

The effects of dietary thiamin on voluntary ethanol drinking and ethanol metabolism in the rat

By K. ERIKSSON, LEENA PEKKANEN AND MAIJA RUSI

The Research Laboratories of the State Alcohol Monopoly (Alko), Box 350, SF-00101 Helsinki 10, Finland

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1. The influence of a deficiency or surplus of thiamin in the diet on voluntary ethanol consumption, ethanol elimination rate and blood acetaldehyde concentration was studied in rats.
2. Both the high-thiamin diet containing 20 mg thiamin hydrochloride/kg and the thiamin deficient diet containing no measurable thiamin produced obvious functional effects on thiamin metabolism in rat tissues after 4 weeks as demonstrated by measurements of the blood transketolase (sedoheptulose-7-phosphate: D-glyceraldehyde-3-phosphate glycolaldehyde-transferase; EC 2.2.1.1) activity and the extent of thiamin pyrophosphate-stimulation of the enzyme.
3. During the first week on the test diets the prospective ethanol free-choice groups had 1.72 M-ethanol as their only drinking-fluid. Subsequently they had a choice between ethanol and tap water for three weeks. During the free-choice period the rats on the high-thiamin diet drank only one-fifth as much ethanol as the rats given the optimum diet with 4 mg thiamin hydrochloride/kg.
4. The thiamin-deficient rats showed a significant tendency to increase ethanol drinking, when intake was expressed relative to total energy intake, but their intake of ethanol on a g/kg body-weight basis was approximately the same as that of the group given the optimum-diet.
5. The observed differences in voluntary ethanol drinking associated with different levels of dietary thiamin cannot be explained by changes in the ethanol elimination rate or the acetaldehyde accumulation in blood during the oxidation of ethanol.

Observations that dietary factors markedly alter the *ad lib.* consumption of ethanol by experimental animals presented with a choice of water and ethanol were first made nearly three decades ago. One of the first findings was that rats on diets lacking B-vitamins increased their voluntary ethanol intake (Brady & Westerfeld, 1947; Williams *et al.* 1949). On the basis of such observations Williams (1950) originated his genotrophic theory on alcohol consumption, in which a genetically-determined exceptionally-high requirement for some nutrient was suggested to be involved in the genesis of human alcoholism. Although Williams' (1950) theory as such has been rejected as being too simplified for the etiology of alcoholism in man, it has been repeatedly shown that with experimental animals voluntary consumption of ethanol can be clearly increased by dietary factors. Such increases have been reported with restricted food intake (Westerfeld & Lawrow, 1953), with a diet of poor nutritive value (Williams *et al.* 1955; Register *et al.* 1972) and with diets relatively high in fats (Pekkanen *et al.* 1978), low in carbohydrates (Lester & Greenberg, 1952), high in proteins (Mirone, 1957; Brown & Hutcheson, 1973), deficient in B-vitamin complex (Brady & Westerfeld, 1947) or deficient in specific B-vitamins, such as thiamin, riboflavin, pyridoxine or niacin (Mirone, 1957; Brown, 1969). Correspondingly, voluntary ethanol consumption has been shown to return to the initial level after supplementing the deficient diets with B-vitamins (Beerstecher *et al.* 1951; Mardones, 1951; Register *et al.* 1972). In particular, the deficiency of thiamin has been associated with an increase in voluntary ethanol drinking in animals (Beerstecher *et al.* 1951; Mardones, 1951; Purdy & Lee, 1962; Brown, 1969) although there is some evidence suggesting a more complex relationship (Senter & Sinclair, 1968; Bass & Lester, 1977). The effect of very high levels of thiamin on ethanol consumption

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in intact animals had not been previously examined and, therefore, was studied in the present experiment.

Of the possible mechanisms regulating voluntary ethanol drinking of experimental animals we examined the changes in the levels of blood acetaldehyde during ethanol oxidation. It has been suggested that the level of blood acetaldehyde in some way limits the amount of ethanol an animal will drink (Schlesinger *et al.* 1966; Sheppard *et al.* 1970; Eriksson, 1973; Amir, 1977). Theoretically, dietary factors might be able to affect the accumulation of acetaldehyde during ethanol metabolism, since they are known to influence to some extent the rate of ethanol oxidation (Horn & Manthei, 1965; Pawan, 1968; Vitale & Coffey, 1971; Sedman *et al.* 1976; Lindros *et al.* 1977), which is one of the determinants of the acetaldehyde levels. One example is protein intake: low intakes cause a greater acetaldehyde concentration during ethanol oxidation and also reduce voluntary ethanol consumption (Lindros *et al.* 1977; Pekkanen *et al.* 1978). Consequently, in the present study, the effects of high and low thiamin intakes on acetaldehyde accumulation were examined to see if this was the mechanism by which voluntary ethanol consumption was affected.

MATERIALS AND METHODS

Test animals and diets

The test animals were 3-month-old male rats of a mixed strain derived from cross-breeding Wistar, Sprague-Dawley and Long-Evans animals in our laboratory (Eriksson *et al.* 1976). The animals were individually housed in galvanized cages with a mesh bottom in a room maintained between 22 and 24° and approximately 55% relative humidity. The ethanol free-choice situation, where animals can choose between water and 1.72 M-ethanol (100 ml/l) to drink, has been developed by Eriksson (1969) and has been described in more detail by Pekkanen *et al.* (1978).

The basal diet was made from vitamin-free casein (ICN Pharmaceuticals Inc., Cleveland, Ohio, USA), rice starch and maize oil so that 0.20 of the total energy was derived from protein, 0.65 from carbohydrate and 0.15 from fat. The energy content was 1420 kJ/kg fresh diet. The optimum-diet contained 4 mg thiamin hydrochloride/kg (Hoffmann-La Roche, Basle, Switzerland), 8 mg riboflavin (Merck, Darmstadt, Germany) and 15 mg nicotinamide (Hoffmann-La Roche), which were the highest recommendations for the rat in the nutrient requirement tables (Jelinek, 1967; Joubert, 1967; Coates *et al.* 1969; (US) National Research Council, 1972). The thiamin-deficient diet contained no added thiamin; and on analysis, neither the rice starch nor the diet as a whole contained detectable levels of thiamin. The high thiamin diet contained 20 mg thiamin hydrochloride/kg fresh diet, which was five times the optimum diet level. The exact content of other vitamins and minerals in the diets has been described previously (Pekkanen *et al.* 1978).

Experimental procedure

The rats were randomly assigned to six groups of eight to nine animals each: ethanol-high-thiamin, ethanol-thiamin-deficient, ethanol-optimum-diet, water-high-thiamin, water-thiamin-deficient and water-optimum-diet. The three groups given water were included to determine the effects of the test diets on growth rates, energy and water consumption and ethanol metabolism. For 3 weeks all groups received *ad lib.* access to the optimum diet and tap water, and then the groups were given their test diets for 4 weeks. During the first of these 4 weeks, the groups given ethanol had an ethanol habituation period in which 1.72 M-ethanol (100 ml/l) was their only drinking fluid, in order to get used to its taste and learn the physiological effects, and then during the remaining 3 weeks they had a choice between the ethanol and water.

Table 1. *Body-weights (g) of the rats at the beginning of the study (initial) and after receiving one of the test diets for 4 weeks (final)†*

(Mean values and standard error of mean; no. of animals/group in parentheses)

Dietary regimen		Initial body-wt.		Final body-wt.	
Drinking procedure	Thiamin status	Mean	SEM	Mean	SEM
Ethanol choice	Thiamin deficient‡ (8)	358	16	281	6**
	High thiamin§ (8)	360	17	379	15
	Optimum (8)	337	18	368	21
Without ethanol choice	Thiamin deficient (9)	362	8	266	11***
	High thiamin (8)	397	16	423	14
	Optimum (8)	355	23	382	24

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: ** $P < 0.01$, *** $P < 0.001$.

† For details, see pp. 3-7.

‡ Contained no detectable amounts of thiamin.

§ Contained 20 mg thiamin hydrochloride/kg.

|| Contained 4 mg thiamin hydrochloride/kg.

Measurement of ethanol elimination rate and blood acetaldehyde

Ethanol elimination rate and acetaldehyde were measured in the animals, first before the test diets were presented and then after the 1st, 2nd and 4th weeks on the test diets. The rats were injected intraperitoneally with 1.5 g 2.17 M-ethanol (100 g/l saline (9 g sodium chloride/l))/kg body-weight and the ethanol and acetaldehyde levels in the tail blood were measured 30, 100, 140, 180 and 220 min after the injection with head-space gas-liquid chromatography as described previously (Eriksson *et al.* 1977).

Measurement of blood transketolase (sedoheptulose-7-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde-transferase; EC 2.2.1.1) activity

At the end of the study the blood samples for enzyme assays were taken from the hearts of the Nembutal-anaesthetized animals. The erythrocyte transketolase activity was measured from the whole-blood haemolysate according to the methods of Schouten *et al.* (1964). The activity of transketolase was expressed in international units, where one international unit was defined as the number of μmol sedoheptulose-7-phosphate formed/min per l. The extent of enzyme saturation was determined by adding thiamin pyrophosphate (TPP) to the reaction: the TPP effect was expressed as the percentage increase in the production of sedoheptulose-7-phosphate in the presence of added TPP. The chemicals were obtained from Boehringer Mannheim (West-Germany).

Statistical treatment of the results

Because of the lack of homogeneity of variance, a non-parametric test, the Mann-Whitney U-test, was chosen for testing the statistical significance of the differences between the groups.

RESULTS

Body-weight and energy intake

Symptoms of thiamin deficiency in rats are characterized by loss of appetite, decreased intake of liquid and loss of ability to maintain their body-weights. In the present study the ethanol-thiamin-deficient group ate only 0.39 times as much food as the ethanol-optimum-diet group and lost a mean of 77 g body-weight; the water-thiamin-deficient group ate only

Table 2. Daily consumption of energy (kJ/kg body-weight) derived from food and ethanol of rats during the experimental periods†

Dietary regimen		Thiamin status		(Mean values and standard error of mean; no. of animals/group in parentheses)															
				Optimum-diet period			1st test-diet week: ethanol habituation						2nd, 3rd and 4th test diet weeks: ethanol free-choice						
				Food		Ethanol		Total		Food		Ethanol		Total		Food		Ethanol	
Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM		
Ethanol choice	Thiamin deficient† (8)	655	76	439	29***	145	10	583	37**	250	19***	62	11	312	27***				
	High thiamin‡ (8)	588	16	431	29***	128	11***	559	36***	629	38	10	1***	639	38				
	Optimum (8)	609	33	604	36	169	4	774	36	649	47	64	18	713	39				
Without ethanol choice	Thiamin deficient (9)	669	13	625	27***			625	27***	320	64**			320	64**				
	High thiamin (8)	544	44	562	28***			562	28***	622	30			622	30				
	Optimum (8)	569	28	757	43			757	43	669	39			669	39				

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: ** $P < 0.01$, *** $P < 0.001$.

† For details, see pp. 3-7.

‡ Contained no detectable amounts of thiamin.

§ Contained 20 mg thiamin hydrochloride/kg.

|| Contained 4 mg thiamin hydrochloride/kg.

Table 3. Daily consumption of water (ml/kg body-weight) and 1.72 M-ethanol (100 ml/l) of rats during the experimental period†
 (Means and standard error of mean; no. of animals/group in parentheses)

Drinking procedure	Dietary regimen		Optimum-diet period		1st test-diet week: ethanol habituation		2nd, 3rd and 4th test-diet weeks: ethanol free-choice		Total		
	Thiamin status	Water	Ethanol	Water	Ethanol	Water	Ethanol	Water	Ethanol	Water	
		Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Ethanol choice	Thiamin deficient, † (8)	78	5	61	4*	38	4*	26	5	64	6***
	High thiamin, § (8)	84	4	54	5***	73	5*	3	0***	76	5
	Optimum, (8)	86	5	73	2	58	6	30	7	88	3
Without ethanol choice	Thiamin deficient (9)	88	6	81	7	59	4**	59	4**	59	4**
	High thiamin (8)	77	6	81	8	81	6	81	6	81	6
	Optimum (8)	90	3	86	4	89	5	89	5	89	5

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

† For details, see p. 7.

‡ Contained no detectable thiamin.

§ Contained 20 mg thiamin hydrochloride/kg.

|| Contained 4 mg thiamin hydrochloride/kg.

Table 4. Effect of dietary thiamin level on rat erythrocyte transketolase (sedoheptulose-7-phosphate-D-glyceraldehyde-3-phosphate glycolaldehyde-transferase; EC 2.2.1.1) activity and on the percentage stimulation of the enzyme by addition of thiamin pyrophosphate (TPP stimulation %) to the reaction

(Means and standard error of mean; no. of animals/group in parentheses)

Drinking procedure	Dietary regimen		Transketolase activity (μmol sedoheptulose-7-phosphate/min per 1 haemolysate)				TPP stimulation %	
		Thiamin status	Activity without added TPP		Activity with added TPP		Mean	SEM
Ethanol choice	Thiamin deficient† (5)		Mean	SEM	Mean	SEM	Mean	SEM
	High thiamin‡ (6)		7.4	4.0**	16.4	4.2**	258	89*
	Optimum§ (6)		87.4	11.0**	89.5	11.0**	15	6*
Without ethanol choice	Thiamin deficient (7)		38.4	3.3	54.5	4.4	49	11
	High thiamin (7)		4.9	1.1***	12.5	1.5***	237	75***
	Optimum (7)		70.4	4.2***	85.0	6.3*	21	5***
			40.9	6.0	60.3	9.1	49	7

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† Contained no detectable thiamin.

‡ Contained 20 mg thiamin hydrochloride/kg.

§ Contained 4 mg thiamin hydrochloride/kg.

0.50 times as much as the water-optimum-diet group and lost a mean of 96 g (Tables 1 and 2). The food intake of both the thiamin-deficient groups were statistically significantly lower throughout the study ($P < 0.001$) compared to the corresponding optimum-diet group (Table 2). The total energy intakes of the two thiamin-deficient groups were almost exactly the same, but in spite of that the ethanol-thiamin-deficient group lost less weight. Though this loss is not statistically significant, it may suggest that the energy derived from ethanol can be used more efficiently by thiamin-deficient animals than the energy from thiamin-deficient food. Both thiamin-deficient groups showed a reduced total fluid intake (Table 3; $P < 0.01$).

Food intake decreased also in the two high-thiamin groups during the first week on the high-thiamin diet (Table 2; $P < 0.001$), but increased to the intake level of the corresponding optimum-diet group during the ethanol free-choice weeks. The high-thiamin groups showed no change in the total fluid intake (Table 3).

Activity of blood transketolase

The effectiveness of the test diets is also indicated by the changes in erythrocyte transketolase activities (Table 4). The thiamin-deficient groups showed significantly less activity both before ($P < 0.01$) and after ($P < 0.01$) the addition of TPP but a significantly greater percentage stimulation by TPP ($P < 0.05$). The low enzyme activity in the thiamin-deficient groups even after adding an excess of TPP into the reaction indicates a reduced synthesis or increased breakdown of the enzyme protein, which may also be partially the result of secondary nutritional defects induced by anorexia.

In the high-thiamin groups because of the greater amount of thiamin bound to the enzyme there was only a slight increase in the enzyme activity on addition of TPP. Consequently, a percentage stimulation by TPP was significantly lower both in the ethanol-high-thiamin group ($P < 0.05$) and in the water-high-thiamin group ($P < 0.001$) compared to the corresponding optimum-diet group.

Voluntary ethanol consumption

The voluntary ethanol intakes as measured with three different indices are shown in Table 5. A high intake of dietary thiamin was associated with a decrease in voluntary ethanol consumption. The reduction was seen during both the initial habituation week, when the ethanol solution was the only drinking fluid (energy from ethanol in Table 2; $P < 0.001$, and intake of 1.72 M-ethanol in Table 3; $P < 0.01$), and by all the different indices during the 3 weeks when there was a choice between ethanol and water, all three indices being statistically significant at $P < 0.01$ or $P < 0.001$ during the whole free-choice period and during the different free-choice weeks (Table 5).

The effects of thiamin deficiency were more complicated to interpret. There was little difference in the ethanol consumption expressed as g ethanol/kg body-weight between the thiamin-deficient and the optimum-diet groups at any time during the experiment. However, when ethanol drinking was related to the total energy or fluid intake, a slight tendency for an increase was seen. The increase relative to the energy intake was statistically significant during the 2nd ($P < 0.05$) and 3rd ($P < 0.05$) free-choice week and consequently, during the whole free-choice period ($P < 0.05$). The increase could be regarded as the result of reduced food intake.

Ethanol elimination rate and blood acetaldehyde

Table 6 shows the ethanol elimination rates and Table 7 the blood acetaldehyde levels 30 min after ethanol administration. The thiamin-deficient groups showed decreased ethanol elimination rates. The decrease in the thiamin-deficient group receiving ethanol free-choice

Table 5. Changes in daily free-choice consumption of 1.72 M-ethanol (100 ml/l) associated with dietary thiamin level
(Means and standard error of mean; no. of animals/group was eight)

Diet	Ethanol free-choice week	Energy from ethanol (% total)		1.72 M-ethanol intake (% total fluid intake)		Ethanol (g/kg body-wt.)	
		Mean	SEM	Mean	SEM	Mean	SEM
Thiamin deficient†	1st	11.2	1.4	30.7	5.0	1.67	0.32
	2nd	26.7	6.4**	40.4	7.9	2.35	0.68
	3rd	35.5	11.4*	52.9	11.4	2.32	0.50
	Whole period	19.0	2.9**	39.4	5.4	2.08	0.39
High thiamin‡	1st	0.9	0.1***	3.3	0.7***	0.20	0.04***
	2nd	1.7	0.4***	6.1	1.8**	0.35	0.11***
	3rd	2.0	0.4***	7.6	1.1**	0.47	0.07***
	Whole period	1.6	0.4***	5.9	1.1***	0.34	0.04***
Optimum§	1st	10.1	3.2	31.8	9.3	2.03	0.61
	2nd	8.1	2.9	30.6	10.7	2.10	0.71
	3rd	10.9	2.9	32.9	7.5	2.37	0.57
	Whole period	9.5	2.9	31.4	8.2	2.17	0.61

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† Contained no detectable thiamin.

‡ Contained 20 mg thiamin hydrochloride/kg.

§ Contained 4 mg thiamin hydrochloride/kg.

Table 6. *The ethanol elimination rates (mg/kg body-weight per h) of rats after intraperitoneal injection of 1.5 g ethanol†*

(Means and standard error of mean; no. of animals/group in parentheses)

Drinking procedure	Dietary regimen		After the optimum-diet period		After the 1st test-diet week: ethanol habituation		After the 2nd test-diet week: ethanol free-choice		After the 4th test-diet week: ethanol free-choice	
	Thiamin status	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
Ethanol choice	Thiamin deficient‡ (8)	305	6	302	4***	317	7	289	19*	
	High thiamin§ (8)	305	3*	306	9*	296	12	296	7*	
	Optimum (8)	321	6	332	9	320	5	321	6	
Without ethanol choice	Thiamin deficient (9)	311	3	318	5	298	7***	298	10*	
	High thiamin (8)	304	7	307	3	303	10**	318	10	
	Optimum (8)	322	11	315	10	334	5	324	7	

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† For details, see pp. 7-16.

‡ Contained no detectable thiamin.

§ Contained 20 mg thiamin hydrochloride/kg.

|| Contained 4 mg thiamin hydrochloride/kg.

Table 7. *The blood acetaldehyde levels (nmol/ml per kg body-weight) of rats 30 min after the intraperitoneal injection of 1.5 g ethanol†*
 (Means and standard error of mean; no. of animals/group in parentheses)

Drinking procedure	Dietary regimen		After the optimum-diet period		After the 1st test-diet week: ethanol habituation		After the 2nd test-diet week: ethanol free-choice		After the 4th test-diet week: ethanol free-choice	
	Thiamin status		Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Ethanol choice	Thiamin deficient † (8)		18	1	19	2	9	2**	15	3
	High thiamin § (8)		15	2*	16	2	27	6	16	5
	Optimum (8)		25	4	16	4	20	4	19	1
Without ethanol choice	Thiamin deficient (9)		21	6	22	4	10	2***	20	2
	High thiamin (8)		21	3	12	3	21	5	19	5
	Optimum (8)		20	3	13	2	22	2	15	3

Values were significantly different from those of the optimum-diet group by Mann-Whitney U-test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

† For details, see pp. 7-11.

‡ Contained no detectable thiamin.

§ Contained 20 mg thiamin hydrochloride/kg.

|| Contained 4 mg thiamin hydrochloride/kg.

was statistically significant compared to the optimum-diet group after the 1st ($P < 0.001$) and the 4th ($P < 0.05$) week on the thiamin-deficient diet, and in the water group after the 2nd ($P < 0.001$) and the 4th ($P < 0.05$) week on the thiamin-deficient diet. The ethanol elimination rate decreased also in the high-thiamin groups: in the ethanol free-choice group after the 2nd ($P < 0.05$) and the 4th ($P < 0.05$) week on the high-thiamin diet, and in the water group after the 2nd week ($P < 0.01$) on the high-thiamin diet compared to the corresponding values of the optimum-diet group.

The changes in the blood acetaldehyde levels did not follow the ethanol elimination rates very closely. In the thiamin-deficient group receiving ethanol free-choice, acetaldehyde in the blood during the ethanol oxidation decreased after the 2nd week on the thiamin-deficient diet ($P < 0.01$), when there was no change in the ethanol elimination rate. Conversely, in the high-thiamin groups, there were no changes in the blood acetaldehyde level while there were some decreases in the ethanol elimination rates. In contrast in the water-thiamin-deficient group, acetaldehyde was decreased after the 2nd week on the thiamin-deficient diet ($P < 0.001$), and the ethanol elimination rate was also decreased.

DISCUSSION

The test diets clearly produced functional changes in the tissue levels of thiamin, as indicated by the change in the activity and TPP saturation of the transketolase enzyme. Functional thiamin deficiency in the thiamin-deficient groups was also indicated by the reductions in food and fluid intake and body-weight.

In contrast to the previous studies (Beerstecher *et al.* 1951; Purdy & Lee, 1962; Brown, 1969) thiamin deficiency did not produce a clearly marked increase in voluntary ethanol consumption by all three different indices used in the present study. A significant increase can be seen when ethanol drinking is expressed relative to the total energy intake. Some tendency for an increase, even though statistically insignificant, can be seen also when ethanol intake is expressed relative to the total fluid intake. But the intake of ethanol on a body-weight basis was almost the same as in the optimum-diet group. Such discrepancy between the different measurements showed clearly how important it is to express voluntary ethanol consumption with different indices, especially in situations in which the body-weight and food and fluid intake are all changing. It should be noted that Brown (1969) found an increase in ethanol intake in female but not in male animals while Beerstecher *et al.* (1951) reported that the increase was not seen in all animals. It is possible that the discrepancy between the present results and those generally obtained may be due to the use of the ethanol habituation period before the ethanol free-choice period in the current study which has not been done in the other studies. However, the mechanism by which this procedure affected the results is not clear.

In the present study high thiamin intake was clearly associated with a reduction in voluntary ethanol drinking. In previous studies it has been found that adding thiamin to the diet of thiamin-deficient animals decreases their ethanol intake (Beerstecher *et al.* 1951; Mardones, 1951). Our results show that the decrease is not dependent on previous deficiency. The complexity of the situation is emphasized in a recent work of Bass & Lester (1977). The authors found that animals which had been forced to connect the effects of ethanol with recovery from thiamin deficiency, achieved by putting ethanol in the drinking water at the same time as injections of thiamin were given, increased their post-recovery ethanol drinking in a free-choice situation, while the formerly thiamin-deficient animals, whose recovery from thiamin deficiency was not paired with ethanol drinking, did not increase their post-recovery ethanol intake.

The mechanisms by which thiamin intake might affect voluntary ethanol drinking of experimental animals are not known. In the present experiment dietary thiamin levels did

not cause such significant changes in either ethanol metabolism or acetaldehyde levels in the blood, which could have been correlated with ethanol drinking. The decreased ethanol intakes by the high-thiamin rats cannot, therefore, be explained by their blood acetaldehyde levels, which tended to be slightly lower at the end of the experiment than those of the optimum-diet group. This is thus an exception to the general negative correlation seen between acetaldehyde levels and ethanol voluntary consumption (Schlesinger *et al.* 1966; Sheppard *et al.* 1970; Eriksson, 1973; Amir, 1977), and shows that ethanol drinking can be reduced by factors other than acetaldehyde accumulation during ethanol metabolism.

Purdy & Lee (1962) concluded on the basis of their pair-feeding experiment mentioned previously that an increase of ethanol drinking was a result of decreased food intake in the thiamin-deficient rats, since severe food deprivation alone has been shown to increase ethanol drinking (Westerfeld & Larrow, 1953). The applicability of this view that ethanol consumption occurs only as a means of obtaining energy has been criticized because even in a food deprivation situation more complicated mechanisms affecting ethanol drinking in animals are obviously involved (Palfai & Reckhow, 1977). In the present experiment the ethanol consumption of the high-thiamin rats was markedly lower even during the 1st week on the high-thiamin diet, when changes in energy metabolism probably would not have occurred. However, the theory relating energy requirement with ethanol consumption in animals cannot be totally ruled out. Ethanol may provide useful energy through metabolic pathways less affected by thiamin deficiency than metabolism of other nutrients, because ethanol can be metabolized to the Krebs' cycle without the thiamin-requiring pyruvate dehydrogenase (*EC* 1.2.4.1) reaction. Thus drinking ethanol may be useful for an animal by delaying the onset of thiamin deficiency symptoms. However, in addition to its role as one of the most essential vitamins in the over-all energy metabolism, thiamin has an important role in nervous function (Barchi, 1976), and the relation of the latter to ethanol drinking has not been studied.

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