# Kiss to Cross ! Non-invasive Mapping of Cerebellar Dentate Nucleus Projections to the Cerebral Cortex

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**Introduction:** Post mortem connectivity based methods demonstrate that the cerebellar dentate nuclei act as the main center of communication to the cerebral cortex, which provides the general neural substrate. This influences not only the generation and control of movement, but also aspects of cognition and visuo-spatial perception [1,2,3]. With this in mind, an understanding of cerebellar dentate nuclei projections needs to be explained and understood as non-invasively. The cerebellar dentate nuclei have a contralateral connection with the cerebral cortex. However, direct invivo diffusion imaging of this crossing and dentate projections to the cortex via crossing is lacking [4]. DTI/ QBI/ DSI parameters give important information about the tissue microstructure and diffusion, but diffusion imaging is not a direct measurement of connectivity. Thus, prior connectional information is needed from other methods i.e. histology, tracer studies, fMRI, resting state fMRI [5,6,7], MEMRI and others. Based on Tracer studies of the dentate nucleus, we hypothesized that diffusion tractography may show the dentate nuclei's contralateral projections to the cortex and the integration of the resting state fMRI functional connectivity may aid the reliability of the connectional assessment.

**Material and Methods:** Six healthy volunteers (Age: 22-40) were imaged on a 3T Tim Trio scanner (Siemens, Erlangen, Germany). High-resolution **(a) T1** (TR/TE: 2300/ 3.46 ms, 1 mm isotropic resolution, FOV 266, 2 averages) , **(b) T2** (TR/TE: 2000/ 302 ms, 0.8 mm isotropic resolution, FOV 207), **(c) Resting state fMRI** (TR/TE: 3000/ 28 ms, 3 mm isotropic resolution, FOV 192 ) and **(d) diffusion data** 2,5 mm isotropic resolution, 126 diffusion directions, 2 averages, **1-4th subjects** (TR/TE= 9100/ 123 ms, FoV=200 mm, 59 slices, 14b0, b=3000 s/mm2), **5th subject** (TR/TE= 7800/ 112 ms, FoV=216 mm, 54 slices, 1b0, b=2800 s/mm2), **6th subject** (TR/TE= 7700/ 109 ms, FoV=216 mm, 54 slices, 14b0, b=2500 s/mm2 ) data was acquired. Data was preprocessed using FSL [8] i.e. eddy current correction, registration; segmentation using freesurfer [9]; resting state fMRI analysis ( AFNI [10] ); reconstruction and tractography ( FSL, MRtrix [11]) were performed. Diffusion and functional data was analyzed with the dentate nucleus as region of reference. Right and left dentate region of interests (ROIs) were manually delineated using atlas [12], thalamus connectivity based parcellation was performed [13] and the resulting regions were used as target regions for the dentate connectivity based segmentation.

**Results:** Here we present a view on kissing and crossing fiber visual representation, which shows the cerebellar dentate nuclei fibers, projecting to the thalamus, and fails to reach on the contralateral hemisphere [Fig. 1] but qbi resolves this problem [Fig. 2]. Manually delineated dentate and FSL connectivity based thalamus segments are showed [Fig. 2a]. These are important regions to consider for dentate-cortical projections. The Dentate projects to the motor, frontal, temporal and posterioparietal area of cortex via the corresponding thalamic nuclei [Fig. 2]. The dentate connectivity based parcellation depicts the dentate segregated functional regions. The primary motor (red), temporal (blue), sensory (green), pre-motor (yellow), pre-frontal (cool), posterior parietal (copper) and occipital cortex (MGH cortical) are color coded. The corresponding connectivity based thalamic regions are also in same color code and same with the dentate. The dentate shows a segregation within different thalamic areas [Fig. 3]. The resting state data analysis shows positive and negative cross-correlated regions [Fig. 4].

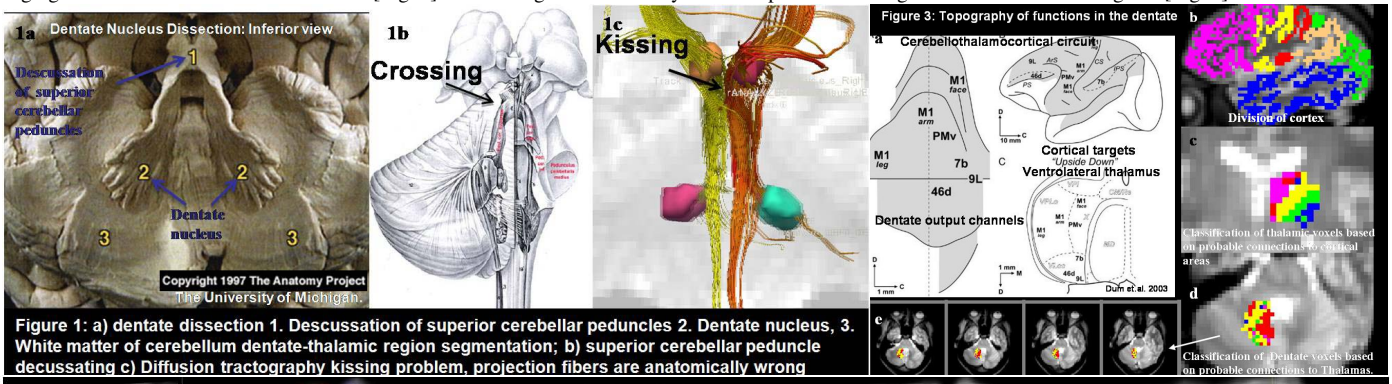


**Figure 1: a) dentate dissection 1. Descussation of superior cerebellar peduncles 2. Dentate nucleus, 3. White matter of cerebellum dentate-thalamic region segmentation; b) superior cerebellar peduncle decussating c) Diffusion tractography kissing problem, projection fibers are anatomically wrong**

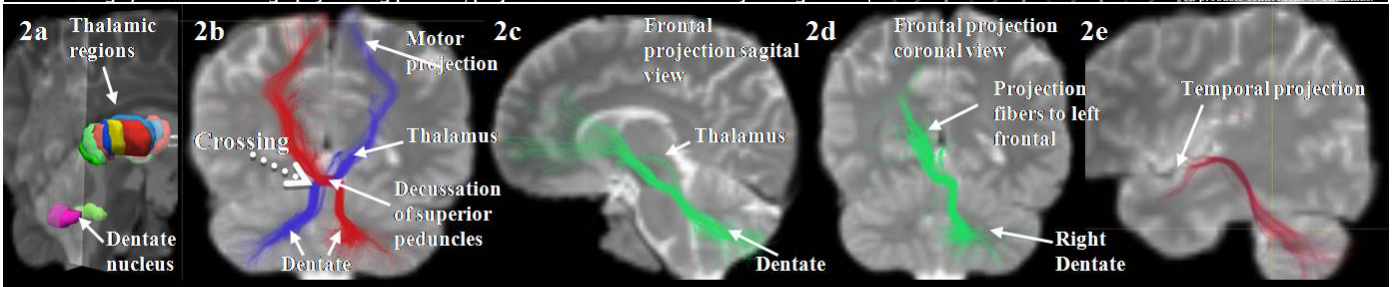


**Figure 2. Dentate to cerebral cortex : a) dentate-thalamic regions b) right and left dentate projection; superior cerebellar peduncle decussating, and projecting to motor area via thalamic motor nuclei. c) Projection fibers from right dentate nucleus to frontal cortex via pre frontal thalamic nuclei. d) coronal view of 'c' e) temporal projection.**

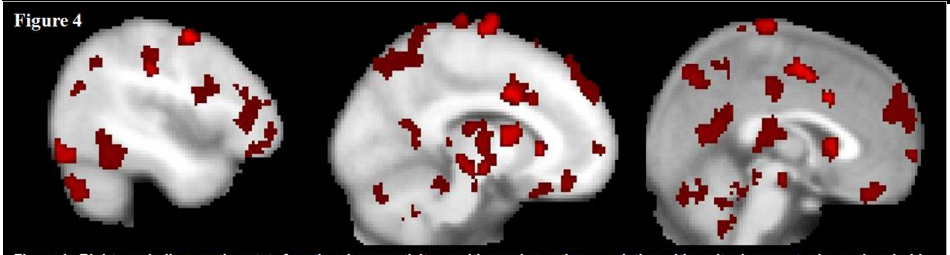


**Figure 4: Right cerebellum resting state functional connectivity: positive and negative correlation with coritcal areas at a lower threshold i.e. left thalamus, frontal medial cortex, frontal lobe, superior frontal gyrus, cigulate gyrus, premotor cortex BA6L, parietal lobe, precuneous cortex, primary motor cortex BA4aL, Occipital cortex, Occipital fusiform gyrus,Broaca's area BA44L, middle temporal gyrus, caudate and some others; interpretation according to MNI, MGH, and Julich atlas available in fslview. (results are not at p 0.05)**

**Conclusion:** The preliminary results indicate that diffusion tractography and functional connectivity reveal interesting and subtle properties of dynamics between the dentate and cortical regions. These findings show consistent invivo contralateral crossing and dentate fiber projections that support the known anatomical pathways and tracer studies results. This represents a milestone of the study of the cerebellar circuit to address clinical and neuroscientific questions. Better MRI-hardware and DSI may provide better results.

**References:** 1. Dum et. al., J. Neuro. 2003; 2. Ramnani N., Nature 2006; 3. Glickstein M., BRAIN 2006; 4. Kumar V. et.al., ESMRMB, WMSG 2008; 5. Friston et.al. J.Cerebral Blood Flow and Metabolism 1993; 6. Biswal B.B. et al, MRM 1995, Neuroimage 1996; 7. Lowe M.J.et al, Neuroimage 1996+1998 ; 8. Smith S.M. et.al., NeuroImage 2004; 9. Fischl B. et.al., Cerebral Cortex, 2004; 10. Cox R., Computers and Biomedical Research 1996; 11. Tournier JD et.al., Neuroimage 2007; 12. Schmahmann JD et.al. 2000; 13. Behrens T.E.J. et.al., Nature Neuro. 2003.