Isotropic High Resolution Diffusion Imaging of Human Habenula in vivo at 7T

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Introduction: The habenula (lat. *habena* meaning rein, Hb) is in control of the human reward system: positive reward is signaled by the dopamine system, whereas disappointment is linked to habenular activation [1,2]. Overactivation of the lateral habenula is associated with depression [3,4]. The habenula is located next to the third ventricle in front of the pineal body and is divided into a medial and lateral part (Fig. 1), which receive input from frontal parts of the brain via the stria medullaris and project down the brainstem via the fasciculus retroflexus [5]. The habenular commissure connecting the nuclei on both hemispheres forms the habenular trigone. Visualization of this structure is difficult because of its small size of approximately 5-9 mm in diameter. Its connectivity is poorly understood in vivo. In the present study, we made use of a high magnetic field strength and a combined approach of reduced FOV acquisition (zoomed imaging) and parallel imaging (GRAPPA), given the name ZOOPPA [6]. With this approach, diffusion-weighted (DW) images with 1 mm isotropic resolution can be obtained at 7T. The high spatial and angular resolution of the data enables efficient DW imaging of the human habenula.

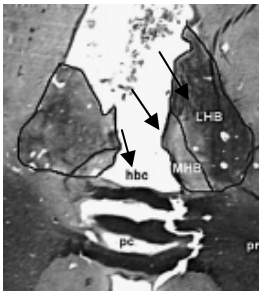

Fig 1: Habenula in a coronal section with combined cell and fibre with Nissl (Cresyl Violet) and Heidenhain-Woelke staining procedures (adapted from [10])
MHB: medial Habenula, LHB: lateral Habenula, HBC: habenular commissure, pc: posterior commissure

Methods: MRI experiments were performed on a 7T whole-body MR scanner (MAGNETOM 7T, Siemens Healthcare, Erlangen, Germany) with a 24-element phased array head coil (Nova Medical, Wilmington, MA, USA). Informed consent was obtained before each study. DW images were acquired with a unipolar Stejskal-Tanner sequence: TR = 10400 ms, TE = 82 ms, FOV =144x150 mm^2, partial Fourier = 6/8, isotropic resolution 1.0 mm^3, 71 slices with 10% overlap, DW with b = 1000 s/mm^2, 60 directions and 4 averages. For the combined approach of zoomed imaging and parallel imaging, outer-volume suppression and GRAPPA was used as described in [6]. A total acceleration factor of 4.2 was used. The total acquisition time was 48 min. The DW images were noise cleaned, corrected for subject motion and co-registered and re-grided to a quantitative T_1-weighted anatomical scan, provided by an MP2RAGE sequence with 0.7 mm isotropic resolution. For all DWI acquisitions, fat suppression was obtained using the method proposed by Ivanow et al. [7]. Multiple fibre orientations were computed in each voxel using the ball-and-2-sticks model [8].

Results and Discussion: Figure 2 shows colour-coded main fibre orientations with significant signal contribution (f-value > 0.05) in coronal and axial brain section containing the human habenula, superimposed on the quantitative high-resolution T1 map and compared with stain sections (Fig. 1) [9,10]. We can identify medial habenular (MHB) nuclei presenting only one fibre orientation running into the anterior-posterior direction (green), whereas the lateral habenula (LHB) shows simultaneously a more superior-inferior orientation (blue). The habenular commissure (HBC) connecting both hemispheres clearly shows a right-left orientation (red). Using probabilistic tractography [8] we can detect stria medullaris and fasciculus retroflexus as two major fibre bundles connecting habenular nuclei with limbic forebrain structures and brainstem (Fig. 3). Whereas fibres from LHB seem to run mainly to the forebrain, tracts from MHB go down to the brainstem and to its commissure as illustrated by streamline tractography using spherical deconvolution [11] (Fig. 4).

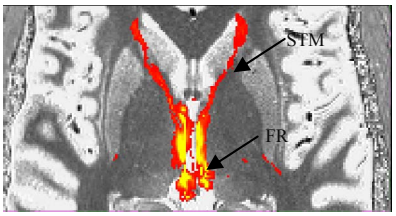

Fig 3: Identification of fibre tracts going out of the habenula (STM:stria medullaris, FR: fasciculus retroflexus)

Conclusion: The combination of zoomed imaging with parallel imaging – ZOOPPA enables DWI acquisitions with 1 mm isotropic resolution at 7T. The data show distinct nuclei of the human habenula in vivo. We identified lateral and medial nuclei with their connecting fibre bundles to the forebrain and the brainstem. The nuclei are clearly visible on the quantitative T_1 map. with a high myelinisation of the LHB and the HBC. Further study of the habenular subdivisions and their role in brain function is likely to improve understanding of the pathophysiology of a wide range of neurologic and psychiatric disorders.

References: [1] Matsumoto, et al. Nature 2007, 447, 1111-5.[2] Ullsperger, et al .J. Neuroscience 2003, 23, 4308-14. [3] Sartorius, et al., Med. Hypotheses 2007, 69, 1305-8. [4] Sartorius, et al., Biol. Psychiat. 2010, 67, 9-11. [5] Hikosaka, et al. J. Neurosci. 2008. 28, 11825-29. [6] Heidemann, et al. OHBM#254 F-PM [7] Ivanov, et al. MRM 2009, 64, 329-26. [8] Behrens, et al. Neuroimag 2007, 34:144-55. [9] Riley, 1943, 259;427. [10] Ranft, et al., 2010, Psych Med, 40, 557-67. [11] Tournier, et al. NeuroImage 2007;35:1459-72.

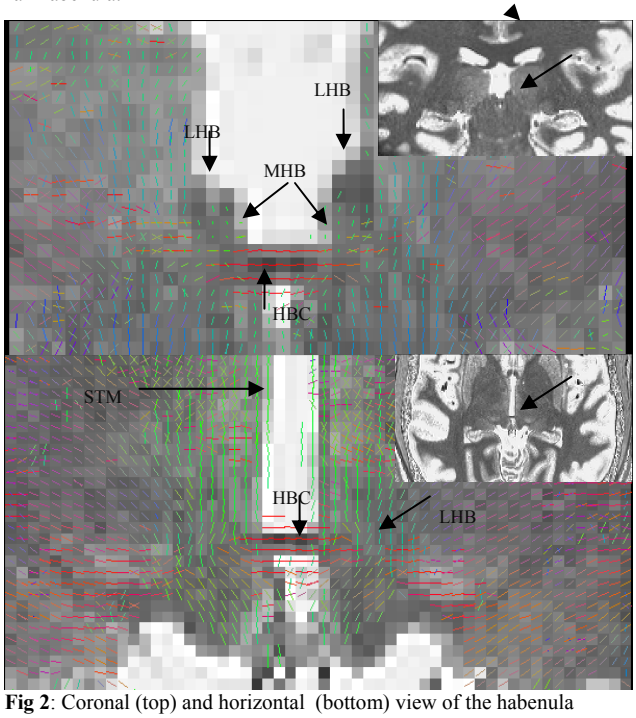

Fig 2: Coronal (top) and horizontal (bottom) view of the habenula diffusion with the color coded vector-orientations (AP:green, SI:blue, RL: red) MHB: medial Habenula, LHB: lateral Habenula, HBC: habenular commissure, STM: Stria medullaris

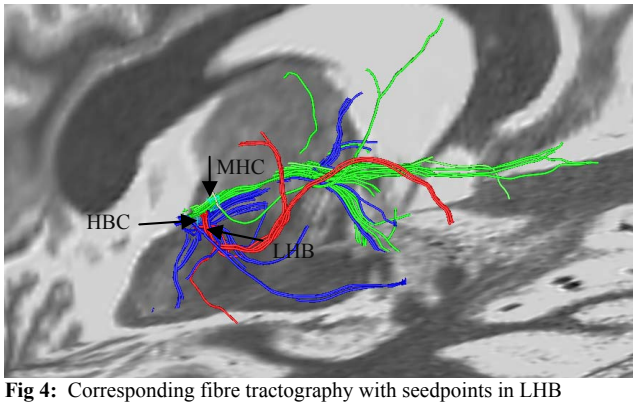

Fig 4: Corresponding fibre tractography with seedpoints in LHB (green), MHB (blue) and HBC (red)