Reorganization of Auditory Cortex in Early-deaf People: Functional Connectivity and Relationship to Hearing Aid Use

Martha M. Shiell[1,2,3], François Champoux[2,3,4,5], and Robert J. Zatorre[1,2,3]

Abstract

■ Cross-modal reorganization after sensory deprivation is a model for understanding brain plasticity. Although it is a well-documented phenomenon, we still know little of the mechanisms underlying it or the factors that constrain and promote it. Using fMRI, we identified visual motion-related activity in 17 early-deaf and 17 hearing adults. We found that, in the deaf, the posterior superior temporal gyrus (STG) was responsive to visual motion. We compared functional connectivity of this reorganized cortex between groups to identify differences in functional networks associated with reorganization. In the deaf more than the hearing, the STG displayed increased functional connectivity with a region in the calcarine fissure. We also explored the role of hearing aid use, a factor that may contribute to variability in cross-modal reorganization. We found that both the cross-modal activity in STG and the functional connectivity between STG and calcarine cortex correlated with duration of hearing aid use, supporting the hypothesis that residual hearing affects cross-modal reorganization. We conclude that early auditory deprivation alters not only the organization of auditory regions but also the interactions between auditory and primary visual cortex and that auditory input, as indexed by hearing aid use, may inhibit cross-modal reorganization in early-deaf people. ■

INTRODUCTION

After sensory deprivation, the brain can reorganize so that the deprived sensory cortex increasingly processes stimuli from other modalities (for a review, see Frasnelli, Collignon, Voss, & Lepore, 2011). In early-deaf people, auditory regions, including the planum temporale (PT; Sadato et al., 2005; Petitto et al., 2000) and primary auditory cortex (Karns, Dow, & Neville, 2012; Fine, Finney, Boynton, & Dobkins, 2005; Finney, Fine, & Dobkins, 2001), are responsive to visual motion stimuli. Although this phenomenon is well established, we know little about the neural mechanisms that underlie this plasticity and the factors that constrain or promote it.

In the current study, we tested people with early deafness varying from profound to severe using fMRI to achieve three goals. The first was to document the location and extent of audiovisual cross-modal reorganization. We used a functional localizer in hearing controls to identify auditory-responsive cortex and compared activation to visual motion in deaf and hearing groups within these regions. On the basis of previous research (Karns et al., 2012; Fine et al., 2005; Sadato et al., 2005; Finney et al., 2001; Petitto et al., 2000), we predicted that deaf people would show visually evoked activity in auditory regions.

The second goal was to investigate possible sources of visual input to reorganized auditory cortex using functional connectivity analysis. This technique examines how functional networks of the brain change under different circumstances. This approach has been used to suggest mechanisms of reorganization in blind people (Collignon et al., 2011; Bedny, Konkle, Pelphrey, Saxe, & Pascual-Leone, 2010; Klinge, Eippert, Roder, & Buchel, 2010; Yu et al., 2008; Liu et al., 2007). It has previously been applied in deaf people to examine interactions within the temporal cortex (Li et al., 2013) and between visual and parietal cortices (Bavelier et al., 2000), but it has not been used to examine the network associated with cross-modal reorganization. In this study, we tested functional connectivity of reorganized auditory cortex to identify candidate areas for the source of cross-modal information. Potential pathways include feedback connections from association areas, direct connections between sensory cortices, and feedforward connections from the thalamus (for a review, see Bavelier & Neville, 2002).

The third goal was to investigate factors that contribute to cross-modal reorganization. Previous research shows that reorganization varies as a function of duration and age of acquisition of deafness (Li et al., 2013; Sadato,

[1]Montreal Neurological Institute, McGill University, [2]BRAMS: International Laboratory for Brain, Music, and Sound Research, Montreal, Canada, [3]CRBLM Centre for Research on Brain, Language, and Music, Montreal, Canada, [4]Université de Montréal, [5]Centre de Recherche Interdisciplinaire en Réadaptation du Montréal Métropolitain–Institut Raymond Dewar

Journal of Cognitive Neuroscience 27:1, pp. 150–163
doi:10.1162/jocn_a_00683

Yamada, Okada, & Yoshida, 2004; Lee et al., 2003) and early language experience (Hirano et al., 2000). To our knowledge, with the exception of one study that looked at reorganization related to sign language use (Lambertz, Gizewski, de Greiff, & Forsting, 2005), no research has examined the effect of residual hearing on reorganization. If cross-modal reorganization is dependent on auditory deprivation, then the degree of cross-modal reorganization will vary according to the degree of auditory deprivation or, reciprocally, the degree of auditory input. One index of auditory input over the lifetime is the number of years during which a person used a hearing aid. We hypothesized that hearing aid use would inhibit cross-modal reorganization of auditory regions, such that deaf people with shorter durations of hearing aid use would show greater reorganization as compared with those with longer durations.

METHODS

Participants

Seventeen early-deaf and 17 hearing controls (6 men, 28 women; mean age = 32.1 years) participated in the study. The groups were matched for age, sex, and handedness. For the deaf participants, information on history of hearing loss, hearing aid use, and sign language use was documented through an interview (Table 1). Participants self-reported their level of hearing loss (profound or severe) based on their audiologists' diagnoses. "Profound" and "severe" are clinical classifications that typically correspond to an average loss for sounds greater than 90 and 70 dB hearing loss (HL), respectively (Harrell, 2002). Ten of the deaf participants reported profound hearing loss since birth, and an eleventh became profoundly deaf at the age of 10 months because of meningitis. The other six deaf participants reported severe hearing loss since birth. In 10 of the 17 deaf participants (seven with profound and three with severe deafness), we additionally tested hearing thresholds (see Methods section 3: Audiological Testing).

All of the deaf participants used a hearing aid at some point during their lifetimes, either because it was introduced by the parents or because it was mandatory while attending public school. Two severely deaf participants did not begin hearing aid use until adulthood. Seven of the profoundly deaf participants stopped using their hearing aids when they left the schools at which they

Table 1. Deaf Participant Characteristics

Code	Age (years)	Age (years) HA Use		Duration HA Use (% Lifetime)	Reported Hearing Loss (dB)	Primary Language
		Start	Stop			
1	30	5	18	43.3	Profound (95.8)	LSQ
2	30	4	12	26.7	Profound	LSQ
3	23	1.5	23	93.5	Profound (95.8)	LSQ
4	51	5	30	49.0	Profound	LSQ
5	26	2	7.5	21.2	Profound (96.7)	LSQ
6	24	4	12	33.3	Profound (96.7)	LSQ
7	23	5	12	30.4	Profound (96.7)	LSQ
8	34	6	13	20.6	Profound (94)	LSQ
9	28	3	28	89.3	Profound (94)	French
10	45	3	44	91.1	Profound	French
11	44	5	Continued	88.6	Profound	LSQ
12	27	6	Continued	77.8	Severe (73)	French
13	37	24	Continued	35.1	Severe	Bulgarian
14	28	4.5	Continued	83.9	Severe	French
15	23	3.5	Continued	84.8	Severe	French
16	43	23	Continued	46.5	Severe (83.75)	French
17	33	12	Continued	63.6	Severe (75)	French

This information was reported by participants. Primary language refers to the language that participants used in their lives during the time of testing, and it does not exclude experience with other languages. For participants in whom we tested hearing thresholds with audiometry (see Methods section), the average threshold in decibels HL is reported in brackets. LSQ refers to *Langue des Signes Québécoise*, the regional sign language. HA = Hearing aid.

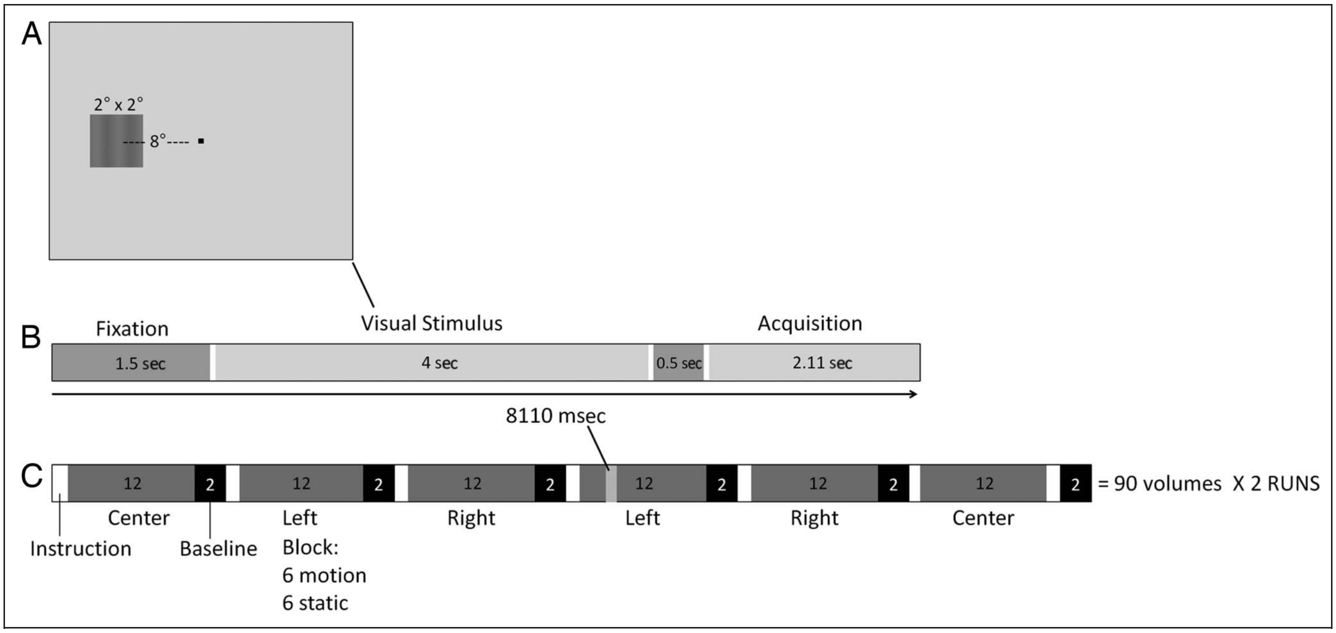

Figure 1. Schematic diagram of the visual fMRI scan. (A) An example stimulus in the left visual field. The lines of the grating moved to the left, right, or remained stationary. (B) A single sparse-sampling trial. (C) The distribution of trials within a run. Stimuli within each visual field (center, left, right) were presented in separate blocks, and motion and static trials were randomly ordered within a block.

had been required to wear them. Three of the profoundly deaf participants and all of the severely deaf participants continued using the hearing aid consistently into adulthood. A fourth profoundly deaf participant used a hearing aid periodically throughout adulthood.

Stimuli and Procedure

The experiment was approved by the ethics review board at the Montreal Neurological Institute. All participants gave informed written consent. For deaf participants who used sign language, a sign language interpreter translated the experimenter's instructions.

Visual fMRI Scan

Previous research shows that neural differences in sensory processing between deaf and hearing people occur for visual motion stimuli (Armstrong, Neville, Hillyard, & Mitchell, 2002). Recent research also indicates that deaf people have enhanced motion detection abilities (Shiell, Champoux, & Zatorre, 2014), as do deaf cats, in whom it has been shown that the enhancement is dependent upon cross-modal activity in the auditory cortex (Lomber, Meredith, & Kral, 2010). On the basis of these data, we designed visual stimuli consisting moving and stationary grayscale sinusoidal gratings (grating size: 2° × 2°, spatial frequency: 1 cycle/degree) with a central fixation cross (0.5° × 0.5°) on a gray background, presented via a projector and mirror system. In each trial, a single grating appeared for 4 sec in either the center, left, or right visual field. The peripheral stimuli were centered 8° to the left or the right from fixation. The temporal frequency of the grating varied such that the lines of the grating appeared to move either leftward or rightward at approximately 1.56°/sec or to remain stationary. An example stimulus is shown in Figure 1.

Scanning occurred on a 3-T Siemens Trio scanner with a 32-channel head coil at the McConnell Brain Imaging Center of the Montreal Neurological Institute. Participants completed two runs of fMRI with visual stimuli. The fMRI runs were separated by a 40-min series of anatomical scans, including a T1-weighted scan (1.0 × 1.0 × 1.0 mm^3 resolution, 176 slices, 256 × 256 matrix, repetition time/echo time = 2300/2.98) which was used for registration. We measured BOLD signal with T2*-weighted gradient echo-planar images (40 slices in an interleaved order, repetition time = 8.11 sec, echo time = 30 msec, voxel size = 3.4 × 3.4 × 3.4 mm^3, matrix size = 64 × 64). Unlike previous studies looking at cross-modal reorganization in the deaf, we chose a sparse-sampling design (Figure 1; Belin, Zatorre, Hoge, Evans, & Pike, 1999; Hall et al., 1999). This design allows for two improvements on previous studies: first, it mitigates the risk that any weak cross-modal activity in the hearing group will be lost among the strong auditory cortical response to the scanner noise, and second, it ensures that any auditory cortex activity measured in the deaf group is not related to vibration of the scanner (Auer, Bernstein, Sungkarat, & Singh, 2007; Levanen, Jousmaki, & Hari, 1998).

The time course of the experiment is illustrated in Figure 1. For each of the visual fMRI runs, we collected 90 volumes, separated into six blocks: two blocks for stimuli in each of the left, center, and right visual fields, with 12 trials in each block. Blocks were preceded by an instruction screen and separated by two baseline trials, during which participants maintained fixation and no grating was presented. Within each block, motion and static trials (six trials for each) were presented in a random order. For each trial, participants fixated the cross, and the grating appeared after 1.5 sec. To ensure that participants attended to the stimuli, we asked them to use a three-button response pad to indicate the type of stimulus presented: either leftward motion, rightward motion, or no motion. This simple task design was chosen to ensure equal performance between groups, thus eliminating the potential confound of behavioral differences when comparing brain activity. Responses could be made at any time after the onset of the grating and before the end of the image acquisition. Image acquisition (2.11 sec) began 0.5 sec after the grating disappeared. We used Presentation software (www.neurobs.com/) to record responses and synchronize the trials with MRI acquisition.

Auditory Localizer fMRI Scan

After the second run of the visual task, hearing participants completed an auditory localizer fMRI scan. This scan consisted of 10 different 8-sec long recordings of nonverbal vocal and environmental sounds taken from Belin, Zatorre, Lafaille, Ahad, and Pike (2000), presented at a comfortable level adjusted for each participant via MRI-compatible insert earphones (Sensimetrics Corporation, www.sens.com/s14/index.html). These stimuli were selected because they encompass a wide variety of acoustical features and are known to produce widespread activation of the auditory cortices; we excluded intelligible speech, however, to avoid activation of language-related regions that may not be strictly auditory in nature. While participants passively listened with closed eyes, we measured BOLD signal with T2*-weighted gradient echo-planar images and a sparse-sampling design identical to that used above but with a repetition time of 10.11 sec. We obtained 40 volumes: 20 with auditory stimuli (each stimulus was repeated twice) and 20 of silent baseline, randomly ordered.

Audiological Testing

For 10 of the 17 deaf participants (seven with profound and three with severe deafness), we confirmed hearing loss by measuring hearing thresholds through audiometry. This testing occurred approximately 2 years after the initial experimental session described above, but all individuals reported that their hearing status was stable over that time. We used a Hughson–Westlake modified procedure (Harrell, 2002) with an AC-40 interacoustic clinical audiometer and headphones. Thresholds were assessed in both ears monoaurally, at 250, 500, 1000, 2000, 4000, and 8000 Hz, with 5-dB steps. In two of the four profoundly deaf participants who used hearing aids at the time of testing and in four of six severely deaf participants, we also tested hearing thresholds binaurally with their hearing aids, in a free soundfield, following the same procedure. For these participants, we additionally obtained spoken word recognition scores: With hearing aids, participants were asked to repeat words played in free soundfield at a comfortable level, using a list of mono- and bisyllabic recorded words in French (Picard, 1984). Responses were scored as either correct or incorrect by the experimenter.

Eye Movements

Although we were unable to track eye movements inside the scanner, we were able to measure the eye movements of 10 deaf and 9 hearing participants during a visual task outside the scanner. The purpose of this testing was to rule out a possible contribution of differences in eye movements across the two groups to any differences in brain activity. For this task, participants maintained fixation on a central cross (size = $0.5° \times 0.5°$) while two grayscale sinusoidal gratings (grating size = $6° \times 6°$, spatial frequency = 0.33 cycle/degree) were presented simultaneously for 500 msec in the left and right visual fields, centered at $-10°$ and $10°$ from fixation. One of the gratings moved whereas the other remained stationary, and participants were asked to indicate which grating was moving. Participants completed an average of 97 trials, while we tracked eye movements of the right eye using an Eyelink 1000 eye tracker (SR Research, www.sr-research.com/EL_1000.html), with a 1000-Hz sampling rate. We recorded the percentage of trials in which participants broke fixation, as defined by the movement of gaze outside a $2° \times 2°$ space surrounding the fixation cross.

fMRI Analysis

Cross-modal Activity

We used FEAT Version 4.1, part of FSL (Smith et al., 2004; FMRI Expert Analysis Tool, FMRIB Software Library, fsl.fmrib.ox.ac.uk) to analyze the fMRI data. Volumes collected during instruction trials were discarded. We applied the following preprocessing steps: brain extraction, motion correction, spatial smoothing with a 7-mm FWHM isotropic Gaussian kernel, grand mean intensity normalization, high-pass temporal filtering (visual and auditory fMRI cutoffs: 243 and 135 sec, respectively). Images were then registered, first with a 6-parameter linear transformation between the T2*- and T1-weighted images of each participant and then with a nonlinear transformation with 12 degrees of freedom to MNI152 standard space (Mazziotta et al., 2001). In three hearing participants, the nonlinear transformations resulted in unacceptable distortions; for these participants, we therefore used linear registration into standard space.

For the visual task, we performed a general linear model (GLM)-based statistical analysis (Worsley & Friston, 1995) in three levels. For the first level, we used FILM with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001) to model the time series of our six task events (motion or static in the center, left, or right visual fields) and the contrast of all motion–static conditions (pooled across visual fields). Six motion correction parameters were also included in the model as covariates of no interest. For the second level, we used FLAME to perform a fixed effects analysis, which combined the results across runs for each participant (Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004; Beckmann, Jenkinson, & Smith, 2003). Finally, we used FLAME to perform a third-level, mixed-effects analysis with automatic outlier deweighting, where group averages and differences between groups were calculated. Areas of significant fMRI response were identified using cluster thresholding with a Z cutoff of 2.3 and corrected for multiple comparisons at $p < .05$, according to Gaussian random field theory (Worsley, Evans, Marrett, & Neelin, 1992). We used a similar analysis strategy for the auditory localizer scan, with a first-level GLM consisting the time course of the auditory stimulus and six motion correction parameters as covariates of no interest, and a second-level mixed-effects analysis to combine results across participants. The results of the auditory localizer scan were cluster thresholded with a Z cutoff of 3.1, and corrected for multiple comparisons at $p < .01$. To identify cross-modal activity in cortical regions that would normally respond to auditory inputs, we did a conjunction analysis between the thresholded auditory localizer results from the hearing group and the contrast of motion-static for the visual fMRI results.

Functional Connectivity

We performed a functional connectivity analysis comparing deaf and hearing groups, with reorganized auditory cortex as our seed region (O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012; Friston, 2011; Friston et al., 1997). We selected the peak voxel (coordinates: 64, −36, 16) from the average cross-modal activity (visual motion–static activity within the auditory localizer) of both deaf and hearing groups. Both groups were included in the seed selection because we did not want to bias a future comparison of groups. It should be noted, however, that the peak voxel obtained from the overall group average was only 4.5 mm away from the peak voxel determined for the deaf group alone (coordinates: 62, −36, 12). We generated a 7-mm-diameter ROI surrounding this voxel and extracted the mean time series from this ROI for each participant. We then continued with a three-level GLM-based analysis, similar to that described above. Here, the first level consisted the events from the original GLM, plus the participant's mean time series from the ROI. The inclusion of the events from the original GLM meant that the functional connectivity analysis detected only those signal changes that were orthogonal to the stimulation paradigm, thus removing the risk of circularity (O'Reilly et al., 2012). With this model, we generated the parameter estimate for the ROI mean time series in each participant and then completed the second- and third-level analyses. Using cluster thresholding with a Z cutoff of 2.3, corrected for multiple comparisons at $p < .05$, there were no significant differences between groups, but several meaningful subthreshold findings were observed that we believed merited further exploration. As such, we chose an uncorrected threshold and considered all voxels above $Z = 3.1$ as significantly different between groups ($p < .001$, uncorrected for multiple comparisons). To examine hemispheric effects in functional connectivity, we did a second functional connectivity analysis with a seed region from the left hemisphere (LH) posterior STG. Here we followed an identical procedure but used the peak group activation in the LH (coordinates: −54, −46, 16) to define the seed region.

Relation to Hearing Aid Use

We wanted to examine the relationship between cross-modal reorganization and auditory input. We made the assumption that deaf participants who use hearing aids are exposed to greater auditory information via their residual hearing than those who do not use hearing aids. Therefore, we quantified residual hearing over the lifetime by taking percentage of lifetime hearing aid use as our measure, because it is sensitive to both the time with and without a hearing aid, both of which may contribute to the degree of cross-modal reorganization, and because it accounts for variability in participant age. Although we also suspected that the age of onset of hearing aid use may affect cross-modal reorganization, our sample did not have a sufficient distribution of this factor to test its effect. We did, however, account for differences in the age of onset in our analysis (see below).

For our analysis of hearing aid use, we first used data from participants with profound deafness only to avoid the potential confound of differences in degree of hearing loss. Of the 11 profoundly deaf participants, one was excluded because she did not use her hearing aid consistently during her adulthood and it was therefore hard to quantify her sound exposure (participant code 3 on Table 1). We also repeated the same analyses with the severely deaf participants included, such that we could explore the effect of hearing aid use more generally. Because of the lower hearing thresholds in the severely compared with profoundly deaf participants, duration of hearing aid use may be an inaccurate measure of auditory input over the lifetime. In particular, two severely deaf participants did not begin hearing aid use until adulthood, most likely because they relied on residual hearing before this time. As such, the relationship between hearing aid use and cross-modal reorganization in the severely deaf group should be interpreted with caution. To test the hypothesis that hearing aid use would modulate cross-modal reorganization, we looked at activity in two ROIs that represented cross-modal reorganization. These ROIs were determined from the results of the above analyses (see Results section below). The first ROI consisted of a 7-mm sphere surrounding the peak voxel for cross-modal activity of the auditory cortex in the deaf group (coordinates: 62, −36, 12). For this ROI, we extracted the mean percent signal change between the motion and static conditions for each participant. The second ROI consisted of a 7-mm sphere surrounding the peak difference in functional connectivity between deaf and hearing participants, which was situated in the LH intracalcarine region (coordinates: −12, −76, 6). From this ROI, we extracted the mean percent functional connectivity for each participant. For both these sets of data, we used a Pearson's test for a correlation with the duration of hearing aid use in percent years of lifetime. We also tested the relationship of these variables in a partial correlation that accounted for the age of onset of hearing aid use.

In addition to testing within the predefined ROI, we wanted to explore whether other auditory regions besides the selected ROI might vary in cross-modal activity according to hearing aid use. To do so, we did a GLM group-level analysis similar to those described above, but including only 10 profoundly deaf participants. For this model, we used duration of hearing aid use (in years) as a regressor and age (in years) as a covariate of no interest. The results were masked with the results of the auditory localizer scan.

RESULTS

Audiological Testing

Hearing loss thresholds, averaged across the frequencies tested, are shown in Table 1. Thresholds were consistent with expectations, given the classification (severe or profound) that was self-reported by the participants. Profoundly deaf participants had thresholds greater than 90 dB HL at all frequencies tested, with the exception of two participants who had thresholds of 85 dB HL at 250 Hz. Two severely deaf participants had thresholds above 90 dB HL for frequencies between 1000 and 8000 Hz, but lower thresholds for 250 and 500 Hz. One severely deaf had thresholds ranging from 25 dB HL to greater than 90 dB HL from low to high frequencies. In five participants who used hearing aids at the time of testing, hearing thresholds improved an average of 39.9 dB HL across frequencies when the hearing aid was worn. For word recognition, the two profoundly deaf participants tested were unable to identify any words with their hearing aids, whereas the three severely deaf participants with hearing aids could correctly identify an average of 62.98% of the words.

Behavioral Performance

All participants accurately identified the direction of motion of the stimulus in the visual fMRI task, and there were no differences between groups in performance (mean correct performance, deaf = 98.65, SD = 1.76;

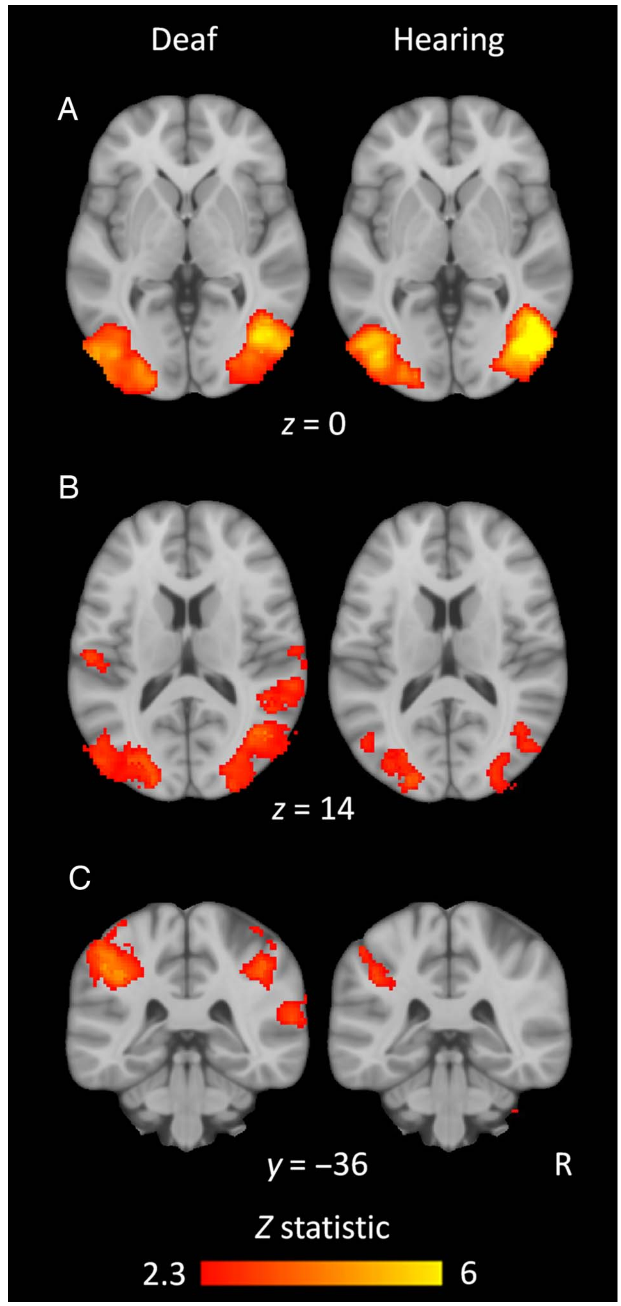

Figure 2. Average activity for the contrast of visual motion–static for the deaf and hearing groups, displayed in MNI152 standard space, $p < .05$ corrected. (A) Both groups showed similar activity in the predicted region for the visual motion processing complex hMT. (B) In the deaf group but not in the hearing, the cluster from the middle lateral occipital region (shown in A) extended into the posterior STG. (C) The deaf group showed extensive activity in response to visual motion, including the IPS, whereas the hearing group's additional activity was limited to the LH IPS.

hearing = 98.94, SD = 1.27; t = −0.54, p = .59, df = 32), indicating that all participants properly attended to the stimuli during the scan. For the eye-tracking task outside the scanner, there were no differences between deaf and hearing groups for the number of trials in which participants broke fixation (group mean percent of trials: deaf = 4.54, SD = 4.04; hearing = 3.38, SD = 2.64; t = 0.74, p = .47, df = 17), which suggests that the groups did not differ in eye movements and that this variable is therefore unlikely to affect any group differences.

fMRI Results

Cross-modal Activity

Visual motion–static. For the contrast of visual motion–static, both groups showed bilateral activity in the middle lateral occipital cortex. This cluster included the posterior inferior temporal sulcus and its ascending limb, which represent the expected location for the motion-sensitive visual area hMT complex (Dumoulin et al., 2000; Figure 2). In the right hemisphere (RH) of the deaf group, but not in the hearing group, this cluster also extended from the occipital cortex through the posterior STS and into the posterior STG (Figure 2). The deaf group additionally showed extensive activity throughout the brain, whereas the hearing group's additional activity was limited to the LH intraparietal sulcus (Figure 2). Because the clusters spanned different anatomical regions to report the coordinates of peak activity, we further thresholded our results with a cutoff of Z = 3.1, such that the reported coordinates would be anatomically meaningful. With this threshold, all remaining voxels within groupings greater than 10 are reported in Table 2. There were no

Table 2. Peak Activations for Visual Motion–Static: Deaf and Hearing Group Averages

Group	*Peak Z Statistic*	*No. Voxels above Z = 3.1*	*Coordinates x*	*y*	*z*	*Hemisphere*	*Anatomical Location*
Deaf	6.45	2731	46	−68	4	R	Middle lateral occipital (including hMT complex)
	5.31	2267	−52	−78	2	L	Middle lateral occipital (including hMT complex)
	4.63	983	−48	−42	48	L	Intraparietal sulcus
	3.94	136	46	−34	40	R	Intraparietal sulcus
	3.99	68	32	−54	50	R	Intraparietal sulcus
	3.55	40	−28	−48	64	L	Intraparietal sulcus
	5.07	315	−36	−12	64	L	Precentral gyrus
	4.12	213	−4	2	48	L	SMA
	3.36	26	14	0	58	R	SMA
	4.01	92	32	−6	56	R	Dorsal premotor cortex
	3.62	27	4	18	32	R	Anterior cingulate gyrus
	3.32	12	−4	16	34	L	Anterior cingulate gyrus
	3.43	27	62	−36	12	R	Posterior STG
	3.59	25	60	−14	28	R	Postcentral gyrus
	3.34	13	−62	−16	26	L	Postcentral gyrus
	3.42	12	−38	−64	−20	L	Fusiform gyrus
	3.33	12	48	−44	18	R	Posterior STS
	3.55	11	−48	−32	24	L	Parietal operculum
	3.54	11	52	−50	12	R	Occipito temporal junction
Hearing	5.98	2797	48	−60	2	R	Middle lateral occipital (including hMT complex)
	5.36	2200	−38	−80	−4	L	Middle lateral occipital (including hMT complex)
	4.23	393	−32	−58	56	L	Intraparietal sulcus

From our cluster-thresholded and corrected results, we applied a further threshold of $Z > 3.1$ and have reported here the peak voxels within the remaining groupings that were greater than 10 voxels. This was done to document anatomically meaningful activations, because the cluster results spanned large regions.

significant differences between groups for the contrast of visual motion–static; however, because we expected that auditory experience may have modulated the degree of STG recruitment, we explored subthreshold trends in subsequent analyses reported below (see Visual Motion Activity within the Auditory Localizer section).

Auditory localizer. In hearing participants, auditory stimuli (versus baseline) activated all of the expected auditory cortices, including bilaterally the transverse gyri, the length of the superior temporal gyri (STG), the PT, and most of the STS.

Visual motion activity within the auditory localizer. Within the region of the auditory localizer, the deaf group showed significant activity in the RH posterior STG for the contrast of visual motion–static (Figure 3). The Harvard–Oxford Cortical structure atlas (FSL: fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases) defined the peak voxel of this activation grouping as supramarginal gyrus, posterior STG, and PT, with respective probabilities of 24%, 18%, and 6%. Although this effect was observed only in the RH at whole-brain corrected levels of significance, we observed a trend for a similar activation in the corresponding region of the LH at an uncorrected threshold of $p < .01$ (peak coordinates: −60, −48, 12; peak $Z = 3.35$; grouping size = 99 voxels). Given the symmetrical location of this activation relative to the RH region and its overlap with the functional localizer, we believe it is more likely to be a true response than a mere statistical artifact. In the LH, there were also several activated voxels within the region of the auditory localizer that were above the temporal plane. These voxels belonged to a cluster that fell primarily on the LH postcentral gyrus (Figure 3).

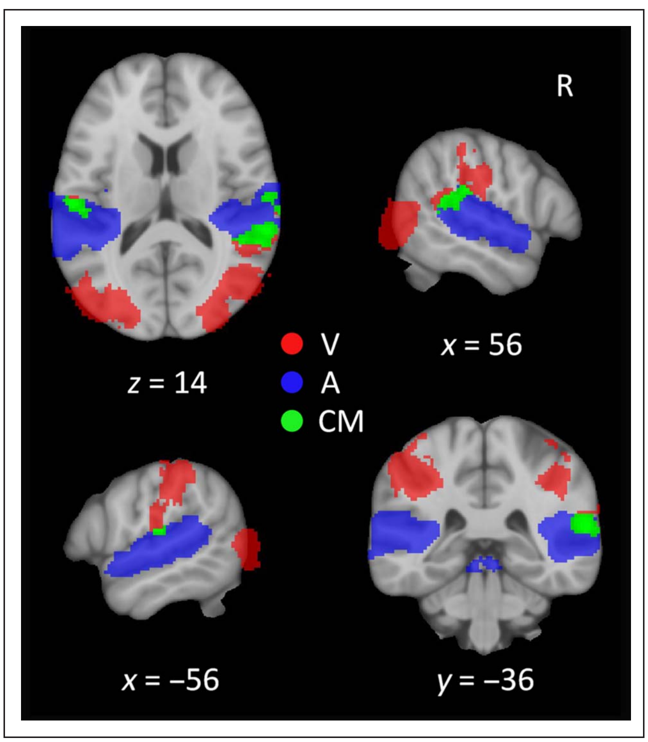

Figure 3. Cross-modal activity (green) in the deaf group, displayed in MNI152 standard space. In the RH posterior STG, visual motion-related activity in the deaf (red, $p < .05$) overlapped with the auditory localizer activity (blue, $p < .01$) from the hearing group. In the deaf group, this cross-modal activity varied with hearing aid use (see Figure 5).

We wanted to check if the cross-modal activity in the deaf group occurred for both the center and peripheral visual field conditions or if it was driven only by the peripheral stimuli. We therefore measured the mean percent signal change in a 7-mm-diameter ROI surrounding the peak voxel of the deaf group activation for the contrast of all motion–static (coordinates: 62, −36, 12). Motion stimuli in both the center (mean percent signal change = 0.092, $SD = 0.106$, $t = 3.58$, $p = .01$, $df = 16$) and peripheral (mean percent signal change = 0.091, $SD = 0.128$, $t = 2.92$, $p = .003$, $df = 16$) visual fields elicited responses within this region, and there was no difference between them for the amplitude of the response ($t = -0.52$, $p = .97$, $df = 16$).

Unlike the deaf group, the hearing group showed no activity for the contrast of visual motion–static within the region of the auditory localizer. Although no differences between groups reached corrected statistical thresholds for visual motion-related activity (as stated in Visual Motion–Static section), we explored the region of the auditory localizer for any trends related to the differences that we found in the group average images. At an uncorrected threshold of $p < .01$, the deaf group showed increased activity as compared with the hearing group in both the LH (peak coordinates: −62, −48, 12; peak $Z = 3.95$, grouping size: 225 voxels) and RH (peak coordinates: 48, −42, 18; peak $Z = 2.85$; grouping size: 15 voxels). In the RH, this activity was part of a larger cluster with a peak that fell on the posterior STS, outside the region of the auditory localizer (peak coordinates: 46, −44, 20; peak $Z = 3.18$; grouping size: 76 voxels). Inspection of the individual data from within these clusters revealed that there was a great deal of variability, which likely accounted for the lack of whole-brain corrected significance. To explore the source of this variability, we therefore performed additional analyses, taking into account hearing aid use, as described below in Hearing Aid Use and Cross-modal Reorganization section.

Functional Connectivity of Reorganized Auditory Cortex

Both deaf and hearing groups showed widespread functional connectivity, with most voxels of the brain showing a significant positive functional connectivity with the seed region in the STG. There was a similar pattern of functional connectivity in both groups, with peak functional connectivities found in the middle temporal occipital junction, the contralateral posterior STG, the inferior

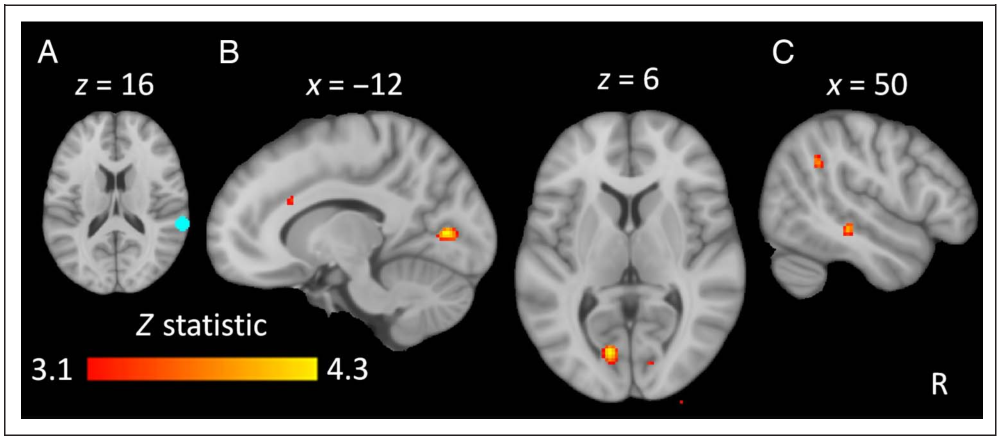

Figure 4. Functional connectivity of RH posterior STG seed, Deaf > Hearing, displayed in MNI152 standard space, $p < .001$ uncorrected. (A) The seed region, selected from the contrast of visual motion–static (see Methods: Functional Connectivity). (B) The largest increase in connectivity between deaf and hearing groups occurred in the LH intracalcarine cortex. (C) There was also a significant difference in the RH supramarginal gyrus and in the RH middle STS.

frontal gyri, and the anterior cingulate gyri. The main question of interest however was how functional connectivity differed across groups. It should be noted that, because the events of the stimulation paradigm were included in the GLM for the functional connectivity analysis, this contrast does not represent differences in the amplitude of response, but rather differences across groups in how the brain regions interact with one another. For this comparison, the greatest difference occurred in an intracalcarine region (Figure 4), where the deaf group showed increased functional connectivity as compared with the hearing. According to the Juelich histological atlas (Eickhoff et al., 2007), this grouping of voxels falls within Brodmann's area 17, primary visual cortex, with 76% probability. This increased functional connectivity was most prominent in the LH. The deaf group also showed a sizeable difference from the hearing group in the RH angular gyrus and smaller differences throughout the brain including in the middle STS. These results are summarized in Table 3. Groupings of 10 or more adjacent voxels with a $Z > 3.1$ are reported ($p < .001$, uncorrected). There were no regions where the hearing group showed increased functional connectivity as compared with the deaf, with the exception of a small grouping of voxels in the LH middle temporal gyrus (peak coordinates: −46, −50, −4; peak $Z = 3.38$; grouping size: 15 voxels).

We wanted to ensure that the difference between groups for functional connectivity in the intracalcarine region could not be attributed to differences in magnitude of response. To do so, we did an ROI comparison of deaf and hearing groups for visual motion-related activity in this region. The ROI consisted of a 7-mm-diameter sphere, surrounding the voxel representing the peak difference between deaf and hearing groups for functional connectivity (coordinates: −12, −76, 6). From this ROI, we extracted the mean percent signal change between the motion and static conditions for each participant. These values were averaged for each group, and we performed a two-tailed t test. There was no difference between groups for the percent signal change in the intracalcarine region (mean percent signal change, deaf = −0.01, $SD = 0.14$; hearing = −0.04, $SD = 0.12$; $t = 0.61$, $p = .549$, $df = 32$).

Functional connectivity analysis with an LH posterior STG seed region showed similar results to the RH seed: The deaf group showed increased functional connectivity in the intracalcarine region, with the peak effect localized at the same coordinates as in the RH analysis (peak coordinates: −12, −76, 6; peak $Z = 3.63$; grouping size: 45 voxels).

Table 3. Peak Differences for Functional Connectivity of RH Post STG, Deaf > Hearing

Peak Z Statistic	*No. Voxels above Z = 3.1*	*Coordinates x*	*Coordinates y*	*Coordinates z*	*Hemisphere*	*Anatomical Location*
4.29	73	−12	−76	6	L	Intracalcarine cortex
4.19	45	−40	0	−18	L	Planum polare
3.98	28	20	−62	64	R	Superior parietal lobule
3.9	38	50	−28	−10	R	Middle STS
3.87	109	48	−48	32	R	Angular gyrus
3.81	24	32	−74	−16	R	Fusiform gyrus

Groupings of voxels greater than 10 are listed.

Hearing Aid Use and Cross-modal Reorganization

In the RH posterior STG of profoundly deaf participants, the mean percent signal change between motion and static conditions correlated with duration of hearing aid use over the lifetime ($r = -.68$, $p = .016$, one-tailed, $df = 8$): Participants who used a hearing aid for longer demonstrated less visually evoked activity in this region (Figure 5). With the severely deaf participants included, we found the same relationship ($r = -.68$, $p = .002$, one-tailed, $df = 14$). This effect remained in both sample groups when we accounted for differences in the age of onset of hearing aid use in a partial correlation (profound deaf only: $r = -.67$, $p = .025$, one-tailed, $df = 7$; all deaf: $r = -.67$, $p = .003$, one-tailed, $df = 13$). We also did a voxel-wise analysis within the region of the auditory localizer to uncover any other potential auditory regions that may vary in cross-modal activity according to hearing aid use in profoundly deaf participants in a more independent, data-driven manner as compared with the ROI approach. At a threshold of $Z = 2.3$ ($p < .01$, uncorrected), we found a small grouping of voxels in the RH post-STS (peak coordinates: 54, −36, 10; peak $Z = 2.77$; grouping size: 22 voxels), where longer durations of hearing aid use were associated with less cross-modal activity. This grouping of voxels overlapped with the independently selected ROI that we previously used to test for a correlation with hearing aid use, with the peaks falling 8.2 mm apart. This convergent result confirms the relationship between hearing aid use and activity in the RH posterior

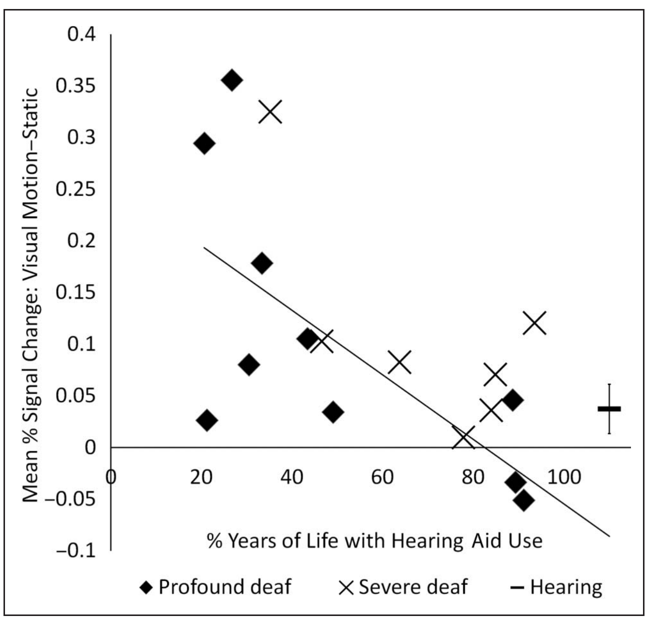

Figure 5. Correlation between duration of hearing aid use and cross-modal activity in RH posterior STG, with a regression line fitted to the profound deaf. This correlation was significant both with and without severely deaf participants included and while controlling for the effects of age of onset of hearing aid use (see Hearing Aid Use and Cross-modal Reorganization section). The horizontal bar represents the mean for the hearing group, with standard error bars.

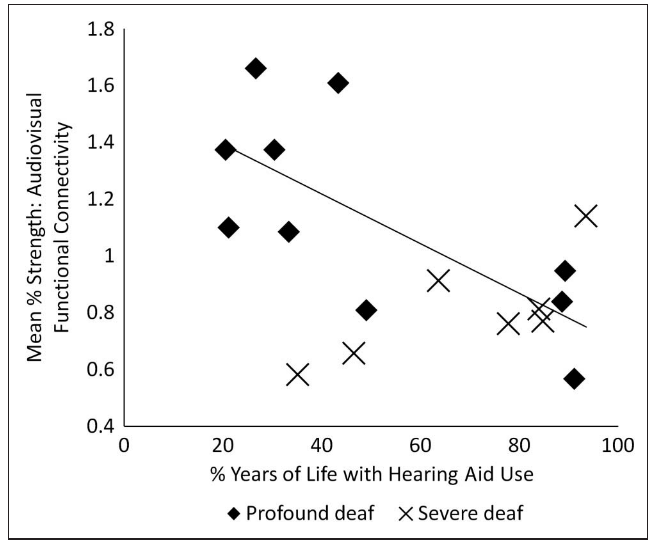

Figure 6. Correlation between hearing aid use and strength of audiovisual functional connectivity, with a regression line fitted to the profound deaf. This correlation was significant both with and without severely deaf participants included and while controlling for the effects of age of onset of hearing aid use (see Hearing Aid Use and Cross-modal Reorganization section).

STG. Also, these analyses help to explain the lack of statistically significant difference in the original contrast of deaf versus hearing: The activity in the deaf group is largely driven by those with the least hearing aid use; thus, without taking this variable into account, there is too much within-group variance for the analysis to be sensitive to the group difference.

Similarly, for profound deaf participants, the percent functional connectivity between the reorganized posterior STG and the LH intracalcarine regions correlated with duration of hearing aid use ($r = -.71$, $p = .011$, one-tailed, $df = 8$): Participants who used a hearing aid for longer durations demonstrated less functional connectivity between the RH posterior STG and the intracalcarine region (Figure 6). The same relationship was found with the severely deaf participants included in the analysis ($r = -.59$, $p = .008$, one-tailed, $df = 14$) and in both sample groups when age of onset of hearing aid use was accounted for (profound deaf only: $r = -.69$, $p = .019$, one-tailed, $df = 7$; all deaf: $r = -.74$, $p = .001$, one-tailed, $df = 13$).

DISCUSSION

We report three principal findings. First, the posterior STG was activated by visual motion in deaf people. A conjunction analysis with the auditory localizer results showed that this region responds to auditory stimuli in hearing people, thus confirming that this activity in deaf people is cross-modal. Second, in deaf people more than in hearing, this reorganized auditory cortex was functionally connected to an anterior intracalcarine region, corresponding to primary visual cortex. Finally, both the magnitude of cross-modal activity in the posterior STG and the strength of functional connectivity between this region and the intracalcarine region correlated with duration of hearing aid use: Longer durations of hearing aid use were associated with less cross-modal activity and decreased audiovisual functional connectivity.

Cross-modal Reorganization of Posterior STG

The visual motion-related activation in the deaf bordered the posterior PT and extended into the posterior STS. The response in the deaf reached a corrected level of significance in the RH with a weaker focus in a symmetrical location in the LH. Several previous studies with deaf people have identified consistent findings of visual motion-related activity in similar regions: bilaterally or unilaterally in the PT (Fine et al., 2005; Sadato et al., 2005; Petitto et al., 2000) and bilaterally in the posterior STS (Bavelier et al., 2001). These prior studies reported more robust group differences than our findings, which is likely attributable to differences in the participant sample: Whereas previous studies tested only sign language users with profound deafness, we included a heterogeneous mix to explore variability related to auditory exposure.

Previous research suggests that cross-modal activity in this region is modulated by attention (Fine et al., 2005; Bavelier et al., 2001). Although we did not manipulate attention in our design, we found no evidence for attentional differences between groups: The groups performed equally well at identifying the stimulus inside the scanner and at maintaining fixation in a task outside the scanner. Furthermore, we did not see differences in brain activity between groups in any region, including attentionally modulated visual regions (Fine et al., 2005; Bavelier et al., 2001). Given these observations, we do not believe that differences in attention can explain our finding. Additionally, we think it is unlikely that our results are driven by sign language experience in the deaf group: Previous research shows that, although the posterior STG is responsive to sign language (Petitto et al., 2000), visual activity in this region occurs nonetheless when differences in language use between deaf and hearing groups are controlled for (Cardin et al., 2013; Fine et al., 2005; Bavelier et al., 2001). Finally, although nearby regions to our activation have been implicated in biological motion processing (for a review, see Allison, Puce, & McCarthy, 2000), given that our stimuli were quite unlike biological motion, we do not believe that our activation represents an enhancement of this type of processing.

An important question in the study of cross-modal reorganization is whether cross-modal activity occurs in auditory regions (operationally defined as regions that respond to sound) or in adjacent regions. Our auditory localizer provides independent confirmation that the visual activation in the posterior STG falls in a region that normally responds to auditory inputs, thus illustrating that the visual activity in the deaf was cross-modal. However, because our auditory ROI was defined in the hearing group and then applied to the deaf group, it cannot account for possible morphological changes occurring in these regions after deafness, such as shifts in the borders of auditory subregions (Wong, Chabot, Kok, & Lomber, 2013). As well, we cannot exclude the possibility that the region within the auditory localizer may be multisensory. Numerous studies have localized activity in nearby regions related to audiovisual integration (for a review, see Hein & Knight, 2008), including audiovisual motion integration (Lewis & Noppeney, 2010), and unisensory visual motion (e.g., Antal, Baudewig, Paulus, & Dechent, 2008). Indeed, according to one model, all sensory regions may have multimodal properties (Pascual-Leone & Hamilton, 2001). By this reasoning, our results may represent a takeover of visual inputs in a normally multisensory region, driven by a lack of auditory inputs. Regardless as to whether this region is considered unimodal auditory or multisensory in hearing people, it has been implicated in auditory spatial processing (Rauschecker, 1998), including auditory motion processing (e.g., Baumgart, Gaschler-Markefski, Woldorff, Heinze, & Scheich, 1999). One interpretation of our activation is that it represents the substitution of the visual modality for the auditory to accomplish the spatial processing functions that are normally completed in this region (Meredith et al., 2011). A similar interpretation has been suggested to explain cross-modal activity in blind people (for a review, see Voss & Zatorre, 2012).

Functional Connectivity

On the basis of the reasoning that the source of cross-modal activity will show enhanced interactions with reorganized auditory regions, our finding of increased audiovisual functional connectivity in deaf people (Figure 4) is consistent with the hypothesis that visual information in the reorganized posterior STG arrives from visual cortex via corticocortical connections. Consistent with this suggestion, a feedforward interaction between these regions has previously been suggested, via dynamic causal modeling, during audiovisual motion integration in hearing people (Lewis & Noppeney, 2010). Our result may reflect a preexisting anatomical connection between visual and cortical regions that is fortified after auditory deprivation. Other possible mechanisms include a connection formed after deafness or a difference in online processing between groups. However, given that functional connectivity only represents a temporal correlation, we cannot rule out the possibility that this effect reflects an interaction other than feedforward corticocortical connectivity, such as an enhancement of reciprocal information transfer, or connection through an intermediary region. Increased functional connectivity between reorganized auditory cortex and RH angular gyrus and middle STS suggest that feedback from parietal regions and interactions within the temporal lobe may play a role. Nevertheless, the findings indicate that the deaf process visual information not only via changes within auditory cortices, as shown previously, but also via changes to the corticortical interactions of auditory and visual cortices.

Interestingly, the increased audiovisual functional connectivity in deaf people was found around the anterior portion of the calcarine sulcus, which typically represents peripheral visual fields (e.g., Engel, Glover, & Wandell, 1997). This is of note, considering that behavioral enhancements to deaf vision are often selective for peripheral function (Bavelier, Dye, & Hauser, 2006). As well, direct anatomical connections from peripheral regions of V2 to caudal auditory regions have been identified in macaques (Falchier et al., 2010), which supports the argument that such direct connections could therefore be enhanced during development in those deprived of auditory input.

Auditory Experience and Cross-modal Reorganization

Because the duration of hearing aid use represents a measure, albeit approximate, of the amount of auditory input that each participant received during his or her lifetime, the correlations between cross-modal reorganization and duration of hearing aid use (Figures 5 and 6) support the hypothesis that auditory deprivation leads to cross-modal reorganization. Because long-term hearing aid users also tended to be oral language users, our findings suggest that auditory language input, arguably one of the most salient inputs delivered through residual hearing, may also be important for cross-modal reorganization. These findings suggest that long-term hearing aid use, even in profoundly deaf people, might be sufficient to inhibit cross-modal reorganization via preservation of auditory neuronal function. The inverse relationship is also possible: The development of cross-modal reorganization may encourage shorter durations of hearing aid use, perhaps because the reorganization prevents an individual from deriving much benefit from the hearing aid. In either case, these correlations are clinically relevant, given that cross-modal reorganization is associated with poorer outcomes after cochlear implantation (Doucet, Bergeron, Lassonde, Ferron, & Lepore, 2006; Lee et al., 2001, 2006). They are also consistent with the suggestion that hearing aid use is associated with better outcomes after cochlear implantation (Santarelli, De Filippi, Genovese, & Arslan, 2008). Our study was not designed to evaluate the role of the age at which the hearing aid was first used; although this factor may be relevant, the correlation with duration of hearing aid use held even after covarying out the age of start.

Although the correlations were statistically significant for a group that included all deaf participants, duration of hearing aid use may not be an accurate measure of auditory input for participants with severe deafness who were more likely, by virtue of their better hearing thresholds, to receive auditory input even without hearing aids. As well, given their better hearing thresholds, severely deaf participants may have received more auditory input than profoundly deaf participants during hearing aid use. Although we did not have a large enough sample size to test for an effect of hearing loss levels in this study, we would predict that the severely deaf people would show less cross-modal reorganization than the profoundly deaf because of their increased auditory exposure. This hypothesis is consistent with previous research, which found less cross-modal activity in response to sign language after severe as compared with profound deafness (Lambertz et al., 2005).

In addition to acting as a measure of auditory input, duration of hearing aid use captures differences in the usefulness of auditory information that an individual receives. As reported by comments from some of our participants, the auditory input received through hearing aids was primarily used to complement speechreading for oral language use. This usage of hearing aids is reflected in the language use of our sample. For example, all of the profoundly deaf participants had experience with sign language, but those who reported proficient speechreading were found only among the long-term hearing aid users. Long-term hearing aid users also tended to report primary use of oral language rather than sign language and, within the severely deaf group, some obtained above-chance performance in spoken word identification when wearing their hearing aids. As such, our measure, duration of hearing aid use, likely captures not only the amount of auditory input but also how this input is used, particularly for language. As speech constitutes one of the most important environmental auditory signals, it is likely that the processing of speech sounds was an important factor influencing our findings. The specific importance of this factor in cross-modal reorganization should be examined in greater detail in future research, particularly with respect to profoundly deaf people who use primarily oral language.

Although we used a correlation analysis to capture the statistical significance of our effect, visual inspection of Figure 5 suggests a more complex relationship: Long-term hearing aid users show little cross-modal activity, whereas short-term hearing aid users vary. Such variability has been noted in previous studies of deaf people (e.g., Bavelier & Neville, 2002). Importantly, our results demonstrate this variability even when the sample is limited to early and profoundly deaf participants, which highlights the need for more research into other potential contributing factors beyond the ones studied here.

Conclusion

Our results demonstrate that early auditory deprivation leads not only to functional reorganization of the auditory cortex but also to enhanced interactions between auditory and primary visual regions. Reorganization varies with years of hearing aid use, suggesting that it is driven by the nature and amount of input from the auditory system. These findings can guide future research on the anatomical correlates of cross-modal reorganization.

Acknowledgments

This work was supported by grants to R. J. Z. from the Canadian Institutes of Health Research, the Canada Fund for Innovation, and the Natural Sciences and Engineering Research Council and by a Centre of Excellence for Commercialization and Research award to the Montreal Neurological Institute. F. C. was supported by grants from the Natural Sciences and Engineering Research Council of Canada and Fonds de Recherche Santé Québec. M. M. S. was supported by a Vanier Canada Graduate fellowship. We thank the staff of the McConnell Brain Imaging Centre for their assistance with acquiring the data, P. Fournier for assistance with audiology procedures, and all of the participants for their cooperation.

Reprint requests should be sent to Martha M. Shiell, Montreal Neurological Institute, McGill University, 3801 rue University, Cognitive Neuroscience Unit, Room 256, Montréal, QC, Canada, H3A 2B4, or via e-mail: martha.shiell@mail.mcgill.ca.

REFERENCES

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences, 4,* 267–278.

Antal, A., Baudewig, J., Paulus, W., & Dechent, P. (2008). The posterior cingulate cortex and planum temporale/parietal operculum are activated by coherent visual motion. *Visual Neuroscience, 25,* 1–10.

Armstrong, B. A., Neville, H. J., Hillyard, S. A., & Mitchell, T. V. (2002). Auditory deprivation affects processing of motion, but not color. *Brain Research, Cognitive Brain Research, 14,* 422–434.

Auer, E. T., Jr., Bernstein, L. E., Sungkarat, W., & Singh, M. (2007). Vibrotactile activation of the auditory cortices in deaf versus hearing adults. *NeuroReport, 18,* 645–648.

Baumgart, F., Gaschler-Markefski, B., Woldorff, M. G., Heinze, H. J., & Scheich, H. (1999). A movement-sensitive area in auditory cortex. *Nature, 400,* 724–726.

Bavelier, D., Brozinsky, C., Tomann, A., Mitchell, T., Neville, H., & Liu, G. (2001). Impact of early deafness and early exposure to sign language on the cerebral organization for motion processing. *Journal of Neuroscience, 21,* 8931–8942.

Bavelier, D., Dye, M. W. G., & Hauser, P. C. (2006). Do deaf individuals see better? *Trends in Cognitive Sciences, 10,* 512–518.

Bavelier, D., & Neville, H. J. (2002). Cross-modal plasticity: Where and how? *Nature Reviews Neuroscience, 3,* 443–452.

Bavelier, D., Tomann, A., Hutton, C., Mitchell, T., Corina, D., Liu, G., et al. (2000). Visual attention to the periphery is enhanced in congenitally deaf individuals. *Journal of Neuroscience, 20,* 1–6.

Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2003). General multilevel linear modeling for group analysis in fMRI. *Neuroimage, 20,* 1052–1063.

Bedny, M., Konkle, T., Pelphrey, K., Saxe, R., & Pascual-Leone, A. (2010). Sensitive period for a multimodal response in human visual motion area MT/MST. *Current Biology, 20,* 1900–1906.

Belin, P., Zatorre, R. J., Hoge, R., Evans, A. C., & Pike, B. (1999). Event-related fMRI of the auditory cortex. *Neuroimage, 10,* 417–429.

Belin, P., Zatorre, R. J., Lafaille, P., Ahad, P., & Pike, B. (2000). Voice-selective areas in human auditory cortex. *Nature, 403,* 309–312.

Cardin, V., Orfanidou, E., Ronnberg, J., Capek, C. M., Rudner, M., & Woll, B. (2013). Dissociating cognitive and sensory neural plasticity in human superior temporal cortex. *Nature Communications, 4,* 1473–1478.

Collignon, O., Vandewalle, G., Voss, P., Albouy, G., Charbonneau, G., Lassonde, M., et al. (2011). Functional specialization for auditory-spatial processing in the occipital cortex of congenitally blind humans. *Proceedings of the National Academy of Sciences, U.S.A., 108,* 4435–4440.

Doucet, M. E., Bergeron, F., Lassonde, M., Ferron, P., & Lepore, F. (2006). Cross-modal reorganization and speech perception in cochlear implant users. *Brain, 129,* 3376–3383.

Dumoulin, S. O., Bittar, R. G., Kabani, N. J., Baker, C. L., Le Goualher, G., Pike, G. B., et al. (2000). A new anatomical landmark for reliable identification of human area V5/MT: A quantitative analysis of sulcal patterning. *Cerebral Cortex, 10,* 454–463.

Eickhoff, S. B., Paus, T., Caspers, S., Grosbras, M.-H., Evans, A. C., Zilles, K., et al. (2007). Assignment of functional activations to probabilistic cytoarchitectonic areas revisited. *Neuroimage, 36,* 511–521.

Engel, S. A., Glover, G. H., & Wandell, B. A. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. *Cerebral Cortex, 7,* 181–192.

Falchier, A., Schroeder, C. E., Hackett, T. A., Lakatos, P., Nascimento-Silva, S., Ulbert, I., et al. (2010). Projection from visual areas V2 and prostriata to caudal auditory cortex in the monkey. *Cerebral Cortex, 20,* 1529–1538.

Fine, I., Finney, E. M., Boynton, G. M., & Dobkins, K. R. (2005). Comparing the effects of auditory deprivation and sign language within the auditory and visual cortex. *Journal of Cognitive Neuroscience, 17,* 1621–1637.

Finney, E. M., Fine, I., & Dobkins, K. R. (2001). Visual stimuli activate auditory cortex in the deaf. *Nature Communications, 4,* 1171–1173.

Frasnelli, J., Collignon, O., Voss, P., & Lepore, F. (2011). Crossmodal plasticity in sensory loss. In A. M. Green, E. C. Chapman, J. F. Kalaska, F. Lepoce (Eds.), *Enhancing performance for action and perception* (1st ed., Vol. 191, pp. 233–249). Philadelphia, PA: Elsevier.

Friston, K. J. (2011). Functional and effective connectivity: A review. *Brain Connectivity, 1,* 13–36.

Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage, 6,* 218–229.

Hall, D. A., Haggard, M. P., Akeroyd, M. A., Palmer, A. R., Summerfield, A. Q., Elliott, M. R., et al. (1999). Sparse temporal sampling in auditory fMRI. *Human Brain Mapping, 7,* 213–223.

Harrell, R. W. (2002). Pure-tone evaluation. In J. Katz (Ed.), *Handbook of clinical audiology* (5th ed., pp. 71–87). Baltimore, MD: Lippincott Williams & Wilkins.

Hein, G., & Knight, R. T. (2008). Superior temporal sulcus—It's my area: Or is it? *Journal of Cognitive Neuroscience, 20,* 2125–2136.

Hirano, S., Naito, Y., Kojima, H., Honjo, I., Inoue, M., Shoji, K., et al. (2000). Functional differentiation of the auditory association area in prelingually deaf subjects. *Auris Nasus Larynx, 27,* 303–310.

Karns, C. M., Dow, M. W., & Neville, H. J. (2012). Altered cross-modal processing in the primary auditory cortex of congenitally deaf adults: A visual-somatosensory fMRI study with a double-flash illusion. *Journal of Neuroscience, 32,* 9626–9638.

Klinge, C., Eippert, F., Roder, B., & Buchel, C. (2010). Corticocortical connections mediate primary visual cortex responses to auditory stimulation in the blind. *Journal of Neuroscience, 30,* 12798–12805.

Lambertz, N., Gizewski, E. R., de Greiff, A., & Forsting, M. (2005). Cross-modal plasticity in deaf subjects dependent on the extent of hearing loss. *Cognitive Brain Research, 25,* 884–890.

Lee, D. S., Lee, J. S., Oh, S. H., Kim, S. K., Kim, J. W., Chung, J. K., et al. (2001). Cross-modal plasticity and cochlear implants. *Nature, 409,* 149–150.

Lee, H. J., Giraud, A. L., Kang, E., Oh, S. H., Kang, H., Kim, C. S., et al. (2006). Cortical activity at rest predicts cochlear implantation outcome. *Cerebral Cortex, 17,* 909–917.

Lee, J. S., Lee, D. S., Oh, S. H., Kim, C. S., Kim, J.-W., Hwang, C. H., et al. (2003). PET evidence of neuroplasticity in adult auditory cortex of postlingual deafness. *The Journal of Nuclear Medicine, 44,* 1435–1439.

Levanen, S., Jousmaki, V., & Hari, R. (1998). Vibration-induced auditory-cortex activation in a congenitally deaf adult. *Current Biology, 8,* 869–872.

Lewis, R., & Noppeney, U. (2010). Audiovisual synchrony improves motion discrimination via enhanced connectivity between early visual and auditory areas. *Journal of Neuroscience, 30,* 12329–12339.

Li, Y., Booth, J. R., Peng, D., Zang, Y., Li, J., Yan, C., et al. (2013). Altered intra- and interregional synchronization of superior temporal cortex in deaf people. *Cerebral Cortex, 23,* 1988–1996.

Liu, Y., Yu, C., Liang, M., Li, J., Tian, L., Zhou, Y., et al. (2007). Whole brain functional connectivity in the early blind. *Brain, 130,* 2085–2096.

Lomber, S. G., Meredith, M. A., & Kral, A. (2010). Cross-modal plasticity in specific auditory cortices underlies visual compensations in the deaf. *Nature Neuroscience, 13,* 1421–1427.

Mazziotta, J., Toga, A., Evans, A., Fox, P., Lancaster, J., Zilles, K., et al. (2001). A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). *Philosophical Transactions of the Royal Society, Series B, Biological Sciences, 356,* 1293–1322.

Meredith, M. A., Kryklywy, J., McMillan, A. J., Malhotra, S., Lum-Tai, R., & Lomber, S. G. (2011). Crossmodal reorganization in the early deaf switches sensory, but not behavioral roles of auditory cortex. *Proceedings of the National Academy of Sciences, U.S.A., 108,* 8856–8861.

O'Reilly, J. X., Woolrich, M. W., Behrens, T. E. J., Smith, S. M., & Johansen-Berg, H. (2012). Tools of the trade: Psychophysiological interactions and functional connectivity. *Social Cognitive and Affective Neuroscience, 7,* 604–609.

Pascual-Leone, A., & Hamilton, R. (2001). The metamodal organization of the brain. In C. Casanova & M. Ptito (Eds.), *Progress in brain research* (Vol. 134, pp. 427–445). Philadelphia, PA: Elsevier.

Petitto, L.-A., Zatorre, R. J., Gauna, K., Nikelski, E. J., Dostie, D., & Evans, A. C. (2000). Speech-like cerebral activity in profoundly deaf people processing signed languages: Implications for the neural basis of human language. *Proceedings of the National Academy of Sciences, U.S.A., 97,* 13961–13966.

Picard, M. (1984). L'audiometrie vocale au Québec français. *Audiology, 23,* 337–365.

Rauschecker, J. P. (1998). Parallel processing in the auditory cortex of primates. *Audiology and Neurotology, 3,* 86–103.

Sadato, N., Okada, T., Honda, M., Matsuki, K., Yoshida, M., Kashikura, K., et al. (2005). Cross-modal integration and plastic changes revealed by lip movement, random-dot motion and sign languages in the hearing and deaf. *Cerebral Cortex, 15,* 1113–1122.

Sadato, N., Yamada, H., Okada, T., & Yoshida, M. (2004). Age-dependent plasticity in the superior temporal sulcus in deaf humans: A functional MRI study. *BMC Neuroscience, 5,* 55–61.

Santarelli, R., De Filippi, R., Genovese, E., & Arslan, E. (2008). Cochlear implantation outcome in prelingually deafened young adults. *Audiology and Neurotology, 13,* 257–265.

Shiell, M. M., Champoux, F., & Zatorre, R. J. (2014). Enhancement of visual motion detection thresholds in early deaf people. *PLoS One, 9,* e90498.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage, 23,* S208–S219.

Voss, P., & Zatorre, R. J. (2012). Organization and reorganization of sensory-deprived cortex. *Current Biology, 22,* R168–R173.

Wong, C., Chabot, N., Kok, M. A., & Lomber, S. G. (2013). Modified areal cartography in auditory cortex following early- and late-onset deafness. *Cerebral Cortex, 24,* 1778–1792.

Woolrich, M. W., Behrens, T. E. J., Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2004). Multilevel linear modelling for fMRI group analysis using Bayesian inference. *Neuroimage, 21,* 1732–1747.

Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of fMRI data. *Neuroimage, 14,* 1370–1386.

Worsley, K. J., Evans, A. C., Marrett, S., & Neelin, P. (1992). A three-dimensional statistical analysis for CBF activation studies in human brain. *Journal of Cerebral Blood Flow & Metabolism, 12,* 900–918.

Worsley, K. J., & Friston, K. J. (1995). Analysis of fMRI time-series revisited—Again. *Neuroimage, 2,* 173–181.

Yu, C., Liu, Y., Li, J., Zhou, Y., Wang, K., Tian, L., et al. (2008). Altered functional connectivity of primary visual cortex in early blindness. *Human Brain Mapping, 29,* 533–543.