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Thalamus segmentation using multi-modal feature classification: Validation and pilot study of an age-matched cohort

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ABSTRACT

Automatic segmentation of the thalamus can be used to measure differences and track changes in thalamic volume that may occur due to disease, injury or normal aging. An automatic thalamus segmentation algorithm incorporating features from diffusion tensor imaging (DTI) and thalamus priors constructed from multiple atlases is proposed. Multiple atlases with corresponding manual thalamus segmentations are registered to the target image and averaged to generate the thalamus prior. At each voxel in a region of interest around the thalamus, a multidimensional feature vector that includes the thalamus prior as well as a set of DTI features, including fractional anisotropy, mean diffusivity, and fiber orientation is formed. A random forest is trained to classify each voxel as belonging to the thalamus or background within the region of interest. Using a leave-one-out cross-validation on nine subjects, the proposed algorithm achieves a mean Dice score of 0.878 and 0.890 for the left and right thalami, respectively, which are higher Dice scores than the three state-of-art methods we compared to. We demonstrate the utility of the method with a pilot study exploring the difference in the thalamus fraction between 21 multiple sclerosis (MS) patients and 21 age-matched healthy controls. The left and right thalamic volumes (normalized by intracranial volumes) are larger in healthy controls by 7.6% and 7.3% respectively, compared to MS patients (though neither result is statistically significant).

1. Introduction

The thalamus is a key subcortical structure located between the cerebral cortex and midbrain. It relays sensory and motor signals to the cerebral cortex and regulates consciousness, sleep, and alertness (Sherman and Guillery, 2000). It is composed of gray matter and myelinated fibers and has connections to nearly every major region in the brain. Fig. 1 shows an example of a manual segmentation of the thalamus overlayed on three views of the corresponding magnetic resonance image (MRI) and as a volume rendering. The thalamus can be subdivided into thalamic nuclei based on histological or functional criteria (Ziyan et al., 2006). The medial and lateral geniculates (Morel, 2007), two small thalamic nuclei located inferior to the main body of the thalamus, are identified by arrows in Fig. 1. The geniculates can be difficult for automatic algorithms to segment due to their low contrast compared to surrounding tissue in T1-w MRI, resulting in an inaccurate estimation of the thalamic volume. Changes in thalamic volume are correlated with many neurodegenerative diseases including multiple sclerosis (MS) (Cifelli et al., 2002; Houtchens et al., 2007), Alzheimer's disease (Braak and Braak, 1991; Zarei et al., 2010), schizophrenia (Byne et al., 2002; Cullen et al., 2003; Danos et al., 2003), and Parkinson's disease (Jellinger, 1999). Thus, accurate segmentation of the thalamus is an important part of understanding and managing neurological diseases and using an automatic segmentation method can facilitate this task.

Our work is motivated by prior studies on the change in volume of the thalamus in multiple sclerosis. Cifelli et al. (2002) manually outlined thalamic volumes in 14 secondary progressive MS patients and 14 healthy controls (HCs). After normalizing to the intracranial volume (ICV), the mean thalamic volume of the MS patients was 17% smaller compared to HCs. Cifelli et al. (2002) also performed a postmortem study

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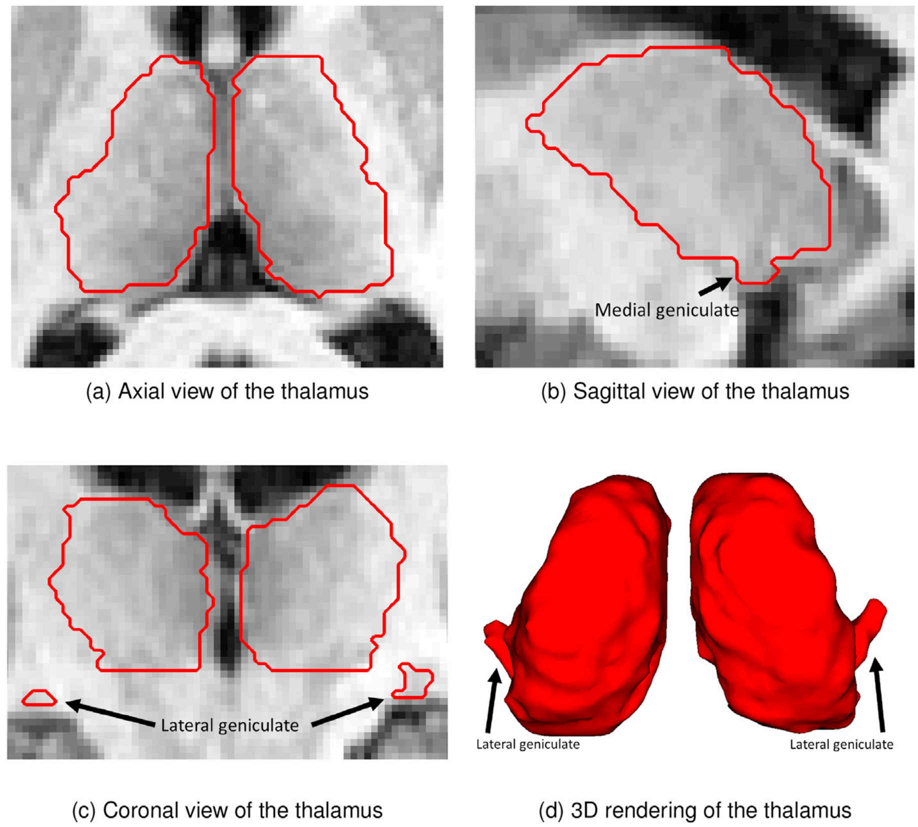

Fig. 1. Examples of the thalamus anatomy (outlined as a red contour) overlaid on a T1-w MRI. The black arrows in the coronal and sagittal views as well as in the volumetric rendering show the locations of the medial and lateral geniculates.

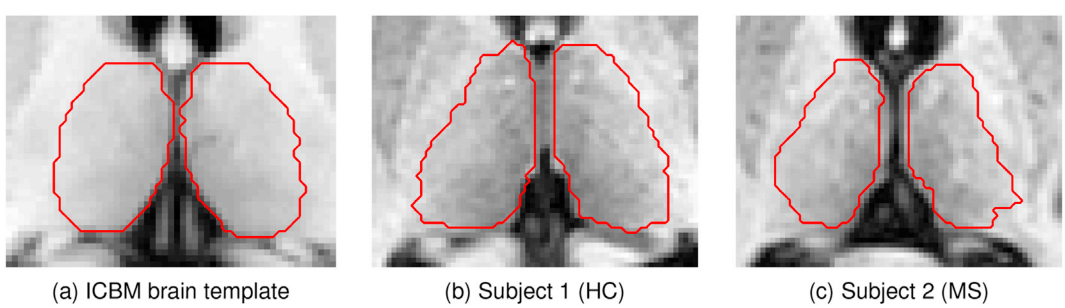

Fig. 2. Examples of the atlases with the manual segmentation of the thalamus outlined in red.

using a set of 13 secondary progressive MS patients and 13 HCs and found a decrease in thalamic volume of 21% between MS patients and HCs. Houtchens et al. (2007) studied the change in thalamic volume in 79 MS patients (62 relapsing-remitting, 16 secondary progressive, 1 primary progressive) and 16 HCs. The thalami were segmented using an edge-finding tool followed by manual correction; a decrease of 16.8% in thalamic volume normalized to ICV was reported. Wylezinska et al. (2003) studied 14 relapsing-remitting MS patients and 14 HCs and reported a 25% decrease in normalized thalamic volume. A significant inverse correlation between normalized thalamic volumes and disease duration was also reported by Wylezinska et al. (2003). The thalamic volumes and ICV in the study by Wylezinska et al. (2003) were segmented manually by an experienced operator. Such studies could be replicated and extended more readily by using an accurate automated algorithm for thalamus segmentation.

Previous methods developed for thalamus segmentation have used T1-weighted (T1-w) MRI alone. Early work by Collins et al. (1999) proposed augmenting a probabilistic atlas with tissue labels. Bazin and Pham (2008) built upon these ideas by combining statistical and topological atlases to find subcortical structures, while observing tissue classification requirements. More sophisticated methods incorporate shape, or spatial priors, such as shape models, topological correction, or spatial information. For example, Patenaude et al. (2011) incorporated prior anatomical information using explicit shape models. Fischl et al. (2002) (in a method called FreeSurfer) proposed using spatial information of relative locations of subcortical structures as a prior. These single probabilistic atlas approaches were replaced with multi-atlas-based segmentation techniques in which multiple atlases are registered to the target image and the deformed labels are fused and transferred to the target (Aljabar et al., 2009; Asman and Landman, 2013). The benefit of multi-atlas techniques is that by fusing the results from multiple atlases, it reduces the effect of errors from any single atlas. However, none of these algorithms incorporate the diffusion properties exhibited both inside and surrounding the thalamus which can be captured from diffusion tensor imaging (DTI).

DTI is an MRI modality that measures the diffusion of water in tissues