High-throughput, Python-based processing pipeline for pre-clinical MRI data

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Experimental Setup

MRI System

Figure 1: The MRI data was acquired with a 9.4T BioSpec Bruker system (Bruker, BioSpin, Ettlingen, Germany). We used 25 C57BL/6J mice (10-12 weeks, male), which underwent photothrombosis to induce focal lesions or sham surgery and received 6x MRI (T2-weighted, DTI, rs-fMRI) during a 4 week experiment. Animal fixation is enabled by an animal carrier like shown and includes tooth and ear holder to minimizes the motion of the head relatively to the scanner during the MRI data acquisition.

Behaviour Tests

Figure 2: Illustrations of three behavioural tests **Grid Walk Test** (top left) evaluates the sensorimotor co-ordination of the limbs by observing exact paw placement on a metal mesh. **Rotating Beam Test** (left) to assess fine coordination and balance deficits. The beam is coupled to a motor which rotates the beam clockwise with 6 rpm. Speed and distance of the mouse is influenced if the right or left hindlimb slips. **Cylinder Test** (right) examines the rodents asymmetrical behaviour as they explore the environment. If the rodent straightens up, the contacts of the front limbs with the cylinder wall are counted.

3D Template / 3D Allen Brain Atlas

Figure 3: (left side) An anatomical MRI template (Neuprop template) was developed by merging 30 independent MRI datasets. This template lies perfectly over the annotations of the Allen Brain atlas (right side) and helps to associate MRI date to atlas regions

Monitoring for Regression

Figure 4: Screenshot of the DASYLab monitoring. The software record all monitoring information on the current session and is necessary for subsequent regression.

Quality Measurement

Signal-to-Noise Ratio

Figure 5: Automatic noise variance estimation have been designed from the knowledge that this background mode can be represented by a density function. The pipeline measures SNR with three well know full-automatic SNR calculation, by using the algorithm of Brummer et. al. , Chang and Sijbers

Bias Field Correction

Correction with MICO / **Correction with N3**

Coefficient of variations (CV) MICO vs. N3

Figure 6: To measure the bias field of MRI data we tested the well known N3-against MICO algorithm. MICO (Multiplicative intrinsic component optimization) has so far only been clinically tested and is fully integrated into the pipeline (top left) Brain extraction after MICO bias field correction (top right) brain extraction after N3 bias field correction (left) Coefficient of variations of whole mouse brain over 15 individuals.

Registration

Figure 7: The brain structures of the T2 weighted MRI show time stronger times weaker deformation caused by the experimental stroke. It is necessary that the registration is able to describe those deformation in a sufficient manner, like shown in the figure. Therefore, we used a the combination of an affine and non-linear transformation.

Acknowledgements/Disclosure

Pipeline flowchart

Functional & Structural MRI · Database · Behavior · Convert

T_2 Map · DTI · rsfMRI

SNR · e^x-Fit

Preprocessing — Bias correction / Skull stripping

Stroke Mask

Allen Brain Atlas · Neuprop Template

Registration — Affine / BSpline / Resample

Incidence Map

SRC files / Tracking / Connectometry

DSI - Studio

Connectivity Matrix

Feature Extraction

Classification — Restricted ✓ / Not-Restricted ✗

4D → 3D / Skull stripping

Preprocessing · Motion Corr. · Regression · Monitoring

Preprocessing — Bias correction / Skull stripping

Filter · Registration · FSL - Nets

Resulting Features

Stroke Volume [%]

Affected Regions

Connectivity Graph of DTI

Adjacency matrix of rsfMRI

Figure 9: Defining effective features is in our case a difficult task. The figure shows the manifoldness of our data. We ca extract the lesion size (upper left) and affected regions (upper right) over the time. The DTI and rsfMRI processing will end up with adjacency matrices (lower right) and graphs (lower left), which tends to a huge amount of graph theoretical properties e.g. connectivity, efficiency, transivety.

Structural Similarity Measurement

Figure 8: Quantitative quality assurance of registration procedure by using structural similarity index measurement (SSIM). Two independent observer registered 15 brain MRI data manually with the Allen brain reference atlas (ARA) by using a point based registration. The median of the similarity between the 1st observer (Obsv. 1) and 2nd observer is 0.915. The similarity of automated registration to 1st observer and 2nd observer differs from the reference value with 0.021 and with 0.025. Thus, the registration shows that it has a sufficient ability to associate MRI to MRI data. Based on this initial transformation, the registration to DTI and rsfMRI is determined.