High Field, High Resolution Imaging of Brain Iron

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Abstract. High field, thin-slice imaging at 3T has been used to study the T2-shortening associated with brain iron content. Computer post-processing techniques have been used to increase the visibility of voxels with short transverse relaxation times. A number of possibly iron-rich regions either not previously identified or infrequently identified are visualized in this process. This enhances the promise of iron-dependent MR contrast for the study and monitoring of neurological diseases related to iron dysmetabolism.

Introduction: It has long been known (1) that mineralized iron particles associated with tissue ferritin provide an endogenous contrast mechanism in brain leading to decreased T2 in specific brain regions. The resulting signal hypointensity is increased at higher field strengths (2,3). This effect is prominent in the basal ganglia and the dentate nucleus of the cerebellum and corresponds well to regions of high iron concentration identified by post-mortem Perls staining (1,4). It is shown here that, through a combination of high field (3T) imaging using thin slices and computer post-processing, a large number of small brain nuclei and cortical regions with rapid transverse relaxation compared to surrounding regions can be consistently identified.

Methods: The studies reported here involved six healthy adult volunteers, aged 62 or less, and used a two-echo spin-echo sequence (TR = 4000, TE= 30, 80, single NEX, 20 cm FOV, 256x128 matrix, 55 contiguous coronal slices each 1.5 mm thick, scan time of 11 m). The resulting voxel size was 0.78 x 1.56 x 1.5=1.83 mm^3. As T2 is somewhat ambiguous for materials that are heterogeneous within a voxel, an 'effective T2', T2E, was calculated for each voxel by use of

$$T2E = (TI2 - TI1) / \ln[S1 / S2]$$

Here S1 and TI1 are the signal intensity and echo time of the first echo image, etc. The 55 coronal slices cover a region 8.25-cm thick extending from the dentate nucleus in the cerebellum to the tip of the temporal lobe. A segmentation algorithm was used to exclude voxels from outside the brain and T2E was calculated for each of the remaining voxels.

Results/Discussion: Specially written software was used to analyze the T2E distribution for each volunteer. Fig. 1 shows the mean percentage cumulative distribution of voxels with T2E less than the indicated value. This distribution has a tail at lower T2E values which corresponds largely to known high iron regions within the basal ganglia. However, this technique also identifies a number of voxels in other brain regions, many of which correspond to the locations of smaller nuclei or nuclei of lower iron content (Fig. 2). These regions include the subthalamic nuclei, the superior and inferior colliculi, the mammillary bodies, the habenular nuclei, the pineal gland, the lateral geniculate bodies and other regions. Inferior to the anterior commissure a region of low T2E in the vicinity of, but perhaps not identical with, the nucleus basalis is consistently seen. Because of the importance of this nucleus in Alzheimer's disease this region should be studied carefully in these patients. It is also of interest that in some regions a thin line (one voxel wide) of low T2E voxels is detected running parallel to the boundary between cortex and the subjacent white matter. A similar line is also seen at some locations along the ependymal lining of the lateral ventricles. Such regions have been identified previously as iron rich in Perls-stained specimens (1,4) but not in MRI, presumably because of their small total volume.

It should be emphasized that it has not been demonstrated that elevated iron is the only source of short T2E values, e.g., RF penetration may affect T2E in some regions. However, in one subject studied at multiple field strengths the effect was much weaker at 1.5 T and stronger at 4T. Also, Perls-staining in humans (1,4) and rats (5) has also identified many of the new low T2E regions as iron rich.

Conclusion: It is shown that high field, high resolution MRI can identify many short T2 voxels in addition to those traditionally associated with high iron content in MRI. High field research scanners at 7T and 8T now exist, and 3T scanners are becoming widely available. A large number of neurodegenerative diseases have been linked to the possibility of abnormal iron metabolism (6). Because of this and the rapid rate of new genetic and molecular biological findings regarding iron metabolism (7-9), the likelihood of a significant role for high-field MRI in diagnosing and monitoring these diseases continues to increase.

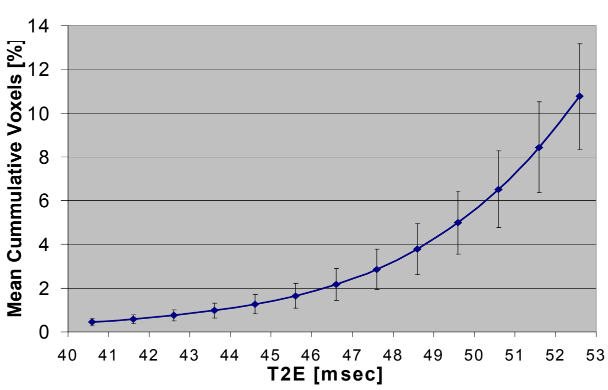

Fig. 1. Mean (over six subjects) of the cumulative percentage of voxels with T2E less than the given value. The error bars represent one standard deviation for this group.

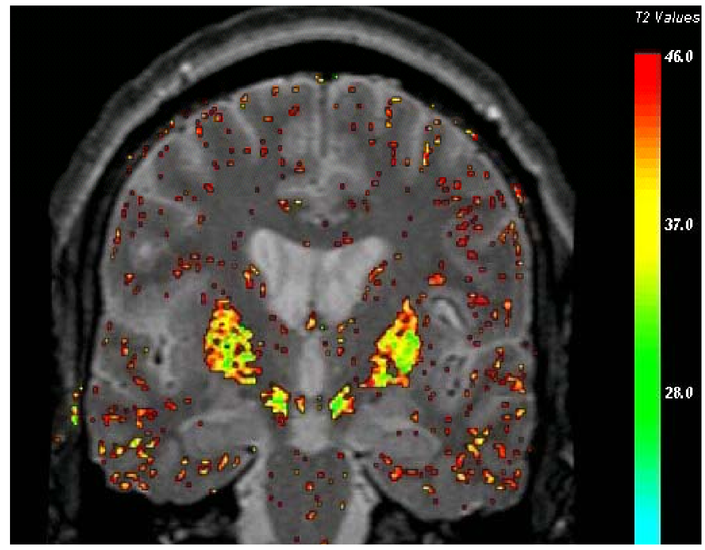

Fig. 2. Coronal section at the level of the globus pallidus and pars reticularis of the substantia nigra. To enhance visibility, voxels with T2E less than 46 msec have been identified, highlighted and registered with the first echo image.

References

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