The Behr Pupil Revisited
ANISOCORIA FOLLOWING CEREBROVASCULAR ACCIDENTS

BY PETER HERMAN (BENZUR), M.D.

Abstract:

Three hundred and sixty-three cases of cerebral infarction were reviewed; 19 had anisocoria. Eighty percent had the larger pupil contralateral to the hemispheric lesion. The mydriasis was associated with long tract signs in all instances. If the abnormal pupil and long tract signs are not on the same side, the long tract signs are the most accurate evidence of the side of the hemispheric lesions.

When the pupil was 4 mm or larger and reacted sluggishly, the prognosis was poor.

The mechanism of the production of the anisocoria is still uncertain; the lesion is probably "cortical" and in the contralateral hemisphere.

Additional Key Words

- long tract signs
- hemispheric lesions
- mydriasis
- extra-ocular movements

In 1879, Behr¹ (at that time one of the most prominent ophthalmologists in Hamburg) described two cases of gunshot wounds of the head with brain injury and lesions of the optic tracts which were associated with a larger pupil on the contralateral side associated with a field defect. Since then, the Behr pupil (as it has come to be known) has been mentioned in the neuro-ophthalmological literature occasionally.²³ The study of Lowenstein⁵ suggests that the explanation Behr offered for the pupil inequality (lesion in the optic tract) is not valid. Furthermore, in a variety of CNS injuries, such as cerebral infarction, this pupil inequality is present, as recognized later by Behr, and persists for a sufficient time to attract the attention of neurologists.

This study was undertaken in order to find out under what circumstances this anisocoria occurs and to determine its topical diagnostic value and prognostic significances.

Methods

A retrospective study consisting of analysis of 363 charts with the major admission diagnosis of cerebral infarction was done. Cases with ocular pathology, previous eye operation, local trauma and active blood serology were excluded. The cases were collected from three different hospitals (Bellevue Hospital, New York University Hospital, and the VA Hospital, New York, New York).

To serve as a control to this study, 100 charts taken at random from the VA Hospital and the Mount Sinai Hospital were reviewed.

Results

Analysis of the 363 charts provides the bulk of this report.

Nineteen cases out of 363 (about 5%) were noted to have unequal pupils. In 12 cases (80%), the larger pupil was on the side contralateral to the hemispheric lesion and associated with focal neurological signs (weakness of cranial nerves VII or XII, or weakness of the limbs, sensory disturbances, field defect, Babinski’s sign). In three cases (20%) the larger pupil was situated on the same side as the hemispheric lesion. In four cases, the findings were either bilateral or insufficient to allow topical localization (cases 3, 4, 6, and 10).

In two cases with ipsilateral mydriasis and proved pathology (cases 8 and 11), the long tract signs correctly localized the lesion, and the pupil, therefore, was misleading.

Table 1 shows the associated field defects and extra-ocular movements (EOM) as well as the long tract signs which have helped in establishing a topical diagnosis. Four of the five times a visual field defect was described; it was homonymous and on the same side as the larger pupil. Many of these patients were stuporous or comatose and visual field examination could not be satisfactorily performed.

In eight cases, the eye position was described. There was conjugate deviation toward the lesion in five and one showed nystagmus in attempted gaze toward the lesion. In two cases, the oculomotor examination was described as "no EOM."

The facial nerve involvement was present on the expected side six of nine times (table 1). Motor weakness, Babinski’s sign and sensory changes were the most common of long tract signs — present in 15 cases.

Ten patients had a pupil recorded as "4 mm" or more; two survived. The six patients with larger pupils (> 4 mm), who died, were comatose. In each instance the pupil remained the same size or increased in size until death. In the two patients (Nos. 12 and 17) who survived and had pupils 4 mm or larger, the pupil was the same size one week and two weeks later; initial examination revealed one to be "alert" and the other "confused postictally." In two patients the outcome was not clear. Table 2 summarized the course of the patient, the changes in the pupil, and the contributory pathological data.
<table>
<thead>
<tr>
<th>Pt. no.</th>
<th>Pupil size and reaction</th>
<th>Ocular signs</th>
<th>Other cranial nerve involvement</th>
<th>Long tract sign</th>
<th>Alertness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R = 2.5 mm, L = 2 mm, reacting</td>
<td>R homonymous hemianopia</td>
<td>R VII</td>
<td>R hemiparesis, R Babinski</td>
<td>Lethargic</td>
</tr>
<tr>
<td>2</td>
<td>“Small,” L &gt; R, poorly reacting</td>
<td>Eyes deviated to R, R nystagmus</td>
<td>Not known</td>
<td>L Babinski</td>
<td>Comatose</td>
</tr>
<tr>
<td>3</td>
<td>R = 4 mm, L = 2 mm, nonreacting</td>
<td>Oculocephalics: 0, Ciliospinal: 0</td>
<td>Gag: 0</td>
<td>R hyperreflexia, bilateral Babinski</td>
<td>Comatose, bilateral decerebration</td>
</tr>
<tr>
<td>4</td>
<td>R = 5 mm, L = 4 mm</td>
<td>Oculocephalics: 0, Eyes midline</td>
<td>L corneal &gt; R</td>
<td>Bilateral Babinski</td>
<td>Comatose</td>
</tr>
<tr>
<td>5</td>
<td>R = 4 mm, L = 2 mm, R sluggish</td>
<td>Eyes deviated to R</td>
<td>L VIII, corneal R &lt; L</td>
<td>L hemiplegia, bilateral Babinski</td>
<td>Alert</td>
</tr>
<tr>
<td>6</td>
<td>L &gt; R</td>
<td>Not known</td>
<td>Papilledema, Corneals: 0</td>
<td>DTR: 0</td>
<td>Comatose</td>
</tr>
<tr>
<td>7</td>
<td>R &gt; L</td>
<td>Eyes deviated to L</td>
<td>L corneal &gt; R</td>
<td>R hemiplegia, R Babinski</td>
<td>Comatose</td>
</tr>
<tr>
<td>8</td>
<td>L &gt; R, irregular</td>
<td>No EOM</td>
<td>R VII</td>
<td>R hemiplegia, R Babinski</td>
<td>Alert</td>
</tr>
<tr>
<td>9</td>
<td>L &gt; R</td>
<td>None</td>
<td>L VII</td>
<td>Bilateral Babinski, L hemiparesis</td>
<td>Awake, OMS</td>
</tr>
<tr>
<td>10</td>
<td>L = 3 mm, R = 2 mm, reacting</td>
<td>L homonymous field defect?</td>
<td>L VII</td>
<td>None</td>
<td>Awake, OMS</td>
</tr>
<tr>
<td>11</td>
<td>R = 4 mm, L = 3 mm, reacting</td>
<td>L homonymous field defect, head and eyes deviated to R decreased</td>
<td>L VII, L corneal Babinski</td>
<td>None</td>
<td>Unresponsive</td>
</tr>
<tr>
<td>12</td>
<td>L = 5 mm, R = 4 mm, reacting</td>
<td>None</td>
<td>L VII</td>
<td>L hemiplegia</td>
<td>Postictal confusion</td>
</tr>
<tr>
<td>13</td>
<td>L = pinpoint, R = dilated, nonreacting</td>
<td>Head deviated to R</td>
<td>Corneals: 0</td>
<td>R clonus, bilateral Babinski</td>
<td>Comatose</td>
</tr>
<tr>
<td>14</td>
<td>R = 4 mm, L = 3 mm, reactive</td>
<td>R homonymous field cut</td>
<td>Tongue to L</td>
<td>None</td>
<td>Disoriented, dysphasia</td>
</tr>
<tr>
<td>15</td>
<td>L &gt; R</td>
<td>None</td>
<td>L VII, L VII</td>
<td>L-side weakness</td>
<td>Awake, OMS</td>
</tr>
<tr>
<td>16</td>
<td>R &gt; L</td>
<td>None</td>
<td>R VII palsy</td>
<td>R hyperreflexia, R Babinski, R hyposensory deficit</td>
<td>Alert, dysarthric</td>
</tr>
<tr>
<td>17</td>
<td>L = 4 mm, R = 3 mm, both reacting</td>
<td>Nystagmus in R lateral gaze</td>
<td>L homonymous field extinction</td>
<td>None</td>
<td>Alert</td>
</tr>
<tr>
<td>18</td>
<td>L = 5 mm, R = 3 mm</td>
<td>Not moving eyes to L</td>
<td>None</td>
<td>None</td>
<td>OMS</td>
</tr>
<tr>
<td>19</td>
<td>L = 4 mm, R = 3 mm</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>L-side weakness</td>
</tr>
</tbody>
</table>

L = left, R = right, 0 = no response, OMS = obtunded mental state.
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Analysis of 50 charts taken at random from a VA hospital and 50 charts from a university hospital revealed only one case of anisocoria and this in a patient with cerebral infarction.

Discussion

Figure 1 shows schematically the cortical and subcortical structures involved in pupillary control. This includes the parasympathetic nucleus (Edinger-Westphal), stimulation of which results mainly in pupillary constriction, and the hypothalamus6,7 main sympathetic relay, which upon excitation induces dilatation of the pupil. These constitute the most important subcortical structures for dilatation and constriction of the pupil.

The pathways by which pupillodilator fibers from the cortex reach the hypothalamus are not well defined. From the hypothalamus fibers pass through the tegmentum of the midbrain, the reticular substance of the pons and medulla, laterally, in the anterolateral columns of the cervical and probably first two thoracic cord segments8,9 (Budge's center). Thus, the fibers ascend through the sympathetic chain to the superior cervical ganglion and the dilator muscle of the pupil.

The cerebral pathways for pupillary constriction are not convincingly demonstrated either. Fibers from the occipital lobe are thought10 to travel in the lateral ventricle wall and then to the lateral geniculate and thalamus, finally synapsing in the E-W nucleus. Pupillary constricting fibers from the frontal lobe4 have been described.

Stimulation of the cerebral hemisphere, prefrontal, parietal and occipital lobe as well as the corona radiata and internal capsule produce pupillary changes. Dilatation is obtained most often from the above structures with or without horizontal conjugate eye movements.7,8,11-13 At times, constriction of the pupil occurs with frontal and occipital lobe stimulation.4,8,9,10,12 Constriction of the pupil is mostly associated with disjunctive movements such as convergence or divergence.14

Evidence for pathways producing dilatation independent of the peripheral sympathetic system was presented as early as 1900 by Parsons,2 who obtained dilatation of pupils by cortical stimulation after bilateral cervical sympathectomy.

What, then, is the site of the lesion producing the larger pupil in our cases?

The persistent associated severe deficit (paralysis, sensory changes, field defect) suggests destruction of cortical and subcortical gray and white matter, and one must entertain the possibility that the larger contralateral pupil is due to destruction of crossed frontal or occipital fibers going to the parasympathetic nucleus of Edinger-Westphal and resulting in

\[ \Sigma \text{DILATOR PUPILLAE} \]

\[ \Sigma \text{CONSTRICTOR PUPILLAE} \]

Redrawn from Cogan and Gray

FIGURE 1

Schematic drawing showing the cortical and subcortical structures involved in pupillary control.

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<table>
<thead>
<tr>
<th>Pt. no., sex, age, race</th>
<th>Pt. course</th>
<th>Pupil course</th>
<th>Contrast procedures</th>
<th>Other neurological procedures</th>
<th>Tentative diagnosis and associated conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 M</td>
<td>Comatose, death 2 days postoperatively</td>
<td>Equal</td>
<td>None</td>
<td>None</td>
<td>L frontoparietal mass clot (at autopsy)</td>
</tr>
<tr>
<td>2 M</td>
<td>Comatose 10 days</td>
<td>Not known</td>
<td>None</td>
<td>Clear LP</td>
<td>Cerebral infarction secondary to emboli versus thrombosis, ICH, R/O subdural</td>
</tr>
<tr>
<td>3 M</td>
<td>Comatose, death in 3 days</td>
<td>Not known</td>
<td>Deep intrahemispheric bilateral hemorrhage</td>
<td>LP: pink</td>
<td>ICH, SAH</td>
</tr>
<tr>
<td>4 M</td>
<td>Comatose, death in 2 days</td>
<td>Became &quot;midsize&quot;</td>
<td>None</td>
<td>Not known</td>
<td>Cerebral infarction versus carotid occlusion, hypertension, ICH, hypertensive ASHD</td>
</tr>
<tr>
<td>5 M (70 years, white)</td>
<td>Deepening of coma, death in 24 hours</td>
<td>Repeat examination, R - 6, L - 4</td>
<td>None</td>
<td>L calorics: only L eye deviates, R calorics: OK, Calorics: no response</td>
<td>Cerebral infarction versus carotid occlusion, hypertension, ICH, hypertensive ASHD</td>
</tr>
<tr>
<td>6 F (61 years, white)</td>
<td>Comatose</td>
<td>Rapidly equal, large and fixed</td>
<td>None</td>
<td>None</td>
<td>L MCA stenosis, R/O subdural, L MCA occlusion (Stokes-Adams)</td>
</tr>
<tr>
<td>7 F (85 years, white)</td>
<td>Transferred comatose</td>
<td>Not known</td>
<td>None</td>
<td>None</td>
<td>R MCA stenosis, hypertension</td>
</tr>
<tr>
<td>8 F (66 years, white)</td>
<td>Alert but dysphasic</td>
<td>Not known</td>
<td>None</td>
<td>EEG: recent cerebral infarction, L</td>
<td>R MCA stenosis, recent cerebral infarction (at autopsy)</td>
</tr>
<tr>
<td>9 (51 years)</td>
<td>Improved</td>
<td>Pupil &quot;normal&quot; in one day</td>
<td>Bilateral carotid occlusion, R vertebral 90% stenosis</td>
<td>None</td>
<td>R cerebral infarction, R multiple cerebral infarct (at autopsy)</td>
</tr>
<tr>
<td>10 F (72 years, white)</td>
<td>Death in 3 weeks</td>
<td>Not known</td>
<td>48 hours later pupil still unequal</td>
<td>R MCA occlusion</td>
<td>R cerebral infarct, hypertensive ASHD, seizure disorder, Recent basilar occlusion, infarcts, both thalami and L occipital lobe, R midbrain (at autopsy)</td>
</tr>
<tr>
<td>11 F (55 years, white)</td>
<td>Death in 7 weeks</td>
<td>48 hours later pupil still unequal</td>
<td>R MCA occluded (99%)</td>
<td>None</td>
<td>R cerebral infarction, hypertensive ASHD, seizure disorder, Recent basilar occlusion, infarcts, both thalami and L occipital lobe, R midbrain (at autopsy)</td>
</tr>
<tr>
<td>12 M (51 years, white)</td>
<td>Improved</td>
<td>Pupil still unequal after 2 weeks</td>
<td>RP MCA occluded (99%)</td>
<td>None</td>
<td>R cerebral infarction, hypertensive ASHD, seizure disorder, Recent basilar occlusion, infarcts, both thalami and L occipital lobe, R midbrain (at autopsy)</td>
</tr>
<tr>
<td>13 M (77 years, white)</td>
<td>Death several hours after admission</td>
<td>Unchanged</td>
<td>None</td>
<td>LP: clear</td>
<td>L = left, R = right, MCA = middle cerebral artery, ACA = anterior cerebral artery, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, ASHD = atherosclerotic heart disease.</td>
</tr>
</tbody>
</table>
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the loss of parasympathetic tonus.

Dysfunction of the contralateral hemisphere as site of pupillary disturbance agrees well with the work of Warwick and others.14, 15 They have shown that the oculomotor fibers and associated parasympathetic outflow are mostly direct and not crossed. The pupil inequality is probably not due to lesions of the subcortical stations, i.e., hypothalamus or E-W nucleus, since in such cases the anisocoria is very marked in the range of 4 to 5 mm, a magnitude difference we have not usually seen. The larger contralateral pupil found, after removal of the cerebral cortex in the cat (nine of 12 experiments), provides experimental support for a contralateral cerebral lesion. In the same paper the authors report on finding 19 cases of hemiplegia with a larger pupil on the side of weakness.

The pupillary changes were strongest after the cerebral infarction.

In the diencephalon and brain stem, most any vigorous electrical stimulation will cause pupillary dilatation.18, 19 This may be due to stimulation of the extensive mesencephalic reticular formation and subsequent changes in the level of consciousness rather than to direct stimulation of pupillary fibers.

Authors recently have shown convincingly that, contrary to what Behr thought, disturbances in the afferent pupillary arc do not cause anisocoria.5, 10 The possibility of dealing with an incomplete ipsilateral Horner syndrome rather than an enlarged contralateral pupil is unlikely since other signs of sympathetic dysfunction were lacking. Moreover, it was shown recently that lid ptosis is probably the most sensitive and earliest index of sympathetic dysfunction, in at least in sympathetic lesions in the cervico cord. A pressure mechanism acting on the third nerve is an unlikely consideration. In such cases the dilated pupil is in the majority of cases (75%) on the side of the cerebral lesion,15, 20 is markedly dilated, does not respond to light, and rapidly reverts to normal size with medical or surgical relief of the pressure. Furthermore, no uncal herniation was described in our cases that came to autopsy.

The anisocoria described may persist for years and will eventually be found as long as five years later in cerebral infarction cases with persistent severe deficit. A survey of 30 patients with severe neurological sequelae of cerebral infarction necessitating nursing homes revealed anisocoria in nine patients, the pupil being seven times larger on the side of the long tract signs. Mecholyl, 2.5% (three drops), was instilled in each eye to detect a cholinergic de-innervation effect. In all but one case the pupil size did not change. In darkness, the pupil size increased bilaterally but the anisocoria persisted.

Summary

Three hundred and sixty-three cases of cerebral infarction were reviewed. Nineteen had anisocoria.

In 80% of the cases, the larger pupil was situated contralaterally to the hemispheric lesion; it was associated with long tract signs in all cases and with a visual field deficit in four of five cases in which fields were examined. When the pupil and the long tract signs are not on the same side, the latter is a more reliable indicator of the side of the hemispheric lesion.

In 60% of the cases the patients were awake, while the remainder were obtunded or comatose. A pupil 4 mm or larger and reacting very sluggishly implies a poor prognosis.

This anisocoria does not necessarily disappear with improvement in general condition or with immediate medical treatment, and may last for years.

The mechanism is still uncertain; the lesion is probably "cortical" and in the contralateral hemisphere.

Recognition of a larger static pupil (Behr pupil) contralaterally situated to the hemispheric lesion in cerebrovascular accidents and associated with long tract signs is important and should not be confused with a dilated or dilating ipsilateral pupil due to direct pressure on the third nerve and implying a neurological emergency.

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