Inter hemispheric transfer time and axon diameter properties of the corpus callosum

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Introduction: The corpus callosum (CC) is one of the largest fiber systems in the brain connecting and transferring information between the two hemispheres. Previous histological studies showed that the axon diameter distribution varies significantly at different parts of the CC (1). Axcaliber is a diffusion MRI methodology the thorough analysis of multi-diffusion time, high b value DWI acquisition, allows the estimation of the axon diameter distribution (ADD) (2). This method was implemented in-vivo for measuring the ADD along the CC of the rat and segmenting it to its neuro-anatomical components. In this study we aimed to examine the inter-hemispheric transfer time (IHTT) and its relation to different axonal properties of the CC. For this purpose we have implemented AxCaliber on a human 3T scanner and used the Poffenberger paradigm (3) for measuring the IHTT for two CC domains: tactile/sensory and visual.

Methods:

Behavioral paradigm: Visual-motor and Tactile trails:13 right handed subjects (6 male and 7 female), underwent a manual RT task according to Poffenberger paradigm (3). In the visual experiment, subjects were required to press a button in response to lateralized presented stimuli while maintaining fixation in the center of the screen. In the tactile experiment subjects were required to press a button in response to a tactile stimuli in dorsal mid-calf. Median RT determined for each of the four visual/tactile hemi-field (left visual/tactile vs. right visual/tactile fields: LVF vs RVF, LTF vs. RTF)) and by hand (left vs. right: LH vs. RH) conditions. Then, the RT-based IHTT (crossed-uncrossed difference [CUD]) was calculated by subtracting the average RT of the two uncrossed response conditions (LVF-LH, RVF-RH/LTF-LH, RTF-RH) from the average RT of the two crossed conditions (LVF-RH, RVF-LH/LTF-RH, RTF-LH).

MRI protocol:6 right handed subjects underwent MRI scan (GE 3T MRI). The experimental protocol consisted of a series of diffusion-weighted spin-echo echo-planar-imaging acquisitions. The experiment was repeated for 4 different diffusion times: 27.7ms, 47.4ms, 67.7ms and 87.7ms with the following parameters of TE = 137.5ms, 123.7ms, 112.7ms and 106.7ms respectively. The rest of the parameters where fixed: δ =21ms, TR=6,000 ms, FOV=192mm and resolution of 1.5x1.53mm^3 (acquired at the saggital plane).28 diffusion gradient increments (linearly from 0 to 4G/cm) were applied only along the x-direction, which is perpendicular to the CC . Voxel-by-voxel analysis was performed on the mid-sagittal slice using the AxCaliber framework (4). The out parameters of AxCaliber (the gamma function parameters as well as the volume fraction of the diffusion components) were used as an input to a clustering algorithm (k-means) with 4-5 clusters.

Results and Conclusions: Behavioral results match the previous findings with the Poffenberger paradigm (Fig. 1). The IHTT for stimuli presented to the ipsilateral side were shorter than the contralateral side in the visual trails and in the tactile one. We were also able to reconstruct the asymmetric IHTT phenomenon and find that the CUD from the right to the left hemisphere is faster than the CUD from the left to the right hemisphere. Using AxCaliber we were able to segment the CC to distinct regions (Fig. 2) corresponding to the genu (cluster 1), body (clusters 2 and 3) and splenium (clusters 4/5) for all subjects. Although the computed ADD are only relative and not absolute number due to the low gradient strength and long gradient pulse, their shape seems to be in excellent agreement with the literature: The most anterior part of the CC (the genu) exhibited a narrow ADD with a small mean diameter (2.1 μm) (Fig. 3). The cluster that represents the body of the CC, which corresponds to fibers that connect the somato-sensory cortex, exhibited the broadest ADD of all measured clusters with mean diameter of 3.55 μm. More posterior parts (splenium of the CC, that connects the visual areas) exhibited a narrower ADD than the body. These micro-structural differences are the base for the behavioral reaction time (IHTT, Fig. 1) differences between the two domains. This work presents in-vivo measurements of the Human relative axon-diameter distribution. AxCaliber was able to reconstruct the diameter distribution within the Human corpus callosum and demonstrate that ADD corresponds to known morphometry in the CC. Further investigation of the relation between white matter micro-structure and behavioral or electro-physiology (through EEG) should be performed. Such studies can set AxCaliber and similar diffusion based measures of white matter micro-structure as the first in-vivo indication of white matter physiology.

Fig.1: Behavioral results of the visual (A) and tactile(B) trails.

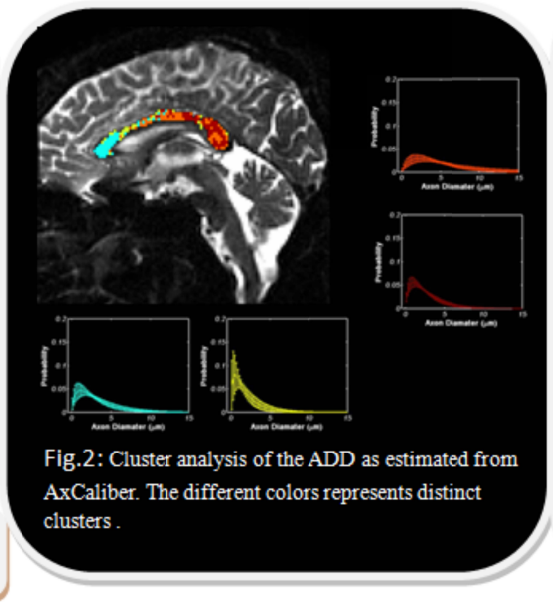

Fig.2: Cluster analysis of the ADD as estimated from AxCaliber. The different colors represents distinct clusters .

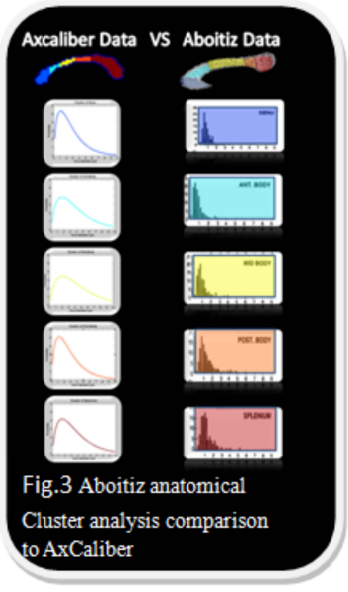

Fig.3 Aboitiz anatomical Cluster analysis comparison to AxCaliber

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