SPECIAL ARTICLES

ABSENCE OF AUDIOGENIC SEIZURES IN WILD NORWAY AND ALEXANDRINE RATS[1]

NUMEROUS observers[2, 3] have reported that loud sounds of high frequency have a profound effect on the behavior of rats. They produce in the rats a high state of excitement characterized by wild undirected running and culminating in a convulsive seizure. In all instances the rats were of the common Norwegian variety which have been bred and raised under laboratory conditions for many generations. It occurred to us to determine whether wild rats taken directly from their native haunts would also show these convulsive seizures when exposed to loud sounds of high frequency.

Opportunity to make these observations came incidentally to other studies on a large number of wild Norway and Alexandrine rats which were trapped alive in alleys, cellars, yards, factories and granaries. Essentially the same technique of auditory stimulation was employed as in previous experiments on the production of convulsive seizures in the domesticated rat. Air-blast, key jingling and air-driven Galton whistle served as stimuli. One hundred and twenty-six wild Norway rats and fifteen wild Alexandrine rats were tested. Stimulation periods were of five minutes duration, with three minutes rest interposed between the different stimuli. In most instances, the rats were tested within a few days after being trapped, but in a few cases they were not tested for several weeks. Seven of the wild Norway rats were selected at random and subjected to daily auditory tests for a period of 27 days.

None of the wild Norway or Alexandrine rats showed either the preliminary high states of excitement or the culminating convulsive seizures; nor did they show any fear responses such as retreats from the hissing air-blast, a common reaction of the domesticated rat to this form of stimulation. On the contrary, they exhibited definitely aggressive behavior in attacking and attempting to bite the metal nozzle of the air-blast apparatus.

The most obvious explanation of the absence of audiogenic seizures in the wild rat is that the convulsions may be a characteristic of domestication. In agreement with this explanation Farris and Yeakel[4] have reported that wild Norway rats bred in the laboratory for 19 generations showed an even greater susceptibility to seizures than their albino relatives. It is evident that if the wild rat showed any such response in its natural environment it would not survive very long.

Some of the factors which may influence the appearance of fits under conditions of domestication are: (1) the progressive inbreeding of a sensitivity to sounds of high frequency; (2) dietary deficiencies produced by the laboratory stock diets; (3) the effects produced by confiement in small cages; (4) the lack of practise in meeting new situations; and (5) endocrine changes.

That dietary factors may play an important part we know from the fact that domesticated rats which never before manifested audiogenic seizures show them when placed on a diet deficient either in magnesium,[5] thiamin[6] or pyrodoxine.[7] It is quite possible that many of the stock diets fed domestic rats may be deficient in one or more of the minerals and vitamins which are essential for prevention of convulsive seizures. Some of our studies indicate that Purina dog chow, which is widely used as a stock diet, is deficient in thiamin. It was found that domestic rats on this diet showed the audiogenic seizures with great regularity, but failed to exhibit them when allowed to drink freely from bottles filled with a solution of thiamin chloride. In regard to the wild rats, it may be pointed out that despite their life in burrows, in alleys, yards and cellars, they may actually have a wider and better assortment of foodstuffs, especially of minerals and vitamins found in the earth, than their domesticated brothers and sisters raised in modern laboratories. In trapping several thousand rats we have found them in general to be strong, vigorous and free from signs of dietary deficiency, such as loss of hair, dermatitis, poor teeth, etc., often in spite of heavy infestation with internal parasites.

Some evidence at hand indicates that the lack of experience in meeting new situations may play an important part in the production of seizures in the domestic rats. These rats, bred for many generations in the sheltered environment of laboratory cages, have long been deprived of the opportunity or necessity of meeting and adjusting quickly and adequately to new situations. Wild rats, on the contrary, owe their very existence to their ability to react adequately to constantly changing situations encountered in their environments, and in so doing have developed strong patterns of aggressive behavior. Consequently, the laboratory-bred animals would be more disposed to conflict and breakdown in the presence of novel situations than their wild relatives.

The importance of being able to make any kind of

[1] Aided by a grant to Curt P. Richter from the Committee for Research in Endocrinology.

[2] C. T. Morgan and J. D. Morgan, *Jour. Comp. Psychol.*, 27: 505, 1939.

[3] F. W. Finger, *Am. Jour. Psychol.*, 55: 68, 1942.

[4] E. J. Farris and E. H. Yeakel, *Jour. Comp. Psychol.*, 35: 73, 1943.

[5] H. D. Kruse, E. R. Orent and E. V. McCollum, *Jour. Biol. Chem.*, 96: 519, 1932.

[6] R. A. Patton, H. W. Karn and C. G. King, *Jour. Comp. Psychol.*, 32: 543, 1941.

[7] H. Chick, M. M. El Sadr and A. N. Worden, *Jour. Biochem.*, 34: 595, 1940.

a response to the experimental situation is brought out by the observation that domestic rats show the fits with less regularity when allowed to run back and forth between the main cage and a small adjoining cage, even though the sound stimulus still follows them.[8] In the wild rat the strong aggressive behavior may serve as an energy outlet or a buffer, which prevents the organism from reaching an explosive level.

Whatever the reason for the absence of auditory fits in the wild rats and their presence in the tame domestic rats we have here an interesting example of behavior differences caused by domestication.

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CHANGES IN ACID-SOLUBLE PHOSPHORUS COMPOUNDS IN THE BRAIN IN POLIOMYELITIS[1]

UNTIL very recently the study of chemical and metabolic pathology of the central nervous system in poliomyelitis was entirely neglected. Racker and Kabat[2] demonstrated that the brain tissue of mice infected with poliomyelitis virus showed a decreased rate of anaerobic breakdown of glucose while oxygen consumption was unimpaired. Recent metabolic studies[3] suggest that this change is specific for poliomyelitis and is not produced by other neurotropic viruses. A decreased lactic acid content of the brain in poliomyelitis has been reported.[4]

The present paper is a preliminary report on changes in acid-soluble phosphorus compounds in the brain in poliomyelitis.

Swiss albino mice four to six weeks of age were infected by intracerebral inoculation of poliomyelitis virus of the Lansing strain. When definite paralysis appeared, the mice were sacrificed by immersion in a mixture of solid CO_2 and ethyl alcohol. Normal mice were treated in a similar manner. The mice were stored in a dry ice box for from several days to two weeks and then the brains were carefully removed. Three brains were pooled for each determination to make a total weight of tissue of approximately one gram. Phosphocreatine, adenosine triphosphate and residual organic phosphate were determined by the method of Stone.[5]

The results are presented in Table I. It is evident that there are marked changes in these compounds in poliomyelitis: adenosine triphosphate increases, while phosphocreatine and residual organic phosphate decrease. The value for adenosine triphosphate for normal mouse brain is similar to that reported by Stone[5] while his normal values for phosphocreatine and residual organic phosphate are somewhat higher than those in Table I. Despite considerable variation, the differences between poliomyelitic and normal brain are clearly significant statistically by use of the "t distribution."[6]

TABLE I

THE EFFECTS OF POLIOMYELITIS ON ACID-SOLUBLE PHOSPHORUS COMPOUNDS OF THE MOUSE BRAIN*

	Phosphocreatine	Adenosine triphosphate	Residual organic phosphate
		NORMAL	
	10.8	16.3	23.2
	10.6	14.8	22.2
	9.46	17.0	22.3
	10.5	20.0	22.84
	2.1	17.5	5.2
	6.65	17.1	9.45
	6.83	15.9	25.97
Mean	8.13	16.95	18.74
		POLIOMYELITIS	
	5.55	23.9	0.80
	1.38	28.0	3.20
	2.38	26.5	7.47
	0.63	24.0	2.50
	0.46	22.1	4.14
	5.83	32.7	0.90
	4.59	33.3	1.11
	5.68	15.0	13.32
Mean	3.44	25.71	4.18
t	3.28	3.65	4.5
Per cent. change from normal	−56.6	+51.7	−77.6

* P per 100 grams of brain tissue.

The changes in acid-soluble phosphorus compounds observed in the brain in poliomyelitis can not be explained on the basis of greater autolysis in the infected tissue, since autolysis would decrease rather than increase the adenosine triphosphate content.[5] The intracellular parasite, the virus, might, in the course of its growth and multiplication, break down nucleoproteins of the cell or might interfere with dephosphorylation of adenosine triphosphate to produce an increase of the latter compound in the brain tissue. The marked changes in acid-soluble phosphorus compounds suggest the possibility of a considerable interference with energy mechanisms and carbohydrate metabolism of the neurons by the virus infection.

Summary: Preliminary studies indicate that the content of adenosine triphosphate is greatly increased in the brain of the mouse infected with poliomyelitis virus. On the other hand, phosphocreatine and residual organic phosphate are markedly decreased in the infected brain.

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[8] W. J. Griffiths, *Comp. Psychol. Monog.*, 17: 1, 1942.

[1] Aided by a grant from the National Foundation for Infantile Paralysis. The author is at present with the Division of Chemotherapy, National Institute of Health, Bethesda, Maryland.

[2] E. Racker and H. Kabat, *Jour. Exp. Med.*, 76: 579, 1942.

[3] M. Nickle and H. Kabat. Unpublished observations.

[4] H. Kabat, D. Erickson, C. Eklund and M. Nickle, SCIENCE (in press).

[5] W. E. Stone, *Jour. Biol. Chem.*, 135: 43, 1940.

[6] F. E. Croxton and D. J. Cowden, "Applied General Statistics." New York: Prentice-Hall, Inc., 1940.