

# Imaging gray matter myelin content of human auditory cortex: resolving a major architectonic division and hemispheric differences in-vivo

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## INTRODUCTION

- The present study takes advantage of recent developments in MRI to map the patterns of myelination within the gray matter of the human superior temporal lobe. Specifically, we obtained quantitative mappings of an imaging parameter sensitive to myelin content (R1) and did so in living human subjects.
- The goals of this study were twofold. The first goal was to examine whether auditory cortical areas, and primary auditory cortex in particular, can be differentiated in-vivo in individual subjects. This goal was motivated by the fact that the inability to anatomically differentiate cortical areas in-vivo, in individual subjects, has been a major obstacle to understanding structure/function relationships in the human auditory cortex. Classical histological literature suggests that auditory koniocortex (i.e., primary auditory cortex) can be distinguished based on heavy myelination [1-3]. We, therefore, hypothesized that auditory koniocortex might be resolvable in mappings of R1. The second goal of this study was to examine whether there are hemispheric differences in gray matter myelin content. This goal was motivated by the well-known functional and anatomical asymmetries of the temporal lobe [4-9].

## METHODS

We use the imaging parameter R1 (1/T1) as an indicator of tissue myelin content

- R1 reflects the amount of random tumbling of water molecules, which is restricted by the lattice of myelinated fibers and depends on their size, configuration and density.

- High correlation between MR signal and myelin content is evident from
  - the gray/white matter contrast on conventional T1-weighted MR images.
  - direct comparison between MR images and myelin stains from the same postmortem specimens [10-14].

### Imaging

- Subjects (N = 5): right-handed, normal hearing thresholds, no known neurological abnormalities

- Imager Strength: 1.5 Tesla; Coil: head coil

- Pulse Sequence: FLASH at 3,5,20 and 30 degrees for four subjects and 5,10,20 and 40 degrees for one subject (TR = 20ms, TE = 7.72ms, resolution = 1.0x1.3x1.0mm)

### Data Analysis

- R1 was estimated for every voxel in the brain:

$$S = PD \sin \alpha \frac{1 - e^{-TR \cdot R1}}{1 - \cos \alpha e^{-TR \cdot R1}} e^{-TE \cdot R2}$$

- Cortical gray matter was segmented using a R1-weighted volume synthesized from multiple FLASH data sets to achieve high contrast between gray and white matter [FreeSurfer, 15,16].

- R1 was averaged across the depth of the gray matter at finely spaced points on the cortical surface.

- The gray matter R1 values were mapped onto the cortical surface.

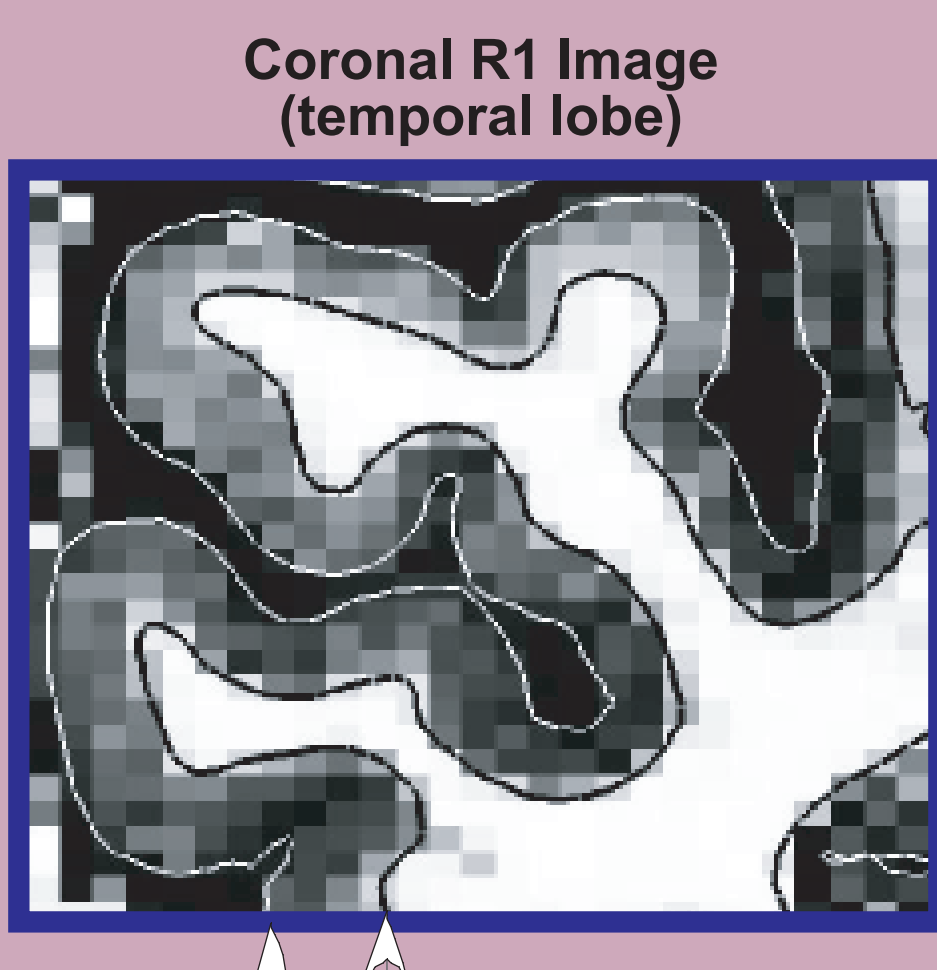
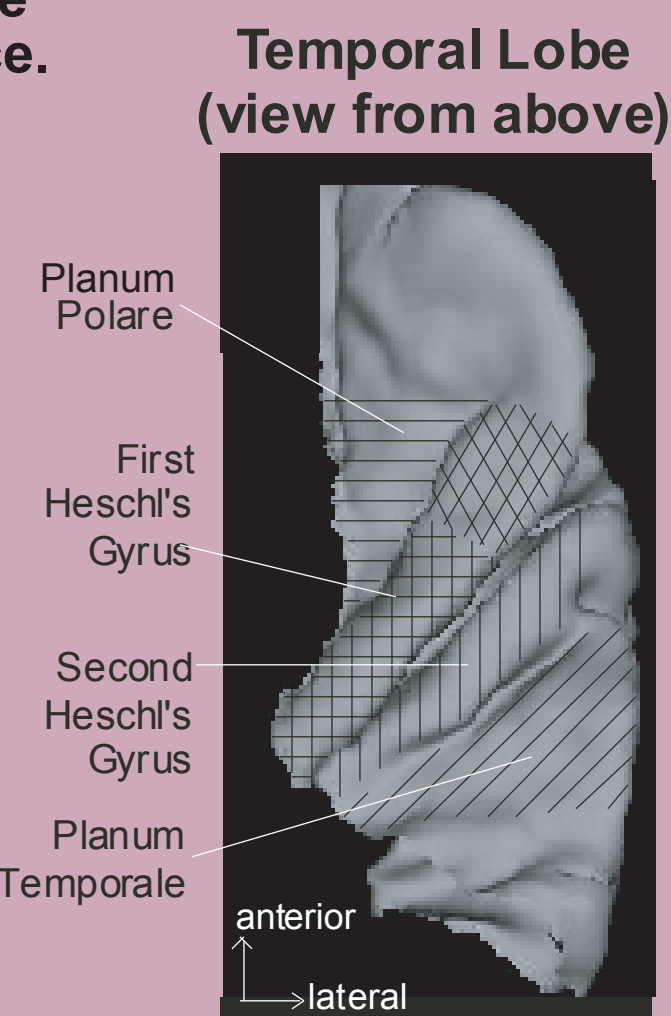


Figure 1. Coronal slice through the temporal lobe showing the spatial distribution of R1 at the resolution of the original images. The grayscale value for each pixel indicates the magnitude of R1 (estimated from multiple image data sets). Black and white lines indicate the gray matter/CSF and gray/white matter borders, as determined by segmentation procedure.

### Defining Regions Of Interest (ROIs)

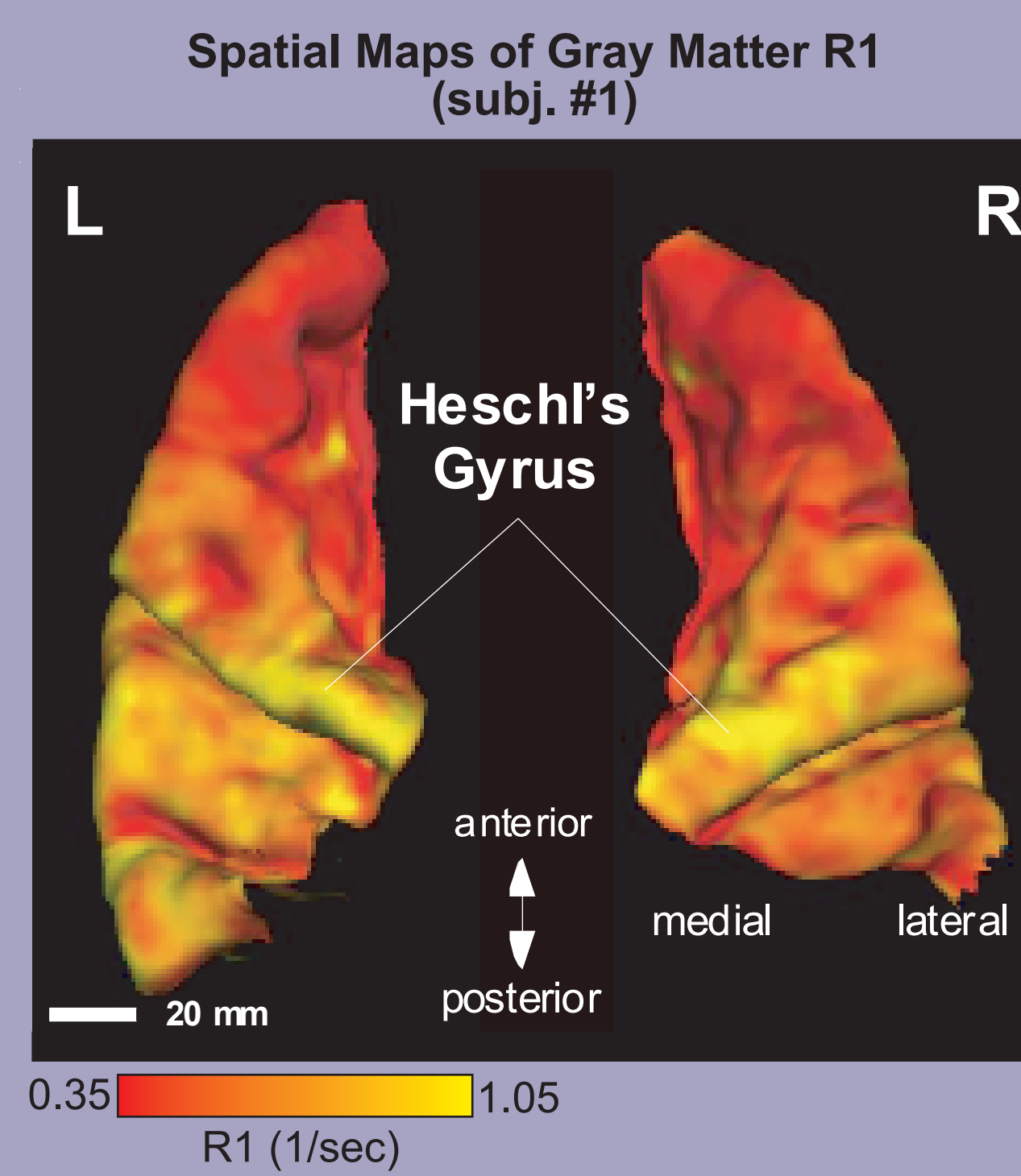
- Gross anatomical landmarks were used to delineate ROIs on the superior temporal lobe (Figure 2).

Figure 2. ROIs displayed on a 3-D reconstruction of the right superior temporal lobe in one subject (#5).



## RESULTS

### Spatial Variations in Gray Matter R1 on the Superior Temporal Lobe



- Gray matter R1 was low, overall, on planum polare, intermediate on planum temporale, and high on Heschl's gyrus. This pattern was highly repeatable across subjects.

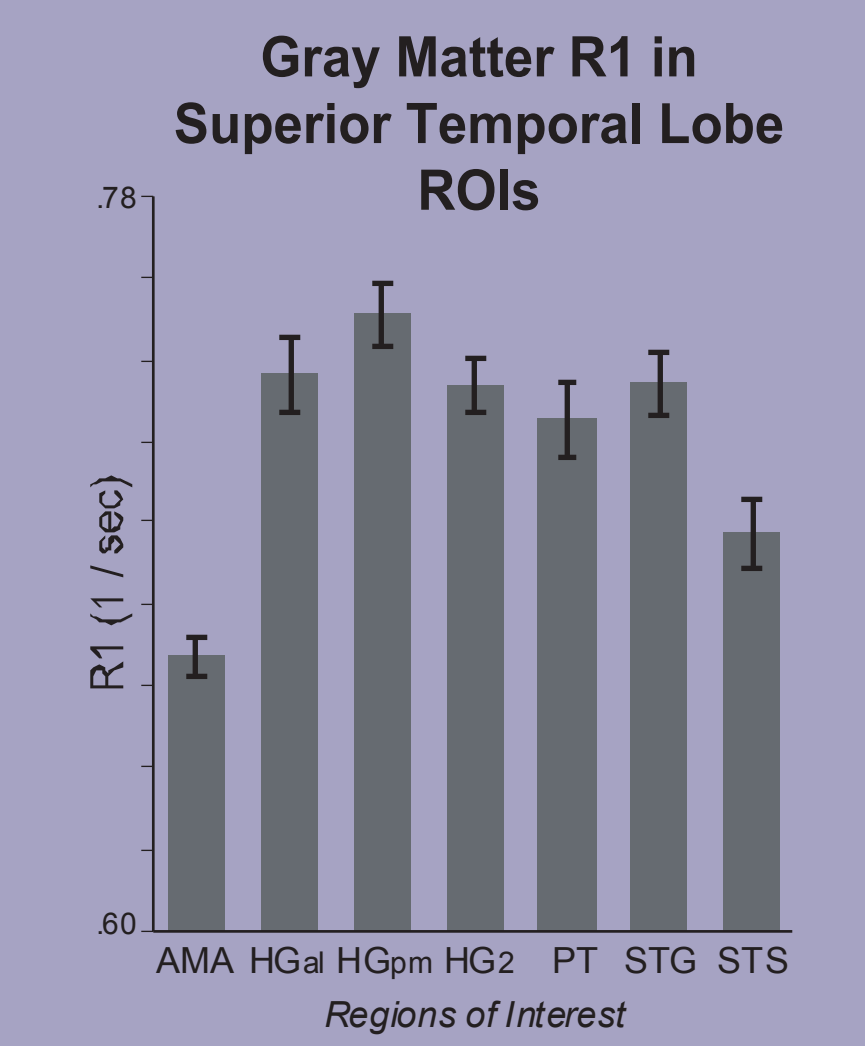


Figure 3. Typical maps of gray matter R1 on the superior temporal lobe. The maps correspond to the left and right hemispheres of one subject. R1 maps are spatially smoothed using an approximation to isotropic Gaussian filter.

Figure 4. Mean gray matter R1 for different ROIs on the superior temporal lobe. Error bars indicate one standard error of the mean across subjects.

### Regions of Highest R1 on the Superior Temporal Lobe

- The regions of highest R1 always overlapped the postero-medial aspect of Heschl's gyrus (the first when there were two).
- High R1 regions were never seen in planum polare, on the superior temporal gyrus, or within the superior temporal sulcus.

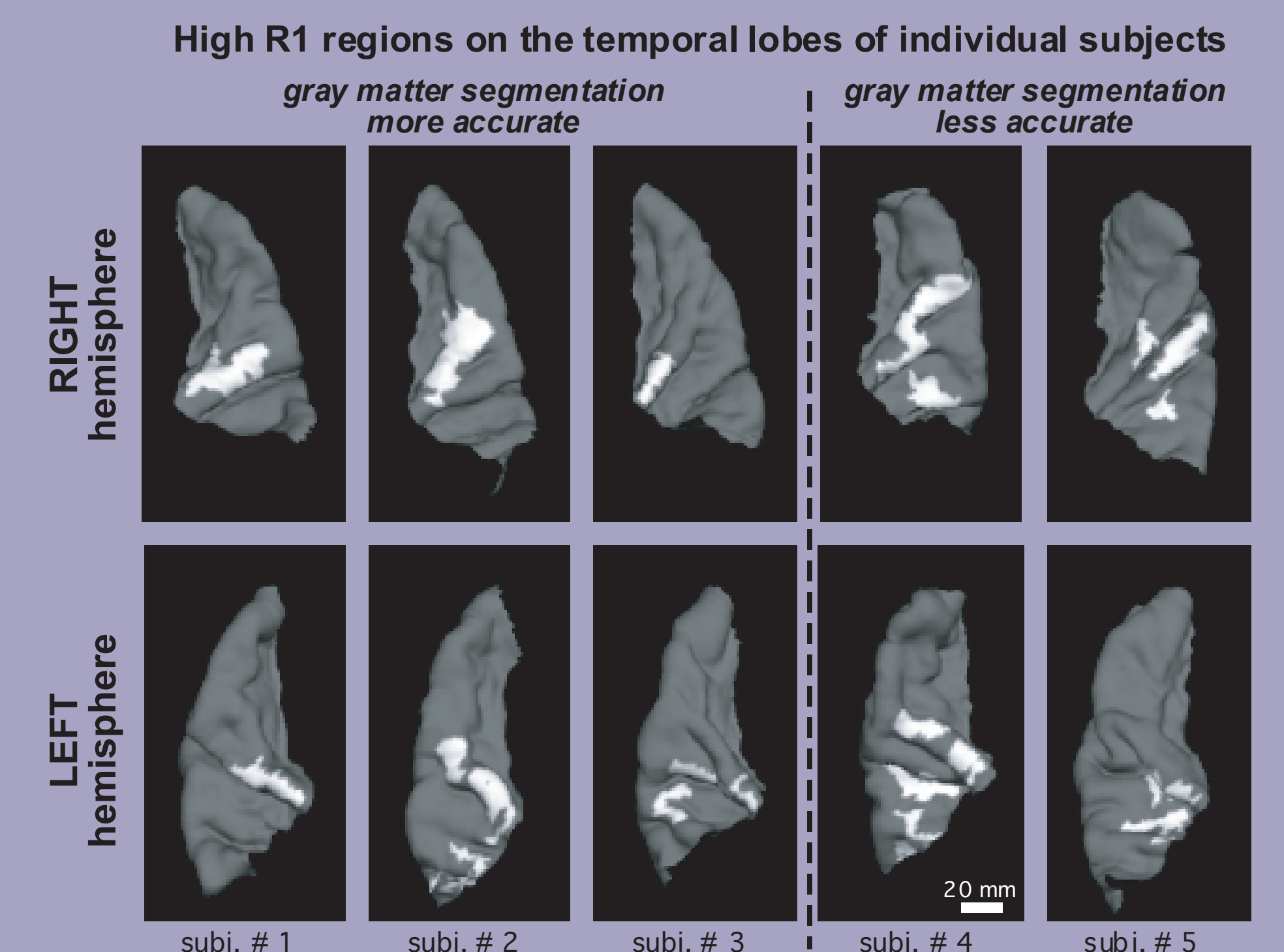
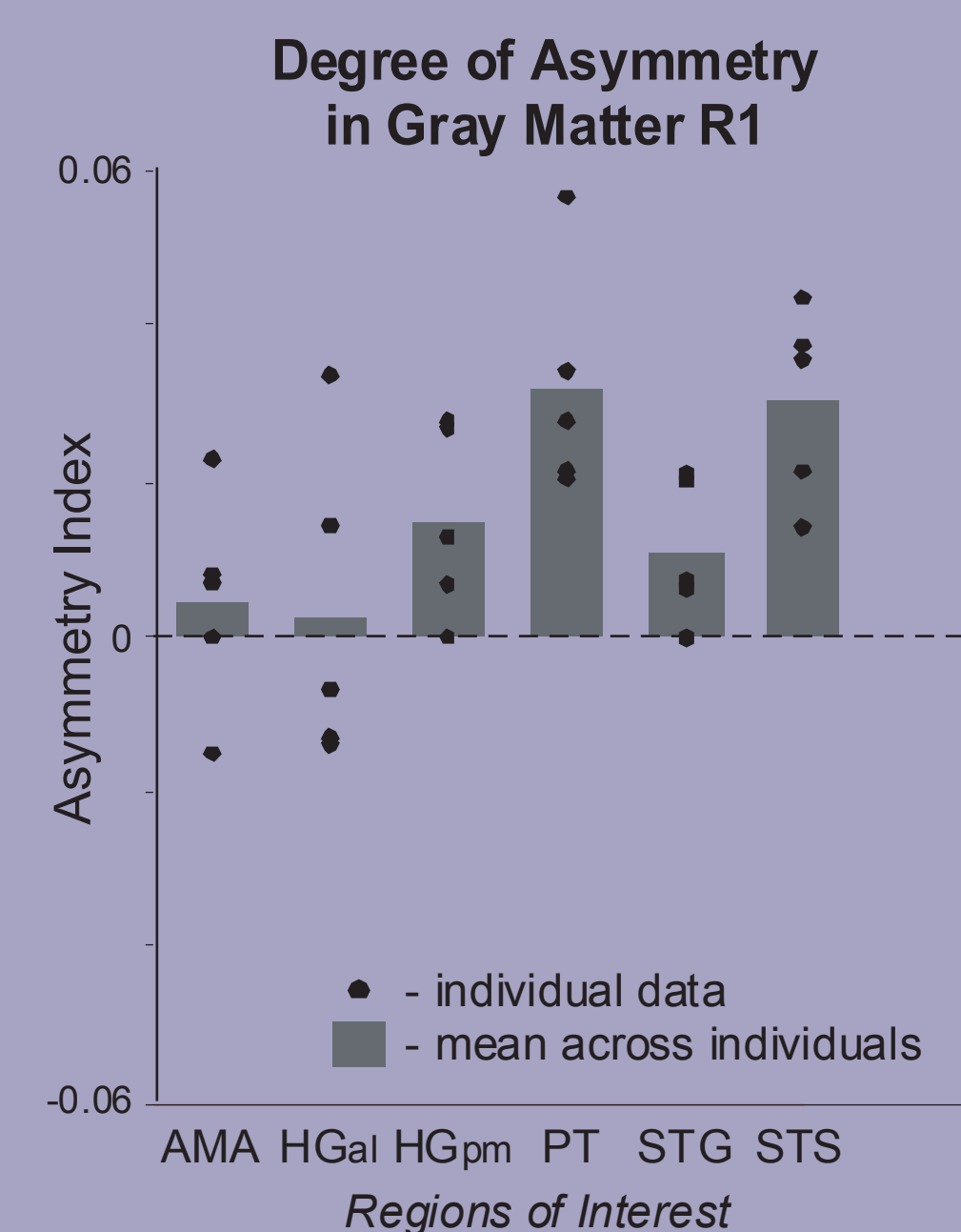


Figure 5. Regions of high R1 on the superior temporal lobe. Each panel shows either the right (top) or left (bottom) superior temporal lobe of a given subject. Maps were processed as follows: First, the maps were thresholded to only show data for points with R1 greater than 80% of the difference between the minimum and the maximum R1 on the temporal lobe. The threshold was defined in the narrow range of values (determined separately for each hemisphere) where spatial change in R1 was rather abrupt. After thresholding, small (less than 50mm<sup>2</sup>) isolated clusters of high R1 were removed for the ease of visual examination. There were no regions of high R1 on the lateral face of the temporal lobe or within sulci (i.e., in regions that cannot be seen). Dashed vertical line separates subjects #4 and #5 in whom gray matter segmentation was more accurate than in subjects #1 and #3.

### Hemispheric Differences



- Gray matter R1 was generally greater on the left compared to the right temporal lobe.
- Asymmetry was most prominent in posterior regions of the superior temporal plane (PT, HGpm), on STG and within STS.

Figure 6. Degree of R1 asymmetry on the superior temporal lobe. For each ROI and subject, an asymmetry index was calculated as the difference in R1 between the left and right sides divided by the sum. Each black circle indicates the index for a particular subject. Gray bars indicate mean across subjects. Dashed horizontal line at zero indicates no asymmetry.

## DISCUSSION

This study shows, for the first time, that gray matter R1 can be estimated and mapped over the surface of the temporal lobe in living humans. Given the strong relationship between R1 and myelin content, we interpret spatial variations in R1 as variations in overall gray matter myelin content. This interpretation is supported by the fact that the regional differences in R1 (between planum polare, Heschl's gyrus and planum temporale) agree with observations of gray matter myelination in histological tissue [1-3]. While in agreement with previous histology, the present approach also provides a very different view of gray matter myelination i.e., quantitative, spatially continuous mappings in living humans.

### High R1 on Heschl's gyrus: A marker for koniocortex?

We suggest that the high R1 regions on Heschl's gyrus coincide with some or all of auditory koniocortex because (1) high R1 likely indicates heavy myelination [10-14], (2) heavy myelination is a prominent and well-documented feature of auditory koniocortex [1-3], and (3) auditory koniocortex in humans typically overlaps postero-medial Heschl's gyrus [1-3,17-20]. Additional information (e.g., gray matter laminar structure) and technological improvements (e.g., improving quality of gray matter segmentation and parameter optimization) may be needed to define the borders of the auditory koniocortex with greater accuracy and reliability. The present study suggests, however, that auditory cortical areas can be delineated based on gray matter architecture directly in living human subjects. Auditory areas identified in this way could provide a common framework for interpreting functional neuroimaging data and enable assignment of specialized functions to particular areas.

### Hemispheric Differences

- The present study provides evidence for a left-right difference in the myelination of the gray matter of the temporal lobe. While hemispheric differences in gross morphology and function of the temporal lobe have been demonstrated previously [4-9], hemispheric differences in gray matter myelination, either in-vivo or ex-vivo, have not.
- The leftward bias in gray matter myelination may be a structural substrate for (1) preferential processing of rapid acoustic changes in the left hemisphere, and/or (2) left-hemispheric specializations for speech and language in humans.

### Implications

The present study lays a groundwork for identifying abnormalities in gray matter myelination in clinical populations and tracking structural changes associated with therapy and learning. Examining people with temporal processing deficits (e.g., dyslexia; 21) may be especially interesting given the crucial role for myelin in maintaining the timing of neural activity. Studying gray matter myelination in clinical populations using R1 mappings is especially practical since the required data can be obtained in a short period of time using conventional scanners and protocols.

## CONCLUSIONS

- Gray matter R1, an indicator of myelin content, can be reliably mapped in individual living subjects.
- The region of high R1 overlapped Heschl's gyrus and may provide a marker for auditory koniocortex.
- Greater gray matter myelination was observed on the left compared to the right temporal lobe. This asymmetry may be a substrate for higher fidelity temporal processing on the left as well as for left-hemispheric speech and language specializations.

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## Acknowledgements

Support provided by NIH/NIDCD R21DC006071, P01DC00119, P41RR14075, P30DC005209 and Athinoula Martinos Scholarship.