depressed or even abolished the evoked potentials in all experiments (Figure 3) with a maximum of 2–10 mni after injection (Figure 1, curve 4). The dosage-dependent alteration of the evoked responses corresponds to the diverging results obtained with LSD[1–8], with DMT only a depression was observed in optically[4] and acoustically[20] evoked potentials. Extent of diminution of evoked potentials and time of recovery were dependent on given dosage, but again the first injection was more effective than the following applications. The increase of evoked responses observed in 2 experiments with low dosage of DMT may be due to the depressing effect on spontaneous background activity leading to an improved signal to noise ratio in the primary afferent channel. With higher dosage the transmission in the synapses of the sensory pathway is increasingly impaired and this results in a diminution or even abolition of the evoked potentials.

Discussion. It is evident from our results that DMT in dosages leading to hallucinations in man does not affect only the synaptic transmission in the lateral geniculate body but also the phasic response and the spontaneous activity of retinal ganglion cells. The depressing effect of DMT on the spontaneous activity is in correspondence with its action on other neurons[14,17], but does not fully agree with the LSD results of MOURIZ-GARCIA et al.[8]. The DMT-caused alteration of the spontaneous activity might be of some relevance for the origin of optic hallucinations: as described previously[18,21,22], maintained illumination decreases the discharge rate of retinal ganglion cells; the depression of the spontaneous activity caused by DMT might be interpreted by the brain as 'light' and this may contribute to the origin of abnormal reactions within brain structures which are also influenced, leading to hallucinations. Basing on the known interaction of LSD and DMT with 5-HT in other brain regions, especially raphe neurons[14,15], and on the activity depressing effect of intracarotidal 5-HT on retinal ganglion cells[23], the DMT action on the activity of retinal neurons may be interpreted as indirect evidence for the existence of 5-HT as a transmitter in those retinal synapses, which are of special importance for the origin and/or transmission of spontaneous activity. That 5-HT was not yet found may be due to the high incidence of dopaminergic neurons in the retina[24], by whose fluorescence 5-HT terminals may be concealed[25].

Zusammenfassung. Intravenöse Injektionen von DMT (1–5 mg/kg) bewirkten neben einer Verkleinerung der visuell evozierten corticalen Potentiale und der lichtinduzierten phasischen Reaktionen retinaler Neurone auch eine starke Verminderung der Spontanaktivität in Einzelfasern des N. opticus. Die Befunde sprechen für eine Beteiligung retinaler Mechanismen beim Zustandekommen optischer Halluzinationen und lassen 5-HT als retinalen Transmitter vermuten.

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[20] O. H. ARNOLD, K. BURIAN, G. GESTRING, O. PRESSLICH and B. SALETU, Electroenceph. clin. Neurophysiol. *30*, 170 (1971).
[21] W.-D. HEISS and H. BORNSCHEIN, Pflügers Arch. ges. Physiol. *286*, 1 (1965).
[22] R. W. RODIECK, J. Neurophysiol. *30*, 1043 (1967).
[23] M. STRASCHILL, Vision Res. *8*, 35 (1968).
[24] S. G. KRAMER, Invest. Ophthal. *10*, 438 (1971).
[25] K. FUXE, T. HÖKFELT and U. UNGERSTEDT, Adv. Pharmac. *6A*, 235 (1968).
[26] Supported by the Österreichischen Fonds zur Förderung der wissenschaftlichen Forschung.

Effect of Hydrocortisone on the Ultrastructure of the Small, Granule-Containing Cells in the Superior Cervical Ganglion of the Newborn Rat

Small cells with an intense formaldehyde-induced catecholamine fluorescence are present amongst sympathetic nerve cells in the superior cervical ganglion of adult[1,2] and newborn[3] rats. Electron microscopic studies have shown that these cells contain round granular vesicles, about 100 nm in diameter, in the ganglia of both adult[4] and newborn[5] rats. Administration of hydrocortisone has been shown to cause a 10-fold increase in the number of the small, intensely fluorescent cells in the sympathetic ganglia of newborn, but not adult, rats[6]. The present study was undertaken to investigate the ultrastructure of such newly formed catecholamine-containing cells.

Twelve newborn rats of the Sprague-Dawley strain were i.p. injected with 20 mg/kg body weight of hydrocortisone acetate daily for 7 days. They were killed 1 day after the last injection, together with untreated controls of the same age. The superior cervical ganglia were removed and processed for electron microscopy using a procedure generally found useful in the present laboratory[7]. Following a brief initial fixation in 1% osmium tetroxide in 0.1 *M* phosphate buffer (pH 7.4), the tissue was diced and replaced in the same fluid for 30 min; it was then washed in the buffer for 10 min and post-fixed in buffered 5% glutaraldehyde for 30 min. After a 10 min buffer wash the tissue was replaced in buffered 1% osmium tetroxide for 30 min. Following a short rinse in distilled water, it was block-stained in aqueous saturated uranyl acetate for 1 h, dehydrated in a graded acetone series, infiltrated in a mixture of equal volumes of acetone and Araldite, and finally embedded in Araldite. Thin sections were cut with a Huxley-Cambridge ultramicrotome, double-stained with a satured aqueous solution of uranyl acetate followed by lead citrate[8] and subsequently examined with a Hitachi 11 B electron microscope.

Small, granule-containing cells with typical appearance[4,5] were observed in the control ganglia. In the ganglia of the hydrocortisone-treated rats, the small granule-containing cells were much more numerous; a cluster of such cells in the ganglion of a hydrocortisone-injected rat is illustrated in Figure 1. Round vesicles with a dense core

[1] O. ERÄNKÖ and M. HÄRKÖNEN, Acta physiol. scand. *58*, 285 (1963).
[2] O. ERÄNKÖ and M. HÄRKÖNEN, Acta physiol. scand. *63*, 511 (1965).
[3] O. ERÄNKÖ and L. ERÄNKÖ, Progr. Brain Res. *34*, 39 (1971).
[4] M. R. MATTHEWS and G. RAISMAN, J. Anat. *105*, 255 (1969).
[5] L. ERÄNKÖ, Brain Res. *46*, 159 (1972).
[6] L. ERÄNKÖ and O. ERÄNKÖ, Acta physiol. scand. *84*, 125 (1972).
[7] J. W. HEATH, B. K. EVANS, B. J. GANNON, G. BURNSTOCK and V. B. JAMES, Virchows Arch. Abt. B. Zellpath., *11*, 182 (1972).
[8] E. S. REYNOLDS, J. Cell Biol. *17*, 208 (1963).

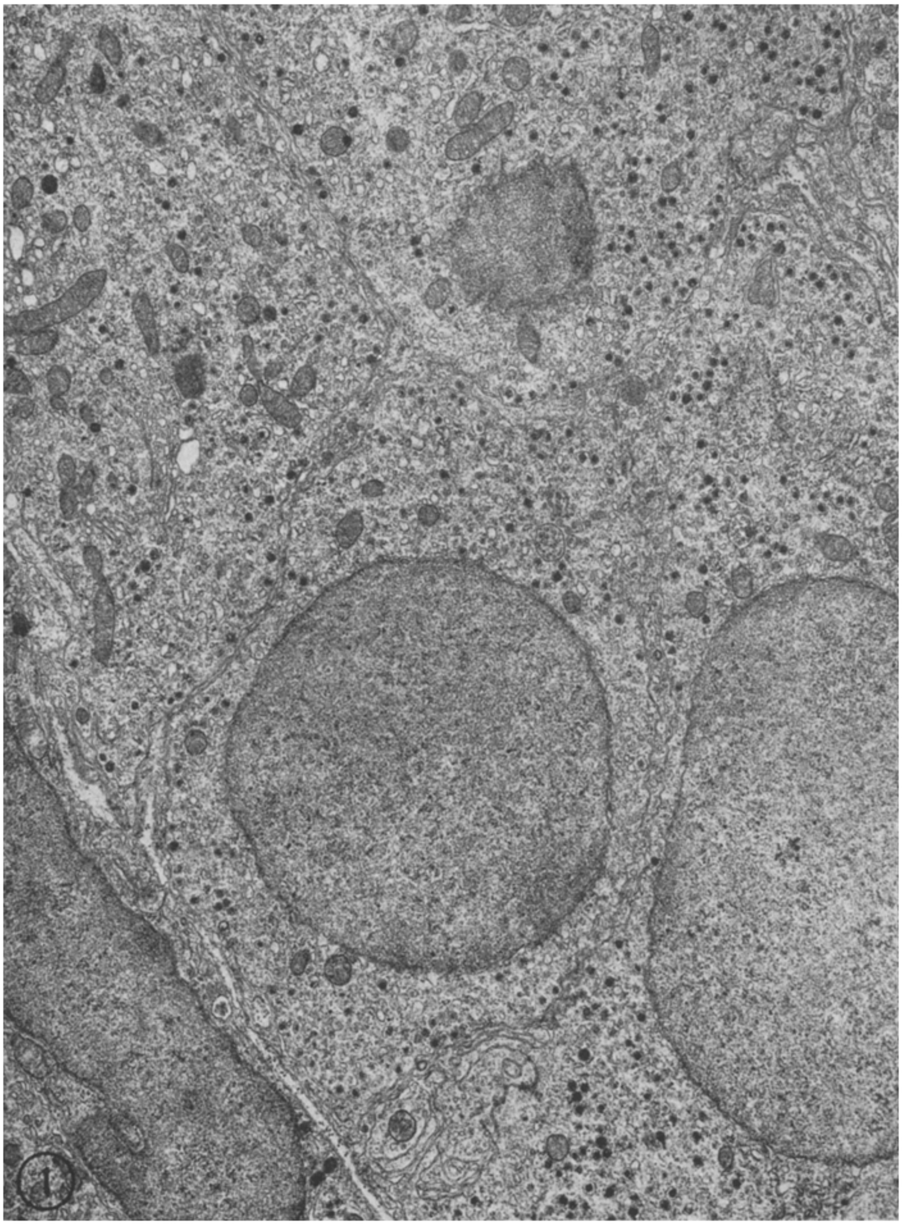

Fig. 1. Low power photomicrograph of part of a cluster of small granule-containing cells from a hydrocortisone-treated rat given 20 mg/kg hydrocortisone acetate daily for 7 days. × 13,000.

were seen throughout the cytoplasm, their number being increased as compared with those in the small granule-containing cells of untreated rats. The diameter of the granular vesicles was about 100 nm both in the control and in the hydrocortisone-treated rats (Figure 2a, b). The electron density of the contents of the vesicles ranged from low to high in both control and hydrocortisone-treated rats, but vesicles with cores of high density were much more numerous in the small granule-containing cells of the treated group (Figure 2b, cf. a).

The observation of the present study that hydrocortisone causes an increase, both in the number of the small granule-containing cells and in the number of the granular vesicles in them, strongly suggests that catecholamines in the newly formed cells are mainly stored in the granular vesicles (as in similar cells of normal rats), rather than in the cytoplasm outside them, an alternative considered earlier[6]. This is in agreement with the observations made in a recent study on the effect of hydrocortisone on cultures of newborn rat sympathetic ganglia, in which an increase in the number of the small, intensely fluorescent cells and in the intensity of their fluorescence was paralleled by an increase in the number of small granule-containing cells and an increase in the number of granular vesicles in them[9].

The significance of the variation in the electron density observed in the present study between individual granular vesicles of the hydrocortisone-injected rats may reflect either variation in the amine concentration of the central granule or differences in its amine composition. This matter should be further studied because the histochemical significance of the method of fixation employed in the present study (osmium-glutaraldehyde-osmium) has not been established. However, it is of interest that, in

[9] O. ERÄNKÖ, J. W. HEATH and L. ERÄNKÖ, Z. Zellforsch, *134*, 297 (1972).

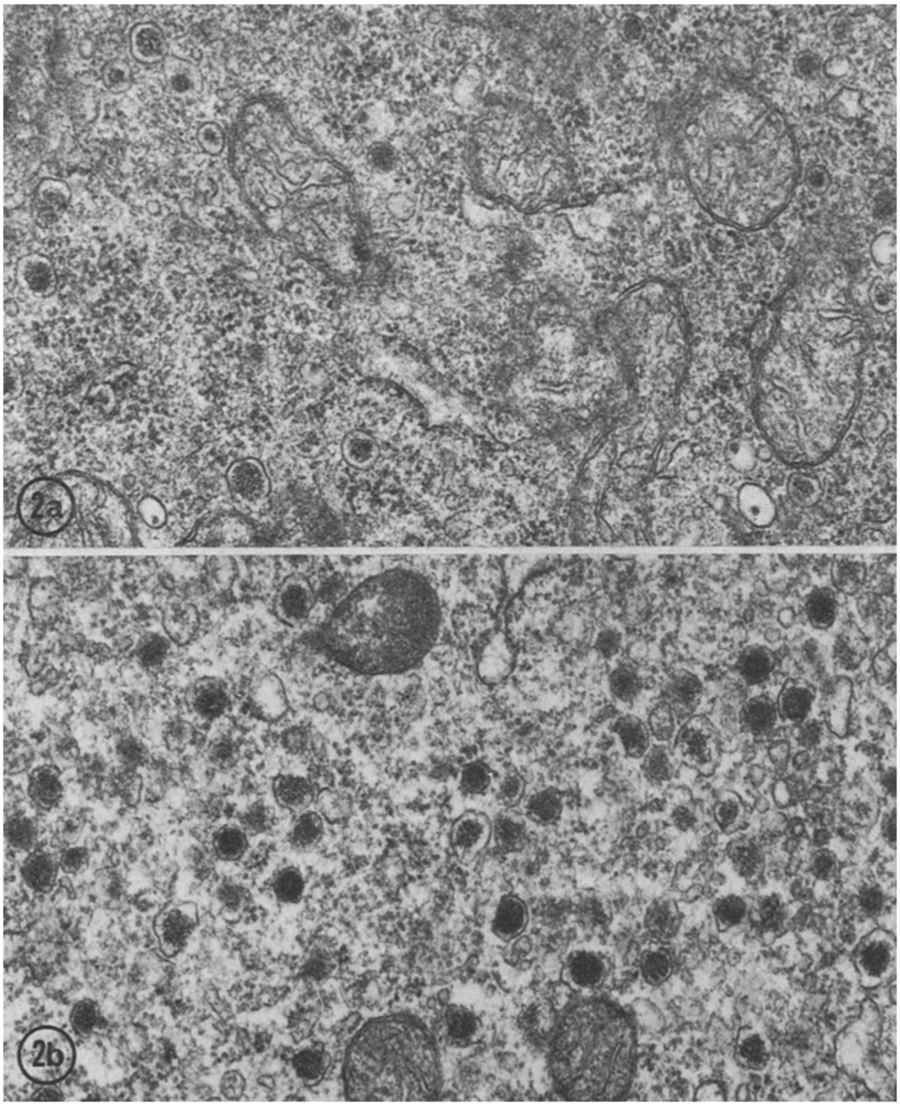

Fig. 2. Areas of the cytoplasm of small granule-containing cells. a) Control rat. The diameter of the granular vesicles is about 100 nm. The cores of the granular vesicles vary in electron density from low to high, but most cores are of low density. × 50,000. b) Hydrocortisone-treated rat. The diameter of granular vesicles and the range in electron density of their cores are similar to that of controls but most granular vesicles have cores of high density; 20 mg/kg/day hydrocortisone acetate for 7 days. × 50,000.

material fixed first in glutaraldehyde and then in osmium, the adrenaline-containing vesicles contain cores of low electron density and the noradrenaline-containing vesicles contain cores of high electron density[10,11]. Granules of both low and high density have been observed in the small granule-containing cells in hydrocortisone-containing cultures after glutaraldehyde-osmium fixation, while only highly dense granules were seen in control cultures[9]. Previous chemical observations have shown that hydrocortisone causes the appearance of adrenaline in the extra-adrenal chromaffin cells, which normally contain only noradrenaline, both in vivo[12] and in vitro[13], suggesting that hydrocortisone may cause the formation of adrenaline also in the small granule-containing cells of the sympathetic ganglia. However, the increase in electron density of the granular vesicles of the small granule-containing cells of hydrocortisone-treated rats observed in the present study using primary fixation in osmium tetroxide more probably reflects an increase in the amine concentration in the vesicles[14].

Zusammenfassung. Hydrocortison-Injektionen führen bei neugeborenen Ratten zu einer Vermehrung der kleinen granulahaltigen Zellen im Ganglion cervicale craniale und zu einer Vermehrung der granulären Vesikeln im Zytoplasma dieser Zellen.

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[10] R. E. Coupland and D. Hopwood, J. Anat. *100*, 227 (1966).
[11] H. Watanabe, Am. J. Anat. *130*, 305 (1971).
[12] O. Eränkö, M. Lempinen and L. Räisänen, Acta physiol. scand. *66*, 253 (1966).
[13] R. E. Coupland and J. D. B. MacDougall, J. Endocrin. *36*, 317 (1966).
[14] This study was supported by the National Health Foundation of Australia, the Australian Research Grants Committee and the Sigfrid Jusélius Foundation, Finland.
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