₂(15)O PET. *J Comput Assist Tomogr* 1991;15:369–375.
- Hofmann E, Preibisch C, Knaus C, Muller J, Kremser C, Teissl C: Non invasive direct stimulation of the cochlear nerve for functional MR imaging of the auditory cortex. *AJNR Am J Neuroradiol* 1999;20:1970–1972.
- Ito J, Sakakibara J, Iwasaki Y, Yonekura Y: Positron emission tomography of auditory sensation in deaf patients and patients with cochlear implants. *Ann Otol Rhinol Laryngol* 1993;102:797–801.
- Johnsrude IS, Giraud AL, Frackowiak RSJ: Functional imaging of the auditory system: The use of positron emission tomography. *Audiol Neurootol* 2002, in press.
- Klinke R, Kral A, Heid S, Tillein J, Hartmann R: Recruitment of the auditory cortex in congenitally deaf cats by long-term cochlear electrostimulation. *Science* 1999;285:1729–1733.
- Kral A, Hartmann R, Tillein J, Heid S, Klinke R: Delayed maturation and sensitive periods in the auditory cortex. *Audiol Neurootol* 2001;6:346–362.
- Lazeyras F, Boex C, Sigrist A, Cosendai G, Terrier F, Pellizone M: Auditory cortex activation by direct cochlear implant electrical stimulation. *Neuroimage* 2001;13:5905.
- Lee DS, Lee JS, Oh SH, Kim SK, Kim JW, Chung JK, Lee MC, Kim CS: Cross-modal plasticity and cochlear implants. *Nature* 2001;409:149–150.
- Lustig LR, Leake PA, Snyder RL, Rebscher SJ: Changes in the cat cochlear nucleus following neonatal deafening and chronic intracochlear electrical stimulation. *Hear Res* 1994;74:29–37.
- McDermott KB, Ojemann JG, Petersen SE, Ollinger JM, Snyder AZ, Akbudak E, Conturo TE, Raichle ME: Direct comparison of episodic encoding and retrieval of words: An event-related fMRI study. *Memory* 1999;7:661–678.
- McIntosh AR, Cabeza RE, Lobough NJ: Analysis of neural interactions explains the activation of occipital cortex by an auditory stimulus. *J Neurophysiol* 1998;80:2790–2796.
- Menon RS, Ogawa S, Strupp JP, Ugurbil K: Ocular dominance in human VI demonstrated by functional magnetic resonance imaging. *J Neurophysiol* 1997;77:2780–2787.
- Mummery CJ, Patterson K, Hodges JR, Price CJ: Functional neuroanatomy of the semantic system: Divisible by what? *J Cogn Neurosci* 1998;10:766–777.
- Nagase S, Miller JM, Dupont J, Lim HH, Sato K, Altschuler RA: Changes in cochlear electrical stimulation induced Fos expression in the rat inferior colliculus following deafness. *Hear Res* 2000;147:242–250.

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- Naito Y, Hirano S, Honjo I, Okazawa H, Ishizu K, Takahashi H, Fujiki N, Shiomi Y, Yonekura Y, Konishi J: Sound-induced activation of auditory cortices in cochlear implant users with post- and prelingual deafness demonstrated by positron emission tomography. *Acta Otolaryngol* 1997;117:490–496.
- Naito Y, Okazawa H, Honjo I, Hirano S, Takahashi H, Shiomi Y, Hoji W, Kawano M, Ishizu K, Yonekura Y: Cortical activation with sound stimulation in cochlear implant users demonstrated by positron emission tomography. *Brain Res Cogn Brain Res* 1995;2:207–214a.
- Naito Y, Okazawa H, Honjo I, Takahashi H, Kawano M, Ishizu K, Yonekura Y: Cortical activation during sound stimulation in cochlear implant users demonstrated by positron emission tomography. *Ann Otol Rhinol Laryngol Suppl* 1995;166:60–64b.
- Naito Y, Tateya I, Fujiki N, Hirano S, Ishizu K, Nagahama Y, Fukuyama H, Kojima H: Increased cortical activation during hearing of speech in cochlear implant users. *Hear Res* 2000;143:139–146.
- Neville HJ, Lawson D: Attention to central and peripheral visual space in a movement detection task: An event-related potential and behavioral study. I. Normal hearing adults. *Brain Res* 1987a;405:253–267.
- Neville HJ, Lawson D: Attention to central and peripheral visual space in a movement detection task: An event-related potential and behavioral study. II. Congenitally deaf adults. *Brain Res* 1987b;405:268–283.
- Neville HJ, Lawson D: Attention to central and peripheral visual space in a movement detection task. III. Separate effects of auditory deprivation and acquisition of a visual language. *Brain Res* 1987c;405:284–294.
- Nishimura H, Doi K, Iwaki T, Hashikawa K, Oku N, Teratani T, Hasegawa T, Watanabe A, Nishimura T, Kubo T: Neural plasticity detected in short- and long-term cochlear implant users using PET. *Neuroreport* 2000;11:811–815.
- Nishimura H, Hashikawa K, Doi K, Iwaki T, Watanabe Y, Kusuoka H, Nishimura T, Kubo T: Sign language ‘heard’ in the auditory cortex. *Nature* 1999;397:116.
- Obler R, Kostler H, Weber BP, Mack KF, Becker H: Safe electrical stimulation of the cochlear nerve at the promontory during functional magnetic resonance imaging. *Magn Reson Med* 1999;42:371–378.
- Okazawa H, Naito Y, Yonekura Y, Sadato N, Hirano S, Nishizawa S, Magata Y, Ishizu K, Tamaki N, Honjo I, Konishi J: Cochlear implant efficiency in pre- and postlingually deaf subjects: A study with H₂(15)O and PET. *Brain* 1996;119:1297–1306.
- O’Leary DS, Andreason NC, Hurtig RR, Hishwa RD, Watkins GL, Ponton LL, Rogers M, Kirchner PT: A positron emission tomography study of binaurally and dichotically presented stimuli: Effects of language and directed attention. *Brain Lang* 1996;53:20–39.
- Pelizzone M, Kasper A, Hari R, Karhu J, Montandon P: Bilateral electrical stimulation of a congenitally-deaf ear and of an acquired-deaf ear. *Acta Otolaryngol* 1991;111:263–268.
- Petitto LA, Zatorre RJ, Gauna K, Nikelski EJ, Dostie D, Evans AC: Speech-like cerebral activity in profoundly deaf people processing signed languages: Implications for the neural basis of human language. *Proc Natl Acad Sci USA* 2000;95:13961–13966.
- Poldrack RA: Imaging brain plasticity: Conceptual and methodological issues – a theoretical review. *Neuroimage* 2000;12:1–13.
- Ponton CW, Don M, Eggermont JJ, Waring MD, Kwong B, Masuda A: Auditory system plasticity in children after long periods of complete deafness. *Neuroreport* 1996;8:61–65.
- Ponton CW, Don M, Waring MD, Eggermont JJ, Masuda A: Spatio-temporal source modeling of evoked potentials to acoustic and cochlear implant stimulation. *Electroencephalogr Clin Neurophysiol* 1993;88:478–493.
- Ponton CW, Eggermont JJ, Don M, Waring MD, Kwong B, Cunningham J, Trautwein P: Maturation of the mismatch negativity: Effects of profound deafness and cochlear implant use. *Audiol Neurootol* 2000;5:167–185.
- Rettenbach R, Diller G, Sireteanu R: Do deaf people see better? Texture segmentation and visual search compensate in adult but not in juvenile subjects. *J Cogn Neurosci* 1999;11:560–583.
- Roder B, Teder-Salejarvi W, Sterr A, Rosler F, Hillyard S, Neville N: Improved auditory spatial tuning in blind humans. *Nature* 1999;400:162–166.
- Rombouts SA, Scheltens P, Machielson WC, Barkhof F, Hoogenraad FG, Veltman DJ, Valk J, Witter MP: Parametric fMRI analysis of visual encoding in the human medial temporal lobe. *Hippocampus* 1999;9:637–643.
- Suarez H, Mut F, Lago G, Silveira A, De Bellis C, Velluti R, Pedemonte M, Svirsky M: Changes in the cerebral blood flow in postlingual cochlear implant users. *Acta Otolaryngol* 1999;119:239–243.
- Teissl C, Kremser C, Hochmair ES, Hochmair-Desoyer JJ: Magnetic resonance imaging and cochlear implants: Compatibility and safety aspects. *J Magn Reson Imaging* 1999;9:26–38.
- Truy E, Deiber MP, Cinotti L, Manguiere F, Froment JC, Morgon A: Auditory cortex activity changes in long-term sensorineural deprivation during crude cochlear electrical stimulation: Evaluation by positron emission tomography. *Hear Res* 1995;86:34–42.
- Tyler RS, Fryauf-Bertschy H, Kelsay DM, Gantz BJ, Woodworth GP, Parkinson A: Speech perception by prelingually deaf children using cochlear implants. *Otolaryngol Head Neck Surg* 1997;117:180–187.
- Weber BP, Neuburger J, Goldring JE, Santogrossi T, Koestler H, Battmer RD, Lenarz T: Clinical results of the CLARION magnetless cochlear implant. *Ann Otol Rhinol Laryngol Suppl* 1999;177:22–26.
- Weeks R, Horwitz B, Aziz-Sultan A, Tian B, Wessinger CM, Cohen LG, Hallett M, Rauschecker JP: A positron emission tomographic study of auditory localization in the congenitally blind. *J Neurosci* 2000;20:2664–2672.
- Wong D, Miyamoto RT, Pisoni DB, Sehgal M, Hutchins GD: PET imaging of cochlear-implant and normal-hearing subjects listening to speech and nonspeech. *Hear Res* 1999;132:34–42.
- Young JP, O’Sullivan BT, Gibson WP, Mitchell T, Sanli H, Withall A, Cervantes R: Assessment of auditory cortical function in cochlear implant patients. *Neuroimage* 1998;7:S384.