Studying Developmental Brain Connectivity in Chimpanzees using High-Resolution Diffusion MRI

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Introduction

The evolutionary origin of human brain function and its connectivity is not yet well understood. This knowledge gap may be closed by comparing human brain connectivity with that of great apes, (e.g., Chimpanzees) (1,2). However, ethical concerns about primate research prohibit neuroimaging research on great apes (3). Therefore, evolutionary neuroscience relies on a small number of previously acquired diffusion MRI (dMRI) data. We here present a novel approach for dMRI data acquisition in great apes, utilizing post-mortem chimpanzee brains from naturally deceased animals originating from African wildlife field-sites, sanctuaries, and European zoos. We optimize and compare the achievable dMRI quality for post-mortem dMRI acquisitions on a human and preclinical MRI system using two different sequences. The resulting data quality allowed an isotropic resolution of 500µm which represents the highest dMRI resolution yet achieved in great apes.

Methods

Tissue Samples
The wild animal brains used for this research originate from African wildlife field-sites. The captive animal brains originate from African animal sanctuaries and European zoos. The brains were extracted within a post-mortem interval of only 2-24h and immersion-fixed with 4% paraformaldehyde in PBS and immersed in Fomblin for scanning.

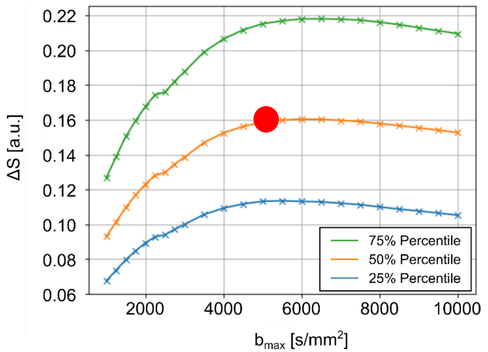
Pre-scan for Optimal Diffusion-Weighting
Optimal diffusion-weighting was determined using pre-scans, acquired using a 3T Connectom MRI System (Siemens Healthineers, Germany). Diffusion-weighted pre-scan acquisitions were acquired with a low isotropic resolution of 2mm in 22 diffusion shells, ranging from b=1.000s/mm^2 to b=10.000s/mm^2. Diffusion-contrast was assessed per shell, as the diffusion signal difference between the main and perpendicular DTI orientation per voxel, ΔS.

MRI Acquisitions and System Comparison
High-resolution dMRI sequences with optimal diffusion parameters and an isotropic resolution of 500µm were set up on two different MRI systems – a 3T Connectom and a 9.4T Bruker Biospec 94/30. Both systems feature a minimum 30 cm wide magnet-bore accommodating entire chimpanzee brains (5). Diffusion MRI sequences were optimized for high-resolution image quality under consideration of system-specific hardware constraints (6–9) (Table). Voxel wise SNR of the b=0s/mm^2 data was calculated for both systems on one brain.

Data Processing
Data processing included debiasing (11), denoising (12), temperature drift correction, and correction of sample movement and distortion (13). The temperature drift correction compensates for tissue diffusivity that increases with temperature over time, due to heating (Fig. 3). For this purpose, a volume-specific factor is calculated, which scales signal intensities to match steady-state temperature conditions. Initial tractography and visualization of the processed dataset was performed using brainGL.

MRI System	Siemens Connectom	Bruker Biospec 94/30
Field Strength	3.0 T	9.4 T
RF Coil	Siemens 32 Ch Head Coil	Bruker 154 mm
Gradient System	G_{max}=300 mT/m Slew=200 T/m/s	G_{max}=300 mT/m Slew=1040 mT/m/ms
Encoding Strategy	3D Segmented EPI Multi Echo dMRI, 4 Echoes	3D Segmented EPI Double EPI Sampling
Spin Echo	Single Spin Echo with Sinc RF Pulse	Double Spin Echo with Adiabatic 180° RF Pulses
Resolution	0.5 mm isotropic	0.5 mm isotropic
Repetition Time	1000 ms	1000 ms
Echo Time	72, 94, 116, 138 ms	58.9 ms
Segmentation Factor	26	32
Matrix Size	256 x 208 x 144	240 x 192 x 144
Phase Encoding	LR	LR
Diffusion Directions	60	58

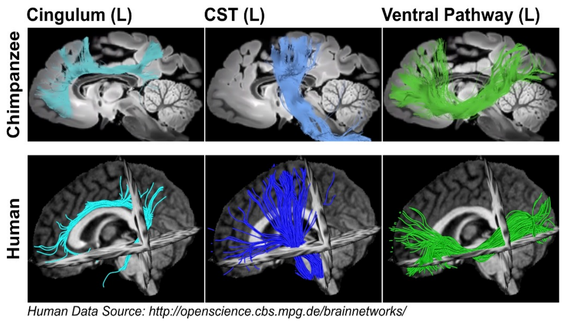
Diffusion Contrast Assessment



Assessment of optimal diffusion-weighting The DTI contrast, ΔS, was assessed between 22 diffusion-weightings, ranging from b=1.000s/mm^2 to b=10.000s/mm^2. The plot displays the whole volume distribution of ΔS of one representative brain. The optimal diffusion-weighting was chosen as the b-value generating the highest median contrast (b=5.000s/mm^2).

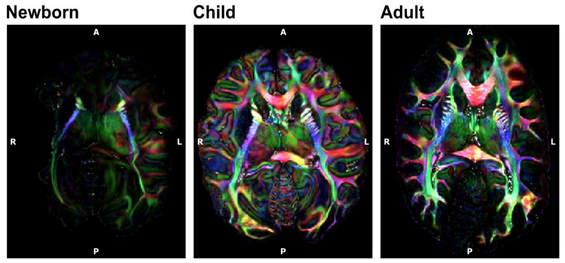
Reconstructions from Preclinical MRI System and Project Status (**Top**) The high-resolution dMRI data enables tractography on fine spatial levels. Three respective tract reconstructions are depicted: Cingulum (turquoise), Corticospinal Tract (blue) und Ventral Pathway (green) (**Bottom**) Diffusion data were acquired from various age groups, enabling a developmental comparison between chimpanzees.

High Resolution Fiber Tract Reconstruction

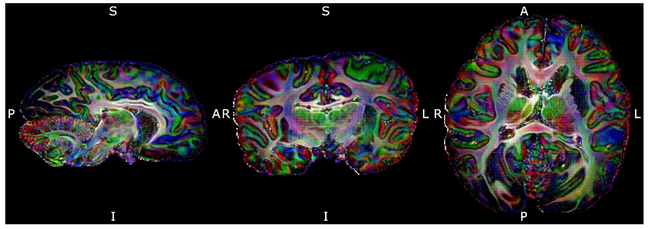


Human Data Source: http://openscience.cbs.mpg.de/brainnetworks/

First Chimpanzee dMRI Data from Different Ages

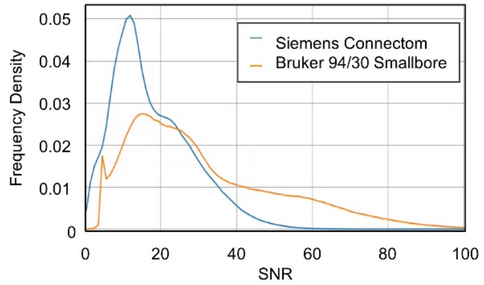


High Resolution DTI Reconstructions from Preclinical Scanner



Preclinical Scanner Acquisition Data Quality The 500µm isotropic high-resolution dMRI data, acquired at the preclinical 9.4T MRI system allow mapping the structural connectivity of the chimpanzee brain with unprecedented image resolution. (LR – Left Right, AP – Anterior Posterior, SI – Superior Inferior)

SNR Scanner Comparison



Comparison of Post-Mortem dMRI Sequences (**Top**) Employed MRI acquisition hardware and sequences (**Bottom**) The SNR comparison between Siemens Connectom Bruker Biospec Acquisitions indicated an increased SNR for the preclinical Bruker system.

Discussion

- We present the highest resolution dMRI data yet collected in great apes (specifically chimpanzees)
- The dMRI data allow tractography reconstructions to compare structural connectivity between chimpanzees and humans.
- The non-invasive selection of naturally deceased animals from the wild provides access to brains of all ages.
- Enables novel access to the development of ape brain connectivity and allows to relate the brain structure to behavioral characteristics.

References

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