Local volume changes of the corpus callosum from 3D MR images of wildtype and knockout mouse brains

G. Hamarneh[1], J. Chen[1], N. Lifshitz[1], J. Henderson[2], M. Henkelman[1]
[1]Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada

Synopsis

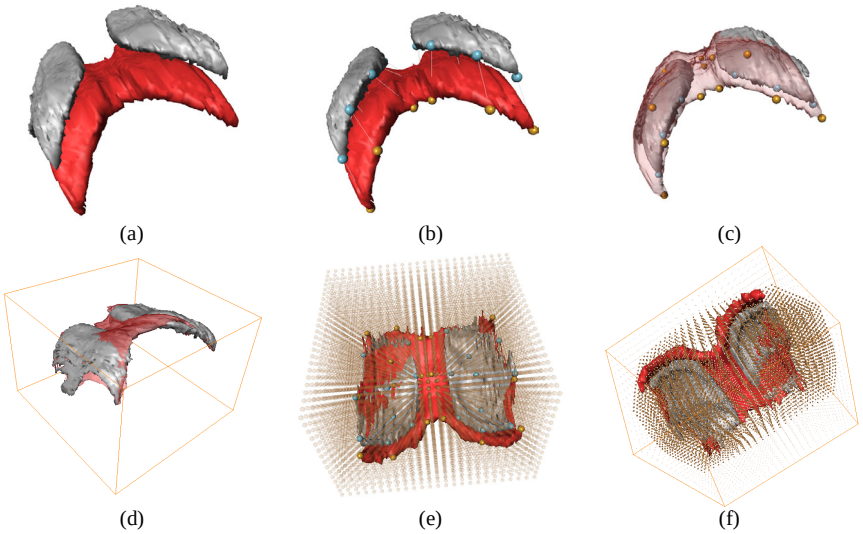
We characterize 3D local volume changes of the corpus callosum from MR images of wildtype and neuro-transgenic fixed mouse brains. We demonstrate how the measurement technique could be used for detecting morphological phenotypes for mutant mouse screening.

Methods

We calculated local volume changes of wildtype and mutant mouse brain structures from the deformation field that maps the correspondence between structures. The deformation field encodes how each tri-ordinate (u,v,w) of a uniform lattice in the wildtype mouse image space is displaced to (U,V,W) in the mutant mouse image space. To establish this spatial correspondence for the wildtype and neuro-transgenic corpora callosa pair (denoted wCC and tCC, respectively), we segmented the wCC and tCC from the MR images (Figure 1a) using Livewire, a semi-automatic segmentation tool provided by Amira software (TGS, San Diego, CA). We then selected homologous wCC-tCC landmarks (Figure 1b) and calculated a rigid transformation to align them (Figure 1c). We thereafter applied thin plate splines (TPS) interpolation to deform the wCC landmarks and surface to tCC (Figure 1d) as dictated by the new corresponding landmarks resulting from the rigid transformation (Figure 1c). The vertices (u,v,w) of a 3D uniform grid in the image space of wCC (Figure 1e) are also transformed using TPS into the new warped grid (U,V,W) (Figure 1f). We then calculated the local volume change according to (see [1] for details):

$$d(u,v,w) = \det\left\{\nabla\left[U(u,v,w), V(u,v,w), W(u,v,w)\right]\right\}$$

where ∇ denotes the gradient of a vector function and det{.} denotes the determinant of a matrix. The deformation function $d(u,v,w)$ measures the expansion or shrinkage required to register wCC to tCC.



(a) (b) (c) (d) (e) (f)

Figure 1. Deformation field calculation (see text for details). wCC rendered in red and tCC in gray.

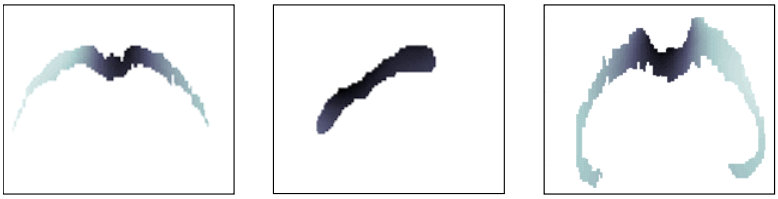
Results

The brains of wildtype and transgenic knockout (Nuk^1/+) 129/SV mice were fixed and imaged (7-T, spin echo, TR 1500ms, TE 30ms, 15.4 hours, 384x192x192 matrix of 40μm^3 isotropic resolution). We first present total volume results (Table 1). Note the decrease in total volume in the transgenic brain and tCC.

Table 1. Total volume measurements.

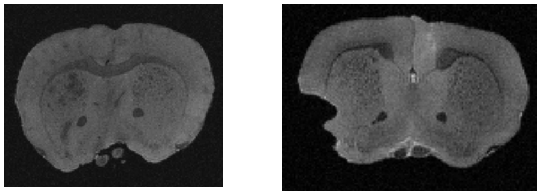
	wildtype volume		knockout volume	
structure	mm^3	normalized	mm^3	normalized
Brain	468.07	1.00	323.55	1.00
CC	11.69	0.0250	5.64	0.0174

By performing local volume change measurements we are able to visualize the relative volume reduction throughout the CC (Figure 2) which clearly shows CC shrinkage in the mid-sagittal region. This is also visible in the coronal MR cross sections (Figure 3), where the CC shrinks/disappears towards the mid-sagittal region in the knockout mouse.



(a) (b) (c)

Figure 2. Local volume change measurements. (a) Coronal, (b) mid-sagittal, and (c) transversal cross sections through wCC. Darker areas mean more volume reduction.



(a) (b)

Figure 3. MRI coronal cross sections through the (a) wildtype and (b) transgenic mouse brains.

Conclusion

We presented a technique for characterizing local volume changes from 3D deformation fields in high resolution MR images of mice. By quantifying localized morphological changes, this measurement technique provides additional insight not attainable by total volume measurements alone. We demonstrated the measurement of local volume changes and the detection of regions of abnormal morphology from a deformation field obtained with the assistance of a human operator. However, we envision and are working on replacing the semi-automatic segmentation and manual landmark labeling with automated image segmentation and registration techniques, thus providing a fully automated screening system for morphological phenotypes.

Acknowledgments

We thank John G. Sled for the helpful discussions.

References

[1] C.A. Davatzikos, M. Vaillant, S. Resnick, J.L. Prince, S. Letovsky, and R.N. Bryan. A Computerized approach for morphological analysis of the corpus callosum Journal of Computer Assisted Tomography, 20(1):88-97, 1996.