Enhanced T1-weighted myelin contrast across lamina at 7T; in-vivo, ex-vivo, and histology

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Introduction: Modern neuroimaging methods allows the investigation of the functional and structural organization of the human cerebral cortex. One of the recent advances has been the visualization of myelination patterns over the cortical surface (1). It has been shown that cortical myelin content can be estimated in vivo to identify a large number of cortical areas using population average myelin maps and the T1, T2 ratio (2,3). Histology indicates that a number of brain regions also show myelin increases localized within the cortical gray matter; however, within-area myelination at a sub-mm scale is harder to visualize, especially outside the striate cortex. The purpose of this work was, first, to use a T1-w MPRAGE modified for strong contrast between low and high myelin content within gray matter (3,4), in order to visualize calcarine and extra-calcarine laminar intensity variations in both in-vivo and ex-vivo data and second, to validate the results by comparing in-vivo and ex-vivo images and ex-vivo images with histology. These laminar variations can be associated with the stria of Gennari and lines of Baillarger, for striate and extra-striate locations respectively.

Methods: Ex-vivo: Two formalin-fixed coronal brain slices were placed in a plastic formalin-filled container. Images were acquired at 7 Tesla (Philips Healthcare, Cleveland, OH, USA) with a volume transmit and 32-channel receive head coil (Nova Medical, Wilmington, MA, USA). Images were acquired with the 3D T1-w MPRAGE adjusted for ex-vivo imaging, accounting for the T1/T2 relaxation of brain tissue after formalin fixation:: TE: 7.7/3.5ms, flip: 8 deg, resolution 400 µm isotropic, 80 slices, TI:280ms, Time delay (TD): 2s, yielding a ~15% contrast difference between high and low myelin gray matter. T2*-w gradient echo images were acquired as a further laminar anatomical reference (TR/TE: 75/20ms, resolution 180 µm isotropic, 278 slices). Histology: striate and extra-striate areas were sampled and 4µm-thick sections were cut and stained with Luxol Fast Blue – Periodic Acid Schiff for myelin. Laminar Profiles: Corresponding MRI samples were manually segmented based on the T2*-w images, the segmentation was aligned on the T1-w images, and laminar profiles were extracted from 0.36mm diameter cylinders, extending from the gray/white (matter) border to the gray/CSF border. About 100 profiles were extracted from each region, and for each profile the signal of each voxel was normalized using the z-score. Laminar profiles from each area were derived from 1000 bootstrapped datasets. For each dataset, estimates of peak location were derived. For the histological samples, the laminar analysis was limited to a single 4µm-thick section, 2D rectangles were built from the gray(GM)/white(WM) border till the gray/CSF border; 2D images were rescaled to 15*15µm^2. In-vivo: Images were obtained with the 3D T1-w MPRAGE, optimized for in-vivo data acquisition with the following parameters: TD = 6s and TI = 1200ms. TR/TE 8/3ms, flip angle: 8 deg, voxel size = 500 µm isotropic. 60 coronal slices, bandwidth 202Hz/px, turbo factor: 275, and adiabatic inversion (4). 4 to 6 scans were acquired per participant, motion corrected and averaged. Laminar analysis of in-vivo data was identical to the ex-vivo data. Contrast was inverted for visualization purposes.

Results: Histological, T1-w, and T2*-w laminar profiles from the striate area of the ex-vivo sample showed a characteristic pattern, with a monotonic increase towards the pial surface and a local minima identified around the middle of cortical gray matter ($p<0.001$) representing the highly myelinated stria of Gennari (Fig. upper row). The stria of Gennari was also identified in the in-vivo T1-w data at the level of the striate fissure (Fig. upper row; in-vivo). Moving dorsally and ventrally with respect to the striate cortex, we reliably identified a similar structure on the histological and T1-w ($p<0.001$) laminar profiles, but not on T2*-w laminar profiles (Fig. lower row, $p>0.05$, ns). In-vivo, extra-striate areas well outside the striate cortex also showed a reliable, high-contrast structure around the middle of cortical gray matter in T1-w laminar profiles (Fig lower row; in-vivo). The same result was replicated across all 4 participants.

Discussion & Conclusions: We can reliably identify a structure located in the middle of the cortical gray matter that extends beyond striate cortex in ex-vivo and in-vivo images using the modified T1-w MPRAGE. On extra-striate portions of the brain, this structure likely represents the two separated lines of Baillarger (5). Due to their close proximity (internal layer IV and internal layer V) the two lines cannot be separated into the distinctive components at the available acquisition resolutions, and the images show instead a uniform structure in the extra-striate cortex that represents the two merged lines of Baillarger. The high sensitivity achieved with the T1-w MPRAGE sequence used provides the basis for studying intra-area (laminar) structure in humans, in vivo.

References

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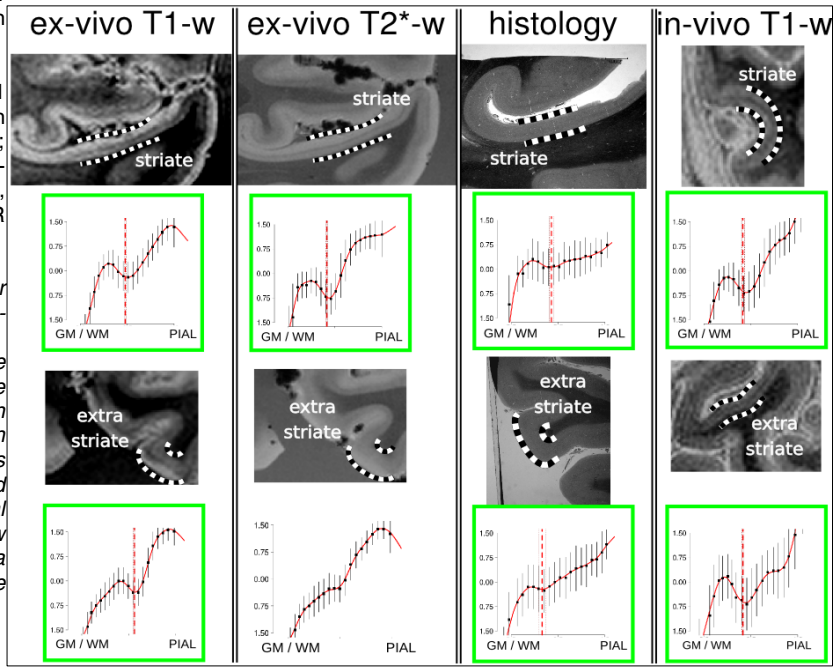

Sample portions and corresponding laminar profile of ex-vivo T1-w, T2-w, histology and in-vivo T1-w data.*
The upper half shows images and the corresponding laminar profiles from the striate samples. The lower half shows images from an extra-striate location. A green line is drawn around laminar profile plot if a local minima was identified in more than 75% of the bootstrapped profiles on a single area (z-test, $p<0.0001$). Local minima were found in all histology and T1-w samples. For the T2-w sample local minima could be found only at the level of the striate cortex, but not for locations outside the striate*