

Quantitative Analysis of the Displacement of the Anterior Visual Pathway by Pituitary Lesions and the Associated Visual Field Loss

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PURPOSE. To evaluate quantitatively the relationship between the displacement of anterior visual pathway structures by pituitary tumors and visual field damage with the goal of improving diagnosis and management.

METHODS. Subjects had pituitary macroadenomas and both magnetic resonance imaging (MRI) and static perimetry. Neuroradiologists measured the displacement of anterior visual pathway structures and right–left tumor asymmetry. To quantify the degree and laterality of visual field loss, we used algorithms from the neurologic hemifield test to analyze each right–left pair of visual fields with respect to temporal asymmetry, the proportion of loss that was temporal, total asymmetry, and total damage. We compared these metrics with the displacement of anterior visual pathway structures and tumor asymmetry.

RESULTS. Of 114 subjects, 64 (56%) were male and the median age was 57 years (range, 14–88). The summation of vision loss in both eyes and the proportion of temporal loss were statistically significantly related to the maximum displacement of the anterior visual pathway (both $P < 0.001$ for fit of linear regression). The relationship between the asymmetry of visual field loss in the two eyes and the subjective assignment of tumor asymmetry on MRI did not achieve statistical significance ($P = 0.06$ by analysis of variance).

CONCLUSIONS. Displacement of the anterior visual pathway by pituitary tumors is associated with both the total amount of visual field loss and the proportion of temporal visual field loss. Although there was right–left asymmetry of vision loss in some subjects, it was not related to the subjective assessment of tumor asymmetry.

Keywords: pituitary, macroadenoma, visual field

Our understanding of the relationship between tumors of the pituitary and loss of visual field extends back at least as far as Cushing in 1915. He and his colleagues reported a series of cases that included examples of bitemporal, homonymous, amaurotic (blind in one or both eyes), and “unclassified” defects in patients with pituitary adenomas.¹ Subsequent small studies also have reported similar mixtures of visual field defects in patients with pituitary tumors.^{2–4} In some instances, study results have been biased by the selection of only those patients with objective vision loss.⁵ Analyzing only those subjects with some type of vision loss makes it impossible to communicate important concepts like the overall incidence of vision loss in the overall population, which may help with clinical decision making.

More recently, the quantitative nature of modern visual field testing has been applied to the relationship between the size of pituitary tumors and the visual field defects they cause. For example, Lee et al.⁶ demonstrated that the volume of the tumor was correlated with the total amount of visual field loss as measured by the Mean Deviation parameter of the Humphrey Field Analyzer.

To determine if there were as yet undescribed quantitative relationships between the displacement of the anterior visual

pathway by pituitary macroadenomas by neuroimaging and their associated visual field loss, we designed a study to assess those potential relationships. To advance our understanding beyond prior work that has relied on overall visual field loss, we assessed quantitatively the laterality and asymmetry of the visual field loss both between regions of the visual field and between eyes. Such quantitative analyses are a first step toward potential decision support tools that might draw a clinician’s attention to visual field results that are suggestive of a chiasmal lesion but do not present as a clear bitemporal defect. Furthermore, this kind of analysis is well suited to finding relationships between functional deficits of vision and the structural correlates found on magnetic resonance imaging (MRI). If such relationships are found, and are strong enough, it may be possible to provide equal-quality care for less cost.

METHODS

After review and approval by the Johns Hopkins University School of Medicine Institutional Review Board, we identified 185 patients in our radiology information system with a diagnosis of “pituitary macroadenoma” associated with at least

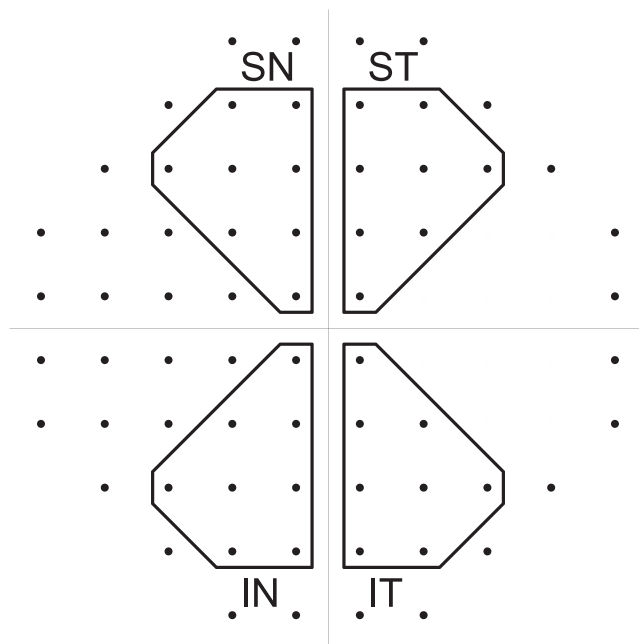


FIGURE 1. Depiction of the four regions of the visual field used in this study: superior nasal (SN), superior temporal (ST), inferior nasal (IN), and inferior temporal (IT), superimposed on the standard 30-2 pattern of visual field test points for a right eye. The regions were defined to be symmetric and to avoid the physiological blind spot (*open circles*).

one relevant MRI study. Subjects were included if at least one dimension of their pituitary adenoma was 10 mm or greater. Sixty-six patients were excluded because they did not have visual field testing available or because they had other underlying diseases such as stroke, glaucoma, ocular or intracranial trauma, retinal artery occlusion, retinal diseases, amblyopia, or unrelated optic neuropathy that may also affect the visual field. The analysis of the relationship between the MRI and subjective visual field findings from this group has been reported previously.⁷

The displacement of the prechiasmatic optic nerve, optic chiasm, and postchiasmatic optic tract by the pituitary macroadenoma was measured using electronic calipers on the original image data. The displacement was measured from the location of the normal side, or, when both sides were elevated, based on the expected deviation from the normal position based on anatomic landmarks. When two reviewers disagreed by 3 mm or more, the senior neuroradiologist (DMY) adjudicated and his measurement was used. Adjudication was necessary in 4/57 (7%) moderate displacement cases where the two neuroradiologists assigned values that differed by at least 3 mm.

All visual field tests were performed using a Humphrey Field Analyzer (HFA-II; Carl Zeiss Meditec, Inc., Dublin, CA, USA). Test patterns were either 24-2 or 30-2, and strategies included Swedish Interactive Threshold Algorithm (SITA) or full threshold. An additional five subjects who had field testing were excluded after review due to either an unreliable test or to a lack of digital data for the visual field results.

For each visual field test, we calculated scores proportional to the degree of visual field loss in each of four quadrants: superior nasal, superior temporal, inferior nasal, inferior temporal (Fig. 1). The scores for each point in each region were calculated in the same way previously described for the neurologic hemifield test (NHT).^{8,9} In brief, each point was assigned a score based on its pattern deviation probability: 0 if > 10%, 2 if > 2% and ≤ 10%, 5 if > 1% and ≤ 2% and 10 if ≤ 1%.

TABLE. Characteristics of Study Subjects, Their Visual Fields, and the Asymmetry of Their Tumors on Magnetic Resonance Imaging

Characteristic	Median
Age, median (range)	57 (14–88)
Sex	
Male	64, 56%
Female	50, 44%
Visual field defect	
Bitemporal	29, 25%
Mixed, bitemporal plus	19, 17%
Normal	26, 23%
Nonspecific	27, 24%
Monocular	11, 10%
Homonymous	1, 1%
Other	1, 1%
Asymmetry of tumor on MRI	
Right	15, 13%
Left	26, 23%
None	73, 64%

The scores from each point in a region (Fig. 1) then were added to summarize the total visual field loss in that region.

The regional scores from each right/left pair of visual fields were used to assess aspects of visual field loss that might be related to features of the pituitary tumor. These analyses included (1) the proportion of all visual field loss that was in the temporal regions of both eyes (sum of scores in the superior and inferior temporal regions in both eyes divided by the sum of scores in all regions from both eyes); (2) the asymmetry of temporal vision loss (sum of scores in the temporal regions of the right eye minus the sum of scores in the temporal regions of the left eye); (3) the total amount of visual field loss (sum of scores in all regions in both eyes); and (4) the asymmetry of total vision loss (sum of all region scores in the right eye minus the sum of all region scores in the left eye). The focus on the temporal visual hemifield is based on the anatomic–physiological relationships between the involved structures.

The relationships between the maximum displacement of the anterior visual pathway structures and total visual field damage and temporal visual field damage were modeled with linear regression. Models were generated for the amount of displacement of structures anterior to the chiasm, for the displacement of the chiasm, and for the maximum displacement (anterior to, at, and posterior to the chiasm). Note that there is overlap in these populations, so a single subject may have more than one region affected. Analysis of variance was used to assess the relationships between tumor asymmetry on MRI and the asymmetry of temporal visual field loss, the asymmetry of the proportion of temporal visual field loss, and the asymmetry of total visual field loss.

To determine the relationship between any of the calculated visual field parameters and any displacement of the anterior visual pathway, we performed receiver operating characteristic (ROC) analysis for each.

We performed all statistical analyses using R (version 3.2.2, <https://www.r-project.org>; in the public domain). This study adhered with the tenets of the Declaration of Helsinki.

RESULTS

The characteristics of the 114 study subjects, their visual field defects, and the presence of asymmetry on MRI are reported in

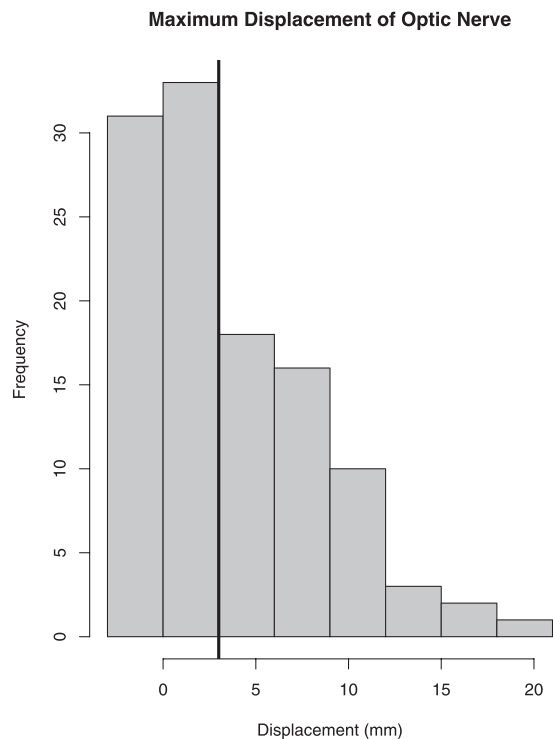


FIGURE 2. Distribution of maximum anterior visual pathway structure displacement on MRI. Tumors not contacting the optic nerve were assigned a value of -1 . The vertical line represents the value of 3 mm used to define the maximum extent of “mild” displacement for this study.

the Table. The median displacement of the anterior visual pathway structures on MRI was 4 mm (range, 0–21) (Fig. 2).

The relationship between total visual field loss and maximum displacement of the anterior visual pathway structures was statistically significant ($P < 0.001$, Fig. 3) with an R^2 value of 0.41. The R^2 values obtained for the relationship between total visual field loss and the displacement anterior to (80 subjects) and at (86 subjects) the chiasm were also statistically significant ($P < 0.001$) and similar (0.38 and 0.40, respectively). Similarly, the relationship between the proportion of temporal visual field damage and the displacement of the anterior visual pathway structures was statistically significant ($P < 0.001$, Fig. 4), but the R^2 value was 0.11. As with the models using total visual field loss, the results for displacement of structures anterior to and at the chiasm produced similar R^2 values (0.14, 0.08, respectively).

The relationship between right–left asymmetry of total visual field damage and qualitative asymmetry of tumors on MRI approached but did not achieve statistical significance (Fig. 5, $P = 0.06$). There were no statistically significant differences in right–left asymmetry in temporal visual field damage based on tumor asymmetry on MRI (Fig. 6, $P = 0.6$).

With any displacement of the anterior visual pathway as the outcome, the area under the ROC curve was 0.72 for total visual field damage, 0.71 for maximum (right versus left eye) damage, 0.68 for the proportion of damage in the temporal hemifields, and 0.46 for right–left asymmetry in temporal visual field loss.

DISCUSSION

Utilizing quantitative analysis of both MRI and visual fields from patients with pituitary macroadenomas, we have demonstrated

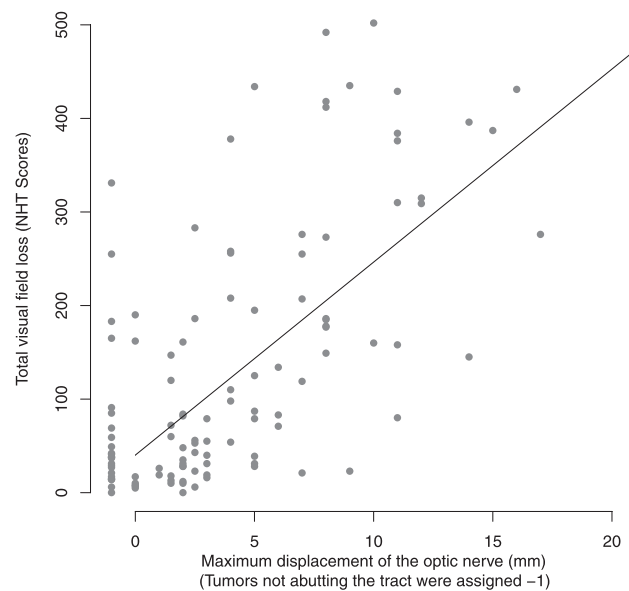


FIGURE 3. Relationship between the total amount of visual field loss in all four quadrants and the maximum displacement of the anterior visual pathway structures. The line depicts the results of linear regression. The R^2 for the correlation between the two parameters is 0.41.

a statistically significant relationship between the amount by which a pituitary tumor displaces the anterior visual pathway and the total amount of visual field damage. This suggests that, perhaps as expected, damage to the optic nerve and chiasm is at least partially due to the mechanical effect of the tumor itself. On the other hand, the R^2 value for this relationship is 0.41, indicating that less than half of the variability in the amount of visual field loss is explained by our measures of displacement alone. The area under the ROC curve for total visual field loss as a predictor of visual pathway displacement was also modest (0.72). Given the nature of this relationship, it is not possible to

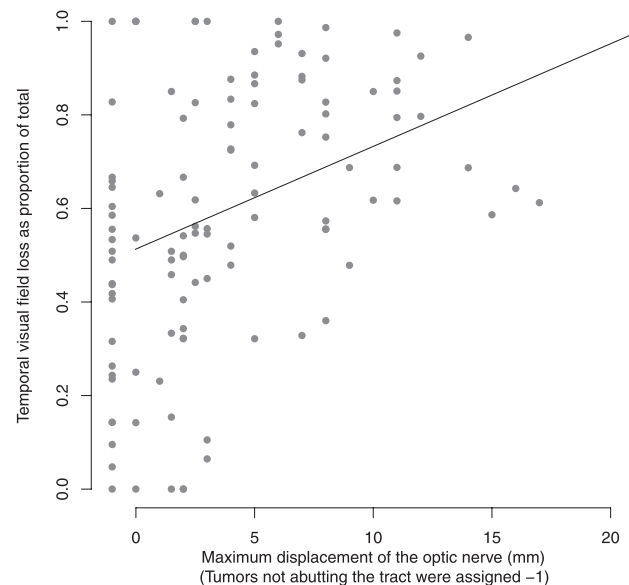


FIGURE 4. Relationship between the proportion of visual field loss in the temporal quadrants and the maximum displacement of the anterior visual pathway structures. The line depicts the results of linear regression. The R^2 for the correlation between the two parameters is 0.11.

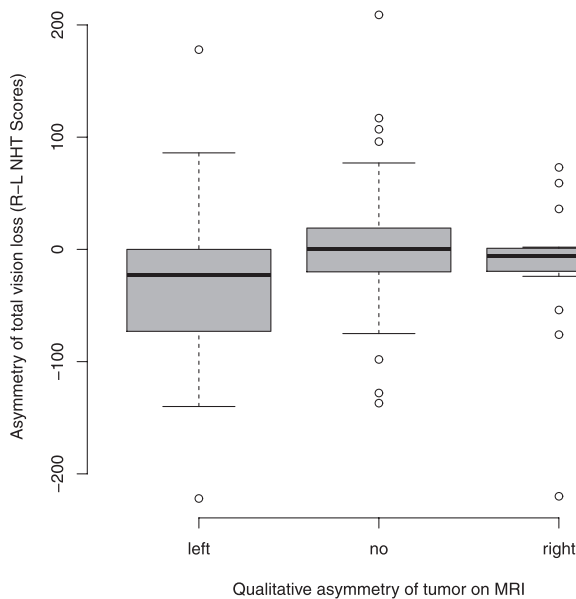


FIGURE 5. The asymmetry of total visual field loss between right and left eyes of subjects and qualitative right-left asymmetry on MRI. There are no statistically significant differences between the right, left, and no categories.

suggest a change in current practice—altering patterns of referral to ophthalmology based on MRI findings, for example.

We similarly found a significant relationship between the proportion of visual field loss that was in the temporal regions and the amount of optic nerve and chiasmal displacement. This analysis had been predicated on the classic teaching that pituitary tumors cause bitemporal defects in the visual field. Again, although the linear relationship was significant, the R^2 value was even lower than that found for the relationship between total visual field loss and the degree of displacement (0.11). The results for models using just displacement of structures anterior to the chiasm or the chiasm itself were similar. Together, these findings suggest that one or more other factors are relevant to the relationship between the amount by which pituitary tumors displace the anterior visual pathway and the associated visual field loss. There are a variety of such potential factors, including inflammation in the region of the tumor, the growth rate of the tumor, the consistency of the tumor, and local compromise of blood flow. Necrosis of tumors as they outgrow their blood supply or intratumoral hemorrhage may also play a role in the relationship between tumor-induced displacement and the damage to the anterior visual pathway. There are also anatomic considerations that may need to be better described and analyzed, including the length of the intracranial optic nerve and the initial spatial relationship between the optic pathway and the pituitary. Any of these could be risk factors for optic nerve dysfunction in the absence of a direct mechanical effect of the tumor. It also may be that not all tumor contact with anterior visual pathway structures is equivalent in terms of causing visual dysfunction and that more detailed information about where the contact occurs would be important to collect. We also have no information about the duration of contact between the tumor and nerve that could be an underlying cause of differential damage for the same amount of displacement. Finally, it may be that there is sufficient noise in the measurement of the tumor, the visual field, or both that the underlying relationships are not being measured precisely.

The results reported herein need to be considered in light of the fact that the data were collected retrospectively. There

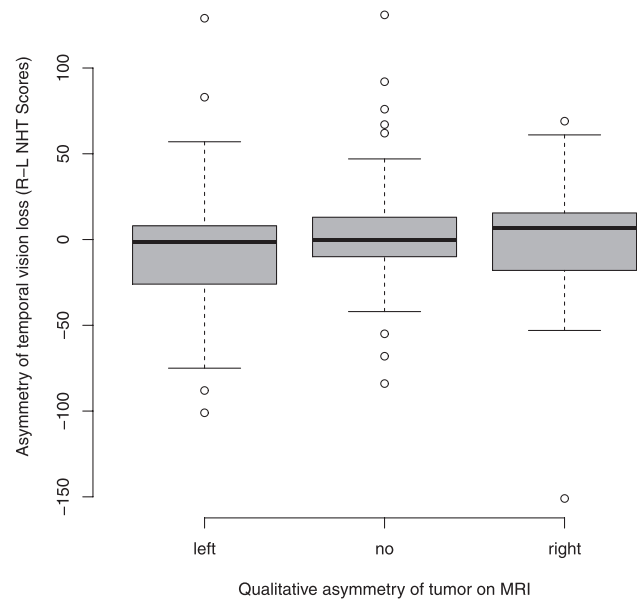


FIGURE 6. The asymmetry of temporal visual field loss between right and left eyes of subjects and qualitative right-left asymmetry on MRI. There are no statistically significant differences between the right, left, and no categories.

also may be an inherent selection bias in our results because only subjects who had both MRI and visual field testing were included. In other words, there may be systematic reasons for which the persons included in the study had both tests done at our institution that also would alter the relationships we evaluated. These potential issues could be overcome by a future, prospective study of all patients presenting with pituitary macroadenomas. Such a study might add to the work described here by clarifying the relationships between structure and function to such a degree that it could be possible to determine which features on MRI predict if and when it is necessary to send such patients for neuro-ophthalmologic evaluation. Such a result could help make the care of these patients more efficient by limiting the need for additional office visits.

In summary, using quantitative assessments of optic nerve displacement by pituitary macroadenomas and visual field damage, we have identified statistically significant relationships between the two. The correlations are weak, however, suggesting that additional potential factors should be evaluated in future work. We also found no clear relationship between the right-left asymmetry of tumors and the vision loss they caused. This may be because no such relationship exists or, again, that alternative factors need to be considered when designing future studies.

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