In vivo Diffusion Spectrum imaging disentangles white and gray matter connectivity in the human cerebellum

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Background: The cerebellum is a complex brain structure, which plays a major role in movement control and cognitive-emotional processing[1]. A number of congenital and acquired diseases affect cerebellar anatomy and function such as inherited and acquired ataxias, tumors, and stroke. To date, most of the knowledge of cerebellar structure has been obtained through invasive ex vivo approaches[2], conventional structural MRI [3] and diffusion tensor imaging [4, 5]. Available data are, however, incomplete and fail to accurately render cerebellar white and grey matter connectivity. Therefore, in clinical practice, non-invasive and accurate tools supporting markers of disease progression and prognosis are strongly desired. **Objectives:** Based on the histological knowledge of the intricate fiber-structure of the cerebellum, we hypothesized that high-angular resolution diffusion spectrum imaging (DSI) could provide an accurate depiction of cerebellar connectivity of both white and gray matter. **Methods:** Four healthy female subjects (Age: 26±4) underwent magnetic resonance DSI at 3 T (Trio a Tim System, Siemens, Erlangen, Germany) using a pre-product 32 channel head coil. (TR/TE=6600/138, FoV=212 mm, 34 slices, 2.2 mm isotropic resolution, 258 diffusion directions, b=8000 s/mm^2, 2 repetitions of 28 min each). High-resolution MPRAGE (TR: 2400 ms, TE: 3.59 ms, 0.8 mm isotropic resolution, FOV256x256) was acquired for anatomical reference. DSI tractography was performed based on a streamline algorithm using the TrackVis software[6]. On the basis of MPRAGE images and an MRI cerebellum atlas[7], 3D ROIs were selected to identify: 1) the intra-cortical cerebellar connectivity; 2) the three cerebellar peduncles, 3) the cerebellar deep nuclei (Nucleus Fastigial, Globose, Emboliform and Dentate) and their connectivity and 4) the connections of some brainstem structures (inferior olive and red nucleus), spinal cord and thalamus (ventral lateral ad intralaminar nucleus) to the cerebellum. **Results:** We disentangled - for the first time *in vivo* - the intra-cortical intersection of fiber-trajectories perpendicular to the cortical surface plane (Purkinje cells dendrites and axons, Golgi cell dendrites, climbing and mossy fibers) into the parallel network constituted by granule cells axons (figure 1). DSI tracking also provided new insight into the complex connectivity of the cerebellar deep nuclei (Nucleus Emboliform-figure 2 A, Globose and Fastigial-figure 2B and Dentate-figure 2C). In addition, we accurately and simultaneously visualized the inferior, middle and superior cerebellar peduncles as well as the rubro-cerebellar tract, the olivo-cerebellar tract, the posterior spino-cerebellar tract, and the connections between the cerebellum and the thalamus (figure 3). Results were consistent in all 4 subjects. **Conclusion:** Using DSI, we could unravel for the first time *in vivo* the complex cerebellar connectivity, both in white and gray matter. We overcame the intrinsic low-sensitivity of the DSI method by careful optimizations of the acquisition protocol and the use of a 32-channel surface coil array at 3T (2-3 fold SNR increase). Though further technical optimizations should aim at shorten the scanning time, DSI clearly proves to be a promising technique for identifying prognostic and monitoring markers of diseases affecting the cerebellum.

References : 1.Schmahmann J. et al., 2006; 2.Van Essen DC, 2002; 3. Makris N et al., 2005; 4. Salamon N et al., 2007; 5. Habas C et al., 2007; Wang R et al., 2007; 7. Schmahmann J. et al., 2000.