The myelin g-ratio is defined as the ratio of the inner to the outer diameter of the myelin sheath. This ratio provides a measure of the myelin thickness that complements axon morphology (diameter and density) with high specificity for assessment of demyelination in diseases such as multiple sclerosis. Previous work has shown that an aggregate g-ratio map can be computed using a formula that combines axon and myelin density measured with quantitative MRI. In this work, we computed g-ratio weighted maps in the cervical spinal cord of nine healthy subjects. We utilized the 300 mT/m gradients from the CONNECTOM scanner for estimating the fraction of restricted water (fr) with high accuracy using the CHARMED model. Myelin density was estimated using the lipid and macromolecular tissue volume (MTV) method, derived from normalized proton density (PD) mapping. The variability across spinal level, laterality and subject were assessed using a three-way ANOVA. The average g-ratio value obtained in the white matter was 0.76 +/- 0.03, consistent with previous histology work. Coefficients of variation of fr and MTV were respectively 4.3% and 13.7%. fr and myelin density were significantly different across spinal tracts (p = 3x10(-7) and 0.004 respectively) and were positively correlated in the white matter (r = 0.42), suggesting shared microstructural information. The g-ratio did not show significant differences across tracts (p=0.6). This study suggests that fr and myelin density can be measured in vivo with high precision and that they can be combined to produce a map robust to free water pool contamination such as cerebrospinal fluid or veins and weighted by the myelin g-ratio. Potential applications include the study of early demyelination in multiple sclerosis and the quantitative assessment of remyelination drugs.

Quantitative magnetic resonance imaging (qMRI) aims to quantify tissue parameters by eliminating instrumental bias. We describe qMRI theory, simulations, and software designed to estimate proton density (PD), the apparent local concentration of water protons in the living human brain. First, we show that, in the absence of noise, multichannel coil data contain enough information to separate PD and coil sensitivity, a limiting instrumental bias. Second, we show that, in the presence of noise, regularization by a constraint on the relationship between T1 and PD produces accurate coil sensitivity and PD maps. The ability to measure PD quantitatively has applications in the analysis of in-vivo human brain tissue and enables multisite comparisons between individuals and across instruments.
In order to better understand whether white matter structural deficits are present in strabismic amblyopia, we performed a survey of the tissue properties of 28 major white matter tracts using diffusion and quantitative magnetic resonance imaging approaches.

Anorexia nervosa (AN) is a serious eating disorder that typically emerges during adolescence and occurs most frequently in females. To date, very few studies have investigated the possible impact of AN on white matter tissue properties during adolescence, when white matter is still developing. The present study evaluated white matter tissue properties in adolescent girls with AN using diffusion MRI with tractography and T1 relaxometry to measure $R_1$ (1/T1), an index of myelin content. Fifteen adolescent girls with AN (mean age = 16.6 years ± 1.4) were compared to fifteen age-matched girls with normal weight and eating behaviors (mean age = 17.1 years ± 1.3). We identified and segmented 9 bilateral cerebral tracts (18) and 8 callosal fiber tracts in each participant's brain (26 total). Tract profiles were generated by computing measures for fractional anisotropy (FA) and $R_1$ along the trajectory of each tract. Compared to controls, FA in the AN group was significantly decreased in 4 of 26 white matter tracts and significantly increased in 2 of 26 white matter tracts. $R_1$ was significantly decreased in the AN group compared to controls in 11 of 26 white matter tracts. Reduced FA in combination with reduced $R_1$ suggests that the observed white matter differences in AN are likely due to reductions in myelin content. For the majority of tracts, group differences in FA and $R_1$ did not occur within the same tract. The present findings have important implications for understanding the neurobiological factors underlying white matter changes associated with AN and invite further investigations examining associations between white matter properties and specific physiological, cognitive, social, or emotional functions affected in AN.

Models of diffusion MRI within a voxel are useful for making inferences about the properties of the tissue and inferring fiber orientation distribution used by tractography algorithms. A useful model must fit the data accurately. However, evaluations of model-accuracy of commonly used models have not been published before. Here, we evaluate model-accuracy of the two main classes of diffusion MRI models. The diffusion tensor model (DTM) summarizes diffusion as a 3-dimensional Gaussian distribution. Sparse fascicle models (SFM) summarize the signal as a sum of signals originating from a collection of fascicles oriented in different directions. We use cross-validation to assess model-accuracy at different gradient amplitudes (b-values) throughout the white matter. Specifically, we fit each model to all the white matter voxels in one data set and then use the model to predict a second, independent data set. This is the first evaluation of model-accuracy of these models. In most of the white matter the DTM predicts the data more accurately than test-retest reliability; SFM model-accuracy is higher than test-retest reliability and also higher than the DTM model-accuracy, particularly for measurements with (a) a b-value above 1000 in locations containing fiber crossings, and (b) in the regions of the brain surrounding the optic radiations. The SFM also has better parameter-validity: it more accurately estimates the fiber orientation distribution function (fODF) in each voxel, which is useful for fiber tracking.
Properties of human brain tissue change across the lifespan. Here we model these changes in the living human brain by combining quantitative magnetic resonance imaging (MRI) measurements of R1 (1/T1) with diffusion MRI and tractography (N=102, ages 7-85). The amount of R1 change during development differs between white-matter fascicles, but in each fascicle the rate of development and decline are mirror-symmetric; the rate of R1 development as the brain approaches maturity predicts the rate of R1 degeneration in aging. Quantitative measurements of macromolecule tissue volume (MTV) confirm that R1 is an accurate index of the growth of new brain tissue. In contrast to R1, diffusion development follows an asymmetric time-course with rapid childhood changes but a slow rate of decline in old age. Together, the time-courses of R1 and diffusion changes demonstrate that multiple biological processes drive changes in white-matter tissue properties over the lifespan.

Visual processing in the magnocellular pathway is a reputed influence on word recognition and reading performance. However, the mechanisms behind this relationship are still unclear. To explore this concept, we measured reading rate, speed-discrimination, and contrast detection thresholds in adults and children with a wide range of reading abilities. We found that speed discrimination thresholds are higher in children than in adults and are correlated with age. Speed discrimination thresholds are also correlated with reading rates but only for real words, not pseudo-words. Conversely, we found no correlations between contrast detection thresholds and the reading rates. We also found no correlations between speed discrimination or contrast detection and WASI subtest scores. These findings indicate that familiarity is a factor in magnocellular operations that may influence reading rate. We suggest this effect supports the idea that the magnocellular pathway contributes to word reading through an analysis of letter position.

A central finding of functional MRI studies is the highly selective response of distinct brain areas in the occipital temporal cortex to faces and places. However, little is known about the association of white matter fibers with the processing of these object categories. In the current study we used DTI-based tractography to reconstruct two main fibers that connect the occipital lobe with the anterior temporal lobe (inferior longitudinal fasciculus-ILF) and with the frontal lobe (inferior fronto-occipital fasciculus-IFOF) in normal individuals. In addition to MRI scans subjects performed face, scene and body recognition tasks outside the scanner. Results show that recognition of faces and scenes were selectively associated with separate parts of the ILF. In particular, face recognition was highly associated with the fractional anisotropy (FA) of the anterior part of the ILF in the right hemisphere. In contrast, scene recognition was strongly correlated with the FA of the posterior and middle but not the anterior part of the ILF bilaterally. Our findings provide the first demonstration that faces and places are not only associated with distinct brain areas but also with separate parts of white matter fibers.

The vertical occipital fasciculus (VOF) is the only major fiber bundle connecting dorsolateral and ventrolateral visual cortex. Only a handful of studies have examined the anatomy of the VOF or its role in cognition in the living human brain. Here, we trace the contentious history of the VOF, beginning with its original discovery in monkey by Wernicke (1881) and in human by Obersteiner (1888), to its disappearance from the literature, and recent reemergence a century later. We introduce an algorithm to identify the VOF in vivo using diffusion-weighted imaging and tractography, and show that the VOF can be found in every hemisphere (n = 74). Quantitative T1 measurements demonstrate that tissue properties, such as myelination, in the VOF differ from neighboring white-matter tracts. The terminations of the VOF are in consistent positions relative to cortical folding patterns in the dorsal and ventral visual streams. Recent findings demonstrate that these same anatomical locations also mark cytoarchitectonic and functional transitions in dorsal and ventral visual cortex. We conclude that the VOF is likely to serve a unique role in the communication of signals between regions on the ventral surface that are important for the perception of visual categories (e.g., words, faces, bodies, etc.) and regions on the dorsal surface involved in the control of eye movements, attention, and motion perception.

2013


Neurons within a small (a few cubic millimeters) region of visual cortex respond to stimuli within a restricted region of the visual field. Previous studies have characterized the population response of such neurons using a model that sums contrast linearly across the visual field. In this study, we tested linear spatial summation of population responses using blood oxygenation level-dependent (BOLD) functional MRI. We measured BOLD responses to a systematic set of contrast patterns and discovered systematic deviation from linearity: the data are more accurately explained by a model in which a compressive static nonlinearity is applied after linear spatial summation. We found that the nonlinearity is present in early visual areas (e.g., V1, V2) and grows more pronounced in relatively anterior extrastriate areas (e.g., LO-2, VO-2). We then analyzed the effect of compressive spatial summation in terms of changes in the position and size of a viewed object. Compressive spatial summation is consistent with tolerance to changes in position and size, an important characteristic of object representation.

Mezer, A, Yeatman JD, Stikov N, Kay KN, Cho N-J, Dougherty RF, Perry ML, Parvizi J, Hua LH, Buttspauly K et al.. 2013 Quantifying the local tissue volume and composition in individual brains with magnetic resonance imaging. Abstract [65]

Here, we describe a quantitative neuroimaging method to estimate the macromolecular tissue volume (MTV), a fundamental measure of brain anatomy. By making measurements over a range of field strengths and scan parameters, we tested the key assumptions and the robustness of the method. The measurements confirm that a consistent quantitative estimate of MTV can be obtained across a range of scanners. MTV estimates are sufficiently precise to enable a comparison between data obtained from an individual subject with control population data. We describe two applications. First, we show that MTV estimates can be combined with T1 and diffusion measurements to augment our understanding of the
tissue properties. Second, we show that MTV provides a sensitive measure of disease status in individual patients with multiple sclerosis. The MTV maps are obtained using short clinically appropriate scans that can reveal how tissue changes influence behavior and cognition.


Visual neuroscientists have discovered fundamental properties of neural representation through careful analysis of responses to controlled stimuli. Typically, different properties are studied and modeled separately. To integrate our knowledge, it is necessary to build general models that begin with an input image and predict responses to a wide range of stimuli. In this study, we develop a model that accepts an arbitrary band-pass grayscale image as input and predicts blood oxygenation level dependent (BOLD) responses in early visual cortex as output. The model has a cascade architecture, consisting of two stages of linear and nonlinear operations. The first stage involves well-established computations-local oriented filters and divisive normalization-whereas the second stage involves novel computations-compressive spatial summation (a form of normalization) and a variance-like nonlinearity that generates selectivity for second-order contrast. The parameters of the model, which are estimated from BOLD data, vary systematically across visual field maps: compared to primary visual cortex, extrastriate maps generally have larger receptive field size, stronger levels of normalization, and increased selectivity for second-order contrast. Our results provide insight into how stimuli are encoded and transformed in successive stages of visual processing.

2012


The present invention provides methods to detect degenerative processes and abnormalities in soft tissues at high spatial resolution, high signal-to-noise ratio and short scanning times, based on quantitative tissue properties. These methods might provide a useful tool to detect and assess abnormalities in soft tissues and to monitor disease progression.

2011


Diffusion imaging and bound pool fraction (BPF) mapping are two quantitative magnetic resonance imaging techniques that measure microstructural features of the white matter of the brain. Diffusion imaging provides a quantitative measure of the diffusivity of water in tissue. BPF mapping is a quantitative magnetization transfer (qMT) technique that estimates the proportion of exchanging protons bound to macromolecules, such as those found in myelin, and is thus a more direct measure of myelin content than diffusion. In this work, we combined BPF estimates of macromolecular content with measurements of diffusivity within human white matter tracts. Within the white matter, the correlation between BPFs and
Diffusivity measures such as fractional anisotropy and radial diffusivity was modest, suggesting that diffusion tensor imaging and bound pool fractions are complementary techniques. We found that several major tracts have high BPF, suggesting a higher density of myelin in these tracts. We interpret these results in the context of a quantitative tissue model.

2009


Functional MRI (fMRI) has become one of the leading methods for brain mapping in neuroscience. Recent advances in fMRI analysis were used to define the default state of brain activity, functional connectivity and basal activity. Basal activity measured with fMRI raised tremendous interest among neuroscientists since synchronized brain activity pattern could be retrieved while the subject rests (resting state fMRI). During recent years, a few signal processing schemes have been suggested to analyze the resting state blood oxygenation level dependent (BOLD) signal from simple correlations to spectral decomposition. In most of these analysis schemes, the question asked was which brain areas "behave" in the time domain similarly to a pre-specified ROI. In this work we applied short time frequency analysis and clustering to study the spatial signal characteristics of resting state fMRI time series. Such analysis revealed that clusters of similar BOLD fluctuations are found in the cortex but also in the white matter and sub-cortical gray matter regions (thalamus). We found high similarities between the BOLD clusters and the neuro-anatomical appearance of brain regions. Additional analysis of the BOLD time series revealed a strong correlation between head movements and clustering quality. Experiments performed with T1-weighted time series also provided similar quality of clustering. These observations led us to the conclusion that non-functional contributions to the BOLD time series can also account for symmetric appearance of signal fluctuations. These contributions may include head motions, the underlying microvasculature anatomy and cellular morphology.

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