Chapter 5

Activation in primary auditory cortex during silent lipreading is determined by sex

Abstract

Recent studies investigating whether the primary auditory cortex (PAC) is involved in silent lipreading gave inconsistent results. We used Positron Emission Tomography to identify which areas in the temporal lobe process visible speech, with a focus on the PAC. Subjects were tested on lipreading numbers and only the eighteen best lipreaders were included in the study (9 female, 9 male). Each subject was scanned while either watching a movie with a speaker silently articulating numbers (lipreading condition) or watching a static image of the same speaker (baseline condition). Subjects were instructed to respectively repeat internally the seen number or the number ‘one’. Compared to the baseline condition, silent lipreading activated temporal areas in both hemispheres with the largest activations in the left hemisphere. When the whole group was examined, no activation in the primary auditory cortex was found. But when investigating the two sexes separately, the female group did demonstrate an activation of the left PAC. There was no significant activation in the right female PAC or in the left and right male PAC. This sex difference in activation pattern indicates that males and females use different neural strategies to come to the same performance in lipreading and explain previous inconsistent results where no differentiation for sex was made.
Introduction

Lipreading is the ability to perceive language by watching the lip, tongue, and jaw movements of a speaker. Hearing impaired persons use lipreading to compensate for their hearing loss, but also with normal hearing, lipreading facilitates the perception of speech, particularly in noisy surroundings (Erber, 1975). The influence of these visual cues is normally outside the awareness of normal hearing persons. Lipreading is a natural skill in hearing impaired and in normal hearing persons. Short-term training only slightly improves the ability in lipreading, but longterm reliance on visual speech perception, like in congenitally deaf subjects, does affect the lipreading performance (Bernstein, 2000, 2001; Summerfield, 1992).

The influence of vision on heard speech is demonstrated when the visual image and auditory signal don’t match. An example in daily practice is a dubbed movie, which results in a disturbing feeling. Another example of visual images not matching the auditory signal is the phenomenon known as the McGurk effect, where an auditory illusion originates from lip movements that do not match the auditory syllables (e.g. auditory /ba/ combined with visual /ga/ is perceived as /da/) (McGurk and MacDonald, 1976).

Apparently, in speech perception, normal hearing subjects do not only rely on auditory cues, but also visual cues have an influence. This was confirmed by brain-language studies that revealed a modulation of temporal region responses when speech sounds were simultaneously presented with visual lip movements (Sams et al., 1991; Mottonen et al., 2002; Besle et al., 2004; Ojanen et al., 2005). Even when visible speech is presented alone, it affects auditorytemporal regions. Silent lipreading (only visible speech) produces activation of the temporal lobe, with secondary auditory cortex activation being consistently reported (Calvert et al., 1997; Ludman et al., 2000; MacSweeney et al., 2000; Campbell et al., 2001; Bernstein et al., 2002; Calvert & Campbell, 2003; Paulesu et al., 2003). Whether this activation of temporal areas during silent lipreading is restricted to hierarchically higher...
order association areas or whether it also involves primary auditory cortex (PAC) remains unsolved (e.g. Calvert et al., 1997; Bernstein et al., 2002). It is generally assumed that primary sensory cortices are devoted to one sensory modality only, in this case hearing. This theory has exceptions, like in early deaf subjects where the primary auditory cortex has been activated by visual stimuli (Finney et al., 2001) and reciprocally in early blind subjects (Cohen et al., 1997; Weeks et al., 2000), indicating the ability of the brain to reorganize after loss of a sensory modality. But the debate on whether or not the PAC is activated during silent lipreading concerns normal hearing subjects. If this activation would indeed be found, it would indicate variability for input modality in primary cortices. This study was designed to investigate whether or not the primary auditory cortex is involved in processing visible speech.

Materials and Methods

Subjects

Eighteen healthy, right-handed volunteers participated in this study (9 males, 9 females), their ages ranged from 18 to 27 years (mean 21 years) for the males and from 19 to 25 years (mean 22 years) for the females. All volunteers gave written informed consent according to the Declaration of Helsinki. The Medical Ethics Committee of the University Medical Center Groningen approved the study. None of the subjects had any history of psychiatric or neurological disorders. Prior to the scanning, subjects were tested for their hearing thresholds using standard audiometric measures (all subjects had thresholds < 20 dBHL, for 0.25-8 kHz) and were tested on their lipreading ability using the same silently articulated numbers as during scanning. As stated above, lipreading is a natural skill and it is difficult to train subjects in lipreading to reach a higher level of performance (Summerfield, 1992). Therefore, only subjects who scored more than 75 % on the lipreading test were included in this study. On the day of scanning,
the lipreading test was again conducted while subjects were positioned in the scanner.

**Data Acquisition**

Regional cerebral blood flow (rCBF) was measured using $[^{15}\text{O}]$-water and a Siemens Ecat Exact HR+ PET scanner operated in three-dimensional mode with a 15.5 cm axial field of view. The scanner acquires 63 slices simultaneously. Each subject was scanned 12 times for the distribution of $[^{15}\text{O}]$-water with a 10 minutes interval between two scans to allow for decay. Each scan was performed after an intravenous bolus injection of 500 MBq of $[^{15}\text{O}]$-water per scan. Except for the first scan, scanning started 30 s prior to injection, to account for background activation. Ten seconds before injection, the stimulus was started. After injection, data were collected during 120 s. A scan specific calculated attenuation correction was performed to minimize interscan displacement-induced variance (Reinders et al., 2002).

**Experimental design**

The experimental design is adopted from Calvert et al. (1997) and is similar to the designs used by MacSweeney et al. (2000), Campbell et al. (2001) and Paulesu et al. (2003). It consists of a baseline and lipreading condition. During the lipreading condition, participants viewed a movie of the whole face of a speaker silently articulating numbers (no auditory speech) with an interval of 3 s and were instructed to silently repeat the viewed numbers. During the baseline condition, subjects viewed a static image of the speaker with the same interval of 3 s. Subjects were instructed to repeat the number ‘one’ each time the face appeared to control for subvocalization and to focus attention. Each condition was presented 6 times in a random order. For the baseline, the same set of images was shown 6 times, for the lipreading condition 6 different sequences of numbers were made to avoid
the effect of learning throughout scanning. Subjects had earplugs to reduce surrounding noise and were trained not to move lips or tongue when silently repeating numbers.

Data analysis

The 2000 version of Statistical Parametric Mapping (SPM2: software from the Wellcome Department of Cognitive Neurology, London, UK) was used for spatial transformations (realignment, transformation into standard stereotactic space and smoothing with a isotropic Gaussian kernel of 8 mm FWHM) and statistical analysis (Friston et al., 1995). An ANOVA estimated the following parameters: two groups (male and female), two conditions (lipreading and baseline) and the mean perfusion to normalize for global flow differences (Multigroup, conditions and covariates). Each scan was scaled to a mean global activity of 50 ml/100ml/min. Hypotheses about regionally specific condition effects were tested comparing the estimates, using linear compounds or contrasts. The resulting set of voxel values for these contrasts constituted the associated SPM of the t-statistics. The significance threshold used for the analysis was p<0.05 corrected for multiple comparisons with False Discovery Rate (Genovese, C. R., Lazar, N. A. & Nichols, T., 2002) with an extent cluster threshold of more than 8 voxels. The results are displayed on the smoothed anatomical MRI template of SPM2.

Pekkola et al. (2005) stated that the signal changes in the PAC due to lipreading might be weaker compared to activation elicited by auditory stimulation and therefore they conducted a region of interest (ROI) analysis in the PAC. A ROI analysis of the PAC is also more appropriate since it gives the overall statistical result for the PAC i.e. it is both more specific and sensitive. Our a-priori hypothesized areas, i.e. the left and right PAC, were defined using the SPM Anatomy toolbox (Eickhoff et al., 2005) and MarsBaR toolbox was used for the ROI analyses (MARSeille Boîte À Région d'intérêt, Tzourio-Mazoyer et al., 2002). Specifically, we created anatomical ROI's
based on the three-dimensional probabilistic cytoarchitectonic maps from the SPM Anatomy toolbox (Eickhoff et al., 2005).

A correct identification of the PAC is essential for correct interpretation of the data. Several authors reported intersubject variability in size and location of the PAC (Penhune et al., 1996; Leonard et al., 1998; Morosan et al., 2001; Rademacher et al., 2001b). To account for this problem of variability in size and location of the PAC, the individual brains were normalized into a standardized stereotactic frame and to remove residual variance in brain structure a Gaussian smoothing filter of 12 mm was applied. Furthermore, we identified the PAC using probability maps, based on the cytoarchitecture of 5 male and 5 female brains (Morosan et al., 2001; Rademacher et al., 2001b; Eickhoff et al., 2005). The inclusion of both male and female brains is essential since it has been found that the proportional volume of the PAC is bilaterally larger in females (Rademacher et al., 2001a).

To compensate for differences in stereotactic space between SPM and the Anatomy toolbox, a linear transformation was applied to the anatomical ROI’s. MarsBaR was then used to conduct the statistical analyses on these ROI’s independently i.e. lateralization was not investigated. The statistical procedure in MarsBaR is the same as in SPM, but instead of analyzing on a voxel-by-voxel basis like SPM does, all voxels in a region are averaged and hence inferences about the whole region can be made. Also in MarsBaR, contrasts were considered significant at $p<0.05$. 

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Results

In this chapter, we only report and discuss the temporal areas involved in silent lipreading. Comparing lipreading with the baseline in all 18 subjects, an activation cluster was observed in the temporal lobe of both the left and right hemisphere. The cluster in the left hemisphere involved parts of the superior and middle temporal gyrus and fusiform gyrus (Brodmann areas 21, 22 and 37) (Figure 1A and Table1). The cluster in the right hemisphere covered a smaller part of the superior and middle temporal gyrus at the junction of the temporal and occipital lobe (BA 22 and 37). The activation in the left and right superior temporal regions covered the planum temporale (secondary auditory region) but did not cover the medial part of Heschl’s gyrus, where the primary auditory region is located (see Figure 1B).

Activation in the PAC was investigated with a region of interest analysis. Results of the whole group (females and males) did not reveal activity in the left or right PAC; the mean activity had a p-value of 0.356 and 0.646 for the left and right PAC respectively. But when the female group was analyzed separately, significant activation in the left PAC was revealed (p=0.042) (Figure 2). They did not show significant activation in the right PAC (p=0.366). Males on the other hand showed no significant activity in the left (p=0.879) or right PAC (p=0.804). The difference between men and women in activity of the left PAC was significant with p=0.021.
Figure 1. Full-color in appendix. Spatial distribution of significant increases in brain activation of the whole group (9 males and 9 females) when comparing lipreading to the baseline. Activations are superimposed on the smoothed anatomical template of SPM2. Clusters are significant at p<0.05 FDR corrected for multiple comparisons. R=right, L=left hemisphere. (A) Activations in the cerebral cortex as an overlay on the volume rendered template. The activation cluster in the left temporal lobe is much larger than the cluster in the right homologue. (B) A horizontal slide 7 mm above the anterior commissure (z=7). The probabilistic cytoarchitectonic maps of the left and right primary auditory cortex are displayed in blue (Eickhoff et al., 2005). This slide shows that the significant activations (in red) do not cover the primary auditory regions.
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Table 1. Clusters of significant* voxels for lipreading minus baseline of the whole group (males and females) located in the temporal lobes. Only the highest peaks of activation are reported for each cluster, with corresponding stereotaxic (Talairach) coordinates and t-value. *Significant at cluster level for p<0.05 FDR-corrected for multiple comparisons, extent threshold 8 voxels, voxel size 2x2x2 mm. Brain regions were identified using the Talairach atlas and the stereotactic atlas of the human brain of Mai et al. (Talairach and Tournoux, 1988; Mai et al., 1997)

<table>
<thead>
<tr>
<th>Brain region (Brodmann Area)</th>
<th>Number of voxels in cluster</th>
<th>Side</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fusiform Gyrus</td>
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<td>Left</td>
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<td>-49</td>
<td>-16</td>
<td>6.54</td>
</tr>
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<td>-44</td>
<td>7</td>
<td>6.32</td>
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<tr>
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<td>-35</td>
<td>5</td>
<td>5.33</td>
</tr>
<tr>
<td>Mid. Temporal Gyrus</td>
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<td>Right</td>
<td>44</td>
<td>-62</td>
<td>5</td>
<td>5.67</td>
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<tr>
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<td>-64</td>
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<td>4.71</td>
</tr>
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<td></td>
<td>59</td>
<td>-35</td>
<td>9</td>
<td>4.65</td>
</tr>
</tbody>
</table>

Figure 2. Regional cerebral blood flow during lipreading relative to the baseline of each group, based on all voxels in the left or right PAC (with a global mean flow of 50 ml/100g/min). Error bars indicate the 90% confidence interval of the mean across subjects per condition. * = Significant (p<0.05) in- or decrease in perfusion during lipreading relative to the perfusion of the baseline of the group, ** = Significant (p<0.05) difference between the two groups.
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Discussion

The present study was designed with a lipreading condition and a static face baseline condition and with the instruction of internal repetition. We adopted the design of (Calvert et al., 1997), who was the first to report PAC activation during lipreading. One of the drawbacks of this design is the lack of a moving content in the baseline condition. It is however unlikely that this difference in moving content between the two conditions explains the activation of the PAC in females and its absence in males. Another possible constraint is the use of internal repetition, which disallows the investigators to monitor the subjects’ performance or attention. The use of internal repetition was used in previous studies that did find (Calvert et al., 1997) or did not find (MacSweeney et al. 2000; Campbell et al., 2001; Paulesu et al., 2003) PAC activation during lipreading. Because we wanted to contribute to the debate on involvement of the PAC during silent lipreading, we choose the task of internal repetition to closely resemble the previous studies.

The voxel-wise analysis of SPM did not have enough power to detect significant activation of the PAC in the whole group, nor in the two groups separately. Like Pekkola et al. (2005), we used region of interest analysis to reach maximal statistical power in the study of PAC activation during lipreading. A difference in power between the two analyses might be expected. Pooling the data of all voxels in the PAC gives a reduced standard error, resulting in a higher t-value and hence more power. And indeed, with this ROI analysis we did find a significant activation of the left PAC in females but not in males and this sex difference in PAC activation was significant. Of course, caution has to be made when pooling data to improve sensitivity. However, in this study, a priori defined regions were used and the significant activation in the left PAC, as shown in figure 2, shows a contrastvalue that is not uncommon for PET activation studies. This clearly indicates that the reported results are true effects and not an artifact of shifting thresholds.

Our study contributes to the debate on whether or not the PAC is
involved in silent lipreading by showing that PAC involvement depends on the sex of the experimental group, with only females having activation in the left PAC during lipreading. Literature showed inconsistent results concerning the involvement of the PAC. A few studies found PAC activation (Calvert et al., 1997; Pekkola et al., 2005), whereas other studies only found secondary auditory cortex activation (Campbell et al., 2001; Bernstein et al., 2002; Paulesu et al., 2003). In these previous studies, sex was not investigated as an explanatory parameter. Some of these studies didn’t mention the sex of their volunteers (Calvert et al., 1997; Bernstein et al., 2002; Olson et al., 2002). On the other hand, Campbell et al. (2001), Calvert et al. (2003) and Pekkola et al. (2005) noted the number of male and female subjects in their volunteer group, but only the results of the whole group were displayed. And in a third group of studies, PAC activation was found in only one of the subjects, but the sex of these individuals was not noted (Ludman et al., 2000; MacSweeney et al., 2000). Finally, Paulesu et al. (2003) and Sekiyama et al. (2003) investigated only male subjects and they found no activation in primary areas during silent lipreading, which is in agreement with our results for the male group.

Our results show a larger activation cluster in the left than in the right hemisphere, although no formal test for lateralization was performed, and the ROI analysis showed that the left PAC was activated in the female group. This is in agreement with previous results on laterality in lipreading (Campbell et al., 1996; Smeele et al., 1998). Also heard speech is strongly left lateralized in subjects (for review see Tervaniemi & Hugdahl, 2003). On the other hand, face-processing is largely based in the right hemisphere (Rhodes, 1985). As Campbell (1998a) stated: while the right hemisphere could sometimes show a speed advantage in analyzing facial speech images, it is the left hemisphere that is critical for categorizing speech.

Although the present chapter focuses on activation in the PAC, possible activation differences in visual areas between males and females might be of interest for the discussion of the PAC results, namely the seen sex
differences in the PAC might be due to a sex difference in the first processing modality. Therefore we also investigated the visual areas (to be published separately). A region of interest analysis in the visual areas did not show a correlation with the sex differences in the PAC. Hence, the differences in the PAC are not a mere result of a higher visual activation in females.

Activation of the primary auditory cortex in females during visible speech processing suggests that there is more variability for input modality than had been suspected (Campbell, 1998b). In the case of normal hearing subjects, activation of the PAC was assumed only to occur in purely auditory processing. The present results show a relation between visual input and PAC activation. These findings raise questions about how the PAC is embedded in the visible speech network and about its function. With the current PET design, these questions can not be answered but literature gives us strong indications about the pathway and function.

There are two possible pathways which may connect the PAC into the visible speech network: 1) either the PAC is activated in an early stage through a subcortical relay station or 2) the information is processed from the primary visual cortex to associative areas, including higher order auditory areas, which in turn have projections to the primary auditory cortex, i.e. a late involvement of the PAC. In the latter, the PAC is activated because of associations with heard speech. Our study design does not allow us to determine the time course of activated areas. However, when Nishitani and Hari (2002) measured cortical activation sequences in subjects viewing verbal lip forms with whole-head magnetoencephalography (MEG), they found that cortical activation progressed from the occipital visual areas to the superior temporal cortex, from there to the inferior parietal lobe, proceeding to the inferior frontal lobe (area of Broca) and ending in the primary motor area. It must be noted that Nishitani and Hari (2002) only found activation in the secondary auditory areas. But it is known from monkey studies that secondary and primary auditory areas are reciprocally connected (e.g. Kaas and Hackett 1998). If the early involvement theory would be more likely, the
activation of the superior temporal regions had to be detected together with the occipital areas or even sooner, which was not found by Nishitani and Hari (2002). Based on this MEG-study, we think that the involvement of the PAC in the present study results from a late involvement mechanism of the PAC through association cortices.

What can be the function of involvement of the PAC during silent lipreading? One possible explanation was stated by the group of Campbell et al. (2001). In one study they did find activation in the PAC (Calvert et al., 1997), but in others they didn’t (Campbell et al., 2001). They explained these seemingly contradictory results in terms of familiarity of the subjects with the voice of the seen speaker, i.e. activation in temporal areas specialized for acoustic speech processing may reflect a form of acoustic imagery, capturing the voice qualities of the speaker (Campbell et al., 2001). However, this explanation of Campbell et al. (2001) seems unlikely because other studies demonstrated that auditory verbal imagery is associated with activity in secondary but not in primary auditory areas (Jancke and Shah, 2004). Moreover, none of our subjects, neither from the male nor from the female group, knew the speaker. Thus, we conclude that familiarity with the speaker’s voice can not account for the involvement of the PAC in the female group. The involvement of the PAC probably reflects the fact that for normal hearing subjects the sight of the speaker is usually accompanied by heard speech and visual and auditory speech perception is tightly connected.

But then the question remains why would females exhibit more activation in the PAC than males? It is generally believed that women have better language skills than men and in general females also perform better on lipreading tasks than their male counterparts (Watson et al., 1996; Kimura, 1999). A better lipreading ability is accompanied by larger activation in temporal brain areas (Ludman et al., 2000). But because all our subjects had similar performance scores on the lipreading test and because we used a fixed set of lipreading items, it is unlikely that a difference in lipreading ability causes the sex difference in PAC activation. However, it is
possible that females have a different strategy for lipreading than males and hence involve different cortical areas for processing the visible speech, even though both groups had the same level of performance. Hence, we can only speculate about the function of PAC involvement during silent lipreading. Differences in lipreading strategy might be linked to differences in active listening of the primary auditory cortex, i.e. the female brain might attend more to the (normally accompanying) auditory sound than the male brain. Activation in primary auditory cortex during silence as part of an auditory attention system has been demonstrated by Hunter and colleagues, but no sex differences were investigated (Hunter et al., 2006). Hence it is possible that females connect the visible speech image to the associated auditory speech sound thereby activating not only secondary, but also primary auditory areas. Males, on the other hand, only activated secondary auditory areas, which might indicate that they rely less on the auditory counterpart of the visible speech image than females.

In conclusion, our data show that only females significantly activate the left primary auditory cortex during visible speech processing. These results suggest that a different neural network is involved in lipreading in the two sexes. Both groups scored high on the test and this indicates that neither pattern of activity is superior to the other in terms of performance in the present lipreading task. This study contributes to the ongoing debate on whether or not the PAC is involved in silent lipreading by showing that this involvement of the PAC depends on the sex of the experimental group.
References


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