effect against epileptic seizures however they were evoked. On the contrary taurine and homotaurine were effective in the protection against the epileptic seizures evoked by cobalt, but were not effective against the physostigmine and strychnine evoked convulsions.

Nevertheless while taurine (0.5 g–3 experiments) had practically no protective action on the epileptic focus and was only partially effective on the diffusion of the seizure activity, homotaurine, at equimolecular doses (3 experiments), was totally effective against cobalt evoked seizures of both hemispheres. Furthermore the homotaurine perfusion caused a synchronized EEG tracing.

A single i.p. injection (100 mg/kg) of taurine or homotaurine, did not protect rats against convulsions due to hyperbaric oxygen, nevertheless, as shown in Table 1, homotaurine (500 mg/kg) given i.p. three times at 12 h intervals, significantly protected rats against hyperbaric oxygen convulsions.

In conclusion our results confirm the anticonvulsive action of taurine (Barbeau & Donaldson, 1973; Van Gelder, 1972) and show that homotaurine is considerably more potent than taurine in preventing epileptic seizures evoked by cobalt and hyperbaric oxygen.

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Brain levels of the potent analgesic etorphine in rats and their functional significance

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Pharmacological data and *in vitro* binding studies suggest the existence of specific opiate receptors. However, *in vivo* measurements of opiate narcotics in the CNS in general fail to correlate with the functional condition (e.g. analgesia, tolerance, dependence). Such a lack of correlation most probably results from the diffuse distribution of these compounds in tissues, with only a minor drug fraction attached to specific receptors.

With potent narcotics that are effective in very small doses and low total tissue concentration, the ratio between the amount of drug at receptor sites and the latter may be more favourable. Indeed this is somewhat substantiated with the potent morphine-like drug etorphine labelled with tritium ([^{3}H]-ET) in the work of Dobbs (1968), that we have confirmed and expanded using more reliable techniques (i.v. administration of [^{3}H]-ET and identification of [^{3}H]-ET in tissue by TLC).

Table 1 Effect of cyprenorphine on [^{3}H]-etorphine levels in rat brain

Expt. no.	Treatment (μg/kg) [^{3}H]-etorphine (i.v.)	Cyprenorphine	Brain levels of etorphine 15 min after injection (ng/g ± s.d.)	No. of animals
I	2	–	0.69 ± 0.03	4
	2	100 (i.p. 30 min before)	0.43 ± 0.09	4
II	20	–	8.87 ± 1.54	3
	20	100 (i.p. 30 min before)	5.89 ± 0.49	3
	20	400 (i.p. 30 min before)	3.38 ± 0.23	3
III	20	–	9.96 ± 2.78	4
	20	100 (i.v. 5 min after)	4.40 ± 1.34	4

Tritium labelled (15 and 16 position) etorphine, S.A. 3.6 Ci/mM was injected into male Sprague Dawley rats (180-200 g). Analysis consisted of liquid scintillation radioassay of TLC purified acetone homogenates of individual brains. The means relative to cyprenorphine treated animals were all significantly different ($P < 0.01$) from those of corresponding controls, based on Student's t test (expt. no. I and III) or analysis of variance (expt. no. II).

Table 1 shows that animals treated with the narcotic antagonist cyprenorphine (CYP) had reduced brain concentration of [^{3}H]-ET. After the injection of 20 μg/kg [^{3}H]-ET, brain levels in CYP pretreated animals were reduced to a different extent depending on the dose ratio [^{3}H]-ET/CYP (expt. II). Such a different degree of reduction in [^{3}H]-ET levels was consistent with the effectiveness of the antagonism (partial or complete inhibition of catatonia) elicited by CYP. The comparison of the results obtained with the dose of CYP constant (e.g. 100 μg/kg, expt. I and II) and changing the amount of [^{3}H]-ET injected, did not indicate a relation between the dose ratio [^{3}H]-ET/CYP and the degree of reduction of [^{3}H]-ET levels.

The brain/plasma ratio of [^{3}H]-ET was approximately the same (about 4 : 1) irrespective of whether 0.2, 2 or 20 μg/kg [^{3}H]-ET had been injected; after 20 μg/kg this ratio was determined up to 3 hours. Fifteen minutes after injection the distribution of [^{3}H]-ET determined in the brainstem, hemispheres, and cerebellum was uneven; they presented concentrations in decreasing order, the one of cerebellum being about one-third that of the brainstem. Similar ratios between the concentrations in these brain regions were found regardless of the dose of [^{3}H]-ET injected (0.2, 2 or 20 μg/kg). Pretreatment with CYP prior to the administration of 20 μg/kg [^{3}H]-ET resulted in the similar reduction of [^{3}H]-ET levels in all brain regions except the cerebellum; [^{3}H]-ET in the spinal cord was also reduced. Other antagonists (i.e. nalorphine and naloxone) were also effective in reducing [^{3}H]-ET brain levels, while no such reduction could be evidenced with agonists (i.e. morphine and heroin) using several dose schedules and experimental conditions.

In view of the latter finding, the reduction in brain etorphine levels by opiate antagonists that we have reported cannot be at present regarded as the result of displacement of etorphine from specific mutual binding sites and therefore its nature remains to be determined.

[^{3}H]-etorphine was kindly provided by Reckitt & Colman, Hull, England.

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Effect of growth hormone deficiency on brain serotonin metabolism

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In recent years considerable evidence has been accumulated for the participation of brain serotonin (5-HT) in the neurohormonal control of anterior pituitary function; less attention has been paid to the effects of hormones on central 5-HT metabolism. Such an aspect has been considered in this investigation which has explored the possibility that plasma levels of circulating hormones may influence brain 5-HT metabolism.

In Sprague-Dawley female rats, hypophysectomized (hypox) two weeks before, brain tryptophan (TP) and 5-hydroxyindolacetic acid (5-HIAA) were significantly higher than in age-matched intact controls: (TP 6.9 ± 0.3 vs 3.4 ± 0.2 μg/g; 5-HIAA 0.65 ± 0.02 vs 0.39 ± 0.01 μg/g, respectively). Brain 5-HT levels were practically unchanged.

Since no change in tryptophan hydroxylase activity has been reported following hypophysectomy, the present results on 5-HT metabolism in hypox rats, could be explained by an increased TP availability in brain serotoninergic neurones.

Among the several physiological factors whose lack could be responsible for the effect present after pituitary ablation, growth hormone (GH) deserves particular attention. It is known in fact that GH has a profound effect on amino acid disposition.

Treatment of hypox rats with bovine GH (NIH B-17, 1 mg i.p. daily x 7 days), reduced considerably brain TP and 5-HIAA (TP 4.9 ± 0.2 vs 7.1 ± 0.3 μg/g; 5-HIAA 0.54 ± 0.03 vs 0.64 ± 0.01 μg/g, respectively) and did not modify 5-HT levels.

These results suggest that GH deficiency could be responsible at least in part for the altered 5-HT metabolism present in hypox rats.

Consistent with this view are the findings that in mature female dwarf mice (dw/dw) of Snell-Bag strain, which are selectively deficient in GH, brain