a cystinuric patient indicate that further investigations into the pathogenesis of cystinuria must consider sulfhydryl-disulfide interaction between cysteine and cystine and must explain the observed differences in renal and intestinal transport.

SAMUEL THIER
MAURICE FOX
STANTON SEGAL
National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Maryland
LEON E. ROSENBERG
National Cancer Institute, Bethesda 14, Maryland

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2 January 1964

Reciprocal Activities of the Ventromedial and Lateral Hypothalamic Areas of Cats

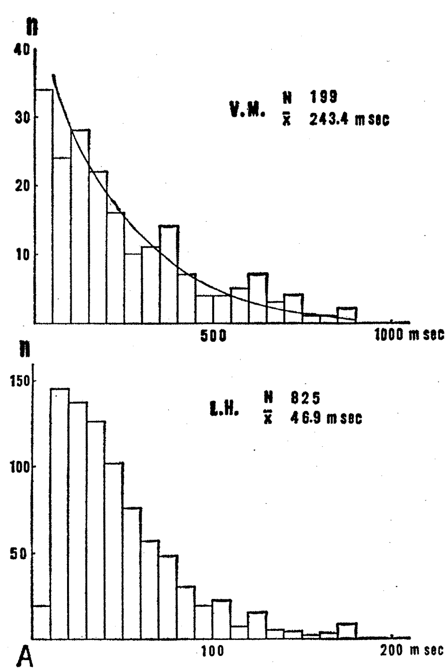
Abstract. *Statistical treatment of recordings of spontaneous unit discharges from the ventromedial nucleus and the lateral area of the hypothalamus (the activities in one area being recorded while the other was stimulated) revealed significant reciprocal relations. The concept that glucose-sensitive neurons are present in the ventromedial nucleus was supported by the effects on the spontaneous unit discharges of injecting glucose and other solutions intravenously.*

The important role of the hypothalamus in the nervous regulation of food intake has already been emphasized. Bilateral lesions in the lateral hypothalamic area (LH) of mammals cause aphagia and those in the ventromedial hypothalamic nucleus (VM) induce polyphagia (*1*). Electrical stimulations of the former through chronically implanted electrodes elicit feeding behavior (*2*), while stimulations of the latter suppress it (*3*). The results of several electroencephalographic studies of these regions supported the behavioral experiments (*4*). In this report we describe analytical studies of the activities of single neuronal units in the lateral hypothalamic area and in the ventromedial hypothalamic nucleus, yielding information on the reciprocal activities of these areas (*5*).

Cats were anesthetized with ether and made to respire artificially through tracheal cannulae. Glass pipette recording microelectrodes and concentric, bipolar, metal-stimulating electrodes were inserted in the ventromedial hypothalamic nucleus (F 11.5, S 1.2, H-5, according to Jasper's atlas) and the lateral hypothalamic area (F 11.5, S 3.5, H-4) at the level of the VM. Electrode locations were later verified histologically. (Insertions were successful in 18 out of 29 cats.) When a stable series of spontaneous unit discharges was detected, tetanic shocks of 20 to 50 cy/sec for a few seconds (pulse duration 0.05 msec; current strength 10^{-6} to 10^{-5} A) were applied through one of the stimulating electrodes. This was followed by intracarotid injections of test solutions (0.3 ml of 10 percent glucose; 10 percent NaCl, Tyrode solution or water). Tactile, auditory, or visual stimuli did not affect the hypothalamic neurons under investigation.

Simultaneous recordings of spontaneous unit discharges in the LH and VM of more than 1 minute duration were attained in seven cats. The frequency of the discharges was usually low in the VM (2 to 7 cy/sec) and high in the LH (8 to 20 cy/sec). The distributions of the time intervals of the spontaneous unit discharges (discharge intervals) and the number of discharges per second (discharge frequency) were compared with simple theoretical distributions, and the significance of the differences was estimated by the Chi-square test.

In all VM recordings, the discharge interval closely resembled the exponential distribution and the discharge frequency the Poisson distribution ($p < .05$ to 0.01) (Fig. 1), like the spontaneous miniature end-plate potential (*6*). On the other hand, in all LH recordings, the discharge interval did not fit the exponential distribution but the Gaussian curve described the discharge frequency ($p < .05$ to 0.01) (Fig. 1). It was confirmed theoretically that even when different class intervals were used (different scales on the abscissa), the patterns of discharge intervals did not correspond to the exponential distribution. Thus, completely



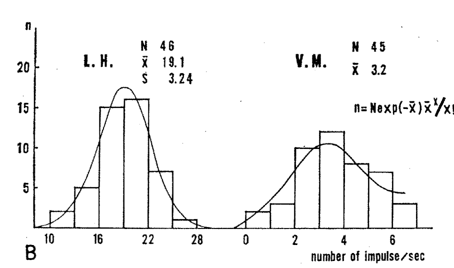


Fig. 1. Spontaneous unit discharge patterns in cats under ether anesthesia. *A*, Distribution of intervals between successive discharges recorded simultaneously in the ventromedial hypothalamic nucleus (VM, top, in a series of 199 potentials) and in the lateral hypothalamic (LH, bottom, 825). Ordinate: n is the number of intervals between $x + \Delta x$. The mean interval $\bar{x}$ is shown. The solid curve was plotted according to $n = N\left(\frac{\Delta x}{\bar{x}}\right)\exp\left(\frac{-x}{\bar{x}}\right)$. *B*, Distribution of number of spontaneous unit discharges per second in the VM (right) and the LH (left). The discharge pattern of the VM closely corresponds to the Poisson distribution and that of the LH to the Gaussian distribution.

random discharges were indicated in the VM, but a more or less systematic pattern of discharges was indicated in the LH.

Termination of ether inhalation increased the frequency of spontaneous unit discharges in the VM and decreased it in the LH, completely reversing both discharge patterns in all instances; that is, in the VM, the discharge interval no longer fitted the exponential distribution but the discharge frequency corresponded to the Gaussian one ($p < .05$ to .01), and in the LH, the discharge interval and frequency corresponded to the exponential and Poisson distributions, respectively ($p < .05$ to .01). This may explain the encephalographic patterns in unanesthetized cats where low-voltage, fast waves usually appear in the VM and slower ones in the LH (*7*). The changes in spontaneous unit discharge patterns may indicate some synaptic control which is influenced by anesthesia not only in the VM and LH, but also in other places such as the amygdaloid nucleus.

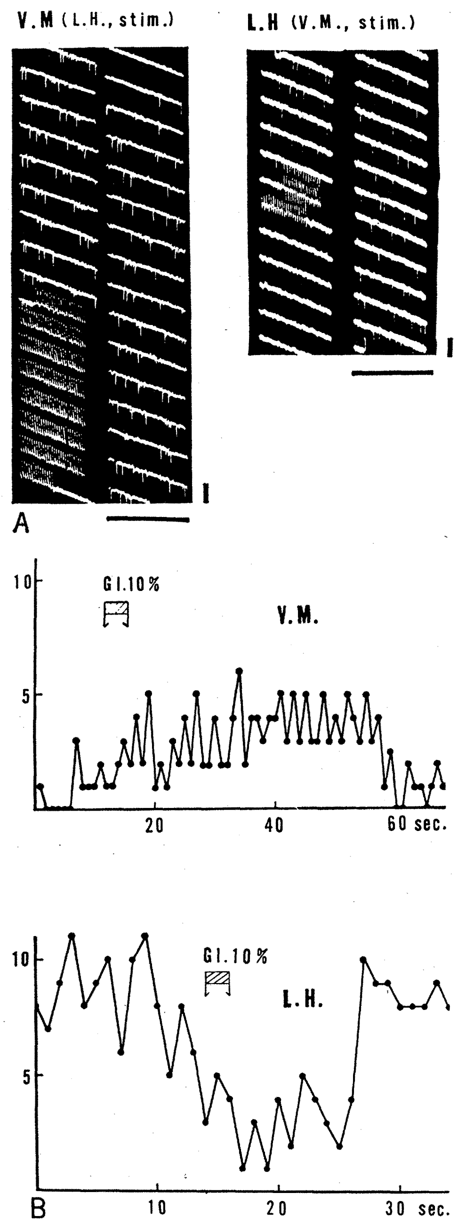


Fig. 2. Effect of electrical stimulation. *A*, From top to bottom and from left to right, (left) spontaneous unit discharges in the VM were reduced in frequency and even ceased for a few seconds by tetanic stimulation of the LH, (shown by artifacts in middle of left columns); (right) discharges in the LH were also decreased by stimulation of the VM. Two different preparations; time, 1 second. *B*, Effect of glucose solution. Number of discharges per second (ordinate) in the VM (top) and LH (bottom) were changed in frequency by injection of 0.3 ml of 10 percent glucose at the time shown. Abscissa, time.

With tetanic stimulation of the LH, discharges in the VM (21 of 25 neurons) decreased or even ceased, while discharges in the LH (15 of 16 neurons) increased up to about twice the former frequency during stimulation and even several seconds afterward, gradually returning to the original frequency (Fig. 2 *A*). The frequency of discharges increased up to about 200 percent in the VM and decreased in the LH when the intensity of stimulation was increased, probably because the stimulating current spread into the VM. Thus, the VM depression was not due to the spreading depression. With stimulation of the VM, the frequency in the LH decreased or ceased and then recovered (9 out of 10 neurons) in a manner similar to that when the LH was stimulated (Fig. 2 *A*). These results also indicate reciprocal relations between the VM and LH.

In 9 VM neurons of 13 and in 2 LH neurons of 30, the frequency of spontaneous unit discharges increased up to about 200 percent during or after injection of glucose solution. This effect sometimes lasted more than 30 seconds (Fig. 2 *B*). Glucose solution decreased the frequency to about half in 16 out of 30 neurons in the LH (12 were uneffected), but the original frequency was recovered several seconds after the injection (Fig. 2 *B*). On the other hand, injection of water accelerated the discharge in 12 out of 13 LH neurons. Sodium chloride solution increased the frequency in the LH (6 of 9 neurons), indicating that the glucose effects were not due to osmotic effect (except in 2 LH neurons). Tyrode's solution, used in control experiments, had no effect, and spontaneous unit discharges recorded from incorrect insertions were not influenced at all by any of the above treatments. This evidence seems to support the concept that glucose sensitive neurons are present in the ventromedial hypothalamic nucleus (*8*).

YUTAKA OOMURA*, KATSUMI KIMURA
HIROSHI OOYAMA*, TAKASHI MAENO
MATASABURO IKI, MAKOTO KUNIYOSHI
Department of Physiology, Faculty of Medicine, Kagoshima University, Japan

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* Present address: Department of Physiology, Faculty of Medicine, Kanazawa University, Japan.

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Pteridines as Pigments in Amphibians

Abstract. *Extracts of brightly colored skins from nine amphibian species were analyzed chromatographically. In yellow skin in which xanthophores predominated, relatively large quantities of sepiapterin were found, while in red skin which was laden with erythrophores, three drosopterins were most prevalent. Frozen sections of skin indicated that pteridines were present within chromatophores, either alone or accompanied by carotenoids. It is concluded that sepiapterin and three drosopterins are utilized as pigments in amphibians and it is suggested that other less brightly colored pteridines also function in this respect. It no longer seems proper to make the tacit assumption that bright pigmentation of amphibians is due only to the presence of carotenoids.*

The ubiquity of integumental carotenoids among amphibians, together with the occurrence of yellow, orange, or red chromatophores which lose their color after treatment with fat solvents, has led to the general assumption that bright coloration of amphibians results from the presence of carotenoids in