Tuning to interaural time difference in human auditory cortex

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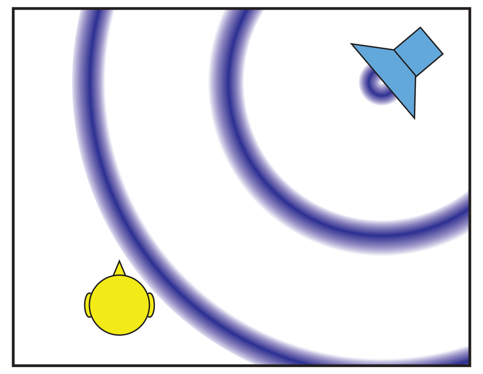
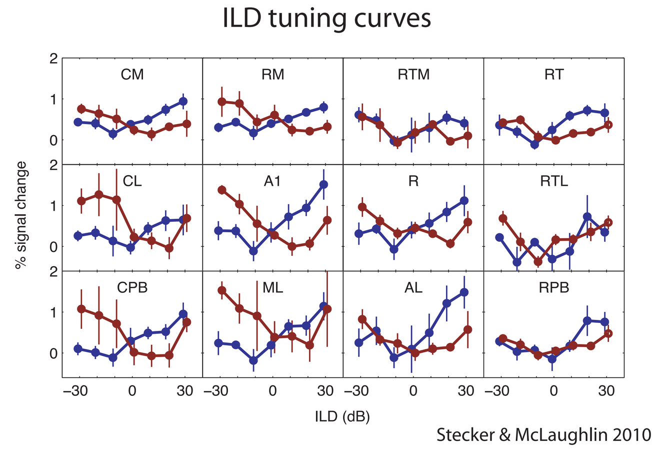
Cortical tuning to auditory space



- Interaural time and level differences ("ITD" and "ILD"): important binaural cues for sound localization.
- Although auditory cortex (AC) is necessary for sound localization (e.g., Malhotra et al. 2004), the representation of ITD & ILD and their relationship in AC (e.g., Johnson & Hautus 2010) remains poorly understood.
- Neural recordings of cortical sensitivity to ILD in animal models suggest broad contralateral tuning (Higgins et al. 2010; Middlebrooks & Pettigrew 1981; Stecker et al. 2005). There is less evidence examining ITD processing in the cortex (Kelly & Phillips 1991; Reale & Brugge 1990), or directly comparing the two cues.
- In human AC, neuroimaging data suggests contralateral tuning for ILD (Stecker & McLaughlin 2010). For ITD, fMRI evidence is mixed – for (Krumbholz et al. 2005; von Kriegstein et al. 2008) and against (Woldorff et al. 1999; Zimmer et al. 2006) contralateral tuning.
- Nature of stimuli and selection of cue values (von Kriegstein et al. 2008) may be important.



Question: Do ITD and ILD cues differentially modulate the hemodynamic response in human AC?

Methods

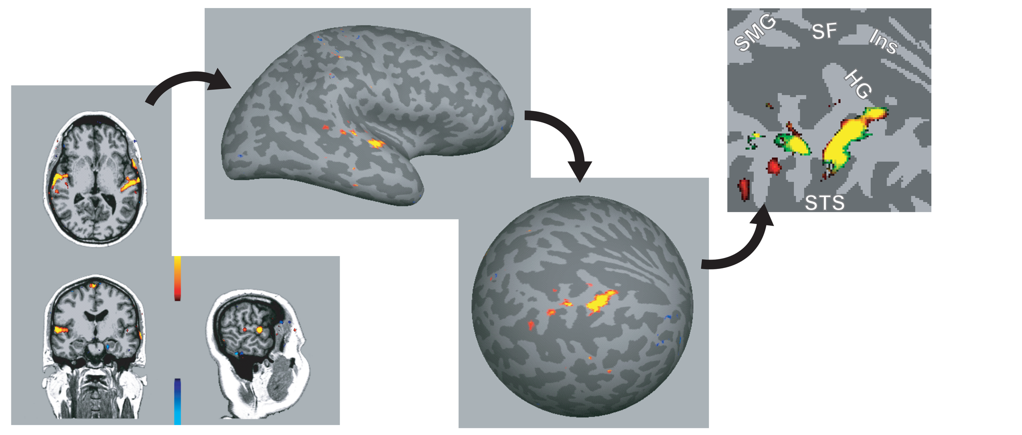
3 experiments (10 normal-hearing, right-handed subjects per experiment) presenting varying stimuli:

ILD at 4000 Hz: Narrowband Gabor click trains (4000 Hz carrier frequency, 2-ms interclick interval) varying across ILD (+/-30, 20, 10, 5, 0 dB ILD), or silence (-10 dB SPL).

ITD at 4000 Hz: Narrowband Gabor click trains (4000 Hz carrier frequency, 2-ms interclick interval) varying across ITD (+/-1500, 800, 500, 200, 0 μs ITD), or silence (-10 dB SPL).

ITD in noise: Broadband Gaussian noise burst trains (1-ms bursts, 10-ms interclick interval) varying across ITD (+/-1500, 800, 500, 200, 0 μs ITD), or silence (-10 dB SPL).

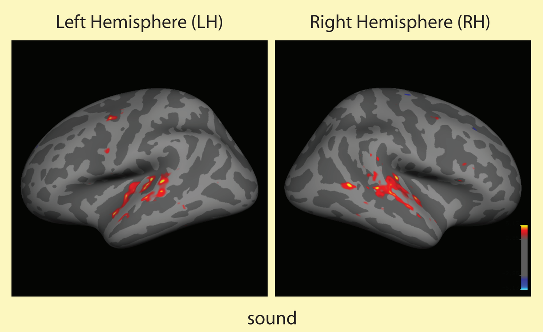
Stimuli	Stimuli 1-s in duration. Average binaural level: 80 dB SPL. Stimuli contain 4 trains of 16 clicks each. Interstimulus interval jittered from 1 - 5-s. Binaural presentation via piezo insert earphones (Sensimetrics S14) in ear defenders.
Task	Respond to infrequent pitch change (1.2-ms ICI) with button press.
Design	Event-related design. Continuous carryover paradigm (Aguirre 2007): each stimulus condition presented both preceding and following every other condition. 2 runs of 201 stimulus presentations per subject.
Imaging	BOLD echoplanar imaging (Philips, 3 Tesla). Continuous imaging (TR = 2-s). 42 3-mm slices, 2.75 x 2.75-mm in-plane resolution.
Analysis	3D functional preprocessing: motion corr., high-pass filtering (100 s), and denoising in MELODIC (FSL). Fixed-effect cross-run individual analyses in FEAT (FSL). Individual cortical surface extraction, projection to average surface with smoothing of 5 FWHM, and random effects cross-subject analysis on surface performed in Freesurfer. Response curves plotted in MATALB for top 1000 voxels responding in MATLAB group analysis.

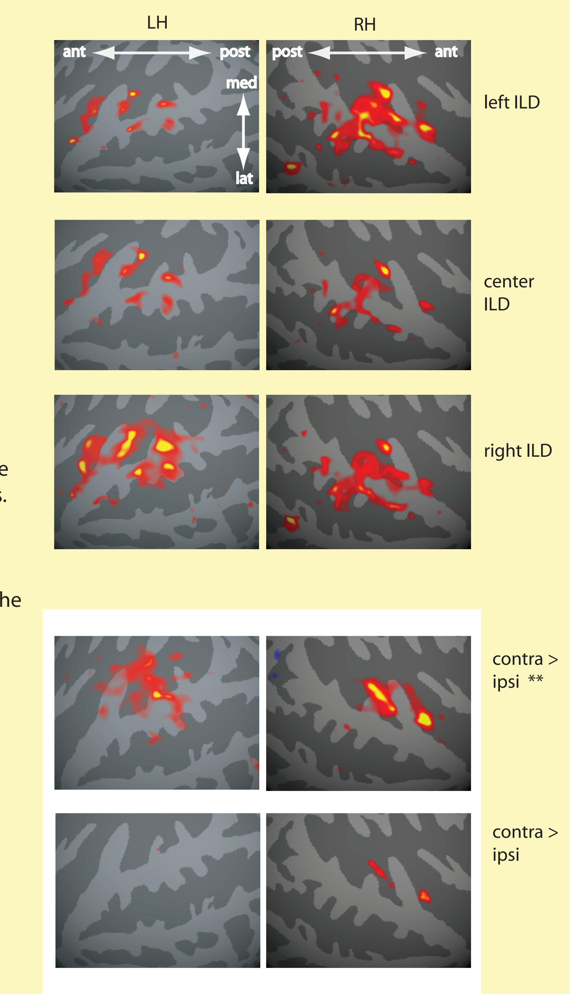


Abbreviations HG: Heschl's gyrus; Ins: insular cortex; SF: Sylvian fissure; SMG: supramarginal gyrus; STG: superior temporal gyrus; STS: superior temporal sulcus

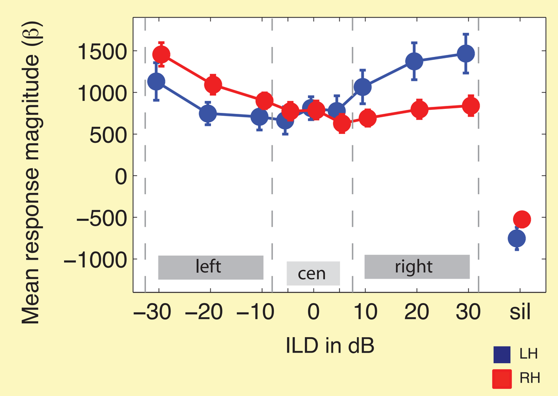
More pronounced contralateral tuning to ILD than ITD

ILD at 4000 Hz



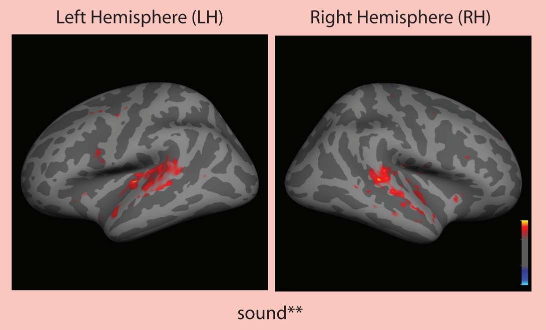


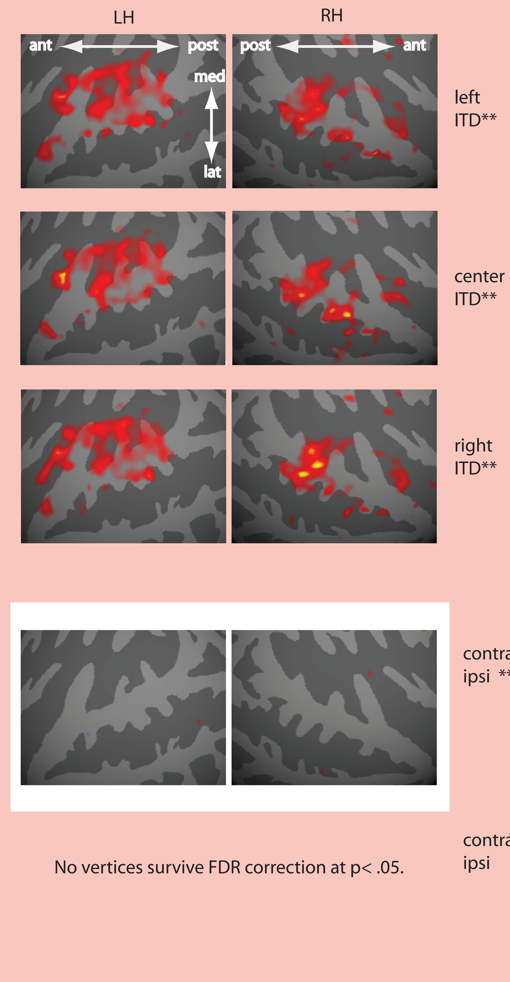
Above and right: Cortical maps of sensitivity to ILD at 4000 Hz plot on a normalized brain (FSaverage) vertices with significant group BOLD response (FDR correction at p< .05, except where noted**) to ILD values imposed on narrowband click trains.
Below: Response-ILD function plots average response magnitude across the top 1000 vertices in AC responding to varying ILD values. Error bars: S.E.M. across subjects.
In both hemispheres, there is contralateral tuning, i.e., the response to contralateral sound is greater than to ipsilateral, though in the BOLD maps this difference appears to be greater in the right than the left hemisphere.



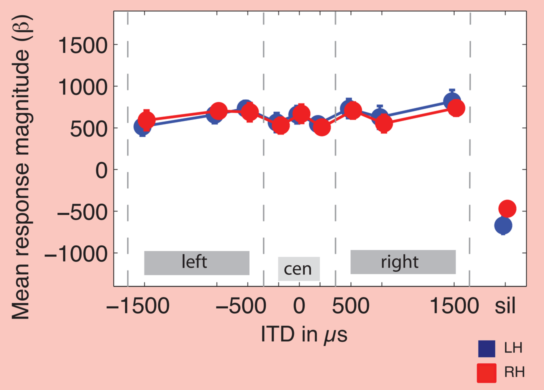
**p< .01, uncorr.

ITD at 4000 Hz



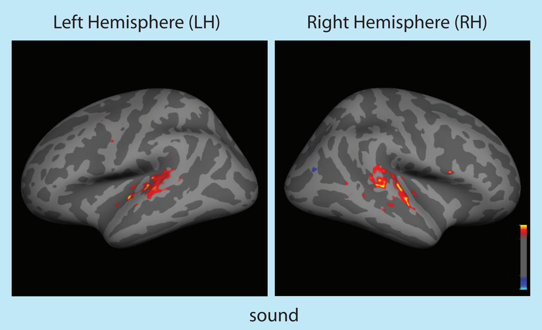


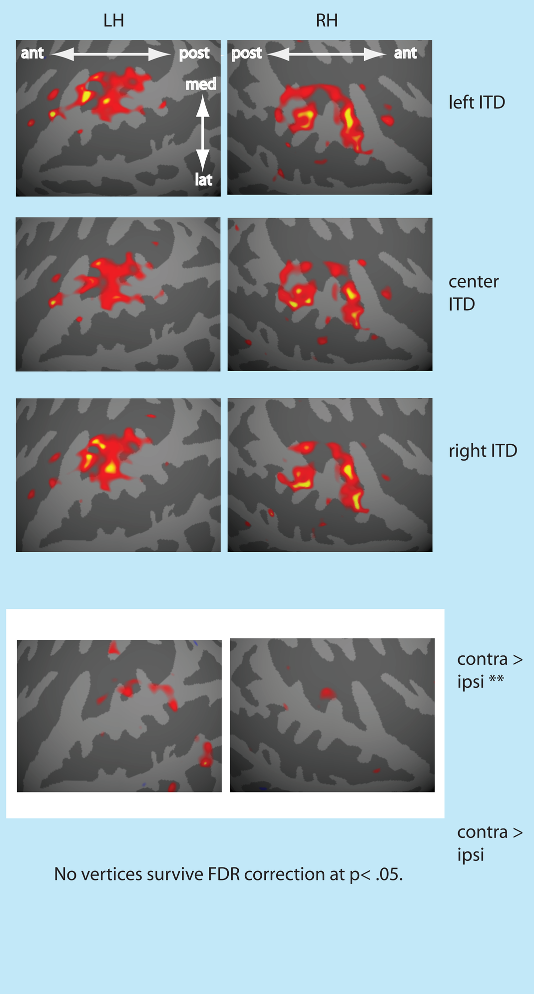
Above and right: Cortical maps of sensitivity to ITD at 4000 Hz plot on a normalized brain vertices with significant group BOLD response to ITD values imposed on narrowband click trains. Formatting as in previous ILD figure. Note that no vertices in any of the conditions survived FDR correction at p< .05.
Below: Response-ITD function. Formatting as in previous ILD figure.
Neither the BOLD maps nor the response-ITD function suggest that there is contralateral tuning in either hemisphere.



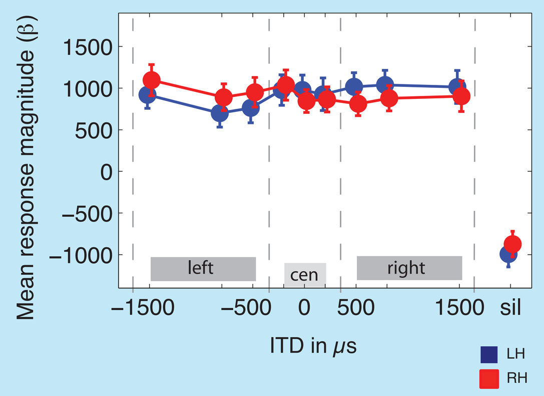
**p< .01, uncorr.

ITD in noise





Above and right: Cortical maps of sensitivity to ITD in noise plot on a normalized brain vertices with significant group BOLD response to ITD values imposed on broadband noise bursts. Formatting as in previous ILD figure.
Below: Response-ITD function. Formatting as in previous ILD figure.
The response-ITD function for ITD in noise shows a small contralateral tuning effect. The difference between response to contralateral and ipsilateral sound is not great enough to survive FDR correction at p< .05 in the BOLD maps.



** p< .01, uncorr.

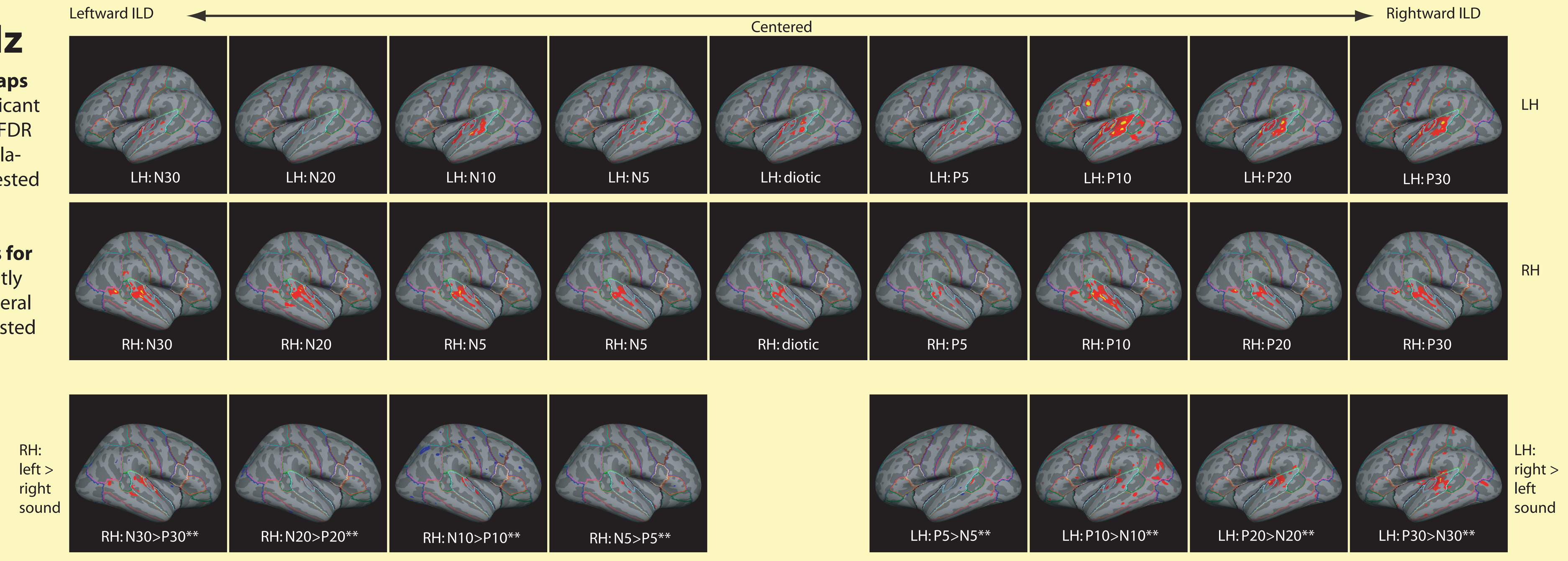
Activation maps across ILD and ITD cue values

ILD at 4000 Hz

Top two rows: activation maps across ILD values plot significant effects (group-level analysis; FDR correction at p< .05) of stimulation across vertices at each tested ILD.

Bottom row: Contrast maps for ILD plot vertices of significantly greater response to contralateral than ipsilateral ILD at each tested value (p<.01, uncorr.).
Red:-yellow: C>I; blue: I>C.

Consistent with other data (Johnson & Hautus 2010; Krumbholz et al. 2007) contrast maps suggest greater contra tuning in LH, similar RH response across hemifields.



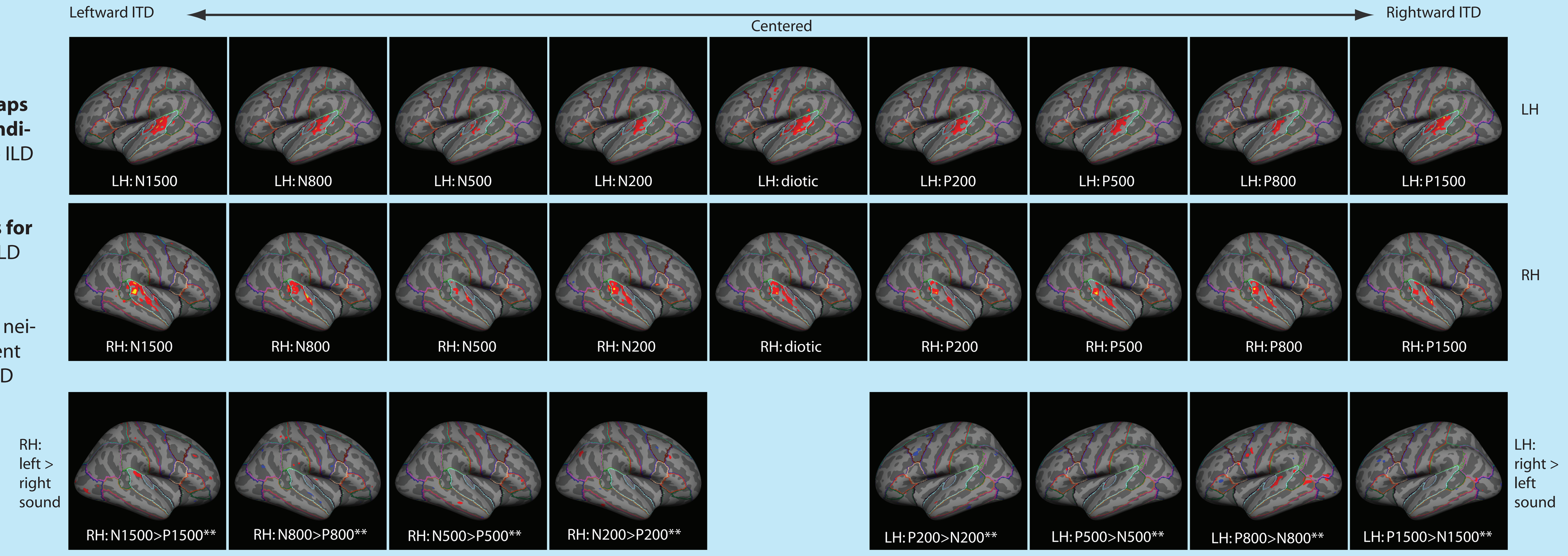
**p< .01, uncorr.

ITD in noise

Top two rows: activation maps across ITD values (noise condition). Formatting identical to ILD maps above.

Bottom row: Contrast maps for ITD. Formatting identical to ILD contrast maps above.

Unlike the ILD data, however, neither LH nor RH show consistent contralateral tuning across ITD values.



Discussion

- Response to ILD at 4000 Hz is contralaterally tuned.
  - Tuning function is non-monotonic – i.e., response enhanced at both contra and extreme ipsi ILD values – thereby reducing contralateral tuning effect as measured.
  - Consistent with previous reports (Johnson & Hautus 2010; Krumbholz et al. 2007), data suggest hemispheric asymmetries in contralateral tuning effect.
- Response to ITD at 4000 Hz does not show contralateral tuning, while response to ITD in noise shows a small effect.
- A few prior fMRI studies have shown weak (Krumbholz et al. 2005) or stimulus-limited (von Kriegstein et al. 2008) contralateral tuning. Possible reasons for present finding of reduced contralateral tuning for ITD vs. ILD:
  - Small magnitude of effect for ITD (Krumbholz et al. 2005; Werner-Reiss & Groh 2008). Present study may lack sufficient power due to parametric stimulus design or continuous imaging paradigm.
  - The BOLD signal, particularly as analyzed in traditional fMRI studies, may not reflect cortical ITD representations potentially involving:
    - Distributed codes across populations of panoramic neurons (Stecker et al. 2003; Werner-Reiss & Groh 2008)
    - Highly local codes (Imig & Adrián 1977)
    - Coding by excitatory/inhibitory "opponent" populations (McAlpine et al. 2001; Stecker et al. 2005)
    - Coding by temporal spike patterns (Furukawa & Middlebrooks 2002)
- Sensitivity to ITD may be reduced at the level of the cortex. May be dependent on attention/task.
- Stimulus history may affect response to ITD (Malone et al. 2002) more than ILD. This was modeled in the present experiments, but not in past studies.

Future Directions

- More fully examine effect of stimulus history on results.
- Conduct time course and MVPA analyses of data.
- Perform future experiments manipulating behavioral task.

Acknowledgments

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