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Automatic segmentation of the lateral geniculate nucleus: Application to control and glaucoma patients

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HIGHLIGHTS

- We provide an automatic LGN segmentation method, which is objective, efficient, valid and applicable.
- We find the LGN asymmetry and LGN atrophy along with the human age.
- We find that the bilateral LGN volumes shrinks in glaucoma patients and the LGN volumes are correlated with clinical parameters in patients.

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ABSTRACT

Background: The lateral geniculate nucleus (LGN) is a key relay center of the visual system. Because the LGN morphology is affected by different diseases, it is of interest to analyze its morphology by segmentation. However, existing LGN segmentation methods are non-automatic, inefficient and prone to experimenters' bias.
New method: To address these problems, we proposed an automatic LGN segmentation algorithm based on T1-weighted imaging. First, the prior information of LGN was used to create a prior mask. Then region growing was applied to delineate LGN. We evaluated this automatic LGN segmentation method by (1) comparison with manually segmented LGN, (2) anatomically locating LGN in the visual system via LGN-based tractography, (3) application to control and glaucoma patients.
Results: The similarity coefficients of automatic segmented LGN and manually segmented one are 0.72 (0.06) for the left LGN and 0.77 (0.07) for the right LGN. LGN-based tractography shows the subcortical pathway seeding from LGN passes the optic tract and also reaches V1 through the optic radiation, which is consistent with the LGN location in the visual system. In addition, LGN asymmetry as well as LGN atrophy along with age is observed in normal controls. The investigation of glaucoma effects on LGN volumes demonstrates that the bilateral LGN volumes shrink in patients.
Comparison with existing methods: The automatic LGN segmentation is objective, efficient, valid and applicable.
Conclusions: Experiment results proved the validity and applicability of the algorithm. Our method will speed up the research on visual system and greatly enhance studies of different vision-related diseases.

1. Introduction

The lateral geniculate nucleus (LGN) is the primary visual relay center of the brain that receives retinofugal fibers and transmits visual information to the visual cortex (Sherman and Koch, 1986). The structure and function of the LGN (Schneider et al., 2004; Zhang et al., 2010; McKetton and Schneider, 2012; McKetton et al., 2013) and its relationship with other structures of the visual

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pathway (such as optic tract and primary visual cortex (Kupfer et al., 1967; Andrews et al., 1997)) have been extensively studied. The LGN is affected by ophthalmological diseases such as myopia (von Noorden et al., 1983; von Noorden and Crawford, 1992; Miki et al., 2003; Barnes et al., 2010) and glaucoma (Gupta et al., 2009; Weber et al., 2000; Dai et al., 2011; Chen et al., 2013) and hence of clinical interest. But all these quantitative MRI studies are based on manual or semi-automatic segmentation methods that are prone to human error of judgment. This limits existing analysis methods in their objectivity, efficiency, validity and applicability of LGN measurements, making conclusions based on them less deterministic.

Except for aforementioned manual or semi-automatic LGN segmentation methods, another method is to apply LGN atlas to guide LGN segmentation by registering it to the individual space. Only two LGN atlases exist to date: the Talairach atlas (Lancaster et al., 2000) and the WFU PickAtlas (Maldjian et al., 2003). However, both were built based on postmortem sections of a single case of a 60-year-old French female. The brain size in these sections was smaller than the average brain sizes because the brain of the subject was atrophied because of old age and death. Thus, the segmented LGN using these prior atlases as a reference point underestimates the true LGN volume compared to those reported in previous studies (Andrews et al., 1997; Putnam, 1926; Zvorykin, 1980), seriously limiting the validity of LGN morphology. In addition, using a single case as a reference point does not consider that LGN volumes vary between subjects and vary along with human age (Li et al., 2012). Thus, prior atlases cannot be used to objectively, reliably and validly determine the normative LGN volume, which is needed as a reference for any MRI studies of the LGN such as to study the influence of age, hemispheric asymmetry, sex, disease, etc. We believe that only a fully automatic LGN segmentation method could overcome the limitations in previous studies.

In this paper, we proposed an automatic LGN segmentation method based on structural MRI imaging. The validity of segmentation method was proved by comparing with the manually segmented LGN as well as LGN location in visual system. The applicability of the method was demonstrated by investigating the property of LGN volumes in normal controls and glaucoma effects on LGN volumes.

2. Materials and methods

2.1. Subjects & MRI image acquisition

2.1.1. Dataset 1

We chose healthy subjects from the publicly available Information extraction from Images (IXI) database (http://www.brain-development.org/) and applied their T1-weighted images and DTI images in this study. The IXI database contained T1-weighted images from 580 normal subjects and DTI images from only 397 normal subjects from Hammersmith Hospital and Guy's Hospital (scanning parameters can be found on the official website: http://www.brain-development.org/). We excluded several subjects if one of the following criteria applied: (i) subjects without T1-weighted images or DTI images; (ii) no age or sex information was available; and (iii) the images failed to be properly recognized during the image processing. Finally, 280 normal subjects aged 20–84 years (age ± SD = 51.32 ± 15.38, male/female: 115/165, age distribution: Fig. S1) were taken from the IXI database and further analyzed.

2.1.2. Dataset 2

All the subjects in Dataset 2 were recruited by Beijing Tongren Hospital. The Medical Ethics Committee of the Beijing Tongren Hospital approved this study and all participants have signed the informed consent form after explained the nature and design of the study. Dataset 2 included 25 primary open angle glaucoma (POAG) patients (age: 44.6 ± 13.0 years, male/female: 11/14) and 25 age-sex-matched normal controls (age: 36.8 ± 11.6 years, male/female: 13/12). All participants were right-handed Chinese. The normal controls were checked to assure that (1) they had no eye diseases or glaucoma; (2) they had no psychiatric disorders; (3) they had no smoking or drinking in the past three months. The subjects in glaucoma group were diagnosed as POAG by experts in Beijing Tongren Hospital. All patients (1) had no other eye diseases; (2) had no psychiatric disorders; (3) no smoking or drinking in the past 3 months.

The patients voluntarily chose to take further examinations including retinal nerve fiber layer (RNFL), cup-to-disk ratio (CDR) and visual field (VF). The demographic data of patients is shown in Table 1. Complete clinical parameters of 14 patients were collected.

Table 1
Demographic data of primary open angle glaucoma patients. "√" represents the information is available, "–" represents the information is not available.

No.	Sex	Age	RNFL		CDR		VF	
			Left	Right	Left	Right	Left	Right
1	F	17	√	√	√	√	√	√
2	F	47	√	√	√	√	√	√
3	M	56	–	–	–	–	√	√
4	M	59	√	√	√	√	√	√
5	M	52	√	√	√	√	√	√
6	M	60	√	√	√	√	√	√
7	F	56	–	–	√	√	√	√
8	F	23	–	–	–	–	–	–
9	M	68	√	√	√	√	√	√
10	M	18	√	√	√	√	√	√
11	F	46	–	–	–	–	–	–
12	M	28	–	–	–	–	√	√
13	F	48	√	√	√	√	√	√
14	F	58	√	–	√	√	√	–
15	M	29	√	√	√	√	√	√
16	F	47	–	–	–	–	–	–
17	F	40	√	√	√	√	√	√
18	M	55	√	√	√	√	√	√
19	F	22	–	–	√	√	√	√
20	F	21	–	–	–	–	–	–
21	M	75	√	√	√	√	√	√
22	F	41	√	√	√	√	√	√
23	M	59	√	√	√	√	–	–
24	F	47	–	–	–	–	√	√
25	F	44	√	√	√	√	√	√

All participants were scanned in a GE 3 T scanner to acquire T1-weighted structural MRI images with the following scanner parameters: TR/TE = 8.9/3.5 ms, slice thickness = 1 mm, flip angle = 13°, matrix = 256 × 256, FOV = 24 × 24 cm^2, slice number = 209, and slice resolution = 0.9999 × 0.9375 mm^2.

2.2. Automatic LGN segmentation

The pipeline of automatic LGN segmentation is shown in Fig. 1. The main procedure includes image preprocessing, prior mask production and LGN delineation by region growing. The steps were as follows:

2.2.1. Image preprocessing

For image preprocessing, all subjects' T1-weighted images were firstly performed correction of non-uniform intensity by using the N3 algorithm (Sled et al., 1998). Then skull stripping was done for the whole brain, which was subsequently segmented to label neuroanatomical structures in the human brain using a method described in (Fischl et al., 2002), which is performed by the software FreeSurfer (Version 5.0.0, https://surfer.nmr.mgh.harvard.edu). Thereafter, the ventral diencephalon area (VDC) was chosen