

# Evidence for the role of the right auditory cortex in fine pitch resolution

Krista L. Hyde<sup>a,b,c,\*</sup>, Isabelle Peretz<sup>b,c</sup>, Robert J. Zatorre<sup>a,c</sup>

<sup>a</sup> Montreal Neurological Institute, McGill University, 3801 University Street, Montreal, Quebec, Canada H3A 2B4

<sup>b</sup> Department of Psychology, University of Montreal, C.P. 6128 succ. Centre-ville, Montreal, Quebec, Canada H3C 3J7

<sup>c</sup> International Laboratory for Brain, Music and Sound Research (BRAMS), Montreal, Quebec, Canada

Received 18 January 2007; received in revised form 4 September 2007; accepted 5 September 2007

Available online 14 September 2007

## Abstract

The neural basis of human pitch perception is not fully understood. It has been argued that the auditory cortices in the two hemispheres are specialized, such that certain right auditory cortical regions have a relatively finer resolution in the frequency domain than homologous regions in the left auditory cortex, but this concept has not been tested directly. Here, we used functional magnetic resonance imaging (fMRI) to test this specific prediction. Healthy volunteers were scanned while passively listening to pure-tone melodic-like sequences in which the pitch distance between consecutive tones was varied in a parametric fashion. As predicted, brain activation in a region of right lateral auditory cortex, corresponding to the planum temporale, was linearly responsive to increasing pitch distance, even across the fine changes in pitch. In contrast, the BOLD signal at the homologous left cortical region was relatively constant as a function of pitch distance, except at the largest pitch change. The results support the model of relative hemispheric specialization and indicate that the right secondary auditory cortex has a finer pitch resolution than the left.

© 2007 Elsevier Ltd. All rights reserved.

**Keywords:** fMRI; Hemispheric functional specialization; Normal brain; Planum temporale

## 1. Introduction

Pitch is the perceptual correlate of acoustic frequency and can be considered along at least two perceptual dimensions, pitch height and pitch chroma (Shepard, 1982). Pitch height, is related to spectral energy distribution and is illustrated by the octave on the keyboard. In contrast, pitch chroma, or the cycle of notes within the octave, provides a basis for acoustic patterns (melodies). Several studies have investigated the processing of sequential or melodic pitch, which is critical for musical perception, however, its neural correlates are not fully understood.

Many findings have shown that musical pitch processing preferentially involves right auditory cortical structures. For example, studies of brain-lesioned patients have shown that the right auditory cortex is critical for melody discrimination (Milner, 1962), perception of missing fundamental pitch

(Zatorre, 1988), perception of melody in terms of its global contour (Peretz, 1990), direction of pitch change (Johnsrude, Penhune, & Zatorre, 2000), and in using melodic contextual cues in pitch judgments (Warrier & Zatorre, 2004). Consistent evidence comes from neuroimaging studies of normal subjects, showing that right secondary auditory regions are central in various aspects of musical pitch processing, such as in melodic processing (Patterson, Uppenkamp, Johnsrude, & Griffiths, 2002; Zatorre, Evans, & Meyer, 1994), in the maintenance of pitch while singing (Perry et al., 1999), and in imagery for tunes (Halpern & Zatorre, 1999). In contrast, left auditory regions seem to be specialized for rapid temporal processing as required in speech (e.g. Belin et al., 1998; Jancke, Wustenberg, Scheich, & Heinze, 2002; Phillips & Farmer, 1990; Zaehle, Wustenberg, Meyer, & Jancke, 2004).

Zatorre, Belin, and Penhune (2002) have recently proposed that the auditory system has developed two parallel and complementary systems, one in each hemisphere, specialized for differential resolution in the spectral and temporal domains, as a need to optimally process incoming simultaneous spectral and temporal acoustic information from the environment. A similar proposition has been made by Poeppel (2003), who suggested that different time integration windows characterize the left and

\* Corresponding author at: McConnell Brain Imaging Center, Montreal Neurological Institute, McGill University, 3801 University Street, Montreal, Quebec, Canada H3A 2B4. Fax: +1 514 398 8949.

E-mail address: krista.hyde@mail.mcgill.ca (K.L. Hyde).

right auditory cortices. Support for this model of hemispheric asymmetry comes from neuropsychological (Robin, Tranel, & Damasio, 1990), electrophysiological (Liegeois-Chauvel, Giraud, Badier, Marquis, & Chauvel, 2001) and neuroimaging studies (Boemio, Fromm, Braun, & Poeppel, 2005; Brechmann & Scheich, 2005; Jamison, Watkins, Bishop, & Matthews, 2006; Schönwiesner, Rubsamen, & von Cramon, 2005; Zatorre & Belin, 2001). The present investigation was based on a study by Zatorre and Belin (2001), in which normal subjects were scanned while passively listening to pure-tone sequences that varied parametrically either in terms of spectral complexity or temporal rate. Pure-tones (or sine wave tones) are tones with a single frequency, in contrast to complex tones that are made up of multiple frequencies. Responses to the spectral features were weighted towards right auditory areas, whereas responses to the temporal features were weighted towards the left. These findings were interpreted as reflecting that the right auditory cortex has a finer spectral resolution, whereas the left has a higher temporal resolution, but this explanation was not tested directly, and it has not been universally accepted (Scott & Wise, 2004).

Here, we used functional magnetic resonance imaging (fMRI) to test the prediction arising from the hemispheric specialization hypothesis that the right auditory cortex is more sensitive to small spectral changes relative to the left. Subjects were scanned while passively listening to pure-tone melodic-like sequences in which the pitch distance between consecutive tones was varied in a parametric fashion. We reasoned that if the right auditory cortex (particularly secondary auditory regions) has a higher resolution for spectral change, then it should show correlated changes in the BOLD response as a function of even small changes in the pitch of a pure-tone sequence; the left auditory cortex, should show increased BOLD response only to large changes in pitch. In other words, a high resolution for spectral change (as in the right auditory cortex) should result in a high sensitivity to small spectral changes, whereas a coarser spectral resolution (as in the left auditory cortex) should result in a lower sensitivity when stimulus frequency changes are small. This hypothesis is based on the assumption that there exist neural populations with frequency selectivity. We expand on this theory in Section 4.

## 2. Methods

### 2.1. Subjects

Ten healthy right-handed volunteers (half of each gender; mean age: 25.3; S.D.: 4.4 years) participated in the present study. All subjects were right-handed as assessed by an adapted form of the Edinburgh inventory (Oldfield, 1971). All subjects had normal hearing as determined via standard audiometric testing, and had no formal musical training. The present protocol was approved by the Montreal Neurological Institute Ethics Review Board, and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects gave informed written consent prior to their inclusion in the present study.

### 2.2. Behavioral experiment

Prior to scanning, subjects were tested in a pitch discrimination task to ensure that they could discriminate the pitch changes used in the subsequent fMRI

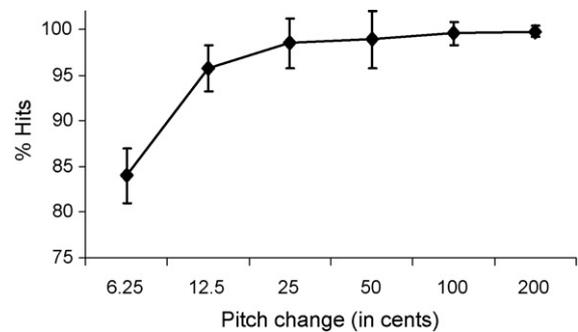


Fig. 1. Pitch discrimination behavioral task results. Performance of  $n = 10$  subjects expressed as mean percentage of hits (i.e. a “yes” response when there was a change) as a function of pitch change. Error bars represent standard errors.

experiment. The task was based on one used in a previous study (Hyde & Peretz, 2004), however, here, we used smaller pitch distances. Subjects were presented with a series of 360 five-tone isochronous sequences in which all tones were pure-tones (from now on referred to as simply ‘tones’ when describing these stimuli), each of 100 ms in duration and with 250 ms between tones. On half of the trials, all five tones were of the same pitch (1046 Hz), but on the other half, the fourth tone was altered by either a rise or fall in pitch at one of the following distances: 6.25, 12.5, 25, 50, 100, or 200 cents (where 1 cent is a unit of equal log frequency separation; 1 semitone = 100 cents). Subjects were asked to press a “yes” button whenever they detected a change and a “no” button when they were unable to detect a change. The stimuli were presented bilaterally through Sennheiser HD450 headphones in a quiet room, at an intensity level of 70 dB SPL-A in a random order. The test lasted about 10 min.

The mean performance of the ten subjects in the pitch discrimination task as a function of pitch change is shown in Fig. 1. The results are expressed uniquely as mean percentage of hits (i.e. a “yes” response when there was a change), since subjects did not make any false alarms (i.e. a “yes” response when there was no change). As can be seen, normal listeners perform well above chance ( $p < 0.001$ ) at the smallest pitch changes of 6.25 and 12.5 cents, and perform at ceiling at all pitch distances including and above 25 cents.

### 2.3. fMRI experiment

#### 2.3.1. Stimuli

Stimuli consisted of seven melodic-like tone sequences, each consisting of 21 pure-tones. The pure-tone sequences all had the same pitch contour starting at 1046 Hz (corresponding to the musical note C6) as shown in Fig. 2, but was modified parametrically in terms of pitch distance between consecutive tones. The pure-tone sequences were presented at one of the following seven pitch distances between tones (from smallest to largest): 0 (fixed pitch), 6.25, 12.5, 25, 50, 100, or 200 cents. The center value for all pure-tone sequences was 1046 Hz. All pure-tones were generated using MITSYN software (Henke, 1976). Each tone was 100 ms in duration, with 250 ms between tones, and the total duration of each pure-tone sequence was 7350 ms (or 7.35 s). A waveform of one pure-tone at 1046 Hz is presented in Fig. 2B.

#### 2.3.2. Task design

Subjects were scanned while passively listening to the pure-tone sequences. A passive paradigm was used so as to optimize the comparison of results to the Zatorre and Belin (2001) study. Subjects heard the pure-tone sequences binaurally at a level of ~80 dB sound pressure level via Siemens MR-compatible pneumatic sound transmission headphones. There were two stimulus ‘conditions’: (1) pitch (either fixed pitch at 0 cents between tones, or pitch change at each of 6 levels: 6.25, 12.5, 25, 50, 100, or 200 cents), (2) and a baseline condition of silence. On each ‘trial’, one stimulus condition was presented, either a pure-tone pitch sequence (either fixed pitch, or pitch change), or a silence condition. Each ‘run’ was comprised of 78 trials: 15 trials for the fixed-pitch level, 48 pitch-change trials (8 trials for each of 6 pitch change levels), and a baseline condition of silence (with 15 trials). For each subject, there were 2 runs (with 78 trials each). For each subject, the 78 trials were presented in a randomized

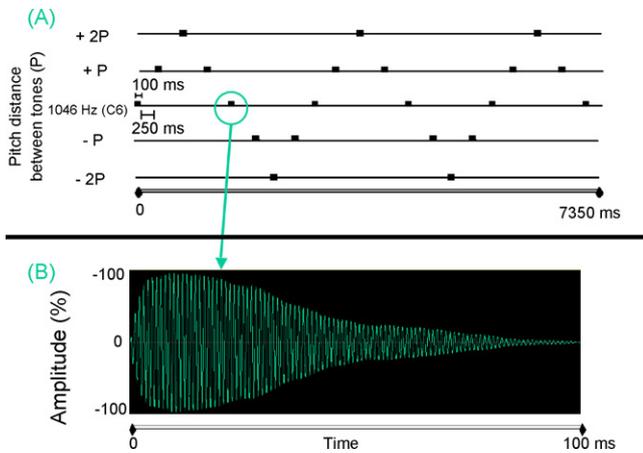


Fig. 2. Pure-tone sequence used in the fMRI study. (A) shows a pure-tone melodic-like sequence, where each black square corresponds to one tone, and the pitch distance between consecutive tones ( $P$ ) in cents is shown along the vertical axis from a center pitch of 1046 Hz corresponding to the musical note C6. (B) shows a waveform of a single pure-tone from a pure-tone sequence used in the fMRI study. The frequency of the pure-tone is 1046 Hz, where amplitude is represented along the  $y$ -axis as a percentage (from  $-100\%$  to  $+100\%$ ), and the time window is represented in milliseconds (ms) along the  $x$ -axis.

order within and across the two runs using Media Control Functions software (MCF, Digivox, Montreal, Canada). Each run lasted about 15 min. A schematic of the fMRI scanning paradigm used is presented in Fig. 3. As shown, each scan acquisition lasted 2 s, and each trial (lasting 7.35 s) was presented 0.4 s after each acquisition. A long inter-acquisition time of 10 s was used in order to minimize the noise-artifact from the scanner on the participants' ability to hear the stimuli. This also serves to avoid scanner noise contamination of the blood oxygenation level-dependent (BOLD) response on the stimuli in the auditory cortices (Belin, Zatorre, Hoge, Evans, & Pike, 1999).

### 2.3.3. fMRI parameters and analysis

Scanning was performed on a Siemens (Erlangen, Germany) Vision 1.5 T MRI scanner at the Montreal Neurological Institute. A high-resolution T1-weighted anatomical scan was obtained for anatomical localization for each subject [echo time (TE), 9.2 ms; repetition time (TR), 22 ms; matrix size,  $256 \times 256$ ; voxel size,  $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$ ], followed by two series of 78 T2\* gradient echo-planar images. A headcoil was used to obtain 20 interleaved slices spanning the whole brain, and oriented along the Sylvian fissure (TE, 50 ms; TR, 10 s; matrix size,  $64 \times 64$ ; voxel size,  $5 \text{ mm} \times 5 \text{ mm} \times 5 \text{ mm}$ ).

In-house software (Collins, Neelin, Peters, & Evans, 1994) was used in the pre-processing of the BOLD images. The images were first spatially smoothed using a 12 mm full-width at half-maximum Gaussian blurring kernel, corrected

for motion, and then were linearly transformed into standard stereotaxic space corresponding to the MNI/Talairach ICBM152 template (Collins et al., 1994). Next, statistical analysis based on a general linear model with correlated errors was performed on the BOLD data using FMRISTAT software (Worsley et al., 2002). Covariate analyses considering the BOLD response over all seven pitch distances were performed in order to investigate which brain areas showed activity that correlated in a linear fashion with increasing changes in pitch. In order to test for a non-linear relationship between BOLD activity and pitch distance, subtraction analyses were performed, including four contrasts as follows: (1) all pitch-change conditions were summed and compared to silence as a control contrast, (2) the fixed-pitch condition was compared to silence to identify the brain areas responsive to fixed-pitch information, (3) a contrast of all pitch-change conditions relative to fixed pitch was performed to identify the brain areas responsive to change pitch information, and (4) the largest pitch (200 cents) was compared to the fixed pitch (0 cents) condition to determine the regions responsive to the largest pitch change in particular.

In determining a minimum threshold for statistical significance for the covariation and subtraction analyses, we used a volume of interest (VOI) approach. As compared to a whole-brain statistical analysis, defining a VOI search volume in which differences are predicted, one restricts the number of multiple comparisons to be performed, which allows the use of a lower threshold value and hence greater sensitivity within the VOI. Based on the results from Zatorre and Belin (2001) study, we expected that the auditory cortices would be specifically responsive to the pure-tone sequences used here. Accordingly, the VOI used here corresponded to previously defined anatomical probability maps of bilateral auditory cortical areas, including the primary auditory cortex, which is found in the medial portion of Heschl's gyrus (HG; Penhune, Zatorre, MacDonald, & Evans, 1996) and an area of secondary auditory cortex, the planum temporale (PT; Westbury, Zatorre, & Evans, 1999). The outlines of the probability maps for the right and left PT as defined by Westbury et al. (1999) are indicated by white arrows in Fig. 4A. The statistical threshold applied for the VOI, including the predicted auditory areas with volume of  $9301 \text{ mm}^3$ , was  $t = 3.3$  at  $p < 0.05$ , corrected for multiple comparisons based on random field theory (Worsley et al., 2002).

## 3. Results

### 3.1. Imaging results

#### 3.1.1. Covariation analyses

The covariation analysis considering the BOLD response across the seven pitch distances revealed a peak activation lateral to the right primary auditory cortex, in the right PT ( $x = 64$ ,  $y = -22$ ,  $z = 4$ ;  $t = 3.7$ ; Fig. 4A). This right PT peak falls well within the probability map for the right PT as defined by Westbury et al. (1999) as indicated by the white outlines in

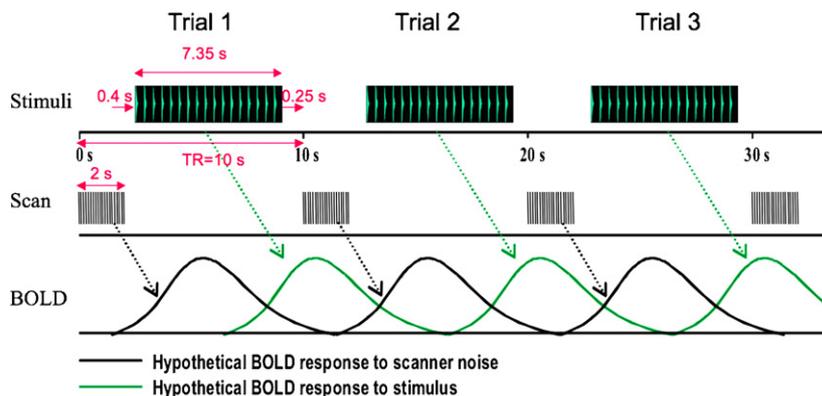


Fig. 3. Schematic of fMRI scanning paradigm. The stimulus presentation, corresponding scan acquisition and hypothetical BOLD response to the scanner noise and to the stimulus are shown.

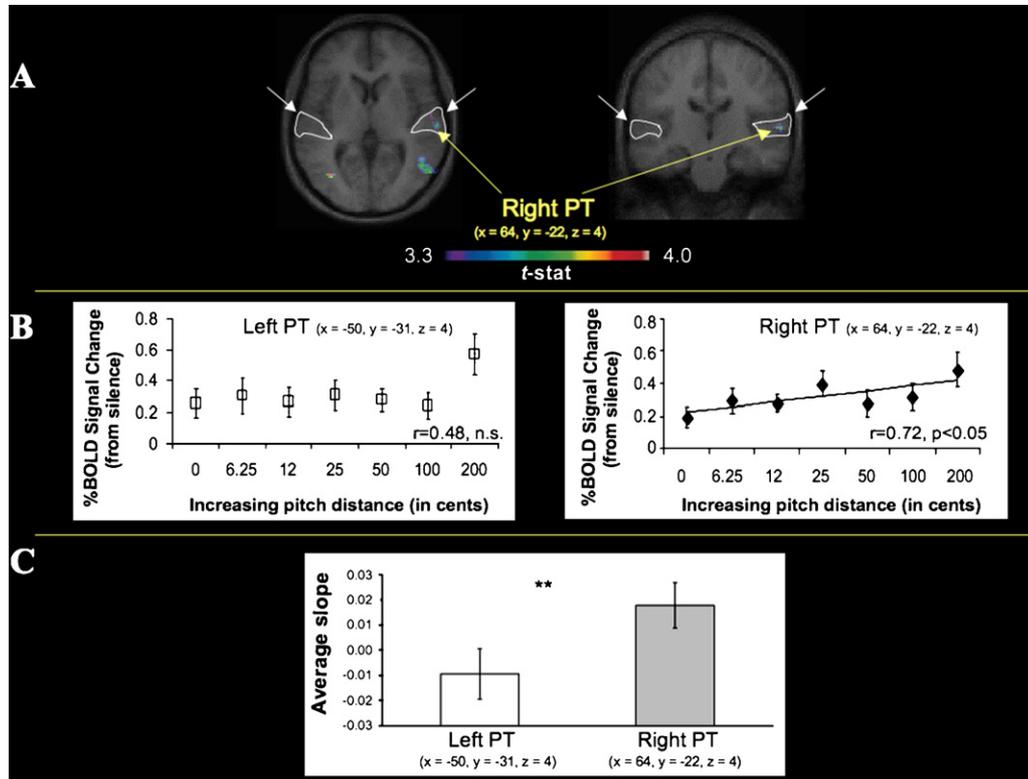


Fig. 4. fMRI results: covariation analyses. (A) Group ( $n = 10$ )  $t$ -statistical map for the covariation analysis superimposed on the group average anatomical MRI. The right side of the brain image corresponds to the right side of the brain. Horizontal and coronal sections are shown on the left and right of the figure, respectively; the right PT peak activation at the voxel with the highest  $t$ -value within the right auditory VOI ( $x = 64, y = -22, z = 4; t = 3.7, p < 0.05$ , corrected), is indicated by yellow arrows. Outlines of the probability maps for the right and left PT as defined by Westbury et al. (1999) are indicated by white arrows. (B) Correlations of % BOLD signal change as a function of increasing pitch distance at the right PT peak voxel shown in (A), and at the voxel with the highest  $t$ -value within the left auditory VOI, corresponding to the left PT ( $x = -50, y = -31, z = 4; t = 1.6, p > 0.05$ , corrected). Pearson  $r$ -values are indicated for the BOLD response at the right and left PT peaks. A trend line is drawn to demonstrate the significant ( $*p < 0.05$ ) positive linear trend at the right PT. (C) Average slopes of the % BOLD signal at the left and right PT shown in (B). The \*\* indicates a significant result at  $p < 0.01$  (one-tailed  $t$ -test). Error bars represent standard errors. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Fig. 4A. In addition, there was an area of activation anterior to the right PT peak ( $x = 58, y = -12, z = 2; t = 3.3$ ; Fig. 4A), though slightly less significant, corresponding to the antero-lateral belt cortex. There were no significant left auditory activations in this analysis. There was also some activation outside the defined VOI, in the middle temporal gyrus, bilaterally (Fig. 4A). However, we do not discuss this result further here since we were specifically interested in the response of the auditory cortices to the pitch stimuli.

In order to investigate the % BOLD signal change (as compared to silence) across all pitch distances, we extracted the BOLD signal at the voxel with the highest  $t$ -value within the right auditory VOI, corresponding to the right PT peak described above ( $x = 64, y = -22, z = 4; t = 3.7, p < 0.05$ , corrected). Calculating the correlation from these extracted values revealed a significant positive linear trend ( $r = 0.72, p < 0.05$ ), where the BOLD signal increased as a function of increasing pitch distance (Fig. 4B, right panel). For comparison, we also extracted the BOLD signal at the voxel with the highest  $t$ -value within the left auditory VOI, although it was not significant ( $x = -50, y = -31, z = 4; t = 1.6, p > 0.05$ , corrected), which falls just within the probability map for the left PT by Westbury et al. (1999).

In contrast to the right PT voxel, there was no significant linear correlation at the left PT voxel ( $r = 0.48, p > 0.05$ ), but rather a non-linear trend such that the BOLD signal increased only at 200 cents (Fig. 4B, left panel). This effect is explored further in the subtraction analyses (below).

Next, we tested whether there was a significant difference in the degree of change in the BOLD signal as a function of small pitch distances between hemispheres. To this aim, we calculated the mean slope values of the BOLD data over all 10 subjects at the right and left PT peaks described above for the first 6 conditions (i.e. 0–100 cents), and contrasted these values across hemispheres. We defined ‘small’ pitch distances as 0–100 cents, excluding the largest pitch condition of 200 cents, on the basis of the present data, which showed that the left PT is not sensitive to changes in the pitch stimuli until the largest pitch distance of 200 cents. The average right PT slope was significantly greater than the left [ $t(9) = 3.13, p < 0.01$ , one-tailed  $t$ -test; Fig. 4C], whereas the left PT on average had a slope that was not significantly different from zero [ $t(9) = 0.92, p > 0.3$ ; Fig. 4C]. The same results were obtained when we performed the same analyses, but considering two different spherical regions of interest (ROIs) of 5 and 10 mm<sup>3</sup>, respectively, centered around the

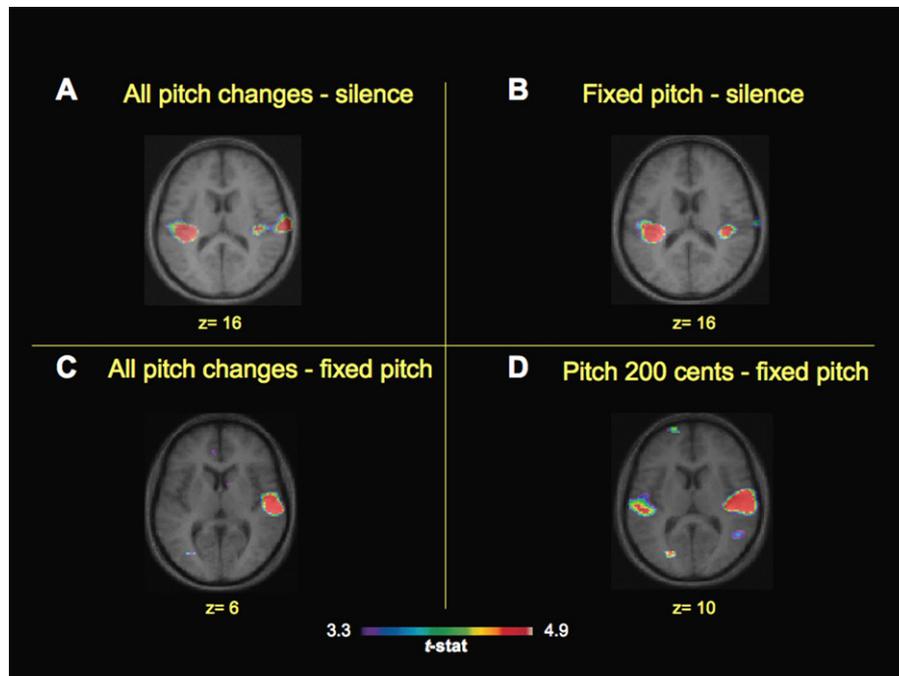


Fig. 5. fMRI results: subtraction analyses. (A–D) Group ( $n = 10$ )  $t$ -statistical maps for the four different contrasts, each of which are superimposed on the group average anatomical MRI. Images are shown as horizontal sections.

voxel with the highest  $t$ -value within the larger auditory VOI, on both the right and the left.

### 3.2. Subtraction analyses

As expected, comparing the sum of all the pitch-change conditions (i.e. 6.25–200 cents) versus silence, revealed significant bilateral activation centered around primary and nearby secondary auditory cortices (Fig. 5A), while the contrast of fixed-pitch minus silence revealed significant bilateral activation in only the medial portion of HG, likely within primary auditory cortex (Fig. 5B). Comparing the sum of all the pitch-change conditions (i.e. 6.25–200 cents) versus the fixed-pitch condition, revealed significant activation in only the right PT ( $x = 58$ ,  $y = -22$ ,  $z = 6$ ;  $t = 5.9$ ; Fig. 5C), in a location very comparable to that shown in the covariation analysis. Of greatest interest was the contrast of largest pitch distance (200 cents) minus fixed pitch (0 cents) because this contrast evaluates the presence of a non-linear response on the left side. It indeed revealed significant bilateral activation in both primary and secondary auditory areas including the PT and the superior temporal gyrus (STG) (Fig. 5D).

## 4. Discussion

### 4.1. Relative functional asymmetry of the auditory cortex

In the present study, we aimed to test whether the right auditory cortex is more sensitive to small pitch changes relative to the left. As expected based on the hemispheric specialization hypothesis, we found that the right auditory cortex was indeed differentially responsive to small pitch changes, whereas the

left was not. Both the covariation analyses and the contrast of all pitch-change conditions minus fixed pitch yielded significant activation specifically in the right PT, lateral to HG. As predicted, the right PT showed correlated changes in activity as a function of relatively small pitch changes (i.e. less than 200 cents) (Fig. 4). In contrast, the left PT showed a relatively constant BOLD signal across pitch distances less than 100 cents, but showed an increased BOLD response at the largest pitch distance of 200 cents as suggested by the extraction of the peak voxel within the VOI (Fig. 4B) and confirmed by the subtraction analyses (Fig. 5D). Thus, our data provide support for the model of relative hemispheric asymmetry where the right auditory cortex has a higher resolution in the pitch domain relative to the left, as suggested in other functional imaging studies (Jamison et al., 2006; Schönwiesner et al., 2005; Zatorre et al., 2002). These results are also consistent with findings from a study that used intracerebrally recorded auditory evoked potentials in humans and showed neurons in the right auditory cortex were more sharply tuned to frequency as compared to those on the left (Liegeois-Chauvel et al., 2001).

This difference in frequency resolution between the hemispheres may account for why brain activation and pitch distance were linearly related in the right auditory cortex but not the left. However, to explain specifically why the BOLD signal increases as a function of increasing pitch difference, one needs to make two assumptions: first, that there exist neural populations with frequency selectivity, and second that a degree of neuronal adaptation is occurring in our paradigm. The first assumption is amply documented in the neurophysiological literature (see Tramo, Cariani, Koh, Makris, & Braida, 2005 for a review) and there is also a reasonable basis to presume that adaptation effects are pertinent. Adaptation reflects the

phenomenon of reduced responses to repeated presentation of a specific stimulus, and has been measured via fMRI in many cortical regions, including visual areas, prefrontal cortex and auditory cortex (see Grill-Spector, Henson, & Martin, 2006 for a review). Similarly, in the present study, we propose that auditory cortical neurons in both hemispheres may undergo adaptation in response to the repeating melodic-like pure-tone sequences, which lasted for over 7 s. The effect of adaptation would presumably diminish as a function of increasing pitch distance. This is because increasing the pitch distance between tones in the repeating pure-tone sequence results in a wider pitch range, thus activating a greater number of distinct frequency-tuned auditory neural populations that have not yet ‘adapted’ to the auditory stimulus. From this perspective, in the present study, one would expect a positive correlation between brain activation and pitch distance in both hemispheres due to the fact that neuronal adaptation decreases with increasing pitch distance. However, a positive linear trend is seen only in the right auditory cortex, which we interpret as evidence that right auditory cortical neurons are more sharply tuned than left auditory neurons.

The interpretation that the left auditory cortex does respond to pitch changes, but only when they are relatively large, is consistent with the idea that the hemispheric asymmetry is relative and not absolute. Support for this relative asymmetry comes from the study of patients with temporal-lobe excisions that encroached upon the right HG and secondary auditory cortex lateral to HG, similar to the region found here that was sensitive to pitch change (Johnsrude et al., 2000). These patients were able to judge the direction of pitch change between two tones, but had significantly elevated difference thresholds on this task, as compared to patients with more anterior right temporal excisions, sparing the lateral HG area, or to patients with left temporal excisions, and normal controls (Johnsrude et al., 2000). These authors suggested that this phenomenon could be explained by the idea that the patients with right lateral HG excisions could use their intact left auditory cortex to accomplish the task, but the less fine-grained representation of pitch in the left hemisphere would lead to a higher threshold. The pitch direction threshold of these right temporally excised patients was about 200 cents and is strikingly similar to the left PT BOLD/interval function found here of 200 cents. The remarkable convergence of these findings across these two studies serves to identify a perceptual threshold for the left auditory cortex for judging the direction of pitch change in the range of 200 cents.

#### 4.2. Hierarchical pitch processing in the auditory cortex

Although several prior studies (Jamison et al., 2006; Johnsrude et al., 2000; Patterson et al., 2002; Schönwiesner et al., 2005; Zatorre & Belin, 2001) converge with the present study in implicating a network of right secondary auditory areas in the processing of spectral variations, the results across these studies (including the present study) do not correspond to exactly the same auditory regions. These differences are likely related to stimuli differences between experiments. For example, in their fMRI study, Schönwiesner et al. (2005) employed

novel noise-like stimuli that were perceptually unrelated to speech and music, but contained acoustic characteristics of both. When these stimuli were made more spectrally complex, brain activation was weighted to the right auditory cortex, with the strongest asymmetry in an area of secondary auditory cortex at the border of the antero-lateral PT and STG, very similar to the right auditory areas of activation found in our study. However, in contrast to the present study, both the right and left primary auditory cortices were sensitive to the spectral variations. This trend may be accounted for by the fact that complex spectral stimuli, as used by Schönwiesner et al. (2005), are known to produce more activation than pure-tones as those used here, in HG and bilaterally on the lateral supratemporal plane (Hall et al., 2002; Wessinger et al., 2001). Moreover, the highest degree of spectral spacing used in that study (about one-third of an octave) was much coarser than the pitch changes used here (smaller than one-sixth of an octave).

The right PT activation found in our study is posterior (by about 20 mm) to the anterior superior temporal area that was found to be responsive to spectral changes in the studies by Zatorre and Belin (2001) and Jamison et al. (2006). In these two studies, the spectral stimuli used consisted of a random pure-tone sequence that spanned a fixed range of one octave. In contrast, in our study, the pure-tone sequences were not at all random, but rather formed ‘melodic-like’ patterns with a fixed contour, and only varied in spectral range. From this perspective, the more posterior activation found here, may reflect that the processing of a fixed melodic contour involves more postero-lateral secondary auditory areas, whereas the presentation of random tones favors more antero-lateral secondary auditory areas. Regardless of the specific localization of contour processing, the present result is consistent with the findings by Zatorre and Belin (2001) and Jamison et al. (2006) that the hemispheric asymmetry in spectral processing is most apparent in regions beyond the primary auditory cortex. It is noteworthy to mention that the latter is also true in the processing of pitch in speech, where the right PT plays a preferential role in the processing of pitch changes in speech prosody (e.g. Gandour et al., 2004; Meyer, Steinhauer, Alter, Friederici, & von Cramon, 2004).

Converging evidence for the importance of non-primary auditory areas to pitch processing also comes from recent neurophysiological findings in the marmoset (Bendor & Wang, 2005). This study revealed the existence of pitch-sensitive neurons that respond with a consistent firing pattern to a variety of complex tones (“missing fundamental” stimuli) that perceptually correspond to a given pitch. The cortical region identified, near the antero-lateral border of the primary cortex and secondary auditory (or belt) cortex, is compatible with our findings here.

Both functional (Patterson et al., 2002) and anatomical (Hackett, Preuss, & Kaas, 2001) findings indicate a hierarchy of pitch processing, where the center of activity moves antero-laterally away from the primary auditory cortex, with more complex pitch pattern processing. For example, in a recent fMRI study that sought to identify the main stages of melody processing in the auditory pathway, spectrally matched sounds that produce no pitch, fixed pitch, and melodies were all found to

activate HG and PT, while more complex melodies activated regions beyond these areas including the STG and planum polare (Patterson et al., 2002). Consistent with this notion of hierarchical pitch processing, in the present study, the processing of fixed pitch implicated primary auditory cortex bilaterally, while the processing of changing pitch sequences implicated secondary auditory areas as well, including the PT and STG, and with a right-weighted lateralization.

## 5. Conclusion

The present data provide further evidence for the preferential involvement of right secondary auditory areas in the processing of sequential pitch information. The results are consistent with the predictions derived from the tradeoff model of relative hemispheric specialization, and provide more direct evidence than available previously that the secondary auditory cortices in the two hemispheres differ in their spectral resolution.

## Acknowledgements

We thank Marc Schönwiesner for his helpful comments on this manuscript, Marc Bouffard and Pierre Ahad for their expertise and assistance, as well as the staff of the McConnell Brain Imaging Centre. This work was supported by funding from the Canadian Institutes of Health Research.

## References

- Belin, P., Zatorre, R. J., Hoge, R., Evans, A. C., & Pike, B. (1999). Event-related fMRI of the auditory cortex. *Neuroimage*, *10*, 417–429.
- Belin, P., Zilbovicius, M., Crozier, S., Thivard, L., Fontaine, A., Masure, M. C., et al. (1998). Lateralization of speech and auditory temporal processing. *Journal of Cognitive Neuroscience*, *10*, 536–540.
- Bendor, D., & Wang, X. (2005). The neuronal representation of pitch in primate auditory cortex. *Nature*, *436*, 1161–1165.
- Boemio, A., Fromm, S., Braun, A., & Poeppel, D. (2005). Hierarchical and asymmetric temporal sensitivity in human auditory cortices. *Nature Neuroscience*, *8*, 389–395.
- Brechmann, A., & Scheich, H. (2005). Hemispheric shifts of sound representation in auditory cortex with conceptual listening. *Cerebral Cortex*, *15*, 578–587.
- Collins, D. L., Neelin, P., Peters, T. M., & Evans, A. C. (1994). Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. *Journal of Computer Assisted Tomography*, *18*, 192–205.
- Gandour, J., Tong, Y., Wong, D., Talavage, T., Dziedzic, M., Xu, Y., et al. (2004). Hemispheric roles in the perception of speech prosody. *Neuroimage*, *23*, 344–357.
- Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: Neural models of stimulus-specific effects. *Trends in Cognitive Sciences*, *10*, 14–23.
- Hackett, T. A., Preuss, T. M., & Kaas, J. H. (2001). Architectonic identification of the core region in auditory cortex of macaques, chimpanzees, and humans. *Journal of Comparative Neurology*, *441*, 197–222.
- Hall, D. A., Johnsrude, I. S., Haggard, M. P., Palmer, A. R., Akeroyd, M. A., & Summerfield, A. Q. (2002). Spectral and temporal processing in human auditory cortex. *Cerebral Cortex*, *12*, 140–149.
- Halpern, A. R., & Zatorre, R. J. (1999). When that tune runs through your head: A PET investigation of auditory imagery for familiar melodies. *Cerebral Cortex*, *9*, 697–704.
- Henke, W. L. (1976). *An interactive dialogue language for time signal processing*. Cambridge, MA: MIT Research Laboratory of Electronics.
- Hyde, K. L., & Peretz, I. (2004). Brains that are out of tune but in time. *Psychological Science*, *15*, 356–360.
- Jamison, H. L., Watkins, K. E., Bishop, D. V., & Matthews, P. M. (2006). Hemispheric specialization for processing auditory nonspeech stimuli. *Cerebral Cortex*, *16*, 1266–1275.
- Jancke, L., Wustenberg, T., Scheich, H., & Heinze, H. J. (2002). Phonetic perception and the temporal cortex. *Neuroimage*, *15*, 733–746.
- Johnsrude, I. S., Penhune, V. B., & Zatorre, R. J. (2000). Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain*, *123*(Pt 1), 155–163.
- Liegeois-Chauvel, C., Giraud, K., Badier, J. M., Marquis, P., & Chauvel, P. (2001). Intracerebral evoked potentials in pitch perception reveal a functional asymmetry of the human auditory cortex. *Annals of the New York Academy of Sciences*, *930*, 117–132.
- Meyer, M., Steinhauer, K., Alter, K., Friederici, A. D., & von Cramon, D. Y. (2004). Brain activity varies with modulation of dynamic pitch variance in sentence melody. *Brain and Language*, *89*, 277–289.
- Milner, B. A. (1962). Laterality effects in audition. In V. Mountcastle (Ed.), *Inter-hemispheric relations and cerebral dominance* (pp. 177–195). Baltimore, USA: Johns Hopkins University Press.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*, 97–113.
- Patterson, R. D., Uppenkamp, S., Johnsrude, I. S., & Griffiths, T. D. (2002). The processing of temporal pitch and melody information in auditory cortex. *Neuron*, *36*, 767–776.
- Penhune, V. B., Zatorre, R. J., MacDonald, J. D., & 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.
- Peretz, I. (1990). Processing of local and global musical information by unilateral brain-damaged patients. *Brain*, *113*(Pt 4), 1185–1205.
- Perry, D. W., Zatorre, R. J., Petrides, M., Alivisatos, B., Meyer, E., & Evans, A. C. (1999). Localization of cerebral activity during simple singing. *Neuroreport*, *10*, 3979–3984.
- Phillips, D. P., & Farmer, M. E. (1990). Acquired word deafness, and the temporal grain of sound representation in the primary auditory cortex. *Behavioural Brain Research*, *40*, 85–94.
- Poeppel, D. (2003). The analysis of speech in different temporal integration windows: Cerebral lateralization as ‘asymmetric sampling in time’. *Speech Communication*, *41*, 245–255.
- Robin, D. A., Tranel, D., & Damasio, H. (1990). Auditory perception of temporal and spectral events in patients with focal left and right cerebral lesions. *Brain and Language*, *39*, 539–555.
- Schönwiesner, M., Rubsamen, R., & von Cramon, D. Y. (2005). Hemispheric asymmetry for spectral and temporal processing in the human antero-lateral auditory belt cortex. *European Journal of Neuroscience*, *22*, 1521–1528.
- Scott, S. K., & Wise, R. J. (2004). The functional neuroanatomy of prelexical processing in speech perception. *Cognition*, *92*, 13–45.
- Shepard, R. N. (1982). In D. Deutsch (Ed.), *The psychology of music* (1st ed., pp. 344–390). New York: Academic.
- Tramo, M. J., Cariani, P. A., Koh, C. K., Makris, N., & Braid, L. D. (2005). Neurophysiology and neuroanatomy of pitch perception: Auditory cortex. *Annals of the New York Academy of Sciences*, *1060*, 148–174.
- Warrier, C. M., & Zatorre, R. J. (2004). Right temporal cortex is critical for utilization of melodic contextual cues in a pitch constancy task. *Brain*, *127*, 1616–1625.
- Wessinger, C. M., VanMeter, J., Tian, B., Van Lare, J., Pekar, J., & Rauschecker, J. P. (2001). Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging. *Journal of Cognitive Neuroscience*, *13*, 1–7.
- Westbury, C. F., Zatorre, R. J., & Evans, A. C. (1999). Quantifying variability in the planum temporale: A probability map. *Cerebral Cortex*, *9*, 392–405.
- Worsley, K. J., Liao, C. H., Aston, J., Petre, V., Duncan, G. H., Morales, F., et al. (2002). A general statistical analysis for fMRI data. *Neuroimage*, *15*, 1–15.
- Zaehle, T., Wustenberg, T., Meyer, M., & Jancke, L. (2004). Evidence for rapid auditory perception as the foundation of speech processing: A sparse temporal sampling fMRI study. *European Journal of Neuroscience*, *20*, 2447–2456.

- Zatorre, R. J. (1988). Pitch perception of complex tones and human temporal-lobe function. *Journal of the Acoustical Society of America*, *84*, 566–572.
- Zatorre, R. J., & Belin, P. (2001). Spectral and temporal processing in human auditory cortex. *Cerebral Cortex*, *11*, 946–953.
- Zatorre, R. J., Belin, P., & Penhune, V. B. (2002). Structure and function of auditory cortex: Music and speech. *Trends in Cognitive Sciences*, *6*, 37–46.
- Zatorre, R. J., Evans, A. C., & Meyer, E. (1994). Neural mechanisms underlying melodic perception and memory for pitch. *Journal of Neuroscience*, *14*, 1908–1919.