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Organization of Human Auditory Cortex: Responses to Frequency Modulated Sounds

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Graduate Program in Neuroscience

A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

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ORGANIZATION OF THE HUMAN AUDITORY CORTEX: RESPONSES TO FREQUENCY MODULATED SOUNDS

(Thesis format: Monograph)

by

Diedre D. De Souza

Graduate Program in Neuroscience

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science

The School of Graduate and Postdoctoral Studies
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Abstract

Functional Magnetic Resonance Imaging (fMRI) was used to investigate the extent, magnitude and patterns of brain activity in response to frequency-modulated sounds. We examined this by manipulating the direction (rise vs. fall) and the rate (fast vs. slow) of a series of iterated rippled noise (IRN) bursts. Participants were presented with auditory stimuli while functional images of the cortex were obtained. Univariate analyses revealed more widespread activation within auditory cortex in response to frequency-modulated sweeps compared to steady-state sounds. Furthermore, multivoxel pattern analysis (MVPA) was used to determine whether regions within auditory cortex were involved in feature-specific encoding. The pattern of activity within auditory cortex showed a high degree of consistency for the rate dimension, suggesting this pattern of activity infers representational information. Additionally, activity patterns for direction were not distinguishable, which suggests this coding occurs over a neural activity pattern not distinguishable at the level of the BOLD response.

Keywords: frequency modulation, auditory cortex, auditory belt, parabelt, Heschl’s gyrus, multivoxel pattern analysis (MVPA), functional magnetic resonance imaging (fMRI)
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During verbal communication, our auditory system is charged with the task of deciphering which stimuli are important and integrating this information in order to perceive the incoming message. This process occurs amidst competing sound sources and yet the human auditory system is capable of decoding auditory speech both accurately and efficiently. It is thought that the auditory cortex is organized in a hierarchical fashion in order to support the processing of complex auditory signals such as those found in speech. According to past research, a core region of cortex known as Heschl’s gyrus responds to any acoustic stimuli, including pure tones, while brain areas peripheral to this region respond to stimuli that are more spectrally and temporally complex (Chevillet, Riesenhuber, & Rauschecker, 2011). Convergent support for this notion has come from a variety of research methodologies including functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG) and electrophysiological recordings just to name a few (Godey, Atencio, Bonham, Schreiner, & Cheung, 2005; Heinemann, Rahm, Kaiser, Gaese, & Altmann, 2010; Mendelson, Schreiner, Sutter, & Grasse, 1993).

The majority of research conducted on the topic of auditory cortical organization has employed steady-state stimuli; sounds with unchanging center frequencies or static noise. Although these sounds lack the dynamic temporal dimensions that are typical in vocalizations, studies have provided much insight into how cortical pathways may be connected to support the integration and processing of spectrally complex acoustic cues. Work by Merzenich and Brugge (1973) revealed that the superior temporal plane (STP) of macaque auditory cortices is organized tonotopically according to frequency, a finding that is consistent with research from other animal models including owl monkeys.
(Atencio et al., 2007), squirrel monkeys (Godey et al., 2005) and cats (Mendelson et al., 1993). They were able to accomplish this by using microelectrodes to record neuronal firings from neurons located within the auditory cortex of macaques. Since much of what is currently known about the organization of human auditory cortex has been inferred from animal models, converging findings such as these serve to further validate such inferences.

Spectral complexity is concerned with the distribution of energy associated with a sound; as the number of frequency elements contributing to a given sound increases, so does the spectral complexity of the acoustic signal. However, a different acoustic element found in vocal productions, frequency modulation, also plays an especially important role in human speech and the vocalizations of animals (Cheung, Nagarajan, Schreiner, Bedenbaugh, & Wong, 2005; Solis and Doupe, 1997). Of interest is the extent to which auditory cortex is specifically tuned to frequency modulations.

The role of frequency modulation in language comprehension can be easily demonstrated by taking a closer look at phonemic processing and how subtle changes in temporal features affect the perception of speech sounds. The production of any given phoneme results in a concentration of acoustic energies known as formants or resonant frequencies. The resonant frequencies produced during the articulation of phonemes depend on the design of the vocal tract as well as the positioning of the tongue. Additionally, because speech is produced in a dynamic fashion, the formant frequencies produced are seldom constant or steady-state, meaning that individual formant frequencies tend to change at differing rates over time (Hillenbrand, Getty, Clark, & Wheeler, 1995). These frequency changes are significant because the information
contained in both frequency modulation and formant transitions (the combination of the different formants produced for a single utterance) are critical for phonemic identification and phonemic perception (Alfredo, 1993; Stevens & Klatt, 1974; Swinney, & Prather, 1980). For example, changing the rate of a consonant’s formant transitions will lead to the perception of either /b/ (50 ms) or /w/ (150 ms) in a syllable-initial position. Likewise, changing the direction of change of the second formant’s (F2) transition will change a /b/ to /d/ (Miller & Liberman, 1979). The importance of frequency modulation in phonemic discrimination suggests that this component of acoustic signals should be given more attention. Thus, the present research focuses specifically on the neural correlates of detecting and identifying such frequency changes.

The process of phonemic identification is not completely understood, but significant progress has been made over the past decade (Liebenthal, Binder, & Spitzer, 2005). Research by Alfredo (1993) emphasized an important distinction between phonemic identification and phonemic perception. While phonemic perception is concerned with the unconscious experience, phonemic identification deals with the conscious awareness of phonemes and, as such, recruits additional cortical regions such as inferior frontal gyrus (IFG) (Patterson & Johnsrude, 2008). An important caveat is that individuals need not identify a phoneme in order to perceive it or utilize the information it conveys. Another point worth mentioning is that phonemic perception follows a bottom-up processing structure and phonemic identification involves a combination of top-down and bottom-up processes. Our investigation into the existence of a processing hierarchy for frequency-modulated sounds will provide further insight into how the acoustic components of phonemes are processed.
Numerous prior studies have used fMRI to localize and visualize functional activity within auditory cortex. Wessinger, Buonocore, Kussmaul, and Mangun (1997) performed one of the first studies that used fMRI to demonstrate frequency-specific responses thereby providing insight into the organization of human auditory cortex. It has since been repeatedly demonstrated that complex stimuli, as measured by bandwidth size and temporal variation, result in numerous activation foci within the auditory cortex that are larger and more extensive than the regions activated by pure tone stimuli (Rauschecker, Tian, & Hauser, 1995; Wessinger, VanMeter, Tian, Van Lare Pekar, & Rauschecker, 2001). Hall et al. (2002) were able to demonstrate that harmonic tones, a type of complex sound, produced more activation in auditory cortex than pure tones. Additionally, when the temporal feature of the acoustic signal was manipulated, they found that frequency-modulated tones produced more activation than steady-state tones.

Likewise, Chevillet et al. (2011) used three classes of acoustic stimuli: pure tones, band-pass noise (BPN, created by applying a upper and lower limit frequency filter allowing frequencies within the defined limit to contribute to the acoustic signal) and species-specific vocalizations (spoken vowels). These auditory signals varied in their level of spectral complexity, allowing the authors to define a structural and functional hierarchy within auditory cortex. According to their findings, pure tones elicited activation in the auditory core, commonly defined as Heschl’s gyrus, BPN elicited activation in the auditory core as well as areas both medial and lateral to the auditory core; the regions medial and lateral to the auditory core are commonly referred to as the auditory belt. Lastly, vocalizations elicited activation in core, belt, and parabelt regions. The parabelt region represents the portion of auditory cortex that is peripheral to the auditory belt. The
recruitment of additional brain areas with increasing complexity of the auditory signal was not symmetrical; rather, it proceeded in an anterior, lateral, and ventral direction in reference to the auditory core. These results also contradict previous findings, which stated that core auditory cortex responds indiscriminately to all auditory signals. This study revealed that although the auditory core responds to all auditory signals, the intensity of the activation within the auditory core is dependent on the spectral complexity of the stimuli. Imaging studies such as this have proven to be particularly useful in localizing the neural networks involved in auditory processing. Although the temporal features were not manipulated in this study, it did demonstrate that creating auditory stimuli that are not only temporally complex, but also spectrally complex, is key to investigating frequency modulation as it pertains to vocalizations.

More recently, there has been a shift whereby more studies are concerned with investigating the neural representations of frequency modulation in primary auditory cortex. A variety of frequency-modulated stimuli have been used throughout the field including linear (Nelken & Versnel, 2000), sinusoidal (Liang, Lu, & Wang, 2002) and logarithmic frequency-modulated sweeps (Mendelson et al., 1993). Similar to the way tonotopic maps were elucidated, many of these studies used both multi-unit and single unit recordings to map representations of frequency modulation. Since frequency modulation necessarily consists of two dynamic features, namely direction and rate, the maps were created by measuring peak neuronal responses for a given rate of modulation and a given direction. Using this method, Mendelson et al. (1993) determined that neurons located in the primary auditory cortex of cats were systematically distributed according to the rate and direction of frequency-modulated sweeps and that the
organization of the two features was independent. This means that the preference of a given neural unit for a particular direction of frequency-modulated sweep has no bearing on its preference for a particular rate of frequency-modulated sweep. The finding that these two features of frequency modulation are independently organized lends support to the notion of a hierarchical representation of acoustic signals in the auditory cortex. It points to the existence of multiple hierarchical networks whereby higher levels are involved in processing the more complex acoustic features, such as the rate and direction of frequency-modulated sweeps, as well as integrating incoming information from lower levels of the hierarchy.

A study by Washington and Kanwal (2008) provided further insight into the neural representations of frequency modulation in the auditory cortex of mustached bats. This work is of particular interest because bats are thought to have one of the most specialized auditory systems since they rely on it not only for communication but also for finding food and for navigation by way of echolocation. Furthermore, this study focused on a subregion of auditory cortex known as the Doppler-shifted constant frequency processing (DSCF) area. The DSCF area is important for several reasons; it represents the largest subregion of the mustache bat’s auditory cortex, it is especially sensitive to spectrally and temporally complex stimuli, and it shows hemispheric lateralization for bat calls similar to the hemispheric specialization we see in humans for language (Kanwal & Rauschecker, 2007). This study revealed several key findings regarding the neural structure and organization of the DSCF. First, it revealed the presence of neurons that respond preferentially to either pure tones or frequency-modulated sweeps. This feature of neuronal selectivity was also demonstrated in cats (Mendelson et al. 1993), and
monkeys (Kusmierek & Rauschecker, 2009). Specifically, 75% of the neuronal population for which recordings were obtained showed a preference for frequency-modulated sweeps compared to steady-state pure tones. Likewise, frequency-modulated selective neurons also showed preferences for a particular direction and rate of frequency modulation. Based on the similarities between bats and humans regarding the use of vocalizations and the lateralization of neural involvement pertaining to species-specific vocalization, this study serves as a comparable model for the expectations one may have regarding the organization of human auditory cortex.

While the methodologies used in the studies mentioned above provide compelling evidence in support of a hierarchical organization within the auditory cortex, these invasive approaches are not appropriate for use on humans. In light of this, imaging studies have emerged as the alternative. A study by Zattore and Belin (2001) revealed results similar to that of the Washington and Kanwal (2008) study discussed above. Using positron emission tomography (PET), they were able to examine both the spectral and temporal variation of sounds within human auditory cortex. In order to manipulate the temporal dimension, participants were presented with two steady-state pure tones of differing frequency in an alternating fashion. The time period between the presentations of each alternating stimulus was increased progressively. In order to manipulate the spectral dimension, the auditory stimuli were presented at a constant rate with the number of frequencies contributing to the auditory signal increasing over time. The authors found bilateral activation of the core auditory cortex in response to temporal variation, and bilateral activation of the anterior superior temporal areas in response to spectral variation. Additionally, they found that activation in response to the temporal features
was left lateralized while responses to the spectral features were right lateralized. Interestingly, the finding that both temporal processing and language processing is left lateralized provides some support for the role of frequency modulation in verbal communication. However, this study used linear pure tone sound bursts. Pure tones are auditory signals consisting of a single concentration of acoustic energy that results in a single frequency band. This poses a particular problem regarding its relevance to speech, as pure tones do not capture the spectral complexity of speech or species specific vocalizations, even when layered, as was done in this experiment.

To summarize then, prior research has demonstrated that the spectral and temporal quality of an acoustic signal greatly influences neuronal responses within the auditory cortex. Therefore, when employing a manipulation involving frequency modulation, some consideration should be given to the parameters that describe this acoustic feature. There is some consensus regarding the threshold for identifying the direction of frequency-modulated sweeps. According to Schouten (1985) and Gordon and Poeppel (2002), the minimum duration of a frequency sweep required to correctly identify its direction is 20 ms. While the current study is not concerned with the identification of frequency-modulated sweeps, using this information to guide stimuli development ensures the auditory signals used will fall within the limits of our perceptual abilities. Unfortunately, there is no such consensus regarding directional sensitivity of frequency modulations; a specific threshold for the frequency range that must be traversed in order to perceive the direction of frequency change as yet to be determined.

The stimuli used in many of the studies discussed were often pure tones. However, these pure tones do not provide the spectrotemporal complexity required to
properly study the auditory cortex in its entirety. As discussed above, pure tone stimuli tend to activate only core auditory regions, while sounds possessing a more complex spectrotemporal array elicits activation in a broader range of auditory cortex, including the core region and areas peripheral to the core (e.g., Rauschecker et al. 1995).

Ultimately, speech is composed of wide-band acoustic signal and, given its importance, it’s quite reasonable to expect some sort of specialization within the auditory cortex for processing and integrating these individual features. For that reason the present study used iterative rippled noise (IRN) for stimulus creation. IRN is a type of broadband noise with discernible spectral and temporal regularities (Swaminathan, Krishnan, Gandour, & Xu, 2008). This enabled us to circumvent issues related to using narrowband stimuli such as pure tones, and instead capture the general spectral complexity typical of speech. Furthermore, we were able to manipulate the center frequency so that the rate and direction of frequency modulation could be investigated.

*Motivation for the Present Study*

This study concerns the neural processing of frequency modulation features that are critical for language comprehension. The intention was to examine how the human brain processes and differentiates the rate and direction characteristics of these stimuli and, in particular, whether different subregions of auditory cortex respond preferentially to these features of speech. We accomplished this by investigating patterns of brain activation in auditory cortex in response to steady state versus frequency-modulated stimuli.

Based on work by Chevillet et al. (2011), we hypothesized that the auditory
cortex would respond differentially to steady-state tones compared to frequency-modulated sweeps, yielding different levels and patterns of activation for the two classes of stimuli. Although their work did not specifically investigate the effects of frequency modulation, it did look at how acoustic signals of varying spectral complexity influenced brain activation. From this it is expected that the element of frequency modulation does increase the complexity of the acoustic signal and should therefore elicit differential activation within primary auditory cortex compared to steady state tones. Furthermore, frequency modulation should yield activation outside the auditory core regions relative to steady-state sounds, extending into peripheral areas such as belt and parabelt regions (Rauschecker et al. 1995, Kusmierek & Rauschecker, 2009). Differential activation of the auditory cortex in response to different sound complexities, e.g., frequency modulated vs. steady-state sounds, would support the notion that the auditory cortex is indeed organized in a hierarchical manner. Also, we will examine whether the rate of change in frequency (fast vs. slow) influences the degree and extent of activation in specific subregions of auditory cortex. A finding such as this would suggest that the auditory cortex is functionally organized in a way that distinguishes different rates of modulation. Lastly, we will examine whether the direction of frequency change (rise vs. fall) also yields differential activation, again suggesting the brain respects this division in auditory stimuli.

Additionally, there is currently some debate regarding the functional hierarchy previously defined in monkeys (Merzenich & Brugge, 1973; Rauschecker et al. 1995; Kikuchi et al. 2010) and in humans (Chevillet et al. 2011). The inferences drawn from animal models and the type of auditory stimuli used are the two major areas of concern.
The design of this study should provide some insight into the role of core auditory cortex in processing stimuli of varying complexity. It has been previously demonstrated that these core regions respond discriminately to auditory signals both in the magnitude of the activation (Chevillet et al. 2011) and in the pattern of the activation (Hsieh, Fillmore, Rong, Hickok, & Saberi, 2012). This study intends to address these issues by performing both univariate analyses and multivoxel pattern analysis (MVPA). While conventional neuroimaging analyses are useful for detecting regional activation differences, they do not provide any information regarding the representational content of voxels within a given region. On the other hand, it has been shown that MVPA is capable of detecting activation patterns in regions of interest (ROIs) even in the absence of average activation differences (Mur, Bandettini, & Kriegeskorte, 2009; Hsieh et al. 2012).

Methods

Participants

Sixteen neurologically healthy adult participants were recruited for this study (eight females, eight males) ages: 20-28 years. All participants were right-handed, monolingual native English speakers with normal audition by self-report. One female participant was excluded from further analyses due to scanner artifacts discovered post-acquisition. Informed consent was obtained from each participant in accordance with the University of Western Ontario Medical Research Ethics Board.

Stimuli

The auditory stimuli consisted of 100 ms Iterative Rippled Noise (IRN) bursts, a
type of broadband noise that has been manipulated in a way that produces a perceived pitch contour while maintaining broadband characteristics similar to human speech (Figure 1; Swaminathan, Krishnan, Gandour, & Xu, 2008). IRN stimuli were created in Matlab (MathWorks, 2010) at a 44.1 KHz sample rate (16-bit quantization); there were four dynamic (changing center frequency) stimulus conditions; Rise-Fast, Rise-Slow, Fall-Fast, and Fall-Slow. Three stimuli were created for each condition, in which the initial and final frequency of the sweep was varied (Table 1). All frequency modulations varied on a linear scale. Stimuli in the ‘Fast’ conditions had an FM rate of 20 octaves/s; the FM rate in the ‘Slow’ condition was 5 octaves/s. The Steady-State condition consisted of an IRN with a constant center frequency of 500, 1000, and 2000 Hz.

Figure 1. Spectrograms of frequency modulated sweeps from each of the five conditions; Fall-Fast (FF), Fall-Slow (FS), Steady-State (SS), Rise-Slow (RS) and Rise-Fast (RF). Note that the dark bands reflect the center frequencies and the corresponding slopes depict the rate at which the center frequency changes.
Table 1. Acoustic parameters of the IRN stimuli

<table>
<thead>
<tr>
<th>Condition</th>
<th>Onset Frequency (Hz)</th>
<th>Offset Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rise - Fast</td>
<td>500</td>
<td>2000</td>
</tr>
<tr>
<td></td>
<td>750</td>
<td>3000</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>4000</td>
</tr>
<tr>
<td>Fall - Fast</td>
<td>2000</td>
<td>500</td>
</tr>
<tr>
<td></td>
<td>3000</td>
<td>750</td>
</tr>
<tr>
<td></td>
<td>4000</td>
<td>1000</td>
</tr>
<tr>
<td>Rise - Slow</td>
<td>500</td>
<td>750</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>1500</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>3000</td>
</tr>
<tr>
<td>Fall - Slow</td>
<td>3000</td>
<td>2000</td>
</tr>
<tr>
<td></td>
<td>1500</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>750</td>
<td>500</td>
</tr>
<tr>
<td>Steady – State</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>2000</td>
</tr>
</tbody>
</table>

*Note:* The onset and offset frequencies for the Steady-State conditions are identical because the center frequencies for this particular manipulation did not change over time.

Stimuli were presented binaurally during scanning via MR compatible headphones (Sensimetrics Model S14). Participants were instructed to passively listen to the stimuli, and were allowed to adjust the volume to their desired level of comfort. We employed a block design and a sparse scanning paradigm, in which subjects heard the stimuli during silent gaps between scanner volume acquisitions (Figure 2). Following each scan, subjects heard trains of a single IRN stimulus (or silence) presented nine times with a 1700 ms inter-stimulus interval. This 900 ms stimulus train was flanked by 50 ms of silence, to eliminate potential masking effects of scanner gradient noise. Each block consisted of five repetitions of this stimulus train. A single stimulus condition was presented within a given block with each condition presented three times during each run.
for a total of 15 blocks per run. Each block was followed by a 13-second null-stimulation period during which no stimulus was played during the inter-scan gaps.

Figure 2. A schematic of the sparse scanning paradigm embedded within a block design. The top graph shows how each run was organized into blocks where silent blocks alternate with one of the five stimuli conditions. Auditory stimuli were presented during the silent inter-scan gaps in order to minimize acoustic masking. A 50 ms period of silence flanked both ends of the 900 ms stimulus train. During the rest blocks, scans were obtained with no stimuli presented during the inter-scan interval.

Scanning was divided into eight scanning runs of 15 blocks each, for a total of 24 blocks per condition over the entire scanning session. Participants were instructed to passively listen to the audio stimuli. A silent movie was displayed via a projector for the sole purpose of keeping the participant alert for the duration of the scan.

*fMRI Imaging*

Images were acquired using the 3.0 Tesla Siemens TIM Trio Scanner located at the Robarts Research Institute in London Ontario. The scanner was fitted with a 32-channel head coil. Functional images were acquired in an axial orientation using an iPAT
parallel acquisition sequence (GRAPPA, generalized auto-calibrating partially parallel acquisition; acceleration factor 2). A total of 1200 T2*-weighted functional scans were acquired over eight runs (voxel size = 3 x 3 x 3 mm; FOV = 192 x 192 mm; TA = 1.6 s, plus 1 second inter-scan gap, yielding an effective TR = 2.6 s; TE = 30 ms; matrix size: 64 x 64 x 28). Twenty eight slices per volume were obtained, providing full coverage of temporal and occipital lobes, but only partial coverage of the upper portion of the cerebrum. Specifically, coverage excluded portions of the somatosensory cortex, somatomotor cortex and superior parietal lobe. Prior to functional scanning we obtained a whole-brain high resolution (T1-weighted) anatomical image (MPRAGE; GRAPPA acceleration factor = 2; TR = 2.3 s, TE = 2.98 ms, Flip angle = 9 degrees, matrix size: 256 x 256 x192; voxel size = 1 x 1 x 1 mm).

Univariate Analysis

Imaging data were analyzed using the AFNI software package (Cox, 1996). All functional scans were motion corrected using a 3d rigid body transform (AFNI 3dvolreg). Since the anatomical scan was performed first in each session, all functional scans were reregistered to the first functional volume of the first run. The functional scans were then used to create subject-wise statistical parametric maps. This process involved creating a general linear model (GLM, AFNI 3dDeconvolve) composed of six regressors; five condition regressors (Fall-Fast, Fall-Slow, Rise-Fast, Rise-Slow, Steady-State), and a single motion parameter estimate calculated as the root mean square of the six motion parameters. Each task predictor was modeled as a boxcar function with a duration of 13 s convolved with a canonical hemodynamic response function. In order to make group-
related comparisons regarding changes in brain activity, the structural scans and statistical maps for all participants were spatially normalized by transformation to the Talairach and Tournoux (1998) template using an automatic registration procedure (least-squares cost function; AFNI \texttt{@auto_tlrc}). After transformation, the statistical maps of each participant were resampled to a resolution of $1\text{mm}^3$ and spatially filtered with a 5mm FWHM Gaussian kernel.

Using the single subject statistical maps, groupwise analyses were performed using a one-sample $t$-test. The first contrast of interest involved comparing activation in response to Steady-State sounds versus frequency-modulated sweeps (Rise-Fast + Rise-Slow + Fall-Fast + Fall-Slow). The purpose of this contrast was to investigate the existence of specialized regions within auditory cortex for processing the time varying components of acoustic signals. Importantly, this contrast enabled us to investigate the effect of frequency modulation on auditory processing while abstracting away from the spectral complexity of the acoustic stimuli. The second and third contrasts of interest were concerned with the different components of frequency modulation, namely rate and direction. More specifically, we were interested in determining whether specialized sub-regions existed to facilitate processing of these acoustic features. In order to examine the effect of rate, the data were collapsed across direction yielding the following comparison; Rise-Fast + Fall-Fast versus Rise-Slow + Fall-Slow. If there are indeed brain regions containing rate-selective neurons, one should anticipate a difference in either the extent or the magnitude of activation. Similarly, to investigate the effect of sweep direction, data were collapsed across rate as follows; Rise-Fast + Rise-Slow versus Fall-Fast + Fall-Slow. Once again, differences in the extent and or magnitude of activation would suggest
the existence of specialized brain regions within auditory cortex for processing particular features of acoustic signals.

**Multivariate Analysis**

Data were also analyzed using a multivariate approach using SPM5 (Welcome Department of Imaging Neuroscience; http://www.fil.ion.ucl.ac.uk/spm/; implemented in Matlab) and the AA automatic analysis library (https://github.com/rhodricusack/automaticanalysis). The processing of individual subject data for the purpose of performing multivoxel pattern analysis (MVPA) followed the default procedures proscribed by the AA library: slice-time correction was performed followed by subsequent realignment of all volumes to a reference image to minimize the impact of movement during data acquisition. No spatial smoothing was performed. As with the univariate analysis, a GLM was created for each participant using each condition as an individual regressor.

The ROIs used in these analyses were adapted from a previous study (Linke, Vincente-Grabovetsky, & Cusack 2011). In this study, participants were asked to listen to a series of pure tones. Univariate analyses were then used to contrast brain activity in response to these pure tones versus baseline. Based on this contrast, the ROIs were functionally defined using a total of six ROIs drawn from Linke et al. (2011): combined left and right auditory cortex, combined left and right Heschl’s gyrus, left auditory cortex, right auditory cortex, left Heschl’s gyrus, and right Heschl’s gyrus. Details regarding the size and location of each ROI can be found in Table 2.
Table 2. Location and voxel size for each ROI used in the MVPA analyses. ROIs were drawn from Linke et al (2011).

<table>
<thead>
<tr>
<th>Location</th>
<th>MNI Coordinate</th>
<th>Cluster Size (mm $^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$X$</td>
<td>$Y$</td>
</tr>
<tr>
<td>Left Auditory Cortex</td>
<td>-52</td>
<td>-24</td>
</tr>
<tr>
<td>Right Auditory Cortex</td>
<td>56</td>
<td>-14</td>
</tr>
<tr>
<td>Left Heschl’s Gyrus</td>
<td>-52</td>
<td>-24</td>
</tr>
<tr>
<td>Right Heschl’s Gyrus</td>
<td>56</td>
<td>-14</td>
</tr>
</tbody>
</table>

A GLM was fitted to the data set, for each subject, by modeling each predictor as a box-car function convolved with the canonical hemodynamic response. There were five regressors, each reflecting an experimental condition of the current study. The time course of each voxel was obtained for each regressor and the corresponding beta weights were extracted for all voxels within a given ROI. These beta weights were subsequently used to perform Pearson correlations which resulted in a 40 x 40 similarity correlation matrix. The size of the matrix is dependent on both the number of conditions and the number of runs comprising the scanning session. Since every condition within each run constitutes a variable on both axes of the matrix and there are eight runs and five conditions, this yields a matrix with 40 x 40 dimensions, condensed to 5 x 5 by averaging across runs.

The contrasts of interest here were directed at investigating the dynamic features of frequency modulation; rate (fast vs. slow), and direction (rise vs. fall). To accomplish this, certain elements (those that represented either rate or direction) of the correlation matrix were selected and subjected to a two-sample t test. More specifically, we first
computed the within-category correlation to determine how consistent the pattern of activity is for each category. We then calculated the between-category correlations in order to compare brain activity patterns in response to different categories of stimuli. Lastly, a two–sample $t$ test was performed to determine whether the within-category correlations (fast vs. slow or rise vs. fall) were stronger than the between-category correlations (rate vs. direction). Significant differences here would suggest that the ROIs under investigation encode information regarding the different categories of the stimuli. All analyses were first performed in native (single subject) space. The single subject statistics were averaged prior to the calculation of group level statistics, which allowed us to determine whether the particular ROI under investigation encoded representational content of acoustic features.

Results

Univariate Analysis

The first contrast was used to investigate the existence of specialized regions for processing frequency modulation. To accomplish this we compared neural activity in response to all dynamic frequency-modulated sweeps (Rise-Fast, Rise-Slow, Fall-Fast, and Fall-Slow) to the Steady-State sounds. The frequency-modulated sweeps resulted in significantly more activation within auditory cortex compared to Steady-State sounds, $p < 0.001$. The results, illustrated in Figure 4 and Table 3, revealed robust activation throughout auditory cortex including regions such as superior temporal gyrus (STG), superior temporal sulcus (STS), precentral gyrus, and postcentral gyrus. Some of these regions comprise what has been previously defined as belt and parabelt regions. Additionally, there seemed to be a greater extent of activation in the left hemisphere
compared to the right hemisphere. This could suggest the possibility of hemispheric lateralization for processing frequency-modulated sweeps.

Figure 3. A contrast of all frequency-modulated sweeps vs. steady-state sounds reveals robust activations in both right and left hemispheres. The group statistical maps displayed here were superimposed on a standardize brain map (Talairach & Tournoux, 1988). Threshold was set to $p < 0.001$.

Table 3. Talairach and Tournoux (1988) coordinates of the peak voxel activation for frequency-modulated sweeps vs. steady-state sounds contrast in each cluster

<table>
<thead>
<tr>
<th>Location</th>
<th>Coordinates</th>
<th>Cluster Size (mm$^3$)</th>
<th>$p$ Value</th>
<th>$t$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Auditory Cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Activation</td>
<td>62 23 11</td>
<td>7,414</td>
<td>$9.7 \times 10^{-4}$</td>
<td>4.156</td>
</tr>
<tr>
<td>Center of Mass</td>
<td>50 22 12</td>
<td>7,414</td>
<td>$9.7 \times 10^{-4}$</td>
<td>4.156</td>
</tr>
<tr>
<td>Right Auditory Cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Activation</td>
<td>-50 11 10</td>
<td>6,314</td>
<td>$9.7 \times 10^{-4}$</td>
<td>4.156</td>
</tr>
<tr>
<td>Center of Mass</td>
<td>-54 18 11</td>
<td>6,314</td>
<td>$9.7 \times 10^{-4}$</td>
<td>4.156</td>
</tr>
</tbody>
</table>
Additionally, a conjunction map was created to illustrate similarities and differences among the brain regions activated for Steady-State sounds and frequency-modulated sweeps. The conjunction map was created by identifying regions that were significantly activated for steady-state sounds (steady-state > baseline in green), those that were significantly activated for frequency-modulated sweeps (frequency-modulated > baseline in red) and areas of common activation in blue. It shows that there are areas of overlap, primarily within core auditory cortex. It also shows that the extent of the area activated is larger for the frequency-modulated sweeps compared to the steady-state stimuli.

![Figure 4](image.jpg)

**Figure 4.** Conjunction map for all subjects showing areas of common activation (blue) as well as unique areas of activation (red and green). Here, dynamic refers to the combination of all the frequency-modulated conditions.

For the second set of analyses, we assessed whether the regions responsible for processing these frequency-modulated sweeps could be further subdivided into distinct
brain areas. More specifically, we were interested in identifying areas showing preferential activation to the rate or directional component of frequency modulation. In order to investigate the effect of rate (fast vs. slow) on neural processing, the two levels of direction were conflated yielding the following contrast; Rise-Fast + Fall-Fast vs. Rise-Slow + Fall-Slow. In a similar fashion, to assess the effect of direction on neuronal activation, data were collapsed across the different levels of rate yielding a similar contrast (Rise-Fast + Rise-Slow vs. Fall-Fast + Fall-Slow). A one-sample \( t \)-test was used to determine whether the contrasts outlined above were significant. A contrast of the different rates (fast vs. slow) of frequency modulation did not yield any significant difference in the level of activation within the auditory cortex. Additionally, when the two levels of direction (rise vs. fall) were contrasted, there was no significant difference in the extent or magnitude of activation.

**Multivariate Analysis**

As stated previously, the ROIs for MVPA were obtained from a previous study that used region of maximum activation to functionally define auditory cortex and Heschl’s gyrus (Linke et al., 2011). This analysis was performed to measure whether neurons in the auditory cortex encoded information regarding the representational content of acoustic signals. More specifically, we were interested in determining whether neurons encoded representational content pertaining to the rate or direction of frequency-modulated sweeps. Data from each voxel within a given ROI were retrieved. This information was used to calculate the correlation of the pattern of activity between all frequency-modulated sweep blocks across subjects. The results for each ROI are listed in
Table 4. The significant contrasts are depicted in bold font.

Table 4. Results of the statistics performed on Pearson correlation ($r$) values for MVPA contrasts.

<table>
<thead>
<tr>
<th>ROIs</th>
<th>Rate: fast vs. slow</th>
<th>Direction: fall vs. rise</th>
<th>Self correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right + Left Auditory Cortex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.0214 (0.0153)</td>
<td><strong>0.0134 (0.0050)</strong></td>
<td>0.0098 (0.0113)</td>
</tr>
<tr>
<td>$t$</td>
<td>1.4544</td>
<td><strong>2.7820</strong></td>
<td>0.8949</td>
</tr>
<tr>
<td>$p$</td>
<td>0.1715</td>
<td><strong>0.0166</strong></td>
<td>0.3884</td>
</tr>
<tr>
<td><strong>Right + Left Heschl’s gyrus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td><strong>0.0357 (0.0113)</strong></td>
<td>0.0123 (0.0069)</td>
<td>0.0135 (0.0084)</td>
</tr>
<tr>
<td>$t$</td>
<td><strong>3.2813</strong></td>
<td>1.8581</td>
<td>1.6619</td>
</tr>
<tr>
<td>$p$</td>
<td><strong>0.0066</strong></td>
<td>0.0878</td>
<td>0.1224</td>
</tr>
<tr>
<td><strong>Left Auditory Cortex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.0186 (0.0157)</td>
<td>0.0070 (0.0040)</td>
<td>0.0120 (0.0113)</td>
</tr>
<tr>
<td>$t$</td>
<td>1.2379</td>
<td>1.7983</td>
<td>1.1039</td>
</tr>
<tr>
<td>$p$</td>
<td>0.2394</td>
<td>0.0973</td>
<td>0.2913</td>
</tr>
<tr>
<td><strong>Left Heschl’s gyrus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td><strong>0.0314 (0.0131)</strong></td>
<td>0.0144 (0.0077)</td>
<td>0.0026 (0.0111)</td>
</tr>
<tr>
<td>$t$</td>
<td><strong>2.5004</strong></td>
<td>1.9370</td>
<td>0.2449</td>
</tr>
<tr>
<td>$p$</td>
<td><strong>0.0279</strong></td>
<td>0.0766</td>
<td>0.8106</td>
</tr>
<tr>
<td><strong>Right Auditory Cortex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.0177 (0.0141)</td>
<td>0.0089 (0.0082)</td>
<td>0.0085 (0.0117)</td>
</tr>
<tr>
<td>$t$</td>
<td>1.3076</td>
<td>1.1242</td>
<td>0.7550</td>
</tr>
<tr>
<td>$p$</td>
<td>0.2155</td>
<td>0.2829</td>
<td>0.4648</td>
</tr>
<tr>
<td><strong>Right Heschl’s gyrus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td><strong>0.0360 (0.0153)</strong></td>
<td>0.0139 (0.0094)</td>
<td><strong>0.0230 (0.0105)</strong></td>
</tr>
<tr>
<td>$t$</td>
<td><strong>2.4483</strong></td>
<td>1.5416</td>
<td><strong>2.2855</strong></td>
</tr>
<tr>
<td>$p$</td>
<td><strong>0.0307</strong></td>
<td>0.1491</td>
<td><strong>0.0413</strong></td>
</tr>
</tbody>
</table>

Note: Significant contrasts are depicted in bold.

The first contrast examined whether different rates of frequency modulation (fast vs. slow) would yield different patterns of activation. The results revealed rate-specific activity patterns in right Heschl’s gyrus, left Heschl’s gyrus and the combination of right and left Heschl’s gyrus. The effect for sweep direction was significant only when the left...
and right auditory cortices were combined into a single ROI. However, direction-related patterns of activity in several ROIs did approach significance; right and left Heschl’s gyrus, left auditory cortex and left Heschl’s gyrus. These results suggest that the auditory cortex may be more sensitive to changes in rate than to changes in the direction of frequency-modulated sweeps. This idea will be explored further in the discussion section. Visual representations of the correlation matrices resulting from the contrasts discussed above are found in Figures 5 and 6.
Figure 5. Mean correlation of activity patterns within (diagonal) and across (off-diagonal) frequency modulated sweeps. Higher correlations are depicted in black and lower correlations are shown in lighter colours. The figures on the left outline areas comprising the Heschl’s gyrus ROI. The figures on the right depict the mean correlation matrices (darker shades depict higher correlations) for the rate contrast in a) left Heschl’s gyrus; b) right Heschl’s gyrus, and c) the combination of left and right Heschl’s gyrus. FF = Fall-Fast, FS = Fall-Slow, RF = Rise-Fast, RS = Rise-Slow.
Discussion

The primary goal of this study was to investigate the organization of human auditory cortex to determine its organization for supporting the processing of complex acoustic signals. Of particular interest is how this organization supports the processing of acoustic features that are salient in speech related sounds. We chose frequency modulation as the acoustic feature of interest because it plays a crucial role in phonemic production and perception. Since we are ultimately interested in making judgments about frequency modulation as they pertain to speech, much attention was given to the design of the auditory stimuli employed in this study. Past research has demonstrated that regions within auditory cortex respond differentially to speech versus non-speech sounds (Binder et al., 2000; Whalen et al., 2006). There are numerous reasons for this including, but not limited to, the spectrotemporal complexity as well as the semantic meanings of
speech. For these reasons, it was important that the auditory stimuli used in the current study possess the physical features of speech such as spectral complexity while simultaneously lacking any language related components. As a result, IRN stimuli were used. These stimuli afforded us the ability to manipulate the center frequency of a spectrally complex acoustic signal without conveying the perception of language.

We first wanted to investigate whether frequency-modulated sweeps and steady-state sounds elicited different responses in both the extent and magnitude of brain activation. By contrasting brain regions that were activated in response to the two classes of stimuli (frequency-modulated sweeps vs. steady-state sounds), we were able to demonstrate that there are indeed differences in both the extent and magnitude of activation within both core and belt auditory cortex. This was an important finding because it suggests the existence of brain regions sensitive to frequency modulation and supports further investigations into how the components of frequency-modulated sweeps are processed. This finding is also consistent with research by Chevillet et al. (2011) who also demonstrated the existence of a similar type of organization for simple tones versus natural speech; specifically, there is increased recruitment of brain regions peripheral to the auditory core as the spectrotemporal complexity of the auditory signal increased. The present study extends this finding by illustrating that this effect can be driven by the temporal characteristics of speech stimuli. The steady-state sounds used in the current study were as spectrally complex as the frequency-modulated sweeps; the only difference was the time varying nature of the frequency-modulated stimuli. It appears then that this temporal modulation drives greater activation both within core regions and also within the surrounding belt regions.
Perhaps even more interesting is the lateralization of activation in response to frequency-modulated sweeps. The left hemisphere displayed a greater extent of activation than the right hemisphere. This finding lends further support to the role of frequency modulation in language processing given the possibility that the left hemisphere is specialized for processing the salient auditory features that are the components of more complex acoustic signals such as speech. For instance, the finding is in line with previous research that demonstrated that rapid temporal auditory inputs are predominantly processed in the left hemisphere (Zatorre & Belin, 2001). Furthermore work by Joanisse and Gati (2003) identified the IFG and the STG as regions that are involved in processing the rapid time varying components of acoustic signals. Importantly, these areas are sensitive to rapid temporal cues in both speech and nonspeech sounds suggesting they may be specialized for processing time varying elements of acoustic signals in general.

The first analysis was instrumental in permitting us to delve into our second contrast of interest because it demonstrated that frequency-modulated sweeps and steady-state sweeps were not processed in the same way. It therefore served as the go-ahead to perform the second set analyses, which focused on specific components of frequency modulation by determining whether rate and direction elicited differences in the extent and or magnitude of activation. This contrast did not yield any significant differences in the extent or magnitude of activation. However, this finding should not be very surprising considering what is currently known about the auditory cortex as it pertains to processing frequency modulation, the response properties of neurons located in this region, as well as their organization on a macroscopic level. Electrophysiology work with monkey (Tian, Rauschecker, 2004) and cat models (Mendelson et al., 1993) has revealed the existence of
rate-selective and direction-selective neurons. However, the selectivity of these neurons is not mutually exclusive meaning that a given rate-selective neuron will respond to a range of frequency-modulated sweeps, but, it will respond most strongly to a specific rate. The same is true for direction-selective neurons. While these rate-selective and direction-selective neurons are in fact located within the auditory cortex, the way in which they are distributed makes it rather difficult to differentiate regions that show preferences for either rate or direction using traditional univariate approaches. Thus the lack of differences in these activation maps does not mean these two features are not differentiated in auditory cortex.

To further investigate neural processing of the rate and direction of frequency-modulated sweeps, MVPA was performed on both auditory cortex and Heschl’s gyrus. To clarify, Heschl’s gyrus was defined as the region representing primary auditory cortex and consists mainly of core auditory regions. On the other hand, the auditory cortex refers to a larger region of the temporal lobe, which includes Heschl’s gyrus, as well as belt, and parabelt regions. This second type of analysis is especially adept at detecting differences in the patterns of brain activity in the absence of gross activation differences. The first analysis investigated whether fast frequency-modulated sweeps elicited more similar patterns of brain activity than slow frequency-modulated sweeps. We found that the pattern of neural activity evoked for fast frequency modulations was differentiable from those evoked by slow sweeps, for all combinations of Heschl’s gyrus (right, left, and right + left). Further analyses showed that fast frequency-modulated sweeps elicited more similar patterns of activity that were distinct from the patterns of activity elicited by sweeps with a slower rate. When this contrast was performed on the auditory cortex
ROIs, which were significantly larger in extent, the effect was no longer present. This finding further supports the idea that core auditory cortex (i.e., Heschl’s gyrus) is in fact sensitive not only to static frequency information, but also more complex acoustic information related to rate of change. That this effect was more significant in the left hemisphere may provide additional support to idea that the left hemisphere is specialized for processing the more rapid temporal cues associated with acoustic signals.

The second contrast involved comparing the patterns of brain activity in response to the different directions of frequency modulation. When left and right auditory cortex was combined into a single ROI, the patterns of activity were significantly correlated for sweeps with the same direction (i.e. rise or fall). When looking at the other ROIs (right auditory cortex, left auditory cortex, left Heschl’s gyrus, right Heschl’s gyrus, and the combination of right and left Heschl’s gyrus), this effect was trending toward significance. A recent study by Hsieh et al. (2012) revealed the existence of direction-selective regions specifically in right primary auditory cortex and left STG using MVPA. One reason this present study did not yield strongly lateralized results for direction-selective activity patterns may be due to the population studied or the type of acoustic stimuli used. The participants in the Hsieh et al. study (2012) were native speakers of Mandarin, a population that may show increased sensitivity to frequency modulation. Mandarin is a tonal language, and native speakers have previously been shown to be better able to detect changes in frequency modulation compared to non-tonal language speakers (Giuliano, Pfordresher, Stanley, Narayana, & Wicha, 2011). Additionally, the stimuli used in the two studies were different. While the present study used IRN, the study by Hsieh et al. (2012) used a series of pure tone sweeps. This discrepancy in
spectrotemporal complexity may also account for some of the differences observed. The lack of spectral complexity renders the stimuli less noisy, which may allow changes in direction to become more salient.

While it has previously been demonstrated that increased stimulus complexity results in increased activation in auditory core, it appears that, in this case, the addition of frequency modulation to stimulus complexity was not sufficient to drive these activation differences above threshold. This does not mean, however, that simple and complex acoustic stimuli are processed in the same way. The organization of neurons within these regions (core, belt, and parabelt) varies considerably and has implications for the types of analyses that will prove useful in identifying differences in brain activations in response to different acoustic stimuli. While neurons within the auditory core are comprised of smaller, more densely packed neurons, the lateral belt and parabelt regions consists of larger neurons that are less densely packed than core regions. This demonstrates clear anatomical delineations for core, belt and parabelt regions. Furthermore, since structure often dictates function, the morphological differences between these regions suggest a sort of neural specialization according to their corresponding role in auditory processing (Sweet, Dorph-Petersen, & Lewis, 2005). Given the complex architecture at the neuronal level and the large intersubject variability at the macroscopic level, analyses sensitive to sub-voxel grain size of neuronal organization, such as MPVA, should be given serious consideration when investigating the functional role of the auditory cortex.
Conclusions

The current study used fMRI to examine the organization of human auditory cortex for processing frequency modulated auditory stimuli. The results provided some insight into how the auditory cortex processes acoustic elements that are salient in communication signals. We accomplished this by using IRN, which more closely simulates speech characteristics than prior studies using pure tones, and showed that steady-state sounds and frequency-modulated sweeps activated different regions of the auditory cortex. More importantly, we demonstrated the existence of rate-specific activity patterns and a trend towards direction-specific activity patterns. Together, this work supports the view that auditory cortex contains neural populations specifically organized for detecting the types of acoustic features typical of spoken language. However it also illustrates the need to apply advanced data analysis techniques such as MPVA to elucidate differences in patterns of brain activity when gross regions of activation overlap.
References


change (up vs. down) for rapid frequency modulated sweeps. *Acoustic Research Letters Online*, 3(1), 29–34.


directed rostrally along the monkey’s supratemporal plane. *Journal of Neuroscience, 30*(39), 13021-13030.


representational content with pattern-information fMRI – an introductory guide.

Scan, 4, 101-109.


Appendix A
Language History and Experience Questionnaire

Please answer the following questions as truthfully as possible. You may leave blank any question you do not wish to answer.

Age (years): ________  Sex: (circle one) Male / Female

(1) What is your country of birth? ______________________________ If you were not born in Canada, how many years have you lived in Canada? ________

(2) Please list all of the languages you know in the order that you learned them (starting with the earliest):
__________________________________________________________________

(3) Please indicate your highest education level ______________________________
How many years of your education have you had in each language?
Language ________________ Years ______
Language ________________ Years ______
Language ________________ Years ______

(4) What percentage of time are you currently exposed to each of the following languages in your daily activities?

<table>
<thead>
<tr>
<th>Language</th>
<th>Mandarin Chinese</th>
<th>English</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speaking</td>
<td>______</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>Understanding speech</td>
<td>______</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>Reading</td>
<td>______</td>
<td>______</td>
<td></td>
</tr>
<tr>
<td>Writing</td>
<td>______</td>
<td>______</td>
<td></td>
</tr>
</tbody>
</table>

(5) Do you speak any Chinese dialects other than standard Mandarin Chinese?
Please check any that apply:
Cantonese []  Taiwanese []  Other (please specify)__________________

(6) Please rate on a scale of one to five how skilled you consider yourself in the following areas (1: not skilled at all; 5: very skilled):

<table>
<thead>
<tr>
<th>Skill</th>
<th>Mandarin</th>
<th>English</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speaking</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Understanding speech</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Reading</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Writing</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

(7) Are you familiar with the Pinyin writing system? _____

If yes

Rate your familiarity from one to five (5 being the most familiar) ______
At what age did you learn Pinyin? ________
How many years were you taught Pinyin? ________
# Appendix B

## Ethics Approval

Use of Human Participants - Ethics Approval Notice

**Principal Investigator:** Prof. Marc Joanisse

**Review Number:** 18204E

**Review Level:** Delegated

**Approved Local Adult Participants:** 100

**Approved Local Minor Participants:** 0

**Protocol Title:** Investigating Speech Perception and Reading in Chinese Using fMRI

**Department & Institution:** Psychology, University of Western Ontario

**Sponsor:** Canadian Institutes of Health Research

**Natural Sciences and Engineering Research Council**

**Ethics Approval Date:** November 21, 2011

**Expiry Date:** June 30, 2013

**Documents Reviewed & Approved & Documents Received for Information:**

<table>
<thead>
<tr>
<th>Document Name</th>
<th>Comments</th>
<th>Version Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revised UWO Protocol</td>
<td>The reimbursement has been set at $40 to cover costs. A new letter and recruitment ad has been included.</td>
<td></td>
</tr>
<tr>
<td>Increase in number of local Participants</td>
<td>The number of participants has been increased from 60 to 100.</td>
<td></td>
</tr>
<tr>
<td>Change in Study Personnel</td>
<td>Diedre Desouza has been added to the research team.</td>
<td></td>
</tr>
<tr>
<td>Letter of Information</td>
<td></td>
<td>2011/10/06</td>
</tr>
<tr>
<td>Advertisement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HERB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this HERB also complies with the membership requirements for REB’s as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HERB’s periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

Members of the HERB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HERB.

The Chair of the HERB is Dr. Joseph Gilbert. The UWO HERB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

**Signature**

---

*Eris Officer to Contact for Further Information*

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2011-2013 M.Sc. Neuroscience

Honours and Awards:
Ontario Graduate Scholarship
2012-2013

Western Graduate Research Scholarship
2011-2013

Brescia University College Council of Trustees Gold Medal Award
2007

Dr. Pat Devolder Award
2006

The University of Western Ontario Continuing Scholarship
2003-2007

Related Work Experience
Graduate Teaching Assistant
The University of Western Ontario
2011-2012

Research Assistant
The University of Western Ontario
2008

Conference Presentations:
Responses to frequency modulated sweeps. Poster presented at the Lake Ontario
Visionary Establishment conference, Niagara Falls, ON.