Metric distances between hippocampal shapes predict different rates of shape changes in dementia of Alzheimer type and nondemented subjects: a validation study

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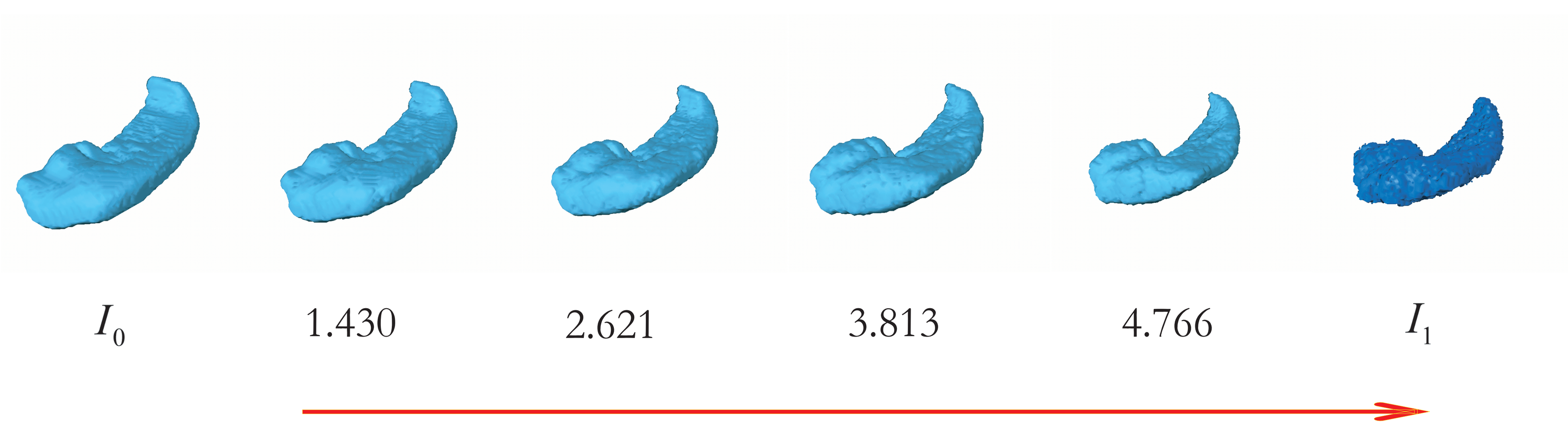
Introduction

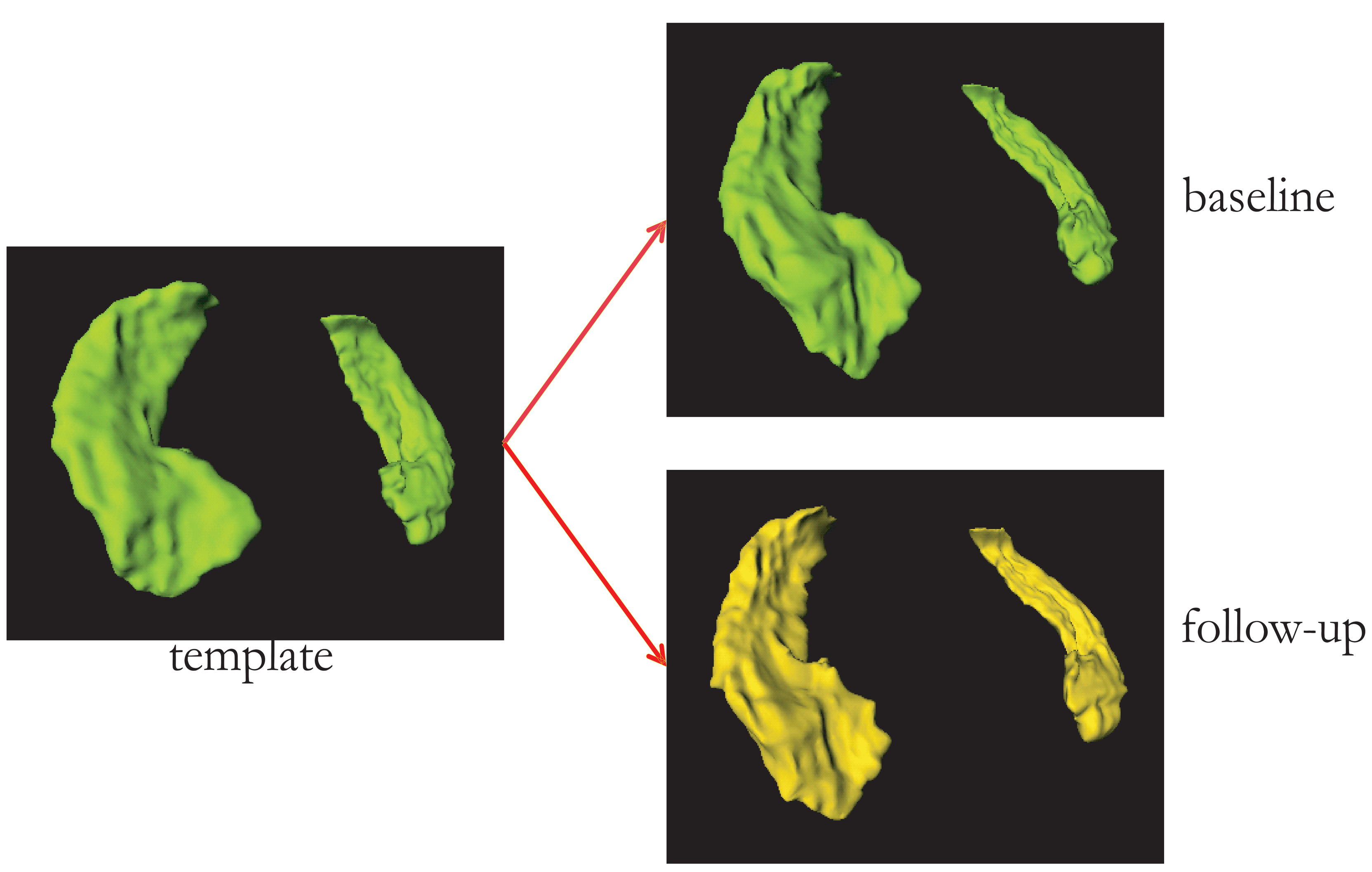
Recent studies have demonstrated the rates at which hippocampal shape in subjects with dementia of Alzheimer type (DAT) change are distinguishable from those in nondemented controls. In particular, Wang et al. [1] used the Large Deformation Diffeomorphic Mapping method [2] that computes diffeomorphisms (one to one, invertible and differentiable maps) between template and target MR subvolumes enclosing the hippocampus. This algorithm is "greedy" in that it computes locally optimal diffeomorphisms for each time-step of the mapping. In contrast, the Large Deformation Diffeomorphic Metric Mapping (LDDMM) method [3] is globally optimal in that it generates diffeomorphisms over the whole time interval of the mapping. LDDMM computes the velocity vectors that transform one binary image of an anatomical structure to another giving a metric distance between the two structures as shown below. The norm ensures smoothness in the space of velocity vector fields, V, that are generated by the group of infinite dimensional diffeomorphisms (which is the generalization of the rotation, translation and scale group), the necessary group for studying shape. The metric distances provide the mathematical notion of what structures are similar and different [4] and could thus be used to predict rates of shape changes over time.



$$d(I_0, I_1) = \sqrt{\int_0^1 \|v\|_V^2 \, dt}$$

Methods

The original data consisted of triangulated graphs of the template hippocamppal surface and the segmented hippocampal surfaces at baseline and follow-up at two years generated by Wang et al. [1] in MR scans from 18 subjects with very mild DAT (CDR 0.5) and 26 age-matched nondemented controls (CDR 0). Respective ages intervals were 73±7 and 74±4.4 years old with scan intervals of 2±0.53 and 2.2±0.37 years. The triangulated graphs were converted to binary images. The figure below shows how LDDMM was applied to the corresponding template-baseline and template-follow-up binary hippocampal segmentations to generate metric distances between the shapes (with respect to the template).



References:

[1] Wang, L. et al. (2003). Changes in hippocampal volume and shape across time distinguish dementia of the Alzheimer type from healthy aging. NeuroImage 20, 667.

[2] Christensen, G.E. et al. (1996) Deformable templates using large deformation kinematics. IEEE Trans. Image Process. 5, 1435.

[3] Beg. M.F. et al. (2005) Computing Large Deformation Metric Mappings via Geodesic Flows of Diffeomorphisms. Int. J. Comp. Vision, 61, 139.

[4] Miller, M.I. et al. (2002) On the metrics and Euler-Lagrange Equations of Computational Anatomy. Ann. Rev. Biomed.

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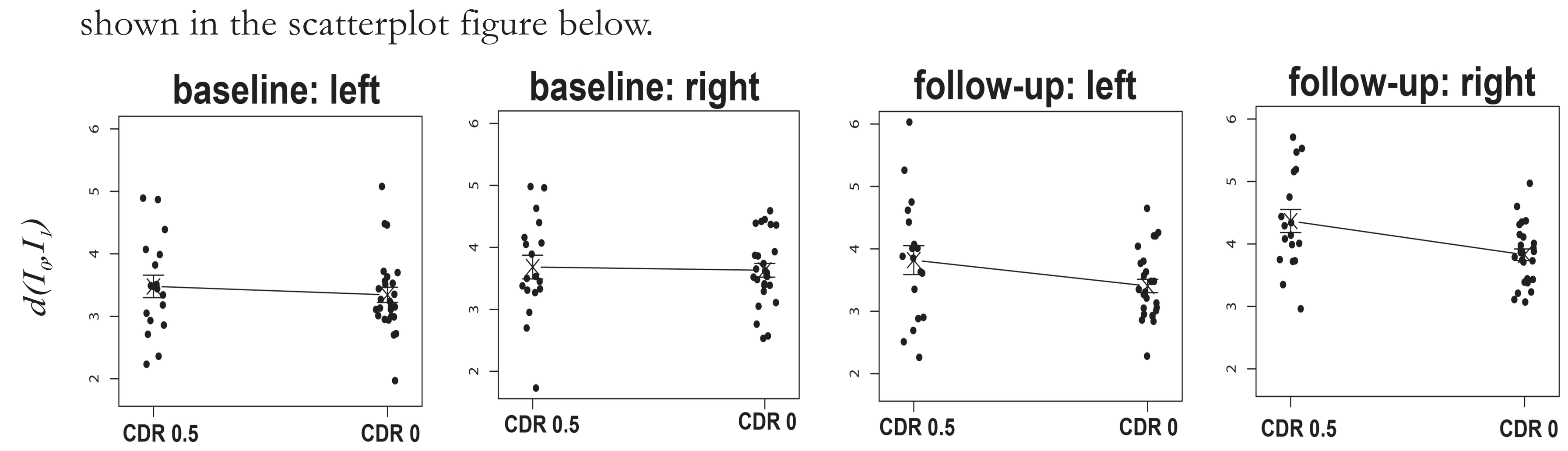
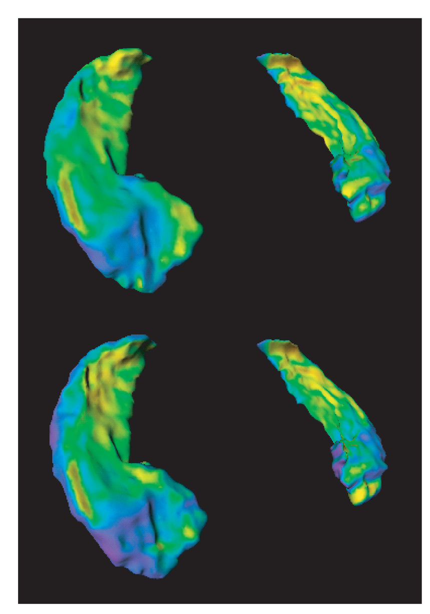
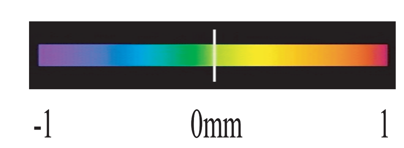
Results

For comparison, the LDDMM generated diffeomorphisms were applied to the template surface and the deformed surfaces were found to be within 0.375mm of those generated by Wang et al. [1] for 90% of the surface vertices (assuming voxel resolution of $0.5mm^3$). Metric distances are shown in the scatterplot figure below.



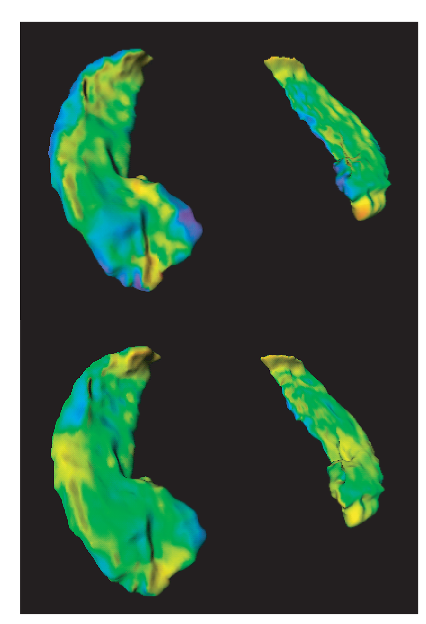
Wilcoxon rank sum and signed rank tests were used to analyze the metric distances with associated p-values presented in tables below with significant ones (<.05) marked with a star. The table below suggests that hippocampal shapes in CDR 0.5 subjects change more over time than in CDR 0 subjects. Next to the table is shape deformation taken from Wang et al. [1] with the group comparisons at baseline shown in the upper panel and that at follow-up in the lower panel.

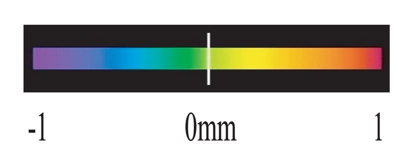




		CDR 0.5 vs CDR 0		
		2-sided	1st < 2nd	1st > 2nd
baseline	left	0.61	0.70	0.30
	right	0.92	0.55	0.46
follow-up	left	0.16	0.92	0.08
	right	0.02*	0.99	0.02*

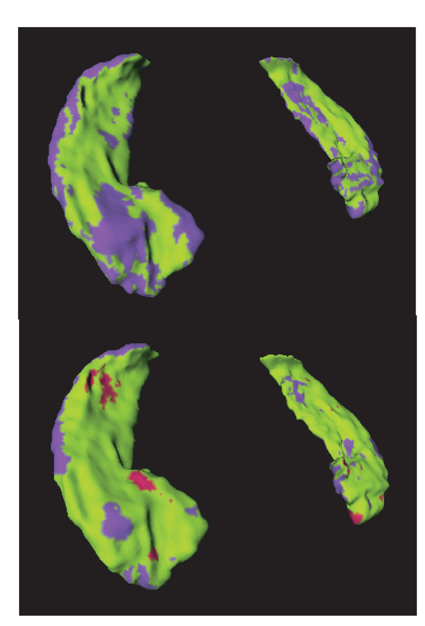
The table below suggests changes in both right and left hippocampi are more noticeable in CDR 0.5 subjects than in CDR 0 subjects with possibly some mild changes in the right in CDR 0 subjects as a result of aging. Shown next to the table are the shape changes across time for CDR 0 (bottom) and CDR 0.5 (top) subjects computed by Wang et al. [1].

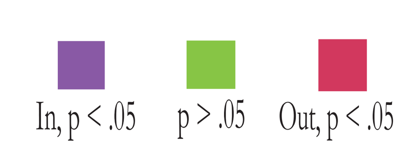




		baseline vs follow-up		
		2-sided	1st < 2nd	1st > 2nd
CDR 0.5	left	0.03*	0.02*	0.99
	right	0.00*	0.00*	0.99
CDR 0	left	0.71	0.36	0.65
	right	0.12	0.06	0.94

The table below suggests some asymmetry in shape changes over time with the effect more pronounced for the right hippocampus. Shown next to the table are the statistical significance of the deformations over time for CDR 0 (bottom) and CDR 0.5 (top) subjects computed by Wang et al. [1] via Wilcoxon's signed rank test with inward in purple (p<.05), outward in red (p<.05), and non-significant deformations (p>.05) in green.





		left vs right		
		2-sided	l < r	l > r
CDR 0.5	baseline	0.35	0.17	0.84
	follow-up	0.04*	0.02*	0.98
CDR 0	baseline	0.06	0.03*	0.97
	follow-up	0.01*	0.00*	0.99

Summary

Thus metric distances can be used as a bio-marker to quantify different patterns of hippocampal shape change over time as well as different rates of hippocampal volume loss distinguishing very mild DAT from healthy aging.

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