Hippocampal and Ventricular Differences in 804 ADNI subjects mapped with Multivariate Tensor-Based Morphometry

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Introduction

Computational anatomy methods are now widely used in clinical neuroimaging to map the profile of disease effects on the brain and its clinical correlates. In Alzheimer's disease (AD), many research groups have modeled localized changes in hippocampal and lateral ventricular surfaces, to provide candidate biomarkers of disease progression for drug trials. We combined the power of parametric surface modeling and tensor-based morphometry to study hippocampal differences associated with AD and mild cognitive impairment (MCI) in 490 subjects (97 AD, 245 MCI, 148 controls) and ventricular differences in 804 subjects scanned as part of the Alzheimer's Disease Neuroimaging Initiative (ADNI; 184 AD, 391 MCI, 229 controls). We aimed to show that multivariate tensor-based surface morphometry (Wang et al., 2009) provides a more powerful way to detect localized anatomical differences than conventional surface-based analysis methods.

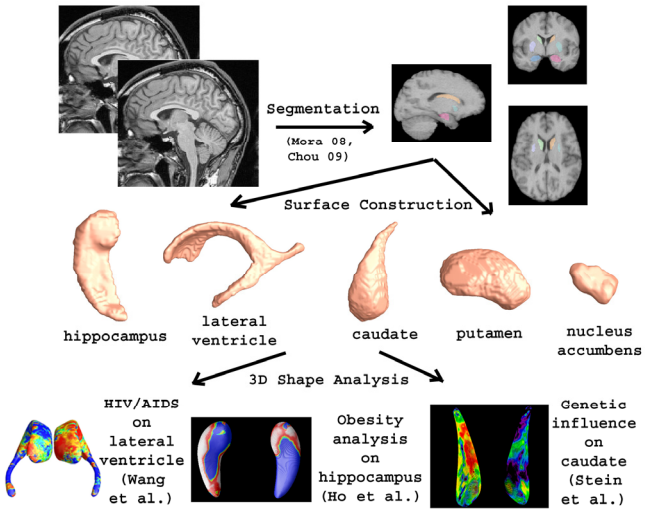

Figure 1. We introduce an automatic 3D subcortical structure morphometry analysis system. Using a method from exterior calculus based on holomorphic differentials, we computed conformal grids on various subcortical surfaces (Wang et al., 2007). A new statistics, multivariate tensor-based morphometry (MTBM) was computed on conformal grids and used to evaluated group differences and correlation with CSF biomarker and clinical decline. The system was used in multiple research projects and demonstrated good accuracy and efficiency.

Methods

We analyzed baseline T1-weighted MRI scans from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset (http://www.loni.ucla.edu/ADNI). First, we extracted parametric surface models of the hippocampus using our adaptive boosting method (N=490; Morra et al., 2008). We also created surface mesh models of the lateral ventricles using our multi-atlas segmentation method that combines multiple fluid registrations to boost accuracy (N=804; Chou et al., 2009). Using a method from exterior calculus based on holomorphic differentials, we induced conformal grids on these meshes (Wang et al., 2007). We left two holes at the front and back of the hippocampus, representing its anterior junction with the amygdala and its posterior limit as it turns into the white matter of the fornix. The hippocampus then represented as an open boundary genus one surface, i.e., a cylinder, and was conformally mapped to a rectangle. To model the lateral ventricular surface, we automatically located and introduced three cuts, based on the topology of the lateral ventricles, in which several horns are joined together at the ventricular "atrium" or "trigone". With holomorphic flow segmentation (Wang et al., 2007), each lateral ventricular surface was automatically partitioned into 3 pieces . Although surface geometry is widely variable across subjects, these zero point locations are stable and intrinsically determined by the surface conformal structures, and the resulting surface partition into component meshes is stable (Figure 2). We registered the hippocampal and lateral ventricular surfaces across subjects using a constrained harmonic map.

As well as examining shape differences using the eigenvalues of the surface deformation tensor, we also used a log-Euclidean metrics (Arsigny et al., 2006), which allows multivariate statistics on the tensors to be computed easily using standard Euclidean formulae. We applied Hotelling's T^2 test to the log-transformed surface deformation tensors.

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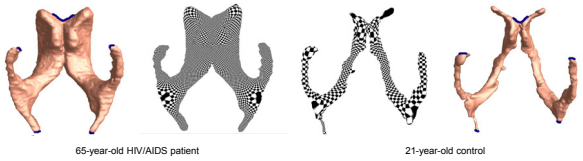

Figure 2 Conformal structure is intrinsic to surface structure. The positions of zero points are very consistent so that it may be used for surface registration.

Results

Hippocampus. Figure 3 shows regions with significant hippocampal shape differences in AD versus MCI, as an example application. We show the statistical *p*-map based on three different local statistics: multivariate TBM, Jacobian determinant and distance to the medial curves (Thompson et al., 2004). All 3 statistics detect consistent morphometric differences, but multivariate TBM gave greatest effect sizes (as shown in the cumulative distribution plots of *p*-values).

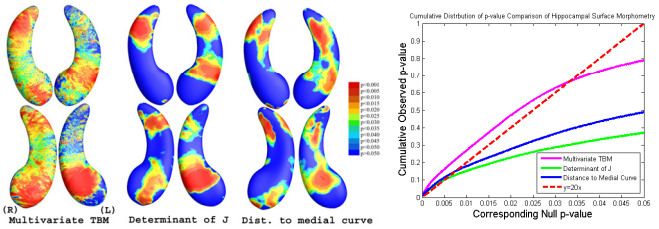

Figure 3. Statistical *p*-map results (left panel) show hippocampal surface shape differences between groups of MCI and AD subjects, using three different statistics: (a) multivariate tensor-based morphometry (MTBM); (b) the determinant of the Jacobian matrix (J) of the surface coordinates; and (c) the radial distance to the medial curve (Thompson et al., 2004). Non-blue colors show vertices with statistical differences, at the p=0.05 level, uncorrected. Multivariate TBM detected anatomical differences more powerfully than the other two statistics. The right panel shows that MTBM yields results that are highly significant using FDR (as they rise above the reference line y=20x).

Lateral Ventricles. Figure 4 shows regions with significant ventricular shape differences in AD versus MCI, using the same 3 statistics. Again, multivariate TBM gave greatest effect sizes; statistics on the surface deformation tensor outperformed scalar summaries of the deformation based on the eigenvalues.

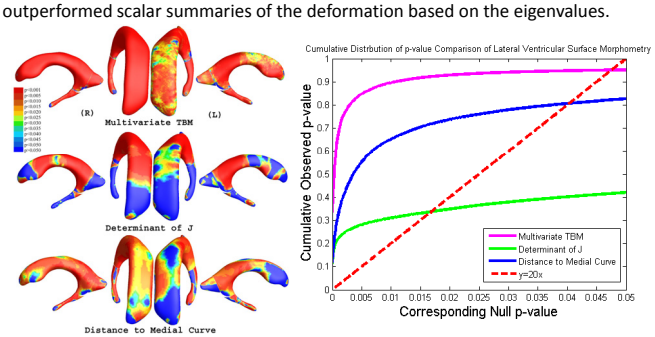

Figure 4. Statistical *p*-map results (left panel) show ventricular surface shape differences between groups of MCI and AD subjects, using three different statistics: (a) multivariate tensor-based morphometry; (b) the determinant of the Jacobian matrix (J) of the surface coordinates; and (c) the radial distance to the medial curve (Thompson et al., 2004). Non-blue colors show vertices with statistical differences, at the p=0.05 level, uncorrected. Multivariate TBM detected anatomical differences more powerfully than the other two statistics. . The right panel shows that MTBM yields results that are highly significant using FDR (as they rise above the reference line y=20x).

Conclusion

In this large subcortical morphometry study, highest effect sizes were given by our novel surface-based analysis method. Our method consists of automated surface extraction, conformal parameterization and partitioning, harmonic mapping, and tensor statistics. This method, proposed in (Wang et al., 2009) is applied here to a large cohort. Future work will use multivariate surface TBM for map-based disease classification and prognosis, and as a candidate biomarker for clinical trials.

Reference:

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