mediate amino acid activating enzymes activities. The amino acid activating enzymes of cerebellum, medulla, and midbrain did not show differences as significant as the incorporation results of the protein of these areas. It seems possible that the results with amino acid activating enzymes represent differences in the enzymes content or variation in the stability of these enzymes. It is not surprising that parallelism does not generally exist between the incorporation results and amino acid activating enzymes activities of various brain areas. Amino acid activating enzymes may not be the limiting factor in protein biosynthesis and may be present in excess to incorporate a radioactive amino acid into proteins of the various brain areas. More definite differences may be in the activity and content of ribosome and transfer enzymes in various brain areas[18].

Zusammenfassung. Untersuchungen an Aminosäure-aktivierenden Fermenten in den diversen Kaninchenhirnregionen, haben gezeigt, dass die Aktivität der Grosshirnrinde am höchsten, die der weissen Substanz des Grosshirns am niedrigsten ist, während sie in den übrigen Hirnteilen in der Mitte liegt.

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5-Hydroxytryptamine Content of Glioma

It is not known whether 5-HT is located in excitable neural tissue or in other types of cell in the central nervous system. The results of experiments in which C^{14} labelled 5-hydroxytryptophan (5-HTP) was injected into animals and its subsequent distribution on autoradiographs examined[1] have suggested that 5-HT may be contained in the glial cells and that its chief action is on the blood vessels around which glial cells cluster.

Information relevant to the location of 5-HT in the central nervous system may also be sought in the 5-HT content of cerebral neoplasms of different cell types and the present study compares estimates of 5-HT in human tissues classified as 'normal' cerebral cortex, 'glioma' and 'meningioma'.

Neoplastic tissues were obtained from two female and five male patients at the time of operation. Their ages ranged from 19 to 71 years. The neoplastic tissues were all from cerebral cortical areas except in case No. 4 where the tumour involved the basal ganglia. The tumours were classified by histological examination of a piece of abnormal tissue adjoining that used for the pharmacological examination. Samples of normal cerebral cortical tissue were also obtained when their removal was necessary for access to the tumour.

The tissues on which 5-HT estimations were to be carried out were collected directly from the operating theatre in containers at 0°C. Pieces of approximately 1 g in weight were extracted with four volumes of acetone according to CORREALE[2] and within 30 min of removal from the body. The brain extracts were taken up in distilled water and assayed biologically on the rat stomach by the method of VANE[3]. The potency of each individual extract was estimated at least four times. Hyoscine 10^{-7} was present in the bathing solution and the active substance assayed was identified as 5-HT by the action of BOL 10^{-7} at the end of each experiment. The methods used have already been fully described[4].

It was necessary to confirm that 5-HT loss after surgical removal occurs at the same rate in normal and neoplastic tissues. Normal tissue left at room temperature (20°C) lost 19% of its 5-hydroxytryptamine content in 24 h whereas the glioma lost 27%. These values are of the same order as those previously reported for cerebral cortical tissues[4].

The results in the Table show the mean 5-HT concentration of extracts from several tissue samples from the same patient. With one exception (case No. 4) and regardless of the nature of the tumour, 5-HT concentrations were found to be lower in the neoplasm than in the adjacent cerebral cortex. The one neoplasm which showed a higher concentration of 5-HT differed from the others in that the tumour involved the basal ganglia. This patient had also previously received high doses of antibiotic (penicillin and streptomycin) and although the oral administration of antibiotics has been found to cause an increase in platelet 5-HT[5] but not of brain 5-HT, the possibility must be considered that if a rise in platelet 5-HT does occur, the concentration of 5-HT may consequently increase in an area such as a neoplasm where the blood brain barrier has suffered a local breakdown. The most pronounced behavioural disturbance was also seen in this patient (No. 4)

5-Hydroxytryptamine (5-HT) concentrations in normal and pathological tissues

Patient No.	Age	Sex	Tumour	5-HT mean ng/g wet weight ± SE (n) Normal frontal lobe	Temporal lobe	Tumour
1	67	F	Meningioma	36.5±3.5 (2)		18.5±3.5 (2)
2	59	M	Meningioma	38.0 (1)		23.5±1.7 (4)
3	23	F	Glioma	54.5±7.5 (2)		20.5±3.5 (2)
4	71	M	Glioma	30.0 (1)		84.3±5.5 (3)
5	27	M	Glioma	59.3±8.1 (4)		31.1±2.8 (5)
6	39	M	Glioma		47.5±3.5 (2)	29.7±0.5 (3)
7	19	M	Oligodendroglioma			16.0±1.0 (2)

[1] G. P. LEWIS, J. Pharm. Lond. *10*, 529 (1958).
[2] P. CORREALE, J. Neurochem. *1*, 22 (1956).
[3] J. R. VANE, Brit. J. Pharmacol. *12*, 344 (1957).
[4] D. JOYCE, Brit. J. Pharmacol. *18*, 370 (1962).
[5] T. J. SULLIVAN, Brit. J. Pharmacol. *12*, 344 (1961).

who suffered from dementia. The six other cases showed few or no mental symptoms.

The objection may be raised that any biochemical dissimilarities between normal and neoplastic tissues may result from the disease process and not from differences in cell constitution. Thus the fact that 5-HT was found in smaller quantities in gliomas than in normal brain does not prove that normal glia contain less 5-HT than nerve cells but constitutes suggestive evidence. It must be noted, however, that two instances of high pressor activity have been reported[5,6] in neoplastic tissues from a child. This is of interest because tumours from young adults or children are likely to be derived from embryonic tissue and are therefore more closely related to true nerve cells.

In this investigation the 5-HT content of both gliomas and meningiomas from adult patients was found to be lower than that of adjacent normal cerebral cortical tissue and the hypothesis that the distribution of 5-HT might be related to a cell type such as the glial cells was therefore not supported[7,8].

Résumé. La teneur en 5-HT de tumeurs intra-crâniennes humaines, déterminée par une méthode biologique, est en général plus faible que celle du cortex cérébral adjacent. Cette observation n'est pas en faveur de l'hypothèse que la 5-HT est localisée dans les cellules névroglies.

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[6] E. BÜLBRING, F. J. PHILPOT, and F. D. BOSANQUET, Lancet I, *1953*, 865.

[7] J. D. P. GRAHAM, Nature, Lond. *183*, 1733 (1959).

[8] This work was carried out at the Institute of Neurology, London. The author wishes to thank Mr. W. MCKISSOK for the human tissues and Dr. J. MARSHALL for helpful discussions. Messrs. May and Baker supplied the 5-hydroxytryptamine creatinine sulphate and generous financial assistance.

Effect of Lysine and Threonine Deficiency on the Endogenous Cholesterol Content of Rat Plasma and Liver[1]

An important stimulus to studies of the relationship between dietary proteins and cholesterol metabolism is the observation that not only the level but also the type of dietary protein is involved in the regulation of the serum cholesterol level in experimental animals (cebus monkey, rat, chicken) maintained on diets containing cholesterol[2,3].

More recently, data have been presented which would suggest that in essential amino acids deficiency, especially in the chicken, balance and imbalance may be of importance in the metabolism of endogenous cholesterol[4,5].

However, in reviewing animal and clinical studies, it appears that in the absence of cholesterol in the diet, relative deficiencies of lysine[4,5], methionine[4], tryptophan[4], and leucine[5] in chickens result in a hypercholesterolemic response, while in adult man fed a rice diet[6,7] which is lysine- and threonine-limited[8], and in children with kwashiorkor, a multiple amino acid deficiency disease, the serum cholesterol is low[9]. Further, the amounts of serum cholesterol, according to SINGAL et al.[10], do not differ in rats on amino acid rations deficient in lysine or in threonine from those observed in animals on an adequate amino acid ration.

In the present communication, the effect on the endogenous cholesterol metabolism in the rat, of low protein isonitrogenous diets deficient in or balanced in lysine and threonine is reported.

For this purpose, both liver and plasma cholesterol values are examined.

Methods. Twenty-four weanling male rats of the Wistar strain, weighing 40 ± 2 g were divided into two groups. The composition of the diets is reported in Table I. As is shown, the diets are isonitrogenous and, following ROSEMBERG et al.[11], lysine and threonine supplemented to obtain better growth and physiological levels of hepatic lipids.

The animals were weighed weekly during the six weeks experimental period, and the daily food consumption was calculated from weight.

Food and water were given *ad libitum*. At the end of the experimental period, plasma was obtained by using the procedure outlined by HANDLER[12].

Table I. Diets used

Ingredient %	1	2
White polished rice	89	89
Salt mixture[a]	4	4
Corn oil	3	3
Cod liver oil	1.5	1.5
Vitamine mixture[b]	1.5	1.5
Diammonium citrate	1	—
L-Lysine HCl	—	0.425
DL-Threonine	—	0.360

[a] K_2HPO_4 322 g, $CaCO_3$ 300 g, NaCl 167 g, $MgSO_4 7H_2O$ 102 g, $CaHPO_4 2H_2O$ 75 g, $FeC_6H_5O_7 6H_2O$ 27.5 g, $MnSO_4 H_2O$ 5.1 g, KJ 0.8 g, $CuSO_4 5H_2O$ 0.3 g, $ZnCl_2$ 0.25 g, $CoCl 6H_2O$ 0.05 g.

[b] At the 1.5% level, the vitamin mixture supplies per 100 g diet: Choline chloride 150 mg—inositol 75 mg—*p*-aminobenzoic acid 75 mg—α-tocopherol acetate 7.5 mg—nicotinic acid 3 mg—riboflavin 1.5 mg—calcium pantothenate 3 mg—thiamine 0.75 mg—pyridoxine hydrochloride 0.75 mg—menadione 0.375 mg—folic acid 0.075 mg—biotin 18.75 μg—vitamin B_{12} (0.1% triturate) 1.500 mg.

[1] Supported by grant from Consiglio Nazionale delle Ricerche, Roma.

[2] O. W. PORTMAN and F. J. STARE, Physiol. Rev. *39*, 407 (1959).

[3] R. E. OLSON and J. W. VESTER, Physiol. Rev. *40*, 677 (1960).

[4] D. JOHNSON JR., G. A. LEVEILLE, and H. FISHER, J. Nutrition *66*, 367 (1958).

[5] M. G. KOKATNUR and F. A. KUMMEROV, J. Nutrition *75*, 319 (1961).

[6] W. KEMPNER, Amer. J. Med. *4*, 545 (1948).

[7] R. E. OLSON, J. W. WESTER, D. GURSEY, N. DAVIS, and D. LONGMAN, J. clin. Invest. *36*, 917 (1957).

[8] R. J. PECORA and J. M. HUNDLEY, J. Nutrition *44*, 101 (1951).

[9] H. E. SCHENDEL and J. D. L. HANSEN, Metabolism clin. and exp. *7*, 731 (1958).

[10] S. A. SINGAL, S. J. HAZAN, V. P. SYDENSTRICKER, and J. M. LITTLEYDM, J. biol. Chem. *200*, 867 (1953).

[11] H. R. ROSEMBERG, R. CULIK, and R. E. ECKERT, J. Nutrition *69*, 217 (1959).

[12] P. HANDLER, J. biol. Chem. *173*, 295 (1948).