

Laser-Doppler Flowmetry and Horner's Syndrome in Patients with Complete Unilateral Damage to the Parasellar Sympathetic Fibers During Cavernous Sinus Surgery

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Aim To determine ocular, sudomotor, and vasomotor components of Horner's syndrome resulting from complete unilateral intraoperative damage to the parasellar sympathetic fibers during cavernous sinus surgery.

Methods Complete damage to the parasellar sympathetic fibers was found in four patients operated for central skull base lesions. Pupilometry, eyelid fissure measurement, Hertel's exophthalmometry, starch iodine sweat test, and laser-Doppler perfusion assessment of bilaterally symmetrical forehead and cheek areas were performed.

Results Pupil diameter was smaller and the eyelid fissure was >2 mm narrower on the affected side in all four patients. Exophthalmometry after the operation never revealed >1 mm difference. Anhydrosis was localized to the medial forehead in three and to the entire forehead in one patient. Average perfusion did not significantly differ between the affected and opposite side of the forehead or cheek.

Conclusions The parasellar sympathetic fibers exclusively innervate the orbit and variably innervate the forehead sweat glands. No conclusion regarding their contribution to the facial vasomotor control could be established.

The anatomical relationships of the cranial nerves III, IV, the first division of the cranial nerve V, and VI, internal carotid artery and its branches, venous compartments and tributaries, and related osseous structures with adjacent dural folds in the cavernous sinus or parasellar space are well described (1,2). The parasellar space contains distinct sympathetic fiber bundles (1,2), which originate from the superior cervical ganglion and travel along the internal and external carotid arteries. Sympathetic fibers around the external carotid artery accompany its branches to supply the majority of the facial blood vessels and sweat glands (3). Sympathetic fibers around the internal carotid artery form the internal carotid nerve, give off caroticotympanic fibers and deep petrosal nerve in the carotid canal, and divide into the larger anterosuperior and smaller posteroinferior group (3-5). Sympathetic fibers inside the parasellar space are distributed systematically rather than in a plexiform arrangement (2,6). Most parasellar sympathetic fibers adhere to the cranial nerve VI, but then leave it usually after a few millimeters to join the first division of the cranial nerve V before entering the superior orbital fissure (5-13).

It has been postulated that the parasellar sympathetic fibers innervate the orbit and contribute to the innervation of blood vessels and sweat glands of an as yet unproven forehead area (3,7-11,13), which would be difficult to ascertain morphologically (2). However, evidence of the parasellar sympathetic fiber function might come from clinical observation.

Our aim was to contribute to the understanding of the facial sympathetic innervation

by analyzing the ocular, vasomotor and sudomotor features of Horner's syndrome resulting from complete unilateral damage to the parasellar sympathetic fibers due to central skull base surgery in four patients.

Patients and methods

Two female and 2 male patients were operated for vascular or tumorous changes of the central skull base at our Department in the last 5 years (Table 1). Patients No. 1 and 3 were operated for parasellar aneurysm of the internal carotid artery. In patient No. 1, the aneurysm originated from the distal part of the horizontal segment and from the anterior loop of the left parasellar internal carotid artery, and was 2.5 cm in diameter. In patient No. 3, the aneurysm was posttraumatic, 3.2 cm in diameter, and originated from the horizontal segment of the left parasellar internal carotid artery. Patient No. 2 was operated for carotid-parasellar fistula, and patient No. 4 for meningioma of the left parasellar space with total sellar destruction and posterior fossa extension.

Continuous 30-minute recording of the steady state facial perfusion, expressed in arbitrary perfusion units, was performed on 11 consecutive postoperative days in patient No. 1, 9 days in patient No. 2, 11 days in patient No. 3, and 8 days in patient No. 4. The laser-Doppler measurements and pupillometry were performed on the same consecutive postoperative days; there were 11 such measurements in patient No. 1, 9 in patient No. 2, 11 in patient No. 3, and 8 in patient No. 4, with a four channel moorLAB® laser-Doppler flowmeter with DP1T-V2 skin

Table 1. Characteristics of the 4 patients who underwent cavernous sinus surgery*

Patient No.	Age (y)	Sex	Pathology	Side	Cranial nerve deficit	
					preoperative	postoperative
1	55	male	parasellar ICA [†] aneurysm	left	no	V [‡]
2	70	female	carotid-parasellar fistula	right	III, IV, VI	III, IV, VI [§]
3	64	male	parasellar ICA aneurysm	left	no	no [¶]
4	34	female	meningioma	right	IV, VI	IV, VI [¶]

*All 4 patients developed ptosis after surgery.

†ICA – internal carotid artery.

‡Cranial nerve deficit recovered completely 6 weeks after the operation, and ptosis recovered substantially (<1 mm difference between the eyelid fissures) after 32 months of follow-up.

§Palsy of the cranial nerves III, IV and VI and ptosis recovered slightly after 28 months of follow-up.

¶Ptosis recovered completely 15 weeks after the operation.

¶¶Palsy of the cranial nerves IV and VI and ptosis recovered substantially (<1 mm difference between the eyelid fissures) after 24 months of follow-up.

probes (Moor Instruments, Millwey, Axminster, UK). Recordings were made in a climate-controlled room at a constant temperature of 22-23°C; there was no airflow in the room (14). A labeled plastic mesh was used for precise positioning of the probes on the patient's forehead and cheeks. Two probes were attached with double-sided adhesive discs to each side of forehead, close to the midline (presumably innervated by the sympathetic fibers around the internal carotid artery) and two more probes were placed on each cheek (presumably innervated by the sympathetic fibers around the external carotid artery). The pupil diameters were measured with a Compact Integrated Pupilograph (AMTect, GmbH, Weinheim, Germany) on the same days as facial perfusion. A starch-iodine sudomotor test was carried out one day before a patient's discharge from the hospital (15). Photographs of the patients were taken on the discharge day and the eyelid fissures were measured. Ptosis was defined as ≥ 2 mm difference between the eye fissures (16,17). The patients underwent Hertel's exophthalmometry (Oculus Optikgeräte GmbH, Wetzlar, Germany) on the discharge day. Exophthalmos was defined as ≥ 1 mm difference between the eyes (18). All patients gave their informed consent and the study was approved by the local Ethics Committee.

Statistical analysis

Wilcoxon signed-rank test was used to compare pupil diameters between the affected and opposite eye and perfusion data between the affected and opposite side of forehead and both cheeks in each patient. The statistical analysis was done with Statistical Package for Social Sciences for

Windows 13.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

Complete damage to the parasellar sympathetic fibers was diagnosed in all four patients after the operation (Table 1). The damage resulted from unavoidable intraoperative injury to the inferior lateral and medial group of the sympathetic fibers surrounding the parasellar portion of the internal carotid artery. Before the operation, ptosis had been present only in patient No. 2, who also had preoperative exophthalmos, conjunctival chemosis, conjunctival hemorrhage, and bruit due to carotid-parasellar fistula. After the surgery, ptosis that could be attributed to the parasellar sympathetic fiber damage was apparent immediately in patients No. 1, 3, and 4 (Table 2). Enophthalmos was never established in any of the patients. In all patients, the pupil diameter on the affected side was significantly smaller than on the opposite side (Table 2). Averaged perfusion data for bilaterally symmetrical medial forehead and middle cheek areas did not differ significantly between the affected and opposite forehead and between the affected and opposite cheek in any of the patients (Table 2). In patients No. 1, 2, and 3, anhydrosis was mostly evident on the medial aspect of the forehead on the affected side (Figure 1A). Only in patient No. 4, the entire forehead on the affected side showed pronounced signs of anhydrosis (Figure 1B).

Discussion

Miosis, ptosis, and forehead anhydrosis were diagnosed in the 4 patients with complete unilat-

Table 2. Postoperative facial perfusion, pupil diameter, and eyelid fissure width in four patients who underwent cavernous sinus surgery*

Patient No.	Forehead perfusion (AU)			Cheek perfusion (AU)			Pupil diameter (mm)			Eyelid fissure (mm)†	
	right	left	<i>P</i>	right	left	<i>P</i>	right	left	<i>P</i>	right	left
1	60.4 ± 44.8	49.9 ± 19.6	0.285	86.2 ± 19.1	110.2 ± 20.4	0.485	6.3 ± 0.3	4.8 ± 0.1	0.018	6	9
2	74.6 ± 33.0	87.8 ± 39.8	0.310	99.6 ± 37.0	123.5 ± 49.5	0.412	4.5 ± 0.1	6.2 ± 0.3	0.007	-	-
3	55.3 ± 18.8	38.0 ± 15.0	0.593	119.1 ± 55.0	125.5 ± 56.6	0.345	5.1 ± 0.3	3.5 ± 0.1	0.004	7	10
4	63.1 ± 25.7	59.7 ± 32.4	0.219	113.0 ± 43.3	110.9 ± 48.8	0.310	5.1 ± 0.5	6.7 ± 0.5	0.005	7	9

*All values are presented as means ± standard deviation based on the measurements performed in patients 1-4 on 11, 9, 11, and 8 consecutive postoperative days, respectively. AU - arbitrary units, recorded over 30 min each postoperative day.

†Obtained from the photographs taken on the discharge day. Not measured in patient No. 2 due to preoperative cranial nerve III palsy and exophthalmos.

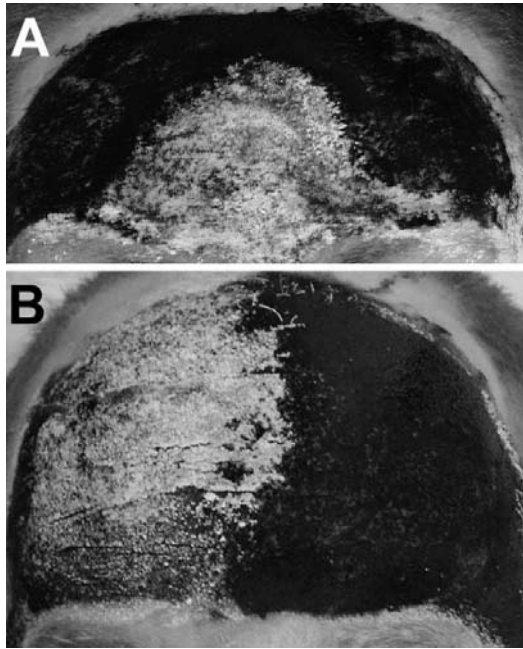


Figure 1. Forehead anhidrosis in patients No. 2 (A) and No. 4 (B). Whitish color indicates areas where the starch-iodine reaction in the presence of sweat failed to occur.

eral damage to the parasellar sympathetic fibers. However, no enophthalmos or deficient vasomotor control could be established.

Injury to the cervical and more distal sympathetic fibers leads to complete or partial Horner's syndrome, traditionally consisting of ptosis, miosis, enophthalmos, facial hyperemia, and facial anhidrosis, which are caused by deficient sympathetic innervation of the iris dilator muscle, the smooth superior tarsal muscle (Müller's muscle), facial blood vessels, and sweat glands (3,19).

The site of the sympathetic lesion can usually be identified from medical history, clinical examination, and findings of pharmacological tests, and imaging studies (20-28). On the other hand, sympathetic fibers form distinct bundles around the internal carotid artery, cranial nerve VI, and the first division of the cranial nerve V. The bundles are diffusely distributed and, therefore, most of the parasellar space lesions manifest themselves without any signs of Horner's syndrome (6). Unavoidable damage to the intracranial sympathetic

fibers during surgery remains the only means of providing conclusive information about the location and extent of damage to date (9).

Issues regarding the ultimate pathway and function of the intracranial sympathetic fibers were initially addressed by Bernard, Mitchell, and Horner (7). In 1979, Parkinson (7,19) also suggested that the answer might come from careful clinical observation of patients with intracranial sympathetic fiber damage due to the lesion itself, neurosurgical procedure, or trauma. Parkinson described two theoretical syndromes that might be caused by damage to the cranial nerve VI or the first division of the cranial nerve V, including the surrounding sympathetic fibers (7). Such damage would result in the palsy of the cranial nerve VI or the first division of the cranial nerve V and complete or partial Horner's syndrome with possible sudomotor and vasomotor changes limited to the forehead.

Our findings support the anatomical observations that the intracranial sympathetic fibers represent exclusive sympathetic inflow to the orbit, because miosis and ptosis were evident in all cases (3). Furthermore, enophthalmos was consistently absent in our patients with Horner's syndrome due to complete damage of the intracranial sympathetic fibers. It seems that enophthalmos may be an illusion caused by narrowing of the eyelid fissure, attributed to ptosis (weakness of the smooth superior tarsal muscle which is part of the levator palpebrae superioris muscle) and to "upside-down" ptosis (weakness of the lower lid retractors, which are an extension of the fascia from the terminal fibers and tendon of the inferior rectus muscle). This is in accordance with previously raised questions about the existence of enophthalmos as one of the signs of Horner's syndrome (29-31).

Miosis and ptosis in our patients improved during the follow-up, which might be attributed to regeneration of the sympathetic fibers from the superior cervical ganglion. However, there have been no reports to date about facial sudomotor

motor or vasomotor fiber regeneration after injury in humans.

Limited data on patients with sympathetic lesion presumably distal to the bifurcation of the common carotid artery (the third-order sympathetic dysfunction) describe the loss of sweating that is usually confined to the medial forehead (3,23,24). The forehead sudomotor pattern was postoperatively always different on the affected side, while the cheek and chin sweating pattern remained bilaterally symmetrical, indicating that sudomotor intracranial sympathetic fibers supply the forehead but have no influence on the cheeks or chin. This is in accordance with observations that the latter two areas receive sudomotor innervation via sympathetic fibers surrounding the branches of the external carotid artery (3,23,24). We were unable to localize anhidrosis exclusively to the medial part of the forehead, as previously reported (23,24), probably because of variable border between the innervation areas of the sympathetic fibers, initially coursing along the internal and external carotid arteries. Nevertheless, the area of anhidrosis correlated with the innervation area of the first division of the cranial nerve V. The variable localization of anhidrosis may also be attributed to sparing of some parasellar sympathetic fiber bundles during surgery, which can be diffusely distributed (6). Our findings support Parkinson's assumption that the intracranial sympathetic fibers ultimately follow the distribution of the first division of the cranial nerve V, a pattern similar to that in the rest of the body (7), although it has proved impossible to follow the dispersed sympathetic fibers accompanying the first division of the cranial nerve V distal to the superior orbital fissure (7). Furthermore, sympathetic activity could be recorded from the first division of the cranial nerve V (32). Recent immunohistochemical studies have confirmed that the first division of the cranial nerve V provides a major sympathetic route to the orbit, although sympathetic fibers have also been

demonstrated in other cranial nerves projecting to the orbit (33).

This is the first report on the application of continuous 30-minute steady state laser-Doppler flowmetry for the analysis of the vasomotor perturbations associated with complete intracranial sympathetic fiber destruction. The lack of statistically significant difference between perfusion data on the affected and opposite side prevented us from drawing any conclusions on the contribution of the vasomotor component of the intracranial sympathetic fibers to different facial regions. There are at least five distinct vasomotor controls that regulate the facial microcirculation as follows: the sympathetic vasoconstriction and vasodilatation, parasympathetic vasodilatation, antidromic vasodilatation, and endothelium-dependent vasodilatation (34-36), all of which could be affected during skull base surgery. Facial microvasculature is usually constricted under thermoneutral conditions due to tonic sympathetic vasomotor control (27,34,35,37). However, facial perfusion after surgery is not solely dependent on the sympathetically mediated blood flow as scalp flap formation and orbitotomy invariably lead to local tissue inflammation, thereby influencing facial perfusion via antidromic or endothelium-dependent mechanisms (35,36). Facial perfusion varies significantly among normal subjects and left-right asymmetry of the forehead microvascular control has been shown previously (14). Therefore, the exclusion of the intracranial sympathetic vasomotor control would be difficult to prove on the basis of average facial perfusion data obtained by laser-Doppler flowmetry.

In conclusion, damage to the parasellar sympathetic fibers, coursing along the internal carotid artery, cranial nerve VI and, hereafter, first division of the cranial nerve V toward the superior orbital fissure, resulted in miosis, ptosis, and forehead anhidrosis. Enophthalmos was absent and laser-Doppler flowmetry failed to reveal deficient facial sympathetic vasomotor control. We believe that the parasellar sympathetic fibers ex-

clusively innervate the orbit and variably innervate the forehead sweat glands, whereas no conclusion regarding their contribution to the facial vasomotor control could be made.

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