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Differential sensitivity to changes in pitch acceleration in the auditory brainstem and cortex

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Abstract

The cortical pitch-specific response (CPR) is differentially sensitive to pitch contours varying in rate of acceleration—time-variant Mandarin Tone 2 (T2) versus constant, linear rising ramp (Linear)—as a function of language experience (Krishnan, Gandour, & Suresh, 2014). CPR and brainstem frequency following response (FFR) data were recorded concurrently from native Mandarin listeners using the same stimuli. Results showed that T2 elicited larger responses than Linear at both cortical and brainstem levels (CPR: Na–Pb, Pb–Nb; FFR). However, Pb–Nb exhibited a larger *difference* in magnitude between T2 and Linear than either Na–Pb or FFR. This finding highlights differential weighting of brain responses elicited by a specific temporal attribute of pitch. Consistent with the notion of a distributed, integrated hierarchical pitch processing network, temporal attributes of pitch are differentially weighted by subcortical and cortical level processing.

Graphical abstract

Keywords

pitch; iterated rippled noise; cortical pitch response; fundamental frequency response; pitch encoding; pitch acceleration; experience-dependent plasticity; functional asymmetry; lexical tone; Mandarin Chinese

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1. Introduction

There is now increasing recognition that the effects of language experience can occur at many levels of sensory, perceptual and cognitive processing that implicate pre-categorical representations (Iverson, Wagner, & Rosen, 2016, and references therein). We also have a better understanding of the effects of language experience on pre-categorical representations at the level of the brainstem and auditory cortex (for reviews, Chandrasekaran & Kraus, 2010; Chandrasekaran, Skoe, & Kraus, 2014; Kraus & Banai, 2007; Kraus & White-Schwoch, 2015; Krishnan & Gandour, 2009, 2014; Krishnan, Gandour, & Bidelman, 2012). Indeed, the brainstem has generally been accepted to be part of a distributed, integrated circuit in language processing that involves both subcortical as well as cortical structures.

Pitch is an auditory perceptual attribute that plays an important role in the perception of speech, language and music. The scalp-recorded brainstem frequency following response (FFR) and the cortical pitch response (CPR) represent pitch-relevant neural activity at brainstem and cortical levels, respectively. The scalp-recorded FFR reflects sustained phase-locked activity in a population of neural elements within the rostral brainstem (Chandrasekaran & Kraus, 2010; Krishnan, 2007) that has been shown to preserve pitch relevant information (Krishnan, 2007; Krishnan & Gandour, 2014). The CPR, similar to the MEG-derived pitch onset response (POR), reflects pitch-specific synchronized neural activity in the auditory cortex. Source analysis (Gutschalk, Patterson, Rupp, Uppenkamp, & Scherg, 2002; Krumbholz, Patterson, Seither-Preisler, Lammertmann, & Lutkenhoner, 2003)—corroborated by human depth electrode recordings (Griffiths et al., 2010; Schonwiesner & Zatorre, 2008)—indicates that the POR is localized to the anterolateral portion of Heschl's gyrus, the putative site of pitch processing (Johnsrude, Penhune, & Zatorre, 2000; Penagos, Melcher, & Oxenham, 2004). The CPR, in addition, is characterized by multiple transient components that may index different temporal attributes of pitch contours (Krishnan, Gandour, Ananthakrishnan, & Vijayaraghavan, 2014; Krishnan, Gandour, & Suresh, 2014). Simultaneous recording of brainstem FFR and cortical CPR responses affords us a window to make a direct comparison of changes in magnitude of pitch relevant neural activity for each cortical and subcortical component. Such comparisons make it possible to draw inferences about their respective roles in the encoding of temporal pitch attributes.

An important temporal attribute of dynamic, curvilinear pitch contours is acceleration rate. Using stimuli that differ in acceleration rate, time-variant vs. constant, language experience effects are not evident in FFR responses to linear rising and falling ramps (Xu, Krishnan, & Gandour, 2006) or even trilinear rising ramps (Krishnan, Gandour, Bidelman, & Swaminathan, 2009). A language-dependent effect, however, is observed in FFR responses when Mandarin listeners, relative to English, are presented with a native lexical tone (Tone 2, T2), a curvilinear pitch contour with changing rate of acceleration. As reflected by CPR components Na–Pb and Pb–Nb (Krishnan, Gandour, & Suresh, 2014), Mandarin listeners show greater peak-to-peak amplitude than English in response to T2 only. Other CPR experiments consisted of stimuli varying in acceleration rate that were not designed to address specifically the question of changing vs. constant acceleration rates. In Krishnan, Gandour, Ananthakrishnan, and Vijayaraghavan (2015), acceleration rates covaried with stimulus duration; with pitch direction and location of peak acceleration (Krishnan,

Gandour, & Suresh, 2015b); and with stimuli that fell inside and outside the normal voice range (Krishnan, Gandour, & Suresh, 2015a). In those experiments, amplitude of neural responses recorded at a frontocentral scalp location (Fz) is larger in Mandarin than English listeners as reflected by both Na–Pb and Pb–Nb. Thus, pitch encoding at both subcortical and cortical levels is acutely sensitive to changes in acceleration rate throughout the duration of native lexical tones.

CPR components have been shown to be differentially-weighted in their sensitivity to particular temporal attributes of pitch. Another well-known attribute of pitch is its *salience*, which is closely related to the strength of temporal periodicity in the stimulus waveform. Using a nonspeech homolog of T2, parametric variation of pitch salience from weak to strong pitch was manipulated by holding acceleration constant (Krishnan, Gandour, & Suresh, 2016). A language-dependent advantage for Mandarin listeners is restricted to the Na–Pb component only. This restriction to Na–Pb suggests that the relative weighting of CPR components vary depending on the sensitivity of neural activity within a particular temporal window to a specific attribute of pitch. In the same study, regardless of language experience, a direct comparison of cortical and brainstem responses further reveal different patterns of relative changes in magnitude along the pitch salience continuum (FFR, monotonic; CPR, non-monotonic). Such patterns suggest that certain attributes of pitch are processed differentially at separate levels along the auditory pathway. In Krishnan, Gandour, and Suresh (2014), T2 is opposed to a linear high rising ramp (Linear). They differ in acceleration rate only, whereas pitch salience and pitch height are fixed. The question remains whether CPR components show differential sensitivity to a time-variant pitch contour relative to one with a fixed rate of acceleration, all else being equal.

Accordingly, the specific aim of this study is to compare the concurrently-recorded cortical CPR data, presented in Krishnan, Gandour, and Suresh (2014), with brainstem data (FFR). A novel approach enables us to view pitch-relevant neural activity at the cortical and brainstem level concurrently and to draw inferences about nature of their coordination. We chose to restrict this follow-up study to Chinese listeners only because CPR effects elicited by T2 and Linear were larger in Chinese listeners than English (Krishnan, Gandour, & Suresh, 2014). In addition, a direct comparison between corresponding sections of T2 and Linear pitch contours (Krishnan, Gandour, et al., 2009), FFR-derived pitch strength of Chinese listeners—but not English—was larger in just those sections of T2 exhibiting higher degrees of acceleration. Importantly, T2 and Linear share the same pitch onset and offset as well as average pitch acceleration rate. Their shared acoustic properties provide an opportunity to isolate the effects of another temporal attribute of pitch: acceleration rate, time-variant vs. constant. Though changes in pitch salience show that the Na–Pb component separates Chinese from English listeners (Krishnan et al., 2016), we hypothesize that the Pb–Nb component of the CPR shows a relatively greater sensitivity to changes from a constant to a time-variant acceleration when compared to Na–Pb and brainstem FFR. If pitch processing at brainstem and cortical levels is differentially sensitive to acceleration rate, we further expect to see differences in the pattern of relative changes in magnitude among CPR and FFR components.

2. Results

2.1. Response morphology of CPR and FFR components

Grand averaged CPR and FFR response waveforms, elicited by T2 (red) and Linear (blue) pitch contours, are displayed in Fig. 1A and 1B, respectively. CPR components are clearly identifiable. The amplitude of the cortical pitch-relevant components (Na, Pb, Nb) are more robust in response to T2 as compared to Linear. FFR time waveforms show more robust periodicity encoding relative to Linear.

2.2. Response magnitude per component and stimulus

Fig. 1C displays the normalized mean response magnitude of T2 and Linear for each component. Results of a two-way (component $\times$ stimulus) ANOVA conducted on normalized amplitude yielded a significant stimulus main effect ($F_{1,18} = 68.78, p < 0.0001, \eta_p^2 = 0.793$) and a marginally significant interaction effect between component and stimulus ($F_{2,72} = 3.43, p = 0.0377, \eta_p^2 = 0.087$). The stimulus main effect showed that T2 was larger in amplitude than Linear. By component, simple effects revealed that response magnitude of T2 was larger than Linear irrespective of component. By stimulus, pairwise comparisons of components failed to reach significance. The fact that T2 elicits more robust responses than Linear in both cortical and brainstem structures underscores the ecological relevance of dynamic, curvilinear pitch contours in natural speech.

2.3. Magnitude of difference between T2 and Linear

Fig. 1D shows the normalized magnitude of the difference between T2 and Linear for each component (Na–Pb, Pb–Nb, FFR). A one-way ANOVA yielded a significant component effect ($F_{2,36} = 6.52, p = 0.0038, \eta_p^2 = 0.266$). Post hoc multiple comparisons showed that Pb–Nb exhibited a larger difference in magnitude than either Na–Pb or FFR. This means that Pb–Nb has heightened sensitivity to changes in rate of acceleration relative to other transient cortical pitch-specific markers as well as to the sustained frequency following response at the level of the brainstem.

3. Discussion

3.1 Transient components of CPR are differentially sensitive to specific temporal attributes of pitch

A comparison with data obtained from an earlier CPR experiment allows us to demonstrate that Na–Pb and Pb–Nb are modulated by differential weighting of particular pitch attributes. These differences in weighting have revealed a relationship between acceleration rate (time-variant, constant) and CPR component (Na–Pb, Pb–Nb). In Krishnan et al. (2016), acceleration rate was uniform across stimuli, whereas pitch salience was varied parametrically from weak to strong. Peak-to-peak amplitude of both Na–Pb and Pb–Nb in the Chinese group gets larger with increasing pitch salience. However, experience-dependent sensitivity to changes in pitch salience is limited to Na–Pb (Chinese > English). A plausible explanation is that neural activity in the Na–Pb time window optimally represents neural processing relevant to pitch salience, and is thus subject to experience-dependent

modulation. We hypothesize that experience-dependent effects are targeted to specific temporal integration windows in which optimal processing occurs for a particular attribute of pitch. In this study, we targeted pitch acceleration. Pitch salience was homogeneous across stimuli; acceleration rate was the only pitch attribute manipulated. T2, relative to Linear, elicits a larger response change in the Pb–Nb time window compared to Na–Pb. This finding supports the view that Pb–Nb, the later CPR temporal integration window, is a pitch-specific, neural marker of changes in acceleration rate that occurs between onset and offset of ecologically-relevant F0 trajectories. Similar changes in the brainstem FFR and the earlier cortical Na–Pb time window further reinforce this notion of differential sensitivity of pitch-relevant neural activity to temporal attributes of pitch.

Our finding of differential sensitivity of pitch attributes is not only congruent with the extant literature, but it brings us closer to a fuller understanding of real-time neural instantiation of tonal features. At the cortical level, a multidimensional scaling analysis of pairwise dissimilarities of mismatch negativity (MMN) responses to Mandarin tones reveals that Chinese listeners, relative to English, are more sensitive to pitch direction than pitch height (Chandrasekaran, Gandour, & Krishnan, 2007). In Cantonese, MMN and P3a are shown to be independent neural components that are differentially sensitive to pitch height and direction, respectively (Jia, Tsang, Huang, & Chen, 2015; Tsang, Jia, Huang, & Chen, 2011). In a Thai tone learning paradigm (Kaan, Wayland, Bao, & Barkley, 2007), English listeners, as reflected by MMN, are more sensitive to early differences in pitch height, whereas Mandarin Chinese are more sensitive to later rapid changes in pitch direction. Though MMN is sensitive to some pitch features, it is neither pitch-specific nor comprised of transient components that are differentially sensitive to temporal attributes of pitch. At the level of the auditory brainstem, FFR responses show that Chinese listeners, relative to English, exhibit more robust pitch representation of those sections containing rapidly changing pitch movements across all four Mandarin tones (Krishnan, Swaminathan, & Gandour, 2009). This early shaping of the auditory signal at a preattentive, sensory level of processing is compatible with the idea that nascent representations of acoustic phonetic features may emerge early along the auditory pathway. Indeed, we have previously shown a strong correlation between neural and behavioral measures at a subcortical, sensory level of the pitch hierarchy (Krishnan, Bidelman, & Gandour, 2010). Such evidence corroborates the view that subcortical pitch encoding plays an important role in shaping tone perception.

3.2 Is there a transformation of neural representation of pitch acceleration from the brainstem to early cortical (Na–Pb) and later cortical (Pb–Nb) pitch-specific components?

A direct comparison of changes in magnitude of pitch-relevant neural activity between responses to constant and time-variant acceleration revealed greater changes for the later cortical pitch component (Pb–Nb) compared to essentially identical changes for the brainstem (FFR) and the earlier cortical pitch component (Na–Pb). One possible explanation is that these different patterns of change reflect differences in the relative weighting of temporal attributes of pitch within a given temporal integration window. Consistent with this viewpoint, the relatively greater sensitivity of Pb–Nb (compared to FFR and Na–Pb) may suggest that the relative weighting is influenced by ecological relevance of specific temporal attributes of pitch. An alternative explanation is that there are fundamental differences in

sensitivity to changes in pitch acceleration among FFR and CPR components. While it is well known that the temporal-based representation of spectrotemporal features relevant to pitch in the brainstem would be more fine-grained than early coarse-grained, labile, and spatiotemporally broader rate-based representations in the auditory cortex (Chechik et al., 2006; Warren & Griffiths, 2003; Winer, Miller, Lee, & Schreiner, 2005; Zatorre & Belin, 2001), this transformation in the pitch encoding scheme alone does not explain the pattern of results observed for FFR and CPR components. The specific pattern of changes observed herein (Pb–Nb > FFR, Na–Pb), are more consistent with the differential weighting explanation. Interestingly, in the case of the brainstem FFR and the earlier cortical Na–Pb component, the pattern of changes elicited by varying pitch acceleration corresponds to those elicited by varying pitch salience (Na only; Krishnan, Bidelman, Smalt, Ananthakrishnan, & Gandour, 2012). Such strong correspondences lead us to hypothesize that brainstem and cortical representations of certain temporal attributes of pitch are shaped in a coordinated manner through corticofugal modulation of subcortical afferent circuitry.

3.3 Conclusions

Pitch-relevant neural activity elicited by manipulation of acceleration rate (constant vs time-variant) at the brainstem and cortical level enables us to assess relative weighting of specific temporal attributes of pitch. As reflected in CPR and FFR response components, the greater changes for Pb–Nb, compared to brainstem FFR and cortical Na–Pb, suggest that relative weighting of a response component varies depending on its sensitivity to a specific pitch attribute within a given time window.

4. Methods

4.1. Participants

Nineteen native speakers of Mandarin Chinese (8 male, 11 female) were recruited from the Purdue University student body to participate in the experiment. All exhibited normal hearing sensitivity at audiometric frequencies between 500 and 4000 Hz and reported no previous history of neurological or psychiatric illnesses. They were closely matched in age (23.1 ± 3.1 years), formal education (15.74 ± 1.7 years), and strongly right handed ($95.20 \pm 7.9\%$) as measured by the Edinburgh Handedness Inventory (Oldfield, 1971). All participants were born and raised in mainland China. None had received formal instruction in English before the age of nine (11.3 ± 1.83 years). Self-ratings of their English language proficiency on a 7-point Likert-type scale ranging from 1 (very poor) to 7 (native-like) for speaking and listening abilities were, on average, 4.3 and 4.9, respectively (Li, Sepanski, & Zhao, 2006). Their daily usage of Mandarin and English, in order, was reported to be 72% and 28%. As determined by a music history questionnaire (Wong & Perrachione, 2007), all participants, except for one, had less than three years of musical training (1.37 ± 1.97 years) on any combination of instruments. None had any training within the past five years. Each participant was paid and gave informed consent in conformity with the 2013 World Medical Association Declaration of Helsinki and in compliance with a protocol approved by the Institutional Review Board of Purdue University.

4.2. Stimuli

Two iterated rippled noise (IRN) stimuli were used to investigate CPR and FFR responses concurrently to time-varying pitch stimuli (Fig. 2, middle right panels). One was of a curvilinear pitch contour modeled after productions of Mandarin Tone 2 (T2) in citation form; the other, a linear rising ramp (Linear). The pitch acceleration rate of T2 changed over the course of the pitch contour (Fig. 2, bottom panel). Unlike T2, the acceleration rate of Linear was constant. Both stimuli, however, shared in common F0 onset/offset (103/131 Hz) and average F0 acceleration (0.112 Hz/ms) (Fig. 2, middle right panels). For further details, see Krishnan, Gandour, and Suresh (2014). By using IRN, we preserve dynamic variations in pitch of auditory stimuli that lack a waveform periodicity, formant structure, temporal envelope, and recognizable timbre characteristic of speech.

Each stimulus condition consisted of two segments (crossfaded with 5ms cos² ramps): an initial 500 ms noise segment followed by a pitch segment, i.e., T2, and Linear (Fig. 2, top panel). The overall RMS level of each segment was equated such that there was no discernible difference in intensity between initial and final segments. All stimuli were presented binaurally at 80 dB SPL through magnetically-shielded tubal insert earphones (ER-3A; Etymotic Research, Elk Grove Village, IL, USA) with a fixed onset polarity (rarefaction) and a repetition rate of 0.94/s. Stimulus presentation order was randomized both within and across participants.

4.3. Brainstem FFR and cortical pitch response acquisition and extraction

4.3.1. EEG acquisition to extract brainstem and CPR responses—Participants reclined comfortably in an electro-acoustically shielded booth to facilitate recording of neurophysiologic responses. They were instructed to relax and refrain from extraneous body movement to minimize myogenic artifacts, and to ignore the stimuli as they watched a silent video (minus subtitles) of their choice throughout the recording session. The EEG was acquired continuously (5000 Hz sampling rate; 0.3 to 2500 Hz analog band-pass) through the ASA-Lab EEG system (ANT Inc., The Netherlands) using a 32-channel amplifier (REFA8-32, TMS International BV) and WaveGuard electrode cap (ANT Inc., The Netherlands) with 32-shielded sintered Ag/AgCl electrodes configured in the standard 10–20-montage. The high sampling rate of 5 kHz was necessary to recover the brainstem frequency following responses in addition to the relatively slower cortical pitch components. Because the primary objective of this study was to characterize the cortical pitch components, the EEG acquisition electrode montage was limited to 9 electrode locations: Fpz, AFz, Fz, F3, F4, Cz, T7, T8, M1, M2. For each stimulus, EEGs were acquired in two blocks of 1000 sweeps each. The experimental protocol took about 2 hours to complete.

4.3.2. Extraction of FFR and CPR—FFR and CPR responses were extracted off-line from the same sweep epoch EEG files. To extract the FFR, EEG files were digitally band-pass filtered (75–1500 Hz, Butterworth zero phase filters with 24 dB/Octave rejection rate). Sweeps containing electrical activity exceeding $\pm 40 \mu\text{V}$ were rejected automatically. Subsequently time domain averaging was performed on three different electrode montages (Fz-to-linked mastoids; Fz-to-linked T7/T8; and Cz-to-linked T7/T8) over an analysis window of 270 ms (from 493 to 763 ms, where 493 represents the onset of the pitch

segment). Each FFR waveform represents the grand average of the FFRs derived from the three electrode montages to a total of 2000 sweeps presented in 2 blocks of 1000 sweeps each.

To extract the CPR components, EEG files were first down sampled from 5000 Hz to 1024 Hz. They were then digitally band-pass filtered (2–25 Hz, Butterworth zero phase shift filter with 24 dB/octave rejection rate) to enhance the transient components and minimize the sustained component. Sweeps containing electrical activity exceeding $\pm 100 \mu\text{V}$ were rejected automatically. Subsequently, averaging was performed on the right temporal (T8), and left temporal (T7) electrode sites using an average reference to evaluate asymmetry effects. The focus here is not to localize the source of the CPRs with just two electrodes, but to characterize the relative difference in the pitch-related neural activity over the widely separated left and right temporal electrode sites. The re-referenced electrode site, Fz–to-linked (T7/T8), was used to characterize the transient pitch response components. It was chosen because both MEG- and EEG-derived pitch responses are prominent at frontocentral sites (e.g., Bidelman & Grall, 2014; Krishnan, Gandour, et al., 2015b; Krumbholz et al., 2003). In addition, this identical electrode configuration makes it possible for us to compare these CPR responses with brainstem FFR responses obtained in this study. An analysis epoch of 1600 ms including the 100 ms pre-stimulus baseline was utilized to average the response across both noise and pitch segments. Only the pitch-specific CPR response was analyzed.

4.4. Analysis of FFR and CPR

FFR analysis procedure was similar to those described in a recent report (Krishnan et al., 2016). Essentially, neural pitch strength was quantified by measuring the magnitude of the F0 component from each response waveform. The spectrum of each response segment was computed by taking the Fast Fourier Transform (FFT) of a time-windowed version of its temporal waveform (Gaussian window, 1 Hz resolution). For each subject, the magnitude of F0 was measured as the peak in the FFT, relative to the noise floor.

Since the focus of this paper is to compare the magnitude of pitch-relevant neural activity at brainstem and cortical levels, only peak-to-peak amplitude of Na–Pb and Pb–Nb components were measured to determine whether variations in amplitude indexed specific aspects of the pitch contour (e.g., pitch acceleration).

4.5. Comparison of CPR and FFR

CPR components are much larger in magnitude than the FFR response (CPR, 3–5 μV ; FFR, 100–300 nV). It is therefore necessary to normalize the raw data to allow for a meaningful comparison of the change in pitch-related neural activity at the brainstem and cortical levels independent of their differences in absolute magnitude. To measure the mean response magnitude of T2 and Linear per component (Na–Pb, Pb–Nb, FFR), each participant's data values were normalized by pooled maximum of T2 and Linear ($x/\text{pooled maximum}$). A two-way ANOVA (SAS®; SAS Institute, Inc., Cary, NC, USA) was performed on normalized response magnitude values for each combination of component (Na–Pb, Pb–Nb, FFR) and stimulus (T2, Linear). To measure the relative change in magnitude of pitch-relevant neural

activity (T2 vs Linear) of each participant's cortical and brainstem responses (Na–Pb vs Pb–Nb; Na–Pb vs FFR; Pb–Nb vs FFR), their data values were normalized per component (Na–Pb, Pb–Nb, FFR) as follows: response change (arbitrary units) = $(T2 - \text{Linear}) / (T2 + \text{Linear})$. A one-way ANOVA was conducted on the normalized magnitude of response change (T2 vs Linear) as measured by cortical (Na–Pb, Pb–Nb) and brainstem (FFR) components. Post hoc multiple comparisons were corrected with a Bonferroni adjustment at $\alpha = 0.05$.

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References

- Bidelman GM, Grall J. Functional organization for musical consonance and tonal pitch hierarchy in human auditory cortex. *Neuroimage*. 2014; 101:204–214. DOI: 10.1016/j.neuroimage.2014.07.005 [PubMed: 25019679]
- Chandrasekaran B, Gandour JT, Krishnan A. Neuroplasticity in the processing of pitch dimensions: A multidimensional scaling analysis of the mismatch negativity. *Restorative Neurology and Neuroscience*. 2007; 25(3–4):195–210. [PubMed: 17942999]
- Chandrasekaran B, Kraus N. The scalp-recorded brainstem response to speech: Neural origins and plasticity. *Psychophysiology*. 2010; 47(2):236–246. PSYP928 [pii]. DOI: 10.1111/j.1469-8986.2009.00928.x [PubMed: 19824950]
- Chandrasekaran B, Skoe E, Kraus N. An integrative model of subcortical auditory plasticity. *Brain Topography*. 2014; 27(4):539–552. DOI: 10.1007/s10548-013-0323-9 [PubMed: 24150692]
- Chechik G, Anderson MJ, Bar-Yosef O, Young ED, Tishby N, Nelken I. Reduction of information redundancy in the ascending auditory pathway. *Neuron*. 2006; 51(3):359–368. DOI: 10.1016/j.neuron.2006.06.030 [PubMed: 16880130]
- Griffiths TD, Kumar S, Sedley W, Nourski KV, Kawasaki H, Oya H, ... Howard MA. Direct recordings of pitch responses from human auditory cortex. *Current Biology*. 2010; 20(12):1128–1132. DOI: 10.1016/j.cub.2010.04.044 [PubMed: 20605456]
- Gutschalk A, Patterson RD, Rupp A, Uppenkamp S, Scherg M. Sustained magnetic fields reveal separate sites for sound level and temporal regularity in human auditory cortex. *Neuroimage*. 2002; 15(1):207–216. DOI: 10.1006/nimg.2001.0949 [PubMed: 11771990]
- Iverson P, Wagner A, Rosen S. Effects of language experience on pre-categorical perception: Distinguishing general from specialized processes in speech perception. *Journal of the Acoustical Society of America*. 2016; 139(4):1799. doi: 10.1121/1.4944755 [PubMed: 27106328]
- Jia S, Tsang YK, Huang J, Chen HC. Processing Cantonese lexical tones: Evidence from oddball paradigms. *Neuroscience*. 2015; 305:351–360. DOI: 10.1016/j.neuroscience.2015.08.009 [PubMed: 26265553]
- Johnsrude IS, Penhune VB, Zatorre RJ. Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain*. 2000; 123(Pt 1):155–163. [PubMed: 10611129]
- Kaan E, Wayland R, Bao M, Barkley CM. Effects of native language and training on lexical tone perception: An event-related potential study. *Brain Research*. 2007; 1148:113–122. S0006-8993(07)00408-8 [pii]. DOI: 10.1016/j.brainres.2007.02.019 [PubMed: 17368579]
- Kraus N, Banai K. Auditory-processing malleability: Focus on language and music. *Current Directions in Psychological Science*. 2007; 16(2):105–110.
- Kraus N, White-Schwoch T. Unraveling the biology of auditory learning: A cognitive-sensorimotor-reward framework. *Trends in Cognitive Sciences*. 2015; 19(11):642–654. DOI: 10.1016/j.tics.2015.08.017 [PubMed: 26454481]

- Krishnan, A. Human frequency following response. In: Burkard, RF, Don, M., Eggermont, JJ., editors. Auditory evoked potentials: Basic principles and clinical application. Baltimore: Lippincott Williams & Wilkins; 2007. p. 313-335.
- Krishnan A, Bidelman GM, Gandour JT. Neural representation of pitch salience in the human brainstem revealed by psychophysical and electrophysiological indices. *Hearing Research*. 2010; 268(1-2):60-66. DOI: 10.1016/j.heares.2010.04.016 [PubMed: 20457239]
- Krishnan A, Bidelman GM, Smalt CJ, Ananthakrishnan S, Gandour JT. Relationship between brainstem, cortical and behavioral measures relevant to pitch salience in humans. *Neuropsychologia*. 2012; 50(12):2849-2859. DOI: 10.1016/j.neuropsychologia.2012.08.013 [PubMed: 22940428]
- Krishnan A, Gandour JT. The role of the auditory brainstem in processing linguistically-relevant pitch patterns. *Brain and Language*. 2009; 110(3):135-148. S0093-934X(09)00042-X [pii]. DOI: 10.1016/j.bandl.2009.03.005 [PubMed: 19366639]
- Krishnan A, Gandour JT. Language experience shapes processing of pitch relevant information in the human brainstem and auditory cortex: electrophysiological evidence. *Acoustics Australia*. 2014; 42(3):166-178. [PubMed: 25838636]
- Krishnan A, Gandour JT, Ananthakrishnan S, Vijayaraghavan V. Cortical pitch response components index stimulus onset/offset and dynamic features of pitch contours. *Neuropsychologia*. 2014; 59:1-12. DOI: 10.1016/j.neuropsychologia.2014.04.006 [PubMed: 24751993]
- Krishnan A, Gandour JT, Ananthakrishnan S, Vijayaraghavan V. Language experience enhances early cortical pitch-dependent responses. *Journal of Neurolinguistics*. 2015; 33:128-148. DOI: 10.1016/j.jneuroling.2014.08.002 [PubMed: 25506127]
- Krishnan A, Gandour JT, Bidelman GM. Experience-dependent plasticity in pitch encoding: from brainstem to auditory cortex. *Neuroreport*. 2012; 23(8):498-502. DOI: 10.1097/WNR.0b013e328353764d [PubMed: 22495037]
- Krishnan A, Gandour JT, Bidelman GM, Swaminathan J. Experience-dependent neural representation of dynamic pitch in the brainstem. *Neuroreport*. 2009; 20(4):408-413. DOI: 10.1097/WNR.0b013e3283263000 [PubMed: 19223793]
- Krishnan A, Gandour JT, Suresh CH. Cortical pitch response components show differential sensitivity to native and nonnative pitch contours. *Brain and Language*. 2014; 138(0):51-60. <http://dx.doi.org/10.1016/j.bandl.2014.09.005>. [PubMed: 25306506]
- Krishnan A, Gandour JT, Suresh CH. Experience-dependent enhancement of pitch-specific responses in the auditory cortex is limited to acceleration rates in normal voice range. *Neuroscience*. 2015a; 303:433-445. DOI: 10.1016/j.neuroscience.2015.07.015 [PubMed: 26166727]
- Krishnan A, Gandour JT, Suresh CH. Pitch processing of dynamic lexical tones in the auditory cortex is influenced by sensory and extrasensory processes. *European Journal of Neuroscience*. 2015b; 41(11):1496-1504. DOI: 10.1111/ejn.12903 [PubMed: 25943576]
- Krishnan A, Gandour JT, Suresh CH. Language-experience plasticity in neural representation of changes in pitch salience. *Brain Research*. 2016; 1637:102-117. DOI: 10.1016/j.brainres.2016.02.021 [PubMed: 26903418]
- Krishnan A, Swaminathan J, Gandour JT. Experience-dependent enhancement of linguistic pitch representation in the brainstem is not specific to a speech context. *Journal of Cognitive Neuroscience*. 2009; 21(6):1092-1105. DOI: 10.1162/jocn.2009.21077 [PubMed: 18702588]
- Krumbholz K, Patterson RD, Seither-Preisler A, Lammertmann C, Lutkenhoner B. Neuromagnetic evidence for a pitch processing center in Heschl's gyrus. *Cerebral Cortex*. 2003; 13(7):765-772. [PubMed: 12816892]
- Li P, Sepanski S, Zhao X. Language history questionnaire: A web-based interface for bilingual research. *Behavioral Research Methods*. 2006; 38(2):202-210.
- Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*. 1971; 9:97-113. [PubMed: 5146491]
- Penagos H, Melcher JR, Oxenham AJ. A neural representation of pitch salience in nonprimary human auditory cortex revealed with functional magnetic resonance imaging. *Journal of Neuroscience*. 2004; 24(30):6810-6815. 24/30/6810 [pii]. DOI: 10.1523/JNEUROSCI.0383-04.2004 [PubMed: 15282286]

- Schonwiesner M, Zatorre RJ. Depth electrode recordings show double dissociation between pitch processing in lateral Heschl's gyrus and sound onset processing in medial Heschl's gyrus. *Experimental Brain Research*. 2008; 187(1):97–105. DOI: 10.1007/s00221-008-1286-z [PubMed: 18236034]
- Tsang YK, Jia S, Huang J, Chen HC. ERP correlates of pre-attentive processing of Cantonese lexical tones: The effects of pitch contour and pitch height. *Neuroscience Letters*. 2011; 487(3):268–272. S0304-3940(10)01374-1 [pii]. DOI: 10.1016/j.neulet.2010.10.035 [PubMed: 20970477]
- Warren JD, Griffiths TD. Distinct mechanisms for processing spatial sequences and pitch sequences in the human auditory brain. *Journal of Neuroscience*. 2003; 23(13):5799–5804. [PubMed: 12843284]
- Winer JA, Miller LM, Lee CC, Schreiner CE. Auditory thalamocortical transformation: structure and function. *Trends in Neuroscience*. 2005; 28(5):255–263. DOI: 10.1016/j.tins.2005.03.009
- Wong PC, Perrachione TK. Learning pitch patterns in lexical identification by native English-speaking adults. *Applied Psycholinguistics*. 2007; 28(4):565–585.
- Xu Y, Krishnan A, Gandour JT. Specificity of experience-dependent pitch representation in the brainstem. *Neuroreport*. 2006; 17(15):1601–1605. [pii]. DOI: 10.1097/01.wnr.0000236865.31705.3a00001756-200610230-00008 [PubMed: 17001276]
- Zatorre RJ, Belin P. Spectral and temporal processing in human auditory cortex. *Cerebral Cortex*. 2001; 11(10):946–953. [PubMed: 11549617]

Figure 1.

Grand average CPR waveforms (**A**) and FFR waveforms (**B**) elicited by T2 (red) and Linear (blue) pitch contours. The cortical pitch-relevant components (Na, Pb, Nb) are highlighted in gray. The waveform amplitude (**A**) waveform periodicity (**B**) and normalized mean response magnitude (**C**) appear to be more robust for T2 as compared to Linear. (**D**) Normalized magnitude difference between T2 and Linear per component (Na-Pb, Pb-Nb, FFR) show that Pb-Nb is larger than either Na-Pb or FFR. These data emphasize that Pb-Nb—a pitch-specific neural generator that indexes temporal regularity in a relatively later time window—exhibits heightened sensitivity to changes in acceleration relative to a fixed rate.

Figure 2.

Waveform (T2) and spectrograms of each stimulus condition (T2, Linear) illustrate the experimental paradigm used to acquire cortical and brainstem responses. The vertical dashed line at 500 ms demarcates the transition from the initial noise segment to the final pitch segment. CPRs and FFRs were extracted from evoked responses beginning with the onset of the pitch. F0 contours (white) are superimposed on their respective pitch segments. Within the pitch segment (top), the waveform shows robust periodicity at a high IRN iteration step ($n=32$); the spectrograms (middle) show clear resolution of dynamic, rising spectral bands corresponding to the harmonics of the fundamental frequency. Corresponding acceleration trajectories (bottom panel) are displayed for the two stimuli. T2 (solid), exemplary of Mandarin Tone 2, and Linear (dashed) both represent time-varying rising pitch contours. Linear exhibits a fixed rate of acceleration. T2 is the only pitch pattern that occurs in natural speech and the only one to exhibit a changing acceleration rate.