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Disturbances of the Hypothalamic Thermoregulation

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Summary

Although compression of the hypothalamus in cases of suprasellar tumour is common, spontaneous dysregulation of body temperature is extremely rare. Bilateral localization of the hypothalamic nuclei and a high grade of compensatory value of temperature regulation may be the reason for this phenomenon.

In the postoperative period temperature dysregulation is observed more often. In order to analyse the influence of diencephalic regulation in these patients classification of the degree of hypothalamic compression is necessary. The problem was studied under experimental and clinical conditions.

1. Experimental studies in rabbits after acute hypothalamic compression and decompression showed a reversible disturbances of temperature regulation.

Hypothalamic compression in dogs resulted in reversible hypothalamic endocrine dysfunction.

2. Clinical observations of body temperature in the period after operation of suprasellar tumors showed similar results.

The temperature study was extended on patients with cerebral trauma and intracranial haemorrhage to differentiate the degree of hypothalamic lesion.

Morphological examinations confirmed alterations localized in the anterior and posterior region of the hypothalamus. The analysis proved the fact that temperature regulation seems to be a highly sensitive parameter of diencephalic function.

Keywords: Thermoregulation; hypothalamic thermoregulation; experimental hypothalamic compression; diencephalic lesion.

Introduction

Hypothalamic temperature regulation seems to be one of the most difficult problems of hypothalamic function. By means of experimental studies some authors have succeeded in localizing areas in the hypothalamus which are connected with temperature regulation in animals. But these models could not be compared with clinical situations.

The following question are discussed:

1. Is observation of body temperature useful in the study of hypothalamic lesions?

2. Do temperature alterations allow predictions about the prognosis?

3. Do we have experimental models for further studies of hypothalamic lesions with clinical purpose?

Within the narrow limit of the hypothalamus, temperature-regulating centres are located in different areas. As shown by Hess, Stoll, and Anderson, the area praeoptica is connected with thermoregulation in the region of the rostral hypothalamus. Under experimental conditions for instance, local heating resulted in "generator potenials" (von Euler), single potential-recording confirmed these results (Nakayama) (receptor system). Beside these areas other zones are located in the caudal hypothalamus and are scattered over a larger region (effector system).

Carlson found two different principles in the system of regulation of body temperature as confirmed by Grote concerning the homeostasis of glucose regulation (Fig. 1).

1. Via the neural pathway.

An immediate reaction is possible via the neural pathway by influencing the sympathetic-parasympathetic system of other neural connections of the hypothalamus.

2. Via the neurohumeral pathway.

The neurohumoral reaction of the hypothalamus provokes a prolonged excreting of releasing hormones, which control the secretion of pituitary hormones.

Both systems are integrated in the hypothalamus and can respond to demands for the adjustment of the ideal values of restraining both agonists and antagonists.

Central receptors are influenced by the blood temperature and at this level the central set point influences the mechanism of regulation . Serotonin and

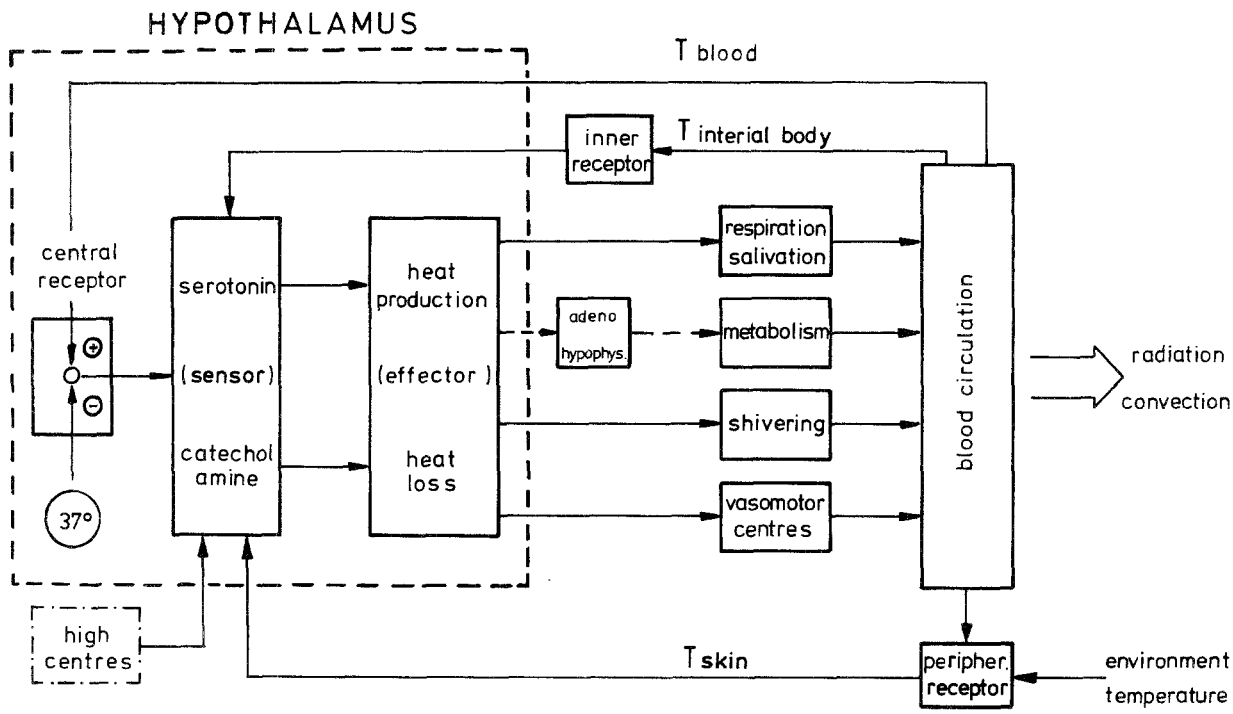

Fig. 1. Central and peripheral mechanisms of temperature regulation. Sensor and effector-system: 1. Via neural (→), 2. Via neurohumoral network (— →)

catecholamines play a part in transmitting the stimulus to the posterior hypothalamus. Stimuli from the periphery and from higher brain centres may interfere at this level.

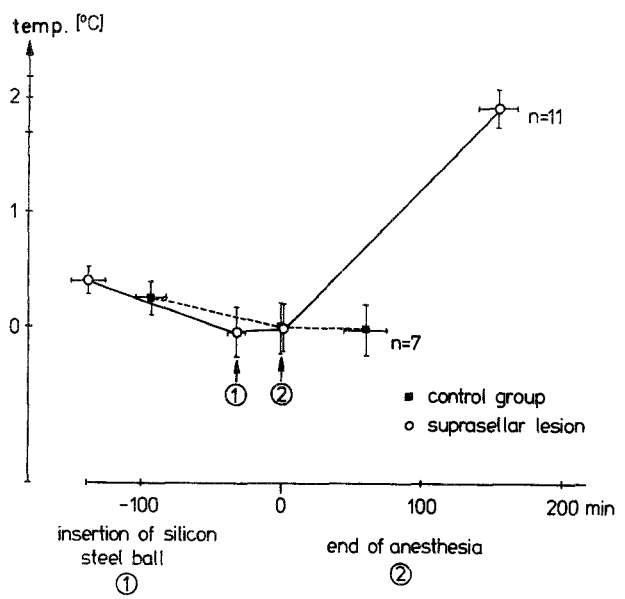

Fig. 2. Temperature course in controls and in rabbits with insertion of silicon steel ball

A set-point for central body temperature is located in the hypothalamus. This point is individually different, but it is extremely constant for each individual. Regulating mechanism start at a central temperature alteration of 0.01 °C (Benzinger).

Experimental Findings

Rabbits

Based on these findings, experimental studies were performed in order to correlate clinical observations with experimental hypothalamic lesions. Since former authors did not imitate suprasellar lesions in experiments, we established an experimental model in order to study suprasellar space occupying lesions causing direct or indirect compression of the hypothalamic structure. Temperature regulation is investigated in rabbits (Fig. 2).

After the implantation of silicone steel balls by microsurgical technique below the chiasm and diencephalic region, body temperature is recorded.

Postoperatively body temperature increases significantly when compared with the control group.

In the acute stage the morphological picture show predominate by diffuse edema of the anterior hypothalamus apparently caused by compression of this area, and as a result of a localized blood brain barrier dysfunction.

In contrast, animals with a chronic lesion, show a much smaller area of scar-like alterations and cell proliferation. No edema is found after 3 weeks. At the

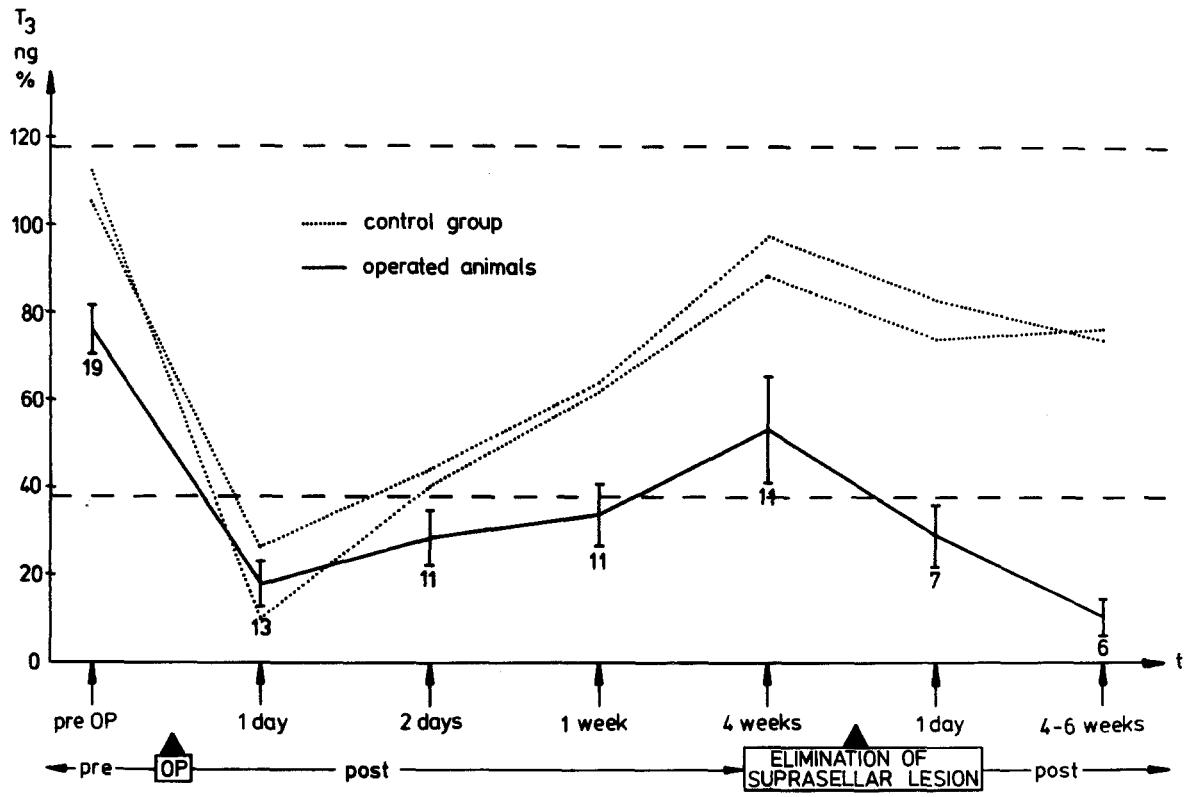

Fig. 3. Serum T_3-level in dogs after insertion of Fogarthy catheter filled with 0.35 ml contrast medium compared with controls

same time, signs of hypothalamic disturbances had ceased. In these cases, restitution had taken place, so that intact areas have compensated for the dysfunction. This type of reaction is typical for bilateral and symmetric areas, which only decompensate in cases of bilateral lesions. In case of an asymmetric lesion, maintainance of function may be ensured by the contralateral structure.

Comparing the acute and chronic findings one sees that reversible lesions predominate if the experimental procedure has been performed carefully.

Dogs

Other investigations with suprasellar space-occupying lesion have been performed on dogs. Fogarthy catheters are implanted by craniotomy below the optic chiasm and filled with 0.35 ml contrast medium.

Temperature regulation could not be studied in the dogs because of technical problems in the postoperative period. But reversible hypothalamic dysfunction due to increased local pressure imitates extracerebral suprasellar lesions. Examination of thyroid function seems to be a proper method since most of the dogs develope severe clinical signs of hypothyroidism. T_3-RIA is found to be the predominant thyroid hormone in dogs.

Since a primary lesion of the thyroid gland could be excluded, the symptoms are therefore caused by a lesion of the hypothalamo-hypophyseal axis (Fig. 3).

The lesion develops in two stages. Initially a reversible hypothalamic lesion with consecutive hypothyroidism develops within the first 4 weeks. After atraumatic removal of the space-occupying lesion by emptying the balloon catheter, a secondary hypothalamic disturbance develops with chronic impairment of thyroid function.

This dysfunction is irriversible even after 6 months of observation.

Clinical Investigations

The results obtained from experimental brain lesions do not always correlate with clinical observations. Rothballer in 1966 was the first to attempt a classification of hypothalamic lesions according to their site.

While temperature dysregulation is extremely rare preoperatively as shown by Lausberg, dysthermia is common in the postoperative phase.

To analyse the different forms of suprasellar lesions

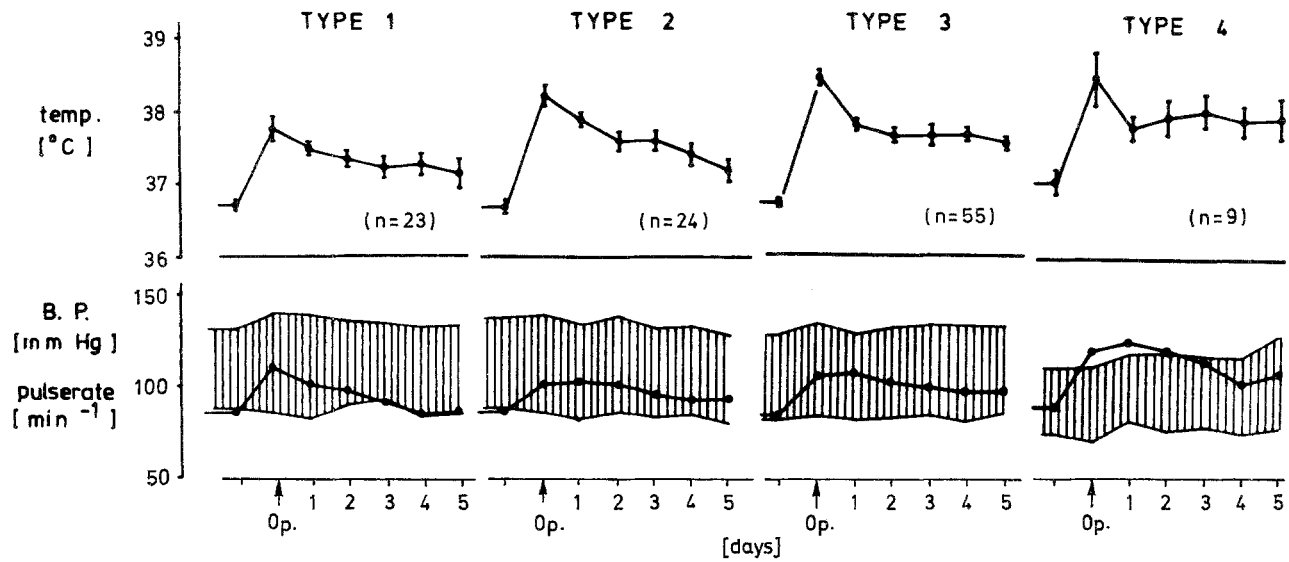

Fig. 4. Temperature values, pulse rate and blood pressure in patients with tumors in the sellar region preoperatively and up to 5 day after operation

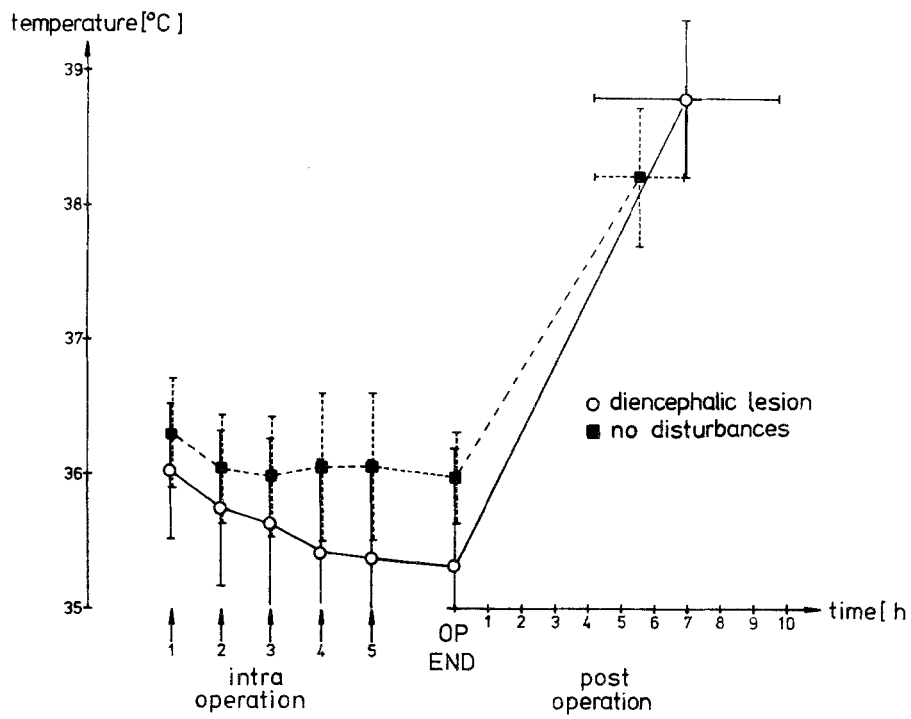

Fig. 5. Course of temperature during operation maximum temperature after end of anaesthesia in patients with and without postoperative diencephalic disturbances

the tumors were classified into 4 different types depending on the degree of hypothalamic compression (7).

Type 1 intrasellar.
Type 2 reaching chiasma.
Type 3 elevation of the floor of the 3rd ventricle.
Type 4 compression of the whole hypothalamus.

Based on this grading, temperature development after operation showed:

No difference according to

1. histological findings (adenoma, craniopharyngeoma);
2. operative approach (transcranial, transsphenoidal).

Significant difference depending on

1. Localisation (Type 1–4) (Fig. 4).

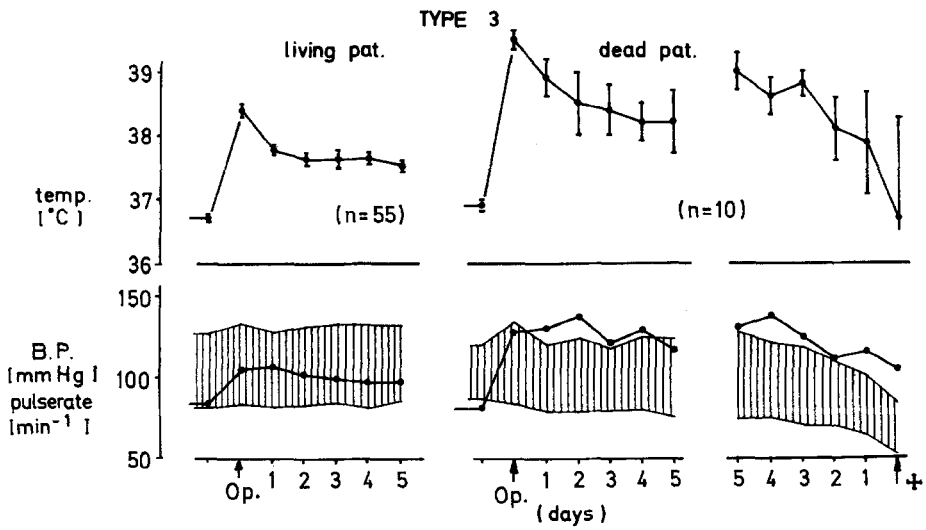

Fig. 6. Temperature, pulse rate and blood pressure in type 3 tumors pre- and postoperatively and in the preterminal phase

2. Patients with and without diencephalic leason (Fig. 5).
3. Surviving—non surviving (Fig. 6).

Head injury, subarachnoid hemorrhage (Fig. 7).

Clinical findings in suprasellar tumors indicated that temperature development is a sensitive parameter for the diagnosis of diencephalic lesions.

In patients with severe head injury and subarachnoid haemorrhage, diencephalic disorders seem to be relevant for clinical deterioration. Temperature studies proved the fact that temperature in significantly different in surviving and non-surviving patients.

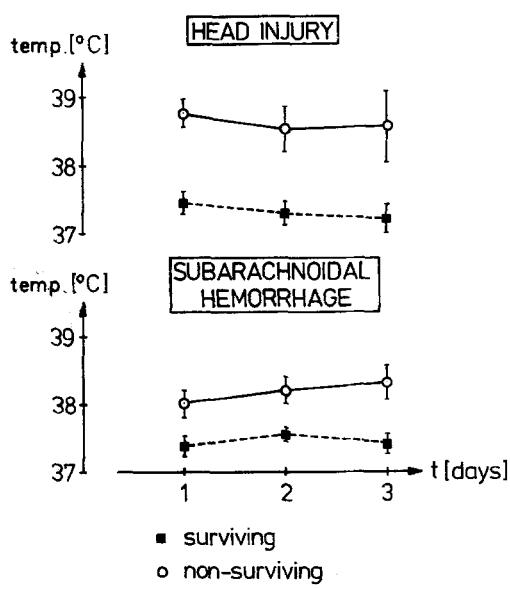

Fig. 7. Mean temperature in the first three days after head injury and subarachnoid haemorrhage in 10 surviving and 10 non-surviving patients

Morphology

The morphological study of the hypothalamus in these patients demonstrated lesions with haemorrhagic and infarcted foci, chiefly in the anterior hypothalamus, which corresponded to the clinical observations. The extent of these foci depended upon the degree of preoperative compression of the hypothalamus. Smaller tumors caused smaller lesions, correspondingly larger tumors produced larger lesions.

In the most severe cases, the tissue damage extended throughout the diencephalon. The most striking feature of the lesions was their symmetry: bilaterally innervated functional areas were damaged.

Both haemorrhagic foci and persistent oedema were found, probably due to venous stasis. The unusual vascular situation of the anterior hypothalamus seems to be responsible for the development of arterial and venous circulatory impairment. Arterial haemorrhage and infarction in the anterior hypothalamus may be produced by occlusion of small branches of the anterior cerebral artery to the anterior hypothalamus. While slow pre-operative tumor growth allows compensatory processes to take place, the rapidity of changes in local pressure and perfusional relations in the postoperative phase put these compensatory mechanism out of action. Thus, postoperatively the zones of oedema cause infarction and haemorrhage foci as well as acute functional disturbances.

In cases of tumors type 3 and 4, displacement of blood vessels was always present. Thus a circulatory disturbance of the hypothalamus must be suspected in addition to the operative damage.

Discussion

The theoretical basis of the pathophysiological mechanism of diencephalic temperature regulation remain controversal. The findings show that the clinical parameters in the acute postoperative period permit assessment of the extent and degree of hypothalamic injury, in the same way as Rothballer demonstrated for the pre-operative period. For this, the pre-operative classification of hypothalamic space-occupying lesions according to the extent of compression is important.

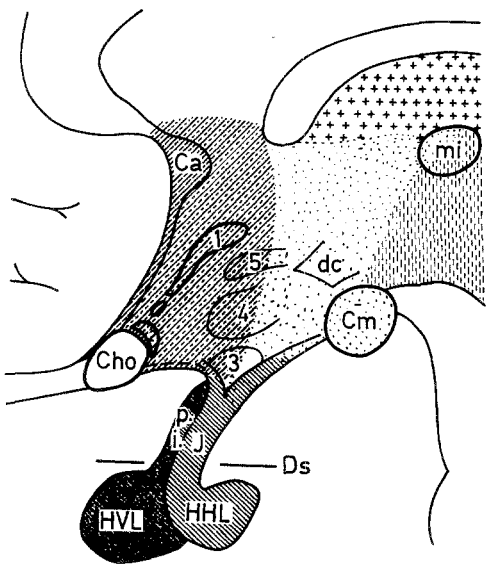

Fig. 8. Regions of blood supply of the hypothalamus and adjacent structures (Lazorthes 1959)

A transient disturbance in temperature regulation is usually evident in case of reversible lesion of the anterior hypothalamus, and a rapid return to normal value indicates that the lesion has regressed.

If the disturbances of regulation are severe and persistent, haemorrhagic foci of infarction may be suspected. Involvement of several regulatory mechanisms can be taken as the sign of widespread hypothalamic damage. The postoperative defects are caused mainly by oedema, the extent of which depends in the degree of hypothalamic compression. For this kind of damage to develop, the following possibilities exist:

Focal oedema may interrupt the functional system by damaging specific cellular areas or neurones. Neuronal stimuli continue without feedback from the periphery and the central receptors. In this situation, hypothalamic deficit may arise, which in turn affects temperature regulation. The regulation of body temperature is based on a summation of neuronal impulses in the hypothalamus, and therefore damage at a single level results in a systemic reaction.

Furthermore microcirculatory changes with disturbance of the blood brain barrier in the region of the hypothalamus may play a dominating role. Since the vascular supply of the hypothalamus results from different arterial regions, primary and secondary dysregulation of blood suppy may follow after operation or trauma or haemorrhage (Fig. 8).

Temperature dysregulation is no isolated sign of diencephalic disorder but reveals a variety of other functional disturbances such as blood pressure, pulse rate, water and electrolyte balance.

These factors may influence regional blood flow in the hypothalamus. As morphological investigations after compression and decompression in rabbits and dogs show, additional secondary lesions seem to lead to rapid deterioration of hypothalamic function.

Conclusion

Neurophysiological, clinical and experimental investigations prove that temperature regulation seems to be a reliable early parameter for the detection of hypothalamic dysfunction. Though temperature recordings of patients with spaceoccupying lesions, severe head injury, or subarachnoid haemorrhage show significant differences between surviving and non-surviving patients, no prognosis can to be drawn from the degree of hypothermia alone.

Temperature dysregulation is proved to be a transient parameter only in acute lesions, while chronic hypothalaic compression show regular body temperature due to compensatory factors in the hypothalamic region. Experimental models are established in rabbits and dogs to study reversible and irreversible hypothalamic lesions which imitate extracerebral suprasellar space-occupying lesions.

These models allow a more extensive investigation of this problem in correlation with clinical purpose.

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