HYPOTHALAMIC LESIONS FOLLOWING CLOSED HEAD INJURY

BY

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Diabetes insipidus is a well recognized sequel of head injury (Porter and Miller, 1946) and the clinical signs and symptoms of hypopituitarism have been described after head injury (Witter and Tascher, 1957). These are well reviewed by the above authors and need not be repeated in the present account, which is concerned with the morbid anatomical findings in the anterior hypothalamus in 106 consecutive autopsies of patients dying soon after severe, acute closed head injuries, i.e. injuries in which the brain was not penetrated by fragments of bone or any foreign substance.

The actual demonstration of lesions in the hypothalamus following closed head injury has not been documented in any sizeable autopsy series. In only two instances has the finding of abnormalities in the hypothalamus been correlated with the presence of clinically obvious post-traumatic hypopituitarism. These were patients described by Schereschewsky (1927) in which haemorrhages were described in the floor of the third ventricle, and Henzi (1952) in which there was atrophy of the supraoptic and paraventricular nuclei.

There is ample reason why traumatic lesions of the hypothalamus should be of significance in the natural history and treatment of cerebral injury. Graschenkov et al. (1965) state that hypothalamic lesions may govern the severity of the sequelae of head injury by affecting adrenaline, acetylcholine and histamine activity, protein and carbohydrate metabolism, capillary permeability and the interaction between the hypothalamus, pituitary and suprarenal cortex. One of the earliest descriptions of the electrolyte disturbances resulting from hypothalamic lesions, was in an experimental account concerning chloride and sugar metabolism by Lewy and Gassmann in 1935. Ishii (1966) claimed the demonstration of a paraventricular hypothalamic centre which controlled the cerebral vascular tone and hence the intracranial pressure. This last is obviously of immense importance in understanding the most serious of surgical problems following cerebral injury.

It is practically impossible in patients with post-traumatic hypopituitarism to tell whether the lesions are in the hypothalamus, pituitary stalk or pituitary gland. Daniel and Treip (1961) demonstrated pituitary lesions in large numbers of patients
dying soon after head injuries. These included anterior lobe infarcts, posterior lobe haemorrhages and partial or complete transection of the stalk. They described how stalk lesions produced anterior lobe infarction by damaging the portal blood supply via the long portal vessels, and diabetes insipidus by denervating the posterior lobe. There is no doubt that these stalk and pituitary lesions are of the utmost importance. However, their existence will only be incidentally confirmed in the present series which sets out to show that lesions higher in the hypothalamus are often present after head injury and should be considered in conjunction with stalk and pituitary lesions when the morbid anatomical basis of post-traumatic hypopituitarism is under examination.

RESULTS

The present autopsy series consisted of 106 patients dying consecutively soon after acute closed head injury.

Preliminary autopsies which prompted this present series showed that microscopically visible lesions were frequently seen in the anterior hypothalamus between the coronal levels of the lamina terminalis and the infundibular recess. Thus following a full autopsy, the brain in each case was fixed in 10 per cent formal saline for more than two weeks. Blocks including the anterior hypothalamus were taken and embedded in paraffin wax. Sections were stained with haematoxylin and eosin, methasol fast blue and cresyl violet or solochrome cyanin for myelin sheaths and Glees silver impregnation for axons.

About half of the injuries were received as a result of road traffic accidents and the majority of the remainder were injuries to children and old people in their homes.

The age distribution of the total 106 patients is shown in fig. 1 with the usual head-injury peaks between 10 and 25 and 45 and 75 years, possibly the ages when people (drivers and pedestrians)
are in the greatest danger on the roads. Figs. 2 and 3 show the age of the 45 individuals with hypothalamic lesions and the 61 without any hypothalamic lesions. These show more young people with hypothalamic lesions.

Table I shows that more males than females had hypothalamic lesions.

The hypothalamic lesions present in 45 (42.5 per cent) of the 106 patients were bilateral in 24 of them. They were of two main types. These were small haemorrhages termed microhaemorrhages, which were present in 31 patients and regions of ischaemic necrosis termed ischaemic lesions, which were present in 26. Both kinds of lesions were present together in 12 cases.

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**Table I.—The Sex Distribution Amongst Individuals With and Without Hypothalamic Lesions**

<table>
<thead>
<tr>
<th>Patients with hypothalamic lesions (45)</th>
<th>Patients without hypothalamic lesions (61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>38</td>
</tr>
<tr>
<td>Females</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>23</td>
</tr>
</tbody>
</table>

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In 31 patients lesions occurred in a somewhat haphazard manner throughout the anterior hypothalamus. These were mainly the ischæmic lesions (fig. 4, Plate XI), but the microhaemorrhages sometimes tended to be anatomically localized in definite regions of the hypothalamus. In 8 patients this was in the subependymal paraventricular nuclei; in 4 it was in the lateral hypothalamus amongst the fibres of the median fore-brain bundle (fig. 5); in 6 it was in the supraoptic nuclei (fig. 6) and in 2 it was in the region of the median eminence of the infundibulum.

The only clinical factor that could be accurately correlated in this series of patients who were almost uniformly comatose during the whole of their time in hospital, was the presence or absence of a lucid interval of consciousness following the head injury and preceding the final coma. A lucid interval of minutes or longer was present in 15 of the 45 cases with hypothalamic lesions, and in 19 of the 61 with no hypothalamic injury. Thus there was no difference and hypothalamic lesions are compatible with a return of consciousness in some cases. An attempt was made to assess the site of major impact to the head in relation to the presence or absence of hypothalamic lesions. Table II shows the findings in those patients in whom this was possible. There were relatively fewer fronto-occipital and more temporoparietal blows in the patients with hypothalamic damage.

**TABLE II.—THE SITE OF CRANIAL IMPACT IN RELATION TO THE PRESENCE OF HYPOTHALAMIC LESIONS**

<table>
<thead>
<tr>
<th>Site of impact</th>
<th>Frontal</th>
<th>Parietal</th>
<th>Temporal</th>
<th>Vertex</th>
<th>Occipital</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with hypothalamic lesions</td>
<td>7</td>
<td>11</td>
<td>8</td>
<td>2</td>
<td>11</td>
<td>39</td>
</tr>
<tr>
<td>Patients with no hypothalamic lesions</td>
<td>13</td>
<td>9</td>
<td>7</td>
<td>6</td>
<td>24</td>
<td>59</td>
</tr>
</tbody>
</table>

There was no difference in the frequency of skull fractures. 37 (82 per cent) of the 45 patients with hypothalamic lesions and 54 (88 per cent) of the 61 with no hypothalamic lesions had fractures of the skull, but there did appear to be some preponderance of fractures involving the middle fossæ in patients with hypothalamic lesions. This is shown in Table III.

**TABLE III.—THE SITE OF SKULL FRACTURES IN RELATION TO HYPOTHALAMIC LESIONS**

<table>
<thead>
<tr>
<th>Site of skull fracture</th>
<th>Anterior fossæ</th>
<th>Middle fossæ</th>
<th>Posterior fossæ</th>
<th>Skull vault</th>
<th>Number with skull fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with hypothalamic lesions</td>
<td>17(45%)</td>
<td>34(92%)</td>
<td>14(38%)</td>
<td>24(65%)</td>
<td>37</td>
</tr>
<tr>
<td>Patients with no hypothalamic lesions</td>
<td>30(55%)</td>
<td>31(55%)</td>
<td>27(50%)</td>
<td>41(75%)</td>
<td>54</td>
</tr>
</tbody>
</table>

Cortical laceration and contusion occurred with equal frequency in patients with hypothalamic lesions and in those without them. Only one of the 45 cases with hypothalamic lesions had no cortical laceration or contusion, and 6 of the patients without hypothalamic lesions had no cortical lesions. Thus if cortical lesions are taken as an index of the severity of the head injury, the great majority of hypothalamic...
lesions occurred in severe head injuries such as made up the bulk of this series, but they could occur in the less severe ones.

Macroscopically notable atheroma of the cerebral arteries made no difference to the incidence of hypothalamic lesions, either ischaemic or haemorrhagic. It occurred in 16 of the 45 patients with hypothalamic lesions, and in 20 of the 61 without them.

Evidence of cerebral anoxia as shown by necrosis of neurons in the cornu Ammonis, was present in 15 of the 45 patients with hypothalamic lesions and in 15 of the 61 without them. Thus there was no significant difference, nor was there any difference in the type of lesion.

The gastric and duodenal mucosa was examined with special care and lesions were found in 6 of the 106 cases. These are shown in Table IV. It can be seen that 4 cases with hypothalamic lesions had gut lesions and 2 of those without. All 6 cases had temporal lobe laceration and all except one had frontal laceration.

Table IV.—Gastric and Duodenal Lesions

<table>
<thead>
<tr>
<th>Cases with hypothalamic lesions</th>
<th>Cases without hypothalamic lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute duodenal kissing ulcers</td>
<td>1. Acute duodenal kissing ulcers</td>
</tr>
<tr>
<td>2. Acute gastric erosion with plasma cell infiltration of the muscle coat</td>
<td>2. Acute duodenal kissing ulcers</td>
</tr>
<tr>
<td>3. Acute haemorrhagic erosion of the duodenum</td>
<td></td>
</tr>
<tr>
<td>4. Haemorrhage through the full thickness of the gastric mucosa</td>
<td></td>
</tr>
</tbody>
</table>

The pituitary gland was examined in 53 of the patients. Lesions, either infarcts or haemorrhages, were present in 14 (28 per cent) of the cases. 8 of these (38 per cent) occurred in the 21 cases with hypothalamic lesions, and 6 (19 per cent) in the 32 patients with no hypothalamic lesions. Haemorrhage into the dural capsule of the gland was much commoner than lesions within the gland, but probably of little significance. Thrombosis of pituitary vessels, as described by Daniel and Treip (1961) was not seen.

Table V shows the distribution of the ischaemic and haemorrhagic lesions, infarcts being confined to the anterior lobe. Two patients had haemorrhages in both the anterior and posterior lobes. There was no predominance of basal fractures of the

Table V.—The Distribution of Haemorrhagic and Ischaemic Lesions in the Anterior and Posterior Pituitary

<table>
<thead>
<tr>
<th></th>
<th>Anterior lobe Infarcts</th>
<th>Anterior lobe Haemorrhages</th>
<th>Posterior lobe Haemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>With hypothalamic lesions</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Without hypothalamic lesions</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
skull in any group. The general impression from these findings is that there is a tendency for hypothalamic and pituitary lesions to occur together in the same patients.

There appeared to be some connexion between secondary brain-stem hæmorrhage and hypothalamic lesions. 28 (62 per cent) of the 45 patients with hypothalamic lesions had secondary brain-stem lesions, whereas 31 (51 per cent) of the 61 without hypothalamic lesions had them.

DISCUSSION

The population of the present series is a typical and fairly representative cross-section of the incidence of closed head injuries from different causes occurring in an industrially advanced urban community.

Comparison of figs. 2 and 3 shows a greater incidence of hypothalamic lesions in younger people. One may postulate that the smaller, firmer brain of the old person is less likely to suffer internal shearing strains of nerve fibres and blood vessels within the cerebral hemispheres. This is pure speculation.

Table I shows a greater incidence of males with hypothalamic lesions, almost certainly due to the greater number of young males who suffer severe head injuries.

The actual cause of the hypothalamic lesions found is not certain. The ischaemically lesions were almost certainly due to shearing of small perforating vessels at the time of impact. Many of the hæmor rhages, or microhæmor rhages, may have been of similar pathogenesis. They are seen often enough elsewhere in the brain where they are often accompanied by encephalolysis of the white matter due to the shearing of nerve fibres (Rand and Courville, 1934, and Strich, 1961). However, the microhæmor rhages localized to the various hypothalamic nuclei bear a remarkable resemblance to lesions found in fatal cases of ruptured cerebral aneurysms (Crompton, 1963). It was thought in these latter that venous engorgement due to raised intracranial pressure might be a pathogenetic factor, and it is possible that this is also the cause in the patients with head injuries. Some of the retinal hæmorrhage seen in fatal head injuries (personal observation) could be accounted for in the same way. Thus not all the hypothalamic lesions found at autopsy may have resulted from injury due to the primary impact. Such lesions have not been reported in the literature as being secondary to cerebral herniation or displacement, and this is not the author’s experience.

The fact that a lucid interval of consciousness before final coma was equally common in cases with and without hypothalamic lesions suggests that these lesions, many of which undoubtedly do occur at the time of impact, are compatible with consciousness.

Table II shows that if the site of impact is analysed in relation to hypothalamic lesions, there is an impression that there are more temporo-parietal and fewer fronto-occipital blows in patients with hypothalamic lesions. Presumably the forces most likely to shear hypothalamic vessels are from side to side, with the upper hypothalamus moving more than the lower. This is supported by the information
in Table III, which suggests a large number of fractures of the middle fossa of the skull base in persons with hypothalamic lesions.

It was thought that arteriosclerosis might render the perforating arteries to the hypothalamus more likely to rupture with shearing strains, and ischaemic lesions more likely to occur if they were narrowed by atheroma, but the figures gave no indication of this. Similarly, it was thought that poor cerebral oxygenation such as could be due to coincident chest injury might increase the incidence of hypothalamic ischaemic lesions. Using the presence of necrosis of the cornu Ammonis as an indication of cerebral anoxia, no such connexion was found. It appears that the harder arteries and poorer oxygenation of the elderly brain do not increase the risk of hypothalamic lesions. This agrees with the implications of figs. 2 and 3.

Acute gastric or duodenal lesions ranging from interstitial haemorrhage in the mucosa and muscle coat to large kissing ulcers were present in 4 of the 45 persons with hypothalamic lesions and in 2 of the 61 without them. These figures do not mean anything, except that they bear out the occurrence of these lesions in acute head injury. The presence of frontal and temporal laceration is likewise of no significance as these are the commonest cortical lesions due to closed head injury.

The incidence of pituitary lesions (28 per cent) was not as high as in the 152 fatal cases of Daniel and Treip (1961), who found these lesions in two-thirds of them. This may be due to their examination of the pituitary being more detailed than in the present series. The incidence of infarcts of the anterior lobe was about the same as theirs. The nature of the lesions was identical to their description, ranging from common capsular hemorrhages through the interstitial hemorrhages of the posterior and anterior lobes to the infarcts of the anterior lobe with characteristic peripheral sparing.

It is probable that lesions of the hypothalamic supra-optic nuclei and infundibulum will produce diabetes insipidus in the same way as stalk transection, by denervating the posterior lobe of the pituitary. The higher the lesions are, the more likely the anterior lobe is to be spared from infarction as its portal vessels will not be involved.

It might have been expected that basal fractures, especially those across the pituitary fossa, would increase the incidence of pituitary lesions. This did not appear to be so, perhaps emphasizing the importance of stalk damage as opposed to actual lobar damage.

Table V hints at a connexion between hypothalamic and pituitary lesions, which suggests that the main damage to the complex is in the lower hypothalamus, infundibulum and upper half of the stalk. This is what one would be led to expect when surmising that movement of the brain within the skull would damage the pituitary stalk and the perforating vessels to the hypothalamus from the anterior cerebral arteries, at about the same level; the base of the brain.

Wolman (1956) and others before him showed that small anterior lobe infarcts can be due to raised intracranial pressure and raised blood pressure. This must be borne in mind, but it is most unlikely that this is the cause of the majority of pituitary lesions found following head injuries.
There was a suggestion that patients with hypothalamic lesions developed secondary brain-stem lesions. This was not pronounced and it is unlikely that it offers any effective support to the assertion of Ishii (1966) that there is a hypothalamic centre which controls cerebral vascular tone and hence the intracranial pressure. However, the possibility of cerebral oedema resulting from hypothalamic damage is still very real.

**SUMMARY**

A detailed pathological examination of 106 fatal cases of acute closed head injury showed that ischaemic or haemorrhagic lesions of the anterior hypothalamus were present in 42.5 per cent. These lesions were most frequent in young people. They were compatible with consciousness and most often followed temporo-parietal blows. They were often associated with fractures of the middle fossa. They tended to be associated with infarction or haemorrhage in the pituitary, probably because injury near the pituitary stalk would damage both the hypothalamic perforating vessels and the pituitary portal vessels.

**ACKNOWLEDGMENTS**

I am grateful to Professor T. Crawford and Mr. Wylie McKissock for their encouragement with this work. I am also indebted to Professor D. Teare and the Westminster City Coroner, Dr. Gavin Thurstan, for the opportunity to perform full autopsies on all these cases of head injury. This work could not have been completed without the technical assistance of Miss Iris Mason made available by the Medical Research Committee of St. George’s Hospital and the technical assistance of Miss Mary Taylor and Mrs. Y. A. Bosley.

**REFERENCES**


(Received 20 August 1970)
Fig. 4.—Large pale ischaemic lesions (I) with well-defined margins, in the anterior hypothalamus and basal ganglia. Haematoxylin and eosin ×2.
Fig. 5.—Microhaemorrhages (M) in the lateral portion of the anterior hypothalamus on one side. Note the associated ipsilateral parietal and temporal lesions with mid-line shift.

To illustrate article by M. Rufus Crompton.

Fig. 6.—Microhaemorrhages (M) in the supraoptic nucleus. Haematoxylin and eosin × 2.