Supplementary Materials for Segmenting Hippocampal Subfields from 3T MRI with Multi-modality Images

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A. Illustration of manual labels of the hippocampal subfields

In the literature, there is still no golden standard or criterion for segmenting the hippocampus into subfields. This issue has been discussed in Yushkevich and many related researchers [1]. In this paper, we follow the segmentation criterion proposed in Thomas et al. [2]. Their original figure (see **Fig. S1**) is cited here to clearly demonstrate the hippocampus subfields formation.

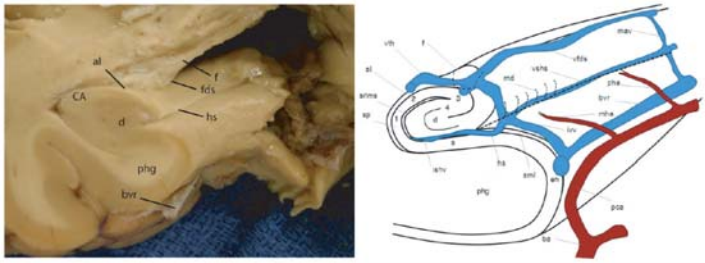

Figure S1 (From Thomas et al. [2]). "*Hippocampal body, gross (left) and schematic (right) coronal-oblique views showing Cornu Ammonis (CA), subfields CA1-4(1-4), alveus (al), dentate gyrus (d), …, subiculum (s)*" [2].

In this paper, we mainly focus on six subfields, i.e., subiculum (Sub), CA1, CA2, CA3, CA4, and dentate gyrus (DG). Our manual labels can be illustrated in **Fig. S2**.

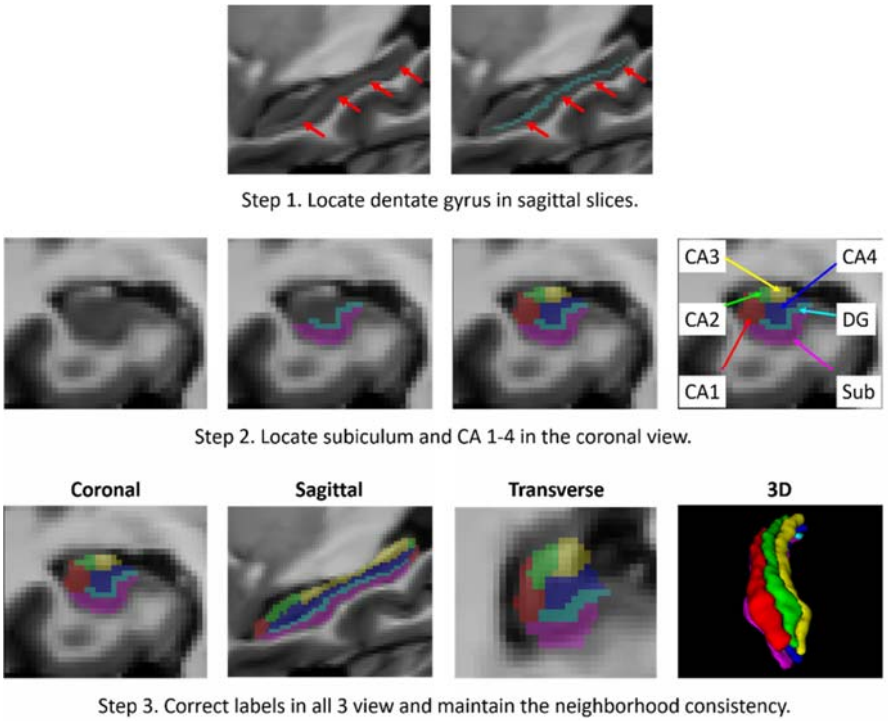

Figure S2. Illustration of manual labelling pipeline.

We start the labeling from the sagittal view using the ITK-snap [3]. First, the dentate gyrus is located, as pointed by the red arrows; see step 1 in **Fig. S2**. We can do this for all the sagittal slices containing the hippocampus. Then, we come to the coronal slices, for locating the subiculum, CA1, CA2, CA3, and CA4 sequentially according to the local intensity (see step 2 in **Fig. S2**). Simultaneously, the mislabeled voxels in dentate gyrus are corrected. After labeling all the subfields in all coronal slices, each slice is double-checked in all 3 views (coronal, sagittal and transverse). Meanwhile, some labels are corrected to maintain the label consistency between neighboring slices. Then, the final labeling results are obtained (see step 3 in **Fig. S2**).

The following **Table S1** compares the average sizes of our hippocampal subfields and those in other works. These sizes are different, mainly due to the use of different labeling criteria. For example, Van Leemput et al. [4] divides the hippocampus into nearly 10 subfields, whereas we just divide it into 6 subfields.

Table S1. Hippocampal subfields size in related works. (unit: mm^3)

	Subiculum	CA1	CA2	CA3	CA4	DG
Ours	893	682	527	479	770	496
Van Leemput et al. [4]	537	340	935		526	
Winterburn et al. [5]	391	858	208		616	
Wisse et al. [6]	1590	3430	154	350	1870	
Whelan et al. [7]	819	1329	-	466	555	642

To evaluate the agreement of the manual labeling on different subjects, we have randomly shuffled the 12 subjects and have them manually segmented again. Then, we have used the two-way random single measure of the intra-class correlation to evaluate the intra 1-observer agreement rate. The intra-class correlation coefficient is r=0.87, the estimation confidence interval is [0.68,0.98], and the p-value equals to $1.91*10^{-13}$, which indicates good agreement over the manual segmentation of all the subjects.

Fig. S3 shows some typical 7T slices and our corresponding manual labels.

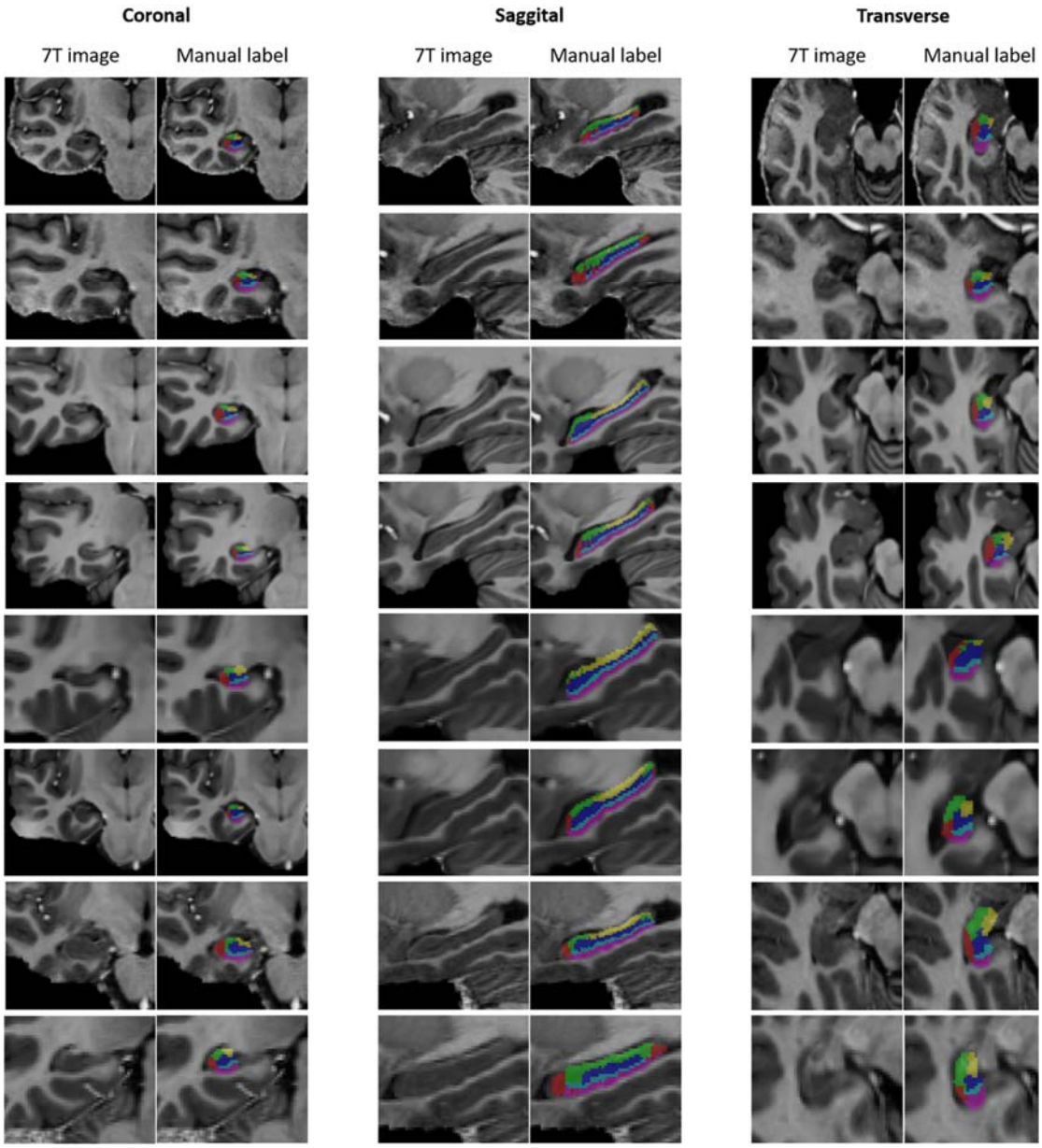

Figure S3: Typical 7T slices and their corresponding manual labels .

Reference

[1]. Yushkevich, P.A., R.S.C. Amaral, J.C. Augustinack, et al., *Quantitative comparison of 21 protocols for labeling hippocampal subfields and parahippocampal subregions in in vivo MRI: Towards a harmonized segmentation protocol.* NeuroImage, 2015;**111**:526-541.

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