Does a pitch center exist in auditory cortex?

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Bendor D. Does a pitch center exist in auditory cortex? J Neurophysiol 107: 743–746, 2012. First published November 2, 2011; doi:10.1152/jn.00804.2011.—Pitch perception is an important component of hearing, allowing us to appreciate melodies and harmonies as well as recognize prosodic cues in speech. Multiple studies over the last decade have suggested that pitch is represented by a pitch-processing center in auditory cortex. However, recent data (Barker D, Plack CJ, Hall DA. Cereb Cortex. In press; Hall DA, Plack CJ. Cereb Cortex 19: 576–585, 2009) now challenge these previous claims of a human “pitch center.”

When you pluck a guitar string the vibrating string produces a sound composed of several spectral components, a fundamental at the frequency of the string’s vibration as well as higher order harmonics at frequencies that are multiples of the fundamental. We do not hear these spectral components as separable and distinct sounds; instead, they get perceptually fused together into a single sound with a pitch equal to the frequency of the fundamental. A remarkable feature of pitch perception is that it does not depend on the fundamental being physically present in the sound, as any subset of harmonics is sufficient for hearing the pitch of the “missing fundamental” (Fig. 1A). Because spectrally different sounds can have the same pitch, the frequency-based neural representation of a sound in the auditory periphery does not explicitly encode pitch, and pitch must be computed at some later stage in the auditory pathway. Although there is general agreement that auditory cortex is essential for pitch perception, whether pitch processing is localized within a single functionally specific region within auditory cortex remains a controversial issue among auditory neuroscientists.

The critical role auditory cortex plays in pitch perception was first demonstrated by Ian Whitfield more than 30 years ago (Whitfield 1980). Whitfield trained cats to discriminate between rising and falling pitches using complex sounds where the spectrum moved in the opposite direction of the pitch. After lesioning auditory cortex bilaterally, cats were no longer able to discriminate pitch changes (although frequency discrimination was still possible).

Two decades later, a region of non-primary auditory cortex (lateral Heschl’s gyrus) was identified as a pitch-processing area using functional magnetic resonance imaging (fMRI) in human subjects (Patterson et al. 2002). In their experiments, Patterson and colleagues used iterated ripple noise (IRN) as an acoustic stimulus, a sound created by taking a sample of broadband noise and adding this noise to itself with a delay (Fig. 1B). There are two major advantages of using IRN. First, pitch salience can be parametrically changed; a weak pitch is perceived with a single delay-and-add iteration, and this pitch strength increases with additional delay-and-add iterations. Next, IRN is acoustically similar to noise, except for it having a salient pitch (which noise does not). By comparing the BOLD signal change between noise and IRN, the region of auditory cortex that responds to a sound’s pitch could be identified. Patterson and colleagues’ finding of a pitch center in lateral Heschl’s gyrus was soon confirmed by a number of studies that collectively utilized a wide range of techniques, including fMRI, MEG, electrophysiology, and structural MRI (Hall et al. 2006; Penagos et al. 2004; Puschmann et al. 2010; Ritter et al. 2005; Schneider et al. 2005; Schönwiesner and Zatorre 2008). Complementing these data in humans, a putative pitch center was identified in monkeys using single-unit recordings (Bendor and Wang 2005). The pitch center in monkeys was located in low frequency auditory cortex near the anterolateral border of primary auditory cortex, an anatomical location potentially homologous to lateral Heschl’s gyrus in humans (Bendor and Wang 2006).

Still, the existence of a pitch center in auditory cortex remains controversial. The majority of fMRI experiments identifying lateral Heschl’s gyrus as a pitch center have used IRN stimuli. Given that pitch can be perceived over a wide range of different acoustic stimuli, pitch responses should still be observed for non-IRN acoustic stimuli. Using five spectrally different acoustic stimuli with the same pitch, Hall and Plack (2009) observed that pitch responses were poorly localized to one region consistently across subjects, with broad activation mainly observed in a region posterior to lateral Heschl’s gyrus (planum temporale). These data suggest that lateral Heschl’s gyrus may be activated by some feature of IRN other than pitch. Analyzing the spectro-temporal representation of IRN, Hall and Plack observed modulations that were not present in the control stimulus (Gaussian noise). Thus pitch responses obtained by a BOLD signal subtraction (IRN – Gaussian noise) could correspond to acoustic differences rather than the presence of a salient pitch.

Barker et al. (in press) examined this idea further by comparing BOLD signal responses to IRN and an IRN stimulus modified to not have a pitch. Barker and colleagues created this “no-pitch” iterated noise stimulus (IRNo) by disrupting the fine structure of IRN, which effectively removed the pitch while keeping the spectro-temporal modulations that were hypothesized to be causing the pitch responses (Fig. 1C). The magnitude of these spectro-temporal modulations increased with the delay-and-add iterations used to generate the IRN and IRNo stimuli. Across the range of iterations used in these experi-
ments, the spectro-temporal modulations for IRN and IRNo stimuli were quantitatively similar, given that they produced similar responses in a computational model of a cochlear filter bank.

Next, 16 human subjects received fMRI scans while listening to IRN and IRNo stimuli with 2, 4, 16, or 64 iterations, as well as two different noise controls. Barker and colleagues (in press) observed that IRN and IRNo stimuli evoked similar regions of activation in auditory cortex. Using a 2\( ^{\text{nd}} \) ANOVA (\( P < 0.001 \), corrected), no significant difference in activity between IRN and IRNo stimuli was observed (at 2, 4, 16, and 64 iterations). Performing a similar analysis using a region of interest approach, this result was confirmed in central Heschl’s gyrus, lateral Heschl’s gyrus, and planum temporale. All three regions of interest did have higher activity when more delay-and-add iterations were used in generating the IRN and IRNo stimuli. While more delay-and-add iterations increase the pitch salience of IRN stimuli, they also increase the magnitude of spectro-temporal modulations for both IRN and IRNo stimuli. These data indicate that IRN activation (relative to noise) can be explained by sensitivity to spectro-temporal modulations in the sound rather than the presence of a salient pitch.

Next, Barker and colleagues (in press) compared the BOLD responses to IRN and IRNo. Only 3 out of 16 subjects showed a significant difference in activity (IRN > IRNo). Furthermore, common voxels of IRN > IRNo activation were only observed in less than half of the subjects: in the left Heschl’s gyrus and left planum temporale (6 out of 16 subjects) and in the right planum temporale near the anterior border of lateral Heschl’s gyrus (7 out of 16 subjects). In contrast to this, the activation from an IRN > noise comparison was more consistent, with 10 out of 16 subjects showing a significant effect. The regions of maximum consistency were on the posterior edge of the right planum polare (14 out of 16 subjects) and in the anterolateral planum temporale (12 out of 16 subjects). While the IRN > noise comparison did activate lateral Heschl’s gyrus, similar to Patterson et al. (2002), the IRN > IRNo comparison did not
activate this region significantly. These data suggest that IRN-related activity in lateral Heschl’s gyrus is more likely a response to spectro-temporal modulations than pitch.

This study highlights the problem of using IRN to study pitch without a proper noise control. While one interpretation of this data is that pitch responses to IRN stimuli do not occur in lateral Heschl’s gyrus, there are several issues to address before we can arrive at this conclusion. First, if a region of the brain is a pitch processing center, could it also be sensitive to non-pitch features of a sound? In monkeys, pitch-selective neurons are colocalized with frequency-tuned neurons that do not respond to missing fundamental sounds (Bendor and Wang 2005). While pitch-selective neurons are generally only found within a specific region of monkey auditory cortex, the heterogeneous composition of this “pitch center” would make it more difficult to identify using a technique such as fMRI. Any difference between two stimuli is reflected in the BOLD signal subtraction, and therefore pitch responses could be obscured by a feature of the control stimulus unrelated to pitch that is enhanced relative to the test stimulus.

A second issue is the lack of agreement between different research groups when investigating pitch responses in lateral Heschl’s gyrus, even when using fairly similar acoustic stimuli (Hall and Plack 2009; Penagos et al. 2004; Puschmann et al. 2010). Minor differences in acoustic stimuli or analysis methods could conceivably enhance or diminish an observed pitch response. For example, the IRN stimuli used by Barker et al. (in press) had a more limited bandwidth (1–2 kHz) than what was previously used by Patterson et al. (2002) (500–4,000 Hz). Although both stimuli produced a pitch, the stimulus used by Patterson et al. had a stronger pitch salience, an attribute that has been linked to larger pitch responses in lateral Heschl’s gyrus (Penagos et al. 2004). Second, the acoustic stimuli used by Barker et al. (in press) were longer in duration (580 ms) than those used by Patterson et al. (200 ms). While increasing the duration of a stimulus doesn’t change its pitch, it puts less emphasis on the onset response and more weight on the sustained response, with the latter potentially having a weaker pitch response as a consequence of neuronal adaptation.

A third point to consider is intersubject variability. Even when group data indicates a significant pitch response in lateral Heschl’s gyrus, individual subjects can have pitch responses nearby but not directly overlapping the group data. This not unique to pitch responses, as even frequency responses to tones will give different activation maps between subjects, indicating that different fields within auditory cortex are not anchored to particular anatomical landmarks (Humphries et al. 2010). Because imaging studies typically average group data using anatomical landmarks, intersubject variability can obscure a significant activation pattern. This approach proved to be problematic during the initial single-unit-based investigations of tonotopy in non-human auditory cortex (Evans and Whitfield 1964; Goldstein et al. 1970). Recording a small number of neurons from each unanesthetized subject and grouping all the data together into an averaged frequency map using anatomical landmarks, these studies failed to demonstrate any reliable tonotopic organization in primary auditory cortex. Repeating these experiments in anesthetized subjects, which permitted the recording of a complete frequency map within a single subject, Merzenich and colleagues (1975) successfully demonstrated a reliable tonotopic organization in primary auditory cortex.
AUTHOR CONTRIBUTIONS

Author contributions: D.B. prepared figures; D.B. drafted manuscript; D.B. edited and revised manuscript; D.B. approved final version of manuscript.

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