

fMRI measurements of sound-level encoding
in the absence of background scanner noise

¹ **Deborah A. Hall ***

¹ **Mark P. Haggard**

¹ **A. Quentin Summerfield**

¹ **Michael A. Akeroyd**

¹ **Alan R. Palmer**

² **Richard W. Bowtell**

¹ MRC Institute of Hearing Research
University Park
Nottingham
UK
NG7 2RD

² Magnetic Resonance Centre
School of Physics and Astronomy
University of Nottingham
Nottingham
UK
NG7 2RD

* Address for correspondence to the first author

Tel : 0115 922 3431
Fax : 0115 951 8503
e-mail : debbie@ihr.mrc.ac.uk

Submitted to : **The Journal of the Acoustical Society of America**

Date of submission : **27 July 2000**

Date of revised manuscript : **1 November 2000**

Short title : fMRI measurements of sound-level encoding

PACS numbers : 43.66.Cb, 43.66.Ba, 43.64.Ri

Abstract

Effects of sound-level on auditory cortical activation are seen in neuroimaging data. However, factors such as the cortical response to the intense ambient scanner noise and to the bandwidth of the acoustic stimuli will both confound precise quantification and interpretation of such sound-level effects. The present study used temporally “sparse” imaging to reduce effects of scanner noise. To achieve control for stimulus bandwidth, we compared 3 schemes for sound-level matching across bandwidth: component level, root mean square power and loudness. The calculation of the loudness match was based on the model reported by Moore et al. (1996). Ten normally-hearing volunteers were scanned using fMRI whilst listening to a 300-Hz tone presented at six different sound levels between 66 and 91 dB SPL and a harmonic-complex tone ($F_0 = 186$ Hz) presented at 65 and 85 dB SPL. This range of sound levels encompassed all three bases of sound-level matching. Activation in the superior temporal gyrus, induced by each of the 8 tone conditions relative to a quiet baseline condition, was quantified as to extent and magnitude. Sound level had a small, but significant, effect on the extent of activation for the pure tone, but not for the harmonic-complex tone, whilst it had a significant effect on the response magnitude for both types of stimulus. Response magnitude increased linearly as a function of sound level for the full range of levels for the pure tone. The harmonic-complex tone produced greater activation than the pure tone, irrespective of the matching scheme for sound level, indicating that bandwidth had a greater effect on the pattern of auditory activation than sound level. Nevertheless, when the data were collapsed across stimulus class, extent and magnitude were significantly correlated with the loudness scale (measured in phons), but not with the intensity scale (measured in SPL). We therefore recommend the loudness formula as the most

appropriate basis of matching sound level to control for loudness effects when cortical responses to other stimulus attributes, such as stimulus class, are the principal concern.

PACS numbers : 43.66.Cb, 43.66.Ba, 43.64.Ri

Introduction

Functional magnetic resonance imaging (fMRI) is a valuable tool for the study of human auditory cortical processing as it can non-invasively measure the topographical organisation of cortical responses to an acoustic signal. fMRI indirectly measures the neuronal population responses through the metabolic consequences of neuronal activity on changes in the ratio of oxygenated to de-oxygenated haemoglobin in the blood (the blood-oxygen-level-dependent, BOLD, response). Here we sought to quantify the effects of sound level on both the extent and magnitude of activation in the auditory cortex and to determine the form of any relationship between them. By using a sparse imaging protocol with silent intervals between image acquisition, responses to sound level were measured in the absence of background scanner noise.

A. Neuroimaging studies of sound intensity

Both fMRI and positron emission tomography (PET) studies have measured systematic changes in auditory activation with sound level, particularly on the supra-temporal plane and superior temporal gyrus (e.g., Jäncke et al., 1998; Lockwood et al., 1999; Millen et al., 1995; Mohr et al., 1999; Strainer et al., 1997). Results have generally indicated a growth in auditory activation with sound level. Understanding brain responses to sound level contributes not only to knowledge of sensory coding, but also to methodological awareness of stimulus control. However, the organising principles of the cortical response to sound level are not yet clear. The lack of a clear consensus on sound-level effects may be a consequence of differences in the range of sound levels presented, particularly if the response saturates at higher levels. Studies have also used different criteria for the specification of sound level; e.g., sound pressure level (Jäncke et al., 1999), sensation level (Lockwood et al., 1999) or dB

relative to a measure of speech intelligibility for each individual subject (Mohr et al., 1999). The ability to exercise control or draw conclusions has also been limited by the coarse quantization or narrow range of levels. Two or three levels are insufficient to determine accurately the shape of the response curve; e.g., to establish whether or not it is linear in dB. The response to sound level has generally been measured across only a few tens of dB relative to the overall system dynamic range of about 120 dB (Viemeister and Bacon, 1988).

B. Effect of the intense background noise in fMRI

fMRI measures of the auditory response to sound intensity in particular risk contamination by the intense background scanner noise. The principal source of noise is the mechanical deformation of the gradient coils caused by the electrical currents flowing in them within the high static magnetic field. For fMRI, the level almost invariably exceeds 100 dB SPL and here was about 127 dB SPL (Foster et al., 2000). For the present study, the acoustic spectrum of the scanner noise was dominated by a harmonic-complex tone ($F_0 = 1.9$ kHz) rising above a background of broadband noise (see Hall et al., 2000, Figure 1).

The scanner noise is a problem for three main reasons. Firstly, it produces its own auditory activation which can overlap with the stimulus-driven auditory response, particularly with conventional imaging protocols where images are acquired at a continuous rate (e.g., Bandettini et al., 1998; Hall et al., 1999; 2000; Shah et al., 1999; 2000; Talavage et al., 1999). This increased baseline level of activation can reduce the size of the experimental effect, and hence reduce the statistical power for detecting stimulus-induced auditory activation. In addition, the supra-threshold magnitude information in the measured response in part reflects an interaction between the responses to the stimulus and to the background noise. Secondly, the

scanner noise can mask the auditory stimulus whenever the stimulus and image acquisition occur close in time. Masking increases the cognitive load for low stimulus levels relative to higher levels, changing the nature of the task by making it harder to detect target stimuli particularly at low sound levels. To overcome masking, presentation levels have tended towards the upper end of the comfortable range of human hearing, and here the cortical response is most likely to saturate. Thirdly, even with hearing protection, the intense background noise can induce a stapedial muscle reflex that alters the sound level transmitted to the inner ear. The level of the sound that triggers this reflex varies across individuals. Although differences in the acoustic reflex threshold do not necessarily reflect differences in loudness perception in normally-hearing listeners (Olsen et al., 1999; Olsen, 1999), imaging studies that use EPI and/or present stimuli towards the upper end of the dynamic range need to consider its effect on sound-level perception.

Temporally sparse imaging can reduce the problems caused by the scanner noise as it intersperses a relatively long period of silence (about 10 s) between bursts of scanner noise and separates the noise in time from stimulus delivery. Sparse imaging minimises perceptual masking and the residual auditory activation effects of the scanner sound. Known effects of intense noise on middle-ear reflexes which may contribute to the masking effects are also thereby minimised. The ability of sparse imaging to detect activation is *not* measurably compromised by the reduction in the number of data averages because sensitivity is maximised by contrasting the peak response with the post-stimulus negative phase of the response (which maximises the percentage change in the BOLD signal between activation and baseline conditions) and, by achieving greater MR signal recovery between image acquisitions (which enhances the BOLD signal-to-noise ratio) (Hall et al., 1998).

C. Requirement for stimulus control

Changes in response magnitude have been used successfully to investigate neural activity patterns associated with different acoustical stimuli including changes in frequency (Talavage et al., 1997), bandwidth (Rauschecker et al., 1997; Wessinger et al., 1997) and pitch strength (Griffiths et al., 1998). When explicitly defining stimulus-evoked activation, it is a potential concern that the observed pattern of activation may partly reflect a response to a separate acoustical property of the stimulus that may not have been tightly controlled across conditions. Evidence to date suggests that both bandwidth (Wessinger et al., 1997) and sound level (Jäncke et al., 1998) have similar effects on the spread of activation on the supra-temporal plane and superior temporal gyrus. Thus, subject to what has been controlled, the two effects may not be easily separable. There may be four possible interpretations for the bandwidth effect as observed. The first explanation, preferred by Wessinger et al. (1997) is that broadband stimuli are intrinsically more effective than pure tones in evoking a neuronal response. This may be especially true in regions of non-primary auditory cortex where neurons respond more strongly to broadband stimuli than to pure tones (Redies et al., 1989). Secondly, the effect of bandwidth could be straightforwardly attributed to the basic spread of auditory excitation across frequency channels, particularly in the multiple tonotopically-organised auditory cortical fields (Merzenich and Brugge, 1973; Thomas et al., 1993). This second explanation is difficult to distinguish operationally from the first. The third explanation draws attention to sound level, an additional acoustical feature that can differ between a pure tone and a broadband stimulus and may therefore be a potential confound. Where details are reported, imaging studies that manipulate bandwidth have sought to control for sound level by equating sound pressure level (e.g., Wessinger et al., 1997).

However, if the bandwidth of a broadband signal is increased while its SPL is held constant, then loudness nevertheless increases. When an increase in bandwidth adds frequency components to separate frequency channels, the loudness model of Moore, Glasberg and Baer (1997) predicts that the excitation pattern widens, increasing the total area and hence the loudness. This result holds true for signals whose bandwidth exceeds the critical bandwidth (e.g., 160 Hz at a centre frequency of 1 kHz) and for signals above about 30 dB SPL (Zwicker et al., 1957; Moore and Glasberg, 1996). As a consequence, the bandwidth effect shown in neuroimaging data may be artefactually overestimated. It is possible that bases for matching other than SPL, such as via a loudness model (e.g., Moore, et al., 1997), would have greater physiological validity at the cortical level. The fourth explanation invokes the consequences of spatial smoothing on voxels that have differing signal-to-noise ratios, where magnitude partly determines extent. If broadband stimuli produce a stronger BOLD response than pure tones, then this is likely to be associated with a greater extent of activation when the statistical map is thresholded at a common probability level.

Further studies are required therefore which control these variables in order to eliminate alternative explanations for the difference in the patterns of activation for pure tones and broadband stimuli. Investigation of the third explanation (the effect of a loudness mismatch) requires control for sound level when measuring other features of the auditory stimulus that drive a particular pattern of cortical response.

D. The present study

The present study quantified effects of sound level on both the extent and magnitude of auditory activation using 300-Hz tones at six sound levels ranging from 66 to 91 dB SPL, in 5-dB increments. The relatively small step size in sound level allowed the determination of the shape of the BOLD response across this intensity

range. By using temporally sparse imaging to overcome masking by the background noise, we were also able to present the tones across a range of naturally occurring sound intensities, the lower end of the range being limited only by the broadband background ambient noise (63 to 68 dB SPL). Ear-defenders attenuated these background levels by about 10 dB at 300 Hz and by about 30 dB between 500 Hz and 10 kHz. There is currently no neuroimaging evidence to favour one sound-level matching scheme over another and so the present study also addressed whether matching based on equal loudness is appropriate for studies of cortical coding. Across normally-hearing listeners, there are individual differences in the slopes of loudness functions measured experimentally (Stevens & Guirao, 1964; Stephen, 1970). Thus, we used a computational method to define loudness (measured in units of phons) that makes no assumptions about individual decision criteria (Moore and Glasberg, 1996; Moore et al., 1997). We investigated the conditions under which activity due to a complex tone approached the activity for a pure tone presented at a higher intensity, but matched for loudness. The design also allowed us to investigate whether bandwidth influences magnitude, as well as extent, of activation; an issue not previously addressed.

I. Methods

A. Subjects

Ten right-handed subjects, aged 20-46, participated in the study. Subjects had no history of neurological impairment. All subjects gave informed written consent and the study was approved by the Nottingham University Medical School ethical committee. Prior to the imaging session, the hearing sensitivity of subjects was measured using pure-tone audiometry. The hearing thresholds of all subjects fell

within the normal range (<20 dB HL) at octave frequencies between 500 and 8000 Hz inclusive.

B. Stimuli and calibration

A harmonic complex signal was synthesized with 16-bit amplitude quantization at a sampling rate of 48 kHz. This stimulus had a fundamental frequency of 150 Hz and was composed of harmonics extending from 300 Hz to 3 kHz inclusive. The harmonics were synthesised with equal amplitude but, as a consequence of the frequency response of the headphones, ranged by 12.6 dB when measured at the ear. The phases of the harmonics were chosen randomly and so stimuli were not specifically selected for their lowest peak factors. This stimulus was then re-synthesized to exploit the full 16-bit digital dynamic range. The harmonic complex was presented at overall levels of 65 and 85 dB SPL (see below for details of the calibration procedure). Next, six 300-Hz pure tones were synthesized. The first had the same amplitude as the 300-Hz component of the 85-dB SPL complex tone, measured at the ear; its level was 66 dB SPL. The remaining five 300-Hz tones had amplitudes that were greater than the 66 dB SPL tone by 5, 10, 15, 20, and 25 dB, i.e., they were presented at levels of 71, 76, 81, 86 and 91 dB SPL (see Table 1). All stimuli were 800 ms in duration, including 10-ms inverted-cosine ramps at onset and offset.

Stimuli were presented diotically through a specially engineered, MR-compatible sound system that delivers acoustic stimuli using electrostatic drivers built into industrial ear defenders (Palmer et al., 1998). The presentation levels reported above were calibrated by mounting the system on KEMAR (Burkhard & Sachs, 1975), equipped with a Brüel and Kjær microphone (Type 4134) connected to a Brüel

and Kjær measuring amplifier (Type 2636), and by measuring the overall power of the stimulus.

The choice of sound levels meant that the 85-dB SPL complex tone was matched in two ways to two different members of the set of pure tones. First, by design, it had the same component level as the 66-dB SPL pure tone. Second, it had approximately the same RMS level (average RMS power = 79 dB, 19 harmonic components) as the 76-dB SPL pure tone (average RMS power = 76 dB). The loudness of all stimuli was also calculated using the computational model of Moore and colleagues (Moore and Glasberg, 1996; Moore et al., 1997). In this model, loudness is a function of the auditory excitation induced by a sound, integrated across frequency (see Figure 1). The background noise level in the scanner room was sufficiently attenuated by the ear-defenders to cause little partial masking and thus had an insignificant effect on the loudness estimates of the stimuli. The loudness estimates of the stimuli are reported in Table 1. The model predicted that none of the pure tones was sufficiently intense to match the loudness of the 85-dB complex tone. Instead, the model predicted that the loudness of the 76-dB and 81-dB pure tones straddled that of the less intense 65-dB complex tone. This model prediction provides a third basis for matching the pure and complex tones for sound level and one that can be evaluated by the stimulus range used in the present study¹.

***** insert Figure 1 and Table 1 here *****

C. Stimulus presentation

The six levels of the pure tone and the two levels of the complex tone defined the eight stimulus conditions of the experiment. Within each condition, ten 800-ms tone bursts were presented in succession separated by 200 ms of silence. The task required target discrimination based on a change in the sound level of the tones.

Targets had an intensity that was 10 dB lower than the non-targets. For example, targets in the 66-dB SPL pure tone condition were presented at 56 dB SPL. To ensure attention to the entire 10 s tone sequence, targets occurred randomly in a ratio of 1:4 and hence could occur more than once in each 10 s sequence. 56-dB targets were at the lowest intensity (in 5-dB steps) that was clearly audible in the MR environment and thus defined the lower end of the intensity range that could be used in the present study. So that the subjects could determine the reference sound level of the non-targets in each epoch, the first two tone bursts in a sequence were always non-targets. Subjects were instructed to press a button with the index finger of the right hand to the occurrence of each target stimulus. A PC logged the times of occurrence of targets and button presses for off-line analysis of detection performance.

One cycle in the experiment consisted of 8 tone conditions followed by a baseline condition and there were 24 such cycles. Tone conditions were ordered so that each condition occurred equally at each of the 8 possible positions within a cycle (according to a Latin-square). Each of the 9 conditions occurred 24 times; giving a total of 216 stimulus epochs and a total experimental time of 39 minutes.

***** *insert Figure 2 here* *****

D. fMRI scanning

The study was performed on a 3 Tesla MR scanner with head gradient coils and a birdcage radio-frequency coil (Bowtell et al., 1994; Bowtell and Peters, 1999). An MBEST echo-planar sequence was used to acquire sets of 16 contiguous coronal images covering the auditory cortex. Each image measured 128 x 128 voxels and the voxel resolution was 3 x 3 x 8 mm. Through-plane voxel resolution was sacrificed in order to achieve better in-plane resolution for the same voxel volume, and hence an adequate signal-to-noise ratio. A set of images took 1072 ms to acquire and these

were acquired every 10.75 s at the transitions between stimulus conditions (see Figure 2). The intense burst of scanner noise produced during image acquisition occurred mostly during the 750-ms silent intervals between stimulus epochs and consequently did not mask the stimuli presented.

E. Image analysis

Image analysis was performed using statistical parametric mapping software (Friston et al., 1995a; <http://www.fil.ion.ucl.ac.uk/spm>) following a standard protocol for each subject. Images were corrected for 3-dimensional head movement using a computational algorithm that minimised the sum of squared differences between the mean image and each image in the time series (Friston et al., 1995b; 1996). For each subject, the amount of motion correction required was generally less than 1 mm in each plane and less than 1° rotation about each axis. Realigned images were spatially smoothed using an isotropic Gaussian kernel of 5 mm full-width-at-half-maximum to enhance the signal-to-noise ratio. For the optimal detection of activated regions, a general smoothness heuristic of twice the voxel size was applied in-plane, while to reduce artifactual bleeding of activation across adjacent images, lighter smoothing was applied through-plane. Image data were not temporally smoothed, since the inter-scan interval exceeded the width of the smoothing kernel. Low-frequency artifacts, corresponding to aliased respiratory and cardiac effects and other cyclical variations in signal intensity, were removed by high-pass filtering the time series at 0.3 cycles/minute.

Image analysis was conducted for each subject using the general linear model. For each time course, 8 *t*-contrasts were performed between each tone condition and the baseline condition. These *t* statistics were computed for all voxels in the brain. Maps of *t* values were transformed to the unit normal distribution to give maps of *Z*

values (referred to as $SPM\{Z\}$). The $SPM\{Z\}$ for each stimulus condition relative to the baseline was thresholded at a probability level of $P < 0.001$ (Z value = 3.09).

For the purposes of descriptive anatomical localisation, the maps of functional activation were overlaid onto brain images for each subject. The location of the auditory cortex can be identified from these images by the position of the Sylvian sulcus, a deep fissure which follows the supra-temporal plane. Viewed coronally, the primary auditory cortex is situated medially on the lower bank of the Sylvian fissure and occupies the transverse temporal gyrus of Heschl (e.g., Penhune et al., 1996). Secondary auditory fields include the lateral convexity of the superior temporal gyrus (e.g., Rivier & Clarke, 1997; Westbury et al., 1999).

F. Extent and magnitude analysis

To investigate systematic changes in the pattern of auditory activation as a function of stimulus intensity, the extent of the activated region and magnitude of the response were calculated separately for each tone contrast and for left and right hemispheres. Extent of activation was defined as the number of activated contiguous voxels in the auditory cortex whose probability of activation exceeded $P < 0.001$. Response magnitude was represented by the percentage change in the MR signal for each stimulus condition relative to the baseline. Image analysis using statistical parametric mapping requires that the data are spatially smoothed. As a consequence, the extent and magnitude of the BOLD response are partly co-dependent such that regions with a particularly high response magnitude will also tend to have the greatest extent. To partly separate the co-dependence of response magnitude and extent, magnitude was computed for a region of fixed size (50 voxels). The 50 voxels were specified by functional, rather than by anatomical, criterion since BOLD contrast images do not specify precise anatomical subdivisions of the auditory cortex. The

region was defined using an overall F -test, which identified regions where there was significant tone activation relative to the baseline. The probability threshold of the F -test was adjusted for each subject to identify a cluster of 50 voxels around the superior temporal gyrus with the greatest F values. Using this criterion, some of those selected voxels did not reach the $P < 0.001$ probability threshold required for the extent measurement. However, this “region of interest” approach ensured that differences in the extent of activation did not inadvertently affect the measure of response magnitude. For example, a positive signal change was not contingent upon an extent that was greater than zero.

II. Results

A. Psychophysical data

Subjects were able to detect the intensity decreases accurately (mean percent correct = 86.9%, StDev across listeners = 19.9%). An ANOVA was calculated for the detection of targets in the pure and complex tone conditions. There was no difference in accuracy of detection across the eight stimulus conditions [$F(7,77)=0.83$, $p=0.57$]. Ability to discriminate the targets was also measured using the d' detection index, taking into account the number of false-positive responses, i.e., button presses to the “non-target” sounds. The resulting d' values ranged from 3.9 (for the 66-dB single tone) to 4.3 (for the 85-dB complex tone), with a mean d' of 4.1. The d' values were consistently high across subjects (ranging from 3.1 for subject 10 to 5.42 for subject 4) indicating that subjects were actively detecting intensity changes for all tones.

B. General pattern of functional activation

All ten subjects showed auditory activation in at least six of the listening conditions relative to the silent baseline. Auditory activation was generally located in

both medial and lateral regions of the superior temporal gyrus. This region includes the primary and secondary areas of the auditory cortex as anatomically defined in Section I.E. Examples of the activation pattern for two subjects are shown in Figure 6. Changes in the activation pattern induced either by increasing sound level or by changing the stimulus bandwidth occurred within a co-occurring region of the auditory cortex suggesting that the activation effects for the manipulations of stimulus level and bandwidth are not easily separable.

Although the experimental design and analysis were not maximally sensitive to the detection of the motor response, in five subjects, task-specific activation most likely to be associated with the finger press was also observed in several cortical regions: the pre- and post-central gyri along the fronto-parietal border containing the primary and secondary motor and somatosensory cortices, and the medial part of the superior frontal gyrus which contains the supplementary motor area and supplementary eye fields (Dejardin et al., 1998; Pickard & Strick, 1996). Three subjects without movement-elicited activation also had the lowest performance scores, perhaps reflecting the greater number of response misses (i.e. fewer button presses).

C. Effect of sound level on the extent of auditory activation

In general, increasing sound intensity generated a spread of activation medially and laterally along the superior temporal plane. The data for all ten subjects for the extent of the activated region in each tone contrast are shown in Figure 3, with the mean and (95%) confidence intervals for each condition (where extent is defined in Section I.F). Four subjects showed bilateral activation in all conditions. The remaining six subjects showed bilateral activation for the pure tones presented at the upper end of the range (91 dB SPL) and for the two harmonic-complex conditions and

unilateral activation for the pure tones presented at the lower end of the range (66 to 86 SPL) (in five subjects, this was in the left hemisphere).

***** insert Figure 3 here *****

Data for the pure tones were subjected to an analysis of variance, with intensity and hemisphere as within-subject factors. There was a significant overall effect of intensity on extent of activation [$F(5,40)=2.46, P=0.05$], with the mean activation/intensity function showing a growth in the extent of activation with increasing level. However, the linear component of the response did not reach significance [$F(1,8)=3.83, P=0.09$]. There was no main effect of hemisphere [$F(1,8)=0.31, P=0.59$]. For the complex tones, a paired t -test showed that extent of activation over both hemispheres did not change with sound intensity [$t(19)=1.35, P=0.20$], nor with hemisphere [$t(19)=0.02, P=0.98$]. Indeed, while some subjects showed an increase in extent for the complex tone as a function of sound level, others showed a decrease. Thus, the data provide (at most) weak evidence for a general increase in the extent of activation for pure tones presented over 66 to 91 dB SPL, but no greater extent for complex tones presented at 85 than at 65 dB SPL.

D. Effect of sound level on the response magnitude

Within the activated auditory area defined in Section I.F., the mean percentage change in the BOLD response ranged from 0.9% in the 66-dB pure-tone condition to 2.5% in the 85-dB harmonic-complex condition. The magnitudes of the auditory response are in the range commonly observed (Hall et al., 1999; Hall et al., 2000). Overall, the mean percentage change in the response to pure tones increased with intensity. The data are plotted in Figure 4. Subjects generally showed a positive response to all of the stimuli relative to the quiet baseline condition, although a relative decrease in the response was seen for two subjects in some tone conditions.

***** insert Figure 4 here *****

Within-subjects analysis of variance for the pure tones showed a significant effect of intensity [$F(5,45)=4.64$, $P<.01$]. Moreover, within-subject contrasts indicated a significant linear change [$F(1,9)=7.48$, $P=0.02$], showing that the overall growth in magnitude as a function of intensity in dB was linear. For the complex tones, the response magnitude was greater at the higher intensity [paired $t(19)=2.30$, $P=0.03$] (see Figure 4). There was no hemispheric effect on the magnitude of activation for either pure [$F(1,9)=0.91$, $P=0.37$] or complex tones [$t(19)=1.76$, $P=0.10$].

E. Correlating measures of extent and response magnitude

The correlation between extent of activation and response magnitude was examined on the data collapsed across hemisphere (Figure 5). The expected positive correlation was high ($r=0.82$, $P<0.001$, $N=80$). As the magnitude of the response increased, so did extent.

***** insert Figure 5 here *****

Although the analyses in Sections II.C and II.D determined the effect of sound level on the extent and magnitude of the response, they did so separately for each stimulus class. If the pattern of auditory activation predominantly reflects a general response to sound level, then the extent and/or magnitude of activation should rise with sound level irrespective of stimulus class. It is therefore powerful to examine, pooled over stimulus class, the relationships between the measures of activation (extent and magnitude) and the two sound-level scales (intensity and the measure of loudness from the model of Moore et al., 1997) as a means of distinguishing between the two bases for sound-level matching. Neither extent nor magnitude of activation correlated with intensity as measured in SPL ($r=0.04$, $P=0.59$ and $r=0.06$, $P=0.48$ ($N=80$) respectively). However, both measures of activation

correlated significantly with loudness as measured in phons ($r=0.36$, $P<0.001$ and $r=0.35$, $P<0.001$). The greater correlation arose from the placement of the two complex tones at higher points of both the activation and the sound-level ranges when stimuli were measured in phons rather than in SPL. This result does not mean that the cortical response reflects loudness coding directly, since the correlations explain barely 10% of the variance in the data. However, it does establish the need to control for loudness when quantifying auditory activation to other stimulus attributes, such as bandwidth.

F. Evaluating the three schemes for sound-level matching across bandwidth

If the observed auditory activation reflected a response to sound level alone, then it should be possible to identify a matching scheme which equates the pattern of activation across both classes of stimulus. Three planned *t*-test comparisons were conducted for those *a priori* matched conditions. The 85-dB SPL complex tone produced a significantly greater extent of activation and response magnitude ($P<0.01$) than the pure tone matched for component level (the 66-dB SPL pure tone) and root mean square level (the 76-dB SPL pure tone). Matching based on the calculated loudness identified the 76-dB and 81-dB pure tones (67.0 and 72.2 phons respectively) as straddling the 65-dB complex tone (69.4 phons) (see Table 1). *t*-test comparisons showed that the complex tone produced significantly more activation ($P<0.01$) than either of these two pure tones in terms of both extent and magnitude of auditory activation. Thus, the complex tone produced a greater response than any of the pure tones matched on the basis of the three schemes. The principle acoustical property that distinguished the pure and the complex tones was that of stimulus bandwidth and we therefore suggest that stimulus bandwidth probably contributed

more strongly to the pattern of auditory cortical activation than did the dB SPL or loudness of that stimulus.

The clearest demonstration of the bandwidth effect is seen by evaluating the degree to which activation is sensitive to changes in bandwidth and insensitive to changes in loudness. Activations (i.e., the SPM{Z} maps) for pairs of tone conditions were superimposed onto brain images for each individual. Two pairs of conditions were contrasted; firstly, the pure tone at 56.8 and 72 phons and secondly, the pure tone at 56.8 phons and the complex tone at 69.4 phons. Visual inspection of these contrast maps permitted the identification of voxels that were activated in one condition, but not in another and vice-versa. An increase in loudness of 15.2 phons activated small regions of auditory cortex. However, an increase in bandwidth, with a similar increase in loudness (12.6 phons), produced a two- to three-fold greater increase in auditory activation (Figure 6). The greater spread of activation with bandwidth than with loudness, illustrated for subjects 2 and 3, is representative of the rest of the group.

***** insert Figure 6 here *****

III. Discussion

This experiment demonstrates that acoustic intensity influenced the pattern of auditory cortical activation when an imaging protocol was used that restricted contaminating effects of scanner noise. Extent and magnitude of activation were positively correlated, as expected, but not perfectly. This result indicates that, for the mapping of cortical responses to stimulus class and sound level, both measures should be extracted. Sound level influenced the extent of activation for pure tones presented at levels of 66 to 91 dB SPL, but not for the complex tones presented at levels of 65

and 85 dB SPL. On the other hand, an increase in sound level was associated with a significant growth in response magnitude for both classes of stimulus. The six increments in dB SPL for the pure tones permitted the magnitude/intensity function to be determined and, for these stimuli, magnitude was found to increase linearly when responses were averaged over all subjects. Using the three sound-level-matching schemes, statistical comparisons between the auditory activation for pairs of stimuli showed that the response was always greater for the complex tone than for the pure tone. Thus, the activated region in the superior temporal gyrus responded differentially both to changes in sound level and in bandwidth, but the effect of bandwidth was the greater.

A. Neurophysiological bases for the auditory activation changes as a function of sound level

Independent physiological knowledge of the neural coding of intensity/loudness enables speculation about the relation between this and the observed changes in the BOLD signal because it drives the neurovascular effects. Sound level may be represented by the activation of units which are distributed within volumes containing units subserving other functions (e.g., Heil et al., 1994; Taniguchi and Nasu, 1993), including the sharpness of frequency tuning to pure tones (Recanzone et al., 1999). The imaging data are at least consistent with these neurophysiological data, as effects of both sound level and bandwidth were found in overlapping regions of auditory cortex. Within the mammalian primary auditory cortex, an orderly spatial organisation of a number of parameters related to the encoding of sound level has been demonstrated, including minimum threshold, dynamic range, best SPL and non-monotonicity of intensity functions (e.g., Heil et al.,

1994), although the present spatial and temporal resolution of the fMRI technique is insufficient to detect these dimensions of cortical representation.

At peripheral levels of the ascending auditory pathway, sound level is represented by the firing rates of neurons at the centre of the excitation pattern (e.g., Liberman, 1978); by the spread of the excitation pattern (e.g, Chatterjee and Zwislocki, 1998) and by the patterns of temporal synchrony of the neuronal firing (e.g., Brosch and Schreiner, 1999; Carlyon & Moore, 1984). However, at the level of the auditory cortex, the neuronal population response to sound level becomes quite complicated: temporal coding has largely disappeared and rate coding is a mixture of both monotonic and non-monotonic neuronal responses to increasing sound level (e.g., Heil et al., 1994; Phillips and Orman, 1984). The combined contribution from neurons that have different rate-intensity functions results in a changing topographical distribution of activity as the sound level of a pure tone is increased. Interestingly, those same authors demonstrated that the cumulative activity across a population increases in a manner similar to the growth of loudness. This is despite (or perhaps because of) the widespread inhibitory effects that are also brought into play at higher sound levels. If the cortical responses entirely reflect processing prior to the auditory cortex, the BOLD response should reflect the increasing cumulative spike count.

Interplay between excitatory and inhibitory inputs can result in non-monotonic rate-intensity functions (Greenwood and Maruyama, 1965; Brugge and Merzenich, 1973). Thus, the physiological response to increasing sound level also involves inhibition of the activity of narrow-band, low intensity-sensitive neurones. Such inhibition is in evidence from the dorsal cochlear nucleus all the way up to the cortex and there are certainly local inhibitory contributions to non-monotonicity at least as high as the inferior colliculus (Yang et al., 1992). At the cortical level, there are

profuse local inhibitory influences (Cox et al., 1992; Manunta and Edeline, 1998; Wang et al., 2000), although a direct local contribution to the observed non-monotonicity of rate-level functions has yet to be demonstrated. Neural inhibition is likely to be metabolically costly and may not be distinguishable from the metabolic cost of excitation. Consequently, if non-monotonicity in cortex receives a local inhibitory contribution, spiking and non-spiking regions would both be costly in terms of their oxygen requirement. Thus, measures based on local haemodynamic changes, such as the BOLD response in fMRI and the rCBF measure in PET, are unable to distinguish neural excitation from local inhibition. Neuroimaging data therefore require careful interpretation where inhibitory, as well as excitatory, responses are likely to be involved. However, despite this fact, an overall increase in oxygen requirement would be predicted along the iso-frequency strip for pure tones with an increase in sound level. This combined increase in both neural excitation and inhibition with increasing sound level may provide the basis for the function observed in the present study.

B. Imaging central auditory responses to sound-level

Although intensity encoding occurs throughout the ascending auditory pathway, the small size of sub-cortical nuclei places them on the limits of detection using current imaging techniques. Using PET, sound-level effects have been observed in a sub-cortical site putatively near the medial geniculate nucleus (MGN) of the thalamus (Lockwood et al., 1999). This result has not been replicated using the better spatial resolution of fMRI possibly due to i) increased physiological motion in the brainstem region and ii) masking by the background scanner noise. Synchronisation of the image acquisition to a fixed point in the cardiac cycle may be required in order to detect brainstem activation reliably (Guimares et al., 1998) by reducing

confounding signal variance from cardiac-related pulsatile brainstem motion. Temporally sparse imaging should also reduce the baseline level of activation to the scanner noise at all levels of the auditory pathway. Thus, it may be profitable for future studies to image sub-cortical structures using cardiac gating in conjunction with a low-noise imaging sequence.

At a higher cortical level, activation has also been reported in a discrete region of the *posterior* superior temporal gyrus in the right hemisphere (Belin et al., 1998) – a region probably located beyond secondary auditory fields. Activation in this brain region was correlated with the difficulty of an intensity-discrimination judgement rather than with sound level per se. Belin et al., attributed the function of this region to the computation of sound-intensity differences. Although our task involved only a simple intensity discrimination, it nonetheless required a sound-level difference judgement and hence one might predict activation in the right posterior superior temporal gyrus. The region of auditory activation did include posterior sections of superior temporal gyrus, but due to the lack of fine spatial localisation of activation, a direct comparison of the localisation of activation between the two studies is not appropriate.

C. Consistency between extent and magnitude measurements of the response to sound level

For increases in sound level, previous studies have generally reported significant increases in the spatial extent of activation and/or the response magnitude (e.g., Jäncke et al., 1997; Lockwood et al., 1999; Mohr et al., 1999). Growth in both the extent and magnitude of the response with sound level is physiologically consistent with a regional increase in the metabolic demands of the underlying neuronal population. Growth in the magnitude of the BOLD response may reflect a

greater change in blood oxygenation as a result of increased neuronal metabolism, while growth in the extent may reflect either recruitment of a larger neuronal population or increased response contribution from draining veins relative to that from the capillary bed.

In general, the extent of activation and the response magnitude both seem to increase as a function of sound level, but this has rarely been demonstrated in the same study. Surprisingly, studies that do report data for both activation measures have failed to demonstrate a clear and consistent effect of stimulus intensity on either one or the other measure. For example, using fMRI, Jäncke et al. (1999) found a significant increase in extent for syllables and pure tones presented at levels of 75, 85 and 95 dB SPL, but no effect on response magnitude. On the other hand, Mohr et al. (1999) found a reliable effect of sound level of monosyllabic words on response magnitude, but not on extent: response magnitude increased significantly as a function of intensity (ranging from 65 to 110 dB C-weighted) and this increase was fairly consistent across subjects, but the extent of activation varied more widely, and less systematically, across subjects. In a PET study however, significant sound-level effects on *both* the extent and magnitude of auditory activation were demonstrated for pure tones (Lockwood et al., 1999). Unlike fMRI, PET produces no intense acoustic noise that may confound the stimulus-driven response. However, the interpretation of the relationship between response magnitude and sound level may not be straightforward because the data suggest an interaction between frequency and level. For example, for a 4-kHz tone, the number of activated voxels in the auditory system and the response magnitude increased strongly across the full 30 – 90 dB SL range, but, for a 500-Hz tone, there was no change in the extent and magnitude of activation between 70 and 90 dB HL, suggesting an approach towards response saturation.

There is also some evidence for saturation of the response measured using fMRI, as Mohr et al's (1999) data suggest that the response magnitude reached a ceiling level at 90 to 95 dB.

In the present study, despite general inter-subject variation, sound level exerted a significant influence across both stimulus types on magnitude, but not on extent of response. Evidence from a reproducibility study concurs with the implication that extent is a less reliable measure of the underlying pattern of activation than is magnitude (Mohr et al., 1999). Up to four-fold variations occurred in the extent of activation between experiments for the same individual, but the response magnitude within activated voxels varied little across sessions. We propose the following explanation for these apparent differences in reliability between measures. "Extent" of activation is defined as the number of voxels whose response exceeds a given probability threshold and so extent can encompass one or more auditory fields. An increase in extent will change the relative contributions of activations arising from these different auditory fields. For example, a large region of activation encompasses a greater proportion of secondary auditory fields compared with the primary auditory field than does a small region. As a consequence, across sound-levels for example, increased extent of activation implies increasingly heterogeneous underlying neuronal and neurovascular responses. In contrast, response magnitude is calculated for voxels within a region that is uniquely specified by the omnibus F test and is fixed across sound-level conditions. Even if multiple auditory fields are embraced, the greater reliability in the effect of sound level on magnitude can be attributed to the contribution of a response that is at least based in the same neurovascular region for a given subject. Hence, less intra-subject variability would be expected in response magnitude than in response extent.

D. Cortical responses to sound level and bandwidth – which is the more potent acoustical feature for fMRI?

When characterising sound-level effects, an increase in activation with intensity will often be hard to dissociate from an increase in activation with loudness because, for pure tones presented in quiet, loudness is a simple monotonic function of intensity (Stevens, 1975). The direct relationship between intensity and loudness can sometimes break down because, when intensity of a sound is held constant, the loudness of that sound changes i) in background noise versus in quiet and ii) as a function of bandwidth.

Firstly, the loudness of a pure tone is reduced by presenting it in a broadband noise (partial masking). This point is of specific relevance to auditory fMRI studies because the intense background noise generated by the scanner would effectively mask a tone stimulus if the signals overlapped in time. Partial masking may arise by suppression of the tone by the noise (Moore et al., 1985), where suppression reduces the excitation level evoked by the tone. Partial masking would encumber interpretation of the effect of stimulus loudness in any fMRI study that uses a conventional imaging protocol in which sets of images are acquired at a rapid rate and image acquisition coincides with stimulus presentation. However, it is unlikely to occur in the present study because the temporally sparse imaging separated the stimulus delivery from the image acquisition (and hence the scanner noise).

With respect to point ii), the sound levels presented in this study achieve some dissociation between intensity and loudness because the set of stimuli embrace such a bandwidth difference. Extent and magnitude significantly correlated with the sound level measured in phons but not in SPL. Since the cortical response to sound level appears to reflect loudness more closely than SPL, loudness may be an important

aspect of cortical encoding. However, clearer demonstrations of a dissociation between the cortical response to intensity and loudness are required before a firm conclusion can be drawn. The data also suggest that bandwidth contributes more strongly to the pattern of activation than sound level. For pairs of tones matched for the same increase in loudness, a greater disparity in the extent of activation was observed when the bandwidth was also increased between tones. Additional activation induced by the complex tone relative to the pure tone was observed spreading medio-laterally along the superior temporal gyrus. Thus, even when sounds of a different bandwidth are matched on the most stringent measure of sound level (i.e., for the loudness match, a complex tone was matched to a pure tone presented at a greater SPL), the bandwidth itself also contributes to the observed activation pattern. This result indicates that potential mismatches in sound level are unlikely to account for much of the increase in the spread of cortical activation for broadband signals relative to pure tones, since the pattern of cortical activation measured was mostly driven by the bandwidth itself. This finding rules out one of the four possible interpretations of the bandwidth effect proposed in the Introduction. It is more likely that the greater spread of activation for the complex tone relative to the pure tone is due either to i) stimuli of a greater bandwidth being more effective than pure tones in driving a response in non-primary auditory fields that lie medially and laterally along the superior temporal gyrus or ii) stimuli of a greater bandwidth leading to a spread of activity across frequency channels in these tonotopically-organised brain regions.

Acknowledgements

This work was partly supported by a Special Project Grant, G9302591, from the Medical Research Council to the Magnetic Resonance Centre, University of Nottingham. We are grateful to Mr Miguel Gonçalves for assistance with the data analysis, and to Dr Brian Glasberg for advice on the implementation of the loudness model.

References

- Bandettini, P.A., Jesmanowicz, A., Van Kylen, J., Birn, R.M., and Hyde, J.S. (1998). "Functional MRI of brain activation induced by scanner acoustic noise," *Magnetic Resonance In Medicine*, **39**, 410-416.
- Belin, P., McAdams, S., Smith, B., Savel, S., Thivard, L., Samson, S., and Samson, Y. (1998). "The functional anatomy of sound intensity discrimination," *The Journal of Neuroscience*, **18**, 6388-6394.
- Brosch, M., and Schreiner, C.E. (1999). "Correlations between neural discharges are related to receptive field properties in cat primary auditory cortex," *European Journal of Neuroscience*, **11**, 3517-3530.
- Bowtell, R., Mansfield, P., Coxon, R.J., Harvey, P.R., and Glover, P.M. (1994). "High-resolution echo-planar imaging at 3.0 T," *MAGMA*, **2**, 241-245.
- Bowtell, R.W., and Peters, A. (1999). "Analytic approach to the design of transverse gradient coils with co-axial return paths," *Magnetic Resonance in Medicine*, **41**, 600-608.
- Brugge, J.F., and Merzenich, M.M. (1973). "Responses of neurons in auditory cortex of the macaque monkey to monaural and binaural stimulation," *Journal of Neurophysiology*, **36**, 1138-1158.
- Burkhard, M.D., and Sachs, R.M. (1975). "Anthropometric manikin for acoustic research," *Journal of the Acoustical Society of America*, **58**, 214-222.
- Carlyon, R.P., and Moore, B.C.J. (1984). "Intensity discrimination: A severe departure from Weber's law," *Journal of the Acoustical Society of America*, **76**, 1369-1376.
- Chatterjee, M., and Zwislocki, J.J. (1998). "Cochlear mechanisms of frequency and intensity coding. II Dynamic range and the code for loudness," *Hearing Research*, **124**, 170-181.
- Cox C.L., Metherate, R., Weinberger N.M., and Ashe, J.H. (1992). "Synaptic potentials and effects of amino-acid antagonists in the auditory-cortex," *Brain Research Bulletin*, **28**, 401-410.
- Dejardin, S., Dubois, S., Bodart, J.M., Schiltz, C., Delinte, A., Michel, C., Roucoux, A., and Crommelinck, M. (1998). "PET study of human voluntary saccadic eye movements in darkness: effect of task repetition on the activation pattern," *European Journal of Neuroscience*, **10**, 2328-2336.
- Foster, J.R., Hall, D.A., Summerfield, A.Q., Palmer, A.R., and Bowtell, R.W. (2000). "Sound-level measurements and calculations of safe noise dosage during fMRI at 3T," *Journal of Magnetic Resonance Imaging*, (in press).

- Friston, K.J., Holmes, A.P., Poline, J.B., Grasby, P.J., Williams, S.C.R., Frackowiak, R.S.J., and Turner, R. (1995a). "Analysis of fMRI time-series revisited," *NeuroImage*, **2**, 45-53.
- Friston, K.J., Ashburner, J., Frith, C.D., Poline, J.B., Heather, J.D., and Frackowiak, R.S.J. (1995b). "Spatial registration and normalization of images," *Human Brain Mapping*, **3**, 165-189.
- Friston, K.J., Williams, S., Howard, R., Frackowiak, R.S.J., and Turner, R. (1996). "Movement-related effects in fMRI time-series," *Magnetic Resonance in Medicine*, **35**, 346-355.
- Greenwood, D.D., and Maruyama, N. (1965). "Excitatory and inhibitory response areas of auditory neurons in the cochlear nucleus," *Journal of Neurophysiology*, **28**, 863-892.
- Griffiths, T.D., Büchel, C., Frackowiak, R.S.J., and Patterson, R.D. (1998). "Analysis of temporal structure in sound by the human brain," *Nature Neuroscience*, **1**, 422-427.
- Guimaraes, A.R., Melcher, J.R., Talavage, T.M., Baker, J.R., Ledden, P., Rosen, B.R., Kiang, N.Y.S., Fullerton, B.C., and Weisskoff, R.M. (1998). "Imaging subcortical auditory activity in humans," *Human Brain Mapping*, **6**, 33-41.
- Hall, D.A., Elliott M.R., Bowtell, R.W., Gurney, E., Haggard, M.P. (1998). "Sparse" temporal sampling in fMRI enhances detection of activation by sound for both magnetic and acoustical reasons. *NeuroImage*, **7**: S551.
- Hall, D.A., Haggard, M.P., Akeroyd, M.A., Palmer, A.R., Summerfield, A.Q., Elliott, M.R., Gurney, E., and Bowtell, R.W. (1999). "Sparse Temporal Sampling in auditory fMRI," *Human Brain Mapping*, **7**, 213-223.
- Hall, D.A., Summerfield, A.Q., Gonçalves, M.S., Foster, J.R., Palmer, A.R., and Bowtell, R.W. (2000). "Time-course of the auditory BOLD response to scanner noise," *Journal of Magnetic Resonance in Medicine*, **43**, 601-606.
- Heil, P., Rajan, R., and Irvine, D.R.F. (1994). "Topographic representation of tone intensity along the isofrequency axis of cat primary auditory cortex," *Hearing Research*, **76**, 188-202.
- Jäncke, L., Shah, N.J., Posse, S., Grosse-Ryken, M., and Müller-Gärtner, H.W. (1998). "Intensity coding of auditory stimuli: An fMRI study," *Neuropsychologia*, **36**, 875-883.
- Liberman, M.C. (1978). "Auditory-nerve responses from cats raised in a low-noise chamber," *Journal of the Acoustical Society of America*, **63**, 442-455.
- Lockwood, A.H., Salvi, R.J., Coad, M.L., Arnold, S.A., Wack, D.S., Murphy, B.W., and Burkard, R.F. (1999). "The functional anatomy of the normal human auditory

- system: responses to 0.5 and 4.0 kHz tones at varied intensities,” *Cerebral Cortex*, **9**, 65-76.
- Manunta, Y., and Edeline, J.M., (1998), “Effects of noradrenaline on rate-level function of auditory cortex neurons: Is there a "gating" effect of noradrenaline?,” *Experimental Brain Research*, **118**, 361-372.
- Merzenich, M.M., and Brugge, J.F. (1973). “Representation of the cochlear partition on the superior temporal plane of the macaque monkey,” *Brain Research*, **50**, 275-296.
- Millen, S.J., Haughton, V.M., and Yetkin, Z. (1995). “Functional magnetic resonance imaging of the central auditory pathway following speech and pure-tone stimuli,” *Laryngoscope*, **105**, 1305-1310.
- Mohr, C.M., King, W.M., Freeman, A.J., Briggs, R.W., and Leonard, C.M. (1999). “Influence of speech stimuli intensity on the activation of auditory cortex investigated with functional magnetic resonance imaging,” *Journal of the Acoustical Society of America*, **105**, 2738-2745.
- Moore, B.C.J., Glasberg, B.R., and Baer, T. (1997). “A model for the prediction of thresholds, loudness and partial loudness,” *Journal of the Audio Engineering Society*, **45**, 224-240.
- Moore, B.C.J., and Glasberg, B.R. (1996). “A revision of Zwicker’s loudness model,” *Acta Acoustica*, **82**, 335-345.
- Moore, B.C.J., Glasberg, B.R., Hess, R.F., and Birchall, J.P. (1985). “Effects of flanking noise bands on the rate of growth of loudness of tones in normal and recruiting ears,” *Journal of the Acoustical Society of America*, **77**, 1505-1515.
- Olsen, S.O. (1999). “The relationship between the uncomfortable loudness level and the acoustic reflex threshold for pure tones in normally-hearing and impaired listeners - A meta-analysis,” *Audiology*, **38**, 61-68.
- Olsen, S.O., Rasmussen, A.N., Nielsen, L.H., Borgkvist, B.V. (1999). “The acoustic reflex threshold: Not predictive for loudness perception in normally-hearing listeners,” *Audiology*, **38**, 303-307.
- Palmer, A.R., Bullock, D.C., and Chambers, J.D. (1998). “A high-output, high-quality sound system for use in auditory fMRI,” *NeuroImage*, **7**, S359.
- Penhune, V.B., Zatorre, R.J., MacDonald, J.D., and Evans, A.C. (1996). “Interhemispheric anatomical differences in human primary auditory cortex: Probabilistic mapping and volume measurement from magnetic resonance scans,” *Cerebral Cortex*, **6**, 661-672.
- Phillips, D.P., and Orman, S.S. (1984). “Responses of single neurons in posterior field of cat auditory cortex to tonal stimulation,” *Journal of Neurophysiology*, **51**, 147-163.

- Picard, N., and Strick, P.L. (1996). "Motor areas of the medial wall: A review of their location and functional activation," *Cerebral Cortex*, **6**, 342-353.
- Rauschecker, J.P., Tian, B., Pons, T., and Mishkin, M. (1997). "Serial and parallel processing in Rhesus monkey auditory cortex," *Journal of Comparative Neurology*, **382**, 89-103.
- Recanzone, G.H., Schreiner, C.E., Sutter M.L., Beitel, R.E., and Merzenich, M.M. (1999). "Functional organization of spectral receptive fields in the primary auditory cortex of the owl monkey," *Journal of Comparative Neurology*, **415**, 460-481.
- Redies, H., Sieben, U., and Creutzfeldt, O.D., (1989). "Functional subdivisions in the auditory cortex of the guinea pig," *The Journal of Comparative Neurology*, **282**, 473-488.
- Rivier, F., and Clarke, S. (1997). "Cytochrome oxidase, acetylcholinesterase, and NADPH diaphorase staining in human supratemporal and insular cortex: Evidence for multiple auditory areas," *NeuroImage*, **6**, 288-304.
- Shah, N.J., Jäncke, L., Grosse-Ruyken M-L, Müller-Gärtner H.W. (1999). "Influence of acoustic masking noise in fMRI of the auditory cortex during phonetic discrimination," *Journal of Magnetic Resonance Imaging*, **9**, 19-25.
- Shah, N.J., Steinhoff, S., Mirzazade S., Zafiris O., Grosse-Ruyken M-L., Jäncke, L., and Zilles, K. (2000). "The effect of sequence repeat time on auditory cortex stimulation during phonetic discrimination," *NeuroImage*, **12**, 100-108.
- Stevens, S.S. (1975). "Psychophysics," New York: John Wiley & Sons. pp28.
- Strainer, J.C., Ulmer, J.L., Yetkin, F.Z., Daniels, D.L., and Millen, S.J. (1997). "Functional MR of the primary auditory cortex: An analysis of pure tone activation and tone discrimination," *AJNR*, **18**, 601-610.
- Talavage, T.M., Ledden, P.J., Sereno, M.I., Rosen, B.R., and Dale, A.M. (1997). "Multiple phase-encoded tonotopic maps in human auditory cortex," *NeuroImage*, **5**, S8.
- Talavage, T.M., Edmister, W.B., Ledden, P.J., and Weiskoff, R.M. (1999). "Quantitative assessment of auditory cortex responses induced by imager acoustic noise," *Human Brain Mapping*, **7**, 79-88.
- Taniguchi, I., and Nasu, M. (1993). "Spatio-temporal representation of sound intensity in the guinea pig auditory cortex observed by optical recording," *Neuroscience Letters*, **151**, 178-181.
- Thomas, H., Tillein, J., Heil, P., and Scheich, H. (1993). "Functional organization of auditory cortex in the Mongolian gerbil (*Meriones Unguiculatus*) 1. Electrophysiological mapping of frequency representation and distinction of fields," *European Journal of Neuroscience*, **5**, 882-897.

- Viemeister, N.F., and Bacon, S.P. (1988). "Intensity discrimination, increment detection, and magnitude estimation for 1-kHz tones," *Journal of Acoustical Society of America*, **84**, 172-178.
- Yang, L.C., Pollak, G.D., and Resler, C. (1992). "GABAergic circuits sharpen tuning curves and modify response properties in the moustache bat inferior colliculus," *Journal of Neurophysiology*, **68**, 1760-1774.
- Wang, J., Caspary, D., and Salvi, R.J. (2000). "GABA-A antagonist causes dramatic expansion of tuning in primary auditory cortex," *NeuroReport*, **11**, 1137-1140.
- Wessinger, C.M., Tian, B., Japikse, K.C., Ghosh, S., Van Meter, J.W., Platenberg, R.C., Pekar, J., and Rauschecker, J.P. (1997). "Processing of complex sounds in human auditory cortex," *Proceedings of the annual mid-winter meeting of the Association for Research in Otolaryngology*, #105, pp27.
- Westbury, C.F., Zatorre, R.J., and Evans, A.C. (1999). "Quantifying variability in the planum temporale: A probability map," *Cerebral Cortex*, **9**, 392-405.
- Zwicker, E., Flottorp, G., and Stevens, S.S. (1957). "Critical bandwidth in loudness summation," *Journal of Acoustical Society of America*, **29**, 548-557.

Footnotes

- 1 As part of the initial stimulus calibration, three of the authors performed an experimental loudness match by adjusting the level of the pure tone until it most closely matched that of the 85-dB SPL complex tone. The authors judged the 86-dB SPL pure tone to match the loudness of the 85-dB complex tone. This experimental match should have yielded approximately the same result as that computed by the loudness model. However, the model assigned the 86-dB pure tone a loudness of 77.3 phons and the 85-dB SPL complex tone a loudness of 86.2 phons (a difference of 8.9 phons). The underestimation of the experimental loudness match may reflect the particular decision criteria used by the three listeners. Because of the uncertainty of the reliability of the experimental match, this is not reported.

(pp11)

Figure Legends

Figure 1. Specific loudness patterns induced by the six 300-Hz pure tones and the two harmonic complex tones according to the model of Moore et al. (1997). The specific loudness pattern is calculated from the physical spectrum after correction for the effects of transmission through the outer and middle ear. The two complex tones generate broader and flatter loudness patterns than those for the pure-tone stimuli. The overall loudness of a sound is obtained by summing the specific loudness (i.e., the loudness per equivalent rectangular bandwidth (ERB)) across the frequency axis, multiplied by two for diotic presentation.

Figure 2. Schematic diagram representing the sparse-temporal-sampling imaging protocol used in the study. In the experimental sequence shown, stimulus conditions are represented by the blocks labelled by intensity (in dB SPL), with a period of silence occurring at every eighth epoch. The solid black lines denote the occurrence of the 1072-ms imaging sequence which occurs mostly in the 950-ms interval between epochs. Image acquisition is repeated every 10.75 s at the offset of each epoch.

Figure 3. Extent of activation across stimulus intensity for pure and complex tones. The responses to the two classes of tones can be represented within the same range of sound intensity, but for clarity are represented side-by-side within each panel, with pure tones on the left and complex tones on the right. Panel (A) shows the extent of activation for all 10 subjects in the left hemisphere and Panel (B) shows the results of the same analysis in the right hemisphere. Panels (C) and (D) show the mean data. Error bars indicate the 95% confidence limits of the means.

Figure 4. Mean percentage response change from baseline for all stimulus conditions within each defined region of auditory activation. Within each panel, pure-tone response are shown on the left-hand side and complex-tone responses on the right-hand side. Results for each hemisphere are plotted for all 10 subjects in Panels A and B. Panels (C) and (D) show the mean response change. Error bars plot the 95% confidence intervals of the means.

Figure 5. The relationship between extent and magnitude of the auditory response for the same data as are plotted in Figures 3 and 4. The extent of activation is defined by the number of voxels whose probability of activation exceeds $P < 0.001$ in the $SPM\{Z\}$. The % signal change from baseline is the averaged signal change across 50 voxels in the auditory cortex, whose probability of activation may not exceed $P < 0.001$. Thus, a positive signal change is not contingent upon an extent that is greater than zero as it is measured using a different procedure. Data are plotted for the 8 stimulus conditions, for all subjects and are shown for the pure tone as filled circles and for the complex tone as open circles.

Figure 6. Activation maps overlaid onto 5 functional images showing greater response to bandwidth than to loudness for two subjects. The effect of a change in loudness is represented by superimposing activations by the pure tone presented at 56.8 and 72 phons onto the same image. In the top row for each subject, red voxels denote significant activation at 72 phons and blue voxels denote significant activation at 56.8 phons. Images in the row below demonstrate the additional change in bandwidth. There is much more activation by the complex tone (shown in red) than

by the pure tone (shown in blue) when the two tones have a similar loudness separation as above (56.8 and 69.4 phons). In all images, voxels in yellow are conjointly activated by both tones. Auditory activation formed a medio-lateral band in the superior temporal gyrus on the lower bank of the Sylvian fissure (regions B). Activation possibly reflecting the motor component of the task can be seen in region A, the medial part of the superior frontal gyrus containing the supplementary motor area, and region C, the left pre/post-central gyri.

Intensity (dB SPL)	Loudness (phons)
<u>Pure tone</u>	
66.0	56.8
71.0	61.9
76.0	67.0
81.0	72.0
86.0	77.3
91.0	82.4
<u>Harmonic complex tone</u>	
65.0	69.4
85.0	86.2

Table 1. Presentation levels for the pure and harmonic complex tones. Intensity (dB SPL) was calibrated using KEMAR (Burkhard & Sachs, 1975). The loudness for the same stimuli was calculated using the computational model of Moore et al., (1996).

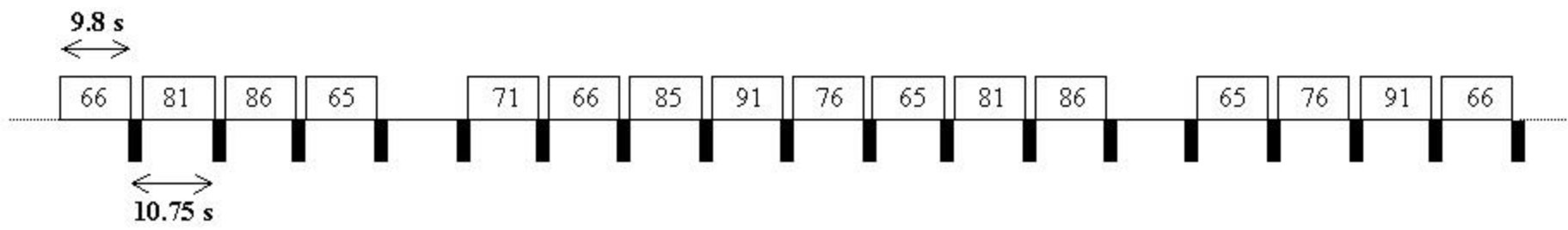


Figure 2

Auditory cortex

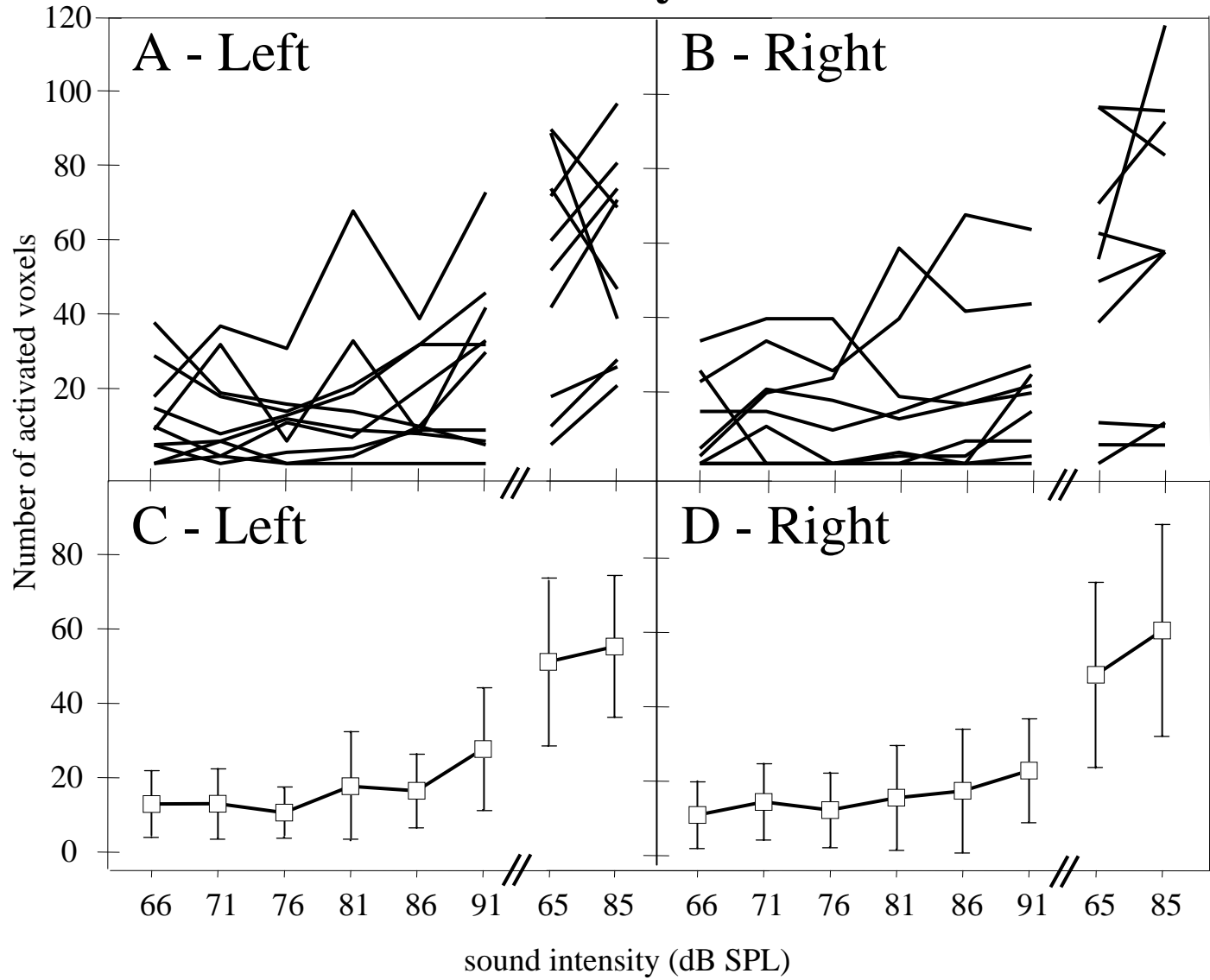


Figure 3

Auditory cortex

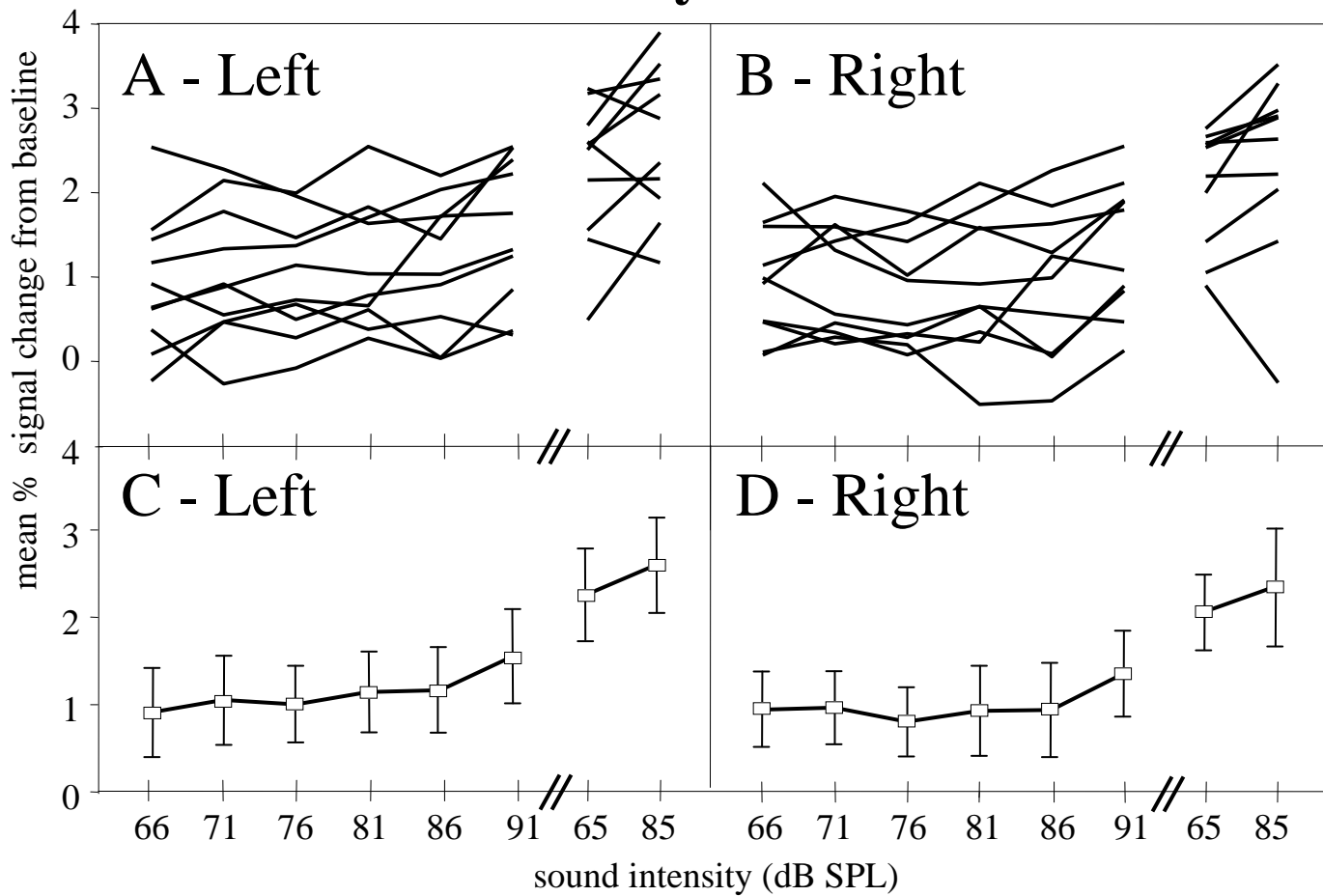


Figure 4

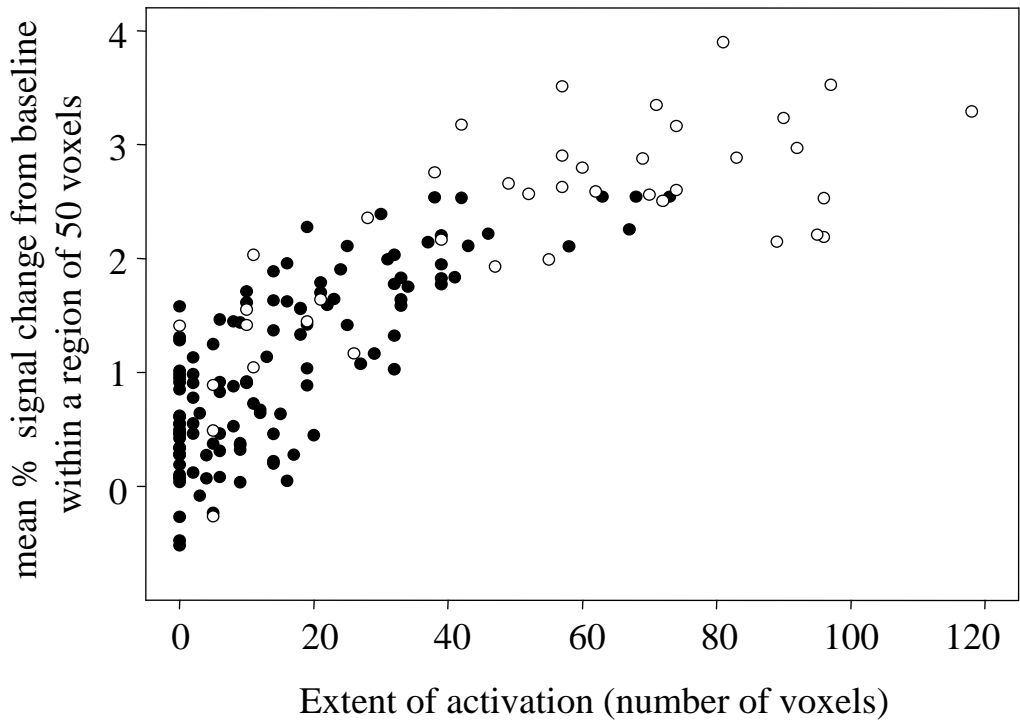


Figure 5

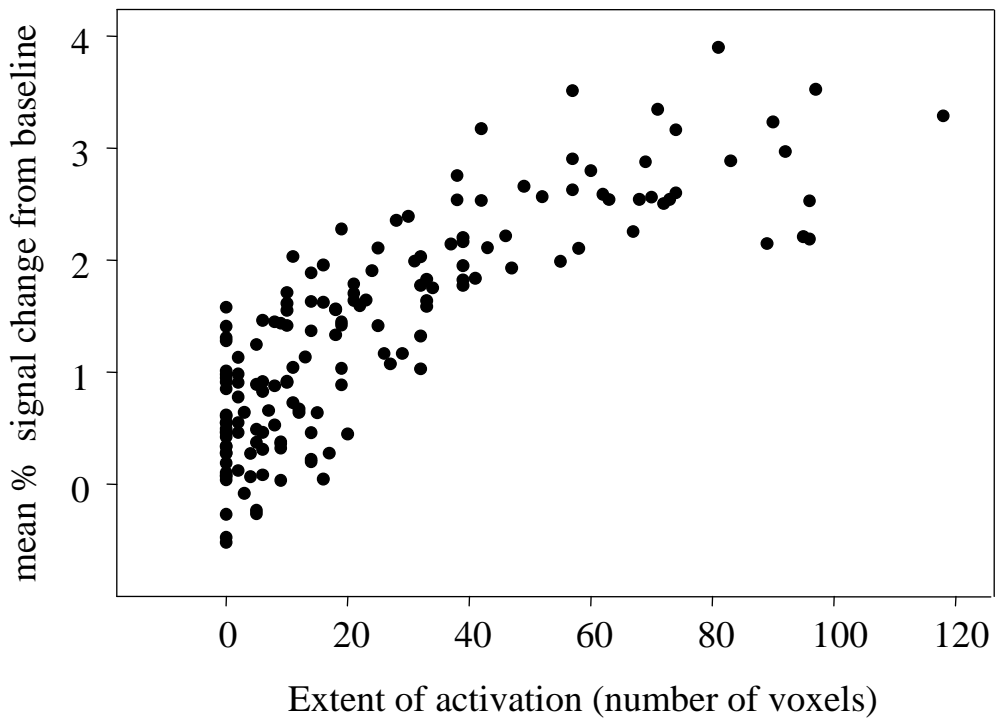
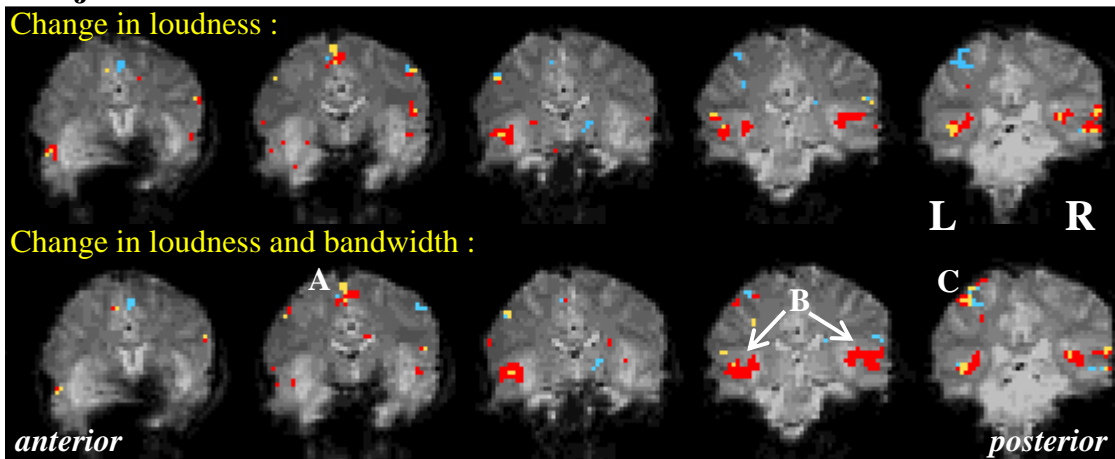
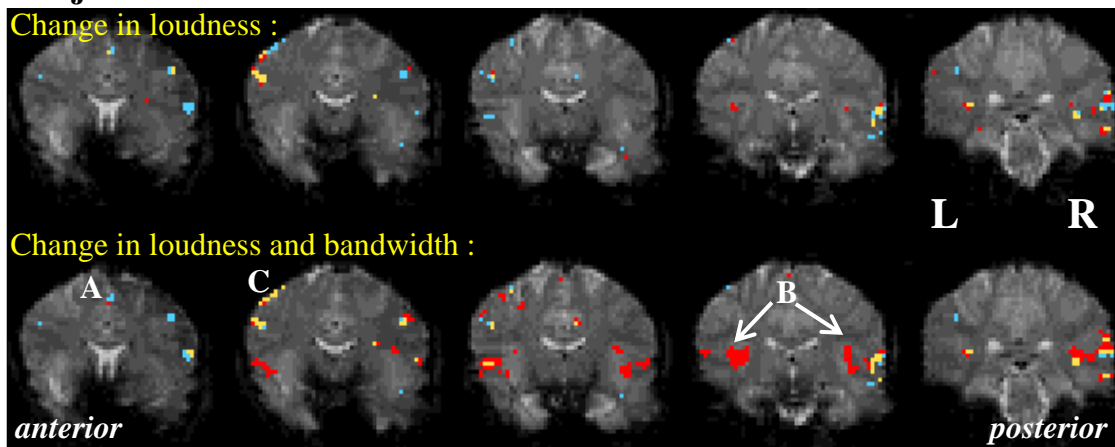


Figure 5

Subject 2



Subject 3



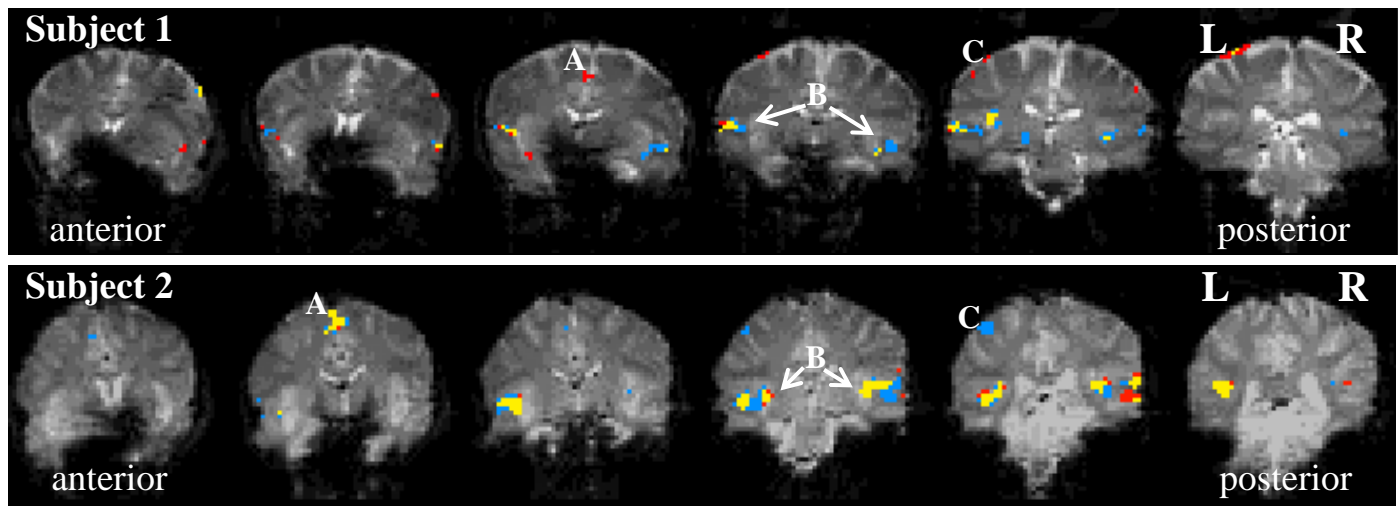


Figure 6