T2 Relaxometry and Volumetry of Postmortem Human Hippocampi

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Introduction: One advantage of postmortem MRI over in vivo imaging is that the in vitro tissue can be held nearly motionless indefinitely, making it possible to perform very high resolution imaging. This opportunity is exploited in the current study. Thirty-eight cadaveric human brains were scanned, and the T_2 values and volumes of the hippocampi were correlated with the subjects' MMSE scores and which hemisphere was imaged (right or left). It was found that in postmortem brain specimens, low MMSE scores are associated with lower hippocampal T_2 values.

Methods: Thirty-eight subjects underwent mini mental state examination (MMSE) while still alive. Within an average of 6.18 hours after death of a subject, the brain was removed from the cadaver, cut into two hemispheres along the midsagittal plane, immersed in 4% formaldehyde solution, and refrigerated at 4° C. After approximately 30 days, each hemisphere was removed from refrigeration and imaged using a 3.0-T MRI scanner (General Electric, Waukesha, WI). A 2D fast spin echo sequence with two echo times was used to acquire proton density weighted and T2-weighted images, in sagittal slices through the hemispheres. The following parameters were used: TR=3.6 s, TE1=13.0 ms, TE2=52.0 ms, FOV=16×16 cm, slice thickness=1.5 mm, acquisition matrix=256×256 zero-padded to 512×512, NEX=6. Total scan time was 31 minutes. T_2 maps were generated. The hippocampus in each hemisphere was manually outlined on the T_2-weighted images as a 3D region of interest (ROI) using AFNI*, as shown in Figure 1. From the selected ROI, the modal T_2 value of the hippocampus and the hippocampal volume (normalized to total hemisphere volume) were calculated. A least-squares linear regression was used to model the hippocampal T_2 values and volumes as functions of MMSE score and left or right hemisphere.

Results: For groups formed based on the MMSE score (higher or lower than 20), the high MMSE group exhibited a higher mean hippocampal volume ($p < .031$). Figure 2 further illustrates this result, displaying T_2 histograms of all hippocampal voxels in the (a) randomized groups and (b) high and low MMSE groups. Linear regression through the data yielded the following equations relating postmortem normalized volume (V) and T_2 of the human hippocampus to MMSE score and left or right hemisphere (LR):

$$V = \alpha_0 + \alpha_1 \cdot LR + \alpha_2 \cdot MMSE \qquad T_2 = \beta_0 + \beta_1 \cdot LR + \beta_2 \cdot MMSE$$

where LR is defined as 0 for left hippocampus and 1 for right. In the volume equation, α_2 was significantly different from zero ($p < .002$), i.e. there was a positive relationship between normalized hippocampal volume and MMSE score. In the T_2 equation, there was some confidence that β_1 and β_2 were not equal to zero, though these observations could not be deemed significant ($p < .09$ and $p < .10$, respectively).

Discussion: This work highlights at least two important findings. First, lower MMSE scores are linked to smaller hippocampal volumes. This correlation has been observed in studies with living subjects[1], where it has been hypothesized that hippocampal atrophy is associated with decreased cognitive function[2]. This association appears to hold true for postmortem brain specimens. Second, the results of this work revealed that in 38 postmortem specimens, the hippocampal T_2 values were higher in right hippocampi than in left hippocampi. Paired comparisons were not possible, since right and left hemispheres from the same subject were not available. Results of this work also suggest that higher T_2 values may be associated with higher MMSE scores, perhaps as a result of iron accumulation.

Figure 1. Typical outlining of a hippocampus (red) on a sagittal T_2-weighted image. Hippocampal outlinings were performed on consecutive slices to produce a 3D region of interest.

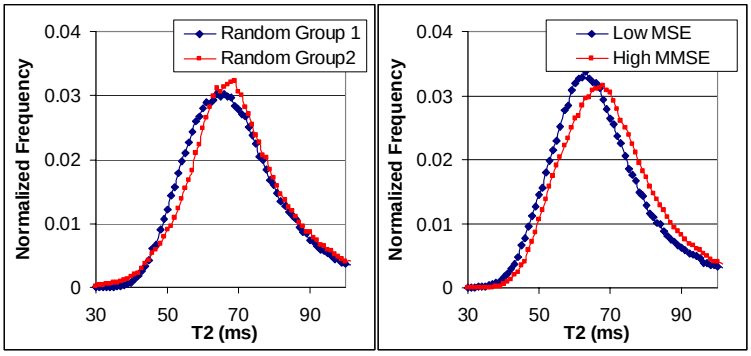

Figure 2. Left: T_2 histograms for all hippocampal voxels of two randomized groups. Peaks of the histogram occur at approximately the same point. Right: T_2 histograms for all hippocampal voxels of a low (< 20) and high (> 20) MMSE group. The histogram for the high MMSE group is shifted approximately 4 ms to the right.

References: [1] DC Steffens et al., Bio Psychiatry, 2000;48:301-309. [2] H Wolf et al., Neurobiology of Aging, 2001;22:177-186.