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Functional plasticity of language-related brain areas after cochlear implantation

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Summary

Using PET, the cerebral network engaged by heard language processing in normal hearing subjects was compared with that in patients who received a cochlear implant after a period of profound deafness. The experimental conditions were words, syllables and environmental sounds, each controlled by a noise baseline. Four categories of effect were observed: (i) regions that were recruited by patients and controls under identical task conditions: the left and right superior temporal cortices and the left insula were activated in both groups in all conditions; (ii) new regions, which were recruited by patients only: the left dorsal occipital cortex showed systematic activation in all conditions versus noise baselines; (iii) regions that were recruited by both groups with a different functional specificity; e.g. Wernicke's area responded specifically to speech sounds in controls but was not specialized in patients; and (iv) regions that were activated in one group more than the other: the precuneus and parahippocampal gyrus (patients more than controls) and the left inferior frontal, left posterior inferior temporal and left and right temporoparietal junction regions (controls more than patients). These data provide evidence for altered functional specificity of the superior temporal cortex, flexible recruitment of brain regions located within and outside the classical language areas and automatic contribution of visual regions to sound recognition in implant patients.

Keywords: PET; language; speech; cochlear implants

Abbreviation: BA = Brodmann area

Introduction

Electrical stimulation of the auditory nerve by a cochlear implant can restore hearing in profound bilateral deafness of sensorineural origin, in subjects who are otherwise neurologically normal. After 2 years of practice, some postlingual cochlear implant patients even recover close to perfect speech comprehension. While these patients are able to perform as well as control subjects in word repetition tasks without lip-reading, the effort and the strategy engaged in such tasks differ from normal and are therefore likely to result in differential recruitment of the cerebral speech perception and production systems. In agreement with another PET study (Wong *et al.*, 1999), we recently identified differences between control subjects and completely rehabilitated cochlear implant patients in the cerebral activation patterns obtained in various passive listening situations (Giraud *et al.*, 2000*b*). These differences were distributed over the left temporal lobe. Left superior temporal regions were overactivated in patients compared with controls, whereas more posterior regions and inferior temporal regions were underactivated. On the basis of the functional neuroanatomy of heard language, as established in normal subjects (Binder *et al*., 2000), these results are interpreted as a functional adaptation within the heard language system, with more resources allocated to phonological analysis at the expense of semantic processing. Semantic processing remained sufficient for correct speech comprehension, as indicated by behavioural data, but was insufficient to produce significant blood flow increases in classical semantic regions (Vandenberghe *et al*., 1996; Mummery *et al*., 1998). These results suggested a flexibility in the recruitment of the language system necessary to achieve successful performance.

However, as the different processing levels were not tested specifically, our analysis was insensitive to functional

reorganization in the language system that might have occurred during deafness and, subsequent to cochlear implantation, during the progressive adaptation to spectrally and temporally degraded sounds. We could not demonstrate positively that the increases in the level of activation observed in patients in regions classically dedicated to phonology were due to enhanced phonological processing, as specificity of these regions could be altered in patients. For similar reasons, decreased activity in semantic regions could not be assigned confidently to decreased semantic processing.

In the present study, we addressed the question of the functional organization of the heard language system after deafness, implantation and successful rehabilitation using an experimental design aimed at functionally segregating phonological and semantic processing. This design comprised conditions in which words and syllables were repeated and environmental sounds named, with matched control tasks involving white noise bursts equated with each of the stimuli in duration and low-pass temporal envelope. To assess the degree of functional specialization within the heard language system, we analysed in each group activations that were (i) common to all sound conditions, i.e. words, environmental sounds and syllables; (ii) specific to speech input, i.e. words and syllables but not sounds; (iii) specific to semantic input, i.e. words and environmental sounds but not syllables; and (iv) specific to words only, as suggested by classical models of auditory word processing (Caplan, 1992). On the basis of the consistency of effects across subjects, differences and commonalities between groups were classified into the following four categories of effect (Table 3): (i) regions recruited by both groups; (ii) new regions recruited only in patients; (ii) regions recruited by both groups but under different task conditions; (iv) regions recruited in one group more than in the other but with no consistent differences between groups.

Methods

Subjects

Six normal right-handed volunteers and six cochlear implant patients (five males in each group, mean age 36.6 years for controls, 53.1 years for patients) participated in a study based on 12 measurements of regional cerebral blood flow with PET, the only neuroimaging technique that can be safely used in the presence of common implants that are not specified as magnetic resonance-compatible (Teissl *et al*., 1999). This study was approved of by the Joint University College London–University College London Hospital Medical Ethics Committee and written consent was obtained from all subjects. All patients suffered from profound bilateral hearing loss [$>$90 dB hearing loss in silence in the best ear without hearing aid within the 0.5–4 kHz range and $<$20% speech comprehension in silence in the best ear with hearing aids set up optimally, in accordance with the NIH (National Institutes of Health, Bethesda, USA) convention, 1995]. Only two patients were perfectly matched in age with the controls. However, as we considered effects that were consistent across subjects, mere age effects cannot account for the effects observed. All subjects were neurologically normal. In particular, no brain diseases were detected in preimplantation magnetic resonance scans. The selection of patients was based on intelligibility performance during clinical tests (scores for word discrimination $>$60% and for sentence comprehension $>$90%). The clinical profile of the patients is summarized in Table 1.

Experimental design

The experimental conditions were: (i) naming the source of environmental sounds (e.g. hear the sound of a dog barking and say ‘dog’), (ii) repeating words matched to sounds by semantic content (e.g. hear the word ‘dog’ and say ‘dog’), (iii) repeating syllables (e.g. ba–ba–ba, dee–dee), saying OK to noise bursts matched to the (iv) sounds, (v) syllables and (vi) words. The last three conditions were used as a low-level auditory baseline and were controlled for articulatory mechanisms. In all conditions, answers were produced silently (mouthing) to prevent auditory processing of the subjects’ own voices.

Prior to PET scanning, patients and controls were asked to identify the sounds and repeat syllables and words. If patients made errors during the first presentation, the stimuli were presented a second time. Only those patients who made no errors during the second presentation of the stimuli were included in the PET experiment. Eye closure and generation of correct (mouthed) responses during PET data collection were controlled by video monitoring. After image acquisition, repetition and naming times were measured in both groups for statistical comparisons. We found no significant difference in repetition times, but patients were slower than controls in naming sounds (time between onset of stimulus and onset of response, 1.2 $\pm$ 0.4 s in controls and 1.7 $\pm$ 0.6 s in patients). However, no specific sound activation was observed in patients despite longer naming times, suggesting that the additional task requirements for naming were non-specific (not different for sounds versus words and syllables). Clinical observations usually indicate increased reaction times in implant patients during word tasks. The absence of differences in repetition times between the two groups was probably due to the familiarity established with the stimuli.

PET data recording

Regional cerebral blood flow was assessed after intravenous injection of water labelled with ^{15}O. The dose received was 9 mCi per injection. Images were acquired with a Siemens CTI III camera. Standardized procedures were used for data acquisition and data analysis. Realignment, normalization and statistics were performed with SPM97d (www.fil.ion.ucl.ac.uk/spm).

Table 1 *Clinical profile of implant patients*

Patient	Sex	Age (years)	Type of deafness	Duration of		Type of cochlear implant	Number of functional electrodes	Side of implant
				deafness	rehab.			
B.H.	M	60	Prog. SNHL	1	0.83	Spectra-22	17	L
L.B.	M	66	Prog. SNHL	2	1.5	Spectra-22	20	R
G.B.	M	56	Ab. SNHL	49	3	Spectra-22	20	L
C.C.	F	42	Ab. SNHL	3	3	Clarion-8	8	R
S.C.	M	33	Ab. SNHL	1	3	Spectra-22	19	R
D.W.	M	52	Prog. SNHL	4	4	Spectra-22	20	R

Ab. = abrupt deafness; Prog. = progressive hearing loss; SNHL = sensorineural hearing loss; rehab. = rehabilitation. *At the time of implantation.

Stimuli

Digitized natural environmental sounds were used. Our stimuli included animate (dog, bird, baby) and inanimate sounds (telephone ringing, drill, car, etc). Syllables were matched to words with respect to the number of syllables, but were made as non-word-like as possible (toto, va, etc.) to prevent implicit processing of syllables as words. For each of the aforementioned stimuli (words, sounds and syllables), we created as a control stimulus a noise burst matched in duration, average amplitude and temporal envelope. All stimuli were presented in free field at a rate of one every 4 s.

Data analysis

The aim of the analysis was to identify effects that were common to patients and controls and effects that differentiated the groups. Ideally, a between-groups comparison requires a random effects analysis based on between-subjects variance. However, since the degrees of freedom for such an analysis depend on the number of subjects, the likelihood of false negatives is high for small numbers of subjects. Conversely, in a fixed-effects analysis the variance and degree of freedom are based on the number of observations (scans). In this case, there may be false-positive results when the within-subjects variance is less than the between-subjects variance. However, this is more of a problem in the analysis of functional MRI time series data than in PET experiments with few observations per condition. Because of the limited availability of suitable patients, it was possible to scan only a small number of subjects. To avoid false-negative results, we used a fixed-effects analysis. To avoid false-positive results, we conducted a second analysis which effectively treated patients as a series of case studies and looked for effects that were consistent across patients relative to controls. The details were as follows.

The first analysis modelled the two groups of subjects independently in a single design matrix. For each group, linear contrasts identified regions that were activated for words – baseline (contrast 1), sounds – baseline (contrast 2), syllables – baseline (contrast 3). The results of these three contrasts were then compared. The results of such second-level comparisons constitute the basis of the present report (Table 2).

Common effects were identified by finding regions that were activated in all three contrasts. This was achieved by conjunction analysis [which sums the three effects and excludes voxels where there are significant differences between the contrasts (Friston *et al*., 1997; Price and Friston, 1997)] and inclusive masking, which includes only those voxels that are significantly activated in each of the contrasts at $P = 0.08$. Given that this masking procedure involved three independent contrasts thresholded at 0.08, its effective error probability is approximately $P < 0.0005$.

Specific effects were identified by contrasting the three first-level effects. For instance, the difference between words and sounds was identified by comparing the results of contrast 1 with contrast 2. These second-level contrasts [e.g. (words – baseline) – (sounds – baseline)] controlled for differences in the acoustic properties of the stimuli, which would not be possible if words and sounds were contrasted directly. In addition, these contrasts were compared across groups to find effects that were common to patients and controls and effects that differentiated the two groups. The latter was achieved by assessing the interaction between contrasts and groups. This is reported at a low threshold ($P < 0.05$) because subtle effects coming from second-level contrasts (e.g. an effect that is speech-specific in one group and responsive to both speech and environmental sounds in the other) are likely to yield low interaction Z scores. However, to safeguard against potential false-positive results while retaining the sensitivity of the fixed effects analysis, a second analysis was performed on individual subjects. We then focused the interpretation of interactions on those effects that were consistently observed in all subjects in one group but no subjects in the other group. The second analysis modelled each subject (patient and control) as an independent subject. Condition-specific effects were calculated, as in the first analysis, for each of the 12 subjects. Differences and commonalities between the patients and controls were assessed by determining the number of subjects in each group who showed a specific effect (as presented in Table 3). The threshold for individual subject effects was set at $P < 0.1$ because the probability of

Table 2 *Analysis (fixed effects, modelling two groups of six subjects) of activations common to all conditions (words, sounds and syllables), specific to phonology (words and syllables but not sounds), semantics (common to sounds and words but not syllables) and words (words but not syllables or sounds) in each group of subjects*

Region	Controls			*Z*	Patients			*Z*	Interaction score
	x	*y*	*z*		*x*	*y*	*z*		
(**A**) Common to all conditions versus matched baselines									
Words syllables sounds									
Left middle sup. temp. (BA 42/22)	–62	–22	8	5.9	–68	–22	4	3.4	NS*
Right middle sup. temp. (BA 42/22)	60	–20	4	5.3	68	–16	6	2.7	NS
	58	0	–2	4.4	64	–8	2	2.9	NS
Left insula	–26	18	–14	3.3	–38	20	2	3.8	NS
					–26	22	–12	3.0	NS
Left inferior frontal (BA 44)	–44	10	26	4.7	NS				2.23
Left post. inferior temporal (BA 37)	–48	–50	–24	3.1	NS† (see B)				1.96
Wernicke's area (BA 22)	NS† (see B)				–64	–44	4	4.4	2.54
Left visual cortex (BA 18)	NS				–12	–74	2	5.5	4.39
	NS				–6	–96	–4	5.4	3.98
Precuneus (BA 19)	NS				–8	–90	40	3.8	3.29
(**B**) Phonology									
(Words syllables) > sounds									
Wernicke's area (BA 22)	–70	–38	6	5.4	NS‡ (see A)				2.54
Left post. inferior temp. (BA 37)	NS‡ (see A)				–46	–46	–14	3.14	2.5
(**C**) Semantics									
Words > (sounds syllables)									
Right temporoparietal (BA 21/39)	60	–68	20	3.7	NS				2.1
Left temporoparietal (BA 21/39)	–58	–54	20	3.2	NS				2.2
(Words sounds) > syllables									
Left parahippocampal gyrus (BA 36)	NS				–20	–40	–10	3.9	2.86

The *Z* score in each group (at $P < 0.001$, uncorrected) and the interaction score between groups (at $P < 0.05$) are provided. Sup. = superior; post. = posterior; temp. = temporal; NS = not significant. *This activation extends posteriorly and medially in controls. An interaction (controls > patients) was found in the posterior superior temporal region at –54, –28, 8 ($Z = 3.54$). †These regions were not significant in these contrasts but were found when analysing activation common to words and syllables, i.e. phonology specific. ‡These regions were non-significant in these contrasts but were found when analysing activation common to all stimuli, i.e. words, sounds and syllables.

such an effect occurring by chance in all six subjects was <0.000001.

We finally investigated the effect of several possible confounds, namely the side of implant and the number of active electrodes. As we found no significant effect of these variables on the functional data, we concluded that these variables could not have affected the data significantly.

Results

Activation common to all stimuli

Activations common to words, environmental sounds and syllables reflect inevitable residual acoustic and articulatory effects, which are accounted for by small differences between the task conditions and their respective baselines.

The baseline tasks controlled successfully for primary auditory processing, as we found no activation in the region of Heschl's gyrus, but activation was observed for both groups in middle regions of the bilateral superior temporal gyri [Brodmann area (BA) 22] and the left anterior insula (Table 2). In controls only (all controls and no patient; Table 3), the activation of the left superior temporal gyrus extended posteriorly and medially (interaction with the patients group at –54, –28, 8). This posterior temporal region did not respond to any sound category in patients and the difference between subject groups was significant ($Z = 3.54$, $P < 0.001$). In controls, we additionally found activation of the left posterior inferior temporal and left inferior frontal regions. Although activation in these regions was higher for controls than for patients, the difference was not significant because of individual variation within both patient and control groups (Table 3).

In patients only, we found activation in Wernicke's area (Fig. 1), the left precuneus and the left dorsal occipital cortex. This latter effect in the visual cortex was observed in every patient. The histogram in Fig. 2 shows that the activity (relative to mean activity for all subjects) was increased locally in every patient (all conditions relative to baseline). None of the controls showed such an effect.

Activation in visual regions could emerge either from increased activation for patients during familiar sound conditions and/or from less activation for patients during the baseline tasks. Reduced activation during the baseline tasks could have arisen if the noise bursts heard during the baseline tasks elicited involuntary eye movements. This hypothesis is based on a previous study that reported deactivation of the

Table 3 *Classification (fixed effects, modelling 12 single subjects) of the regions found in the former analysis (Table 1) according to the number of subjects in each group that showed a specific effect*

Region	Specificity	Number of controls	Number of patients	
Regions common to both groups				Conj.
Left middle sup. temp. (BA 42/22)	Common	6	5	5.50
Right middle sup. temp. (BA 42/22)	Common	5	6	3.69
Left insula	Common	6	6	3.38
Regions recruited by patients only				Int.
Left visual cortex (BA 18)	Common	0	6	4.39
Regions recruited in both groups with different specialization				Int.
Left post. superior temp. (BA 22)	Common	6	0	3.54
Wernicke's (BA 22)	Words and syllables	6	0*	2.5
Regions recruited in one group more than the other but with no consistency across subjects				Int.
Precuneus (BA 19)	Common	1	6	3.29
Left parahippocampal gyrus (BA 36)	Words and sounds	1	6	2.86
Left post. inferior temp. (BA 37)	Phonology	2	4†	2.5
Left inferior frontal (BA 44)	Common	4	3	2.23
Left temporoparietal (BA 21/39)	Words	6	2	2.2
Right temporoparietal (BA 21/39)	Words	3	2	2.1

To consider an interaction positive, we stipulated that the significance of the interaction at the group analysis level (Table 1) should be $P < 0.05$ *and* a difference should be evident at the single subject analysis level ($P < 0.1$ for each individual, which gives $P < 0.00000$ for an effect present in six subjects). The same criteria were required for changes in functional specificity. This conservative definition was adopted to prevent fallacies inherent in the analysis of groups in a fixed-effects model while permitting good sensitivity when studying small samples of subjects. In each region found with the group analysis, we specify the number of subjects in each group that showed the effect and the interaction (Int.) or conjunction (Conj.) (for effects common to both groups) levels. The second column indicates the contrast in which a region was found (Common = common to words, sounds and syllables). *This region was activated by all conditions (words, sounds and syllables) in four patients and by sounds in the other two patients. †This region was common to words, sounds and syllables in four controls and one patient (Int. = 1.96). Post. = posterior; sup. = superior.

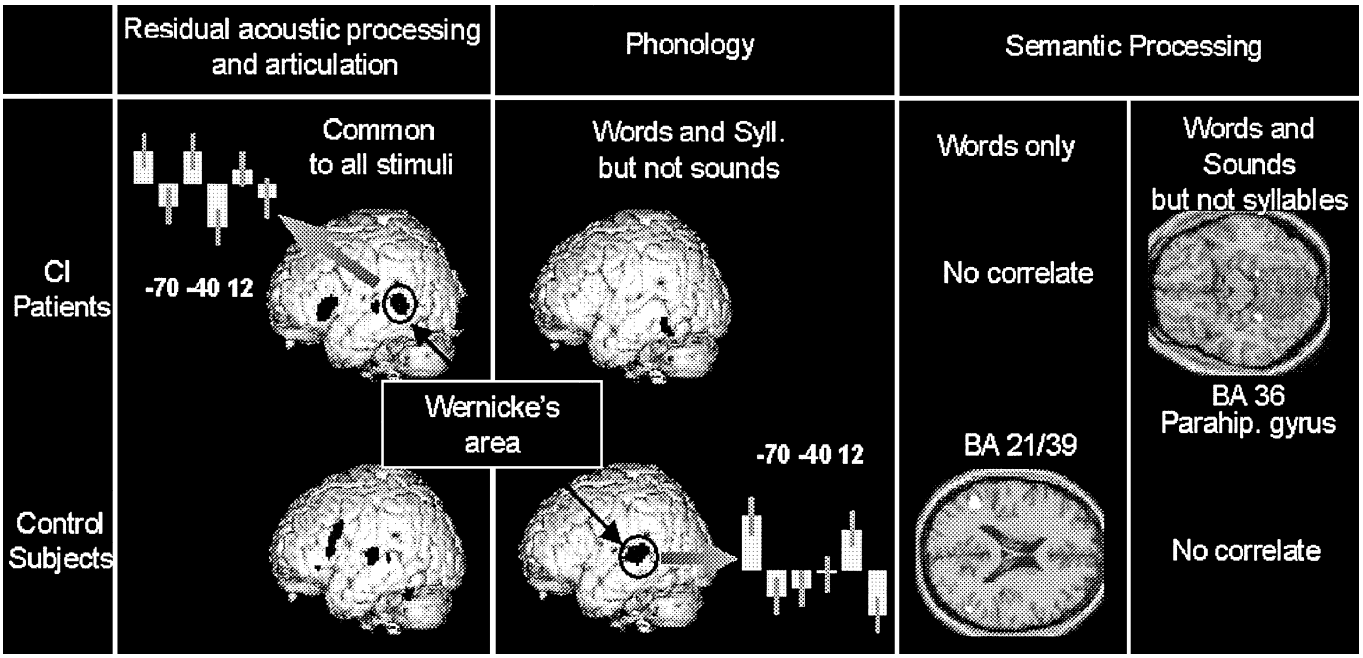

Fig. 1 Condition-specific brain activations in six postlingual rehabilitated cochlear implant patients and six normal-hearing control subjects. The histograms indicate activity variations in both groups relative to the mean of conditions used in the analysis. Activated voxels are displayed at $P < 0.001$, uncorrected. Wernicke's area, phonology-specific in controls, shows a decreased functional specialization in cochlear implant patients. Syll. = syllables; Parahip. = parahippocampal.

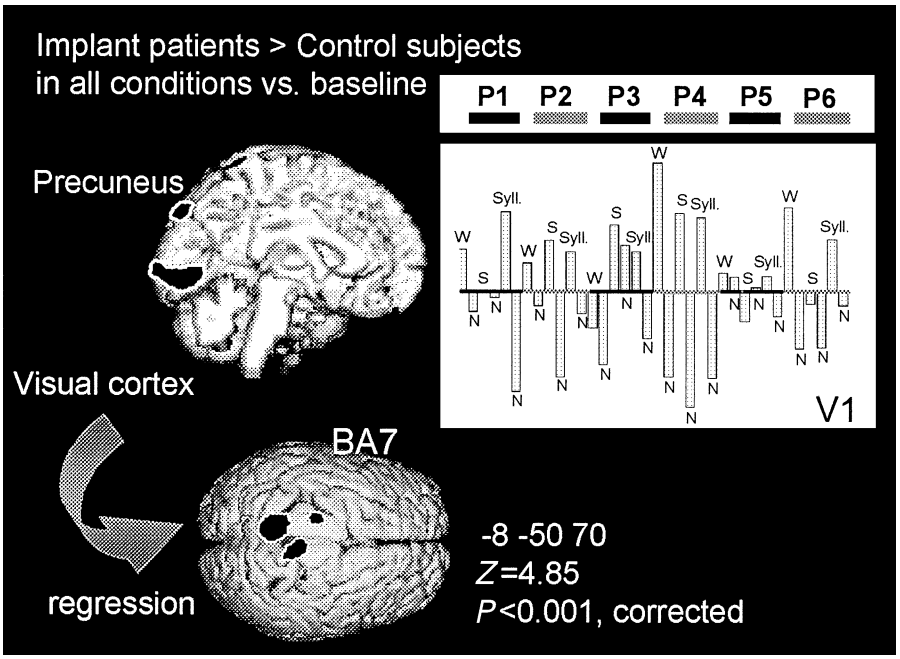

Fig. 2 Brain regions activated more in each cochlear implant patient than in the control subjects, for all stimuli (words, environmental sounds, syllables) against their respective baseline controls. Changes in activity in the visual cortex correlate with activity in superior parietal cortex (BA 7). *Inset*: activity (relative to mean activity in all 12 subjects) in the primary visual cortex of cochlear implant patients (P1 to P6). W = words; S = sounds; Syll. = syllables; N = noise.

visual cortex during involuntary eye movements with eyes closed (Wensel *et al*., 1996). To see whether changes in visual activity reflected involuntary ocular oscillations, we correlated activation in the visual areas with all other voxels in the brain. We used the blood flow variation in one voxel of the visual cortex (the peak in the group analysis: –6, –96, –4) as a covariate of interest (Friston *et al*., 1997; Büchel *et al*., 1998; Morris *et al*, 1998). In patients but not in controls, the activity in the visual cortex covaried with activity in the left superior parietal (–8, –50, 70; $Z = 4.85$) and the anterior cingulate (14, 24, 16; $Z = 3.99$) cortices. There was no correlation in areas associated with eye movements (frontal and supplementary eye fields).

Phonology-specific activation

In controls, Wernicke's area (recruited by all stimuli in patients) was activated by speech sounds but not by environmental sounds. The activity increase in this region for speech stimuli relative to sound naming was observed consistently in all controls, whereas in all patients this region was activated to the same extent during sound naming (see footnote to Table 3).

In patients, the posterior inferior temporal cortex was activated more by speech sounds than by environmental sounds. A similar trend was observed in the control group, but the difference between speech and sound did not reach significance because in the controls, unlike in the patients, this region was also activated in the environmental sound condition. Previous activation studies (Price *et al*., 1996*a*; Warburton *et al*. 1996) and lesion studies (De Renzi *et al*., 1987; Krauss *et al*., 1996; Raymer *et al*., 1997; Foundas *et al*., 1998) suggest a critical role of the left posterior inferior temporal region in naming. In contrast, our results indicate that this region might not be essential for naming sounds. Nevertheless, as the difference between subject groups in this region did not reach our criteria for significance (consistency across subjects), a conclusion about the functional specificity of this region and its possible alteration in patients would require further experiments involving a larger number of subjects in both groups.

Semantic activation

The left parahippocampal gyrus (BA 36) was activated in all patients but in only one control for words and sounds and the group difference reached our criteria for significance ($Z = 2.9$, $P < 0.01$). We found no region in controls where meaningful sounds and words produced greater activation than syllables. However, in another study (Giraud and Price, 2001) involving a larger number of subjects and the same set of stimuli, words and environmental sounds but not syllables activated a left anterior inferior temporal region that has previously been associated with semantic processing (Vandenberghe *et al*., 1996; Mummery *et al*., 1998). In the present study, activation in this area was detected only when the threshold was reduced to $P < 0.05/0.01$.

We also assessed effects specific to words in accordance with classical models of auditory word processing (Caplan, 1992), which postulate a module dedicated to the processing

of auditory word forms. Words specifically activated bilateral posterior temporoparietal regions (BA 21/39), which have been associated with semantic processing in other studies (Démonet *et al*., 1994; Engelien *et al*., 1995; Price *et al*., 1997; Gorno-Tempini *et al*., 1998) even when neither stimuli nor task involves auditory word-form analysis. However, as the bilateral posterior temporoparietal areas were activated in only four controls and two patients, the difference between controls and patients did not reach our criteria for significance. Further studies are therefore required to confirm that normal subjects engaged the semantic system more than patients.

Discussion

Classification and interpretation of the between-groups effects

We segregated several components of the heard language system to identify commonalities and differences in its organization between rehabilitated cochlear implant patients and control subjects. We observed effects common to both groups in the middle regions of the bilateral superior temporal cortices and the left insula, and differences between groups in the posterior superior temporal cortex, Wernicke's area, the inferior frontal cortex (Broca's area), the posterior inferior temporal cortex, the visual cortex, the precuneus, the parahippocampal gyrus and bilaterally in the temporoparietal junction. Using our single-subject analysis (see Methods and Table 3), we established that (i) the visual cortex was the only region that was exclusively and consistently recruited in patients, (ii) the posterior superior temporal region and Wernicke's area were recruited in both groups but with a different functional specialization consistently observed across subjects of both groups, and (iii) all other regions where the group analysis detected an interaction did not meet our criterion for significance.

The interpretation of these results was based on the following logic. (i) Only one group and not the other recruits a region. If a region is recruited in every control but in none of the patients, this means that it is possible to perform the tasks without this region (as all patients managed the task). This suggests that this region, albeit activated in controls, is not critical for the task even in controls (Price *et al.*, 1999*b*). This reasoning is not interchangeable. If patients activate a region that is never activated in controls, this is considered a new region. The status of 'new region' is given only to regions that are activated in all patients and none of the controls. (ii) Both groups recruit the same region but under different task conditions, consistently in every subject of each group. This situation raises a question relative to the functional specialization of the region. If, in patients, a region is recruited in fewer experimental tasks than in controls, we conclude that it is more specialized 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 conclude only that the region is less specialized in patients. (iii) A region is activated in one group more than in the other (statistically) but not systematically in all subjects. In this case, we conclude that the region is contributing flexibly depending on task requirements and individual strategies and that it is not, in general, indispensable. This last interpretation is the only one that is equivalent for both patients and controls.

Activations common to control subjects and cochlear implant patients

Activations in the middle bilateral superior temporal cortices and the left insula were observed both in controls and patients under identical experimental conditions. These shared activations were common to all tasks (environmental sounds, words and syllables) that differed from baseline by acoustic complexity and familiarity. Activation of bilateral auditory association cortices (BA 42/22) reflects the additional auditory processing that corresponds to the acoustic differences between stimuli and baseline, particularly with respect to temporal complexity (Griffiths *et al*., 1998; Giraud *et al*., 2000*a*). The tasks also differed from their corresponding baselines by the fact that the content of the verbal output was determined by the auditory input rather than an acoustically cued standard response (i.e. say 'OK' to each stimulus). As lesion (Habib *et al*, 1995; Dronkers, 1996) and activation (Wise *et al*., 1999) studies implicate the anterior insula in articulation planning, activation in this region is consistent with differences between tasks and baselines at the speech production level.

Regions recruited in patients only

In the absence of visual input (eyes closed), all patients recruited visual regions. In each of them and in none of the controls, sound naming, word and syllable repetition produced larger blood flow increases in the left dorsal occipital cortex than in the baseline task.

There was no correlation of visual cortical activity with activity in areas associated with eye movements, such as the frontal and supplementary eye fields (Sweeney *et al*., 1996), but there was a correlation with activity in the anterior cingulate and left superior parietal cortex, areas associated with attentional control (Posner, 1994; Coull and Nobre, 1998; McIntosh *et al*., 1998). The anterior cingulate is usually implicated under task conditions involving high performance demands (Posner and DiGirolamo, 1998) and has been proposed as the substrate for executive control of cognitive and motor processes (Posner, 1994). The superior parietal region is recruited by directed visual attention (Corbetta, 1998).

Visual activation might reflect learned expectancy (e.g. from lip-reading experience) to process auditory and visual stimuli simultaneously. This hypothesis gains support from

a report by MacIntosh and colleagues, who observed activation of the left dorsal occipital visual cortex in response to an auditory stimulus presented alone after subjects had learned that this stimulus signalled a visual event (MacIntosh *et al*., 1998). Likewise, cochlear implant patients may expect, even in the absence of visual input, to use the visual source of sounds to resolve acoustic ambiguities. This expectation could have arisen from previous dependency on lip-reading to discriminate consonants and a continuing need for visual cues to localize the source of sounds as binaural information is not available.

Differences in regional functional specialization

In all control subjects, Wernicke's area was activated by speech but not by environmental sounds. This phonology-specific response is consistent with the impaired ability to repeat after lesions to this region (BA 22) (Valdois *et al*., 1995). The cochlear implant patients also activated this region for speech but all of them showed equivalent activation for naming environmental sounds. The specialization of the left superior temporal cortex anterior to Wernicke's areas (BA 42 at –58, –28, 8) was also altered in patients. This region was responsive to all sound categories in controls but did not respond consistently in any condition in patients.

These findings can be summarized as follows. (i) In controls, the posterior superior temporal cortex (BA 42) responds more to complex sounds than to modulated white noises, and Wernicke's area (BA 22) responds specifically to speech sounds. (ii) In cochlear implant patients, the posterior region of BA 42 is less specialized in that it does not respond differentially to complex sounds, i.e. environmental and speech sounds, and modulated white noise. Moreover, Wernicke's area (BA 22) shows no specialization for speech sounds. Hence, in patients the functional specialization is less marked in both the left posterior superior temporal cortex (BA 42) and Wernicke's area (BA 22). These observations constitute evidence for flexibility in the functional specialization of the language network depending on the subject's experience. The finding that Wernicke's area responded to all types of stimulus implies that the specialization of Wernicke's area for speech and the human voice (Belin *et al*., 2000) relies on experience. This finding also illustrates that Wernicke's area is not specialized for the most refined physical properties of phonological sounds, but responds to much simpler patterns featuring speech, e.g. white noises modulated at syllabic rate (Giraud *et al*., 2000*a*), which are also present in environmental sounds (in particular in animal sounds, which constituted half of our stimuli). Although Wernicke's area is specialized for speech sounds (Binder *et al*., 2000), it is not uniquely driven by the physical nature of speech stimuli (bottom-up mechanism); it is also driven by the expectations of the system (Bischoff-Grethe *et al*., 2000) and when phonological output is required (Wise *et al*., 2001).

Regions activated in patients more than in controls

The left precuneus was more active in patients, suggesting that, in the absence of visual information, they formed a visual representation (Fletcher *et al*., 1995) of the sound sources which (like memory mechanisms) might help task performance. Consistent with this hypothesis, in all patients activation of the parahippocampal gyrus was found with sounds and words but not with syllables. This region interfaces between visual perception and encoding of stimuli (Buffalo *et al*., 1999; McDermott *et al*., 1999; Rombouts *et al*., 1999) and its activation might reflect the increased mnemonic processes associated with items corresponding to known objects that can be imagined. However, as the precuneus and the parahippocampal region were occasionally engaged by controls (activation in these regions was observed in one control), the systematic recruitment of these regions in patients probably reflects the automatization of a mechanism that is flexibly available also to normal subjects according to the individual strategy when faced with task requirements.

Regions activated in controls more than in patients

Several of the classical language-related regions were less activated in patients than in controls. For instance, the controls but not the patients showed significant activation during the word condition in the temporoparietal junctions (BA 22/39) associated with semantic processing (Démonet *et al*., 1994; Engelien *et al*., 1995; Price *et al*., 1997; Gorno-Tempini *et al*. 1998). Similarly, the controls but not the patients showed significant activation in the left inferior frontal cortex (Broca's area) for words, syllables and sounds. Because the patients could perform the naming and repetition tasks without activating either the temporoparietal or the inferior frontal cortices, these regions may be not be necessary for task performance. Indeed, previous studies have shown that it is the insula and not Broca's area (Donnan *et al*., 1999; Poldrack *et al*., 1999) that is critical to repetition (Dronkers, 1994) and that word repetition can also proceed without recall of semantics.

Interindividual variability of these effects was too large to assign them confidently to functional differences between groups. Although further studies are required to verify their significance, our results suggest that when cochlear implant patients engage in effortful acoustic and phonological processing, this is counterbalanced by reduced activation of the linguistic components that are not critical to the task. Difference in age between groups might also contribute to these effects as they were not consistently observed in all patients.

Conclusion

Our findings are consistent with the following account. In cochlear implant patients, the differentiation between speech

and non-speech sounds is decreased in the auditory and association cortices, which are classically dedicated to complex sound analysis and phonological processing. Coarser segregated processing at early levels is compensated by alternative cognitive strategies involving memory, the formation of mental visual representations of objects that normally produce the sound, and an automatic recruitment of visual attentional mechanisms to process concomitant visual cues. Behavioural and imaging data suggest that, rather than going through phonological and semantic processing in a serial manner, as predicted by the classical models of language processing (Caplan, 1992), patients probably go through a series of concurrent and interactive steps before reaching stable sound recognition. These steps involve regions outside the classical language system to decide whether a sound is speech or not, a word or not, can be associated with an object or not, etc. Enhanced and additional early processing steps (prior to recognition) are paralleled by attenuation of later steps, i.e. processing in semantic and speech production regions that is not critical for the specific task requirements of sound recognition.

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References

Belin P, Zatorre RJ, Lafaille P, Ahad P, Pike B. Voice-selective areas in human auditory cortex. Nature 2000; 403: 309–12.

Binder JR, Frost JA, Hammeke TA, Bellgowan PS, Springer JA, Kaufman JN, et al. Human temporal lobe activation by speech and nonspeech sounds. Cereb Cortex 2000; 10: 512–28.

Bischoff-Grethe A, Proper SM, Mao H, Daniels KA, Berns GS. Conscious and unconscious processing of nonverbal predictability in Wernicke's area. J Neurosci 2000; 20: 1975–81.

Büchel C, Price C, Friston K. A multimodal language region in the ventral visual pathway. Nature 1998; 394: 274–7.

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: 572–99.

Caplan, D. Language. Structure, processing, and disorders. Cambridge (MA): MIT Press; 1992.

Corbetta M. Functional anatomy of visual attention in the human brain. Studies with positron emission tomography. In: Parasuraman R, editor. The attentive brain. Cambridge (MA): MIT Press; 1998. p. 95–122.

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: 7426–35.

De Renzi E, Zambolin A, Crisi G. The pattern of neuropsychological impairment associated with left posterior cerebral artery infarcts. Brain 1987; 110: 1099–116.

Démonet JF, Price C, Wise R, Frackowiak RS. Differential activation of right and left posterior sylvian regions by semantic and phonological tasks: a positron-emission tomography study in normal human subjects. Neurosci Lett 1994; 182: 25–8.

Donann GA, Carey LM, Saling MM. More (or less) on Broca. Lancet 1999; 353: 1031–2.

Dronkers NF. A new region for coordinating speech articulation. Nature 1996; 384: 159–61.

Engelien A, Silbersweig D, Stern E, Huber W, Doring W, Frith C, et al. The functional anatomy of recovery from auditory agnosia. A PET study of sound categorization in a neurological patient and normal controls. Brain 1995; 118: 1395–409.

Fletcher PC, Frith CD, Baker SC, Shallice T, Frackowiak RS, Dolan RJ. The mind's eye—precuneus activation in memory-related imagery. Neuroimage 1995; 2: 195–200.

Foundas A, Daniels SK, Vasterling JJ. Anomia: case studies with lesion localisation. Neurocase 1998; 4: 35–43.

Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 1997; 6: 218–29.

Giraud AL, Lorenzi C, Ashburner J, Wable J, Johnsrude, IS, Frackowiak RSJ, et al. Representation of the temporal envelope of sounds in the human brain. J Neurophysiol 2000a; 84: 1588–98.

Giraud AL, Truy E, Frackowiak RS, Grégoire MC, Pujol JF, Collet L. Differential recruitment of the speech processing system in healthy subjects and rehabilitated cochlear implant patients. Brain 2000b; 123: 1391–402.

Giraud AL, Price C. The constraints functional anatomy places on cognitive models of auditory word processing. J Cogn Neurosci. In press 2001.

Gorno-Tempini ML, Price CJ, Josephs O, Vandenberghe R, Cappa SF, Kapur N, et al. The neural systems sustaining face and proper–name processing. Brain 1998; 121: 2103–18.

Griffiths TD, Büchel C, Frackowiak RS, Patterson RD. Analysis of the temporal structure in sound by the human brain. Nat Neurosci 1998; 1: 442–27.

Habib M, Daquin G, Milandre L, Royere ML, Rey M, Lanteri A, et al. Mutism and auditory agnosia due to bilateral insular damage. Role of the insula in human communication. Neuropsychologia 1995; 33: 327–39.

Krauss GL, Ficher R, Plate C, Hart J, Uematsu S, Gordon B, et al. Cognitive effects of resecting basal temporal language areas. Epilepsia 1996; 37: 476–83.

McDermott KB, Ojemann JG, Petersen SE, Ollinger JM, Snyder AZ, Akbudak E, et al. Direct comparison of episodic encoding and retrieval of words: an event-related fMRI study. Memory 1999; 7: 661–78.

McIntosh AR, Cabeza RE, Lobaugh NJ. Analysis of neural interactions explains the activation of occipital cortex by an auditory stimulus. J Neurophysiol 1998; 80: 2790–6.

Morris JS, Friston KJ, Buchel C, Frith CD, Young AW, Calder AJ, et al. A neuromodulatory role for the human amygdala in processing emotional facial expressions. Brain 1998; 121: 47–57.

Mummery CJ, Patterson K, Hodges JR, Price CJ. Functional neuroanatomy of the semantic system: divisible by what? J Cogn Neurosci 1998; 10: 766–77.

Poldrack RA, Wagner AD, Prull MW, Desmond JE, Glover GH, Gabrieli JD. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. Neuroimage 1999; 10: 15–35.

Posner MI. Attention: the mechanisms of consciousness. [Review]. Proc Natl Acad Sci USA 1994; 91: 7398–403.

Posner MI, DiGirolamo GJ. Executive attention: conflicts, target detection and cognitive control. In: Parasuraman R, editor. The attentive brain. Cambridge (MA): MIT Press; 1998. p. 401–24.

Price, CJ, Friston, KJ. Cognitive conjunction: a new approach to brain activation experiments. Neuroimage 1997; 5: 261–70.

Price CJ, Moore CJ, Humphreys GW, Frackowiak RS, Friston KJ. The neural regions sustaining object recognition and naming. Proc R Soc Lond B Biol Sci 1996a; 263: 1501–7.

Price CJ, Wise RJ, Warburton EA, Moore CJ, Howard D, Patterson K, et al. Hearing and saying. The functional neuro-anatomy of auditory word processing. Brain 1996b; 119: 919–31.

Price CJ, Moore CJ, Humphreys GW, Wise RJS. Segregating semantic from phonological processing during reading. J Cogn Neurosci 1997; 9: 727–33.

Price CJ, Green DW, von Studnitz R. A functional imaging study of translation and language switching. Brain 1999a; 122: 2221–35.

Price CJ, Mummery CJ, Moore CJ, Frackowiak RS, Friston KJ. Delineating necessary and sufficient neural systems with functional imaging studies of neuropsychological patients. J Cogn Neurosci 1999b 11: 371–82.

Raymer AM, Foundas AL, Maher LM, Greenwald ML, Morris M, Rothi LJ, et al. Cognitive neuropsychological analysis and neuroanatomic correlates in a case of acute anomia. Brain Lang 1997; 58: 137–56.

Rombouts SA, Scheltens P, Machielson WC, Barkhof F, Hoogenraad FG, Veltman DJ, et al. Parametric fMRI analysis of visual encoding in the human medial temporal lobe. Hippocampus 1999; 9: 637–43.

Sweeney JA, Mintun MA, Kwee S, Wiseman MB, Brown DL, Rosenberg DR, et al. Positron emission tomography study of voluntary saccadic eye movements and spatial working memory. J Neurophysiol 1996; 75: 454–68.

Teissl C, Kremser C, Hochmair ES, Hochmair-Desoyer IJ. Magnetic resonance imaging and cochlear implants: compatibility and safety aspects. J Magn Reson Imaging 1999; 9: 26–38.

Valdois S, Carbonnel S, David D, et al. Confrontation of PDP models and dual-route models through the analysis of a case of deep dysphasia. Cogn Neuropsychol 1995; 12: 681–724.

Vandenberghe R, Price C, Wise R. Josephs O, Frackowiak RS. Functional anatomy of a common semantic system for words and pictures. Nature 1996; 383: 254–6.

Warburton E, Wise RJ, Price CJ, Weiller C, Hadar U, Ramsay S, et al. Noun and verb retrieval in normal subjects. Studies with PET. [Review]. Brain 1996; 119: 159–79.

Wenzel R, Bartenstein P, Dieterich M, Danek A, Weindl A, Minoshima S, et al. Deactivation of human visual cortex during involuntary ocular oscillations. Brain 1996; 119: 101–10.

Wise RJ, Greene J, Büchel C, Scott SK. Brain regions involved in articulation. The Lancet 1999; 353: 1057–1.

Wise RJS, Scott SK, Blank SC, Mummery CJ, Murphy K, Warburton EA. Separate neural subsystems within 'Wernicke's area'. Brain 2001; 124: 83–95.

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.

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