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Naso-temporal asymmetry and contraction anisocoria in the pupillomotor system

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Abstract ● **Background:** Differences between the pupillomotor sensitivity of nasal and temporal retinal hemifields may contribute to the relative afferent pupillary defect (RAPD) seen in optic tract or pretectal lesions. To understand the architecture of the pupillary pathway, it is necessary to know the size and the prevalence of such naso-temporal differences and also of contraction anisocoria (unequal direct and consensual pupillary responses) in normal individuals. The results of previous studies have been only partially consistent. ● **Methods:** We registered the direct and consensual pupillary light reactions in both central retinal hemifields of 42 healthy subjects by means of IR video pupillography. Stimuli were generated under mesopic conditions on a computer screen as half-circles with 4.6 cd/m² and 10 deg radius. Stimulus duration was 200 ms with a stim-

ulation interval of 4 s.

● **Results:** The nasal retina was significantly more sensitive than the temporal retina, and the direct pupillary reactions were significantly larger than the consensual reactions. For the nasal retina, direct pupillary reactions exceeded the consensual reactions, whereas there was nearly no difference between direct and consensual reactions for the temporal retina. ● **Conclusion:** RAPD in optic tract damage or pretectal lesions cannot be explained by the only slightly more sensitive nasal retina. Considerably more input would be needed from the contralateral than from the ipsilateral retina into the optic tract. The nearly equal direct and consensual pupil reactions when stimulating the temporal retina suggest an input of temporal retina to both sides of the pretectum. Such a crossing of temporal fibres may take place in the chiasm.

Introduction

Differences between nasal and temporal retina have great importance in view of their separate projection to the brain. Lesions of the afferent visual pathways affect the two hemiretinae differently. The visual fibres from nasal retina cross in the chiasm, whereas the fibres from temporal retina project ipsilaterally. This decussation is assumed to be about 53:47 (crossed:uncrossed) on the basis of the histological study by Kupfer et al. [33]. Nevertheless, the afferent path of the pupillary fibres from retina to the pretectum and further to the pupillomotor nu-

clei in the Edinger-Westphal complex is still not known exactly. Patients with unilateral lesions of the optic tract [6, 7, 9, 37–39, 42, 47, 49], as well as certain unilateral thalamic or midbrain lesions [16, 17, 26, 31, 50, 54], show a marked relative afferent pupillary defect (RAPD) with the swinging-flashlight test in the eye contralateral to the lesion. This RAPD usually amounts to between 0.3 and 0.9 log units [31, 47, 53], which means that the eye contralateral to the lesion needs more than twice as much light for the same pupillary reaction as the ipsilateral eye. A much greater input from one retina into the contralateral than into the ipsilateral optic tract would re-

quire a considerably more effective nasal than temporal retina in pupillomotor sensitivity. Only a subtle naso-temporal asymmetry of retinal pupillomotor sensitivity has been described by several authors in the past [7, 13, 29, 34, 50].

A further crossing of the pupillary path takes place in the midbrain: each pretectal nucleus in the primate has input to both Edinger-Westphal nuclei with contralateral predominance [8, 22, 41, 45]. Such an asymmetric crossing in the pretectum is required for "contraction anisocoria" (greater direct than consensual pupillary reaction). With an asymmetric crossing in the chiasm and a predominantly contralateral midbrain projection, a larger direct than consensual pupillary reaction occurs when only one eye is illuminated. Although it was believed to be a pathologic abnormality by some investigators [28, 35], this contraction anisocoria has been reported by several authors [1, 35, 44, 55].

There are unclear differences between retinal hemifields with regard to contraction anisocoria. Illumination of the nasal retina causes a larger direct than consensual pupillary contraction. Illumination of the temporal retina, however, has been reported to give a larger consensual than direct contraction by some authors [5, 13, 36] and equal reactions in both eyes by others [43, 55].

This study was intended to help to clarify these apparent contradictions in a large number of healthy subjects with low stimulus intensity. We looked for the prevalence and the amount of contraction anisocoria in each retinal hemifield, i.e. the difference between direct and consensual reaction when stimulating one retinal hemifield in one eye. We tried to find out whether there were differences in pupillomotor sensitivity between the nasal and the temporal retina.

Methods

Infrared (IR) video computer pupillography was performed in 42 healthy subjects aged 21–39 years. The subject looked into a "black box". In a semitransparent mirror the subject could see the stimuli generated from a computer on monitor 1 at a distance of 30 cm (Fig. 1). The pupil reactions were registered by an IR-sensitive video camera behind the mirror. IR light (880 nm) was emitted from an array of IR-LEDs fixed at the camera aperture (confocal illumination). The picture of the camera was digitized by a frame grabber card and evaluated online by a computer. The pupil was detected by the corneal first Purkinje reflex of about 0.1 mm of size generated by the IR-LEDs. Starting from the Purkinje reflex, a horizontal and a vertical line of the pupil's picture were scanned. The pupil's edges could be detected by a steep change in IR light reflection: A bright fundus reflex contrasted with a very dim iris reflex. The pupil diameter was then determined as the mean of the horizontal and the vertical diameter. The two diameters had to be in a certain ratio for a correct determination of pupil diameter. The spatial resolution in measuring the pupil size was 0.05 mm. Consensual recording of the pupillary light reflex was possible by occluding one eye with an IR filter and recording the pupil reactions through this filter while the other eye observed the stimuli.

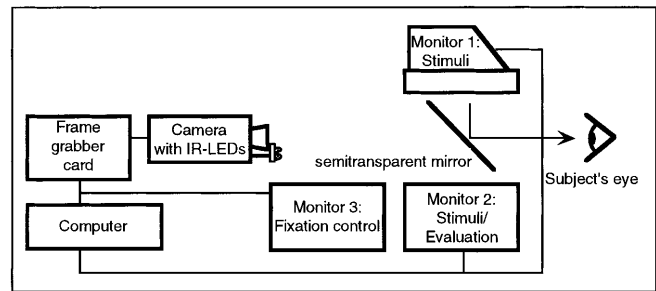


Fig. 1 IR pupillography. Stimulation and registration device for the pupillary light reflex

The examiner could observe the frame grabber card picture on monitor 3 outside the box as well as the stimuli sequence on monitor 2.

With a test series in five subjects, we evaluated which stimulus size, luminance and location should be used to obtain reproducible pupillary responses.

For our study, the stimuli were presented on a monitor as white half-circles with 10 deg radius and a horizontal offset of 1 deg from the fixation point. This offset was not implemented for the first 20 subjects. Stimulus luminance was 4.6 cd/m², monitor background luminance 1 cd/m² (mesopic conditions, stimulus contrast 0.78). Stimulus duration was 200 ms with an interval of 4 s between two stimulus presentations.

After 10 min adaptation, nasal and temporal retinal hemifields were stimulated 5 times each in both eyes. Pupillograms were registered sequentially, directly and consensually, thus testing four different channels for each eye. With our device, we were not able to perform simultaneous registration of direct and consensual responses. Statistical analysis showed no effect of order.

The pupillograms were evaluated offline by applying a curve-fitting procedure. By this means, the parameters of the pupillary movements could be determined more exactly. An artefact rejection process indicated inaccurate fits and those measurements were discarded. As parameter for the retinal pupillomotor sensitivity we chose the amplitude of the pupillary contraction in millimetres. The data were evaluated by analysis of variance (ANOVA) for repeated measurements. The ANOVA was weighted by the number of measurements obtained for each stimulus condition.

Results

With our stimulus conditions, most subjects had larger direct than consensual pupillary reactions for the nasal retina (contraction anisocoria). For the temporal retina, the direct reactions were in most cases also slightly larger than the consensual ones, but there were many subjects who presented the inverse relation (Fig. 2). The amount of contraction anisocoria was always smaller than 0.5 mm.

The ANOVA showed that the mean direct pupillary reaction clearly exceeded the mean consensual reaction for the nasal retina (0.71 mm vs 0.63 mm). For the temporal retina, direct and consensual reactions were nearly equal (0.64 mm vs 0.61 mm). This influence of the retinal hemifield on the direct-consensual difference was significant ($P=0.013$, Fig. 3).

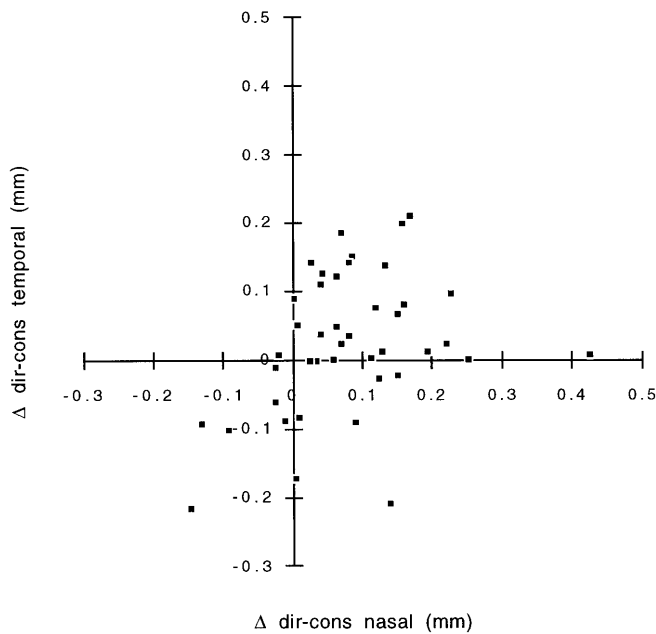


Fig. 2 Differences between direct and consensual light reflex (contraction anisocoria) for the nasal and for the temporal retinal hemifield (mm of amplitude). Each point represents one subject with the nasal mean difference plotted against the temporal mean difference

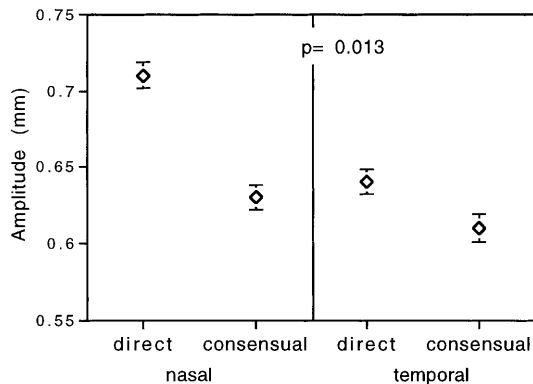


Fig. 3 Direct versus consensual pupillary reactions for the nasal and the temporal retinal hemifield (means \pm SE of both eyes of 42 individuals)

The direct–consensual difference for the nasal hemifield (0.08 mm) was highly significant ($P < 0.01$ Student's *t*-test). At least a 5% significant direct–consensual difference was also found for the temporal hemifield (difference 0.03 mm). The 95% confidence intervals for the direct–consensual differences – nasal (0.056; 0.104) and temporal (0.006; 0.056) – indicate that, for the temporal retina, the direct and consensual reactions should be considered as more or less equal.

A direct reaction of 0.71 mm and a consensual reaction of 0.63 mm for the nasal retina correspond to a ratio

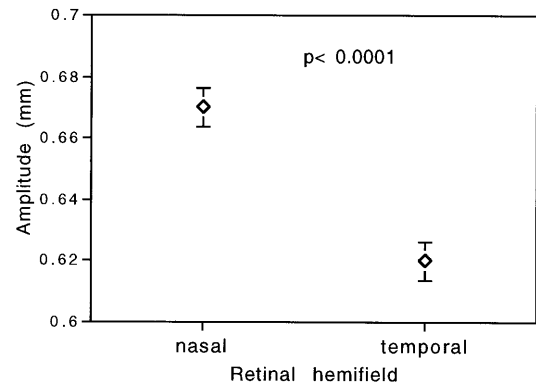


Fig. 4 Nasal versus temporal stimulation (means \pm SE of direct and consensual measurements and of both eyes of 42 individuals)

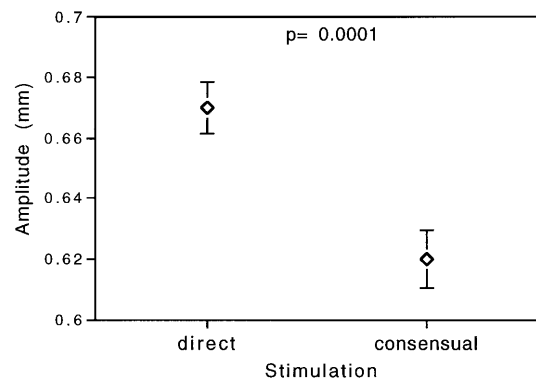


Fig. 5 Direct versus consensual stimulation (means \pm SE of nasal and temporal stimulation and of both eyes of 42 individuals)

of 1.13 (direct:consensual=53:47). For the temporal retina, 0.64 mm of direct reaction and 0.61 mm of consensual reaction give a ratio of 1.05 (direct:consensual=51:49).

The nasal retina proved to be significantly more sensitive than the temporal retina (Fig. 4). The differences in the pupillary reactions were subtle (nasal 0.67 mm, temporal 0.62 mm; mean difference 0.05 mm). The mean naso-temporal ratio of 1.08 corresponds to a sensitivity of 52:48 (nasal:temporal).

The direct pupillary reactions (0.67 mm) significantly exceeded the consensual reactions (0.62 mm) (contraction anisocoria, Fig. 5) with a mean difference of 0.05 mm. The mean direct-consensual ratio was about 1.08.

Discussion

Because of the variability of the pupillary light reaction (PLR), repeated measurements in many subjects were required [30, 34]. In 84 healthy eyes, we were able to confirm the higher sensitivity of the nasal retina compared

to the temporal retina with our stimulus conditions in the central 10 deg area. The central retina is most effective for pupillomotor input [29], and the central 30 deg visual field covers about 80% of the striate cortex [25].

Our ratio of about 52:48 in favour of the nasal retina is in accordance with a higher density of photoreceptors and ganglion cells in the nasal retinal field [14, 15, 27, 40, 51], but represents only a small asymmetry. As mentioned above, the contralateral RAPD in tract lesions or other unilateral impairment of the afferent path to the pretectum has not been sufficiently explained up to now. For a RAPD of about 0.6 log unit, one must postulate a greater pupillary input from the contralateral eye into one optic tract than that from an only slightly more sensitive nasal retina.

We found larger direct than consensual pupillary reactions, but we observed a difference in this contraction anisocoria between the retinal hemifields. Our results regarding contraction anisocoria when illuminating only one retinal hemifield support the results of Smith and Smith [44] and Wyatt and Musselman [55] rather than those of Cox and Drewes [13] or Martin et al. [36]. All these previous studies like ours, found a larger direct than consensual contraction amplitude for the nasal retina. For the temporal retina, however, we found nearly equal direct and consensual contraction amplitudes as shown by Smith and Smith and by Wyatt and Musselman. Given an asymmetric midbrain crossing (see above), these findings suggest that equal information from temporal retina must reach both sides of the pretectum, i.e. the pretectal olivary nucleus (PON [23]) (cf. Fig. 6).

Recent findings in primates indicate that the entire visual field is represented in each PON [12, 22]. Apart from other possible interpretations, such as cortical projections [12] or an interaction between the two PON [11, 41], these findings are in accordance with a direct projection of fibres from temporal retina to both PON.

The finding of a more extensive direct than consensual reaction when illuminating one eye (i.e. both hemifields together) also is best explained by some temporal fibres also reaching the contralateral PON. This greater input to the PON from the contralateral eye amplifies the asymmetric pretectal crossing required for contraction anisocoria and leads to a greater direct pupillary reaction [50].

Hypothetical projection of pupillomotor fibres

A direct projection of pupillomotor fibres from temporal retina to both PON would imply a decussation of temporal fibres at an unspecified location in the pupillomotor pathway.

If such a partial crossing of temporal pupillary fibres took place in the optic chiasm, there would be sufficient

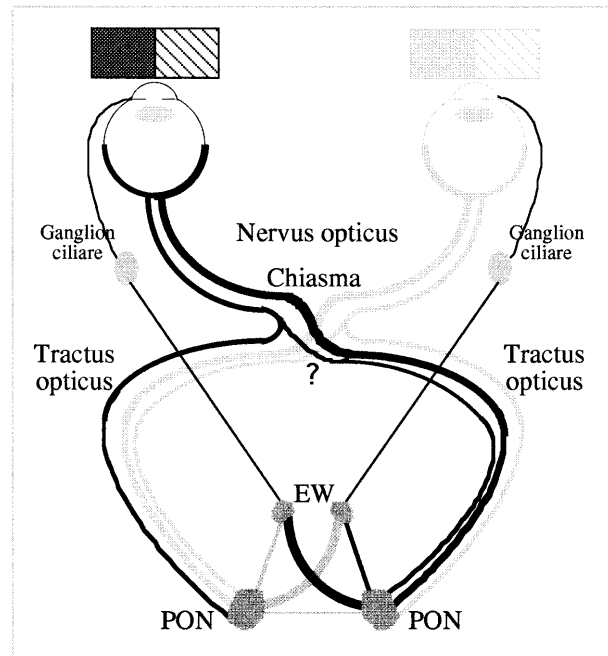


Fig. 6 Hypothetical pathway of the pupillary light reflex from the retina to the pretectum and back to the iris sphincter. Note the partial crossing of temporal pupillary fibres in the chiasm. The projection from the olivary nuclei (PON) to both Edinger-Westphal nuclei (EW) is believed to be predominantly contralateral (see text)

input from one eye into the contralateral optic tract to explain the marked contralateral RAPD in cases of optic tract lesions. This would mean a less strict separation of nasal and temporal fibres in the chiasmal decussation for the pupillomotor than for the visual system.

Some arguments may be cited for such a partial crossing of temporal pupillary fibres in the chiasm: The phylogenetic evolution of the chiasmal crossing runs from completely crossed to partially crossed [34, 48], and the fibres from temporal retina have changed their path. In albinos, the more asymmetric chiasmal crossing is due to temporal fibres also crossing [3]. It is generally agreed that the PLR and the visual system share the same receptors [2, 32, 34]. The ganglion cells contributing to the PLR however probably in part are different from the ganglion cells projecting to the visual cortex. Apart from the M or P system, there is a heterogeneous group of ganglion cells (W cells in the cat) projecting directly into midbrain regions [57]. Although it seems obvious that several different components have an impact on the PLR [4, 21, 56], these ganglion cells seem to have properties appropriate for mediating the PLR with the stimuli we used [18, 34, 57]. As the W-analogous cells are phylogenetically older, it is possible that their fibres cross more completely than those of the M and P cells. W-analogous fibres to the accessory optic system [10, 24] or to the suprachiasmatic nucleus [19] apparently do so. In cats,

40–60% of the W fibres from temporal retina cross in the chiasm [34, 52].

A crossing of temporal fibres in humans would not necessarily be caused simply by the naso-temporal overlap across the vertical midline in primates [20, 46], for such an overlap is small and would also imply nasal fibres running ipsilaterally.

A model of the pupillary light reflex pathway is shown in Fig. 6. The pupillomotor fibres from the nasal retina cross in the chiasm and run to the contralateral PON. Pupillary fibres from the temporal retina project to both PON with a partial crossing in the chiasm. There is a predominantly contralateral projection from the PON to both Edinger-Westphal nuclei (EW) [8, 22, 41, 45]. Each EW has input to the ipsilateral pupil sphincter. Other central structures (cortex, thalamus) that possibly have an impact on the pupil are not considered here because they are probably not directly involved in the PLR. This is a model which is calculated from our results with hemifield stimulation and which is based on neuroanatomical findings in the literature (see above). With a pu-

pillary pathway structured in this way most pupillary phenomena could be explained, such as the RAPD in unilateral lesions of the afferent path.

In unilateral lesions of the optic tract, reduced but not abolished pupillary reactions should then be found in the blind temporal retina. Although stray light as well as threshold problems complicate matters, this indeed seems to be the case [31].

In conclusion, our results of different ratios of contraction anisocoria in both retinal hemifields suggest a partial crossing of fibres from temporal retina to the contralateral PON. Thus, information from temporal retina is inferred to reach both left and right PON. Nasal retina seems to be only slightly more pupillomotor sensitive than temporal retina. A partial crossing of temporal fibres in the chiasm in addition to the crossing of nasal fibres would lead to a larger input from one eye into the contralateral optic tract. This asymmetry of pupillomotor input into the optic tracts could explain the marked RAPD seen in patients with unilateral optic tract lesions or other unilateral disturbances of the afferent pupillary pathway.

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