The Journal of Laryngology & Otology (2008), ***122***, *238–245*.

doi:10.1017/S0022215107008043
Printed in the United Kingdom
First published online 22 May 2007

Main Article

Auditory cortical activation and speech perception in cochlear implant users

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Abstract

Cochlear implantation is generally accepted as a successful means of restoring auditory sensation to profoundly deaf individuals. Although most patients can expect a satisfactory outcome following implantation, some have poor speech perception outcomes. This investigation used [^{18}F]-fluorodeoxyglucose positron emission tomography to measure cortical activity resulting from auditory stimulation in seven 'good' and four 'poor' cochlear implant recipients. Activations were significantly greater in both the primary and association cortices in the good compared with the poor implant users. We suggest that the ability to access the more specialised speech processing abilities of the auditory association cortices helps determine outcome following cochlear implantation.

Key words: Cochlear Implants; Positron Emission Tomography; Outcome Assessment; Sensorineural Deafness

Introduction

Cochlear implantation is now widely accepted as a successful method of restoring the sensation of hearing to the profoundly deaf. It is both a clinically effective and a cost-effective intervention.[1–5] The majority of implant candidates can now expect to obtain a satisfactory outcome from implantation.[2] Post-lingually deafened implant users are often able to have interactive telephone conversations.[5] Speech perception performances have improved greatly over the years, due mainly to a combination of improvements in implant technology and candidate selection.

Despite these improvements in outcomes, some patients derive little or no benefit from implantation. Implant performances range from full speech comprehension to the most basic detection of noise.[1,6–8]

Positron emission tomography (PET) is an imaging technique that enables visualisation and quantification of biochemical processes in living tissues. It has been used to determine changes in regional cerebral glucose metabolism (and hence cortical activity) using the glucose analogue [^{18}F]-fluorodeoxyglucose (FDG).[9–12]

Positron emission tomography has been used to investigate cortical activity in cochlear implant users. This functional neuroimaging technique does not utilise magnetic fields, unlike functional magnetic resonance imaging (MRI), and is safe in implant users.[13]

Herzog and colleagues published one of the earliest reports of the measurement of cortical activity following cochlear implantation.[14] They demonstrated bilateral activation of the auditory cortices in response to unilateral implant activation. The greatest activations were on the side contralateral to the implant. This investigation of four adult cochlear implant users did not detect any differences between subjects who were pre- compared with post-lingually deaf. However, the study did note that the patient with the best outcome following implantation had greater levels of cortical activation than those with poorer outcomes. The patterns of bilateral auditory cortical activity described in implant recipients are similar to those described in normal hearing subjects.[15]

Auditory cortical activations in cochlear implant users are strongly influenced by the nature of the stimulus presented. Speech generates significantly greater activations of the auditory association areas than white noise or pure tones.[16,17] This is not surprising, as the auditory association areas are known to be responsible for the processing of complex auditory signals.[18–20] Similar findings have been described in normal hearing subjects, in whom complex auditory stimuli caused greater activations in association areas, compared with simple stimuli such as pure tones or white noise.[15,21]

Naito and co-workers reported greater auditory association area activity in cochlear implant users than normal hearing subjects following speech

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Accepted for publication: 9 February 2007.

stimuli.[22] These authors suggested that higher levels of neural activation were required to process signals from cochlear implants than from fully functioning cochleas.

Speech perception in cochlear implant users has been shown to be related to auditory cortical activity. Fujiki and colleagues demonstrated greater activations in patients with high compared with low speech perception scores following implantation.[23] A further study by the same investigators reported a significant correlation between auditory cortical activations and implant speech perception.[24] This correlation was present in the association but not the primary auditory areas. A more recent investigation found a positive correlation between speech perception and activations in both the primary and association auditory cortices.[25] As more neurons in the auditory cortices are recruited, implant performance improves. A more recent investigation using single photon emission computed tomography showed that cortical activations were greater in implant users with high speech perception abilities compared with those with poorer outcomes.[26]

The aim of the present study was to compare auditory cortical activations in two groups of post-lingually deafened, fully rehabilitated, adult cochlear implant users: 'good' performers and 'poor' performers. The intention was to add to the existing knowledge on this topic, by utilising both single-subject and statistical parametric mapping group analyses.

Materials and methods

Subjects

Eleven post-lingually deafened adult cochlear implant recipients took part in the study. Patients were recruited from the Manchester Adult Cochlear Implant Programme. They were all under annual review following implantation. They had been using their implants for between 36 and 142 months (mean 71.5; standard deviation 31.1).

Patients' speech perception outcomes were determined using the Bench, Kowal, Bamford sentence test. Patients listened to 32 sentences containing 100 key words which they attempted to identify. The number of key words the patient was able to repeat correctly during the test produced the Bench, Kowal, Bamford sentence test score, expressed as a percentage ranging from 0 to 100 per cent. This was performed in the auditory alone condition using pre-recorded test material from computer files.

The 11 patients were divided into two main groups, as part of a larger study investigating cortical activity in cochlear implant users. 'Poor' patients had Bench, Kowal, Bamford scores of less than 25 (n = four). 'Good' patients had Bench, Kowal, Bamford scores of greater than 80 (n = seven).

The 11 cochlear implant users comprised eight men and three women. All participants were right-handed. Their ages ranged from 52 to 75 years (mean 64.3, standard deviation 6.4). The duration of deafness prior to implantation ranged from seven to 51 years (mean 24.3, standard deviation 18.9). Six patients had their implant in the right ear and five in the left ear. The clinical details of the patients are shown in Table I.

Acoustic stimulation and scanning procedure

Two scans were performed on each patient: a control and an activation scan. These were performed on different days. In both scans, patients were in a dimly lit room and were instructed to sit quietly without moving. In the control state, the implant was switched off and the patients received no auditory input. In the activation state, the patient listened to a complex, pre-recorded story. This was a commercially available compact disk (CD) recording and was delivered from a CD player directly into the implant via a specifically designed cable. The patients were asked to concentrate on the story, and they were questioned about it after the scanning procedure was completed. The activation and control states were prolonged for 32 minutes each, after which the patients were moved to and positioned within the scanner.

Imaging was performed using a General Electric Advance PET scanner (General Electric Medical Systems, Milwaukee, Wisconsin, USA). We studied regional cerebral glucose metabolism using the glucose analogue fluorodeoxyglucose, radio-labelled with fluorine-18, as a measure of neuronal activity. Fifteen minutes after the insertion of a peripherally

TABLE I

CLINICAL FEATURES OF STUDY GROUP*

Age (years)	Sex	Deafness aetiology	Deafness duration (years)	Implant side	Implant use duration (months)	BKB score
63	Female	Streptomycin/TB meningitis	48	Right	50	0
75	Male	Meningitis	51	Right	53	0
62	Male	Streptomycin/TB meningitis	44	Left	87	24
71	Female	Streptomycin/TB meningitis	47	Left	88	18
70	Male	Ménière's	7	Right	48	92
60	Male	Otosclerosis	20	Left	36	82
61	Male	Noise-induced	10	Right	54	96
63	Female	Idiopathic	15	Right	55	100
69	Male	Ototoxicity	8	Left	71	92
52	Male	Ménière's	7	Left	81	98
61	Female	Idiopathic	10	Right	142	90

*Eleven adult cochlear implant recipients. BKB = Bench, Kowal, Bamford sentence; TB = tuberculosis

https://doi.org/10.1017/S0022215107008043 Published online by Cambridge University Press

sited venous cannula, approximately 120 MBq of [^{18}F]-FDG was injected, 2 minutes after the start of the 32-minute activation or control period. Following patient positioning, data acquisition commenced 40 minutes after injection of the [^{18}F]-FDG. Scanning consisted of a 15-minute, three-dimensional (3D) emission scan followed by a 10-minute, two-dimensional (2D) transmission scan (to correct for tissue attenuation) and a 5-minute 2D emission scan (to correct for emission contamination of the transmission scan). Images were reconstructed by fully 3D filtered back projection with reprojection into a $128 \times 128 \times 35$ image matrix (voxel size $1.95 \times 1.95 \times 4.25$ mm) using measured attenuation correction.

Data analysis

Images were registered into standard stereotaxic brain space[27] and smoothed with a 12 mm Gaussian filter using the Statistical Parametric Mapping package SPM99 (Functional Imaging Lab, London, UK). All further analysis and display were performed using in-house developed software running under IDL5.5 (Research Systems, Boulder, Colorado, USA). Images were normalised to the thresholded mean voxel value and masked with a cut-off at 0.8 of this value. The control state was then divided by the activation state, so the resulting image demonstrated cortical activation due to auditory stimulation alone, in terms of percentage changes. This resulting image was overlaid on the standard single subject magnetic resonance T1 image which is part of SPM99. Regions of interest, incorporating the primary auditory cortex and its association areas, were determined with reference to a standard brain atlas,[27] using the template distributed as part of the MRIcro package from the University of Nottingham, UK.[28] The percentage change in [^{18}F]-FDG uptake in these regions of interest was measured for auditory stimulation.

This study was approved by both the Manchester local ethics committee and the administration of radioactive substances advisory committee.

Results

Single-subject analysis

Some measure of auditory cortical activity was present in all 11 implant users. Areas of cortical activation in the good implant users were more extensive than those in the poor implant users. Representative images from four of the patients (two good implant users and two poor implant users) are displayed in Figure 1.

The mean rise, across all patients, in cortical activity in the primary auditory areas was 5.99 per cent for the good implant users and 2.90 per cent for the poor implant users. In the association cortices, the corresponding rises were 8.16 and 2.80 per cent. The mean increases in activity in all auditory areas were 7.62 per cent in the good group and 2.82 per cent in the poor group. The activations were significantly greater in the good than the poor group, in all areas under investigation: primary areas ($p < 0.049$, eight degrees of freedom), association areas ($p < 0.001$, seven degrees of freedom) and all auditory areas ($p < 0.001$, eight degrees of freedom). All of these analyses were performed using Student's *t*-test. These results are summarised in Table II and displayed graphically in Figure 2.

Group analysis

All of the activation states from each group (i.e. good and poor) were analysed together using the Statistical Parametric Mapping package SPM99. Statistical parametric mapping is an approach to image analysis that involves the application of a statistical test to every pixel in a set of images. It can be used to identify voxels that differ significantly from either a control image or another activation image. The results can be expressed as a *p* value or a z score representing the degree of statistical significance. They can also be displayed as a parametric image which is a graphical representation of statistically significant change. There were a total of seven activation states included in the good group analysis and four activation states for the poor group. The cluster size, maximum Z value within the cluster and co-ordinates of the maximum values for the seven good implant users are shown in Table III. The statistical parametric maps (for a representative plane at $z = 0$) generated for the good group are displayed in Figure 3. This method of analysis did not detect any common suprathreshold activations for four poor implant users.

Discussion

This study has shown that good and poor cochlear implant users had significantly different levels of auditory cortical activation in response to speech stimuli. Good implant users had greater neuronal activity in both the primary and association auditory cortices than did poor implant users. The bilateral auditory activations demonstrated in the good implant users were similar to those seen in normal hearing subjects.[15,21]

The convergent results obtained from the single-subject analysis and statistical parametric mapping approach showed greater auditory cortical activations in subjects with better speech perception outcomes from cochlear implantation. These good implant users had significantly greater levels of activity in both the primary and association cortices. The group analysis results, using SPM99, demonstrated large bilateral activations of the auditory areas in the good group. No common activations were detected in the poor group with this approach. This was anticipated, as these implant users had only very low levels of implant-related auditory activity, some of which may have been random 'noise' rather than genuine brain activations in response to implant stimulation.

All of the subjects in the poor group had been deafened through the effects of meningitis. Post-meningitic implant users often have poorer outcomes than those deafened by other causes.[29] This may result from both peripheral and central effects

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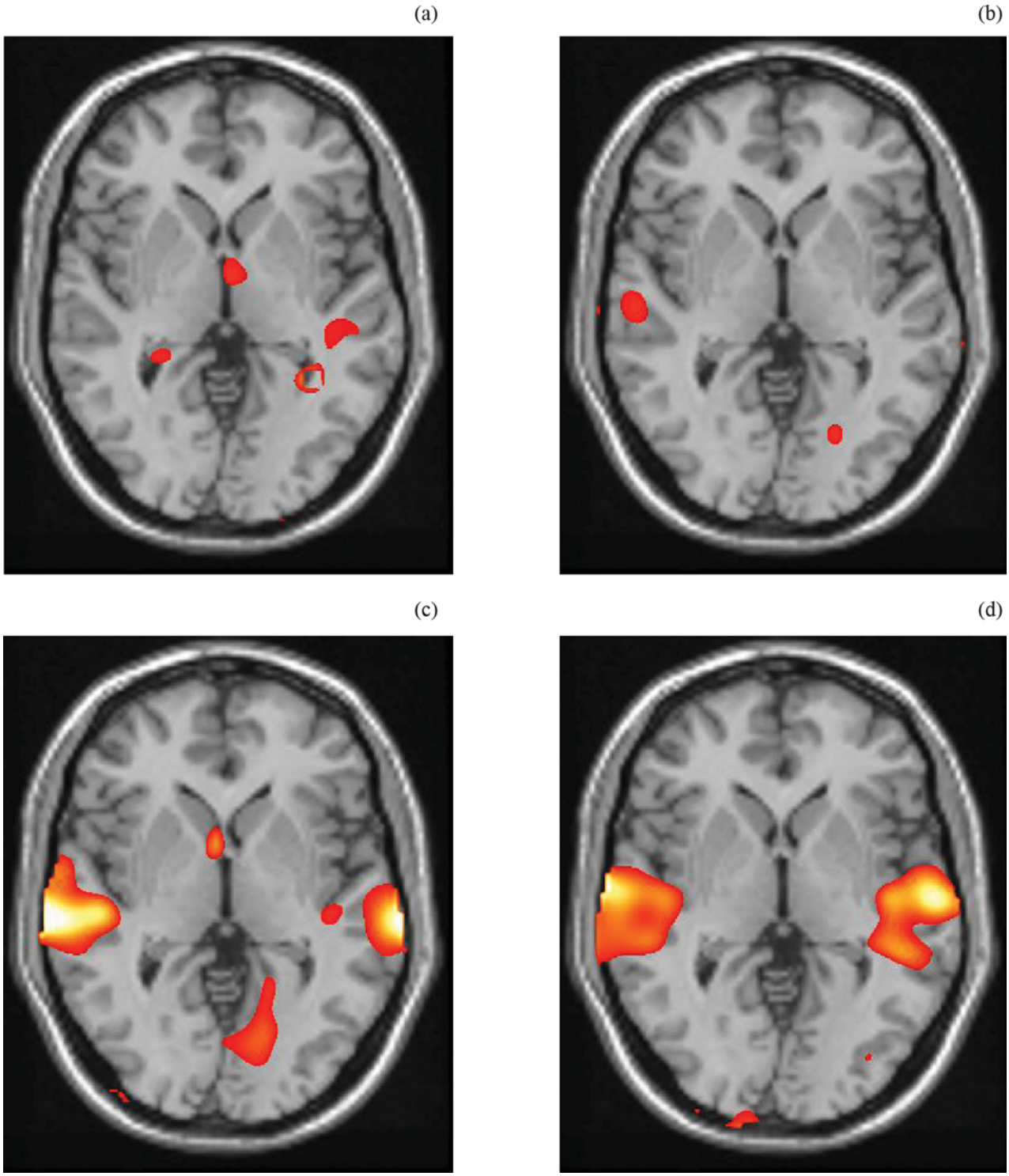

FIG. 1
Patterns of cortical activity generated by auditory stimulation of two 'poor' cochlear implant users (a & b) and two 'good' cochlear implant users (c & d).

of meningitis on the auditory pathway.[30] It is possible that this may have occurred in the subjects in the present study, resulting in their poor outcomes. None of the subjects in the good group were deafened by meningitis. We do not feel the differing aetiologies of deafness between the groups detract from the findings of different levels of cortical activations in the good and poor groups.

Four of the patients studied were female and seven were male. They were part of a larger investigation into cortical activations in cochlear implant users, with a study group of nine women and 11 men. There were no significant differences in cortical activations between male and female implant users (data not shown). This is in agreement with previous functional neuroimaging studies, which have

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TABLE II

INCREASE IN CORTICAL ACTIVITY IN EACH REGION OF INTEREST IN STUDY GROUP*

Region of interest	Increase in cortical activity (mean ± SE) (%)	
	'Good' users	'Poor' users
Primary auditory areas	5.99 ± 1.22	2.90 ± 0.55
Association auditory areas	8.16 ± 0.52	2.80 ± 0.54
All auditory areas	7.62 ± 0.53	2.82 ± 0.48

*Eleven cochlear implant users (good users, $n = 7$; poor users, $n = 4$). SE = standard error

reported that neural processing of speech stimuli is not influenced by gender.[21,31] The selection criteria for the present study were the implant users' annual Bench, Kowal, Bamford sentence scores (determining their allocation to the good or poor groups) and their willingness to participate.

In the present study, the good group consisted of seven subjects, while the poor group only had four. It was believed that four subjects would be a large enough group to establish levels of cortical activation in subjects with poor speech perception outcomes. Given the above findings, and taking into account the fact that one of the main aims of the overall study (of which all subjects were a part) was to investigate how cochlear implant users process speech signals, we did not feel that performing further scans on poor implant users was justified or necessary.

Previous functional neuroimaging investigations of auditory stimulation in cochlear implant recipients have reported results similar to those of the current study. Using radio-labelled inhaled xenon, Parving and colleagues described auditory temporal lobe activations in cochlear implant users.[32] Activations were larger in patients with better speech perception outcomes. The authors concluded by suggesting that functional neuroimaging may have a role to play in predicting outcome following cochlear implantation.

Unlike a recent report by Mortensen *et al.*, we did not find that increased activity in the right temporal or the left inferior prefrontal cortices was associated with a better outcome from implantation.[33] The

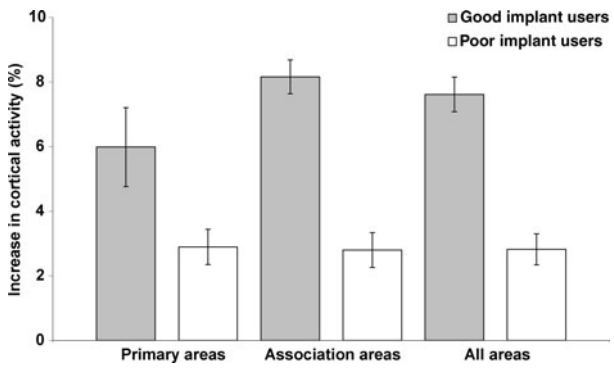

FIG. 2

Mean cortical activations in auditory regions of interest, in the 11 cochlear implant users.

TABLE III

SPM99 ANALYSIS* OF 7 'GOOD' COCHLEAR IMPLANT USERS

Cluster level	Z score	Co-ordinates (x, y, z)
2371	4.68	62, −30, −2
2600	4.51	−64, −18, 12

*Uncorrected p value < 0.0001; extent threshold 50 voxels

report in question compared post-lingually deaf cochlear implant users with good and poor speech perception outcomes. It may be that the results from this and the present study are at variance because of the different scanning protocols or auditory stimuli presented. However, in the previous report, five of the seven subjects in the good group had left ear cochlear implants and four of the five subjects in the poor group had right ear cochlear implants. It has been our observation that cochlear implant users tend to have greater activations in the auditory areas contralateral to the side of implantation.[25] This may account for Mortensen and colleagues' finding of greater right-sided auditory cortical activations in good implant users (who were mainly left ear implant recipients) compared with poor implant users (who were mainly right ear implant recipients).[33]

A comparison of auditory activity in normal hearing subjects, cochlear implant users and an auditory brainstem implant user demonstrated temporal lobe activations in all subjects.[34] The cochlear implant users, but not normal hearing subjects, had significant activations following presentation of multi-talker babble. Reviewing the statistical parametric maps generated in this study, it is also apparent that activations following speech stimuli were also greater in implant users than normal hearing subjects. Comparable results were obtained in an investigation of subjects with normal hearing and those with cochlear implants. This study reported bilateral auditory cortical activation in both groups.[35] The implant users had significant auditory cortical activations in response to multi-talker babble. Unlike the implant users, the normal hearing subjects were able to distinguish between this and meaningful speech stimuli and did not have significant auditory activations. The implant users also had greater temporal lobe activations than normal hearing subjects when listening to sentences. These findings suggest that implant users employ novel neural processing strategies in order to interpret the signals received from their cochlear prostheses.

In the present study, the good implant users had greater activations in the association than the primary auditory cortices following presentation of speech stimuli. This was an expected finding, as this group of implant users had good speech perception abilities. In normal hearing subjects, the primary auditory areas do not show increased activity in response to speech, as opposed to other, less complex stimuli.[36] The association cortices, however, are specialised for speech analysis, and increased activity does occur during speech

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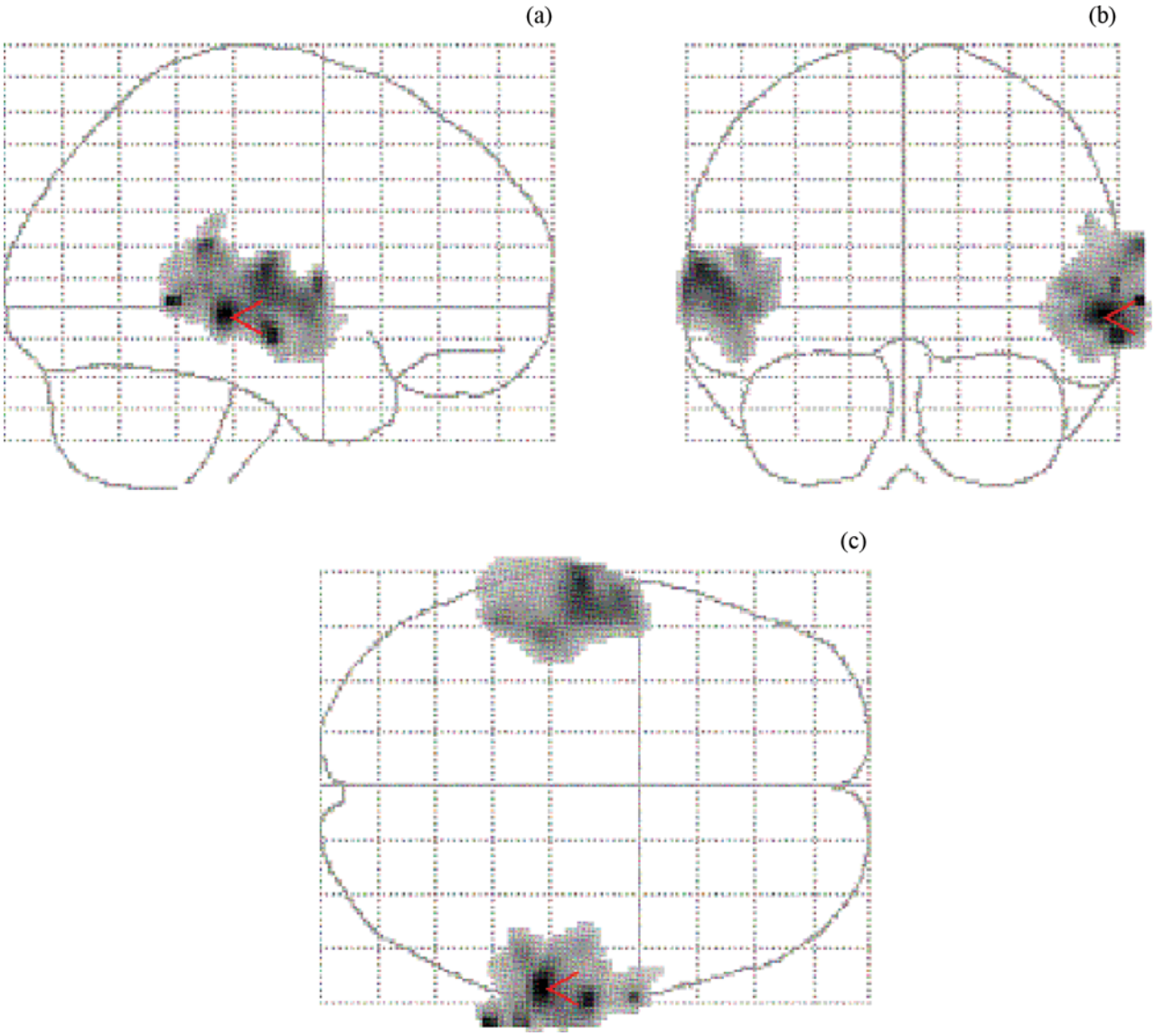

FIG. 3

Brain regions recruited (uncorrected p value < 0.001, extent threshold 50 voxels) by auditory stimulation of 7 'good' cochlear implant users; analysis using SPM99 Statistical Parametric Mapping package. (a) Side view, (b) back view, (c) top view.

processing.[18,36,37] This sub-specialisation of the auditory areas appears to be retained following successful cochlear implantation.

In the poor group of implant users, activations were greater in the primary than the association cortices. This suggests that these subjects were unable to access the higher cortical processes required for the interpretation of speech, which is reflected in their low speech perception outcome scores. The activations in the primary area were significantly less than those seen in the good implant users. All of the subjects in the poor group had long periods of deafness prior to cochlear implantation (range 44–51 years), which is associated with poorer speech perception outcomes.[8,38,39] Our results suggest that recruitment of the speech-processing abilities of both the primary and association auditory cortices play a major role in determining speech perception outcome following cochlear implantation.

Auditory cortical activity has previously been reported to decrease as a function of duration of post-lingual deafness.[40] However, a recent, contradictory investigation suggests that auditory cortical activity decreases transiently in the presence of auditory deprivation and then increases as functional reorganisation occurs.[41] The authors criticised the quantification methods used in the earlier report and speculated that auditory cortical re-innervation by other sensory modalities (i.e. cross-modal plasticity) may account for the increased activity in the auditory areas. As suggested in previous work,[25] we contend that the influence which duration of deafness has on implant speech perception outcomes is mediated, in part, by its effect on auditory metabolic activity.

Accurate prediction of outcome following cochlear implantation is problematic.[8,38,42] The only variable that has been consistently demonstrated as

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a predictor of outcome is duration of deafness prior to implantation; with increasing length of deafness, poorer speech perception results are anticipated.[8,38,43,44] However, at present, only approximately 20 per cent of an individual's implant outcome can be accounted for by known variables.[45]

- **Cochlear implantation is generally accepted as a successful means of restoring auditory sensation to profoundly deaf individuals**
- **This investigation used [^{18}F]-fluorodeoxyglucose positron emission tomography to measure cortical activity resulting from auditory stimulation in seven 'good' and four 'poor' cochlear implant recipients**
- **Activations were significantly greater in both the primary and association cortices in the good compared with the poor implant users**
- **This finding suggests that the ability to access the more specialised speech processing abilities of the auditory association cortices helps determine outcome following cochlear implantation**

In pre-lingually deaf children, the degree of auditory hypometabolism is directly related to implant performance.[46] Following a multivariate analysis, this factor predicted outcome more accurately than did duration of deafness and duration of implant use. It was suggested that if cross-modal plasticity increases auditory cortex metabolism before implantation, then the outcome from implantation will be poor. If cross-modal plasticity occurs, then the auditory neurons used for visual processing cannot be 'reprogrammed' for auditory functions. A recent investigation by the same workers adds to their previous findings and suggests that increased levels of neural processing in the ventral visual pathways are associated with poorer outcomes from implantation.[47] Furthermore, recent PET studies of the cortical responses to promontory stimulation in normal hearing subjects and cochlear implant candidates have suggested that testing temporal processing abilities may be used to predict outcome following cochlear implantation.[48,49] Although functional neuroimaging is currently only used as a research tool in the field of cochlear implantation, we suggest that, ultimately, it will become part of the assessment process for potential implant candidates.

Conclusion

This investigation demonstrated that implant recipients with good speech perception outcomes had significantly greater auditory cortical activations than those with poor speech discrimination ability. Greater levels of activation in the primary auditory areas were present in good implant users than poor implant users, and this may play a role in the recruitment of the association areas. Good cochlear implant users were able to access the more specialised speech processing abilities of the auditory association cortices, whereas poor implant users were not. We suggest that recruitment of the auditory association cortices plays a major role in determining outcome from cochlear implantation.

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Mr K M J Green takes responsibility for the integrity of the content of the paper.
Competing interests: None declared