

ROLE OF VITAMIN E IN THE PREVENTION OF MUSCULAR DYSTROPHY IN GUINEA PIGS REARED ON SYNTHETIC RATIONS

MADSEN *et al.*¹ were the first to attain any notable success in inducing the guinea pig to eat synthetic rations. In the course of their experiments they observed the relatively early appearance of severe muscular dystrophy not unlike the lesions first extensively studied by Goettsch and Pappenheimer.²

When the cod liver oil was removed from the diet, being replaced by other substances which satisfied the A and D requirements, the dystrophies were not prevented but were very notably delayed. It was hence apparent that the dystrophies were not actually caused by the cod liver oil, although they were precipitated and exaggerated in some unknown way by it.

Some three years ago we began the study of the nutritional requirements of guinea pigs with synthetic rations. With a slight modification of the diet of Madsen *et al.*, we have had no difficulty in producing the early severe dystrophies of these observers. This animal material, with the particular diet employed—a diet in which the increased proportion of cod liver oil seems responsible for particularly early and severe dystrophy—appeared ideally adapted for experiments attempting evaluation of the possible role of vitamin E in the prevention of such dystrophies.

A year was spent demonstrating that the administration of 0.75 cc or even of 0.5 cc of wheat germ oil daily to guinea pigs on this diet prevented the development of dystrophies up to the 355th day of life, when the experiment was discontinued. The muscle creatine values in these animals were normal. The controls (without wheat germ oil) all developed typical early dystrophies and in each case were sacrificed when practically moribund at times varying from the end of the first to the end of the third month.

These encouraging results with wheat germ oil led us to a repetition of the experiment employing the pure substance, alpha tocopherol, instead of wheat germ oil. In the midst of this work, several important papers appeared, reporting the employment of alpha tocopherol. Barrie,³ as well as Goettsch and Ritzman,⁴ have shown that alpha tocopherol prevents the development of muscular dystrophy in suckling rats from mothers reared and held on low E—facts which we can confirm. Mackenzie and McCollum⁵ have also reported that alpha tocopherol cures the dystrophy which develops

in rabbits maintained on the Goettsch and Pappenheimer diet, supplemented with 10 per cent. ether extracted wheat germ.

Since Cummings and Mattill⁶ have shown that oxidative reactions initiated by the auto-oxidation of cod liver oil are destructive to vitamin E, we fed the cod liver oil (1 cc per os) and alpha tocopherol (3 mg per os) on alternate days. These guinea pigs likewise remained free of evidence of muscular dystrophy and have now been sacrificed on the 200th day of life, showing normal values for muscle creatine.

It is therefore apparent that in another animal form and with a particular dietary regimen in which an early severe dystrophy of the striated musculature invariably appears, alpha tocopherol acts effectively to prevent the dystrophy.

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A QUANTITATIVE STUDY OF MEANING BY A CONDITIONED SALIVARY TECHNIQUE (SEMANTIC CONDITIONING)

If a human subject has acquired a conditioned reaction to some specific verbal stimulus, let us say the sight of the word "cent," what will be the course of the generalization or the transfer of the conditioning to other words similar in meaning or in visual-auditory form? Will there be more transfer of conditioning to a word like "penny" than to a word like "scent" or will the reverse be true? A number of experimenters have established conditioned responses to verbal stimuli,¹ and most of them have noted transfer from conditioned sensory stimuli to their verbal correlates and *vice versa*.² But in no case was there any attempt to separate the semantic—or meaning-content—factor of the verbal conditioning from its mere visual-auditory form. It is clear, however, that such a separation lies well within the limits of the conditioning technique. By using, for instance, in the transfer tests one series

⁵ C. G. Mackenzie and E. V. McCollum, *SCIENCE*, 89: 370, 1939.

⁶ M. J. Cummings and H. A. Mattill, *Jour. Nutr.*, 3: 421, 1931.

¹ O. P. Kapustnik, in "Fundamental Mechanisms of Conditioned Reflex Activity in Children" (edited by A. G. Ivanov-Smolensky), Moscow-Leningrad, 1930, 11-22 (Russian); N. N. Traugott, E. P. Smolenskaya, N. N. Traugott and V. K. Fadeyeva, L. E. Khozak, T. V. Kovsharova, L. I. Kotliarevsky, in "Studying the Highest Forms of the Neurodynamics of Children" (edited by A. G. Ivanov-Smolensky), Moscow, 1934, 273-450 (Russian); C. V. Hudgins, *Jour. Gen. Psychol.*, 8: 3-52, 1933; G. H. S. Razran, *Arch. Psychol.*, 28: 1-124, 1935; R. Menzies, *Jour. Psychol.*, 4: 75-120, 1937; K. Diren, *Jour. Psychol.*, 3: 291-308.

² Kapustnik, Traugott, Smolenskaya, Traugott and Fadeyeva, Khozak, Kovsharova, Kotliarevsky, Diren and Razran, *loc. cit.*

¹ L. L. Madsen, C. M. McCay and L. A. Maynard, Cornell Univ. Agric. Exp. Sta. Memoir No. 178, 1935; L. L. Madsen, *Jour. Nutr.*, 11: 471, 1936.

² M. Goettsch and A. M. Pappenheimer, *Jour. Exp. Med.*, 24: 145, 1931.

³ M. M. O. Barrie, *Nature*, 142: 799, 1938.

⁴ M. Goettsch and J. Ritzman, *Jour. Nutr.*, 17: 371, 1939.

of words that are similar to the conditioned word in meaning but differ from it in verbal form and another series that are similar in form but differ in meaning, the conditioning values of the two factors may be readily compared and the amount of pure semantic—or meaning—conditioning easily determined.

A preliminary study of this rather significant problem was thus undertaken by the writer with the aid of a list of homophones and synonyms and with the use of salivation as the conditioning technique. Four simple words—*style*, *urn*, *freeze* and *surf*—were flashed on a screen at random order before three subjects who were chewing gum, sucking at lollipops or eating small tea-sandwiches. The subjects' individual eating periods lasted three minutes, in the course of which each word-to-be-conditioned was flashed fifteen times, and altogether five eating periods were made in each experimental session. After each eating period came an eight-minute testing period, during which the subjects' salivations to the exposed words were determined. The determinations were made by means of the writer's "cotton" technique that consists in ascertaining increments in weights of dental cotton rolls inserted under the subjects' tongue for periods of one minute. (With the use of proper control and rotation this technique is highly satisfactory and reliable.) The subjects were not aware of the attempts to condition them and were told that the purpose of the experiment was "to study the effect of eye-fatigue upon digestion." They became conditioned rather quickly, after two or three eating periods, but the tests with the transfer words were begun only on the second experimental session. The transfer words were: *stile*, *fashion*; *earn*, *vase*; *frieze*, *chill*; *serf*, *wave*.

TABLE 1

CONDITIONED SALIVATIONS OF 3 ADULT HUMAN SUBJECTS TO 4 WORDS, THAT HAVE BEEN FLASHED ON A SCREEN WHILE THE SUBJECTS WERE EATING, AND TO 4 HOMOPHONES AND 4 SYNONYMS OF THESE WORDS*

Words	Experimental session				Mean
	2	3	4	5	
Style	234mg.	276	293	218	255
Stile	57%	51%	43%	49%	50%
Fashion	64%	76%	66%	69%	69%
Urn	186	199	234	223	211
Earn	41%	34%	26%	34%	34%
Vase	50%	54%	48%	44%	49%
Freeze	268	308	314	246	284
Frieze	38%	32%	45%	46%	40%
Chill	43%	56%	68%	72%	60%
Surf	190	230	240	310	243
Serf	24%	20%	18%	28%	23%
Wave	46%	52%	68%	58%	56%
Mean for conditioned words	220	253	270	249	249
Mean for homophones	40%	34%	33%	39%	37%
Mean for synonyms ..	51%	60%	63%	61%	59%

* Each entry is a mean of 9 determinations and represents milligrams of net conditioned salivation (minus control salivation) in one-minute periods (the entries for the homophones and synonyms are given in percentages of the main conditioned salivation).

The results are presented in Table 1. The entries

in this table are means of nine determinations, three for each of the three subjects. The entries for the conditioned words, or the words that have actually been associated with the eating, are given in milligrams of net conditioned salivation (minus control salivation) per one-minute periods. The entries for the transfer words are in percentages of salivation of the conditioned words. As seen from the table, by far the greater portion of the transfer conditioning went to the synonyms rather than to the homophones. The average transfer to the former was 59 per cent. and to the latter only 37 per cent., quite a pronounced difference. Furthermore, there was also some evidence that, as the conditioning progressed, the homophones lost some of their transfer and the synonyms gained. Again, while the amount of transfer for different synonyms varied considerably, ranging from 43 per cent. for *freeze-chill* in the first experimental session to 76 per cent. for *style-fashion* in the second experimental session, still in no case was the transfer for any homophone greater than that for its corresponding synonym. Within the limits of the present study the conclusion seems thus to be warranted that verbal conditioning is primarily semantic.³ A subject gets more conditioned to the meaning of a word than to its mere visual-auditory form (although this pure form conditioning is, as seen from the table, by no means negligible). At any rate, the experiment provides an objective method for an experimental attack of a problem that heretofore could be discussed only in the light of subjective introspection or, at best, in the light of gross clinical observation.⁴

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THE GELATIN OF BROM PHENOL BLUE¹

WHILE investigating the kinetics of the fading of brom phenol blue (tetrabromophenolsulfonphthalein) in dilute alkali, we² observed that the completely faded solution, on acidification, became progressively more viscous and in a few minutes set to a clear lemon-colored gel. Although gel formation is not an unusual phenomenon with high molecular weight solutes, the concentration sufficient to produce a stiff jelly is so low as to merit further study from those interested in the mechanism of gelation. Although only a few dyes of its series have been investigated, brom phenol blue appears to be unusual in forming a gel. Phenolphtha-

³ The possibility that the conditioning to the synonym was only indirect, through first recalling the actual conditioned word, was ruled out by a "free association" test.

⁴ Salivation is of course not the only suitable response for dealing with this problem. The galvanic skin response, the pupillary and wink reflexes and indeed any response that is readily conditioned and quantified should, as far as we know, be equally good.

¹ Contribution from the Chemistry Department, Columbia University.

² Amis and LaMer, *Jour. Am. Chem. Soc.*, 61: 905, 1939.