In vivo Imaging of Human Hippocampal Subfields at 7 Tesla

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Introduction:

Hippocampal subfield damage has been associated with Alzheimer's disease, epilepsy, schizophrenia and depression (1-4). Until now, however, hippocampal subfield studies have been limited to animals or post-mortem histopathology. Resolution and contrast-to-noise limitations have limited differentiation of the hippocampal layers at the current clinical 1.5 and 3 T imagers. This restricts the utility of T_2-weighted and FLAIR MRI to drastic changes, *e.g.,* mesial temporal sclerosis that occur only at the end of pathological processes (5,6). Our goal was to test whether the combination of ultra high field, multi-coil array, shimming and T_2^* weighted MRI would resolve hippocampal subfields down to the 100 micron thick dentate granular cell layer (DGCL) that foments neuroprogenitor cells and is implicated in memory formation(8).

Materials and Methods:

Ten healthy volunteers (5 male, 26±6 years old) were enrolled. All gave IRB approved written informed consent. They were imaged at 7 Tesla (Siemens AG) using a 24-element head coil-array (Nova Medical) with 3D MP-RAGE T_1-weighted MRI for anatomic reference; and T_2^*-weighted gradient-echo (*TE/TR*= 25/944 ms) at 232 micron in-plane resolution (0.05 mm^3 pixels) in coronal and sagittal slabs (17 slices 1 mm thick) over the hippocampus, as shown in Fig. 1.

Results:

All hippocampal subfields down to the DGCL were visible in all 10 subjects (*cf.* Fig. 1). Consequently, a 90% confidence interval for the probability that the DGCL would be detected in a random normal subject extends from 84.6% to 100%. Therefore, a diagnostic test that identifies subjects as abnormal when the DGCL is not visualized is expected to have at least 85% *specificity*. All larger subfields were visible in excellent detail and contrast.

Discussion:

Although visualization of all hippocampal subfields is a significant advancement, imaging the DGCL is particularly noteworthy. It size sets the resolution threshold and it is one of only two known neurogenesis loci in the adult brain. The complex processes involved in mitosis leave dividing cells particularly vulnerable to damage and new mutations. This supports the theory that the DGCL is the site of initial injury in many diseases involving the hippocampus.

Conclusion:

The combination of 7 T field, $\mathbf{B_0}$-shim, high count receive-coil arrays and heavy T_2^* weighting is shown to consistently depict hippocampal subfields down to 100 micron in clinically acceptable (14 minute) time. The higher resolution and contrast obtainable at 7 T can, therefore, be applied to earlier detection of pathology in this sensitive circuit. Furthermore, by inference, the resolution and contrast could be used for diagnosis and to monitor subfield-targeted treatment of diseases which have a predilection for the hippocampus.

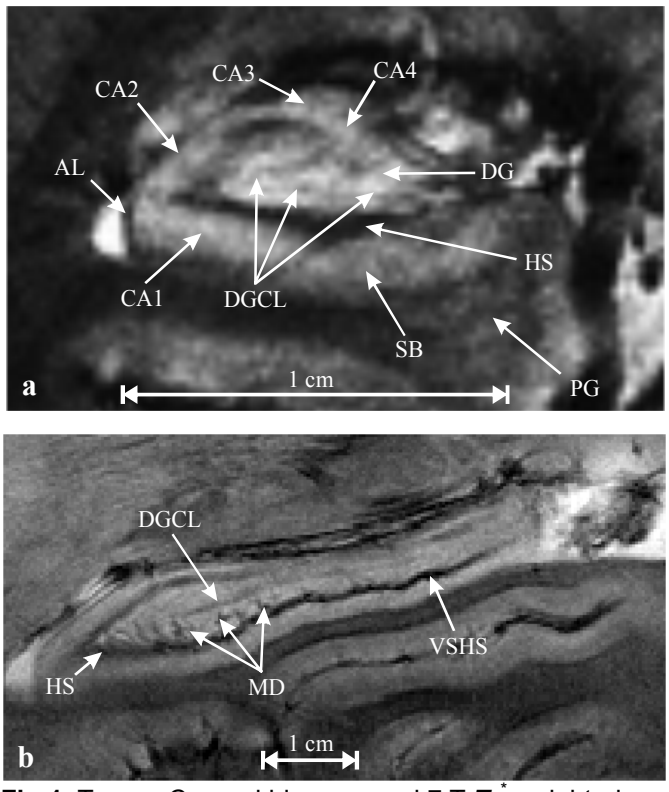

Fig.1. Top, **a**: Coronal hippocampal 7 T T_2^*-weighted MRI. Note the four Cornu Ammonis (CA) subfields CA1…4, Subiculum (SB), parahippocampal gyrus (PG), hippocampal sulcus (HS), Dentate gyrus (DG), alveus (AL) and dentate granule cell layer (DGCL) (arrows). [anatomy according to Fig. 3-54, p. 105 of (7)]. Bottom, **b**: Sagittal view showing the vein of superficial hippocampal sulcus (VSHS), hippocampal sulcus (HS) and margo denticulatus (MD). Note the high contrast the vasculature produces on these T_2^* weighted images.

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