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Lateral Geniculate Nucleus in Hypertensive and Normotensive Glaucoma

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Abstract

Objective: To find whether changes in lateral geniculate nucleus (LGN) can be determined *in vivo* in hypertensive and normotensive glaucoma, and whether these changes correlate with the advancement of glaucoma disease.

Methods and subjects: The authors examined two groups of patients, 9 patients with hypertensive glaucoma (HTG) and 9 patients with different stages of normotensive glaucoma (NTG). The diagnosis was based on a comprehensive ophthalmological examination. The results of both groups were compared with a group of 9 healthy subjects. A comprehensive ophthalmological examination was supplemented by examination of the visual field by means of a fast threshold program. The sum of sensitivity in the field of vision of homolateral halves (range 0 to 22 degrees) was compared with the size of contralateral corpus geniculatum laterale.

Data collected from patients were compared with a group of nine healthy controls.

We carried out MRI tests at 3-Tesla MRI scanner (Philips Achieva TX series release 3.2.1.1) using eight-channel sense head coil.

Results: The measured values were subjected to statistical analysis using the Wilcoxon test and Spearman´s rank correlation coefficient.

The authors proved reduction of LGN in both HTG and NTG (p=0.0000). The LGN reduction dependence on the stage of changes in visual fields was not statistically significant, in HTG for the right half of visual fields (RH VF) and the left LGN r=0.3255, p=0.3926, and for the left half of visual fields (LHVF) and the right LGN r=0.0033, p=0.9934. Similarly, in NTG, statistically significant correlation between RH VF and L LGN (r=0.0496, p=0.1745) and between LHVF and R LGN (r=0.5399, p=0.1335) was not found either. The authors demonstrated median duration dependence in hypertensive glaucoma treatment to the reduction of the LGN. R=-0.4908, p=0.179 for the right LGN and r=-0.7743, p=0.0143 for the left LGN.

Conclusion: The reduction of LGN volume was proved both in patients with HTG and those with NTG.

Keywords: Hypertensive glaucoma; Normotensive glaucoma; Lateral geniculate nucleus; MRI; Changes in the visual field

Abbreviations: GDx: Scanning Laser Polarimetry; HTG: Hypertension Glaucoma; NFI: Nerve Fiber Indicator; NTG: Normal-Tension Glaucoma; PERG: Pattern Electro Retinography; PVEP: Pattern Visual Evoked Potentials

Introduction

In previous studies we demonstrated by means of fMRI and other functional vision examinations the difference between hypertensive and normotensive glaucoma [1-5]. This time we have focused on the possible evidence of differences at the LGN level. The fMRI examinations were carried out on the same individuals of all the three groups [1,3-5].

Glaucoma is still being defined as a chronic progressive neuropathy with excavation and atrophy of the optic nerve and consequent changes in the visual field. This formulation is used for both hypertensive and normotensive glaucoma. Even though we know that the pathogenesis of both diagnoses is different, the therapeutic approaches are very similar.

Since 1993, when Chatuverdi et al. [6] examined glaucomatous damage of LGN in both magnocellular and parvocellular layers in patients with or without glaucoma, there are plenty of studies about LGN damage to be found in literature. Counting ganglion cells of LGN postmortem, greater loss was found in magnocellular cells. No difference showed in parvocellular layers. Weber et al. [7] arrived at similar conclusions in an experimental model as well. Increased intraocular pressure in monkeys disrupted the size, density and number of neurons in the LGN, as well as the LGN volume itself. The high intraocular pressure had a greater influence on the magnocellular cells than on the parvocellular ones (59% *vs.* 31%). The degree of shrinking of the LGN itself (after volume correction) indicated that the loss of magnocellular ganglion cells is 4 times higher than that of parvocellular ones (38% *vs.* 10%). Yücel et al. [8,9] proved that in experimental glaucoma,damages occur not only to magnocellular but to parvo-and koniocellular LGN cells as well. Gupta et al. [10] demonstrated clinical-pathological changes in intracranial parts of the optic nerve, LGN and visual cortical areas in the human glaucoma.

Group of Patients and Methods

Our set of patients included 18 patients, 9 with HTG (3 women and

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6 men aged 41-71 years, mean 49.3) and 9 with NTG (6 women and 3 men aged 28-74 years, mean 60.1). The control group consisted of 9 healthy subjects (4 women and 5 men, aged 24-66 years, mean 43.7) (Table 1). All of them underwent comprehensive eye examinations, including biomicroscopy, gonioscopy, daytime IOP curve, perimetry, GDx NFI, PERG and PVEP. Visual acuity after eventual correction was in all of them 1.0. IOP after CCT correction was lower than 18 mmHg. In the HTG cases after a glaucomatous treatment. None of them had any neurological disease, and structural brain imaging using MRI was normal in all the persons. Perimetric examination was performed by the Medmont device M700 (MedmontPty Ltd, Victoria 3124, Australia) using glaucoma program and fast threshold strategy. The sum of sensitivity in the right halves of the visual fields (RH VF) of each individual was compared with the left LGN, and vice versa (LHVF *vs*. R LGN). The LGN size achieved by MRI studies was performed on a 3-Tesla MRI scanner (Philips Achieva TX series release 3.2.1.1) using eight-channel sense head coil. Multiple sequences were applied: sagittal 3D T1 TFE (TR/TE 8/3, 8, 160-170 slices, acquisition voxel 1×1×1, FOV 240×240, Sense 1.7, NSA 1), axial T2 TSE (TR/TE 3000/80, 28 to 30 slices, 4 mm gap slice thickness 1 mm, FOV 240×240, TSE factor 15, ACQ voxel 0.57×0, 74×4, NSA 1), coronal and axial PDW TSE (TR/TE 3000/12, 50 slices, 2 mm slice thickness gap 0, FOV 120×20, TSE factor 7, ACQ voxel 0.7×0, 89×2, NSA 3). Axial T2 and sagittal T1W 3D TFE images of the brain were obtained for optimal spatial orientation and to rule out any incidental abnormalities along the visual pathways. LGN images were acquired in the coronal and transversal plane, 2 mm proton density weighted, giving a bright signal intensity by low signal intensity of white matter tracts. In all subjects each LGN was visible. Image analysis was performed by one neuroradiologist, who was able to access coronal and axial PDW images of the LGN only. MR image data were analyzed using Extended MR Workspace (Philips, version R2.6.3.1). LGN height was obtained by drawing a perpendicular line from the apex of the convexity to the base of the nucleus. Other diameters of the LGN were obtained in the axial PDW plane in two perpendicular drawings.

Results

The measured values of total sum of sensitivity in homolateral halves of the visual fields (RH VF and LHVF), the sizes of the right (R) and left (L) LGN are shown in tables 1-3. Table 2 gives also the time of treatment of hypertensive glaucoma.

The results were subjected to statistical analysis. Sets were compared using the Wilcoxon paired test, and their mutual correlation using the Spearman correlation coefficient. First, we compared the size of LGN in the control group. The results are shown in figure 2. Then we compared all three sets with one another (Figures 3 and 4).

Gender-Year of birth	LH VF	R LGN	RH VF	L LGN
M-1988	2 295	4.5	2 271	4.7
F-1988	2 051	4.9	2 088	4.3
M-1982	2 210	5.6	2 268	5.3
F-1967	2 219	5.1	2 196	5.1
F-1967	2 176	4.8	2 176	5
F-1965	2 184	4.8	2 177	5
M-1956	2 087	4.6	2 178	4.6
M-1955	2 176	4.9	2 229	4.9
M-1946	2 167	4.3	2 215	4.2

Table 1: Control group.

The sum of sensitivity in the left halves of visual fields LHVF, the sum of sensitivity in the right halves of visual fields RHVF (dB), size of the right (R) LGN, left (L) LGN (mm).

Gender-Year of birth	LH VF	R LGN	RH VF	L LGN	Length of therapy
M-1971	1 483	3.2	1 526	3.6	8
F-1970	1 876	3.6	1 868	3.1	6
M-1962	1 615	3.1	1 493	3.5	7
M-1956	777	3.3	961	3.5	13
M-1953	183	3.3	355	3.5	13
M-1948	1 711	4.1	1 319	4.2	7
F-1950	1 838	3.3	1 890	3.6	9
F-1946	2 048	3.4	1 946	3	15
M-1942	1 038	3	947	2.4	30

Table 2: Group of HTG.

The sum of sensitivity in the left halves of visual fields LHVF, the sum of sensitivity in the right halves of visual fields RHVF (dB), the size of the right (R) LGN, left (L) LGN (mm). Length of glaucoma therapy (in years).

Gender-Year of birth	LHVF	RLGN	RHVF	L LGN
M-1984	2 076	3.6	2 140	3.5
M-1960	2 219	4.1	2 200	4.3
F-1959	2 102	3.6	2 140	3.5
F-1952	1 318	3.4	1 324	3.4
F-1949	2 026	3.6	1 875	3.1
F-1948	1 761	3.9	1 830	3.7
F-1939	1 758	3	1 833	2.9
M-1938	1 017	3.1	991	2.8
F-1938	2 146	3.2	2 149	3.2

Table 3: Group of NTG.

The sum of sensitivity in the left halves of visual fields LHVF, the sum of sensitivity in the right halves of visual fields RHVF (dB), the size of the right (R) LGN, and the left (L) LGN(mm).

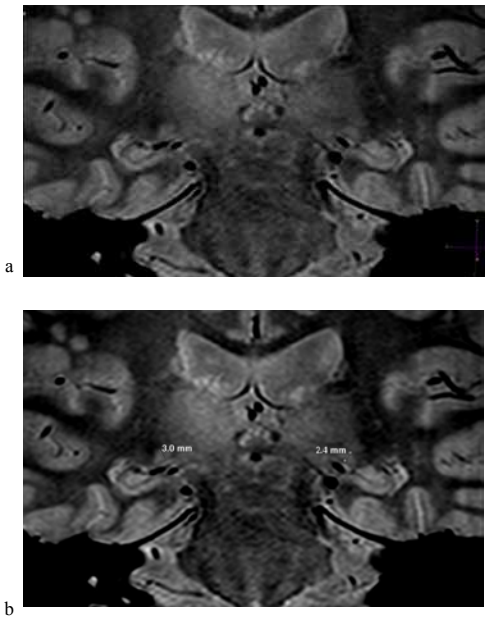

Figure 1: LGN coronal slices in a patient with hypertensive glaucoma (M-1942).

a) Coronal 2 mm proton density weighted lateral geniculate nucleus image. **b)** Coronal proton density weighted LGN with oblique lines showing orientation used for height measurement.

Neuroimaging studies of the LGN with coronal proton density images with 2 mm slice thickness is a technical challenge for MR imaging optimization protocol to consistently identify the LGN

from surrounding white and gray matter structures and for its measurement (Figures 1a and 1b).

Similarly, we sought to determine whether there is a dependency in the size of the LGN on the age of persons. We did not find a statistically significant relationship between the size of the right LGN and age (r=-0.3377, p=0.3741), and similarly neither between the left LGN and the age (r=-0.0588, p=0.8806). Another objective was to find in hypertensive glaucoma, whether there is a relationship between the size of LGN and the duration of glaucoma disease. At the right LGN, we found a mean dependence, which was, however, not statistically significant (r=-0.4908, p=0.1797). At the left LGN we also found a mean dependence but this time a statistically significant one (r=-0.7743, P=0.0143) (Figures 5 and 6). Similar research was not carried out in normotensive glaucoma due to their different pathogenesis.

Relationship between the changes in visual fields (sum of sensitivities in homolateral halves) to the LGN size in hypertensive

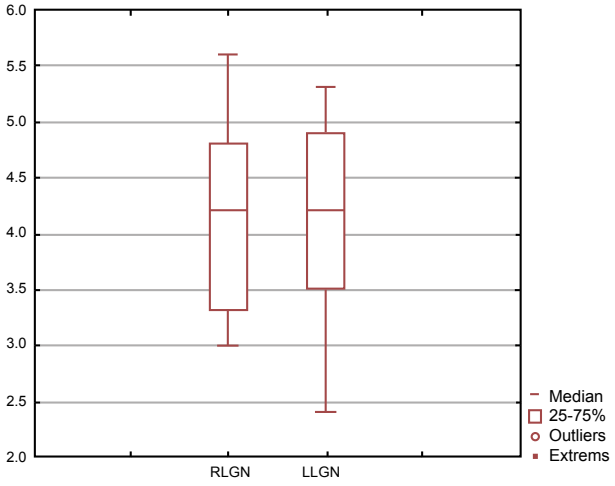

Figure 2: The graph shows the size of the right and left LGN in the control group. Wilcoxon paired test showed no difference between the left and right LGN (p=0.909).

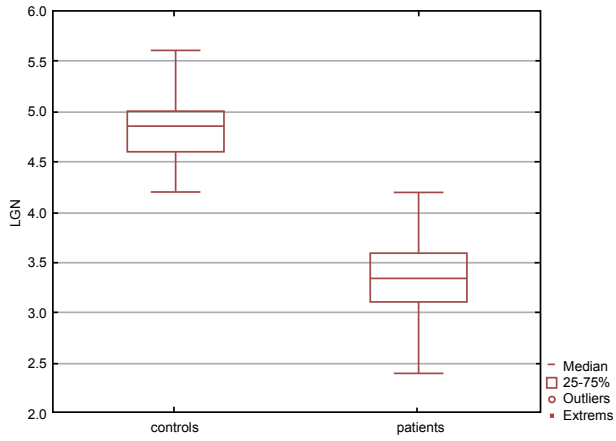

Figure 3: Shows a statistically significant difference inthe total size of LGN in the control group and in the group of hypertensive glaucoma patients (p=0.0000).

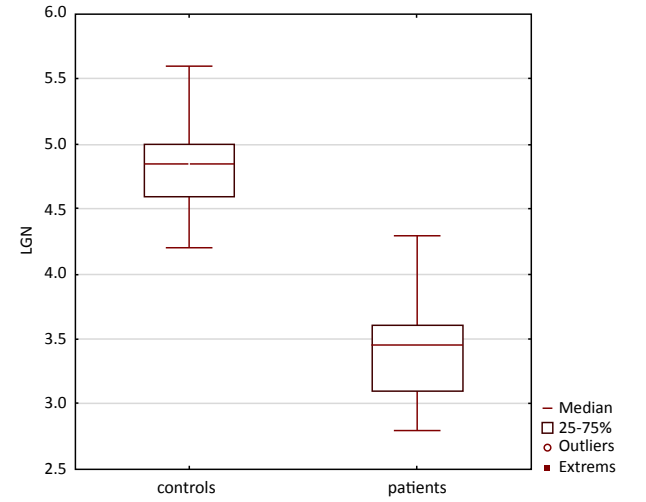

Figure 4: Shows a statistically significant difference in the total size of the LGN in the control group and the group of normotensive glaucoma patients (p=0.0000).

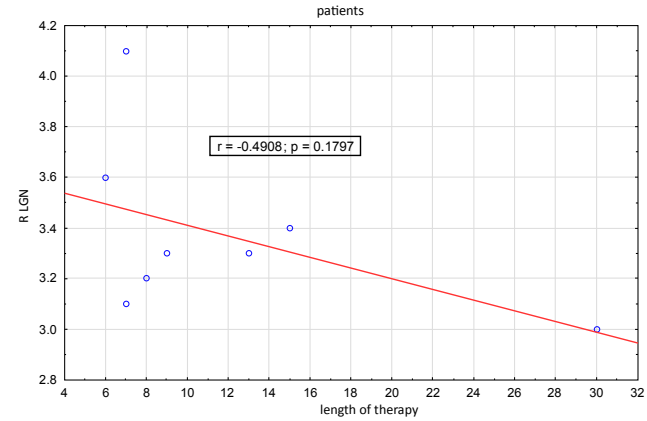

Figure 5: Dependence of the size of the right LGN on length of the hypertensive glaucoma therapy.

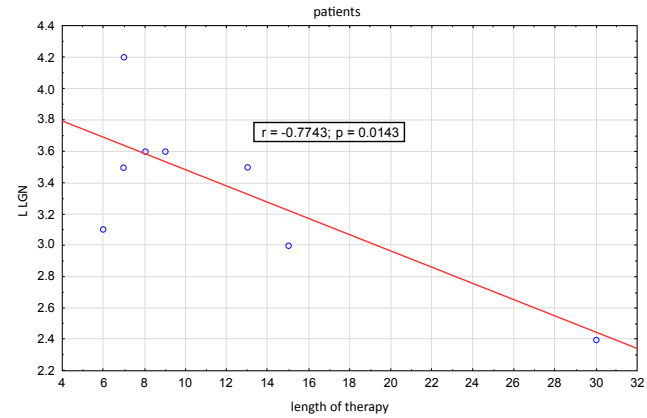

Figure 6: Dependence of the left LGN on length of the hypertensive glaucoma therapy.

glaucoma was not statistically significant. The correlation coefficient between RHVF and L LGN was (r=0.3255, p=0.3926) and between LHVF and R LGN (r=0.0033, p=0.9934).

Similarly in normotensive glaucoma, no statistically significant correlation between RHVF and L LGN (r=0.0496, p=0.1745) and between LHVF and R LGN (r=0.5399, p=0.1335)was found.

Discussion

Recent studies from the last three years demonstrate a LGN reduction not only in experimental animals but in glaucoma patients as well [11-13]. Using positron emission tomography, Shimazawa et al. [14] demonstrated changes of glial activity in LGN in monkeys with experimentally induced hypertensive glaucoma. Doganay et al. [15], using magnetic resonance spectroscopy, found increased ratio of glutamate/creatinine both in the vitreous and in the LGN in glaucoma patients. All these works allege involvement of LGN in the pathogenesis of glaucoma disease. We were interested in the work by Zhang et al. [16] that demonstrated the LGN reduction in patients with normotensive glaucoma. In our previous presentations we demonstrated the difference in the activity of visual cortex in hypertensive *vs.* normotensive glaucoma. In hypertensive glaucoma, in dependence on the progression of glaucoma disease, fMRI activity also decreased. We did not find this effect in normotensive glaucoma [1-4]. Therefore, we were interested in finding the LGN sizes in these glaucoma groups. In hypertensive glaucoma, degeneration of both the LGN and visual cortex due to transneuronal processes is experimentally proven. On the basis of pathogenesis of normotensive glaucoma, changes in front of the visual pathway as well as in the LGN can be expected. This assumption was confirmed by Zhang et al. [16]. Our work also proves the LGN reduction in normotensive glaucoma. Furthermore, we sought to find whether there is a correlation between the changes in the visual fields and LGN sizes. It is possible that we did not achieve the results of Dai et al., who compared the findings in the visual field of one eye always against both LGN [13], because our set of patients was too small (9 persons). We took the sum of sensitivity of homolateral visual fields as credible for afferentation exactly to the contralateral LGN. We have not proven any statistically significant relationship. But our patients did not have the changes of the 5th stage by glaucoma staging system [17] as they had in the work by Dai et al. [13]. We are aware of the age differences in individual groups: HTG–49.3 years, NTG–60.1 years, and the control group 43.7 years. And it is also known that the NTG disease is more common in women and at higher age than HTG. These data influencing the differences are also reflected in our file. The examination was performed in 2010 on the device 3-Tesla MRI scanner (Philips Achieva TX series release 3.2.1.1) using an eight-channel sense head coil. Even if we would like to correct the data subsequently, it was not possible because we upgraded the device to a 32-channel sense head coil in 2011. We managed however to demonstrate the relationship between the duration of hypertensive glaucoma and LGN size.

As for measuring the size of the LGN, Dai et al. [13] used both height and overall volume of the morphological body. The LGN size, the so called height is generally recognized as the most consistent dimension of the MR and histological sections. The MR image and histological section have a similar shape. From our experience, the coronal plane is well viewable, and the height corresponds best to changes of sizes which are the earliest and most extensive at possible LG Natrophy process. Therefore we have used this dimension to determine the size of the LGN.

Conclusions

We can conclude that by means of MRI, changes in the LGN can be demonstrated *in vivo* in both hypertensive and normotensive glaucoma.

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