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The hippocampal formation is a complex, heterogeneous structure that consists of a number of distinct, interacting subregions. Atrophy of these subregions is implied in a variety of neurodegenerative diseases, most prominently in Alzheimer’s disease (AD). Thanks to the increasing resolution of MR images and computational atlases, automatic segmentation of hippocampal subregions is becoming feasible in MRI scans. Here we introduce a generative model for dedicated longitudinal segmentation that relies on subject-specific atlases. The segmentations of the scans at the different time points are jointly computed using Bayesian inference. All time points are treated the same to avoid processing bias.

We evaluate this approach using over 4700 scans from two publicly available datasets (ADNI and MIRIAD). In test–retest reliability experiments, the proposed method yielded significantly lower volume differences and significantly higher Dice overlaps than the cross-sectional approach for nearly every subregion (average across subregions: 4.5% vs. 6.5%. Dice overlap: 81.8% vs. 75.4%). The longitudinal algorithm also demonstrated increased sensitivity to group differences: in MIRIAD (69 subjects: 46 with AD and 23 controls), it found differences in atrophy rates between AD and controls that the cross sectional method could not detect in a number of subregions: right parasubiculum, left and right presubiculum, right subiculum, left dentate gyrus, left CA4, left HATA and right tail. In ADNI (836 subjects: 369 with AD, 215 with early cognitive impairment — eMCI — and 252 controls), all methods found significant differences between AD and controls, but the proposed longitudinal algorithm detected differences between controls and eMCI and differences between eMCI and AD that the cross sectional method could not find: left presubiculum, right subiculum, left and right parasubiculum, left and right HATA. Moreover, many of the differences that the cross-sectional method already found were detected with higher significance. The presented algorithm will be made available as part of the open-source neuroimaging package FreeSurfer.

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