Table III. Distribution of HT in the sediment and in the supernatant of whole brain and 7 brain regions of Sprague Dawley rats, homogenized in a isotonic medium and centrifuged at 100,000 × g during 1 h

Region	HT (ng/g fresh tissue) Sediment a)	Supernatant b)	a/b	HT (%) Sediment	Supernatant
Cerebellum	16.1 ± 3.1 (4)	13.2 ± 0.1 (4)	1.3	54.9	45.1
Pons-medulla	20.8 ± 0.9 (4)	15.0 ± 1.4 (4)	1.3	58.0	42.0
Hippocampus	22.6 ± 2.5 (4)	15.9 ± 1.9 (4)	1.4	58.7	41.3
Cortex	25.4 ± 1.1 (12)	13.9 ± 1.5 (12)	1.8	64.6	35.4
Striatum	54.7 ± 1.4 (4)	20.1 ± 8.0 (4)	2.7	73.8	26.2
Thalamus	128.3 ± 10.6 (6)	46.3 ± 4.5 (6)	2.8	73.5	26.5
Hypothalamus	200.3 ± 12.3 (6)	56.8 ± 5.1 (6)	3.5	77.9	22.1
Whole brain	31.2 ± 0.7 (10)	13.6 ± 0.6 (10)	2.3	69.6	30.4

Homologous regions coming from more than 1 brain were grouped together; cortex, 2 brains; hypothalamus and thalamus, 4 brains; cerebellum, striatum, hippocampus and pons-medulla, 6 brains. Each value represents the mean ± S.E.M. Number of determinations in brackets.

studied, the highest HT levels are registered in the hypothalamus, as has also been demonstrated in the monkey[11] and man[12]. The concentration of HT in the thalamus takes second place in importance except in the New Zealand white rabbit. The HT levels of the striatum and the hippocampus are low and similar to those found in the cortex. Cerebellum, cortex and pons-medulla are poor in HT.

The regional levels of HT in the rat are conditioned both by the histidine concentration[9] and the histidine decarboxylase activity in each region[13]. These 2 parameters are also age-dependent.[9,10]. The regional distribution of the amine in other species could probably be determined by the some factors. In the Fauve de Bourgogne rabbit the regional distribution of HT could correspond to a pre-stabilization level, as the animals used were too young.

After homogenization of the brain of the rat in an isotonic medium and centrifugation at $10^5 \times g$, 70% of the HT was found in the sediment (Table III). An identical distribution was found by SCHANBERG et al.[14] in the case of serotonin. In all areas, the HT content in the sediment is higher than in the supernatant. The ratio, HT concentration in the sediment/HT concentration in the supernatant makes it possible to differentiate between the 2 types of structures: a) cerebellum, pons-medulla, hippocampus and cortex in which the HT concentration in the sediment is less than twice that in the supernatant, b) striatum, thalamus and hipothalamus in which the HT concentration in the sediment is more than twice that in the supernatant.

In the cortex[4] and hipothalamus[15], HT, like other biogenic amines, is found expecially concentrated in the subfractions rich in nerve endings. The analysis of the results of Table III shows that the regions rich in nerve endings have a higher concentration of HT in the sediment, the fraction in which the cell organelles are found.

The presence of the enzymes histidinedecarboxylase[16] and N-imidazolemethyltransferase[15] in the sediment, together with the fact that the intraperitoneal administration of 100 mg/kg of L-histidine, causes a rise in the levels of HT exclusively in this fraction[7], support the interpretation that the HT dectected in the supernatant is synthesized by some of the structures found in the sediment.

Resumen. En las especies estudiadas el hipotálamo es la región mas rica en histamina (HT). En la rata, la mayor proporción de HT se localiza en el sedimento de los homogenizados en medio isotónico centrifugados a $10^5 \times g$; la proporción de HT en el sedimento varia ampliamente de una región a otra.

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Evidence for an Adipokinetic Mechanism in the Ventromedial Hypothalamus

Long-term regulation of feeding appears to be controlled by adipose tissue metabolism. Rats which have been artifically fattened eat little while the excess fat is being catabolized[1]. Conversely, chronic diabetics are vigorous eaters[2,3], possibly because their fat stores are almost totally depleted. In normal animals, the circadian cycle of lipogenesis and lipolysis is paralleled by high and low feeding rates, respectively[4]. The ventromedial hypothalamus (VMH) appears to mediate these behavioral responses: After VMH lesions, rats do not adjust food intake appropriately in response to either body nutrient repletion[5] or depletion[6]. These feeding adjustments may be mediated directly by local nutrient transactions within the medial hypothalamus, for this area of the

brain can retain ^{14}C labelled nutrients to a greater extent than the rest of the brain[7]. The following experiment was designed to determine whether this retention capacity is a consequence of differential incorporation of D-glucose-^{14}C within a lipid subfraction of the medial hypothalamus. If that is the case, it would be conceivable that feeding behavior is controlled by a local adipokinetic mechanism within the brain.

Ten Sprague Dawley albino rats (mean weight $\pm$ SD: 273 $\pm$ 40 g) having free access to food and water were used. Half the animals were of each sex, but since no reliable differences were observed between the 2 groups, all data were pooled. All animals were stomach tubed with 20 μC of uniformly labelled D-glucose-^{14}C in 5 ml of 50% w/v unlabelled D-glucose; 6.5 h later, all animals were anesthetized with Nembutal; brains were removed and frozen. VMH and lateral hypothalamic (LHA) samples were dissected and weighed to 0.1 mg[7]. Individual samples were homogenized and separated by conventional extraction procedures into trichloroacetic acid (30%) soluble, chloroform-methanol (2:1 by volume) soluble, and residue fractions. The extracts were evaporated to dryness and dissolved in 0.3 ml of Soluene®. After addition of 3 ml of scintillation cocktail (4 g PPO and 0.2 g POPOP per liter of toluene), each sample was counted for 50 min.

In all fractions, VMH radioactivity was higher than LHA activity (Table) ($t > 3.90$, $df = 9$, $p < 0.01$, in all 3 cases, correlated t-test). Furthermore, the relative increase in the activity of the VMH lipid fraction, in comparison to the corresponding LHA extract, was reliably higher than the corresponding increases in either the acid soluble or residue fractions ($t > 2.61$, $df = 9$, $p < 0.05$, in both cases).

Although translation of this distribution differential into a behavioral cause is not yet possible, the distinct metabolism of the VMH suggests one unique mechanism whereby the regulation of energy intake may be accomplished: Namely, local VMH metabolism may parallel a critical peripheral process, possibly adipose tissue metabolism, and thereby keep account of lipogenic and lipolytic nutrient transactions within the body. Such a process could be mediated by the insulin sensitive cells which have been demonstrated to reside in the medial hypothalamus[8].

Zusammenfassung. Nach peroraler Verabreichung von ^{14}C-Glukose konnte in den Lipiden des ventromedialen Hypothalamus mehr Radioaktivität nachgewiesen werden als im lateralen Hypothalamus. Dies könnte ein Hinweis für eine Steuerung der Nahrungsaufnahme über den Lipidmetabolismus des medialen Hypothalamus sein.

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DPM ($\pm$ SEM)/10 mg tissue in TCA, chloroform-methanol and residue fractions of ventromedial and lateral hypothalamic brain samples and % differences

Fraction	VMH	LHA	$\frac{\text{VMH-LHA}}{\text{LHA}} \times 100\%$
Trichloroacetic acid	498 ($\pm$ 60)	402 ($\pm$ 34)	24.2% ($\pm$ 5.8)
Chloroform-methanol	317 ($\pm$ 23)	214 ($\pm$ 12)	48.3% ($\pm$ 8.3)
Residue	143 ($\pm$ 8)	115 ($\pm$ 6)	25.9% ($\pm$ 6.7)

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The Effect of Intracellular Potassium Ions on Active Sodium Efflux in Frog Sartorius Muscle

The ion sensitivity of sodium efflux from striated muscle has been the subject of several investigations[1-4]. The activation of sodium outward transport by external potassium ions is abolished by strophantidin[4,5].

While the effects of external Na^+- and K^+-ion concentrations on the glycoside-sensitive Na^+-extrusion have been studied in some detail[6], little is known so far about the effect of internal K^+-ions on active sodium efflux from muscle.

Material and methods. Using pairs of sartorius muscles from the frog *Rana temporaria*, parallel measurements of Na-efflux without and with strophantidin were made and the difference between the respective values was taken to give the data for active Na^+-efflux. The experimental methods were similar to those described by previous authors[4-6]. Muscles were loaded with potassium chloride by immersing them for 6 h in high potassium-Ringer[7,8], containing ^{22}Na. Thereafter the muscle was initially equilibrated for 20 min in non-radioactive solution at the experimental temperature of 20 °C. Measurements of the sodium efflux were then carried out over a period of 45 min at the external K^+ concentrations [K_0], given in the Figure, in presence or in absence of 10^{-5} strophantidin. The time course of the changes in internal potassium [K_i], was obtained from muscles loaded with [^{42}K]-potassium chloride, the ^{22}Na being absent in this case. The [K_i] of these muscles equilibrated with the ^{42}K-solution of known specific activity was computed from the radioactivity remaining in the muscle. In addition the electrolytes were measured at the end of the experiment from perchloric acid extracts with she aid of a Beckman DU

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