Thalamic segmentation and validation with diffusion-weighted MRI

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Target audience Investigators using diffusion-weighted MRI (DWI) data and clustering algorithms, interested in quantitative validation to research and clinical purpose.

Purpose The thalamus is a midline symmetrical structure situated between cortex and midbrain. Myelinated axons emerge from several thalamic nuclei and terminate in the cerebral cortex. We present an algorithm that segments the thalamus based on diffusion-weighted MRI (DWI) data without manual intervention. The key advantage of the approach is provided by the use of so-called dissimilarity-based representations (DBR) to combine data from multiple input sources and modalities into a single metric (Figure 1). The algorithm generates thalamic segmentations and evaluates their accuracy by computing clusters' (a) hemispheric symmetry and (b) quality of the prediction the segmentation produces on an independent set of DWI. We present the methods and illustrate the segmentation results in relation to two thalamic atlases obtained with different approaches[1, 2].

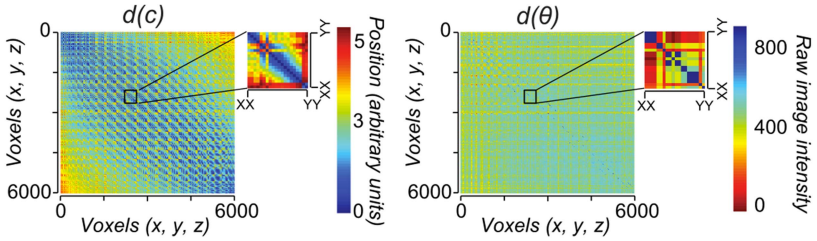

Figure 2 Automatic clustering initialization. Dissimilarity matrix. Left-hand panel, pixels in the image represent the Mahalanobis distance in *mm* between pairs of thalamic voxels. Right-hand panel, pixels in the image represent the Euclidean distance between the demeaned diffusion signal of pair of thalamic voxels.

Methods We acquired DWI data of 5 subjects with 96 diffusion-weighting directions ($b = 4000 s/mm^2$, resolution $1.5mm$ isotropic) at 3T and used the measurements to segment the thalamus. Segmentations were generated by a weighted combination of local diffusion measurements (DW) and spatial coordinates (c). We used *k*-means clustering on the combination of DW and c weighted by the factor α. We performed cross-validation for finding the α that generated the thalamic segmentation with clusters' means $\overline{DW}$ best predicting the measured diffusion properties in a second dataset. We computed the symmetry in terms of the spatial coordinates between the centroids of each thalamic cluster in the left and right hemisphere. Segmentations corresponding to maximizing both accuracy and symmetry were retained (Figure 2).

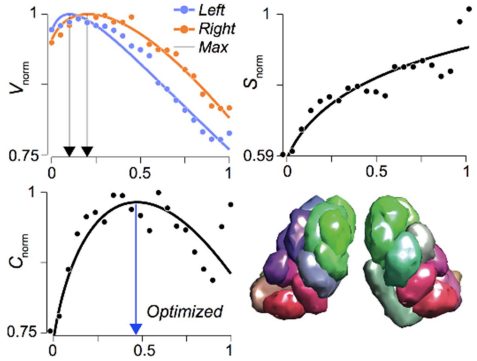

Figure 1 Segmentation optimization. From top left to bottom right: Explained variance (*V*, normalized) in the measured fiber orientation modulation as function of the contribution (α) of clusters' spatial coordinates and predicted fiber orientation distribution. Orange and blue indicate the right and left thalamic segmentations. Explained variance decrease with α. Inter hemispheric symmetry (*S*) of thalamic clusters. Symmetry increases with α. Combined validation metric, *C*. The maximum of the curve indicates the value of α that maximizes both *V* and *S*. Final clustering result.

Results We illustrate the segmentation results in relation to two thalamic atlases obtained with different approaches. These segmentations vary substantially. In addition to the differences in global shape of the thalamus there is also a substantial difference in the way the thalamus can be segmented using different methods. On the one side this difference is expected because the atlases use different data and information to segment (DWI vs. staining), on the other side it is important to be able to compare the different segmentation solutions, i.e. to have a mechanism to establish the quality of segmentations. To this end, our algorithm allows for establishing how well a thalamic segmentation represents the measured data.

Discussion Recently there have been a number of attempts to automatically segment the thalamus[1, 2]. The current method relies on three simple assumptions - fascicles' homogeneity within a nucleus, spatial homogeneity of nuclei, and hemispheric symmetry of the nuclei.

Conclusions Evaluating the accuracy by which a thalamic segmentation represents the measured diffusion properties in the thalamus and the symmetry of the clusters in the two hemispheres provides a suitable metric for automatically and reliably segmenting the thalamus in the living human brain.

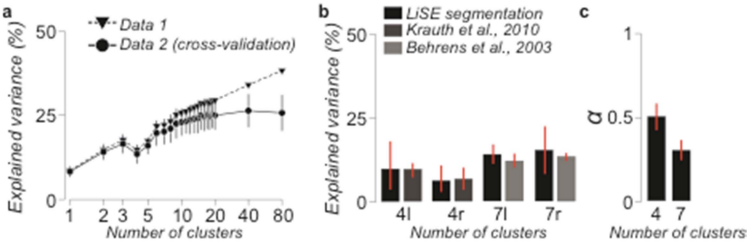

Figure 3 Thalamic segmentations evaluation. a. Cross-validated and non-cross-validated explained variance in the demeaned diffusion signal as function of cluster number in the segmentation (mean ±1 stdev across individual brains). **b.** Comparison of the cross-validated explained variance in the demeaned diffusion signal across thalamic segmentations. **c.** Average α.

References 1. Behrens TEJ, Johansen-Berg H, Woolrich MW et al. Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. *Nat neurosci*, 2003; *6*(7):750-757. 2. Krauth A, Blanc R, Poveda A, et al. A mean three-dimensional atlas of the human thalamus: generation from multiple histological data. *Neuroimage*, 2010; *49*(3):2053-2062.