Quantitative T_2 and T_2* relaxometry of hippocampal subfields

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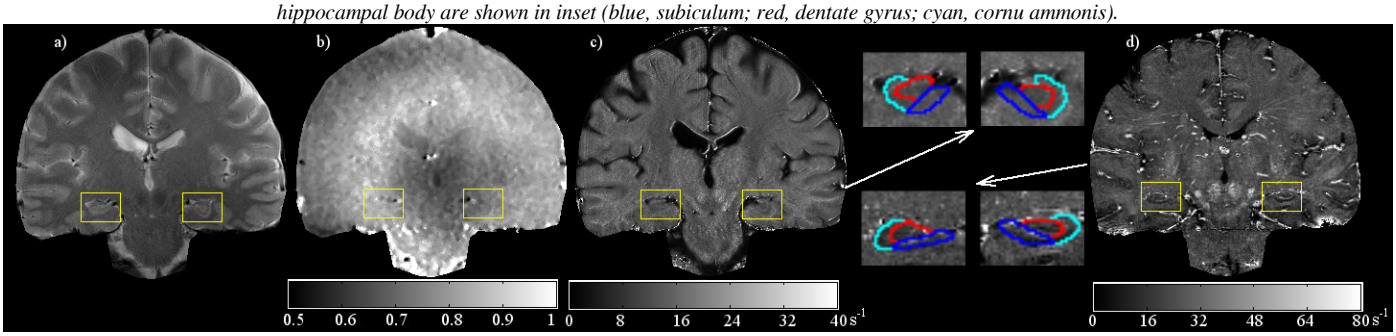
Introduction: Quantitative transverse relaxometry is useful for identifying abnormalities of the hippocampus including epilepsy, Alzheimer disease, depression, and hippocampal sclerosis [1, 2, 3]. Preclinical and post-mortem studies suggest that different disease processes selectively affect hippocampal subfields. Interpretations of these disease processes are still limited to accurate volume measurements of the subfields [4]. Hippocampal subfield T_2 and T_2* mapping can be obtained using high resolution MRI at high magnetic field. Past work has performed T_2* maps, but not T_2. At high magnetic fields, the spin-echo T_2 ($1/R_2$) is more difficult to measure due to radio frequency (RF) tissue heating and RF heterogeneity, while the gradient echo T_2* ($1/R_2$*) may suffer from increased background field gradients, for example near air-tissue interfaces. Moreover, high resolution transverse relaxometry mapping is limited by the need for high signal-to-noise, while maintaining clinically acceptable scan time. For spin echo T_2, tissue heating can be overcome by employing substantially shortened echo train [5] and/or using reduced flip angles with stimulated echo compensation [6] to eliminate T_2 variations from RF heterogeneity. For T_2* linear background fields can be corrected prior to T_2* measurements [7]. The purpose of the study is to investigate the feasibility of quantitative T_2 and T_2* measurements of the hippocampal subfields at 4.7 T.

Methods: Seven healthy subjects (29.7±2.8 years, age range 27-34 years) were scanned at 4.7 T (Varian Inova). All subjects provided informed consent according to the institutional protocol. R_2 maps were acquired using stimulated echo compensation [6] from 2D multiecho spin echo images with 6000 ms repetition time, 13 ms echo spacing, 5 echo train length, 3 mm slice thickness, 4 slices, 6 mm slice gap and 512 x 320 imaging matrix, 256 x 160 FOV, 0.5 mm in-plane resolution; 70 kHz receiver bandwidth; 90°excitation and 165°refocusing pulses; RF pulse duration: 5.3 ms (excitation) & 3.0 ms (refocusing); Total time 15.5 min. R_2* maps were obtained using 3D multiecho gradient echo sequence with 41 ms repetition time, 4.7 ms first echo time, 7.5 ms echo spacing, 13° flip angle, 1.5 mm slice thickness, 512 x 320 x 90 imaging matrix, 0.5 mm in-plane resolution, 90 kHz receiver bandwidth and 17.4 min scan time. The signal decay curves were fit on a pixel-by-pixel basis and bilateral regions of interest (ROIs) were manually drawn on R_2 and R_2* maps for left and right subiculum SUB, dentate gyrus DG and cornu ammonis CA of the hippocampal body. Note CA combines CA1-3 area.

Figure 1: In-vivo (coronal view) of a) raw spin echo image (TE 39 ms); b)Normalized flip angle map; c) R_2 map d) R_2 map at 4.7 T of a healthy control. Subfields of hippocampal body are shown in inset (blue, subiculum; red, dentate gyrus; cyan, cornu ammonis).*



Results: Transverse relaxation times T_2 and T_2* of left and right hippocampal subfields are summarized in the Table 1. With both methods, shortest relaxation times are found in the subiculum that follow similar trend as compared to the previous works [8, 9]. The effect of linear field correction is shown on T_2*. T_2* values are underestimated by 8-12% for uncorrected T_2* maps while 3-8% for T_2* maps with z-component correction only. For intra-rater reliability test, intraclass correlations for different subfields were in the range of 0.83-0.92. Example images and quantitative maps from one volunteer are shown in Fig 1. Fig. 1(c) presents the R_2 map obtained using stimulated echo compensation, and the corresponding normalized flip angle map is shown in Fig 1(b). Typical flip angles for hippocampus were in the range of 152-165^0. Fig. 1(d) shows a linear background field corrected R_2* map. The hippocampal subfields are indicated in the inset for R_2 and R_2*.

Discussion: We demonstrated high resolution R_2 and R_2* maps using high field MRI to enable hippocampal subfield quantitative measures beyond volume, which might be useful for further investigation in hippocampal-related neurodegeneration. T_2 values of subfields were obtained using multiecho spin echo R_2 mapping method [6], using 5 echoes and 165^0 flip angle to keep acceptable specific absorption rate. We obtained similar T_2 values with 165^0 flip angles compared to 180^0 flip angles. T_2* values of hippocampal subfields suggest that there is a significant lengthening in T_2* values obtained with full (xyz) background field correction versus uncorrected and correction with the z only component. Previous work [8] at 7 T demonstrated hippocampal subfield R_2* maps using the linear field correction in the z-direction only and reported T_2* values as follows: SUB 31.1, CA1 = 39.2, CA2+CA3 = 33.3, CA4+DG= 32.8. While another 7 T study [9] reported T_2* values of left and right hippocampal subfields and showed CA separately as CA1-4. Our T_2* values of subfields are in good agreement with their results [8, 9] and we obtained longer T_2* values as expected at 4.7 T (our values combining left and right T_2* values: CA=44.1, DG= 46.5, SUB=36.4). Discrimination between subfields was greater with T_2* than with T_2, although T_2 generally had reduced variability. The changes in T_2 and T_2* values in subfields indicate a similar trend in our study. A limitation of our study was that the CA subfields were grouped rather than separated due to insufficient spatial contrast and resolution. However, the hippocampus was still broken into three distinct subfield territories.

Conclusion: Quantitative MRI relaxometry of hippocampal subfields is possible using both spin echo R_2 and gradient echo R_2* mapping methods. Absolute measures of transverse relaxation rates might be helpful to gain insight into neurological diseases associated with variations between hippocampal subfields.

References: [1] Bernasconi, N, Neurology (2005), 65 (2):223-228; [2] Barnes J, Neurobiol aging (2009), 30:1711-1723; [3] Luo Z, PLOS One (2013), 8 (9); [4] Malykhin NV, Neuroimage (2010), 49:1224-1230; [5] Uddin MN, MRM (2013), 70:1340-1346; [6] Lebel RM, MRM (2010) 64:1005-1014; [7] Volz S, Neuroimage, (2009), 45(4):1135-43; [8] Goubran M, Human Brain Mapping (2013), 35 (8): 3588-3601; [9] Cho ZH Psych. Res. (2010), 44:881-886.

Table 1: Transverse relaxation times for subfields on hippocampal body over seven healthy subjects (age range 27-34 years)

	Left of Hippocampal body			*Right of Hippocampal body*		
	CA	***DG***	***SUB***	***CA***	***DG***	***SUB***
T_2 (ms)	*66.23±5.1*	*70.15±2.6*	*60.72±6.4*	*68.27±2.1*	*67.28±2.2*	*61.14±3.0*
T_2^* (ms) (full correction)	*41.60±1.5*	*47.91±5.2*	*35.68±4.7*	*46.55±4.6*	*45.10±3.0*	*37.15±3.5*
T_2^* (ms) (z-only correction)	*40.02±2.3*	*46.63±6.4*	*34.38±3.2*	*44.43±5.0*	*41.4±2.9*	*34.75±2.8*
T_2^* (ms) (uncorrected)	*38.54±1.8*	*44.13±6.2*	*32.09±3.6*	*42.57±4.37*	*40.13±2.7*	*33.12±4.1*

**CA, cornu ammonis; DG, dentate gyrus; SUB, subiculum. Values are provide as mean ± standard deviation over healthy subjects*