Reversal of Horner’s syndrome

L. J. CAUST AND MARJORIE M. L. PRICHARD

From the Department of Otolaryngology, Radcliffe Infirmary, Oxford, and the Nuffield Institute for Medical Research, University of Oxford

In the course of an investigation in rats into the effect of section of the cervical sympathetic chain on the nasal mucosa, it was noticed that the Horner’s syndrome became reversed when the rats were anaesthetized at various times after the original operation.

As this observation does not appear to have been reported previously, it was thought that a brief account of the finding should be recorded.

EXPERIMENTAL PROCEDURES

In all, 26 albino rats were operated upon: six were males of the Wistar strain, weighing between 315 g. and 387 g. at the time of operation, and 20 were females of the Sprague-Dawley strain, weighing between 197 g. and 305 g.

The operations were carried out with aseptic precautions and under anaesthesia induced by ether and maintained by an ether-oxygen mixture given through an intra-oral tube. In all instances a Zeiss operating microscope was used.

One of two different operations was performed, in every case on the left side: (a) removal of the superior cervical sympathetic ganglion, or (b) section of the cervical sympathetic trunk. The surgical approach was the same in each case. A mid-line incision was made in the skin of the neck, about 3.5 cm. in length, from the mandible to the sternum; any bleeding points encountered during the operation were ligated or packed with absorbable gelatin sponge. By means of blunt dissection just medial to the digastric muscle, the common carotid artery was located. This vessel was traced forwards (rostrally) to the origin of the internal carotid artery, and the superior cervical sympathetic ganglion was then found lying medial and dorsal to the bifurcation. The cervical sympathetic trunk could then be traced as it coursed caudally from the superior ganglion, passing behind the carotid artery from the medial to the lateral side of this vessel.

The superior cervical ganglion was excised in 14 rats. In the other 12 rats a segment of the cervical sympathetic trunk, measuring about 5 mm. in length, was removed about midway between the superior and the inferior cervical ganglia.

At the end of the operation the skin edges were brought together and sutured to close the wound. These sutures were removed under ether anaesthesia one week after operation. The rats were allowed to survive for periods ranging from three weeks to 53 weeks.

In some of the animals the arteries and veins of each retina were examined and photographed under anaesthesia (Fig. 3). The pupils were dilated with cyclopentolate hydrochloride. To make the retinal vessels visible a drop of methyl cellulose was placed on the globe, and a small rectangular cover-slip was then laid on the drop. The cover-slip was supported by plasticine on either side of the eyeball so that its plane was horizontal. Photographs of the retinal vessels were taken with a 35 mm. camera attached to the Zeiss operating microscope, at a magnification of × 2. The negatives were then enlarged × 3 for an assessment of the comparative size of the retinal vessels on the two sides.

OBSERVATIONS

A Horner’s syndrome was apparent on the left side in all 26 rats as soon as the animals had regained consciousness after the original operation. The left eye in each rat showed enophthalmos and ptosis (Fig. 2a). The assessment of any degree of meiosis was found to be too difficult in the albino rat. When fully conscious, the rats in which the ganglion had been removed showed a less marked Horner’s syndrome than did the animals in which the trunk had been cut. In all rats, the Horner’s syndrome became more marked during the first four to six weeks after operation, after which there was no obvious change. It was still present at 53 weeks in the four rats kept for this period.

In the first two experiments, when the rats were anaesthetized for removal of the sutures one week after operation, it was noticed that the Horner’s syndrome became reversed as soon as the animals became unconscious (Fig. 1). Instead of the eye on the denervated side showing enophthalmos and ptosis (Fig. 2a), the sunken globe became protruded and now protruded more than the eye on the un-operated side (Fig. 2b). When the rats recovered consciousness the original syndrome reappeared (Fig. 2c).

Thereafter, all the rats were examined under ether anaesthesia, both at early and various later stages after operation. In addition the effects of anaesthesia

1Sterispon (Allen & Hanburys).

2Cyclogyl (Schieffelin).
with halothane\(^3\) and with trichlorethylene\(^4\) were observed. With each of these three anaesthetic agents, and also with chloroform, the result was the same. Reversal of the syndrome occurred almost invariably. A difference, however, was noted in the degree of reversal between the rats in which the superior cervical ganglion had been removed and those in which the sympathetic trunk had been sectioned. The most marked reversal of the syndrome occurred regularly in the rats which had had the ganglion removed (Table I). These were the animals which, of the two groups, showed a less prominent Horner's syndrome when conscious. The rats in which the sympathetic trunk had been cut, and which in the conscious state showed the most pronounced Horner's syndrome, showed only a relatively slight reversal of the syndrome when they were anaesthetized in the first week or two after the operation. However, with the passage of time the degree of reversal in the latter rats increased and came to approach that seen in the rats whose ganglia had been removed. It should be noted that the three rats

\(^3\)Fluothane (I.C.I.).

\(^4\)Trilene (I.C.I.).

**TABLE I**

<table>
<thead>
<tr>
<th>Horner's Syndrome</th>
<th>One Week after Operation</th>
<th>At End of Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trunk Section</td>
<td>Ganglionectomy</td>
</tr>
<tr>
<td>In conscious state</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td><strong>Under anaesthesia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reversed</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Slightly reversed</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Not reversed</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**FIG. 1.** Rat showing reversal of its left Horner’s syndrome under ether anaesthesia eight weeks after removal of the superior cervical ganglion on the left side. Note the protrusion of the left eyeball. (Enlargement made from a 35 mm. colour transparency.)

**FIG. 2.** Rat three weeks after left superior sympathetic ganglionectomy, showing:

(a) Left Horner's syndrome during consciousness;
(b) reversal of the syndrome under ether anaesthesia;
(c) 10 minutes after (b); with returning consciousness the left Horner's syndrome is beginning to reappear. (Enlargements made from 35 mm. colour transparencies.)

**FIG. 2a**

**FIG. 2b**

**FIG. 2c**
which are listed in Table I as showing only slight reversal in the later series of tests were examined at an earlier stage than the remainder. Because of intermittent infection these particular experiments were terminated at three, 18, and 18 weeks respectively. In the other rats the terminal observations were made up to 53 weeks after operation.

In seven animals in which satisfactory photographs were taken of the retinal vessels under anaesthesia, all showed that the vessels of the left eye, or denervated side (Fig. 3b), were larger in diameter compared with those of the right eye or intact side (Fig. 3a).

In a few instances tranquillizers were given in the hope that these would quieten the rat and enable a photograph to be taken which was good enough to allow actual measurement of the degree of enophthalmos in the conscious state. To this end, injections of thioridazine⁵ and chlorpromazine⁶ were used.

In two rats 3·0 mg. per 100 g. body weight of thioridazine was injected subcutaneously with little or no tranquillizing effect; there was, however, a slight reversal of the Horner’s syndrome in one of these rats (ganglionectomy).

Chlorpromazine was injected intramuscularly into seven rats in a dosage of 0·8 mg. per 100 g. body weight. In all seven animals the drug in this dosage produced a condition resembling catalepsy. When the effect of the drug was maximal, the rats could be placed in any desired position and remained virtually motionless although apparently awake. While in this state, however, the Horner’s syndrome was again completely reversed in all seven animals.

Davis (1929) has shown that in rabbits there is a retro-orbital blood lake, and it was found in the present study that a similar but smaller blood lake is present in the rat. It seemed possible that the reversal of the Horner’s syndrome might be due to engorgement of this lake, due to an increased sensitivity of its muscular walls to circulating adrenalin. To test this possibility, adrenalin was injected subcutaneously into two rats in a dosage of 0·005 mg. per 100 g. body weight. In each rat the injection caused dilatation of both pupils, a more marked dilatation occurring on the denervated side, but there was no change in the ptosis or in the enophthalmos on that side.

SUMMARY AND COMMENT
The reversal of the Horner’s syndrome described above occurred with remarkable constancy, taking place under general anaesthesia with ether, halothane, trichlorethylene, chloroform, and also after the administration of thioridazine and chlorpromazine. The reversal was apparently not due to the peripheral and/or possible central effect of adrenalin liberated from the adrenal medulla under general anaesthesia, since the administration of adrenaline caused no reversal.

The cause of the phenomenon was not found in the present investigation. The reversal was not relevant to the main investigation and the problem was not taken further. The finding is, however, reported as an interesting observation.

REFERENCE

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⁵Melleril (Sandoz).
⁶Largactil (May & Baker).
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L. J. Caust and Marjorie M. L. Prichard

J Neurol Neurosurg Psychiatry 1963 26: 241-243
doi: 10.1136/jnnp.26.3.241

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