High Conspicuity Imaging and Initial Quantification of the Habenula on 3T QSM Images of Normal Human Brain

John Schenck[1], Dominic Graziani[1], Ek Tsoon Tan[1], Seung-Kyun Lee[1], Luca Marinelli[1], Thomas Foo[1], Christopher Hardy[1], Tian Liu[2], and Yi Wang[3]
[1]*MRI Laboratory, General Electric Global Research, Schenectady, New York, United States,* [2]*MedImageMetric, New York, New York, United States,* [3]*Radiology, Cornell Medical College, New York, New York, United States*

Target Audience: Clinicians and scientists interested in the role of the habenula in brain function and neuropsychiatric disorders.

Purpose and Introduction. The habenule are two small (mm-sized) cell masses located in the epithalamus deep in the brain near the midline on either side of the 3rd ventricle. They are adjacent to the pineal gland and are connected by a small fiber tract spanning the 3rd ventricle, the habenular commissure. They are not normally seen as conspicuous components of conventional MRI brain images and they are currently of intense neuropsychological interest as they are implicated to have major roles in normal brain functioning (e.g., decision making, emotion) and in brain dysfunction (particularly depression, but also addiction, anxiety, schizophrenia, etc.). The rapidly growing interest in the role of the habenulae in depression research is evidenced by a search of the PubMed data base for studies linking the habenula to depression which returns 5 results from 2010, 19 from 2013 and 19 from the first half of 2014. We have demonstrated [1] that 3T QSM provides a noninvasive, practical means of localizing and characterizing the susceptibility and volume of the habenulae. Eventually, this role for QSM could provide data on habenular iron, myelination, calcification, etc., and the changes in these parameters with time during normal brain function or as a response to therapy. QSM may provide clinically relevant and objective aid in the diagnosis and treatment of depression and other brain disorders and clarification of the role of the habenula in basic neuroscience.

Methods: Twenty whole-brain datasets (IRB-approved, multi-echo 3T, gradient-echo, SWAN; TR = 50ms; 9 echoes; TE = [4.5; 9.5; 14.4; 19.4; 24.4; 29.4; 34.3; 39.3; 44.3] ms; flip angle = 20°; bandwidth = 244 Hz/pixel; resolution = 0.58x0.75x2 mm^3; 6m 22s scan time) were generated from four normal adult volunteers. These data sets were processed [2,3] to produce whole-brain susceptibility (QSM) maps.

Results: In all cases the QSM images showed small, but very conspicuous, paired structures on either side of the 3rd ventricle and anterior to the pineal gland (Fig. 1 and Table 1). They are nominally 3-5 mm in diameter and are paramagnetic relative to CSF with an average peak relative susceptibility of +0.20 ppm on both left and right. On axial images the iron-containing pulvinar serves as a landmark for the slices containing the habenulae. They are confined to one or two of these 2 mm thick slices. Because of the consistency with the known anatomy of the epithalamus, these paired structures are conjectured to represent a paramagnetic component of the habenular nuclei (which may or may not coincide with the complete anatomical habenula). In a fraction of the cases a neighboring vein produces some ambiguity in the structure's boundary but this is not a significant source of confusion. Two diamagnetic bridges, consistent with the known anatomy of the habenular and posterior commissures, are seen across the 3rd ventricle between the two nuclei.

Table 1. Typical measured susceptibility parameters for four volunteers.

	Left Habenula				Right Habenula			
Volunteer	N_{voxels}	χ_{avg} (ppm)	χ_{max} (ppm)	Volume (mm^3)	N_{voxels}	χ_{avg} (ppm)	χ_{max} (ppm)	Volume (mm^3)
1	19	0.15	0.21	8.4	25	0.14	0.22	11.0
2	29	0.14	0.21	12.7	31	0.14	0.19	13.6
3	26	0.15	0.22	11.4	38	0.14	0.20	16.7
4	11	0.14	0.18	4.8	7	0.12	0.15	3.1

All susceptibilities are in SI units and are referenced to $\chi_{CSF} = 0$. N_{voxels} are the number of local voxels with susceptibility > 0.1 ppm. χ_{avg} is the average susceptibility of these voxels. χ_{max} is the maximum susceptibility in these voxels.

Discussion and Conclusions: Hypointense structures a few voxels in size are sometimes seen in this region on 3T T2-weighted magnitude images and probably correspond to the habenulae, but these are inconspicuous and inconstant findings and conventional MRI is not widely utilized for habenular studies. However, the structures in the QSM images reported here are highly conspicuous and constantly found. Iron has been reported in the habenula of Perls' stained rat brains and is a well-known contrast mechanism in human brain imaging. Most of the QSM contrast seen here in the habenulae almost certainly results from the presence of ferritin iron deposits as has been established in other brain regions (basal ganglia, pulvinar, etc.). The total habenular susceptibility is presumably a superposition of contributions from multiple tissue components including, in addition to iron, myelinated tracts and calciums salts. Recently there have been several pioneering studies of MR imaging of the habenulae and adjacent structures [4-7]. To date these studies have utilized T1, T2 and T2* -weighted images along with diffusion-weighted imaging and functional MRI. To our knowledge, this is the first report of measured habenular susceptibility values utilizing 3T *in vivo* QSM. There is currently intense interest in the role of the habenular nuclei in a wide range of normal brain functions and in important brain disease states including major depressive disorder (MDD), bipolar disorder, schizophrenia, panic and anxiety [e.g., 8,9]. The habenula has been used as a target for deep brain stimulation to treat refractory depression [10]. QSM imaging may provide a useful approach to targeting this nucleus and it may also serve as a guide to less conspicuous nearby target structures.

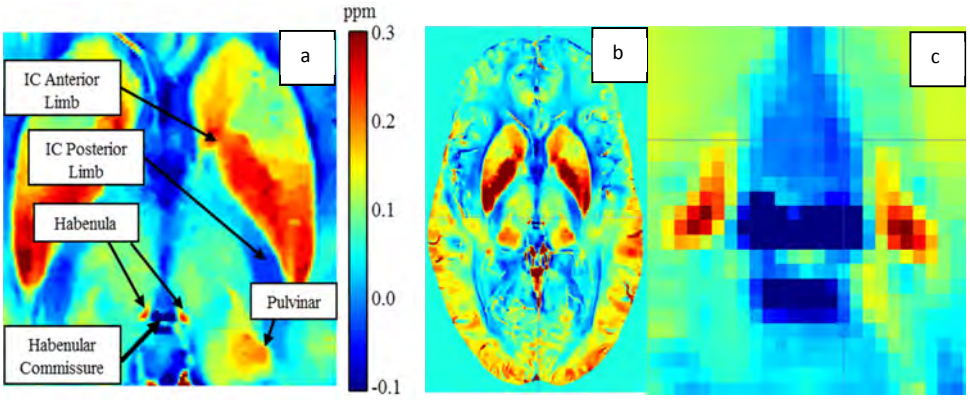

Figure 1. Axial 3T QSM image of a normal volunteer referenced to $\chi_{CSF} = 0$. Not labeled are the prominent iron-rich regions of the basal ganglia – the caudate nucleus, globus pallidus and putamen. IC – internal capsule. a) intermediate magnification. b) low magnification. b) high magnification.

References: 1. Schenck JF, et al. Book of Abstracts. Third International Workshop on Phase Imaging and QSM, Duke University, Durham, NC USA, October 6-8, 2014, 2. Liu T, et al. Magn Reson Med 2013;69:467-476. 3. Liu J, et al. Neuroimage 2012;59:2560-2568. 4. Strotmann B, et al. J Magn Reson Imaging 2014;39:1018-1026. 5. Strotmann B, et al. Front Hum Neurosci 2013;7:878. 6. Lawson RP, et al. Neuroimage 2013;64:722-727. 7. Savitz JB, et al. Biol Psychiatry 2011;69:336-343. 8. Ranft K, et al. Psychol Med 2010;40:557-567. 9. Li B, et al. Nature 2011;470:535-539. 10. Schneider TM, et al. Neurosurgery. 2013;72(2 Suppl Operative):184-193.