is calculated to approx. 11 μm. Cell fragments less than 4–5 μm diameter were not counted). Total mean number was calculated by multiplying numbers of cells in sample sections by factor 10. The semithin sections were stained in toluidine blue at pH 8.5. In the adult rats (3 females of 240–280 g, and 4 males of 345–380 g) mast cells were observed in the mid-brain and in the olfactory lobes. In the olfactory lobes, the mean total number was 168 ± 92 (S.D.) and the mast cells were located in the region of the nucleus olfactorius anterior. In the diencephalon, mast cells were observed in most parts of the thalamus and in the habenular region of the epithalamus. They were located perivascularly as shown in Figure 1. The mean total number was 1700 ± 681 when observed in the toludine blue stained section series. The number of mast cells observed in the section series stained in astra blue did not differ significantly from the figures present. No mast cells were observed in other brain regions, except that a few cells were found in the pia covering different brain regions. They were not included in the figures presented for the adult rats.

In the brains of baby rats (6-day-old: 2 females and 2 males) a few mast cells only were observed in the thalamic neuropil. However, they were plentiful in the part of the pia covering the diencephalon (Figure 2). The caudal limit of the distribution of mast cells here was at the level of the commissura posterior. The mean total number of mast cells in this diencephalic pia of the baby rats was 6136 ± 1031. In addition mast cells were plentiful in the pia-arachnoidea of fissura sagittalis, just behind corpus callosum, and of the lobus olfactorius. They are not included in the figures presented.

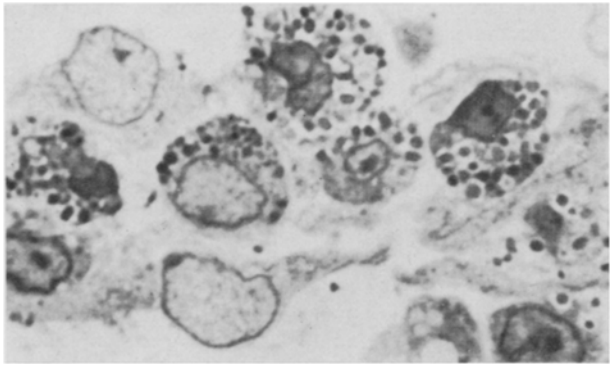

Fig. 2. Light micrograph of semi-thin epon section of mast cells in the dorsal diencephalic pia of baby rat brain. Section stained with toluidine blue. ×1600.

The content of histamine in a rat peritoneal mast cell has been calculated to be approx. 12 pg/cell[12,13], with variations up to a mean of 31.5 pg/cell[14]. Supposing that the amount of histamine in the mast cells of the brain is not far from that in the peritoneal mast cells, 12 pg/cell, the content of histamine in mast cells of the adult rat thalamus is 20.4 ± 8,1 ng. The weight of the thalamic and epithalamic region is approx. 0.14 g (142 ± 3 mg), which means that mast cells in the thalamus of the rat are responsible for 144 ng histamine/g fresh tissue. This is only slightly below the total amount of approx. 160 ng/g tissue that has been observed for this region of the adult rat brain[2]. In the 6-day-old rats, the mean histamine values based on mast cells in the diencephalic pia only should be 73.5 ± 12.3 ng. The brain weight of 6-day-old rats is approx. 0.5 g (506 ± 45 mg). From this figures the total histamine content in the brain of the baby rat, based on mast cells in the thalamic pia only, is 147 ng histamine/g fresh tissue. A maximum of 220–320 ng histamine/g tissue has been observed in the brains of 2-6-day-old rats, with a rapid decline at 10 days[3,15].

Thus, the present observations show that at least one-half of the histamine in the brain of the baby rat might be located in mast cells of the diencephalic pia, and that most of the histamine observed in the thalamus region of the adult rat brain might be based on mast cells in the neuropil of the thalamus and the habenular region of the epithalamus.

Résumé. Des cellules «mast» ont été observées dans les lobes olfactifs, dans le thalamus et dans la région de l'habénula de l'épithalamus chez le rat adulte, et dans la pie-mère dorsale du diencéphale chez le rat nouveau-né de 6 jours. La teneur en histamine de ces cellules pourrait expliquer la présence de la plus grande partie de l'histamine observée par d'autres auteurs dans la région du thalamus chez le rat adulte et au moins la moitié de la teneur totale en histamine dans la cervelle des rats nouveau-nés.

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Gold Thioglucose Induced Terminal Degeneration in Mouse Hypothalamus

It has been reported that the administration of gold thioglucose (GTG) causes necrosis in a discrete part of the hypothalamus[1–3]. Thus 24 adult mice of CPY strain were injected with GTG (Solganol, Bol., Schering A.G., Berlin) i.p. in a dose of 0.5 or 1.0 mg/g body weight. In the first part of the experiment, animals were decapitated 40, 44, 48, 56, 72 and 87 h after injection for histological localization of the necrosis caused by GTG. The tissues were fixed in 4% formaline and embedded in paraffin. Frontal plane serial sections of the diencephalon 7 μm in thickness were made and stained with luxol fast blue and cresylviolet. In the second part of the experiment mice were perfused with Karnowsky solution 40, 48, and 72 h

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after GTG injection. Small tissue blocks containing different parts of the hypothalamus were embedded in durcupan. Sections were cut with a Reichert ultrotome, stained with uranyl acetate and lead citrate. A Tesla BS 413A electron microscope was used for examination. The number of the degenerated terminals were counted on photomontages prepared from the zona externa of the median eminence.

A discrete region of the hypothalamus was damaged, including parts of the arcuate, ventromedial (Figure 1b) and premamillary nuclei (Figure 1c). The size of the lesion was independent of the dose of GTG and the length of time between injection and decapitation. Necrosis was also found in the retrochiasmatic area (Figure 1a) and in the periventricular nucleus but only in a minority of the animals. Other parts of the hypothalamus appeared intact. In 3 mice the ventral hippocampal commissure and the medial part of the dentate gyrus were partially destroyed. Only one of the animals demonstrated necrosis in the medial preoptic nucleus.

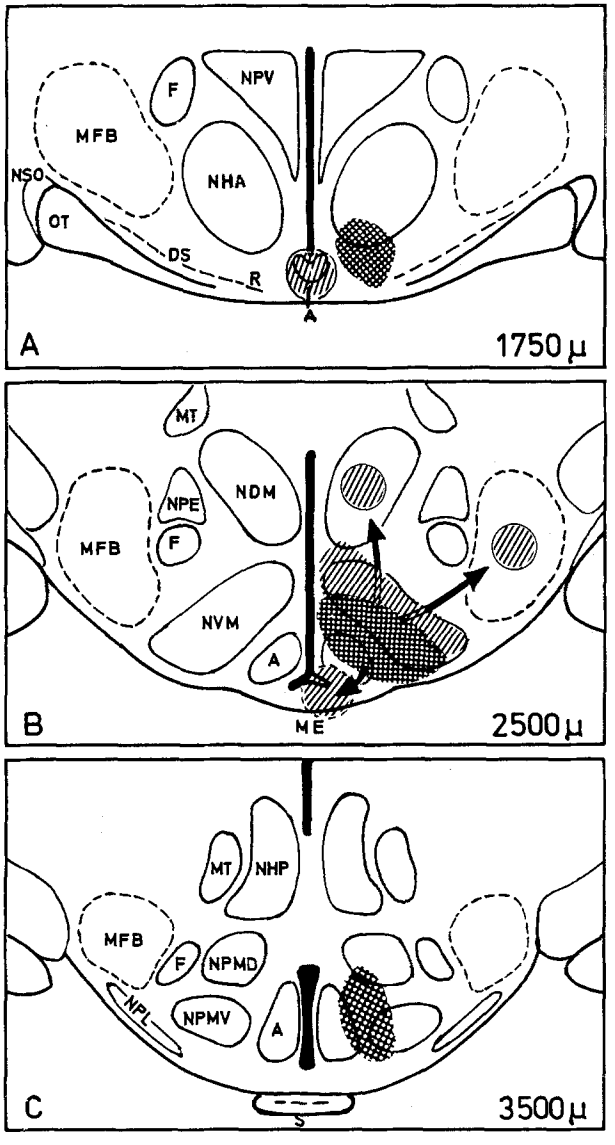

Fig. 1. Frontal hypothalamic sections at a different level from the anterior commissure in µm. F, fornix; OT, optic tract; DS, supraoptic decussations; MT, mamillothalamic tract; S, hypophyseal stalk; MFB, medial forebrain bundle; NPV, paraventricular nucleus; NHA, anterior hypothalamic nucleus; NSO, supraoptic nucleus; R, retrochiasmatic area; NVM, ventromedial nucleus; NDM, dorsomedial nucleus; A, arcuate nucleus; NPF, perifornical nucleus; NHP, posterior hypothalamic nucleus; NPMD, dorsal premamillary nucleus; NPMV, ventral premamillary nucleus; NPL, prelateral mamillary nucleus. :::, Site of the damage caused by GTG. ▒, Regions containing degenerated axon terminals (circles show the tissue samples removed for EM investigations).

Normal tissue elements could not be recognized within the necrotic brain regions. Dark degenerating boutons were found in the undamaged part of the ventromedial nucleus (Figure 2b). At later survival times (72 h), proliferation of astrocytes and oligodendroglial cells (Figure 2b) were observed in the undamaged region of the ventromedial nucleus, as well as an increase in the number of perivascular cells within the basal lamina of the capillaries. These juxtavascular cells[4] contained degenerated cell particles.

Degenerated axon terminals could be observed in the dorsomedial nucleus and in the lateral hypothalamic area among the fibres of the medial forebrain bundle (Figure 2a) and of the supraoptico-hypophyseal tract.

Degenerated axons were also found in the median eminence, especially in the zona externa. The first signs of degeneration consisting of formation of so-called axon cytolysomes[4] were observed 40 h after treatment (Figures 3a and b). After 48 h there appear large degenerated complexes, partially or totaly enveloped by tanycytes. However, at the same time we found free dark degenerating boutons, which characterize the degenerative process at other places in the CNS. At longer survival periods, the engulfed degenerating fragments lose their boundary membranes and are digested by tanycytes or other glial cells. Degenerated axons were repeatedly observed in the perivascular space of the primary portal plexus (Figure 3a). The number of 'lipid' droplets which characterize the tanycytes considerably increased following the treatment.

Although some pathologically altered terminals or tanycytes may be found also in intact animals, the experimental mice (48 h after treatment) have shown a much higher degeneration rate, as can be seen from our quantitative data. On a surface area of 10,000/µm² we found 59 early degenerating terminals and 47 free dark degenerating complexes, 77 tanycyte profiles contained one or more axon fragments. In contrast, on the same area in intact animals, we found 2 axon cytolysomes and 1 tanycytes with ingested axon fragments. In the other areas examined we never found signs of a 'spontaneous' degeneration.

Our findings are consistent with several other anatomical studies of intrahypothalamic fibre connections. Using GTG induced lesions of the ventromedial nucleus, AREAS and MAYER[5] showed degenerating fibres leaving this nucleus and directed towards the dorsolateral hypothalamus. MILLHOUSE[6] traced ventromedial axons directly into the lateral hypothalamus. There are also ventromedial afferents in the periventricular fibre system, some of which probably terminate in the arcuate nucleus[6]. Some of the cell bodies of the arcuate, periventricular, ventromedial, suprachiasmatic and dorsal

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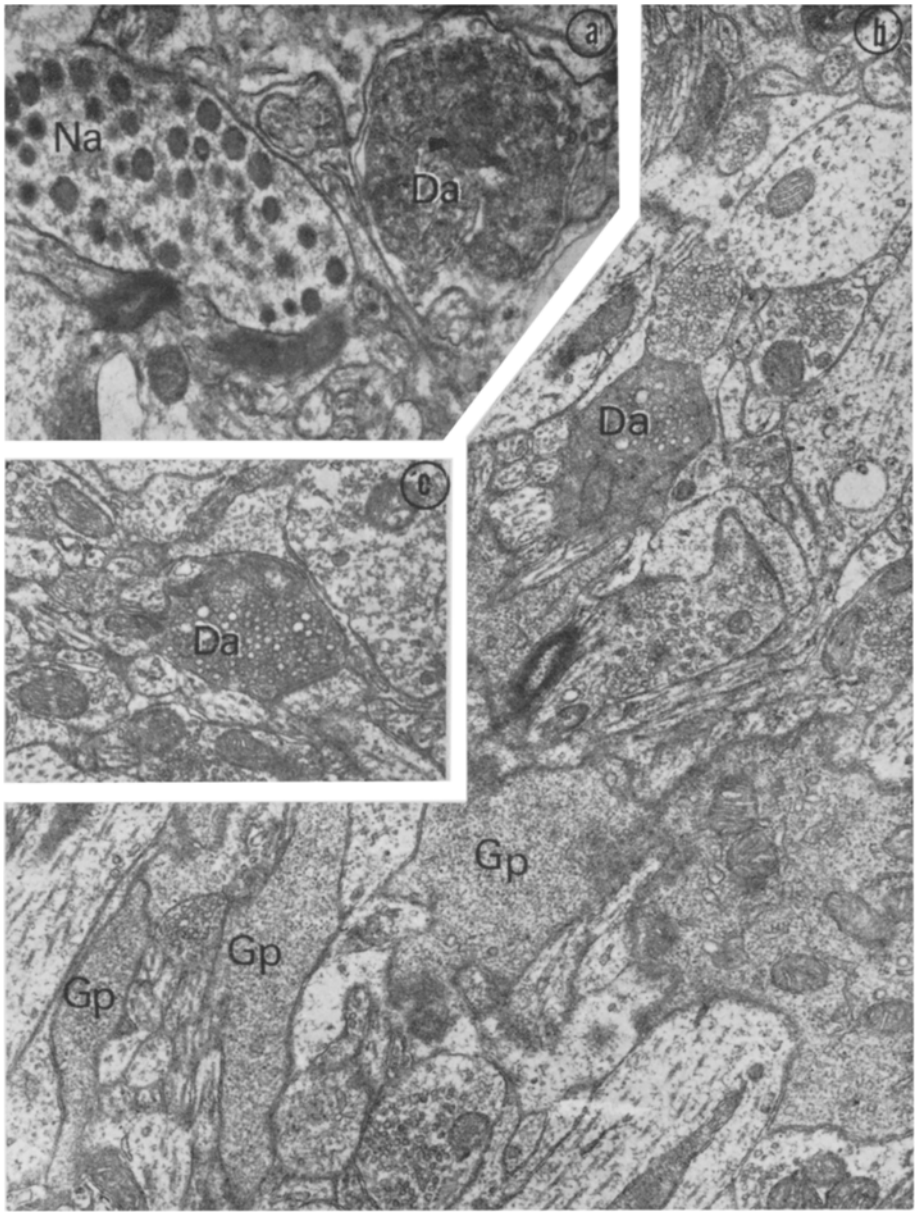

Fig. 2. a) Terminal degeneration in the lateral hypothalamic area. The degenerating axon (Da) is engulfed by glial process. Na, neurosecretory axon. ×22,140. b) Marked proliferation of ologodendroglial (Gp) cell processes in the ventromedial nucleus near to the lesion. ×22,356. c) A degenerating axon terminal is contacted by a dendrite in the arcuate nucleus. ×22,356. The animal was killed 72 h after GTG administration.

premamillary nuclei appear to send fibres into the median eminence[4,7–9].

Our electron microscopic data demonstrate that fibres originating from the ventromedial and arcuate nuclei terminate in the median eminence, dorsomedial nucleus and in cells located in the medial forebrain bundle. Rich intranuclear connections of arcuate and ventromedial nuclei were also verified.

Zusammenfassung. Durch die Gabe von Goldthioglucose bei Mäusen werden Läsionen im N. ventromedialis, N. arcuatus, N. premamillaris dorsalis und ventralis hervorgerufen. Die degenerierten Axonendigungen werden elektronenmikroskopisch in der Eminentia mediana, im N. dorsomedialis und an Zellen des basalen Vorderhirnbündels nachgewiesen. Degenerierte Synapsen sind auch im N. arcuatus und N. ventromedialis zu finden.

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