

subsequent synthetic processes. Such a mechanism cannot account for differences in slopes of the curves, however, and therefore certain preferential esterifying mechanisms for each of the fatty acids must be operative.

Summary. Palmitic-1-C¹⁴ and linoleic-1-C¹⁴ acids were infused into fasted dogs, and fractionation of the serum lipids carried out at time intervals up to 72 hours. Although many similarities were found in the metabolism of these 2 fatty acids, it was observed that linoleic-C¹⁴ acid appeared to 1) persist longer in the plasma as the FFA and 2) to be incorporated preferentially into cholesterol esters and phospholipids.

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1. Stein, Y., Shapiro, B., *Am. J. Physiol.*, 1959, v196, 1238.
2. Dittmer, J. C., Hanahan, D. J., *J. Biol. Chem.*, 1959, v234, 1976.
3. Laurell, S., *Acta Phys. Scand.*, 1957, v41, 158.
4. Fredrickson, D. S., Gordon, R. S., *J. Clin. Invest.*, 1958, v37, 1504.
5. Lipsky, S. R., Haavik, A., Hopper, C. L., McDivitt, R. W., *ibid.*, 1957, v36, 233.
6. Freeman, N. K., *J. Biol. Chem.*, 1957, v227, 449.
7. Hanahan, D. J., Blomstrand, R., *ibid.*, 1956, v222, 677.

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Hypoxic Alteration of Righting Ability and Pain Threshold in Two Mammalian Species.* (26331)

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Although much experimental work has been done in man and animals on pain(1), there are only limited studies on the effects of hypoxia on thermal pain perception(2). Besides studying hypoxic effects on pain thresholds, we were also interested in using the response to pain along with tests of righting ability as indices of body function during hypoxic episodes.

Mammalian species that hibernate survive more severe hypoxia than do non-hibernating species(3,4). Two possible means by which hypoxic tolerance could be greater in one species than another are: a) the more tolerant mammal possesses greater capacity to maintain high functional levels by maintaining tissue oxygenation through greater utilization of physiological regulatory mechanisms or biochemical energy reserves. b) The more tolerant mammal by decreasing metabolism and function, reduces the oxygen requirement to parallel the reduced oxygen supply.

In the present study, an attempt was made

to evaluate the above alternatives as to their role in species differences of hypoxic tolerance. Degree of hypoxic alteration of function as shown in pain threshold and righting ability changes was compared for one hibernating species and one non-hibernating species.

Methods. Experimentally naive, Harlan strain white rats (*Rattus norvegicus*) of 200 to 300 g body weight were the non-hibernators used. Thirteen lined ground squirrels (*Citellus tridecemlineatus*) of 150 to 250 g body weight were the hibernators used.

Pain threshold was determined by using a modification of the method described by D'Amour and Smith(5). The tails of the ground squirrels were shaved prior to the experiment. Animals of both species were restrained either in cylinders or taped to boards. A small hood was placed over the head of the animal through which 1 to 2 liters per minute of air, or an air mixture deficient in oxygen were pumped. The tail was then placed in a trough containing a resistance wire heater. The heater was turned on and the temperature increased at approxi-

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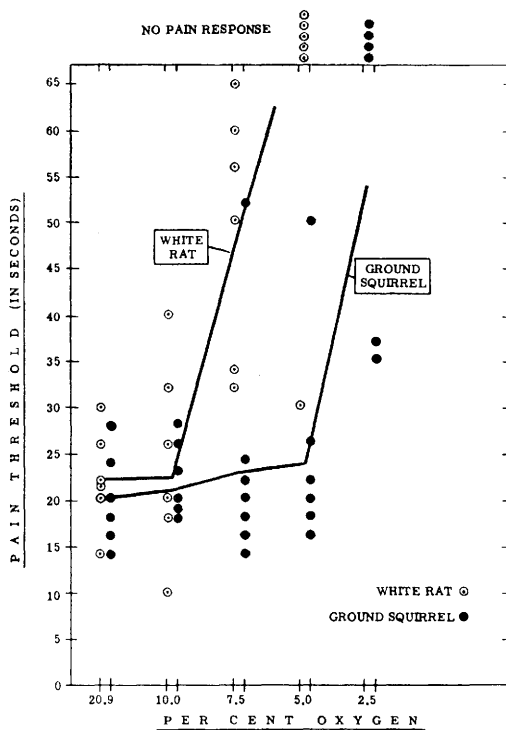


FIG. 1. Effects of varying inspired oxygen percentage on pain threshold (tail flick response time) in white rats and ground squirrels. Each point represents one determination. Curves are drawn through the mean at each oxygen percentage.

mately 4°C per second. The reflex reaction time required for the first definite tail twitch was taken as the pain threshold. In tests where no response was obtained, the tail was removed at the first indication of burning. Hypoxic tests were done after 5 minutes of breathing a low oxygen mixture. The method gave highly reproducible results for both species.

The degree of hypoxia necessary to abolish the righting reflex was determined by placing the animal in a 3 liter jar which could be rotated while air was being pumped out. In one series, the rate of air removal was equivalent to an altitude ascent of 2,000 feet per minute. The end point was taken at the first sign of inability of the animal to right itself in the rotating jar and barometric pressure was then measured.

In a second series, the animals were decompressed to 150 mm Hg in 9 seconds. Time required for loss of righting ability was then measured.

Results. The mean normal pain threshold in our apparatus was 22 seconds in the rat and 19 seconds in the ground squirrel. Little alteration in pain threshold occurred in the rat until the oxygen percentage was below 10 (Fig. 1). Five per cent oxygen abolished pain sensitivity in 5 out of 6 rats. All of the rats survived the brief (about 7 minutes) hypoxic period of 5% oxygen breathing.

The ground squirrels showed no depression of pain sensitivity with air mixtures containing 5% oxygen. Of the 6 animals at 2.5%, 2 still showed a response after 5 minutes. One animal did not survive the test, but 5 animals recovered completely within a few minutes after this hypoxic episode.

Righting ability was less susceptible to hypoxia in the rat for both series of tests (Table I). The rat appeared to fight the hypoxia and struggled to maintain the upright position. At the end of the hypoxic episode, the rat required several minutes to regain consciousness and complete motor control. The ground squirrels on the other hand, made little effort to fight the jar rotation even in the first few seconds of deep hypoxia but seemed content in the supine position. Recovery in the ground squirrel was much faster than that of the rat following hypoxia.

Discussion. Our results from animals are in agreement with those of Stokes *et al.*(2) who found that in men breathing 10% oxygen there was no change in thermal pain perception. These authors could not use with

TABLE I. Barometric Pressure at Which Righting Was Lost.

Animal	No. of obs.	Pressure (mm Hg)	Equivalent oxygen (%)
Rat	6	154.0 $\pm$ 9.0*	4.3
Ground squirrel	6	183.0 $\pm$ 10.0	5.1

Time righting ability remained after 9-second ascent to 38,000 feet (150 mm Hg or equivalent to 4.2% oxygen)

Animal	No. of obs.	Time (sec.)
Rat	9	52.0 $\pm$ 11.0*
Ground squirrel	9	8.1 $\pm$ 1.5

* Mean $\pm$ S.D.

humans the severe hypoxia that we used to alter pain threshold in animals.

In comparison of the 2 species, ground squirrels maintained pain sensitivity with more severe hypoxia than could the rat, but the rat's righting ability was much more susceptible. The response to pain as we measured it may be a spinal reflex(1) while the righting response utilizes higher centers. This indicates that the ground squirrel supported some functions, perhaps at the expense of others, during oxygen deficiency. The greater hypoxic survival of the ground squirrel could be due to partial functional depression which conserves energy for maintenance of more vital functions. Which functions are maintained and how they are maintained, and which are depressed are avenues of future research.

Summary. The response to thermal pain in the rat was decreased by breathing 7.5%

oxygen and abolished with 5% oxygen. The 13 lined ground squirrel had no alteration of response with 5% oxygen but did with 2.5%. However, the righting reflex of the ground squirrel was much more susceptible to hypoxia than that of the rat. Loss of righting ability occurred at a barometric pressure of 183 mm Hg for the ground squirrel and 154 mm Hg for the rat in simulated altitude ascent in a chamber.

1. Beecher, H. K., *Pharmacol. Rev.*, 1957, v9, 59.
2. Stokes, J., III, Chapman, W. P., Smith, L. H., *J. Clin. Invest.*, 1948, v27, 299.
3. Hiestand, W. A., Rockhold, W. T., Stemler, F. W., Stullken, D. E., Wiebers, J. E., *Physiol. Zool.*, 1950, v23, 264.
4. Bullard, R. W., David, G., Nichols, C. T., *Harv. Mus. Comp. Zool. Bull.*, 1960, v124, 321.
5. D'Amour, F. E., Smith, D. L., *J. Pharmacol.*, 1941, v72, 74.

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Threshold and Pattern of Electroshock Seizures in Ataxic Manganese-Deficient Rats.* (26332)

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Offspring of manganese-deficient females exhibit a congenital ataxia characterized by incoordination, loss of equilibrium, retraction of the head, and tremor. This abnormal condition has been shown to result from an irreversible defect or defects occurring between the 14th and 18th days of gestation in rats (1). Recent studies, both physiological and morphological, have revealed abnormalities of the inner ear in manganese-deficient young; these studies indicate that impaired vestibular function may be involved in the etiology of the ataxic syndrome(2,3,4). However, certain manifestations of the ataxia, such as tremor, could not be attributed to loss of vestibular function. It was therefore

of interest to examine another aspect of nervous system function.

The present communication describes experiments investigating brain excitability, as measured by response to electroshock, in offspring of normal and manganese-deficient rats.

Materials and methods. Animals and diets. Ataxic, manganese-deficient offspring were produced by procedures similar to those previously reported(3). Briefly, female rats of the Sprague-Dawley strain were maintained from time of weaning on a fortified milk diet deficient in manganese. Control groups were treated in the same way, except that manganese was added to the diet.[‡] At maturity the animals were mated with normal males.

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