In-vivo quantification of the hippocampal subfields using 4.7T Fast Spin Echo imaging

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Introduction: Changes in the hippocampus have often been implicated to the pathophysiology of many neurological and psychiatric diseases. Despite the fact that hippocampal reduction has been confirmed in many MRI studies, the hippocampal volume loss has not been specified with respect to the detailed underlying structural alterations i.e. hippocampal subfields. A growing number of preclinical studies and limited postmortem data suggest that different diseases can affect the subfields selectively. However, current MRI studies usually measure global hippocampal atrophy instead of measuring volume loss in its subfields. Therefore, research on the hippocampus could benefit from the development of methods that would enable the identification and in-vivo measurement of the hippocampal subfields. The purpose of this study was to delineate and quantify the hippocampal subfields within entire hippocampal structure using ultra-high resolution Fast Spin Echo (FSE) imaging at 4.7T. Previous studies of the hippocampal subfields using high field MRI applications were restricted to parts of the hippocampus [3] or conducted ex-vivo [4].

Methods: Eleven healthy volunteers (5 male and 6 female, age 23-56 years) were studied using a Varian Inova 4.7T scanner. The T2-weighted 2D FSE acquisition employed contiguous 1 mm thick slices with a 90° excitation followed by four 140° refocusing pulses, 90 slices oriented perpendicular to the anterior–posterior commissure line, TE/TR 39/11000 ms, 13.5 min, in-plane matrix 384 x 296, FOV 20 x 20 cm, original resolution was 0.52x0.68x1 mm interpolated to 0.26x0.34x1mm. The resulting images were used for volumetric analysis of the hippocampal subfields (Fig 1). A whole brain T1-weighted 3D MPRAGE sequence (3D axial approach, 256 slices, TE/TR/TI 5ms/1.8s/850ms. 10º flip, 110 views per segment, interleaved sequential encoding, 15 minutes for whole brain, in plane resolution 0.75 x 0.75 x 0.75 mm) was used for intracranial volume (ICV) measurements and hippocampal volume normalization. The regions of interest were traced with a mouse-driven cursor using DISPLAY (Montreal Neurological Institute) software, which displays all three planes simultaneously. Our detailed volumetric protocol for the hippocampus [2] has been previously reported. Quantification of the hippocampal subfields employed an anatomical atlas of the human hippocampus [1] as a reference. Raw volumes were normalized to ICV using the following formula for volume correction: normalized volume = Raw volume / ICV of the same subject x 1000 mm³.

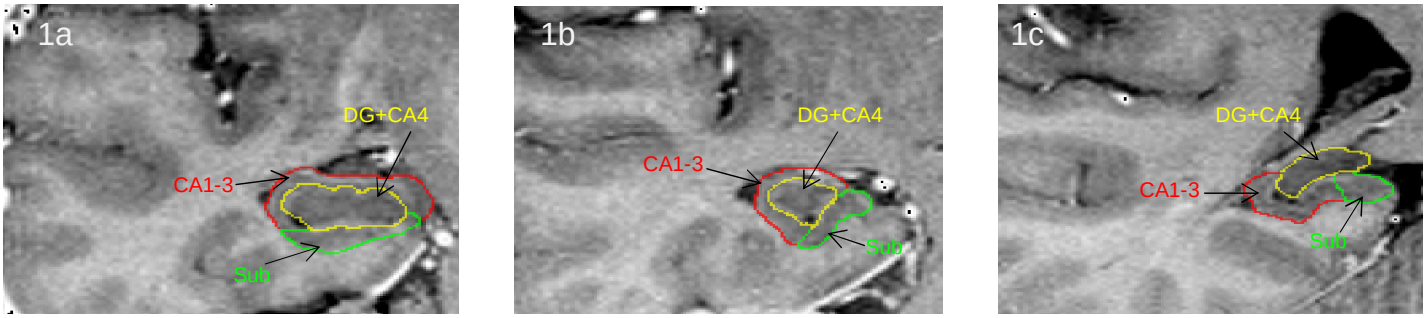
Results: Normalized volumes for hippocampal subfields are shown in Table 1. Values were quite consistent between the two hemispheres. However the percentage distribution of the subfields was different for hippocampal parts: hippocampal tail (CA 1-3 (51.2%); DG+CA4 (38.8%); Sub (10.0%)); hipocampal body (CA 1-3 (34.8%); DG+CA4 (37.6%); Sub (27.6%)); hippocampal head (CA 1-3 (50.7%); DG+CA4 (25.1%); Sub (24.2%)). The biggest part of the dentate gyrus (+CA4) was located in the hipocampal body (42.7%), following hippocampal head (37.0%) and tail (20.3%). In contrast the hippocampal head had the largest part of CA 1-3 (53.1%), following hippocampal body (28.2%) and tail (18.7%). Hippocampal tail had the smallest portion of the subiculum (7.3%) compared to hippocampal head (49.5 %) and tail (43.2%).

Conclusion: For the first time, we have quantified the hippocampal subfields in-vivo within the entire hippocampal formation. Future applications of this technique to psychiatric and neurological disorders may reveal new information about vulnerability of hippocampal subfields to specific pathology.

Table 1 Mean values and standard deviations for hippocampal subfields after normalization to ICV from 11 healthy volunteers.

	Cornu Ammonis (CA 1-3)		Dentate gyrus (DG) +CA4		Subiculum (Sub)		Total hippocampal volume (HC)	
	Left	**Right**	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
Range, mm³	803.6 - 1354.8	839.2 - 1325.2	639.2 - 938.5	690.8 - 912.0	443.3 - 633.6	475.2 - 647.7	1888.7 - 2829.4	2081.3 - 2797.6
Mean ± SD, mm³	1112.8 ± 175.9	1116.9 ± 143.7	791.8 ± 92.9	791.1 ± 70.8	566.9 ± 54.4	582.5 ± 52.7	2471.7 ± 274.7	2490.5 ± 237.9
% of HC	45.0	44.8	32.1	31.8	22.9	23.4	100	100

Figure 1 Delineation of the hippocampal subfields using 4.7T FSE. From left to right: hippocampal head (1a), hippocampal body (1b), and hippocampal tail (1c). Hippocampal subfields: Cornu Ammonis (CA1-3), dentate gyrus (DG) + CA4, subiculum (Sub).



Acknowledgements: This study was supported by the Canadian Institutes of Health Research and personnel support from the Alberta Heritage Foundation for Medical Research.

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