THE HUMAN CONNECTOME PROJECT: ADVANCES IN DIFFUSION MRI ACQUISITION AND PREPROCESSING

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Target Audience: This work will be of immediate interest to scientists studying brain anatomical connectivity, white matter tractography approaches and diffusion MRI acquisition and low-level modelling.

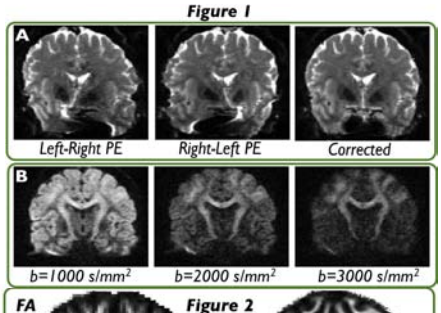
Purpose: The Human Connectome Project (HCP) is an ambitious 5-year effort to map human brain connections and their variability in healthy adults [1], [2]. A consortium of HCP investigators will study a population of 1200 subjects (from ~400 families and including twins and their non-twin siblings) using multiple imaging modalities, along with extensive behavioral and genetic data. In this overview, we focus on diffusion-weighted (DW) MRI and the structural connectivity aspect of the project. We present recent advances in acquisition and preprocessing that allow us to obtain very high-quality *in-vivo* MRI data, while achieving the aim of scanning a very large number of subjects. These advances result from 2 years of intensive efforts in optimising many aspects of data acquisition and processing during the piloting phase of the project. The data quality described here is representative of the datasets that will be released to the community at quarterly intervals, beginning in 2013.

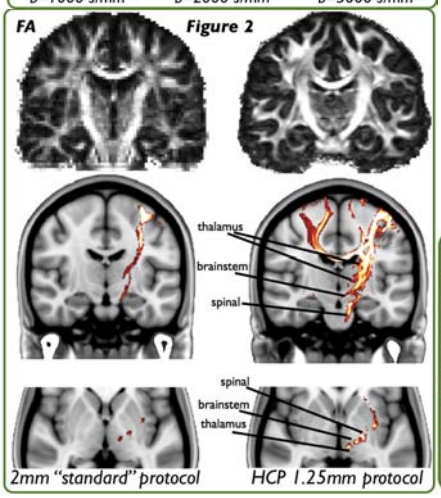
Methods: A Siemens 3T Skyra system is being used to scan all 1200 subjects (started in August 2012). The scanner was modified to include a Siemens SC72 gradient coil with maximum gradient strength of 100 mT/m [1]. High gradient amplitudes are beneficial for DW-MRI, as they allow shortening of the diffusion encoding period and the echo time (TE), and thus increases in the signal to noise ratio (SNR) and decreases in the repetition time (TR). A 32-channel coil is used for parallel receive.

Acquisition Protocol: A major state-of-the-art feature of the acquisition protocol is the achieved acceleration using multiband (MB) excitation [3, 4]. N brain slices can be excited simultaneously, while sharing diffusion preparation, leading to a N-fold reduction in the TR and subsequent scanning time. The final protocol was achieved after extensive piloting that included low and higher level features, such as RF pulse shapes, timings, flip angles, partial Fourier factors, fat saturation options, T1 relaxation effects, phase encoding (PE) directions, monopolar and bipolar sequences, spatial resolution, MB acceleration factors, in-plane accelerations, gradient non-linearities, slice excitation orders, image reconstruction options, subject tolerance and *q*-space sampling schemes. The HCP DW-MRI scans utilise monopolar Stejskal-Tanner pulsed gradients, single-shot 2D EPI acquisition, with 6/8 partial Fourier and MB=3. Spatial resolution is **1.25mm isotropic** (matrix size 144x168) and *q*-space sampling includes 3 shells at b=1000, 2000 and 3000 s/mm^2 (diffusion times are Δ=43.1 ms and δ=10.6 ms). TE and TR are matched across shells (TE=89 ms, TR=5.5s) and phase encoding is applied along the left-right (LR) direction. For each shell, 190 datapoints are obtained, corresponding to 90 DW directions and 5 b=*0*'s acquired twice, with the phase encoding direction reversed for each pair (i.e. LR and RL pairs). Directions are optimised within and across shells (i.e. staggered) to maximize angular coverage using the approach of [5], and form a total of 270 non-colinear directions for each PE direction. Cardiac monitoring during the scan will allow for retrospective cardiac-gating. Total scanning time for whole-brain coverage (110 slices) is ~55 minutes. Note, a similar acquisition would take 3-4 hours with conventional methods and scanners, while also having much less SNR.

Preprocessing: To minimise biases and noise floor effects in tractography [6], magnitude images are reconstructed from the multiple channels using a SENSE R=1 approach [7]. The preprocessing pipeline includes distortion correction and fibre orientation estimation. Distortion correction takes advantage of the complementary information included in the LR/RL pairs and considers susceptibility, eddy-current and head motion induced distortions [8,9]. The susceptibility induced off-resonance field is calculated from b=*0* pairs [8]. This is then fed into a Gaussian process predictor [9] that additionally estimates the eddy-current induced field and the head motion for each volume, allowing the correction of all these distortions in a single resampling step. The preprocessed data are then used in a model-based approach for estimating fibre orientations [10]. This model allows for multi-exponential decay in q-space, by considering a distribution of diffusivities for each voxel, and performs *multi-shell parametric spherical deconvolution*. Fibre orientations and their uncertainty are obtained using a Bayesian inference framework [11] (Rician noise model).

Due to the high performing gradients used and subject positioning limitations of the customized scanner, significant spatial gradient nonuniformities exist [12]. For DW-MRI, these can alter both the actual strength and orientation of any diffusion-sensitising gradient from their nominal values. To account for these artifacts we utilise the corrections in [12] to obtain individual b values and gradient orientations for every voxel. We also correct for geometric distortions caused by the imaging gradients.

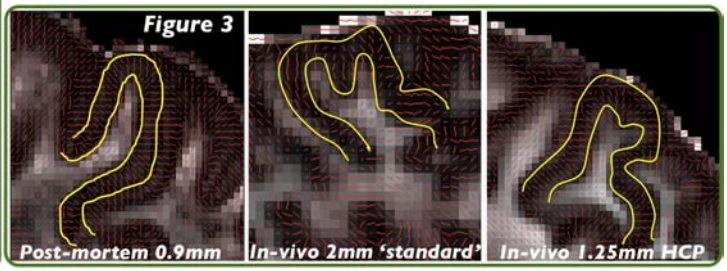




Results & Discussion: Figure 1A illustrates an example of the raw HCP data (two b=0's acquired using reversed PE directions) and the preprocessed data, corrected for susceptibility-induced distortions. Panel B illustrates exemplar DW images (coronal views) after preprocessing, at all three b values acquired. Notice the high SNR of these images, despite the very high spatial resolution. Figure 2 shows a qualitative comparison between the HCP protocol-pipeline and a "standard" DW-MRI protocol (i.e. data acquired at 2mm isotropic resolution on a Siemens 3T Trio). The first row illustrates coronal views of fractional anisotropy (FA) maps. The second and third row show probabilistic tractography results [11] on the different datasets. Path probability maps are presented in coronal and axial views, respectively, when seeding in the hand area of the primary motor cortex. Tractography using the HCP datasets is much more sensitive and reveals known cortical projections that cannot be reconstructed using standard datasets. In addition to connections to the contralateral hemisphere, particular branches are revealed that correspond to cortico-thalamic, cortico-spinal and cortico-bulbar paths.

Another example of the new capabilities the HCP data will offer is the ability to capture cortical radial anisotropy, as shown in Figure 3. This is a feature that has been reported in very high quality and high resolution post-mortem data [13]. It is not evident in "standard" in-vivo data, but is now clear in the HCP datasets.

HCP datasets (including resting-state fMRI, task fMRI, DW-MRI and structural) will be made freely available in early 2013 (http://www.humanconnectome.org) and at quarterly intervals. A new piloting stage has begun to explore DW-MRI acquisitions on a Siemens 7T scanner (200 subjects will be scanned), which also has SC72 gradients and eventual 64 channel receive capability [1]. New acceleration approaches, such as compressed sensing [14], will be explored and combined with multiband. We are also exploring new methods for fibre orientation estimation [15] and tractography, including direct quantification of fibre dispersion [16].



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