

## Pituitary adenoma

### Assessment of modern means of neuro-ophthalmological subjective investigation<sup>◇</sup>

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**ABSTRACT.** The authors tested contrast sensitivity function (C.S.) in a series of 81 patients with pituitary adenoma. In the first part of the study, they compared C.S. with visual acuity (V.A.), desaturated panel D-15 (D-15), automatic static perimetry (A.P). When C.S. was abnormal, there was a high probability of finding an abnormal V.A. and an abnormal D-15. The C.S. attenuation was associated with a change of A.P. when the whole visual field was considered. The authors tried to determine whether the addition of C.S. to the other classical means of visual investigations was useful for the diagnosis. For microadenomas, the best association was A.P.-C.S., the second best association A.P.-D-15. For macroadenomas, the best association was always A.P.-C.S., the second best was Goldmann-C.S.

**Key words:** pituitary adenoma; contrast sensitivity; colour vision test; automated static perimetry; Goldmann perimeter

#### INTRODUCTION

The study of the function of contrast sensitivity (C.S.) has recently come into wide clinical use<sup>1</sup>. Some studies<sup>2-7</sup> have emphasized its role as a means of investigating the compression of the anterior visual pathway. We tested C.S. in a series of 81 patients with pituitary adenoma. In the first part of the study, we compared C.S. with classical

means of investigation: visual acuity (V.A.), colour tests, automatic static perimetry (A.P.). In the second part, we tried to determine whether the addition of C.S. to the other classical means of visual investigation was useful for the diagnosis. Knowing that visual field study remained essential, we tried to find out which association of the tests, according to the size of the tumour, was the best for our purposes. Thus, 50 patients who underwent the complete tests on the same day were evaluated.

#### PATIENTS

Patients seen in our Neuro-Ophthalmology Department with the diagnosis of pituitary ade-

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noma confirmed by surgical and immunocytochemical findings, were included. Non-surgically treated patients were included when a CT scan and/or M.R.I. were highly significant of a pituitary tumour. They were subjected to static and dynamic hormonal investigations (FSH, LH,  $\alpha$ -subunit, PRL, GH, TSH) under combined hypothalamic stimulation<sup>8</sup>. Patients with a previous ophthalmological disease (chronic glaucoma, cataract and retinal disease), with congenital dyschromatopsia or who were known to have an associated disease possibly altering the visual field (multiple sclerosis) were also excluded. Attenuation of C.S. increases with age especially with high spatial frequencies<sup>9, 10</sup>. We limited the use of C.S. to patients younger than 50 years, because of limited equipment<sup>11</sup>. For the highest spatial frequencies, we could not discriminate statistically the normal population from the pathological older than 50 years (unpublished data). Patients unable to undergo tests because of a too bad V.A. ( $< 1/50$ ) or with a serious intellectual deterioration were excluded. Each patient was tested one or several times from June 1987 to June 1989 and underwent a neuro-ophthalmic examination, including a Goldmann perimetry study with two (V4, II2) or three isopters (V4, II2 and I2), an automated static perimetry study of the central 30° with a fast thresholding technique for 94 points and a 4-2-2-2-foveolar threshold determination<sup>12</sup>. The A.P. and the C.S. study were performed on the Vision Monitor<sup>®</sup>, on the same cathode ray tube stimulator. We used vertical sinusoidal stationary gratings presented at 3.50 M sustaining a square of 2.2 × 1.6° of visual angle. The luminance of the background was 100 candela/m<sup>2</sup>. Further details can be found elsewhere<sup>13</sup>. Three colour vision tests were done: Ishihara plates, Farnsworth-15 Hue and the desaturated panel D-15. Only the score of the last test was used in this study; it was

calculated as proposed by Lanthony<sup>14</sup>.

#### First part

C.S. was successively compared to V.A. (278 comparisons), to desaturated panel D-15 (250 comparisons) and to A.P. (272 comparisons) and special attention was given to the central 10° of the visual field. The numbers of the eyes tested were not the same for the different techniques because not all patients were subjected to all of the tests on the same day. Results were recorded as one of two alternatives: 'normal' or 'abnormal' and the  $\chi^2$  test was used. V.A.  $\geq 20/25$  was considered as 'normal'. Automated visual fields were compared to a map of normal subjects, matched for age and included in the device<sup>11</sup>. The results of C.S.<sup>11</sup> and the score of desaturated panel D-15<sup>14</sup> were also compared with a normal population matched for age.

#### Second part

Fifty patients who had all of the tests on the same day were divided into two groups according to the size of their adenoma. Eighteen were microadenomas ( $< 10$  mm), 32 were macroadenomas ( $> 10$  mm). We were aided in the strategic choice of the different tests by an adaptation of the theory of the decision tree<sup>15, 16</sup>. Knowing that the visual field was essential, we tried to propose a planned sequence of diagnostic tests (C.S., colour tests, fundus) for visual investigation. The probability of the risk of anomaly for C.S. or desaturated panel D-15 or fundus was added to the probability of anomaly either for Goldmann or A.P. We obtained numbers allowing a classification of the optimum association of two tests. The calculation was realized separately for microadenomas and for macroadenomas.

RESULTS

First part

Contrast sensitivity and visual acuity  
(Table 1a, b)

Two hundred and seventy-eight comparisons were made. An attenuation of contrast sensitivity was observed in 18% of the eyes, the visual acuity staying normal ( $\chi^2$ ,  $p < 0.05$ ). Only in four eyes was C.S. normal with an abnormal V.A. When C.S. was abnormal, there was a high probability of finding an abnormal V.A. ( $\chi^2$ ,  $p < 0.001$ ) (Table 1a). The probability of finding a global attenuation of C.S. increased when V.A. was less than 20/25 ( $\chi^2$ ,  $p < 0.001$ ) (Table 1b).

Contrast sensitivity and desaturated panel D-15  
(Table 2)

Two hundred and fifty comparisons were made. Desaturated panel D-15 and C.S. were both normal in 60.8% of the eyes and were found both abnormal in 12.8% of cases. In 29 eyes desaturated panel D-15 was abnormal (11.6%), C.S. staying normal; in 37 eyes it was the opposite, C.S. alone being abnormal (14.8%). When C.S. was abnormal, there was a high probability of finding an abnormal desaturated panel D-15 ( $\chi^2$ ,  $p < 0.001$ ).

Contrast sensitivity and automated perimetry  
(Table 3)

Two hundred and seventy-two comparisons were made. C.S. and A.P. were both normal in 54.8% of the cases and both abnormal in 22.1%. In 15.4% of the eyes A.P. was abnormal, C.S. remaining normal; in 7.7% C.S. was abnormal and A.P. staying normal. The attenuation of C.S. was associated with a change of A.P. when the whole

TABLE 1a. Contrast sensitivity and visual acuity: 278 comparisons

		Visual acuity	
		Normal	Abnormal
Contrast sensitivity	Normal	191 68.70%	4 1.43%
	Abnormal	52 18.70%	31 11.15%

TABLE 1b. Contrast sensitivity and visual acuity: 278 comparisons

		Visual acuity	
		$\geq 20/25$	$< 20/25$
Contrast sensitivity	Localized attenuation	48 57.83%	5 6.02%
	Global attenuation	4 4.83%	23 27.71%

C.S. : localized attenuation = attenuation of two spatial frequencies; global attenuation = attenuation of all the spatial frequencies investigated.

visual field was considered ( $\chi^2$ ,  $p < 0.001$ ). With an alteration of the central 10° of the visual field the chances of finding an attenuation of C.S. increased. However, this link was not statistically significant.

TABLE 2. Contrast sensitivity and desaturated Panel D-15: 250 comparisons

		Desaturated panel D-15	
		Normal	Abnormal
Contrast sensitivity	Normal	152 60.8%	29 11.6%
	Abnormal	37 14.8%	32 12.8%

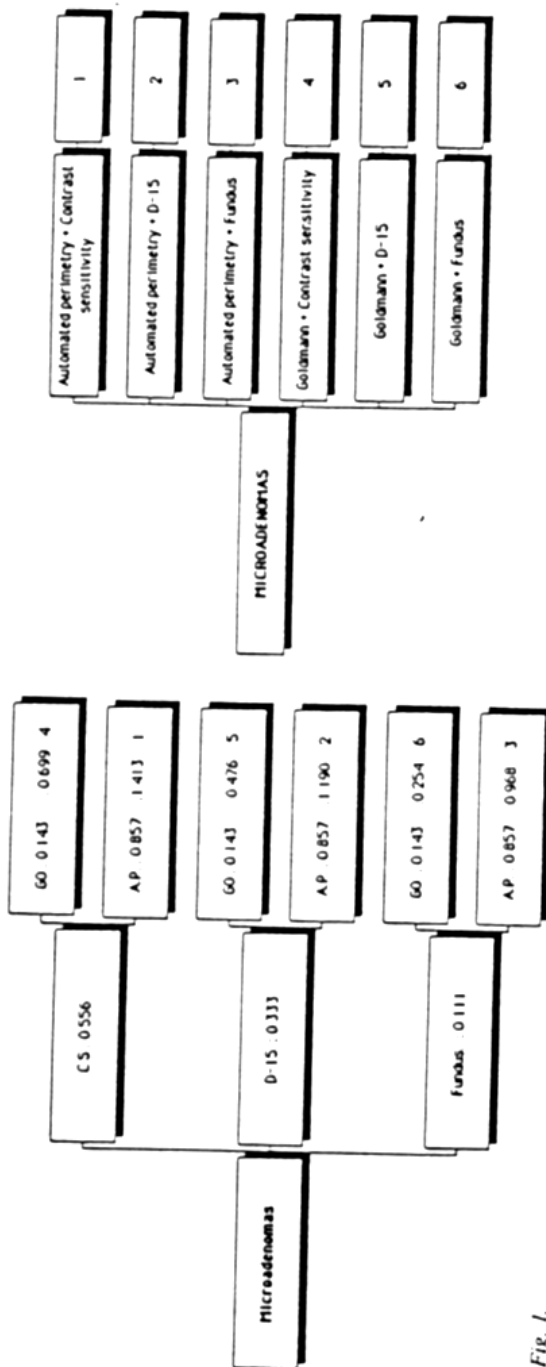


Fig. 1.

Fig. 1. Decision tree in microadenomas. On the left : the calculation; on the right : the classification of the best association of tests. C.S.: contrast sensitivity, D-15: desaturated panel D-15, A.P.: automated perimetry, GO: Goldmann.

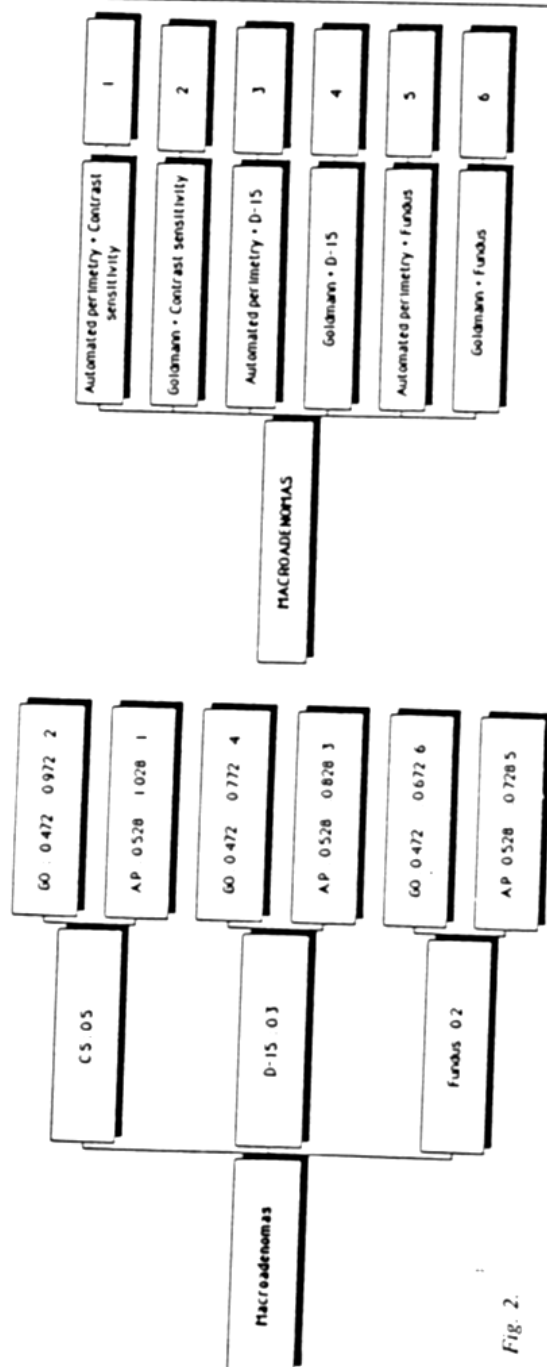


Fig. 2.

Fig. 2. Decision tree in macroadenomas : On the left : the calculation; on the right : the classification of the best association of tests. C.S.: contrast sensitivity, D-15: desaturated panel D-15, A.P.: automated perimetry, GO: Goldmann.

TABLE 3. Contrast sensitivity and automated perimetry: 272 comparisons

		Automated perimetry	
		Normal	Abnormal
Contrast sensitivity	Normal	149 54.77%	42 (26*) 15.44% (9.55*%)
	Abnormal	21 7.72%	60 (52*) 22.05% (19.11*%)

\* alteration of the central 10°.

## Second part

### Analysis of the flow diagrams (Figs. 1, 2)

For microadenomas, the best association was automated perimetry-contrast sensitivity, the second one associated automated perimetry-colour test (Fig. 1).

For macroadenomas, the best association was always automated perimetry-contrast sensitivity, the second best association was Goldmann perimeter-contrast sensitivity (Fig. 2)

## DISCUSSION

The relationships between C.S. and V.A. were well known<sup>1</sup> and the most interesting clinical finding was the association of normal V.A. with an abnormal C.S. The attenuation of C.S. was observed in 18% of our cases, V.A. remaining normal. Our results were close to those of Lorance *et al.*<sup>4</sup> but very different from those of Kupersmith *et al.*<sup>3</sup> who, using Arden gratings, found a reduction of C.S. in 94% of the eyes with 20/20, in patients with an anterior visual pathway compression (irrespective of the type of lesion). The lack of standardization of the different C.S. tests was a limitation for a better comparison. The comparison of C.S. with other visual parameters known as earlier indexes of chiasmatic compres-

sion was interesting. The change of the colour test could be an earlier symptom<sup>17</sup>. In our study, when C.S. was attenuated, there was a high probability of finding a change of colour vision. The importance of the investigation of the central 10° in the early diagnosis of a mid-chiasmatic compression was also established<sup>17</sup>. We found a correlation between C.S. and A.P., but there was no statistically significant correlation when the central 10° was only considered. The place of C.S. in regard to the other tests was difficult to establish. Kupersmith *et al.*<sup>3</sup> assessed that mild defects in Snellen acuity, colour vision, and perimetry did not correlate with the extensive loss of contrast thresholds seen in such patients. We adapted the theory of the decision tree used as a quantified flow diagram in our clinical use. It seemed that Goldmann and automated perimeter were equivalent for the visual assessment of macroadenomas. In this situation, logically, the most important visual field defects were expected and both methods appeared equally sensitive to detect them. In these cases with larger deficits, Goldmann was easier and less tiring for the patients<sup>19, 20</sup>. For the microadenomas, where the visual field defects were usually less important, A.P. seemed an excellent test and the addition of C.S. and colour test useful. Their association was interesting because the visual functions explored were obviously different. Without evidence of radiologically visible mechanic compression, the anomalies observed were difficult to explain. We can conjecture that they could be in relation with hormonal or ischaemic changes in the vicinity of the tumour. At the present time, none of these tests was able to give enough information about the degree of impairment of the visual pathway and of its ability of recuperation after decompression. Further investigations comparing them to 'objective' functional tests such as visual evoked potentials could be interesting.

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## REFERENCES

1. Storch RL, Bodis-Wollner I: Overview of contrast sensitivity and neuro-ophthalmic diseases. In: *Glare and Contrast Sensitivity for Clinicians*. Nadler MP, Miller D, Nadler J (eds), pp 85-112. Springer Verlag 1990
2. Bodis-Wollner I, Diamond SP: The measurement of spatial contrast sensitivity in cases of blurred vision associated with cerebral lesions. *Brain* 99:695-710, 1976
3. Kupersmith MJ, Siegel IM, Carr RE: Subtle disturbances of vision with compressive lesions of the anterior visual pathway measured by contrast sensitivity. *Ophthalmology* 89:68-72, 1982
4. Lorance RW, Kaufman D, Wray SH, Mao C: Contrast visual testing in neurovisual diagnosis. *Neurology* 37:923-929, 1987
5. Jaffe MJ, Caruso RC, Koppelman MCS: Chiasmal compromise: neurosensory characteristics of incomplete recovery. *Clin Vis Sci* 3-4:233-241, 1988
6. Grochowicki M, Vighetto A, Berquet S, Sassolas G: Contrast sensitivity function and pituitary adenoma: a study of forty cases. *Br J Ophthalmol* 74:358, 1990
7. Blamires TL, Reeves B: Longitudinal study of visual dysfunction in patients with perichiasmal lesions. Communication at VIIIth International Neuro-Ophthalmology Symposium Winchester 23-29 June 1990
8. Cohen R, Bouquier D, Biot-Laporte S, Vermeulen E, Claustrat B, Cherpain M-H, Cabrera P, Guidetti P, Ferry S, Bizollon ChA, Sassolas G: Pituitary stimulation by combined administration of four hypothalamic releasing hormones in normal men and patients. *J Clin Endocrinol Metabol* 62:892-898, 1986
9. Ross JE, Clarke DD, Bron AJ: Effects of age on contrast sensitivity function: uniocular and binocular findings. *Br J Ophthalmol* 69:51-56, 1985
10. Neetens A, Smet H: L'emploi de réseaux en neuro-ophtalmologie pour la détermination de la sensibilité au contraste. *Ophtalmologie (Paris)* 1:31-38, 1987
11. Grochowicki M, Vighetto A, Pissavin C: Pseudotumor cerebri. Longitudinal study using contrast sensitivity and automated static perimetry. *Neuro-ophthalmology* 10:97-108, 1990
12. Charlier JR, Defoort S, Rouland JF, Hache JC: Comparison of automated kinetic and static visual fields in neuro-ophthalmologic patients. In: Heijl A (ed): *Proc VIIIth International Perimetry Society Meeting*, pp 3-8. Amsterdam/Milano: Kugler & Ghedini 1989
13. Vighetto A, Grochowicki M, Cousin J: La sensibilité au contraste spatial dans la sclérose en plaques. *Rev Neurol (Paris)* 146:264-270, 1990
14. Lanthony P: Evaluation du Panel D-15 désaturé II: Comparaison entre les tests Panel D-15 désaturé et Farnsworth 100-hue. *J Fr Ophtalmol* 10:579-585, 1987
15. Pauker SG, Kassirer JP: Clinical applications of decision analysis: a detailed illustration. *Sem Nucl Med* 8:324-335, 1978
16. Fineberg HV: Decision trees: construction, uses, and limits. *Bull Cancer (Paris)* 67:395-404, 1980
17. Gajdos-Preuss A, Schaison M, Fontaine M: Manifestations ophtalmologiques des adénomes hypophysaires. *J Fr Ophtalmol* 1:427-438, 1978
18. Frisén L: The earliest visual field defects in mid-chiasmal compression. In: *Proceedings of the 6th International Visual Field Symposium*. Heijl A, Greve EL (eds). Dordrecht (The Netherlands): Dr W Junk Publ 1985
19. Beck RW, Bergstrom TJ, Lichter PR: A clinical comparison of visual field testing with a new automated perimeter, the Humphrey field analyzer, and the Goldmann perimeter. *Ophthalmology* 92:77-82, 1985
20. Glaser JS: The optic chiasm. In: *Current Neuro-Ophthalmology*, vol 1. Lessels S, Van Dalen JTW (eds). Year Book Medical Publishers 1988