

VOLUMETRY OF THE HUMAN MEMORY CIRCUIT: DIFFERENTIAL EFFECT OF AGE ON HIPPOCAMPAL SUBFIELDS AND ASSOCIATED WHITE MATTER VOLUMES



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INTRODUCTION

- The human memory circuit includes thin white matter projections (alveus and fimbria), which emanate from inside the hippocampus and lead out of the medial temporal lobe via the fornix.
- The volumetric trajectory of the hippocampal subfields and, in particular, the above-mentioned white matter (WM) structures have received little attention with respect to healthy aging

HYPOTHESES:

- We hypothesized volumetric decreases would be localized to the CA1 and subiculum hippocampal subfields.
- In addition, decreases amongst all white matter volumes across age was hypothesized.

METHODS

- Manual segmentation** on high-resolution MRI images (T1/T2-weighted, voxel size = 0.3mm isotropic) for five healthy controls (2 male, 3 female, aged 29-57 yrs; mean age = 37).
- Intrarater reliability** performed on two randomly selected hemispheres and evaluated using Dice kappa overlap metric

Table 1. Summary of Intra-rater Reliability

Structure	Left	Right
Alveus	0.90	0.90
Fimbria	0.90	0.86
Fornix	0.87	0.87
Total	0.90	0.89
White Matter		

Average intra-rater reliability was calculated using Dice's volumetric Kappa. A score of 0 represents no overlap between test and retest labels, whereas a value of 1 represents a complete overlap.

- High-resolution atlases¹ were used for the **automatic segmentation** of 297 individuals from the OASIS dataset aged 19-94 years (mean age=44.85 ± 23.43)². **MAGeT Brain segmentation** (previously validated for use in medial temporal automated segmentation³) was used to automatically segment WM using the three high resolution atlases created.

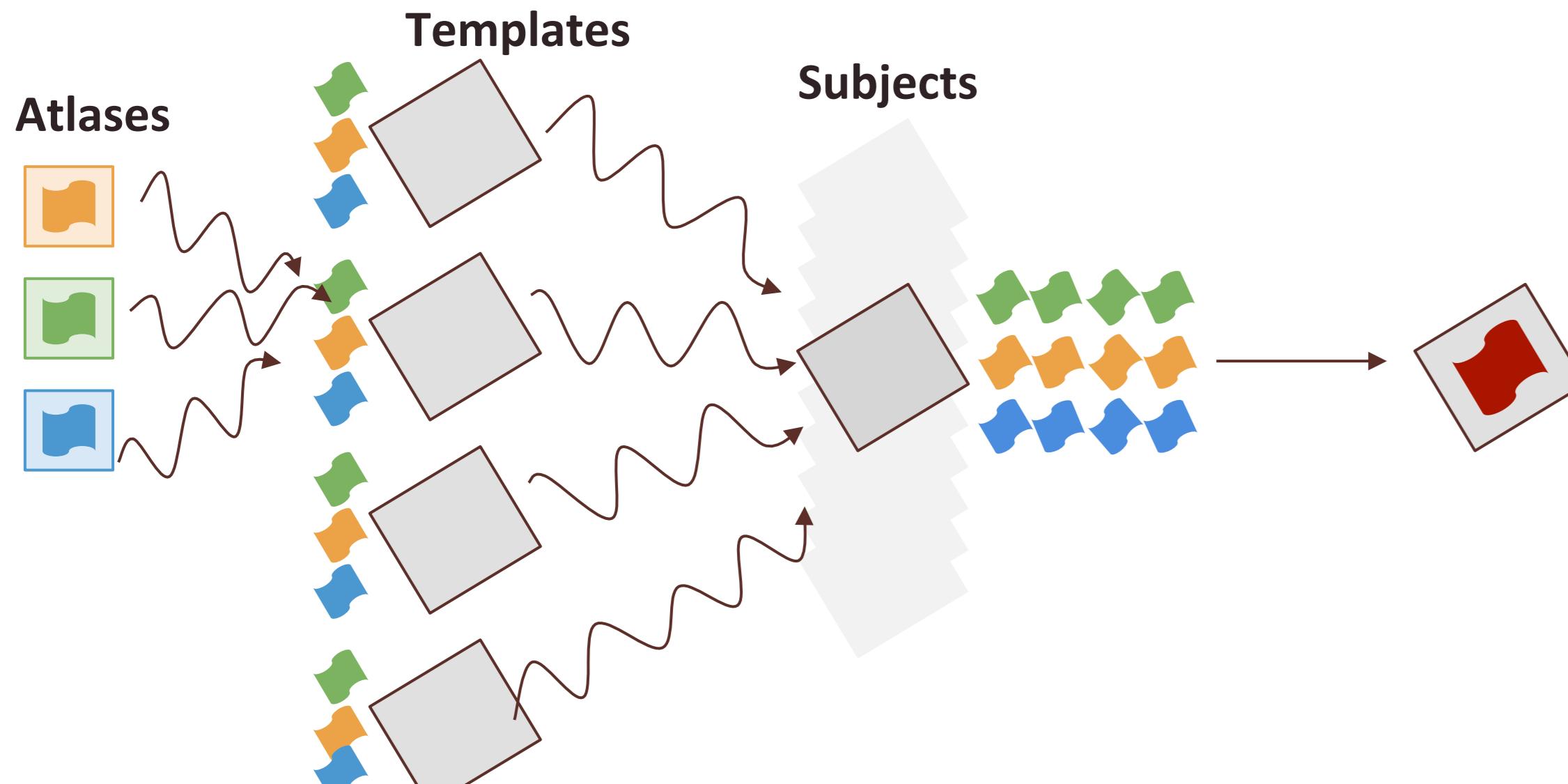


Figure 1. Summary of automatic segmentation process via Multiple Automatically Generated Templates (MAGeT Brain). Each atlas is used to segment a subset of participants (templates). Each template label is then used to segment each subject. All labels for a given subject are then fused to produce one final label.

RESULTS

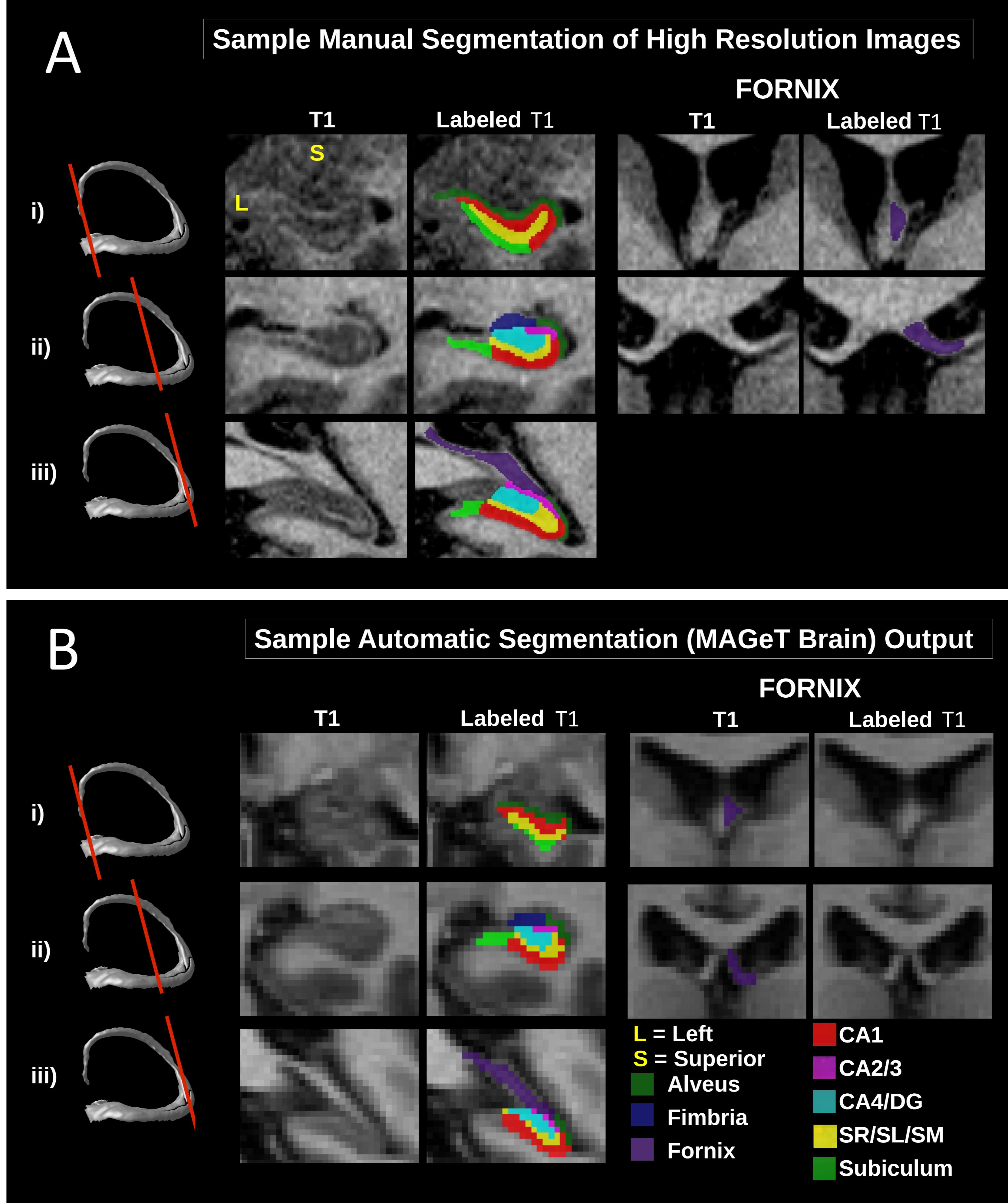


Figure 2. Manual and automatic segmentation for hippocampal subfields and white matter structures. **A:** Sample of high-resolution atlas created for white matter structures. Representative slices of the fornix are also depicted. White matter labels are presented along side hippocampal subfield labels as per Winterburn et al., 2013. **B:** Sample output of MAGeT Brain automatic segmentation. Resulting segmentations were inspected individually for quality control purposes. A total of 19 segmentations failed to reach quality standards (297 scans were used).

Effect Size of Structure Volumes Across Age

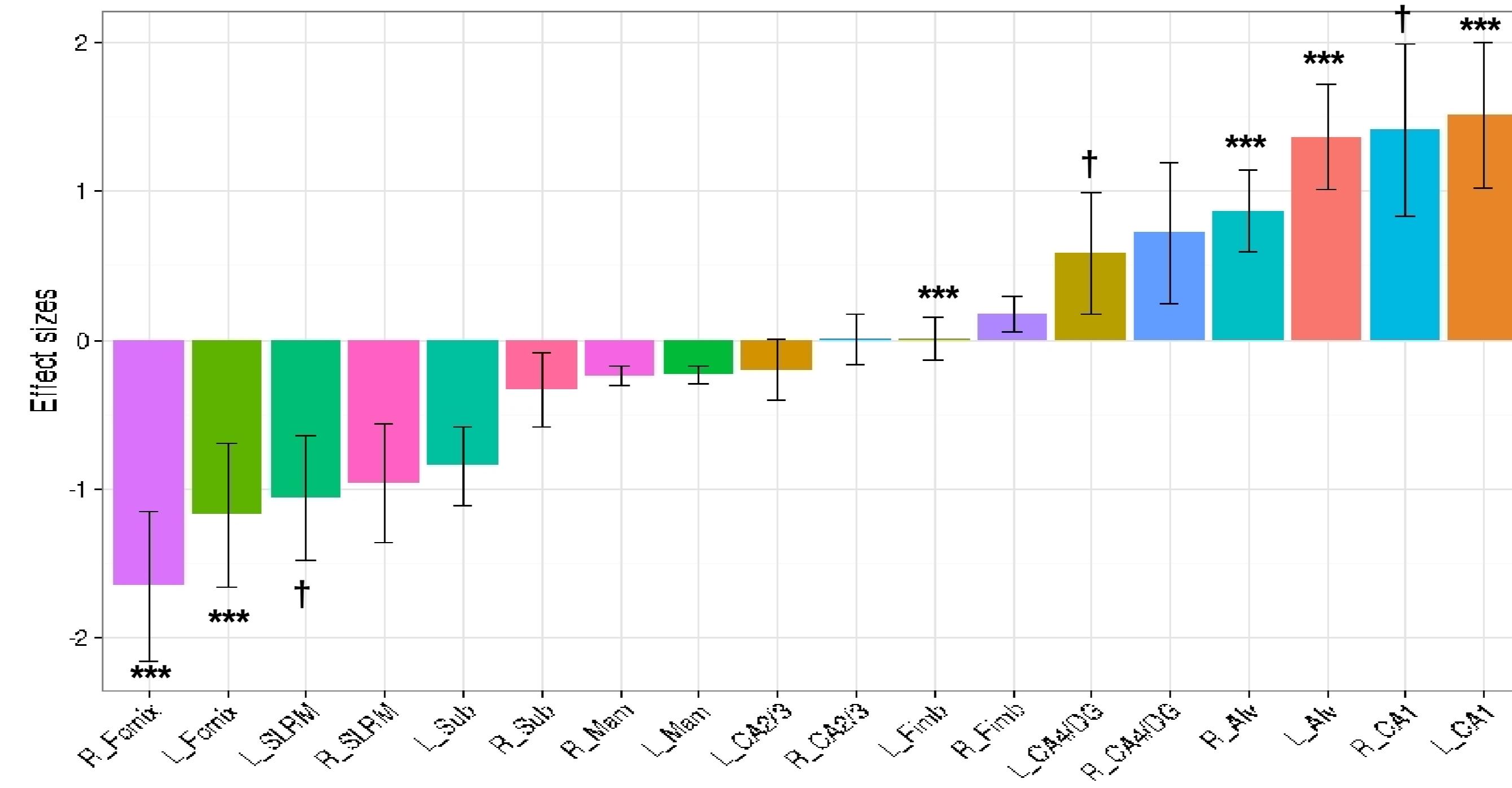


Figure 3. Graph depicting effect size (β values) of structure volumes on age. A general linear model controlling for sex, and total intracranial capacity demonstrated significant volumetric differences across age for the right and left fornix, right and left alveus and left CA1 region. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, † indicates significance prior to bonferroni correction.

SUMMARY

- A general linear model controlling for age, sex and total intracranial volume indicated a significant decrease in left and right fornix volume across age (respectively; $t=-3.27$, $p<0.001$; $t=-4.11$, $p<0.001$). This result is consistent with prior DTI-fornix studies.
- Another contrary to prior literature⁴ was the observed increase in left CA1 volume ($t=4.75$, $p<0.001$).
- The left CA1, SLM and CA4/DG were found to be significant prior to Bonferroni correction.
- Contrary to expected, the alveus was seen to increase bilaterally with age (Left: $t=7.16$, $p<0.001$; Right: $t=6.58$, $p<0.001$)

Here we present evidence of bilateral increases in CA1 and alveus volumes and decreased fornix volume during healthy aging. Previous studies have demonstrated preservation of the CA1 subfield in healthy aging⁴; however, the volumetric trajectory of HC WM remains relatively elusive. Our results suggest preservation of such structures (e.g. the alveus) may be linked to a decreased likelihood of developing neuropsychiatric disorders (e.g. Alzheimer's Disease).

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