• Meta-Analysis •

Magnetic resonance imaging assessment of the lateral geniculate nucleus volume and height in patients with glaucoma: a Meta-analysis

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Abstract

● **AIM:** To evaluate the lateral geniculate nucleus (LGN) volume and height using magnetic resonance imaging (MRI) in glaucoma patients.

● **METHODS:** Literatures retrieval was carried out through PubMed, Web of Science, Embase, and Cochrane Library. Studies that compared the volume and height of LGN in glaucoma patients with that in control subjects were included. The volume and height of LGN were extracted from the included studies. The Review Manager 5.4.1 software was used for the Meta-analysis.

● **RESULTS:** This Meta-analysis included 10 cross-sectional studies, including the eyes of 223 glaucoma patients and 185 healthy controls. Compared with the control subjects, the volume and height of LGN in glaucoma patients measured by MRI were significantly reduced {-29.13 mm^3, 95% [confidence interval (CI): -44.82 to -13.43, P=0.0003; -0.61 mm, 95%CI: -0.78 to -0.44, P<0.00001, respectively]}. Subgroup analysis demonstrated that the differences of LGN volume and height between glaucoma patients and control subjects in the older group were smaller than that in the younger group, and LGN volume decreased with the increase of glaucoma severity.

● **CONCLUSION:** The results demonstrate that the volume and height of LGN are decreased in glaucoma patients, and LGN volume can be considered a parameter of glaucoma severity.

● **KEYWORDS:** magnetic resonance imaging; lateral geniculate nucleus; glaucoma; Meta-analysis

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INTRODUCTION

Glaucoma is an irreversible blindness eye disease, which is characterized by progressive optic nerve degeneration[1]. More and more evidence showed that the disease is a neurodegenerative disease affecting the entire visual pathway, including lateral geniculate nucleus (LGN) and visual cortex[2-3]. The pathophysiological mechanisms of glaucoma are similar to neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease[4]. Therefore, it is critical to understand the pathogenesis between the eye and the brain in glaucoma patients, because it may contribute to the early detection of glaucoma.

Magnetic resonance imaging (MRI) is an imaging tool that can be used to observe the changes of brain structure, function and metabolism[5-6]. Zhang *et al*[7] reported that the diffusivity of optic nerve and optic radiation in glaucoma patients detected by diffusion tensor imaging (DTI) showed abnormal. The Meta-analysis of Li *et al*[8] revealed that the abnormalities of optic nerve and optic radiation detected by DTI in glaucoma patients were corrected to the severity of disease and age. In our previous study, abnormal brain functional connectivity was detected by resting state functional magnetic resonance imaging (fMRI) in glaucoma patients[9]. In addition, a systematic review supported the view that glaucoma is accompanied by abnormal changes in optic nerve, LGN, and other brain regions related to visual function[10]. Moreover, the white matter damage detected by DTI and the abnormalities of visual cortex activity detected by fMRI in glaucoma patients were earlier than the visual field loss[11-12].

LGN is the thalamic relay of visual signals from the retina to the visual cortex, and its pathological changes lead to eye diseases and brain diseases[13]. The autopsy sections of

glaucoma patients showed that magnocellular cell density in the LGN was decreased, which was the first time to describe trans-synaptic degeneration[14]. In the monkey model of experimental glaucoma, it was found that the volume and number of neurons in LGN decreased[15]. Gupta *et al*[16] displayed the imaging evidence of LGN atrophy in glaucoma patients for the first time.

Several studies with MRI had reported that the LGN volume and height in glaucoma patients are reduced compared with those of healthy controls[16-25]. However, the differences in disease severity and age of glaucoma patients in these studies may influence the final results. Therefore, we will conduct a Meta-analysis of the volume and height of LGN measured by MRI in glaucoma patients.

MATERIALS AND METHODS

Search Strategy Two independent reviewers searched the PubMed, Web of Science, Embase, and Cochrane Library databases for all relevant studies from the beginning to January 16, 2023. We used the following Medical Subject Headings (MeSH) terms to determine the relevant studies: "Glaucoma" AND "Geniculate Bodies". There was no limit to language and location. In addition, we searched for more related studies in the list of references. The final decision was made after two independent reviewers reached an agreement. The Meta-analysis was registered at PROSPERO (CRD42022333105).

Inclusion and Exclusion Criteria Inclusion criteria: 1) the volume and height of LGN were measured by MRI; 2) comparison between glaucoma patients and normal subjects; 3) original studies. Exclusion criteria: 1) reviews, case reports, and Meta-analyses; 2) studies conducted in non-human subjects; 3) repeated studies.

Literatures Selection and Data Extraction Two independent reviewers separately evaluated studies, and any disagreements were resolved through discussion. Data were extracted by the two independent reviewers including year of publication, first author, country, age, gender, VF mean deviation (MD), retinal nerve fiber layer thickness (RNFLT), LGN volume and height, manufacturer and magnetic field intensity of the MRI.

Quality Assessment We evaluated the qualities of the included studies based on the Agency for Healthcare Research and Quality (AHRQ) checklist. According to the total score (range: 0-11), the qualities of the studies were divided into three categories: high (score: 8-11), moderate (score: 4-7), and low (score: 0-3).

Statistical Analysis The Review Manager 5.4.1 software was used for the Meta-analysis. Chi-square test and Higgins I^2 test were applied to detect the heterogeneity of studies. According to the I^2 values, the heterogeneity of the studies was divided into three categories: high ($I^2 \geq 50\%$), moderate ($25\% < I^2 < 50\%$), and low ($I^2 \leq 25\%$). The fixed-effect analysis model was used if the heterogeneity is not significant ($I^2<50\%$, $P>0.10$). Otherwise, the random-effect analysis model was applied ($I^2 \geq 50\%$, $P \leq 0.10$). We also used sensitivity analysis and subgroup analysis to determine the sources of heterogeneity, and assessed potential publication bias through the funnel plot. The weighted mean difference (WMD) and its 95% confidence interval (CI) were used for continuous estimates, and $P<0.05$ was regarded to be statistically significant.

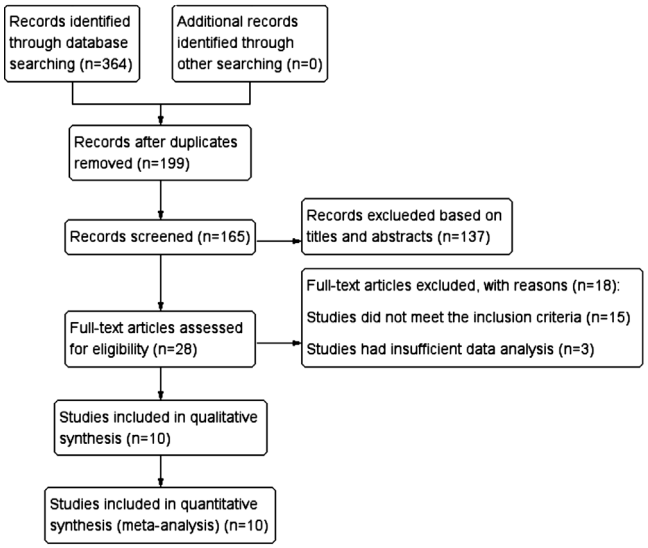

Figure 1 Flow diagram of the article search process for Meta-analysis.

RESULTS

Included Studies and Study Characteristics We conducted the Meta-analysis according to the PRISMA statement. The screening process of related articles was shown in Figure 1. We searched related articles published from inception to January 16, 2023 (PubMed: 124; Embase: 126; Web of Science: 111; Cochrane Library: 3) and excluded 199 duplicate articles. The 137 studies were excluded by reading the titles and abstracts of 165 articles. After reading the full text of 28 studies, 3 studies with insufficient data and 15 studies that failed to meet the inclusion criteria were excluded. As a result, 10 studies were finally included in the Meta-analysis, including the eyes of 223 glaucoma patients and 185 control subjects. Table 1 described the detailed features of the 10 studies. Of the 10 studies, 9 studies included open-angle glaucoma patients, and another one included normal tension glaucoma patients. Based on the AHRQ checklist, we evaluated the qualities of the 10 included cross-sectional studies, and their qualities were moderate (score: 4-7).

Main Analysis

Analysis of the LGN volume in glaucoma patients and controls Of the 10 included studies, 7 studies reported the LGN volume in glaucoma patients[17-18,21-25]. There was high heterogeneity among the 7 studies ($\chi^2=84.45$, $P<0.00001$, $I^2=93\%$), so the data were pooled through the random-effects model (Figure 2). We calculated the WMD of LGN volume

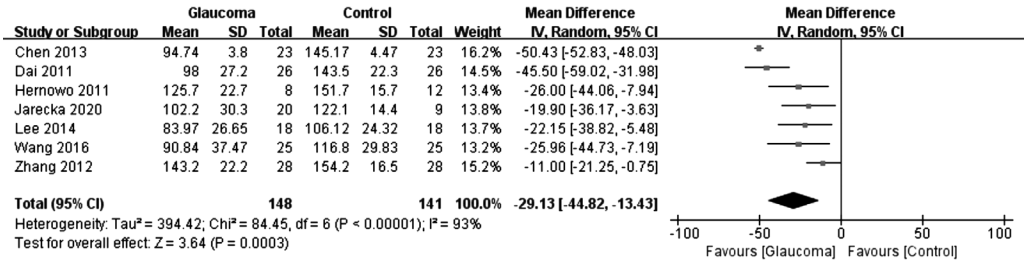

Figure 2 Forest plot of LGN volume in glaucoma patients and controls SD: Standard deviation; CI: Confidence interval; LGN: Lateral geniculate nucleus.

Table 1 Characteristics of studies included in the Meta-analysis

Author, Year	Country	GL	No. of eyes		Age (y)		Sex (M/F)		RNFLT (μm)		VF MD (dB)		MRI		AHRQ score
			GL	Con	GL	Con	GL	Con	GL	Con	GL	Con	Manufacturer	MFI	
Chen, 2013	China	POAG	23	23	35.17	35.13	18/5	18/5	55.62±3.79	111.85±2.00	-	-	General Electric	3	5
Dai, 2011	China	POAG	26	26	35.40	35.40	21/5	21/5	-	-	-	-	General Electric	3	6
Ersoz, 2017	Turkey	POAG	24	24	58.39	57.73	-	-	-	-	-	-	Philips	1.5	6
Furlanetto,2018	Brazil	POAG	41	12	62.90	63.20	18/23	6/6	64.70±10.6	95.40±6.90	-15.39±10.02	-0.38±0.89	Siemens	3	5
Gupta, 2009	Canada	POAG	10	8	63.10	58.60	3/7	3/5	-	-	-12.63±4.18	0.97±1.30	Philips	1.5	6
Hernowo, 2011	Netherlands	POAG	8	12	72.96	-	7/1	-	58.09±8.37	-	-13.72±7.66	-	Philips	3	5
Jarecka, 2020	Poland	OAG	20	9	67.18	70.50	-	-	68.73±14.62	92.80±11.60	-10.48±7.32	0.36±0.70	General Electric	7	5
Lee, 2014	Korea	POAG	18	18	47.60	45.20	8/10	8/10	75.56±16.93	97.17±6.85	-	-	Siemens	7	5
Wang, 2016	China	POAG	25	25	44.64	36.80	11/14	13/12	83.98±17.25	-	-12.42±8.54	-	General Electric	3	6
Zhang, 2012	China	NTG	28	28	54.80	53.90	-	-	-	-	-	-	General Electric	1.5	7

GL: Glaucoma; Con: Control; M: Male; F: Female; OAG: Open-angle glaucoma; POAG: Primary open-angle glaucoma; NTG: Normal-tension glaucoma; RNFLT: Retinal nerve fiber layer thickness; VF: Visual field; MD: Mean deviation; MRI: Magnetic resonance imaging; MFI: Magnetic field imaging; AHRQ: Agency for Healthcare Research and Quality.

between the glaucoma patients and normal subjects, which was -29.13 mm^3 (95%CI: -44.82 to -13.43, P=0.0003). These results demonstrated that the LGN volume of glaucoma patients was decreased compared with normal subjects.

Based on the sensitivity analysis, two studies[17-18] had caused great heterogeneity of the LGN volume in this Meta-analysis. The glaucoma patients were divided into the younger group (age<40y) and the older group (age≥40y) according to their age. As shown in Figure 3, a subgroup analysis according to the age of glaucoma patients showed that there was no heterogeneity (χ^2=0.50, P=0.48, I^2=0 and χ^2=3.53, P=0.47, I^2=0, respectively) in the younger and older group, and indicated that LGN volume decreased both in the younger group (-50.28 mm^3, 95%CI: -52.64 to -47.92, P<0.00001) and the older group (-18.11 mm^3, 95%CI: -24.73 to -11.49, P<0.00001) .

LGN volume may potentially be related to glaucoma severity. Another subgroup analysis according to the glaucoma severity was conducted in studies (Figure 4). The glaucoma patients were stratified into the advanced glaucoma group (RNFLT≤60 μm) and the non-advanced glaucoma group (RNFLT>60 μm) according to their RNFLT[26]. The results found that there was no heterogeneity in the non-advanced glaucoma group (χ^2=0.23, P=0.89, I^2=0), but not the advanced glaucoma group (χ^2=6.90, P=0.009, I^2=86%), and indicated that LGN volume decreased in both the non-advanced glaucoma group (-22.38 mm^3, 95%CI: -32.27 to -12.48, P<0.00001) and the advanced glaucoma group (-39.92 mm^3, 95%CI: -63.63 to -16.22, P=0.001).

Analysis of the LGN Height in Glaucoma Patients and Controls Moreover, 5 studies reported the LGN height of their participants[16-20]. There was moderate heterogeneity among the 5 studies (χ^2=7.74, P=0.10, I^2=48%), so the data are summarized through random effect model (Figure 5). The WMD of LGN height between glaucoma and normal subjects was -0.61 (95%CI: -0.78 to -0.44, P<0.00001). The results demonstrated that the LGN height of glaucoma patients was decreased compared with normal subjects.

As shown in Figure 6, a subgroup analysis of LGN height according to the age of glaucoma patients showed that there was no heterogeneity (χ^2=0.07, P=0.79, I^2=0 and χ^2=1.28, P=0.53, I^2=0, respectively) in the younger group and older group, and indicated that LGN height was decreased both in the younger group (-0.73 mm, 95%CI: -0.79 to -0.67, P<0.00001) and the older group (-0.43 mm, 95%CI: -0.65 to -0.20, P=0.0002).

Publication Bias Funnel plots were applied to assess the potential publication bias. No obvious publication bias was found in the Meta-analysis of LGN volume (Figure 7) and LGN height (Figure 8).

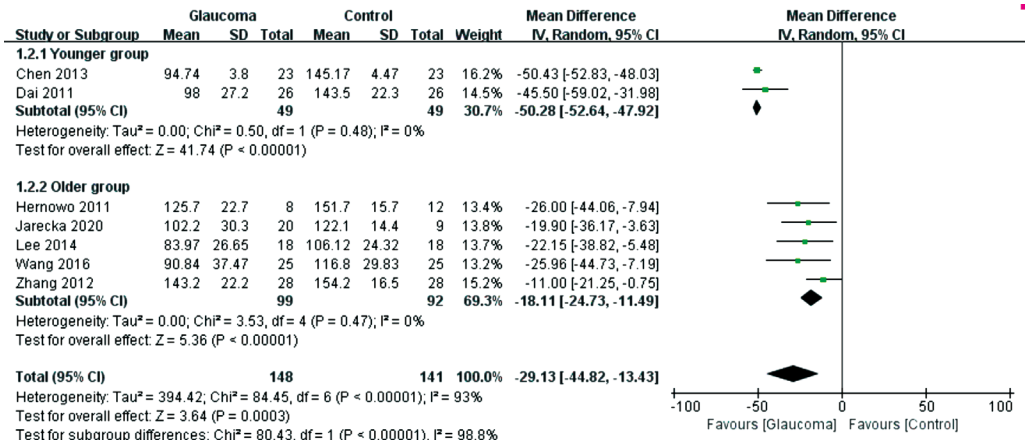

Figure 3 Subgroup analysis of LGN volume according to the age of glaucoma patients SD: Standard deviation; CI: Confidence interval; LGN: Lateral geniculate nucleus.

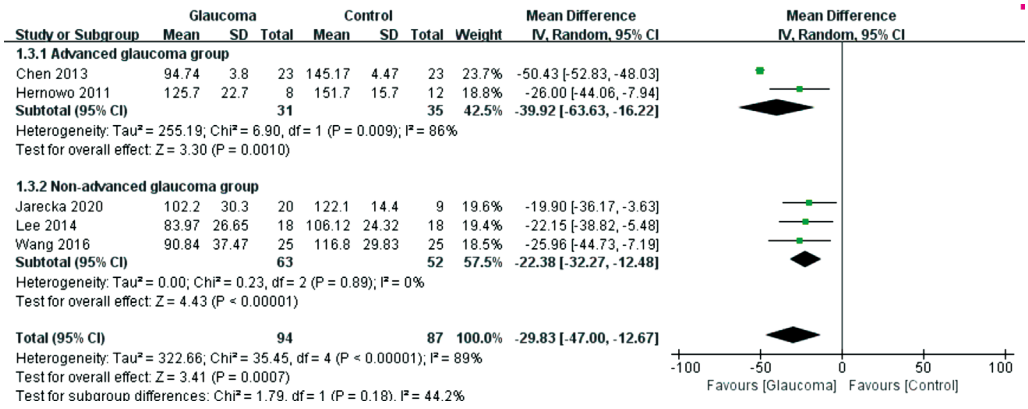

Figure 4 Subgroup analysis of LGN volume according to glaucoma severity SD: Standard deviation; CI: Confidence interval; LGN: Lateral geniculate nucleus.

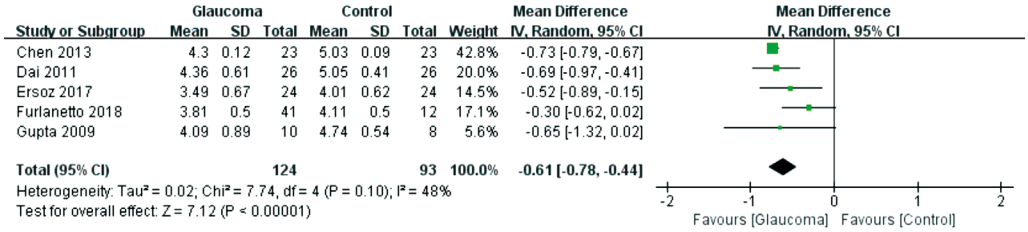

Figure 5 Forest plot of LGN height in glaucoma patients and controls SD: Standard deviation; CI: Confidence interval; LGN: Lateral geniculate nucleus.

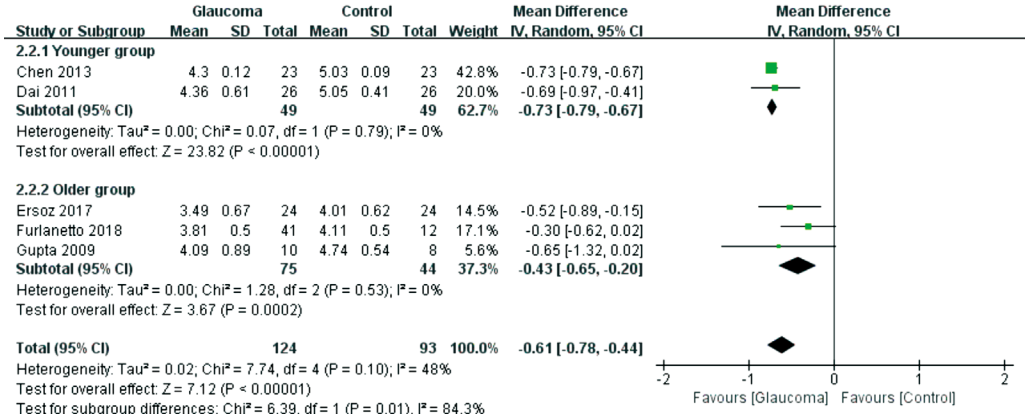

Figure 6 Subgroup analysis of LGN height according to the age of glaucoma patients SD: Standard deviation; CI: Confidence interval; LGN: Lateral geniculate nucleus.

DISCUSSION

We first conducted a Meta-analysis to compare the LGN volume and height of glaucoma patients and healthy subjects, which confirmed the significant changes in LGN volume and height of glaucoma patients. The results demonstrated that the LGN volume of glaucoma patients was decreased compared with control subjects. However, two studies[17-18] had caused great heterogeneity of the LGN volume in this Meta-analysis.

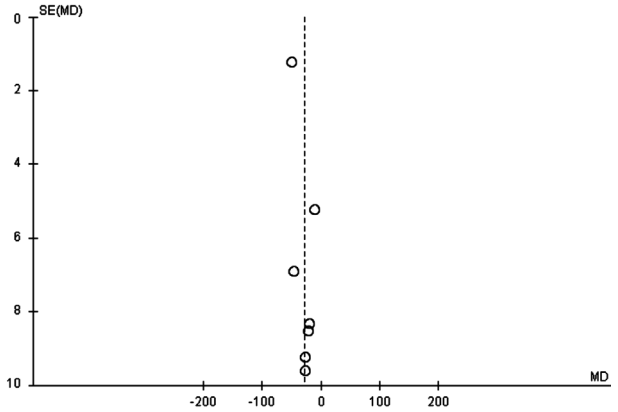

Figure 7 A funnel plot of LGN volume in glaucoma patients and controls SE: Standard error; MD: Mean difference.

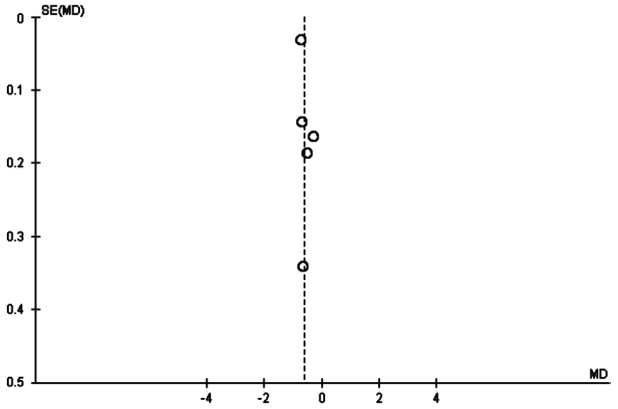

Figure 8 A funnel plot of LGN height in glaucoma patients and controls SE: Standard error; MD: Mean difference.

The characteristics and pathophysiological mechanisms of glaucoma indicate that glaucoma can be regarded as an age-related neurodegenerative disease[27]. Alba *et al*[28] found that age-related degeneration in the capillary structure of LGN may lead to neurodegenerative diseases. Therefore, subgroup analysis according to the age of glaucoma patients was also performed in studies and demonstrated that LGN volume was reduced in both the younger and older group, and no heterogeneity was found in the two subgroups. There was evidence that the loss of optic nerve axons occurs with age[29]. Therefore, we hypothesize that age-related LGN atrophy may exist in normal subjects, which makes the difference of LGN size between glaucoma and control groups in the older group smaller than that in the younger group.

There was a significant difference in LGN volume measured by MRI between the early glaucoma group and the advanced glaucoma group[22,30]. The nasal optic nerve fibers of each eye converges with the temporal nerve fibers of the opposite eye and project to LGN. And there were significant associations between RNFLT and LGN volume observed in glaucoma patients[22,24,31]. Another subgroup analysis based on the glaucoma severity showed that there was no heterogeneity in the non-advanced glaucoma group (RNFLT>60 μm), but not in the advanced glaucoma group (RNFLT≤60 μm), and found that LGN volume decreased in both the non-advanced glaucoma group and the advanced glaucoma group. The heterogeneity of the advanced glaucoma group may be due to the different ages of patients in the two studies[17,21]. Our Meta-analysis found that the volume of LGN decreased with the increase of glaucoma severity and demonstrated that LGN volume could be considered a parameter of glaucoma severity. Dai *et al*[18] showed that both volume and height of the LGN were significantly associated with the glaucoma severity. There were significant correlations between RNFLT and clinical stages with LGN height[19]. Our results showed that the LGN height of glaucoma patients was decreased compared with healthy subjects. Subgroup analysis according to the age of glaucoma patients further demonstrated that LGN height was reduced in both the younger and older group, and no heterogeneity was found in the two subgroups.

Our Meta-analysis found that LGN volume and height measured by MRI were significantly reduced in glaucoma patients. The significant decrease in the volume and height of LGN indicated the diagnostic ability of LGN parameters in differentiating glaucoma patients. Li *et al*[32] discovered that LGN volume and height had good diagnostic accuracy to discriminate glaucoma patients from control subjects.

In addition, Song *et al*[33] reported that mean diffusivity in LGN measured by DTI was higher in glaucoma patients, and it was significantly related to the cup to disc ratio. The abnormalities of LGN and visual cortex in glaucoma patients were observed by diffusion kurtosis imaging[34]. Compared with normal subjects, the fMRI response in the LGN in early glaucoma patients was decreased, and it was significantly correlated with glaucoma severity[35]. Magnetic resonance spectroscopy could measure the metabolites of tissues, and also showed that the glutamate-glutamine/creatin ratios were increased in LGN of glaucoma patients[36]. All the above studies had provided evidences for the LGN damage in glaucoma patients. Moreover, a previous study found that the atrophy degree of neurons in the LGN of glaucoma monkeys treated with memantine was significantly lower than that in the control group[37]. Brimonidine provided neuroprotective effects in glaucoma animal model[38] and improved visual field in glaucoma patients[39]. Considering that glaucoma is a neurodegenerative disease of the eye and the brain, the combination of brain imaging and ophthalmological measurements may contribute to the early diagnosis of glaucoma and guide timely interventions to save the vision of glaucoma patients.

Nevertheless, there are several limitations in our Meta-analysis. First, there may be deviations in manual demarcation, although it is generally believed that manual demarcation can provide

accurate results. Second, other factors such as the types of MRI, race, or handedness might potentially affect the size of LGN. Third, the sample size of the studies was relatively small.

In conclusion, our Meta-analysis demonstrated that the volume and height of LGN were decreased in glaucoma patients, and found that LGN volume could be considered a parameter of glaucoma severity. Finally, these findings indicated that LGN volume and height may be of great value in detecting and monitoring the progression of glaucoma.

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REFERENCES

1 Chan JW, Chan NCY, Sadun AA. Glaucoma as neurodegeneration in the brain. *Eye Brain* 2021;13:21-28.

2 Lawlor M, Danesh-Meyer H, Levin LA, Davagnanam I, De Vita E, Plant GT. Glaucoma and the brain: trans-synaptic degeneration, structural change, and implications for neuroprotection. *Surv Ophthalmol* 2018;63(3):296-306.

3 You ML, Rong R, Zeng Z, Xia XB, Ji D. Transneuronal degeneration in the brain during glaucoma. *Front Aging Neurosci* 2021;13:643685.

4 Saccà SC, Paluan F, Gandolfi S, Manni G, Cutolo CA, Izzotti A. Common aspects between glaucoma and brain neurodegeneration. *Mutat Res Mutat Res* 2020;786:108323.

5 Kasi A, Faiq MA, Chan KC. *In vivo* imaging of structural, metabolic and functional brain changes in glaucoma. *Neural Regen Res* 2019;14(3):446-449.

6 Gracitelli CPB, Gerente VM, Furlanetto RL, Amaro E Jr, Paranhos A Jr. Magnetic resonance imaging for glaucoma evaluation. *J Glaucoma* 2020;29(8):622-626.

7 Zhang QJ, Wang D, Bai ZL, Ren BC, Li XH. Diffusion tensor imaging of optic nerve and optic radiation in primary chronic angle-closure glaucoma using 3T magnetic resonance imaging. *Int J Ophthalmol* 2015;8(5):975-979.

8 Li K, Lu CX, Huang YF, Yuan L, Zeng D, Wu K. Alteration of fractional anisotropy and mean diffusivity in glaucoma: novel results of a meta-analysis of diffusion tensor imaging studies. *PLoS One* 2014;9(5):e97445.

9 Zhang QL, Shu YQ, Li XF, Xiong C, Li P, Pang YL, Ye W, Yang L, Zeng XJ, Zhang X. Resting-state functional magnetic resonance study of primary open-angle glaucoma based on voxelwise brain network degree centrality. *Neurosci Lett* 2019;712:134500.

10 Nuzzi R, Dallorto L, Rolle T. Changes of Visual Pathway and Brain Connectivity in Glaucoma: A Systematic Review. *Front Neurosci* 2018;12:363.

11 Wang R, Tang ZH, Sun XH, Wu LJ, Wang J, Zhong YF, Xiao ZB. White matter abnormalities and correlation with severity in normal tension glaucoma: a whole brain atlas-based diffusion tensor study. *Invest Ophthalmol Vis Sci* 2018;59(3):1313-1322.

12 Murphy MC, Conner IP, Teng CY, Lawrence JD, Safiullah Z, Wang B, Bilonick RA, Kim SG, Wollstein G, Schuman JS, Chan KC. Retinal structures and visual cortex activity are impaired prior to clinical vision loss in glaucoma. *Sci Rep* 2016;6:31464.

13 Qian YZ, Zou JY, Zhang ZH, An J, Zuo ZT, Zhuo Y, Wang DJJ, Zhang P. Robust functional mapping of layer-selective responses in human lateral geniculate nucleus with high-resolution 7T fMRI. *Proc Biol Sci* 2020;287(1925):20200245.

14 Chaturvedi N, Hedley-Whyte ET, Dreyer EB. Lateral geniculate nucleus in glaucoma. *Am J Ophthalmol* 1993;116(2):182-188.

15 Weber AJ, Chen H, Hubbard WC, Kaufman PL. Experimental glaucoma and cell size, density, and number in the primate lateral geniculate nucleus. *Invest Ophthalmol Vis Sci* 2000;41(6):1370-1379.

16 Gupta N, Greenberg G, de Tilly LN, Gray B, Polemidiotis M, Yücel YH. Atrophy of the lateral geniculate nucleus in human glaucoma detected by magnetic resonance imaging. *Br J Ophthalmol* 2009;93(1):56-60.

17 Chen ZQ, Wang JM, Lin FC, Dai H, Mu KT, Zhang H. Correlation between lateral geniculate nucleus atrophy and damage to the optic disc in glaucoma. *J Neuroradiol* 2013;40(4):281-287.

18 Dai H, Mu KT, Qi JP, Wang CY, Zhu WZ, Xia LM, Chen ZQ, Zhang H, Ai F, Morelli JN. Assessment of lateral geniculate nucleus atrophy with 3T MR imaging and correlation with clinical stage of glaucoma. *AJNR Am J Neuroradiol* 2011;32(7):1347-1353.

19 Ersoz MG, Pekcevik Y, Ayintap E, Gunes İB, Mart DK, Yucel E, Türe G. MR imaging of the anterior visual pathway in primary open-angle glaucoma: correlation with octopus 101 perimetry and spectralis optical coherence tomography findings. *Curr Eye Res* 2017;42(7):995-1001.

20 Furlanetto RL, Teixeira SH, Gracitelli CPB, Lottenberg CL, Emori F, Michelan M, Amaro E Jr, Paranhos A Jr. Structural and functional analyses of the optic nerve and lateral geniculate nucleus in glaucoma. *PLoS One* 2018;13(3):e0194038.

21 Hernowo AT, Boucard CC, Jansonius NM, Hooymans JMM, Cornelissen FW. Automated morphometry of the visual pathway in primary open-angle glaucoma. *Invest Ophthalmol Vis Sci* 2011;52(5):2758-2766.

22 Kosior-Jarecka E, Pankowska A, Polit P, Stępniewski A, Symms MR, Kozioł P, Żarnowski T, Pietura R. Volume of lateral geniculate nucleus in patients with glaucoma in 7Tesla MRI. *J Clin Med* 2020;9(8):2382.

23 Lee JY, Jeong HJ, Lee JH, Kim YJ, Kim EY, Kim YY, Ryu T, Cho ZH, Kim YB. An investigation of lateral geniculate nucleus volume in patients with primary open-angle glaucoma using 7 Tesla magnetic resonance imaging. *Invest Ophthalmol Vis Sci* 2014;55(6):3468-3476.

24 Wang JQ, Li T, Sabel BA, Chen ZQ, Wen HW, Li JH, Xie XB, Yang DY, Chen WW, Wang NL, Xian JF, He HG. Structural brain alterations in primary open angle glaucoma: a 3T MRI study. *Sci Rep* 2016;6:18969.

25 Zhang YQ, Li J, Xu L, Zhang L, Wang ZC, Yang H, Chen CX, Wu XS, Jonas JB. Anterior visual pathway assessment by magnetic resonance imaging in normal-pressure glaucoma. *Acta Ophthalmol* 2012;90(4):e295-e302.

26 Lavinsky F, Wu MF, Schuman JS, Lucy KA, Liu ML, Song Y, Fallon J, de Los Angeles Ramos Cadena M, Ishikawa H, Wollstein G. Can macula and optic nerve head parameters detect glaucoma progression in eyes with advanced circumpapillary retinal nerve fiber layer damage? *Ophthalmology* 2018;125(12):1907-1912.

27 Mancino R, Martucci A, Cesareo M, Giannini C, Corasaniti MT, Bagetta G, Nucci C. Glaucoma and alzheimer disease: one age-related neurodegenerative disease of the brain. *Curr Neuropharmacol* 2018;16(7):971-977.

28 Alba C, Vidal L, Díaz F, Villena A, de Vargas IP. Ultrastructural and quantitative age-related changes in capillaries of the dorsal lateral geniculate nucleus. *Brain Res Bull* 2004;64(2):145-153.

29 Calkins DJ. Age-related changes in the visual pathways: blame it on the axon. *Invest Ophthalmol Vis Sci* 2013;54(14):ORSF37-ORSF41.

30 Pankowska A, Matwiejczuk S, Kozioł P, Żarnowski T, Pietura R, Kosior-Jarecka E. Visual tract degradation in bilateral normal-tension glaucoma-cortical thickness maps and volumetric study of visual pathway areas. *J Clin Med* 2022;11(7):1907.

31 Schmidt MA, Knott M, Heidemann R, Michelson G, Kober T, Dörfler A, Engelhorn T. Investigation of lateral geniculate nucleus volume and diffusion tensor imaging in patients with normal tension glaucoma using 7 tesla magnetic resonance imaging. *PLoS One* 2018;13(6):e0198830.

32 Li M, Ke ML, Song YW, Mu KT, Zhang H, Chen ZQ. Diagnostic utility of central damage determination in glaucoma by magnetic resonance imaging: an observational study. *Exp Ther Med* 2019;17(3):1891-1895.

33 Song XY, Zhen PY, Chen AH, Zhao J, Li XJ, Chen YY, Tang WJ, Zhang YY. Diffusion tensor imaging detects microstructural differences of visual pathway in patients with primary open-angle glaucoma and ocular hypertension. *Front Hum Neurosci* 2018;12:426.

34 Xu ZF, Sun JS, Zhang XH, Feng YY, Pan AZ, Gao MY, Zhao H. Microstructural visual pathway abnormalities in patients with primary glaucoma: 3 T diffusion kurtosis imaging study. *Clin Radiol* 2018;73(6):591.e9-591.e15.

35 Zhang P, Wen W, Sun XH, He S. Selective reduction of fMRI responses to transient achromatic stimuli in the magnocellular layers of the LGN and the superficial layer of the SC of early glaucoma patients. *Hum Brain Mapp* 2016;37(2):558-569.

36 Doganay S, Cankaya C, Alkan A. Evaluation of corpus geniculatum laterale and vitreous fluid by magnetic resonance spectroscopy in patients with glaucoma; a preliminary study. *Eye* (*Lond*) 2012;26(8):1044-1051.

37 Yücel YH, Gupta N, Zhang Q, Mizisin AP, Kalichman MW, Weinreb RN. Memantine protects neurons from shrinkage in the lateral geniculate nucleus in experimental glaucoma. *Arch Ophthalmol* 2006;124(2):217-225.

38 Rodrigo MJ, Cardiel MJ, Fraile JM, Mendez-Martinez S, Martinez-Rincon T, Subias M, Polo V, Ruberte J, Ramirez T, Vispe E, Luna C, Mayoral JA, Garcia-Martin E. Brimonidine-LAPONITE® intravitreal formulation has an ocular hypotensive and neuroprotective effect throughout 6mo of follow-up in a glaucoma animal model. *Biomater Sci* 2020;8(22):6246-6260.

39 Scuteri D, Bagetta G, Nucci C, Aiello F, Cesareo M, Tonin P, Corasaniti MT. Evidence on the neuroprotective properties of brimonidine in glaucoma. *Prog Brain Res* 2020;257:155-166.