Hippocampus-Specific fMRI Group Activation Analysis with Continuous M-Reps

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Extended Abstract

Continuous M-Reps. In earlier work [4], we developed a deformable modeling framework called the *continuous medial representation (cm-rep)*, which, in simplest terms, is a continuous analog of the *m-rep* approach by Pizer *et al.* [3]. Cm-reps are deformable templates that have a special property that the skeleton (medial axis) of the template preserves its branching topology (number and configuration of its branches) during deformation. Furthermore, the skeleton of the deforming template is modeled explicitly as a continuous manifold and the exact geometric relationship between the skeleton and the template's boundary is captured. The skeleton-boundary relationship makes it possible to define a special shape-based coordinate system on the interior of the template. One of the coordinate axes connects points on the skeleton to the corresponding (nearest) points on the boundary, while the other two axes parameterize the skeleton as well as the boundary. As argued in [5], this coordinate system is a natural way to parameterize the interiors of anatomical structures to which cm-rep templates have been fitted. It allows us to analyze the distribution of appearance features (intensity, fMRI, DTI) within the structures more or less independently of the differences in the shape of the structures. In this paper, we illustrate the application of such analysis to functional MRI data associated with the hippocampus.

fMRI Study. We designed an fMRI study in which hippocampal activation was highly anticipated. Healthy volunteers (n=18) performed a complex scene encoding task in the scanner. The study followed the block design paradigm. In addition to EPI functional imaging, T_1 anatomical scans were acquired. Standard techniques (SPM, [2]) were used to align functional images to the anatomy, to correct for motion artifacts, to smooth the data temporally and spatially and to compute subject-level statistical maps using the general linear model.

Structure-Specific Group Analysis of fMRI. Whole-brain fMRI group analysis methods such as SPM [2] rely on deformable image registration to normalize

data between subjects. Registration does not always align the hippocampus accurately [1] and such misalignment will, in theory, reduce the statistical significance of intersubject statistical maps. To improve intersubject alignment in the hippocampus, we fit cm-rep templates to manual segmentations of the hippocampus (Fig. 1) and use the cm-rep coordinate system to project subject-level fMRI statistics to a common reference space[3]. We then perform random effects analysis to compute a hippocampus-specific groupwise statistical map.

Results: Improved Sensitivity and Specificity. We compared whole-brain and hippocampus-specific maps generated by SPM and our technique, respectively (Fig. 2). The peaks in the hippocampus-specific map had higher raw t-values and lower corrected p-values than the peaks located near the right hippocampus in the whole-brain map (Table 1). This indicates that our approach is more sensitive and that, in general, the accuracy of intersubject normalization does weigh in on the sensitivity of group analysis, despite the influence of many other sources of error. Furthermore, in most studies, peaks and clusters in the whole-brain activation map are assigned anatomical labels by looking up their coordinates in the Talairach space. Due to normalization errors, peaks resulting from consistent hippocampal activation across subjects may be mislabeled as activation in nearby structures. By restricting its analysis to the hippocampus, our approach aims to increase the likelihood that activation labeled as hippocampal is indeed originating in the hippocampus of each subject. However, specificity is confounded by the fact that spatial smoothing and EPI/T_1 alignment are performed for each subject. In part, our future work will focus on developing structure-focused EPI smoothing algorithms.

References

1. O. T. Carmichael, H. A. Aizenstein, S. W. Davis, J. T. Becker, P. M. Thompson, C. C. Meltzer, and Y. Liu. Atlas-based hippocampus segmentation in Alzheimer's disease and mild cognitive impairment. *Neuroimage*, 27(4):979–90, Oct 2005.
2. R. Frackowiak, K. Friston, C. Frith, R. Dolan, and J. Mazziotta, editors. *Human brain function*. Academic Press USA, 1997.
3. S. M. Pizer, P. T. Fletcher, S. Joshi, A. Thall, J. Z. Chen, Y. Fridman, D. S. Fritsch, A. G. Gash, J. M. Glotzer, M. R. Jiroutek, C. Lu, K. E. Muller, G. Tracton, P. Yushkevich, and E. L. Chaney. Deformable m-reps for 3D medical image segmentation. *International Journal of Computer Vision*, 55(2):85–106, Nov 2003.
4. P. A. Yushkevich, H. Zhang, and J. Gee. Continuous medial representation for anatomical structures. *IEEE Trans Med Imaging*, 2006. to appear.
5. P. A. Yushkevich, H. Zhang, and J. C. Gee. Statistical modeling of shape and appearance using the continuous medial representation. In *Medical Image Computing and Computer-Assisted Intervention, MICCAI*, volume 2, pages 725–732, 2005.

[3] Manual segmentation was performed only for the right hippocampus so our results are currently limited to that structure

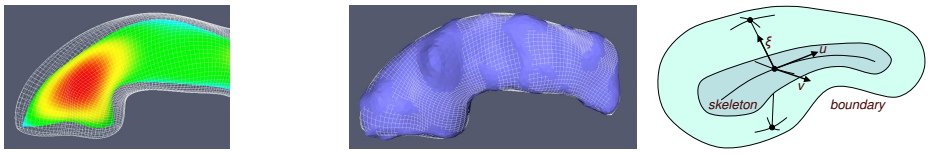

Fig. 1. A cm-rep template fitted to the hippocampus. On the left, the thickness function is plotted in color over the template's skeleton. In the middle, the target segmentation is shown in blue. The shape-based coordinate system is illustrated on the right.

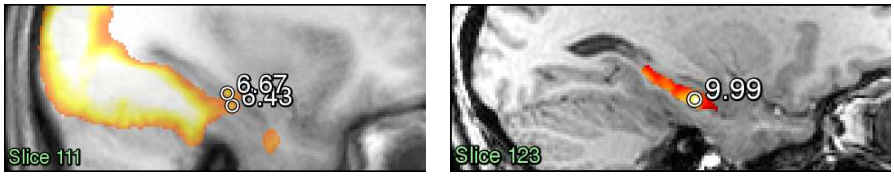

Fig. 2. Examples of sagittal slices through whole-brain (left) and hippocampus-specific (right) group analysis maps. Peaks are identified by circles.

Table 1. Peaks near the right hippocampus in the whole-brain group activation map compared to the peaks in the right hippocampus-specific group analysis map. Abbr.: right cerebrum (RC), parahippocampal gyrus (PHG), right hippocampus (RH). The column P_{hippo} indicates the fraction of hippocampus segmentations, warped into the space of the whole-brain template, that overlap each peak's location.

Peaks in Whole-Brain RFX Map

Tal. Coord.	Talairach Labels	t-Stat	p_{corr}	P_{hippo}
16, -31, -2	RC, limbic lobe, sub-gyral, *, *	7.69	0.033	0
20, -29, 8	RC, sub-lobar, thalamus, gray matter, pulvinar	6.89	0.14	0
31, -22, -9	RC, temporal lobe, sub-gyral, gray matter, hippocampus	6.67	0.21	0.94
33, -6, 27	RC, limbic lobe, uncus, white matter, *	6.47	0.30	0
31, -20, -13	RC, limbic lobe, PHG, gray matter, hippocampus	6.43	0.33	0.82
27, -21, -13	RC, limbic lobe, PHG, gray matter, Brodmann area 6	6.12	0.60	0.94
24, -17, -17	RC, limbic lobe, PHG, white matter, *	6.01	0.74	0.94

Peaks in the Hippocampus-Specific RFX Map

Loc. in RH	t-Stat	p_{corr}	Loc. in RH	t-Stat	p_{corr}
Head, Lateral	9.99	0.00016	Tail, Lateral	8.04	0.0035
Tail, Medial	7.55	0.0082	Body, Lateral	6.45	0.062