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Increased audiovisual integration in cochlear-implanted deaf patients: independent components analysis of longitudinal positron emission tomography data

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Abstract

It has been demonstrated in earlier studies that patients with a cochlear implant have increased abilities for audio-visual integration because the crude information transmitted by the cochlear implant requires the persistent use of the complementary speech information from the visual channel. The brain network for these abilities needs to be clarified. We used an independent components analysis (ICA) of the activation ($H_2{}^{15}O$) positron emission tomography data to explore occipito-temporal brain activity in post-lingually deaf patients with unilaterally implanted cochlear implants at several months post-implantation (T1), shortly after implantation (T0) and in normal hearing controls. In between-group analysis, patients at T1 had greater blood flow in the left middle temporal cortex as compared with T0 and normal hearing controls. In within-group analysis, patients at T0 had a task-related ICA component in the visual cortex, and patients at T1 had one task-related ICA component in the left middle temporal cortex and the other in the visual cortex. The time courses of temporal and visual activities during the positron emission tomography examination at T1 were highly correlated, meaning that synchronized integrative activity occurred. The greater involvement of the visual cortex and its close coupling with the temporal cortex at T1 confirm the importance of audio-visual integration in more experienced cochlear implant subjects at the cortical level.

Introduction

After more than 30 years of clinical application, the efficiency of cochlear implantation to recover auditory functions in deaf adult patients is now firmly established (UKCISG, 2004; Gaylor *et al.*, 2013). Indeed, a fast rate of progress in auditory speech recovery is observed during the first year after cochlear implantation (Lazard *et al.*, 2012). However, despite considerable recovery of auditory performance through the neuroprosthesis, cochlear-implanted (CI) patients maintain a much higher level of word recognition in speech-reading conditions compared with normally-hearing subjects (NHS) even several years after implantation (Rouger *et al.*, 2007). After implantation and during progressive auditory recovery, speech-reading is maintained at a high level because the crude information transmitted by the cochlear implant requires the persistent use of complementary speech information from the visual channel, especially in noisy situations (Fu & Nogaki, 2005; Qazi *et al.*, 2013; Oxenham & Kreft, 2014). Consequently, due to the multisensory nature of language, patients rely principally on visual and visuo-auditory adaptive strategies for speech comprehension (Barone & Deguine, 2011).

Using the McGurk effect (McGurk & MacDonald, 1976), it has been shown that both child (Schorr *et al.*, 2005) and adult (Rouger *et al.*, 2008; Tremblay *et al.*, 2010) CI patients rely more on visual information in the case of incongruent visuo-auditory speech information. However, in pre-lingually deaf patients, the bimodal fusion classically describing the McGurk effect depends on the age at which the implantation is performed (Schorr *et al.*, 2005), suggesting a sensitive period for the development of audio-visual integration. Similar results have been revealed using non-speech stimuli (Gilley *et al.*, 2010), confirming that, following a long period of deafness in early life, the neuronal processing of visual–auditory information is not fully restored by the cochlear implant. In addition, in the post-lingually deaf, the occurrence of a bimodal fusion during the McGurk effect depends on the duration of experience of the implant (Desai *et al.*, 2008). Taken together, these results tend to show that, in CI patients, the ability to integrate visual and auditory speech information requires some adaptive processes, during which the brain has to recalibrate the distorted auditory information with the visual cues provided by lip movements (Barone & Deguine, 2011).

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The efficiency of these adaptive processes is probably very dependent on the capacity of the brain to reorganize after a long period of deafness, during which the visual channel has colonised the auditory areas devoted to speech processing. Indeed, in pre-lingually deaf children, it is now clearly established that such cross-modal reorganisation proscribes a restoration of auditory speech processing (Lee *et al.*, 2001, 2007; Lazard *et al.*, 2013). However, in post-lingually deaf CI patients, cross-modal reorganisation in auditory areas can be actively reversed as long as the patients are recovering auditory functions (Rouger *et al.*, 2012). Further, after implantation, we documented a mutual feedback between each sensory channel, which allows an improvement in speech intelligibility in both the auditory and visual modalities (Strelnikov *et al.*, 2009). Most importantly, this adaptive visuo-auditory synergy developed by CI patients leads to higher skill levels in multisensory integration (Rouger *et al.*, 2007). The main issue now is to understand how visual and auditory information are merged together in the brain of CI patients. Based on psychophysical studies, we predict in cochlear implant users a specific and progressive synergy between the visual occipital areas and the visuo-auditory temporal areas that contribute to improve a multimodal adaptive strategy. Until now, studies of brain activity and cortical reorganisation have focused primarily on auditory or visual processing of speech (Giraud *et al.*, 2001a; Green *et al.*, 2005; Sandmann *et al.*, 2012), although speech is, by nature, a multisensory mechanism (Vatakis & Spence, 2007). The present positron emission tomography (PET) brain imaging study is aimed at revealing the plastic changes that occur in cochlear implant users during visuo-auditory speech processing.

Due to the incompatibility of the cochlear implant with functional magnetic resonance imaging (fMRI), only a few studies have explored brain activation in cochlear implant users using PET scans (Green *et al.*, 2008). Further, in addition to the technical constraints, the cortical reorganisation induced by a long period of deafness creates some limitations in the evaluation of the functional reorganisation that occurs later during auditory recovery. In a PET study aimed at analysing the resting-state activity of patients (Strelnikov *et al.*, 2010), we found that, compared with the controls, profoundly deaf subjects have higher levels of cerebral blood flow in the visual and temporal auditory cortices. These changes of activity levels during the resting state also affect other areas that are critical in speech processing, such as the pre-motor Broca area as well as the posterior temporal cortex, which lies at the crossroads between the perceptual and semantic integration of audio-visual speech (Hickok & Poeppel, 2007; Hocking & Price, 2008). Such specific increases in brain resting-state levels reflect the adaptive strategy of relatively experienced cochlear implant users for the audio-visual integration of speech, and they are further progressively modified following the reactivation of the auditory system through the cochlear implant. The activity level at rest in these speech-related areas progressively increases during the first months following the activation of the implant. Thus, in relatively experienced cochlear implant users, due to high brain activity at rest in speech-related areas, further activation during a specific speech-driven task would probably be of a limited range and scarcely detectable using conventional analysis. In addition to the limitations imposed by the high activity level of the baseline, several studies have now clearly addressed the issue of relationships between resting-state activity and task-induced activities (Northoff *et al.*, 2010; Mastrovito, 2013). Indeed, in classical analysis, differences between conditions are based on the hypothesis of a linearity of brain activation across conditions, an assumption that has been challenged and referred to as the cognitive subtraction problem (Friston *et al.*, 1996). Consequently, a more adapted method of analysis should be applied, a method that should not be biased by differences in resting-state levels. An alternative to the classical statistical parametric mapping in neuroimaging is independent components analysis (ICA; McKeown *et al.*, 1998). This method allows us to break down a set of brain images obtained during different conditions into a number of spatially independent component maps with their associated activation waveforms. These waveforms are then put into correlation with the experimental protocol in order to reveal those whose activity is related to the experimental events. For example, in a paradigm that includes several different experimental conditions in addition to a resting state, we can select those components where activity changes follow the conditions in a similar way for each subject, whatever the magnitude of these variations. This method excludes the problem of cognitive subtractions (Friston *et al.*, 1996) and allows us to assess the dynamic changes in brain activity with great sensitivity across different experimental conditions. Thus, in order to be able to evaluate the plastic reorganisation that occurs during audio-visual speech processing in CI patients, we applied ICA to the brain activity obtained during four experimental conditions, including the resting state and visuo-auditory speech comprehension tasks. This methodological approach revealed significant peculiarities of the cortical network involved in audio-visual speech processing in CI patients.

Materials and methods

A part of the present study includes a previous protocol (Rouger *et al.*, 2012) aimed at analysing the cortical network involved in visual speech processing in CI deaf patients. However, the participants are presently involved in additional protocols (see below) to apply ICA, which constitutes the originality of the study.

Participants

Ten deaf CI patients (aged 35–81 years, mean 53.9 years, seven women, right-handed) (Table 1) and six NHS (aged 20–49 years, mean 34.2 years, all men, right-handed) were involved in this PET neuroimaging study. The participants in both groups were native French speakers with self-reported normal or corrected-to-normal vision and without any previously known language or cognitive disorders. All CI patients had post-lingually acquired profound bilateral deafness (bilateral hearing loss above 90 dB). In the majority of the patients, the etiologies and durations of deafness were unknown (Table 1). The CI patients were recipients of a unilateral cochlear implant, five on the left side and five on the right side. All participants gave their fully informed consent prior to their inclusion in this study, in accordance with local ethics committees (CPPRB Toulouse I, no. 1-04-47, Toulouse, France). Due to cochlear explantation or technical reasons during the PET scan, nine patients passed the PET exam shortly after implantation (T0) and eight at several months post-implantation (T1) (Table 1). The initial PET data were partly the same as in Rouger *et al.* (2012), but the baseline and audio-visual conditions were added to the analysis in the present study.

The age of the subjects could be an issue as hearing function is affected by aging (Erler & Garstecki, 2002; Seidman *et al.*, 2004; Arpesella *et al.*, 2008; Arehart *et al.*, 2011). However, in our limited sample of CI patients, the performances in word discrimination during scan sessions were not correlated with the age of the patients at either T0 or T1 ($P > 0.1$ for both). Further, our strategy in the

TABLE 1. Characteristics of CI patients in the study

No.	Age (years)	Deafness duration (years)	Sex	Implant	Side	Onset (days)	T0 (days)	T1 (months)	Pre-op. (%)	T0 (%)	T1 (%)
CI02	81	> 20	F	Nucleus CI24	R	31	2	X	20	40	X
CI03	39	> 20	M	Nucleus CI24	R	36	X	10	30	X	70
CI04	39	> 20	F	Nucleus CI24	R	35	8	3	50	40	85
CI06	57	> 20	F	Nucleus CI24	L	27	2	15	20	15	40
CI07	69	> 5	M	Medel	L	29	5	11	25	50	90
CI08	39	> 20	M	Nucleus CI24	L	32	9	X	0	20	X
CI09	62	> 5	F	Clarion	L	34	3	4	55	50	90
CI10	64	> 10	F	Advanced Bionics	L	33	9	8	0	20	60
CI11	54	> 20	F	Nucleus CI24	R	33	15	7	45	50	60
CI12	35	> 20	F	Nucleus CI24	R	31	1	6	10	45	60

Onset indicates the time between cochlear implantation and the implant onset. T0, time of the first PET examination, from implant onset; T1, time of the second PET examination, from implant onset. Due to the variation of about 5% between the time of visits, scores should be considered only approximate.

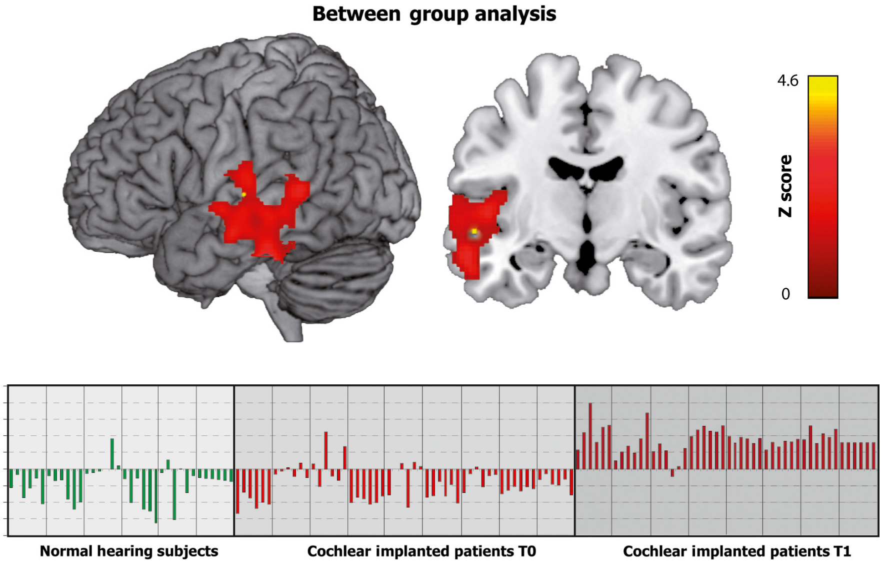

FIG. 1. The peak activity cluster from the between-group analysis in the audio-visual condition. The order of the subject groups is NHS (green bars), T0 and T1 (red bars). There is no difference between NHS and T0 but there is an increase of activity in the T1 group. Each bar corresponds to one image in the audio-visual condition. Activity level per image is shown in arbitrary units where zero is a mean value overall at the given location. The color scale of brain activity indicates *z*-values.

present study was to compare the effect of cochlear implantation with respect to the duration of experiencing the implant during the first months of recovery (T1 vs. T0). In addition, a close inspection of individual data did not seem to reveal any influence of age. Indeed, it can be seen in Fig. 2 that the oldest patient (CI02) had a level and pattern of activity that were similar to all other patients. This is especially illustrative when compared with the youngest patient in our group (CI12). The same applied to her behavioral data. However, to rule out any influence of age, we applied a correlation analysis to the mean peak values observed in individual patients for both the occipital and temporal components (see Results). None of these analyses revealed a significant correlation with age at either T0 or T1 ($P > 0.05$), suggesting that our results were probably not influenced by the aging factor.

Stimuli

The stimuli were French bisyllabic words and meaningless temporally-reversed disyllabic words (non-words) pooled into lists of 40 stimuli each, including 20 words and 20 non-words in random order. The utterances were recorded in a soundproof booth with a professional digital video camera and exported in MPEG2 video format with maximum encoding quality.

Positron emission tomography

The subjects were scanned in a shielded darkened room with their head immobilised and transaxially aligned along the orbitomeatal line with a laser beam, with the position verified before each acquisition. Measurements of the regional distribution of radioactivity were performed with an ECAT HR+ PET camera (Siemens®) with full volume acquisition (63 planes, thickness 2.4 mm, axial field of view 158 mm, in-plane resolution ≈ 4.2 mm). The duration of each scan was 80 s, and about 6 mCi of $H_2{}^{15}O$ was administered to each subject for each individual scan using an automatic injector. There were two runs per condition. Three images were acquired during each run, and eight runs resulted in 24 images per subject.

In each scan, stimulation on the experimental conditions was started at ≈ 20 s before data acquisition and continued until scan completion. Experiment instructions were given to subjects before each tomography and repeated before each scan.

Procedure

Each CI patient was scanned twice. The first tomography (T0) was performed as early as possible after the implant onset. The second tomography (T1) was performed as soon as the patient's auditory speech performance had reached a recognition level in the normal range (Rouger *et al.*, 2007). In the present set of patients, their percent of auditory word recognition was 70 ± 16% (SD) at the time of the second tomography. The words used for testing the patients were disyllabic words classically used by French speech therapists from the Fournier list. They were presented at a comfortable level of about 65 dB.

The following stimulation conditions were used during each PET: rest (R), motor control task (MC), visual speech discrimination task (V) and audio-visual speech discrimination task (AV). An auditory-only condition would also be interesting and has been the aim of most of the previous studies performed in cochlear implant users (for review, see Strelnikov *et al.*, 2014). However, due to the legislative limitations for the radioactive load, the inclusion of this condition was not possible in the present protocol. Based on our previous studies (Rouger *et al.*, 2007) that revealed a strong audio-visual integration in CI patients during progressive recovery, we prioritized specifically a condition of a natural audio-visual speech task.

All of the conditions were performed consecutively in the first run and then repeated in the second run. Thus, there were two runs per condition and the whole study of four conditions included eight runs. In contrast to the classical activity analysis, in the ICA approach randomization of runs is not an important issue because it searches for the correlated variability in time between the patients. We arranged the conditions for each subject in the same order of the addition of cognitive components, i.e. R, MC, V and AV. This uniform approach permitted a diminishment in the variability in time between the subjects.

During the rest condition, subjects lay in the camera with their eyes closed and without any auditory stimulation. The motor control condition consisted of presenting the photographs of the speech therapist in the correct or upside-down position. The subject was to indicate the correct or incorrect position of the picture using mouse buttons; this condition was used to exclude motor activities and factors that are non-specific to speech processing. The visual speech condition was speech-reading; both words and non-words were presented in the visual modality without any auditory stimulation. The audio-visual speech condition consisted of presenting videos with sound. In both the visual and audio-visual speech conditions, subjects had to identify whether or not they recognised the words by using a two-button computer mouse (two-alternative forced choice). The presentation rate was 5 s/word, including visual presentation of the word (about 1000 ms per word including pre-rest and post-rest times) followed by a black screen with a white fixation cross in its centre. The presentation screen was fixed on the PET camera and the sound intensity was fixed at a level of about 60 dB sound pressure level. The order of the presented stimuli in each behavioral task was randomised between the subjects. Patient 3 at T0 and patients 2 and 8 at T1 were excluded from the analyses at corresponding time points due to technical problems with the PET camera leading to poor quality of images (CIP 2 and CIP 3) or due to cochlear explantation cause by an inflammation (CP8).

Data analysis

The neuroimaging data were first analysed with SPM2 software including the standard procedures for image pre-processing (realignment, spatial normalisation to the Montreal Neurological Institute brain template, smoothing with 8 mm isotropic Gaussian kernel), model definition and statistical assessment.

Two types of SPM design matrix were constructed. One type was for group comparison and comprised groups of subjects as regressors: NHS, T0 (neo-user patients) and T1 (relatively experienced patients). Such a matrix was constructed separately for the images from the visual and audio-visual conditions.

Another SPM design matrix was used for within-group analysis and comprised four regressors corresponding to four conditions of the study. Such a matrix was constructed separately for the NHS, T0 and T1 groups of subjects with proportional scaling. The SPM matrices were used only to set regressors for the images entered into the ICA.

The ICA was realised with the Group ICA toolbox GIFT (http://mialab.mrn.org/software/) in MATLAB. The Fast ICA stabilized algorithm was used, and the number of independent components was taken to be equal to 24 in within-group analysis and 50 in between-group analysis, with regular back reconstruction and z-scores as scaling components. In the algorithm of the GIFT toolbox, principal components analysis, covariance matrix calculation and eigen decomposition are implemented prior to the ICA. Multiple regression of activity in the extracted components with regressors from the SPM design matrix were assessed using the r^2 value at $P < 0.01$.

Our initial hypothesis was that the strong visuo-auditory synergy that occurs in cochlear implant users during progressive recovery relies on a strong synergy between the occipital and temporal visuo-auditory areas. Consequently, we selected the components where the maximum activity was in the occipital BA (Brodmann areas) (BA17, 18 and 19) and temporal (BA20–22, 41, 42, 37 and 38) regions. The component with the highest r^2 value at the peak was selected in each of these two regions.

The study conformed to the 2013 WMA Declaration of Helsinki.

Results

Behavioral results

The mean performance of the patients in the PET camera for the visual word recognition was 65.5 ± 10.9% at T0 and 65.9 ± 9.6% (SD) at T1; no significant difference was observed between the two stages post-implantation (paired t-test, $P > 0.6$). Concerning NHS, their performance for the visual word recognition was 56.0 ± 8.6%. This level of performance did not differ from chance (binomial test, $P > 0.3$), which was in our case 50% given 50% of words in the lists. Using signal detection theory, the d' values in CI patients were significantly higher than those observed in NHS (0.95 ± 0.7 vs. 0.29 ± 0.5, Mann–Whitney U-test, $P < 0.01$).

As for the audio-visual word recognition, the mean performance of the patients in the PET camera was 80.4 ± 10.0% at T0 and 89.4 ± 10.0% (SD) at T1. In this case, there was a significant increase of performance between the two stages post-implantation (paired t-test, $P < 0.02$). The audio-visual scores in controls were 100%. The Kruskal–Wallis test across the three groups of subject revealed a significant group effect on the audio-visual score ($P < 0.01$); the controls were significantly superior to the patients at T1 and T0 (Mann–Whitney U-test, $P < 0.01$). We did not find an effect of the implantation site on any of the behavioral scores. There were no significant correlations of behavioral scores with age and no effect of gender was found on these scores.

Neuroimaging results

Between-group analysis

We first applied ICA methods to investigate whether there was a difference between the groups of normal subjects and patients at the early (T0) and later (T1) stages post-implantation. The between-group analysis was performed for each stimulation condition (MC, V and AV) and R, and images from all of the groups were collectively submitted to ICA. As a result, in the between-group analysis, we observed a statistically significant difference for the AV word discrimination task (Fig. 1); the component presented a maximum in the left middle temporal region (coordinates: −60, −10, −2, $r^2 = 0.65$; Table 2). To confirm the group effect in this AV condition, we applied an ANOVA analysis on the activity at the peak of the temporal component; the between-group effect was highly significant ($P < 0.0001$, $F_{2,135} = 130.79$). Because three patients were not included in the experimental protocols (see above), at both the T0 and T1 time points, the repeated-measures analysis of the patients' PET data was not possible. It is of importance that we did not observe a significant difference between NHS and patients at the time of implant activation (T0; $P = 0.96$) but the difference was significant between NHS and patients at T1 ($P < 0.0001$) as well as between the two post-implantation evaluation periods at T0 and T1 ($P < 0.0001$). We used unpaired *t*-tests because not all of the patients had successful PET scan sessions at both the T0 and T1 time points. These results showed that the global between-group effect was caused by a higher visuo-auditory activity at T1, which differed from that observed in controls and at the end of the deafness period. Other significant components in this analysis had peaks outside our regions of interest, i.e. in the frontal and parietal cortex. These peaks could be explained by the higher cognitive load to decipher the sound degraded by the implant and also the related attentional processes. No significant peaks were found in the regions of interest for other conditions in the between-group analysis. We did not find the effect of implantation site on brain activity at T0 or T1.

Within-group analysis

Having established the differential activity between the groups, we proceeded with an analysis within each group (NHS, patients at T0 and T1) in the occipital and temporal region of interest. For each group, we searched for any component in which the activity was correlated with the sequence of the experimental conditions (R, MC, V and AV). In the within-group analysis, components of interest correlated with conditions were found only in CI patients and this was true at the two periods of evaluation T0 and T1. We did not observe any significant components in NHS with peaks in the temporal and occipital regions. However, we observed numerous significant components that largely covered these two regions of interest but had peaks outside these regions. For example, the ICA revealed a component that covered a large region, including the occipital pole and cerebellum, with a peak between them. However, this peak presented stronger activity during the MC than during the V and AV conditions. The location of this peak and its association with the visuo-motor task excluded the component from our focus of interest in the processing of visuo-auditory speech information. In consequence, we have excluded the component presenting such features from our analysis.

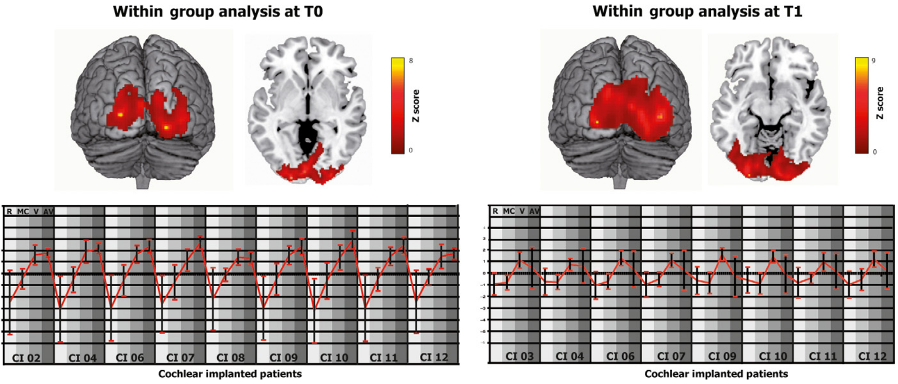

FIG. 2. The peak occipital activity cluster correlated with task in the cochlear implant users at T0 and T1. Left – occipital activity at T0. Right – occipital activity at T1. The mean activity per condition is presented for each subject, and the order of conditions per subject is as follows: R, MC, V and AV. The set of these four conditions constitutes one subject. Error bars represent SDs. Conventions as in Fig. 1.

TABLE 2. Activity at the peaks of the independent components

Region	*x* axis (mm)	*y* axis (mm)	*z* axis (mm)	r^2	*F* (ANOVA)
Group effect in the AV condition					
L middle temporal (BA22/21/37)	−60	−10	−2	0.65	130.79
Condition effect in the T0 group					
L middle occipital (BA17/18/19)	−22	−100	−2	0.86	120.47
Condition effect in the T1 group					
L middle temporal (BA22/21/37)	−62	−12	−2	0.65	29.7
L lingual (BA17/18/19)	−28	−98	−10	0.50	38.7

In patients at T0, a significant component was observed bilaterally in the occipital region with a maximum in the left middle occipital visual region covering BA17/18/19 (Table 2, Fig. 2) and a sub-maximum in the right middle occipital region (coordinates: 16, −102, 12, $r^2 = 0.86$) with a similar spread. To test the effect of conditions on the peak of this occipital component, we applied a repeated-measures ANOVA comparison that yielded significant differences between the four conditions ($P < 0.0001$, $F_{3,159} = 170.4$).

The ICA for patients at T1 revealed two significant components. The first covered a large temporal region in the left hemisphere that included parts of BA22/21/37 (Table 2, Fig. 3). The maximum was located in the left middle temporal region (coordinates: −62, −12, −2, $r^2 = 0.45$). A second set of clusters emerged in patients at T1; it presented a bilateral distribution with a maximum in the left lingual region of the occipital pole (coordinates: −28, −98, −10) and a sub-maximum in the right occipital inferior region (coordinates: 24, −96, −4, $r^2 = 0.50$). The two clusters covered the visual areas BA17/18/19 (Table 2, Fig. 2). The repeated-measures ANOVA comparisons of activity during the conditions yielded significant differences for both the left temporal region ($P < 0.0001$, $F_{3,141} = 31.3$) and left lingual region ($P < 0.0001$, $F_{3,141} = 41.7$).

Comparisons and correlation analysis

The ICA performed within the patients at T1 and T0 revealed two components located in the visual occipital cortex, which might correspond to the same cortical region. Indeed, the overlap of the occipital clusters between T1 and T0 was 90% with respect to T1 and the Euclidian distance between the peaks of these clusters was 10 mm. This analysis demonstrating a large spatial overlap between the occipital clusters strongly suggested that the same region was involved in patients at T0 and T1.

In the between-group (AV condition) and within-group (patients at T1) analysis, two left temporal clusters emerged from the ICA. A specific analysis of the overlap between these two clusters showed that the spatial extent of the left temporal cluster in T1 had a 50% overlap with that obtained in the between-group effect. The Euclidian distance between the peaks of these two temporal clusters was < 3 mm, a value that is within the smoothing of 8 mm. Thus, there was a high coincidence of peaks for the two temporal clusters.

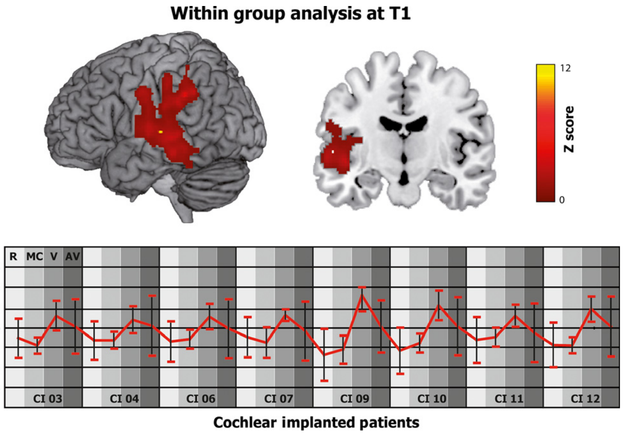

FIG. 3. The peak activity cluster correlated with task in the cochlear implant users at T1, the temporal activation. The mean activity per condition is presented for each subject, and the order of conditions per subject is as follows: R, MC, V and AV. The set of these four conditions constitutes one subject. Error bars represent SDs. Conventions as in Fig. 1.

Concerning the strength of the peaks, as can be seen from Table 2, the highest *F*-values were observed in the left temporal region in the between-group comparison. The *F*-values for the left temporal peak were much lower in the within-group analysis at T1. In addition, the *F*-values were also lower at T1 for the occipital peak compared with the *F*-values for the occipital peak at T0. A relative decrease in the strength of the peaks at T1 may have been due to the variability of neural mechanisms employed by the relatively experienced CI patients.

The ICA methods revealed two regions, one occipital and one temporal, that emerged from the within-group analysis in relatively experienced CI patients at T1. To assess whether the two components observed at T1 were functionally correlated during the experimental conditions, we performed a correlation analysis taking the respective activity at the peak obtained in each sessions (R, MC, V and AV) and across all patients. This analysis led to a highly significant *r*-value of 0.92 ($P < 0.001$; Fig. 4) meaning that the occipital and temporal components covaried with the tasks in the same direction. As some studies reported gender-related differences in brain activity during lip-reading (e.g. Ruytjens *et al.*, 2006), we examined the possible effect of gender on the observed peaks but found no significant effect. We also examined each peak of activity for the correlation with age and for the effect of implantation side, but no such effects were found. Also, no correlations of activity with behavioral scores were found.

Discussion

We originally applied ICA to PET data to analyse the cortical activity during visual and visuo-auditory speech processing in cochlear implant deaf patients. Based on the specific skills in visuo-auditory integration described in CI patients (Barone & Deguine, 2011), we expected to observe some modifications in the normal cortical network involved in integrating visual and auditory speech information. Using ICA in between-group analysis, we showed that relatively experienced patients had greater activity in the left middle temporal cortex compared with neo-users and controls. In within-group analysis of relatively experienced patients, a spatially independent task-related component was also observed in the left middle temporal cortex. Patients at both time periods after implantation had a task-related component in the visual cortex. The time course of temporal and visual activity in relatively experienced patients was tightly coupled. This coupling suggested that visuo-auditory synergy was crucial to adjust cross-modal plasticity, which is necessary for the recovery of speech comprehension in adult CI patients.

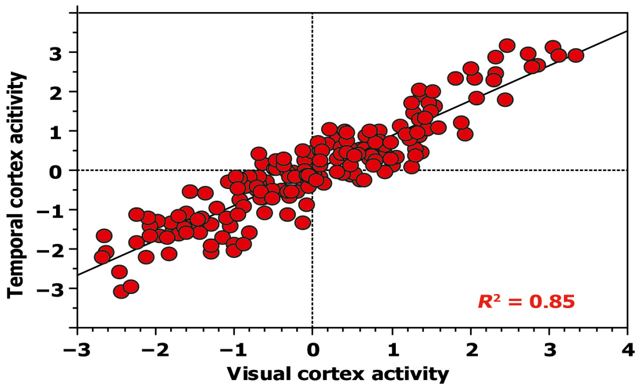

FIG. 4. Relations of the visual cortex activity with left temporal activity in the T1 group.

Occipital and temporal activity in cochlear-implanted patients

An interesting result that emerged from the ICA was a systematic involvement of the visual occipital region in CI patients at both T0 and T1. We propose that the involvement of the visual cortex is related to the role of speech-reading during deafness (T0 component) and during recovery after implantation (T1 component). The independent component involves similar locations at T0 and T1 that include low-level visual areas. Although the spatial extent of the component is large, it mainly corresponds to the central visual field representation and thus probably conveys the representation of the foveal gaze (Schira *et al.*, 2009). This component is probably functionally related to the specific oculomotor strategy developed by deaf subjects for speech-reading (Watanabe *et al.*, 2011). Indeed, speech-reading is the visual compensatory strategy developed by profoundly deaf patients to recover a degree of speech comprehension (Tyler *et al.*, 1997; Kaiser *et al.*, 2003). At the time of implantation, and following a long period of deafness, CI patients develop skills in speech-reading that exceed those observed in NHS. Although some studies report only mild improvement in speech-reading performances after implantation (Gray *et al.*, 1995; Bergeson *et al.*, 2005), there is strong evidence that such a strategy is maintained across time in spite of auditory recovery (Giraud *et al.*, 2001b; Rouger *et al.*, 2007). One reason for preserving the high speech-reading ability is that it contributes to bisensory integration, which improves speech recognition in noisy environments, a challenge for the majority of cochlear implant recipients (Fu *et al.*, 1998). This clearly explains the finding of two clusters emerging in the visual cortex, at both early and late stages after cochlear implantation but not in NHS.

The second important finding is that, in addition to the occipital components, a component in the left temporal cortex turned out to be specific to relatively experienced patients (at T1) in both the between-group and within-group analyses. Further, ANOVA analysis confirmed that the activity in the left temporal area at T1 was higher than that observed at T0, which was at the same level as in NHS. As can be seen in Figs 1 and 3, the cluster covers a large part of the left temporal cortex in its middle and posterior portions, including the auditory cortex in the depth of the lateral fissure. The peaks of the clusters are situated in the middle STG/STS (superior temporal gyrus/superior temporal sulcus), which has been shown to be more active in audio-visual speech than to separate auditory and visual components (Wright *et al.*, 2003). Further, this cortical region is also specifically activated during the matching of auditory and visual stimuli in verbal conceptual processing (Thierry & Price, 2006; Hocking & Price, 2009). Thus, its role consists of mapping the auditory and visual speech information, providing the integrative audio-visual concept. Hence, we hypothesise that the higher activity in the temporal cortex in CI patients at T1 reflected the supranormal (compensatory) audio-visual speech processing described in these patients (Rouger *et al.*, 2007; Barone & Deguine, 2011). The higher activity level observed in the temporal and occipital areas at T1 emphasised the increased cross-modal interplay that takes place in relatively experienced CI patients. This is consistent with the cross-modal activations of low-level visual areas during auditory speech perception in CI patients (Giraud *et al.*, 2001b).

Visual and audio-visual integration in cochlear-implanted patients

Until now, due to the technical limitations imposed by the cochlear implant, only a few brain imaging studies have been performed in CI patients and most of them have emphasised the mechanisms by which the deaf brain processes auditory speech (Lazard *et al.*, 2013). These studies are of importance as they provide evidence of a progressive reactivation of the auditory system by speech sounds (Green *et al.*, 2005; Mortensen *et al.*, 2006). Further, there are indications of brain adaptation to the electrical signal expressed as increased phonological rather than semantic processing in auditory cortical areas (Giraud *et al.*, 2000). When ICA was applied to longitudinal PET data, two cortical regions emerged, the occipital visual cortex and the temporal multisensory areas. The crucial finding concerns the strong correlation between the temporal and visual cortices related to the experience with a cochlear implant. The positive correlation suggests a functional coupling that involves visual and visuo-auditory integration of speech. This coupling may be progressive as long as the patients are experiencing the implant because, in the first months post-implantation, the patients rely more strongly on the visual modality. Later, during auditory recovery, the dominant visual processing is progressively replaced by a bimodal visuo-auditory integration of speech. Indeed, during the first months post-implantation, AV speech comprehension increased significantly to reach a plateau during the first year (Rouger *et al.*, 2007), and such improvement was also visible in the present limited set of patients. However, the non-speech visual takeover in the auditory cortex may interfere with speech recovery (Sandmann *et al.*, 2012).

At T0, the occipital activity in the AV condition is nearly the same as, or in some patients higher than, in the V condition (Fig. 2). If one considers the occipital activity at T1 (Fig. 4), it is higher in each patient in the V condition than in the AV condition, meaning that this area has become more specific to visual perception. However, a supplementary area appears in the posterior temporal region (Fig. 3), which is very similar to the occipital region changes of blood flow between the conditions. Thus, one can conclude that there is a redistribution of blood flow between the occipital and temporal regions at T1 in the V and AV conditions.

We propose that the revealed functional coupling that concerns the visual occipital and visuo-auditory temporal regions reflects, at the neuronal level, the compelling visuo-auditory synergy on which is based the recovery of speech comprehension in CI patients. First, as expected given the classical perceptual benefit derived from multisensory integration, relatively experienced CI patients achieve higher performance in audio-visual conditions compared with auditory-alone conditions (Rouger *et al.*, 2007). It is of importance that a visuo-auditory synergy can lead to the improvement in unimodal speech processing, either auditory or visual. Indeed, audio-visual practice allows a significant increase in perceptual performance in a single modality alone (Frassinetti *et al.*, 2005; Seitz *et al.*, 2006; Strelnikov *et al.*, 2011). Our recent study demonstrated an increase in speech-reading skills in CI patients during the first months of experience of the implant (Strelnikov *et al.*, 2009), suggesting that a strong positive feedback consolidates the decoding of visual cues with auditory information resulting in an increase in speech-reading performance. A similar positive visuo-auditory loop participates in the progressive increase in auditory speech performance in the first months after implantation.

Independent components analysis and classical activations

Due to the interference of the implant with magnetic fields, fMRI studies of CI patients are not possible and PET scan imaging remains the principal method to investigate the brain activity in these patients. Although ICA is already used in fMRI (for review, see Calhoun *et al.*, 2009), to our knowledge, this is the first study that applies ICA to the $H_2{}^{15}O$ activation PET data. Although the spatial resolution of PET is slightly weaker, it has a higher signal-to-noise ratio compared with fMRI (Votaw, 1996), which permits patterns of neural activity to be obtained that are more reliable than in fMRI.

Using the classical SPM paradigm on the same group of subjects with the rest condition subtracted from the stimulation condition, we previously found a difference between T0 and T1 in the right temporal region during speech-reading (Rouger *et al.*, 2012). The classical SPM paradigm is unsuitable to test the difference between T1 and T0 for audio-visual stimulation, which can be related to the increase of the audio-visual network activity at rest in T1 patients (Strelnikov *et al.*, 2010). The present method found a component with a significant group effect in the audio-visual condition with the peak in the left temporal region.

The comparison of the results from different analyses of the same PET images provides a valuable example that demonstrates the complementarities of the two approaches to the neuroimaging data. Spatial ICA finds systematically non-overlapping, temporally coherent brain regions, whereas the classical SPM approach has no spatial criteria but uses strictly voxel-wise statistics. Both voxel-wise and spatial criteria are appropriate in the consideration of brain activity and provide complementary points of view as shown by our results. They suggest that brain activity can be differently modulated by the visual and audio-visual processing at both the level of the activity intensity and the level of its spatial organisation. The combination of the two approaches helps to better understand the diversity of the stimulation-processing strategies in the brain.

Conclusions

The present data establish the neural underpinnings of high audio-visual integration in relatively experienced CI patients by demonstrating the existence of the specific brain network of audio-visual integration with a tight coupling of activity in the visual and auditory cortices. The peculiarities of brain reorganisation in CI patients reflect the adaptive processes of two origins: first, a long-term adaptive mechanism induced by the long period of hearing loss, and second, a comparatively short-term adaptive process corresponding to the reactivation of the auditory system. In both cases, intramodal (visual) and cross-modal (visuo-auditory) reorganisation are crucial in the success of recovery through the cochlear implantation.

From the clinical point of view, this work provides important cues to adapt for clinical rehabilitation strategies after cochlear implantation. The high skills in multisensory integration observed in CI patients should be used to improve the recovery of other auditory functions that are still deficient in cochlear implant users. As visuo-auditory training facilitates perceptual learning in a single modality, we believe that a strong visually- and audio-visually-based rehabilitation during the first months after implantation would significantly improve and hasten the functional recovery of speech intelligibility.

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Abbreviations

AV, audio-visual speech discrimination task; BA, Brodmann areas; CI, cochlear-implanted; fMRI, functional magnetic resonance imaging; ICA, independent components analysis; MC, motor control task; NHS, normally-hearing subjects; PET, positron emission tomography; R, rest; T0, shortly after implantation; T1, several months post-implantation; V, visual speech discrimination task.

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