the genotypes or sexes, despite the fact that the urinary phenylketone excretion of *Dd*[1] females (14.5 ± 1.6 mg%) is almost twice that of *Dd*[1] (8.4 ± 2.1 mg%) males and therefore should have lower brain amines; it may be inferred from these results that a mechanism other than an altered brain amine content is responsible for the seizures. Analytical determination of pseudo(-cholin) esterases revealed, in confirmation of the results with the zymogram tests, a lower amount in *Dd*[1] (132.5 ± 19 mm³ CO_2 evolved/g brain tissue) than in *DD* (186 ± 13 mm³ CO_2)[10]; details of these findings and methodologies will be described elsewhere.

Abnormalities in esterases may correlate with myelin degradation which accompanies the disease; the fact that such abnormalities occurred in all of a number of clinically distinct neurologic disorders of *mice* and also multiple sclerosis of *man* is noteworthy and it may be assumed that non-specific esterases could have basic metabolic significance in normal myelin anabolism. Since it is unlikely that all mutations resulting in a neurologic disorder cause, among other disturbances, esterase deficiency, one may presume that it is a secondary (indirect) effect of the mutant gene.

Zusammenfassung. In Analysen von Gehirn-Zymogrammen verschiedener neurologischer Mäusemutanten wurden Abnormalitäten in Form von Esterasedefiziten gefunden. Da solche neulich auch für die multiple Sklerose des Menschen beschrieben wurden, wird vorgeschlagen, unspezifische Esterasen als signifikant für den normalen Myelinanabolismus zu bewerten.

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The Jackson Laboratory, Bar Harbor (Maine USA), March 20, 1964.

[10] J. P. DAVANZO and H. MEIER, unpublished results; detailed data and methods will be published elsewhere.

Effect of Feeding Pattern on Fatty Acid Oxidation by Rat Liver Slices

Intermittent starvation, i.e. the feeding pattern where periods of food intake alternate with periods of fasting, leads in rats to a series of adaptations which in many parameters differs from the sequelae of simple continuous caloric undernutrition[1]. Apart from a markedly enhanced lipogenesis[2] in intermittently starving rats the rate of oxidative tissue processes is increased, which manifests itself *in vitro* by a higher endogenous respiration of various organs[3] and a higher basal metabolism of the animal[4].

In the present work the *in vitro* oxidation of palmitate-1-C^{14} by liver slices of female Wister rats was investigated: (a) in intermittently starving animals fed during the first week on alternate days and for the rest of the experimental period three times a week; (b) in continuously underfed rats which received daily a reduced food ration, corresponding to $^1/_7$ of the amount ingested by the intermittently starving animals per week; (c) in *ad libitum* fed controls. All groups were given a standard laboratory diet[5] for a period of 7–8 weeks. In the subsequent experiments intermittently starving and *ad libitum* fed male rats were used, which received for a period of 5 weeks either a control diet[6] containing 20 cal.% protein, 20 cal.% fat and 60 cal.% carbohydrate (mainly starch), or a high-fat diet[6] containing 20 cal.% protein, 73 cal.% fat (mainly beef tallow) and 7 cal.% carbohydrate. In all experiments the total food intake in intermittently starving and continuously underfed rats was 30–40% lower than in the controls, which manifested itself by a lower body weight.

The animals were killed by decapitation either in a state of satiety, after having consumed a measured amount of food during the preceding night, or after a subsequent fasting. Liver slices were incubated for 2 h in Krebs-Ringer phosphate buffer with a complex of potassium palmitate (3 μC per sample), with albumin (2.5%); $C^{14}O_2$ was precipitated as $BaC^{14}O_3$ and its radioactivity was estimated. In parallel samples of the liver the protein, glycogen and fat content was estimated.

From the results summarized in the Table it is apparent that the liver slices of intermittently starving rats oxidized in all experimental series twice to three times as much palmitate as those of *ad libitum* fed controls or continuously underfed rats. This applied to the animals killed in a state of satiety as well as to those fasting for 16–48 h prior to sacrifice. The enhanced palmitate oxidation was also very marked in intermittently starving rats on the high fat diet, as compared with animals which ingested the same diet *ad libitum*. The oxidation values were in this case proportionally increased both in the intermittently and *ad libitum* fed groups, most probably as a manifestation of adaptation to a high fat intake.

Essentially the same increase in palmitate oxidation in intermittently starving rats was also found in subsequent experiments, where possible differences in the glycogen content (in fed animals) were compensated by the addition of glycogen to the incubation medium. As the protein and the fat content in the compared liver samples was practically equal, it is unlikely that the above results of palmitate oxidation were substantially influenced by the ratio of the main liver constituents.

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Effect of the feeding pattern on the *in vitro* oxidation of palmitate-1-C^{14} by rat liver slices

Experimental series	Feeding pattern	Diet[a]	Fasting prior sacrifice to (h)	$C^{14}O_2$ as percentage of activity added ± S.E.	P^c
I	Intermittent starvation	S	0	8.95 ± 0.61 (6)[b]	<0.001
	Continuous underfeeding	S	0	3.91 ± 0.33 (6)	
	Feeding *ad libitum*	S	0	3,78 ± 0.27 (6)	
II	Intermittent starvation	S	24	10.59 ± 0.53 (6)	<0.001
	Continuous underfeeding	S	24	2.75 ± 0.23 (5)	
	Feeding *ad libitum*	S	24	2.60 ± 0.25 (6)	
III	Intermittent starvation	S	48	11.21 ± 0.74 (6)	<0.01
	Feeding *ad libitum*	S	48	5.48 ± 0.40 (6)	
IV	Intermittent starvation	C	0	4.65 ± 0.29 (5)	<0.01
	Feeding *ad libitum*	C	0	2.90 ± 0.22 (5)	
	Intermittent starvation	HF	0	12.11 ± 1.13 (5)	<0.01
	Feeding *ad libitum*	HF	0	5.34 ± 0.52 (5)	
V	Intermittent starvation	C	16	6.46 ± 0.67 (5)	<0.01
	Feeding *ad libitum*	C	16	3.18 ± 0.74 (5)	
	Intermittent starvation	HF	16	12.18 ± 1.19 (5)	<0.001
	Feeding *ad libitum*	HF	16	4.76 ± 0.53 (5)	

[a] S = standard laboratory diet; C = control diet; HF = high-fat diet.
[b] Number of animals.
[c] Statistical significance of the difference between the intermittently starving group and the comparable *ad libitum* and continuously underfed group respectively. Differences between the *ad libitum* fed and continuously underfed groups are not significant.

The results obtained provide evidence that in addition to an increased formation of glycogen[7] and body fat[2], which are also found in other similar dietary patterns characterized by larger and infrequent meals[8], the feeding pattern used in our experiments also leads to an increased ability of the organism to oxidize available nutrients, including fatty acids. This metabolic change is further moderated by the composition of the diet, i.e. the predominant substrate available for tissue oxidation.

Zusammenfassung. Intermittierendes Hungern führt bei Albinoratten zu einer 2–3fachen Erhöhung der *in vitro* Oxydation von Palmitat-1-C^{14} bei Leberschnitten. Dies im Vergleich zu *ad libitum* gefütterten oder kontinuierlich unterernährten Tieren.

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Sleep Induced by the Administration of Melatonin (5-Methoxy-N-acetyltryptamine) to the Hypothalamus in Unrestrained Cats

The relatively high level of melatonin in the pineal gland of the mammalian brain[1] suggests that besides its inhibitory action on gonadal function[2] it may also play the role of a modulator substance within the central tryptaminoceptive structures postulated by Brodie and Shore[3]. The recent finding that it is capable of preventing thyroid hyperplasia caused by methylthiouracil[4] also suggests such a possibility.

In the present study, carried out upon 11 adult cats, micro-amounts (15–30 μg) of crystalline melatonin (used as free base) where administered directly through chronically implanted stainless steel cannulae into three subcortical structures according to Jasper, Ajmone-Marsan coordinates: preoptic region (F 14.5 to 15; L 2.5 to 4; H −3 to −4), nucleus centralis medialis (F 9; L 0.0; H 0.0) and to the brain stem reticular formation (F 2 to 3.5; L 3 to 4; H −2 to −2.5). The general behavior of the animals was observed in a relatively sound-proof box and EEG recordings made simultaneously. After 3–5

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