# Toward Clinically Practical T2-Mapping for Neurodegenerative Diseases

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## Introduction

Quantitative imaging techniques, such as T2 mapping, hold great promise for enhancing the utility of MRI for evaluating neurodegenerative diseases. For example, there is much current interest in the role of iron in shortening T2 in various brain regions and its potential to serve as a biomarker of disease presence and progression.[1-3] The studies that have demonstrated this potential invariably require extensive and time-consuming post-processing by analysts skilled in neuroanatomy. Before widespread clinical applications of these techniques can occur, there must be a great increase in the speed and ease with which quantitative information (both global and regional) can be extracted from the images. Simultaneously, these semi-automated techniques must have sufficient accuracy as compared to manual segmentation to capture the significant signs of disease. We present here a semi-automated technique which we have evaluated on 3-tesla images of patients with rare genetic iron storage diseases in which the role of iron in reducing brain T2 is obvious, and also on cohorts of Alzheimer's patients and normal controls in which the proposed effect is much more subtle. Disease-related defects in iron metabolism and storage are accepted as part of the pathology in aceruloplasminemia (aCp)[4] and Hallervorden-Spatz disease (HSD - also known as NBIA)[5] and may also play a role in the pathogenesis of more common diseases such as Alzheimer's and Parkinson's diseases.[1]

## Methods

T1 and T2-weighted MRI images were collected for 37 AD subjects and 46 normal controls as part of an IRB-approved clinical study. Also studied were one patient each with HSD and aCp. T1-weighted images were mapped to Talairach coordinates using AFNI.[6] Regional T2 distributions were extracted from the co-registered T2 images using the Taliarach atlas[7] and subjected to statistical analysis to compare AD cases with normal controls. Regions with possible increases in tissue iron were detected based on analysis of the percentage of voxels with T2 below various empirically chosen threshold values. The thresholds ranged from 30 to 45 ms depending on the T2 distribution within each region. Voxels with T2 >100 ms were taken to represent atrophy-related CSF accumulation and omitted from the analysis. The resulting features were then compared for the aCp and HSD patients as well as for the AD and control groups.

## Results

An increased number of short T2 voxels is associated with the brain iron storage diseases aCp and HSD (Fig. 1). Increased numbers of low-T2 voxels were also found in several brain regions for the AD patients as compared to the controls. These regions include the lentiform nucleus (putamen plus globus pallidus) and the left Brodmann area 34 (see the Table and Fig. 2). These findings support but, of course do not prove, the conclusion that decreased T2 observed in AD is iron related as previously suggested.[8] Additional analysis is underway to investigate the changes in Brodmann Area 34 and to determine the degree to which nearby structures such as the hippocampus and uncus are affected.

For each case the analysis required only 10-15 minutes of postprocessing time by a technician without specific neuroanatomy training. This compares to 4-5 hours required for a trained neuroanatomist to complete a precise manual segmentation. Thus, these results support the contention that clinically relevant T2 mapping can be performed in a semi-automated fashion. This greatly enhances the possibility of widespread clinical utilization of the technique.

| Region | T2 threshold | *p*-value |
|---|---|---|
| Lentiform Nucleus | 30 ms | 0.003 (left)<br>0.005 (right) |
| Putamen | 30 ms | 0.002 (left)<br>0.005 (right) |
| Medial Globus Pallidus | 30 ms | 0.005 (left)<br>0.010 (right) |
| Lateral Globus Pallidus | 30 ms | 0.035 (left)<br>N.S. (right) |
| Brodmann Area 34 | 45 ms | 0.006 (left)<br>N.S. (right) |

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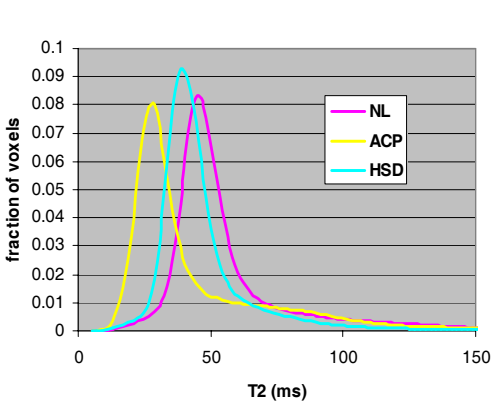


Fig 1. Increased numbers of short T2 voxels (leftward shift of histogram) are associated with the iron storage diseases aCp and HSD.

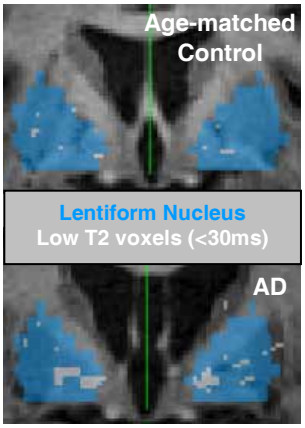


Fig 2. Low-T2 voxels in the lentiform nucleus of a typical AD patient and an age-matched control.