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SPECIFIC HUNGER FOR THIAMINE:

VITAMIN IN WATER VERSUS VITAMIN IN FOOD[1]

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Young, thiamine deficient rats showed a marked and significant preference for diets containing any one of 3 concentrations of thiamine over thiamine deficient diets. The preference appeared whether arbitrary cues were paired with thiamine or not. Less than ½ of the Ss showed an immediate preference for the thiamine diet; more than ½ maintained their preference throughout the 2-week experimental period. In a parallel experiment with thiamine presented in one of 2 water sources, no preferences emerged. An aversion appeared at the highest concentration. It is concluded that thiamine intake is not quantitatively related to thiamine need and that an explanation of thiamine specific hunger in terms of learning by "need reduction" is inadequate.

Specific hungers for several dietary essentials have been reported (for a review see Morgan & Stellar, 1950). For example, rats made deficient in sodium (Richter, 1956) or one of several B vitamins (Scott & Quint, 1946) will manifest a marked preference for the needed substance. The mechanisms involved in this preference behavior are obscure. In particular, the relative roles of instinctive and learned recognition of the needed substance have not been determined. Investigation of the sodium specific hunger has indicated strong instinctive elements in the rat's preference for sodium under conditions of sodium need (Richter, 1956), but little work has been done on the mechanisms involved in other specific hungers.

This paper presents an initial analysis of the response of the vitamin B1 (thiamine) deficient rat to the needed vitamin. Thiamine was selected as the substance to be studied for the following reasons: (*a*) The existence of a specific hunger for vitamin B1 has been clearly demonstrated (Richter, Holt, & Barelare, 1937; Scott & Verney, 1949; Tribe & Gordon, 1955), and supported by evidence of a hunger for the vitamin B complex (Harris, Clay, Hargreaves, & Ward, 1933). (*b*) There is a relatively rapid partial recovery from thiamine deficiency following consumption of this substance. This makes a learning interpretation of thiamine preference in terms of reinforcement more reasonable than for other vitamins.

Scott and Verney (1947, 1949) found that the specific hunger for vitamin B1 in solid food appeared only in animals suffering from considerable thiamine depletion. Animals showed a preference (Scott & Verney, 1947) for an arbitrary flavor which was presented for a time with a diet containing thiamine. On the basis of these findings, it was postulated that the vitamin preference had been learned and had developed through the association of a "feeling of well being" with the ingestion of the thiamine diet (Harris et al., 1933; Scott & Verney, 1947).

The results of Scott's experiments are clear, but his interpretations do not necessarily follow from the results. In light of psychological data on the rat, the learning of a B1 specific hunger would be extremely difficult. This experiment was designed to analyze factors contributing to the B1 preference in deficient animals. The experimental design was similar to Scott's. His procedure was altered and supplemented in a number of significant ways: (*a*) A closer analysis of the data on individual *S*s was conducted in order to obtain more information concerning their daily intake patterns. It was hoped that a day by day analysis would clarify the manner in which the hun-

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ger emerges. (*b*) Thiamine was offered to some *S*s in one of two water tubes; for others it was incorporated in one of two solid diets. (*c*) For some *S*s, arbitrary distinctive cues (e.g., flavor, constant position) were paired with the choice containing thiamine, while for others no such cues were associated with the thiamine choice. The presence of arbitrary distinctive cues should facilitate the development of a learned preference, and help to maintain a preference once established. (*d*) Control *S*s were underfed and maintained at the same weights as deficient *S*s. The control *S*s were not deficient, and had never received thiamine by mouth before their preferences were tested.

Method

Subjects and Apparatus

At the start of the experiment, 90 weanling Sprague-Dawley albino rats of both sexes, aged 21–23 days, were placed in individual cages (10 × 8 × 7 in.). Food and water were always available to all *S*s. The cages were housed in a temperature controlled room with a constant (12 hr. light, 12 hr. dark) light cycle. The *S*s were weighed and the data collected at the same time each day. For basic maintenance, a synthetic B1 deficient diet was employed.[3] The diet was supplemented with varying amounts of thiamine during the food-choice experiments in a manner to be described below. The B1 concentrations chosen represent a range from minimal amounts for growth (1 μg/gm or ⅓ μg/ml) to excessive amounts (100 μg/gm or ml.). Thus, the low concentrations require exclusive selection for *S* to remain healthy and survive, while the high concentrations (100 μg.) provide adequate vitamin in minimal amounts.

Food-Choice Procedure

A 3-week control period followed immediately upon weaning. During this period each *S* was offered B1 deficient diet in two 2-oz. glass food cups. These cups were firmly attached to the front of each cage, approximately 2 in. apart. They were fitted with Bakelite tops in which holes about 1 in. in diameter had been drilled. During the 2-week test period following the control period, the situation was identical except that now only one of the cups contained deficient diet; this diet supplemented with thiamine in concentrations of either 1, 5, or 100 μg/gm was in the other food receptacle. For the last week of the control period, and the 2-week experimental period, food intake from each cup per *S* per diem was recorded. Spillage from each cup was collected and the appropriate compensation made. Occasionally, the spillage was contaminated by water or urine, so that accurate quantitative recovery could not be made. All *S*s were presented with cleaned cups and fresh food on the first experimental day. The appropriate type of fresh food was added to each cup daily after intakes were recorded. Thus, cups containing a preferred diet tended to hold fresher diet. Throughout the 5-week period, *S*s received water ad lib. from standard water bottles.

Ten experimental *S*s were run at each vitamin concentration. Five *S*s had a constant position design, and five a varied position design. In one condition, constant position, the position of the diet containing thiamine was constant for each *S*, either left or right. Each *S* had the same assignment of cups and tops to substances for the entire 2-week experimental period. As a further distinctive cue, the thiamine diets were flavored with .04 cc/kg of oil of anise extract. Rats neither prefer nor avoid anise in this concentration (Scott & Quint, 1946). In the varied position condition, the position of the diet containing thiamine was alternated daily from left to right. After recording intakes from the 5 thiamine and 5 deficient cups from a varied position group each day, the cups were refilled and each *S* was randomly assigned one weighed thiamine and one weighed deficient cup. The varied position groups thus received different cups from day to day, the position of the thiamine cup alternated daily, and no distinctive flavor was incorporated in the thiamine diet.

Five control *S*s were tested in the varied position paradigm for each vitamin B1 concentration. Each *S* was paired by sex and weaning weight to a partner in the experimental group of the same concentration. Throughout the control period, each was fed B1 deficient diet in two cups, in amounts so that his weight approximated the day by day weight of his experimental partner. In addition, each received 60 μg. of thiamine hydrochloride injected subcutaneously every 48 hr. from weaning to the end of the experimental period. This amount of thiamine is considerably in excess of the requirements of these *S*s (Brown & Sturtevant, 1949). Thus, at the start of the experimental period, the controls suffered from semistarvation analogous to that produced by the anorexic symptoms of the vitamin deficiency in the experimentals. Like the experimentals, they had had no previous experience with the thiamine diet. Yet in contrast to them, the controls were by no means vitamin deficient.

Forty-five rats, divided into nine groups of five each were *S*s for the food-choice tests. For each concentration, the groups were matched by sex and weaning weight. The combinations of conditions are summarized in Table 1. The code letters entered in this table will be used as group designations for the remainder of the article.

[3] The basic diet contained, per kilogram: vitamin free casein 250 gm., sucrose 656 gm., corn oil 30 gm., cod liver oil 20 gm., Hegsted salt mixture 40 gm., riboflavin 5 mg., pyridoxine 5 mg., nicotinic acid 50 mg., pantothenate 65 mg., biotin 0.5 mg., folic acid 0.5 mg., vitamin E 100 mg., vitamin K 5 mg., cystine 2 gm., choline 1 gm.

TABLE 1

GROUPS IN FOOD-CHOICE EXPERIMENT
5 Ss PER GROUP

Thiamine concentration µg/gm	Conditions		
	Deficient		Nondeficient
	Position constant	Position varied	Position varied
1	1-C	1-V	1-V control
5	5-C	5-V	5-V control
100	100-C	100-V	100-V control

Liquid-Choice Procedure

The liquid-choice experiment was analogous to the solid-choice experiment. During the 3-week control period, *S*s were offered water in two 100 ml. Richter tubes attached firmly to the front of each cage, approximately 2 in. apart. For the 2-week experimental period, water was available in one of the two tubes, and a thiamine solution of 1/3, 5, or 100 µg/ml in the other. The groups were tested under the position varied, position constant (plus anise .04 cc/l) and control conditions. Liquid intakes from each tube per *S* per diem were recorded for the last week of the control period and the 2-week choice period. It should be noted that in this experiment 1/3 µg/ml B1 was tested instead of the 1 µg/gm concentration of the solid-choice experiment. A concentration of 1 µg/gm would not require virtually exclusive choice of the thiamine source for survival. Rats ordinarily drink more water (milliliters) than they eat (grams) and the thiamine requirement (1 µg/gm) is proportional to the number of calories ingested. Throughout the 5-week experiment, all *S*s received the synthetic B1 deficient diet ad lib. from a single standard food cup.

TABLE 2

GROUP PREFERENCES IN SOLID-FOOD CHOICE EXPERIMENT

Group	Proportion days B 1 preferred[a]	χ^2	Total grams eaten	
			B 1	Deficient
1-C[b]	53.5/61	35**	425	92
1-V	49/68	13*	258	128
1-V control	32/70	.5	516	602
5-C	58/70	30**	958	110
5-V	51.5/70	15**	811	371
5-V control	26.5/70	4.1	533	660
100-C	65/70	51**	1001	179
100-V	64/70	48**	1008	187
100-V control	21.5/70	10*	540	757

[a] Equal intake counted as 0.5.
[b] Three *S*s died before end of experiment.
* $p < .01$ (two-tailed χ^2).
** $p < .001$ (two-tailed χ^2).

In order to minimize vitamin deterioration, the solutions were completely replaced daily. Tap water was added to a concentrated, stock thiamine solution, which itself was prepared twice weekly. The temperatures of water and vitamin solutions were equalized prior to presentation.

As in the solid-choice experiment, 45 *S*s, divided into nine groups of five each were tested. The three groups at each concentration level were again matched for sex and weaning weight. Experimental conditions and code letters for each group are similar to those in Table 1, but the letter "L" is added to distinguish them from *S*s in the food-choice experiment.

RESULTS

At the beginning of the 2-week test period, all experimental *S*s showed marked anorexia and weight loss, the usual first signs of vitamin B1 deficiency. Many of the *S*s spilled large quantities of food. Signs of peripheral neuritis and lack of grooming were not obvious in the 3-week deficient *S*s, but they did appear within the 2 experimental weeks in a few *S*s on the lowest B1 concentrations in food and water. Marked and rapid weight gain and reduction in the amount of food spilled almost invariably followed the ingestion of adequate amounts of thiamine during the test period. Only two *S*s, both in the 1-V group, continued to spill large amounts of food during a good part of the experimental period.

A highly significant preference for the thiamine diet was exhibited by each of the six experimental, solid-food choice groups (Table 2). In terms of total grams eaten in the 14-day test period, *every S* in the 5- and 100-µg. experimental groups preferred the thiamine diet. Fifteen of the 20 *S*s in these groups ate at least twice as much thiamine diet as deficient diet (Table 3). Eight out of 10 *S*s preferred the diet containing 1 µg. of thiamine, seven of these showing at least a 2:1 preference.

As indicated in Tables 2 and 3, none of the control *S*s showed a significant preference for the B1 diet. Each *S* ate approximately equal amounts of each diet or tended to prefer the diet deficient in thiamine.

The preference for the vitamin-rich diet among the experimental groups became *greater* as the concentration of the vitamin

TABLE 3
INDIVIDUAL PREFERENCES IN SOLID-FOOD CHOICE EXPERIMENT

Group	Overall 2:1 pref.[a]	Overall 50% pref.[b]	Terminal pref.[c]	Immediate pref.[d]
1-C	4	4	4	4
1-V	3	4	4	2
1-V control	0	2	0	0
5-C	5	5	5	1
5-V	3	5	2	0
5-V control	0	2	0	0
100-C	3	5	4	2
100-V	4	5	4	2
100-V control	0	1	0	0

[a] B 1 intake at least twice deficient intake (14 days).
[b] B 1 intake greater than deficient intake (14 days).
[c] B 1 intake at least twice deficient intake (last 4 days).
[d] B 1 intake at least twice deficient intake on both Days 1 and 2.

increased. At concentrations of 1 and 5 μg., greater preferences (in terms of number of days on which thiamine was preferred and total grams of each diet eaten) were associated with the constant position design. This effect was greatest for the 1 μg. group (Table 2).

Individual food-intake patterns for the 5-C and 100-V groups are presented in Figures 1 and 2. These figures show that the thiamine preference may develop in many different ways. In a number of instances, position preferences initially interfered with the development of a thiamine preference in the constant position paradigm. These position preferences were altered in favor of the side containing thiamine in all cases but one. This *S*, in the 1-C group, showed a clear aversion to thiamine, and had shown a distinct position preference in the control period to the side later containing the deficient choice. The *S* died after 1 week of the experimental period.

Twenty-three of the 30 experimental *Ss* maintained a clear preference for the thiamine diet until the termination of the experiment (Table 3). In doing so, the 100 μg. *Ss* ingested much more thiamine than they could possibly utilize. This result is interesting when it is considered that the control *Ss* as a group showed a slight aversion to the 100-μg. diet. Individual records of the experimental *Ss* show that no one pattern of food choice predominates in any given experimental situation. Eleven of the 30 *Ss* showed an immediate preference for thiamine, eating at least twice as much of the thiamine diet as deficient diet on both the first and second days (Table 3). Six *Ss* switched from an initial thiamine aversion to a preference, and four *Ss* went through a period of approximately equal intake from

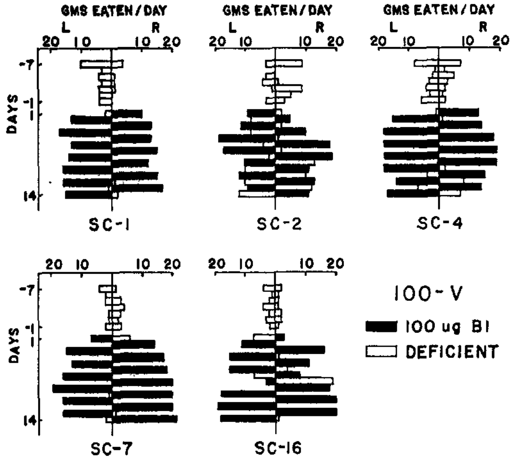

FIG. 1. Individual intake patterns for the five *Ss* in the 100-V group. (Days −7 to −1 are the last 7 days of the control period. Days 1–14 comprise the complete experimental period. For each *S* intake from the left cup is presented in the left column, and that from the right in the right column.)

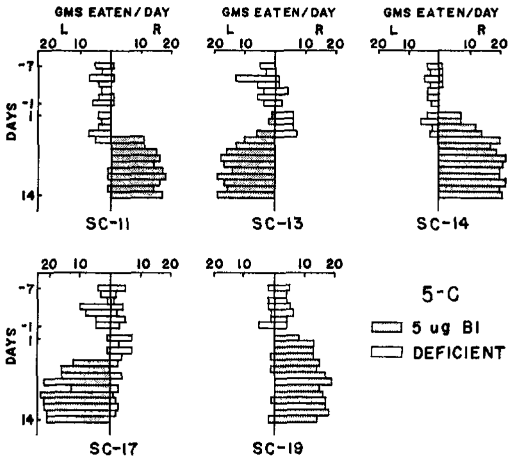

FIG. 2. Individual intake patterns for 5 *Ss* in the 5-C group. (Days −7 to −1 are the last 7 days of the control period. Days 1–14 comprise the complete experimental period. For each *S* intake from the left cup is presented in the left column, and that from the right cup in the right column.)

TABLE 4
Group Preferences in Liquid Choice Experiment

Group	Proportion days B 1 preferred	χ^2	Total ml. drunk	
			B1	Deficient
1/3-C-L[a]	20.5/57	4.5	149	184
1/3-V-L[a]	33.5/64	.14	247	241
1/3-V-L control	35/70	0	653	642
5-C-L	29/70	2.1	557	654
5-V-L	31/70	.91	715	736
5-V-L control	32.5/70	.36	564	615
100-C-L	28.5/70	2.4	547	820
100-V-L	20/70	13**	590	715
100-V-L control	14.5/70	24**	379	742

[a] Some data lost due to early deaths of some *S*s.
** $p < .001$ (two-tailed χ^2).

the two choices for at least 2 days before showing a preference, (e.g., SC-2, Figure 1; SC-14, Figure 2).

The results of the liquid-choice experiment were clearly negative. As Table 4 indicates, both controls and experimentals tended either to avoid the B1 solutions, or to drink these solutions and water in equal quantities. Out of 30 liquid-experimental *S*s one (in the 100-C group) showed a 2:1 preference for the thiamine solution. The 100-μg/ml solutions were clearly aversive to a number of *S*s. All experimental *S*s in the 5 and 100-μg. liquid groups recovered rapidly, showing significant weight gains on the first or second experimental day. None of the 1/3 μg/ml *S*s recovered significantly. Only 2 of the 10 *S*s survived the 14-day experimental period. Four *S*s died, and four were killed during the second week when they showed clear signs of severe, incapacitating deficiency (paralysis, convulsions, and extreme malnutrition).

Discussion

The results of the solid-choice varied position groups are in general accord with the parallel groups from Scott and Verney's experiment (1949). The increased preference for thiamine with increasing concentration that we observed was not reported by Scott and Verney. However, they recorded intake for a 3-week experimental period, and it is possible that preferences for the lower concentrations of the vitamin would remain for longer periods, and thus equalize an initial relative preference for higher concentrations. Scott and Quint (1946), using a choice between 5-μg. thiamine and deficient diets, state: "All the thiamine deficient animals began eating the thiamine containing diet almost exclusively on the first or second day (average 1.3 days) and continued to do so until the sixth to twenty first (average 12.2 days)." In our comparable 5-V group, no *S*s showed a marked (2:1) initial preference (Table 3), and only 11 of 30 experimental *S*s showed such a preference. The maintenance of preference through the 14-day experimental period in many *S*s is consistent with Scott's findings. We have confirmed Scott's basic finding, although our experiment differed from his in a number of ways. Scott and his associates used random alternation of cup positions, and seem to have used the same cups for each *S*. The strain of rats that they employed is not mentioned, nor is the manner in which spillage was handled.

In contrast to the general confirmation of Scott's results, the liquid-choice experiment yielded results contrary to those that would have been predicted from Richter's work (1956). Richter employed a different strain of rats and the concentration (1200 μg/ml) that they responded to dramatically was much higher than any we used. Furthermore, he has been unable to repeat this result.[4] Luria (1953) found that thiamine deficient rats pressed a lever for a thiamine solution (25 μg/cc of water) more than nondeficient rats. This result may have been due to activity level differences. She also claims that thiamine deficient *S*s show less habituation (less aversion developing over time) than nondeficient *S*s in a two water-choice situation with high concentrations of thiamine in one water tube.

In the varied position design, there were a number of cues that *S*s might have associated with the thiamine diet. In addition to the taste and smell of thiamine, the thiamine diet cups tended to contain fresher diet, once a preference for this diet was established in a group as a whole. This is a con-

[4] C. P. Richter, personal communication, 1963.

sequence of the fact that the food in the cups was not completely changed daily, but rather the appropriate diet was added to the remains in each cup daily. It is also conceivable that *S*s learned the daily alternation pattern. The improved performance of the 1 and 5 μg. groups under the constant position as opposed to varied position design implies that these *S*s had some difficulty in discriminating the thiamine in their diets, whereas there is no evidence for such difficulty with the 100 μg. concentration.

The great majority of workers in this area have expressed the view that the thiamine preference is learned, on the basis of the "feeling of well being" produced by ingestion of the vitamin (Harris et al., 1933; Scott & Verney, 1949). Scott and Verney (1947) reported that when thiamine was paired with an arbitrarily imposed distinctive flavor, and then dissociated from this flavor so that the vitamin was in one diet and the flavor in the other, a preference for the flavored diet appeared. This was the primary basis for their conclusion that the preference is a learned appetite. While this finding demonstrates that learning may be instrumental in the *maintenance* of the preference once established, it does *not* critically implicate learning in the initial development of the preference. It is entirely possible that *S*s recognized the thiamine, preferred this diet, associated the arbitrary flavor with the thiamine diet, and then followed the flavor because it was much more distinctive than the vitamin taste and smell.

The hypothesis that *S*s learn a thiamine preference *exclusively* through need reduction (i.e., the beneficial aftereffects of thiamine ingestion) is difficult to maintain in light of some of the evidence reported in this paper and in others. Such an hypothesis requires that a particular response, e.g., eating from a particular food cup, be reinforced by an internal event taking place, at best, minutes after the response has been emitted. Since the rat characteristically sniffs and samples both cups before settling down to one or the other, it is difficult to imagine how it would determine which response pattern was responsible for its physical improvement. Although there are many references to the striking and rapid recovery from deficiency symptoms following administration of thiamine to animals or humans, there is no accurate truly short-term, minute-by-minute record of recovery. Drury, Harris, and Maudsley (1930) found significant recovery from bradycardia in B1 or B complex deficient animals by 1 hr. after vitamin administration. Williams (1961, p. 92) refers to a case of dramatic recovery from infantile (human) beriberi within 30 min. of vitamin administration. However, assuming that effects may manifest themselves within 5–10 min. of ingestion, the establishment of the preference would be a learning feat unprecedented in the animal learning literature.

Four *S*s in our study went through at least 2 days of approximately equal intake of the two choices before showing a thiamine preference. These *S*s developed the preference after they had ingested much of both diets, and were increasing weight and food intake rapidly; in other words, the preference developed in these *S*s after they had made an initial spurt of recovery. The nature of the "need reduction" or "feeling of well being" in this case is unclear.

Finally, the liquid-choice *S*s at the 5 and 100 μg. levels recovered rapidly and yet did not display a preference for thiamine in solution. The ⅓-μg. groups did not recover substantially because they ingested insufficient amounts of the thiamine choice. Thus, under certain circumstances where recovery from deficiency is present, or possible, a preference does not develop. It is possible that a preference for thiamine in water could be demonstrated with different concentrations of thiamine. Richter, Holt, and Barelare (1937) reported such a preference with a very high concentration (1200 μg/ml) of thiamine in water. There may also be a critical low concentration in the range between 1/3 and 5 μg/ml where an adaptive preference would emerge. The 1/3 μg/ml concentration may not have produced a significant enough recovery, while no adaptive preference was necessary for recovery with the 5 μg/ml choice. In any event, it is possible that emergence of a preference based on need reduction was impaired in some way by the aqueous medium of presentation. The thiamine preference may only appear (whatever its mechanism) when the vitamin is presented in a nutritive medium, or in a solid medium. Alternatively, thiamine may only be recognized by a rat when it is hungry, and thus eating food, as opposed to thirsty, and drinking.

The data presented in this paper reveal some unexpected limitations on the conditions necessary for the emergence of a thiamine preference in thiamine deficient rats. The varied patterns of development of the preference, lack of preference when thiamine is in water solution and development of the preference in a few *S*s well on their way to recovery indicate that the mechanism may be complex, and that a simple and straightforward interpretation of the thiamine specific hunger as based on learning through need or drive reduction seems inadequate. The results indicate that when the specific hunger appears in rats, there is no evidence of *regulation* of thiamine intake. Data from the controls clearly demonstrate that the general nutritive lack produced by the anorexia of thiamine deficiency is insufficient cause for the emergence of a thiamine preference.

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