

Attention modulates activity in the primary and the secondary auditory cortex: a functional magnetic resonance imaging study in human subjects

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Abstract

Using functional magnetic resonance imaging, ten healthy subjects were scanned whilst listening to consonant-vowel syllables under three different conditions: (i) a 'no-attention' condition required subjects to ignore the stimuli; (ii) an 'attend' condition requiring attentive listening to stimuli; (iii) a 'detect' condition requiring detection of a specific target syllable. Hemodynamic responses were measured in the primary and secondary auditory cortex. These three conditions were associated with significantly different activations in the primary and secondary auditory cortex. The strongest activations were found for the 'detect' condition, followed by the 'attend' condition. The weakest activation was evident during the 'no-attention' condition. There were also stronger activations in the left hemisphere and within the primary auditory cortex. These results suggest that the primary and secondary auditory cortex play a main role in the selective attention. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

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Attention is a basic mechanism enabling the preferred or attenuated processing of incoming stimuli. In the auditory modality a person can attend selectively to a particular speaker's voice while turning off other, simultaneous, conversations ('cocktail party phenomenon'). Much knowledge on the neural bases of auditory selective attention in humans comes from event-related potential (ERP) and magnetoencephalography (MEG) studies. These studies have shown that the N100 or a later tonic negative shift which is called the 'processing negativity' (PN) (for a review, see Näätänen [11]), elicited by stimuli delivered to the attended ear was considerably larger than the responses elicited by stimuli to the non-attended ear (enhancement effect). Although the time resolution of these techniques is excellent allowing resolution of neural processes down to milliseconds, limited spatial resolution prevents precise localisation of the enhancement effect within primary or secondary auditory cortex. However,

some MEG studies claim to find neuromagnetic dipoles within primary auditory cortex (in particular the right) responsible for the enhancement effect [6]. Recent brain imaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), both with superior spatial but inferior temporal resolution, showed some dependency of the regional cerebral blood flow (rCBF) and the hemodynamic response in the auditory cortex to different attentional loads. However, the results are not uniform ranging from no effect [19] over moderate [21] to strong attentional effects [7,13,18]. Other studies, employing dichotic listening paradigms, thus introducing spatially directed attention, which is partly different from the pure selective attention paradigms, found that attending selectively to the right-ear input (while ignoring the left-ear input) predominantly activated the auditory cortex in the left hemisphere and vice versa [1,12,19]. However, all brain mapping studies performed group analysis by pooling the stereotactically normalized functional data sets. In auditory cortex, this technique has the disadvantage that the highly variable gyral and sulcal morphology of the primary and secondary auditory cortex [16] is not accounted for. This study was designed to reconsider whether selective attention

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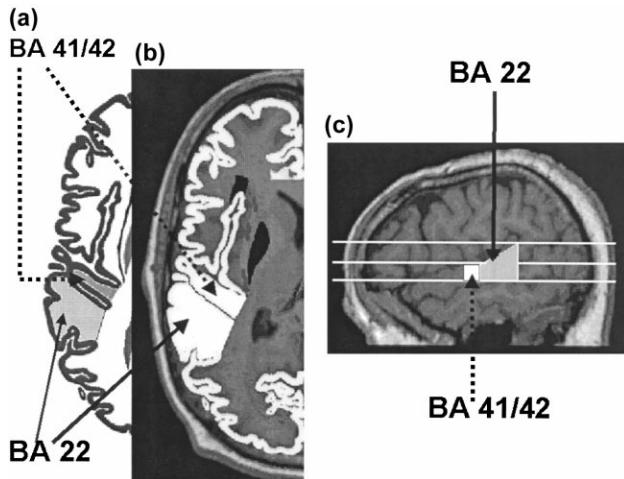


Fig. 1. Description of the anatomical landmarks used to delineate the primary and secondary auditory cortex. (a) Template of the Talairach atlas at $z = 12$ mm with the highlighted primary and secondary auditory cortex; (b) the same Talairach template overlaid onto a MR-scan; (c) sagittal slice demonstrating the inferior and superior borders of the primary and secondary auditory cortex. Upper, middle, and inferior lines representing z -positions at 20, 12 and 4 mm according to the Talairach atlas.

might influence the activity within the auditory cortex by using high resolution fMRI and circumventing group analysis. In particular, we examined whether there is an enhancement effect (i) within primary and secondary auditory cortex, (ii) whether it is different for the primary and secondary auditory cortex, (iii) and whether it is hemisphere dependent. In order to account for the high variability in gyral and sulcal morphology of the auditory cortex, activations in the vicinity of the primary and secondary auditory cortex were measured in individual brains and subjected to conventional statistical analysis.

Ten male right-handed volunteers, from 20 to 40 years of age, without history of neurological or audiological illness, were studied. After a full explanation of the research, subjects gave informed written consent according to a protocol approved by the Ethics Committee of the Heinrich-Heine University, Düsseldorf. Functional MR images were acquired using a 1.5 Tesla Siemens MRI system (SIEMENS Magnetom Vision, Erlangen, FRG), equipped with echo planar imaging (EPI) capability and a standard radiofrequency (RF) head coil for transmit and receive. Pulse sequence parameters were as follows: gradient echo EPI; TR = 6 s; TE = 66 ms; field-of-view (FOV) = 200×200 mm; flip angle (α) = 90° ; matrix size = 64×64 ; resolution = $3.125 \times 3.125 \times 3.0$ mm; interslice gap = 0.3 mm. Sixteen axial slices were oriented in the anterior-posterior commissure (AC-PC) plane, the lowermost slice being 20 mm below the AC-PC line. Additionally, high-resolution, T1-weighted anatomical images of the entire brain were obtained in 3D using the magnetization-prepared, rapid acquisition gradient echo pulse sequence with the following parameters: TR = 11.4 ms; TE = 4.4 ms; $\alpha = 15^\circ$; inver-

sion time = 300 ms; 1 excitation; FOV = 230 mm; matrix = 200×256 ; 128 sagittal slices with 1.25 mm slice thickness.

During scanning the room lights were dimmed and the subjects' eyes were open. Auditory stimuli were presented binaurally using a digital playback system and a magnetically shielded transducer system. The acoustic stimulation system terminated in tightly occlusive headphones allowing unimpeded conduction of the stimulus with good suppression of ambient scanner noise by about 20 dB. During each condition, a series of 48 images were acquired comprising multiple 'baseline' periods (OFF), where subjects heard only the ambient machine noise, alternating with 'activation' periods (ON), where auditory stimuli were delivered. Each series, lasting about 7 min, began with three baseline datasets (15 s interval), followed by 48 datasets during which 'baseline' alternated with 'activation' every 36 s (72 s/cycle, 12 images/cycle, four cycles).

Stimuli were 16-bit, digitally-sampled, consonant-vowel (CV) syllables (/ka/, /ta/, /pa/, /ga/, /da/, /ba/) as previously described [9,15]. One-third of the trials consisted of the target syllable /ta/ for the 'detect' condition. Three experimental conditions were performed. The first condition was to ignore the acoustic stimuli and to concentrate on the hands or the feet (no-attention). In the second condition, a simple listening instruction was given requiring the subjects to attentively listen to the stimuli (attend). During the third condition, subjects were instructed to respond to any occurrence of the target syllable by briefly lifting the left index finger (detect). The order of stimuli was randomised for each subject. Stimulus intensity was 90 dB based on previous findings [9]. To reduce further possible masking of the stimuli by scanner noise, a TR of 6 s was adopted [15]. Stimulus presentation was triggered by the EPI sequence to fall in the interscan gap of 4 s (sequence scanning time = 2 s) resulting in a non-masked presentation of stimuli (four stimuli per sequence separated by an interstimulus interval of 1 s).

Image analysis was performed using SPM96 software [4]. The datasets were realigned, spatially normalized [17], and smoothed with a Gaussian kernel of 8 mm [4,5,17]. The effects of global activity and time were removed using linear regression and sine/cosine functions as confounds. Condition specific effects (no-attention, attend, and detect compared to baseline) were estimated with the general linear model using a delayed box-car waveform. These statistical contrasts were used to create an SPM (Z) and thresholded at a Z -value of 3.09 (corresponding to $P < 0.001$, uncorrected for multiple comparisons). The activated voxels surviving this procedure were superimposed on individual stereotactically normalized high-resolution anatomical scans. Because the activated clusters covered a wide range of auditory cortex, we defined volumes of interest (VOI) in each hemisphere to account for the diversity of the auditory cortex (primary, immediate, and secondary auditory cortex). These VOIs were defined

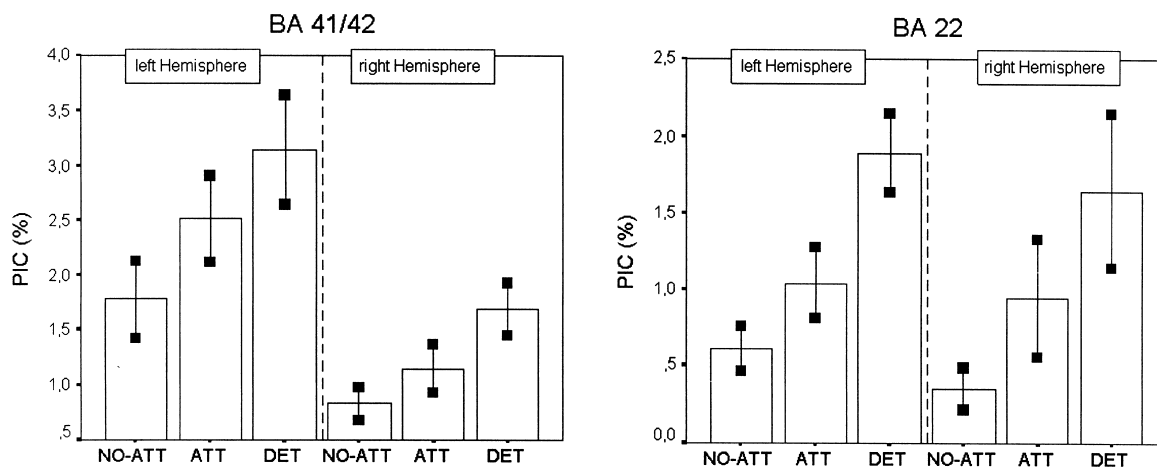


Fig. 2. Mean percent intensity changes (PIC) relative to baseline for the three experimental conditions: NO-ATT, no-attention; ATT, attend; DET, detect. SEM as vertical lines.

according to the Talairach atlas and prominent sulcal and gyral landmarks [8]: (i) the primary and immediate auditory area (Brodmann area, BA 41/42) was defined as a region covering Heschl's gyrus (as defined by the Heschl's sulcus and the first transverse sulcus) on at least three horizontal planes taken from the Talairach atlas ($z = 12$ and $z = 4$); (ii) secondary auditory cortex was defined as being posterior to primary and immediate auditory cortex extending in the inferior and superior directions from plane $z = 0$ and to $z = 20$ (Fig. 1). The posterior border was taken as the bifurcation of the Sylvian fissure into the ramus posterior ascendens and ramus posterior descendens.

Because the exact location of different cytoarchitectonic regions within the auditory cortex is currently unknown, our VOI definitions and Brodmann area (BA) designations should be taken as approximate only. For each VOI, the three highest peak activations (separated by at least half the width of the smoothing kernel (4 mm)) were identified and percent intensity change measures (PIC) relative to baseline were calculated. The three PICs of each VOI were averaged to a mean PIC representing the activity of that VOI. It is worth mentioning that the spatial smoothing of the dataset means that the signal change within a given voxel (and a given peak activation) represents the average signal change in a small region around that voxel, weighted by the smoothing kernel employed (8 mm in all three dimensions). Thus, our intensity measure is a reliable estimate of the activity of a given VOI.

These PICs were subjected to a $3 \times 2 \times 2$ -way analysis of variance with repeated measurements factors (attention: no-attention, attend, and detect; hemisphere: right versus left; area: primary versus secondary auditory cortex). This analysis revealed significant results for the main effects 'hemisphere' ($F(1, 9) = 54.03$, $P < 0.001$), 'area' ($F(1, 9) = 21.8$, $P < 0.001$), and 'attention' ($F(2, 8) = 24.9$, $P < 0.001$). None of the interactions were significant. There was stronger activity in the left hemisphere and within primary auditory cortex. Most

importantly for this study, the result with respect to the 'attention' factor was highly significant and is qualified by increasing PICs with increasing attentional demands (Fig. 2). A trend analysis revealed a highly significant linear trend for the 'attention' factor ($F(1, 9) = 33.9$, $P < 0.001$, $r^2 = 0.79$). No further trend was significant. We also performed a-posteriori analyses by comparing the mean PICs for the three conditions and revealed highly significant differences between the 'no-attention' and 'attend' as well as between the 'no-attention' and 'detect' conditions (all P -values < 0.001). There was no significant difference between the 'attend' and 'detect' conditions, although there was a trend for a larger PIC during the 'detect' condition ($P = 0.15$).

In summary, our auditory stimulation evoked strong hemodynamic responses in primary (BA41/42) and secondary (BA 22) auditory cortex. But most importantly, we found stronger hemodynamic responses in BA41/42 and BA22 when subjects were required to attend to the stimuli or to detect the target stimulus. This enhancement effect is important for several reasons: First, there is an activity increase in BA41/42 and BA22 during the 'attend' and 'detect' conditions compared to the 'non attention' condition although the physical properties of the stimulation remains the same across all conditions. Thus, attention and detection should be responsible for this enhancement effect. Second, this enhancement effect is also found within BA41/42, a brain area for which a direct modulation of activity by attention was hard to measure due to the inter-subject averaging procedure blurring the activations within the primary auditory cortex because of the highly variable gyral and sulcal morphology of that region. With respect to this finding, it is worth mentioning an ongoing controversy as to whether attentional processes might modulate neuronal activity within primary sensory areas. Some researchers suggest that attentional modulation is related to activity in secondary sensory areas [3]. Our data supports the notion that there is modulation of neuronal activity within the

primary auditory cortex due to attentional processes which resembles recent findings in the visual modality [10,20]. These findings might indicate that attention may act upon early stages of information processing. However, the precise mechanism by which early auditory processing is modulated by attention remains unknown. A tonic increase of activity in the auditory cortex might occur in anticipation of a stimulus. Alternatively, there could be a phasic modulation such that each target stimulus elicited a larger response in an auditory target area. In future studies it is necessary to disentangle these two alternatives.

A further result of the present study was the stronger activation in left auditory cortex which is in conflict with the hypothesis of a generally larger activation in the right hemisphere during attention tasks [6]. This stronger activation in left auditory cortex might depend on the verbal stimuli used here which most likely evoked stronger responses in neural networks specialized for verbal processing in the left hemisphere. Whether this left-sided activity dominance will remain when applying non-verbal stimuli has to be investigated further. Finally, we found stronger activations within primary than in secondary auditory cortex. This activation pattern might be due to the simple nature of our stimuli eliciting phonetic rather than complex analyses. These phonetic analyses are most likely processed in the vicinity of primary auditory cortex while more complex auditory analyses require the activity of neural networks located more posterior on the superior temporal gyrus and more inferior in the superior temporal sulcus [2,14].

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