Image registration of mouse brains containing varying amounts of extra cortical CSF

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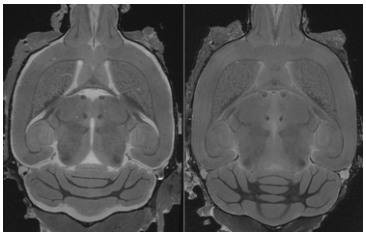
Introduction



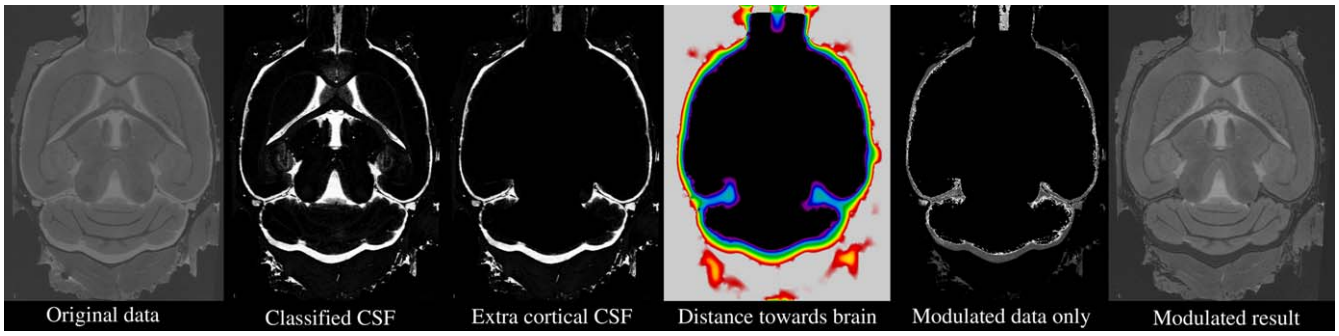
Neuroanatomical abnormalities are important indicators of human disease and their respective mouse models. Using MRI and subsequent image analysis, minute abnormalities in mouse neuroanatomy can be detected. To identify these abnormalities, we utilize a groupwise image registration method based on cross correlation (Kovacevic et al., 2005; Chen et al., 2006). In recent studies we encountered mouse brains with abnormally large and variable amounts of extra cortical CSF. (See figure on the right where a brain with an unusual large layer of extra cortical CSF is shown as well as one with an ordinary amount of CSF.) Given the intensity of background, cortex and CSF in a T2 weighted MRI, a higher correlation is found when matching CSF to cortex compared to matching CSF to background. In some cases this leads to incorrect alignment of the brains. Parts of the extra cortical CSF are sometimes matched to the cortex in other brains. This misalignment can lead to incorrect conclusions about findings in subsequent analyses. To deal with this problem, we considered using mutual information for the image registration; however this does not explicitly control whether the CSF layer is treated as brain tissue or background. We introduce here an automatic approach which will modulate the extra cortical CSF to have it resemble background and thus eliminate this confound to the registration problem.

Methods

The process of modulating the CSF intensity consists of three parts (illustrated in sequence in the figure below). First we will classify the CSF tissue in the brain using a fuzzy classifier. Next, the CSF we are interested in, namely the CSF around the surface of the brain, is identified and finally the intensity of this CSF is modulated so it will appear to be background. The classification of tissues is done using the voxel intensities. To avoid retraining the classifier for each specimen, all brain data sets were normalized prior to classification. The choice of a fuzzy classifier allows for a smooth transition between regions with no modulation and full modulation. Each brain is aligned to an atlas so as to estimate the location of the brain surface and to identify the extra cortical CSF. When voxels inside the cortex are classified as CSF, the modulation of these voxels is towards cortex intensities. On the other hand, voxels outside the brain classified as CSF are modulated towards background intensities. To allow for this calculation, the residual CSF layer was used to create a coordinate system consisting of contours parallel to the brain surface parameterized between 0 and 1 (D_v, distance value). The modulation formula depends on the likelihood of a voxel being CSF (F_v, fuzzy classification value) and D_v. The background intensity is given by I_{bg}, the cortex intensity by I_{cortex}. The constant γ defining the sharpness of Sigmoid curve was 12 in our case. The voxel modulation formula is given as:

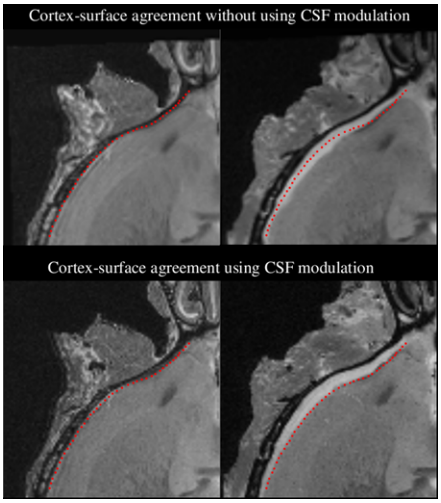
$$\begin{aligned} \text{voxel} &= \text{original voxel intensity} && \text{if } F_v \le 0.1, \\ &= I_{bg} + \alpha * \beta * (I_{cortex} - I_{bg}) && \text{if } F_v > 0.1; \end{aligned}$$

$$\text{Where}: \alpha = 1 - \frac{1}{1 + e^{-\gamma(Fv - 1/2)}} \quad , \quad \beta = 1 - (D_v)^5$$



Results

We have used our modulation strategy in the groupwise registration method. On the right (top row) we see the cortical alignment obtained without the modulation strategy and we observe that part of the CSF is incorrectly aligned with the cortex of another brain. In the bottom row we see that when the CSF was modulated during the registration method, the two cortices were correctly aligned.



Conclusion

In recent studies we encountered brains containing varying amounts of extra cortical CSF. Using our groupwise registration method for analysis of the brains, we found this resulted in incorrect alignment. That would lead to incorrect findings. We have developed a modulation strategy to deal with this extra cortical CSF, alleviating the registration problem.

References

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Kovacevic N, Henderson JT, Chan E, Lifshitz N, Bishop J, Evans AC, Henkelman RM, Chen XJ. (2005) A three-dimensional MRI atlas of the mouse brain with estimates of the average and variability. Cereb Cortex. 15:5 639-45