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12 February 1970; revised 9 June 1970 ■

Monosodium Glutamate: Lack of Effects on Brain and Reproductive Function in Rats

Abstract. *Monosodium glutamate was injected subcutaneously in infant rats of both sexes. The lateral preoptic and arcuate nuclei and median eminence were examined by light and electron microscopy for possible monosodium glutamate effects. As adults, treated animals showed no adverse monosodium glutamate effects on the reproductive system and neural morphology.*

Olney (*1*) reported that a single subcutaneous injection of monosodium glutamate (MSG) in newborn mice (2 to 9 days of age) induced acute neuronal necrosis in several brain areas including the preoptic and arcuate nuclei and median eminence region. Newborn mice which received a series of injections of MSG, when adult showed a syndrome which suggested a complicated neuroendocrine disturbance. These mice exhibited skeletal stunting, marked obesity, and female sterility. Acute brain damage was also found in a newborn rhesus monkey after a single administration of MSG (*2*). This report is concerned with both the acute and long-range effects of MSG upon the development of the brain and reproductive function of male and female rats after a single injection of MSG into newborn animals. The rat was chosen for these studies because Olney (*1*) and Olney and Sharpe (*2*) stated that acute hypothalamic lesions also are produced in rats, and also because injections of hormones (*3*) and drugs (*4*) at a "critical stage" of neonatal development can drastically effect hypothalamic control mechanisms as related to reproduction and sexual behavior.

Male and female rats of the Wistar strain (Simonson Laboratories, California), 3 to 4 days old, received a single subcutaneous injection of MSG. The MSG (Mann Research Laboratories) was injected subcutaneously in a volume of 0.1 ml; the total dose was 4 mg per gram of body weight. This concentration is approximately four times greater than the minimum dosage which produced hypothalamic lesions in newborn mice (*1*) and a newborn monkey (*2*). Control rats were injected with an equal volume of saline. In experiments concerned with the acute effects of MSG on the brain, the animals were killed 3 hours posttreatment. To determine long-range effects of MSG, uniform litters (eight pups per mother) were kept in an environmentally controlled room until weaned. The experiment was terminated at 68 days posttreatment for males and 88 days posttreatment for females. Relative reproductive organ weights were recorded (organ weight per unit body weight). The anesthetized rats were perfused intracardially with normal saline followed by either 10 percent buffered formalin or Flickinger's fixative (*p*H 7.2). Brains perfused with formalin were paraffin embedded, sectioned, and stained with cresyl violet for light microscopy. Brains perfused with Flickinger's modification of Karnovsky's fixative (*5*) were sectioned transversely, and the preoptic nucleus, median eminence, and arcuate nucleus were dissected out. The tissue was washed in 0.2*M* cacodylate buffer (*p*H 7.2), postfixed in 1 percent cacodylate-buffered osmium tetroxide for 1 hour, dehydrated in graded alcohols, and embedded in Epon 812. Silver and gray sections were stained with uranyl acetate followed by lead citrate and examined in a Hitachi HS-7S electron microscope.

Light microscopic examination of the

Table 1. Effect of monosodium glutamate (MSG) injection in infant rats on adult reproductive organ weights. Organ values are the mean ratios of organ weight (in milligrams or grams, as noted below) to body weight (in hundreds of grams), plus or minus the standard error of the mean.

Group	Females			Males			
	No. of rats	Ovaries (mg/100 g)	Uterus (mg/100 g)	No. of rats	Testes (g/100 g)	Seminal vesicles (mg/100 g)	Prostate (mg/100 g)
Control	7	34.7 ± 0.9	162.9 ± 9.4	8	1.02 ± .03	244.9 ± 17.0	120.7 ± 9.9
MSG-treated	8	29.3 ± 1.4*	179.8 ± 10.8	6	1.06 ± .06	287.0 ± 16.8	118.3 ± 3.5

* The difference from the value for the control group is significant at the $P < .01$ level.

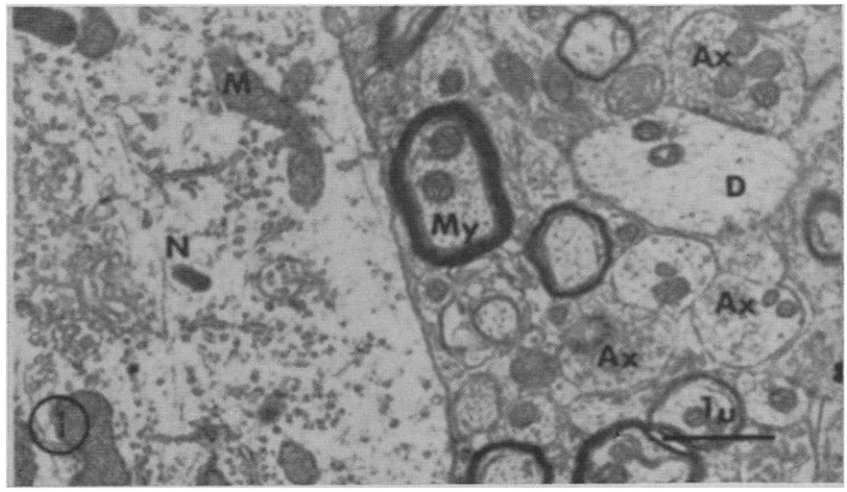

Fig. 1. Neuron (*N*) and neuropil of the lateral preoptic nucleus in an MSG-treated adult rat. *Ax*, axon terminal; *D*, dendrite; *M*, mitochondrion; *My*, myelinated axon (× 16,300).

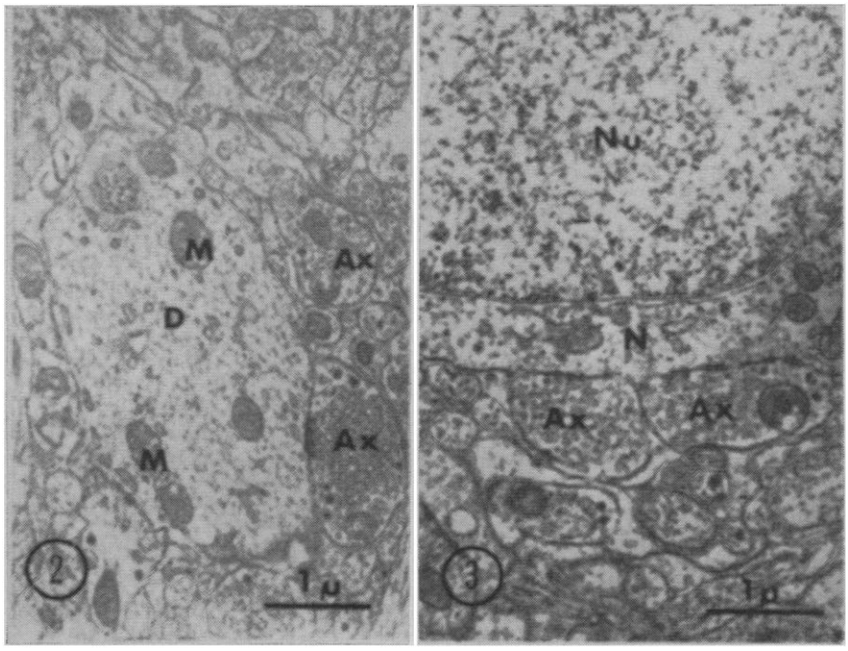

Fig. 2. Dendrite (*D*) in neuropil of median eminence of an MSG-treated adult rat. *Ax*, axon terminal; *M*, mitochondrion (× 15,000). Fig. 3. Neuron and neuropil in the arcuate nucleus of an MSG-treated adult rat. *Ax*, axon terminal; *M*, mitochondrion; *Nu*, nucleus (× 16,300).

brains of the infant rats killed 3 hours after a single injection of MSG failed to reveal any effects upon the lateral preoptic nucleus, arcuate nucleus, and median eminence. The possibility still existed that the single injection of MSG could have produced effects which were not obvious with the light microscope; therefore, the same neural regions from male and female adult rats were examined with the electron microscope. Electron microscopic observations of the lateral preoptic nucleus, arcuate nucleus, and median eminence region did not show any edematous swelling or disintegration of organelles in neurons or neuronal processes such as was illustrated by Olney (*2*) in the infant monkey. There was no indication that such damage had ever occurred (Figs. 1–3). These areas were also examined with respect to distribution of neurons and glia, distribution and size of axon terminals and dendrites, nucleolar size, and distribution of dense-core and clear vesicles. No differences were observed between MSG-treated and control animals.

Not only were no morphological lesions of the brain detectable after MSG treatment, but adult animals also did not manifest any pronounced disturbances with respect to reproductive function. The lack of MSG effect was determined by the following criteria: (i) adult MSG-treated females cycled normally and were capable of mating and producing normal litters; (ii) although the relative ovarian weights were significantly less than the controls (34.7 ± 0.9 versus 29.3 ± 1.4, $P < .01$), no differences were noted when the ovaries were examined histologically; (iii) the relative uterine weights were not significantly different; and (iv) no significant differences were observed in the weights of testes, seminal vesicles, and prostates of MSG-treated males compared to controls (Table 1).

These results fail to duplicate the findings reported in mice and monkey by Olney (*1*) and Olney and Sharpe (*2*). Since the experimental approaches used in the present study and reported by Olney are very similar, it is difficult to determine the cause of the discrepancies at this time. However, the possibility exists that the differences may be due to variation in species susceptibility.

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11 May 1970

Sterols in Recent Marine Sediments

Abstract. *Sterolic fractions have been isolated from Recent marine sediments representing two different environments. The fractions were characterized by infrared spectroscopy and thin-layer chromatography. The major sterols in the fractions were identified by gas chromatography and mass spectrometry. The demonstrated survival of these common plant and animal sterols for several thousand years suggests that these molecules will be useful geochemical indicators.*

Most organic matter produced by a marine community its quickly re-oxidized by the organisms or by inorganic processes. A small fraction escapes oxidation and is deposited in sediments. This small fraction is the object of study for organic geochemistry. The part of this preserved organic matter not bound into kerogen contains most of the preserved biochemicals (*1*).

The high degree of structural diversity of sterols suggests that the sterols might carry significant information with regard to the type of biological community associated with various sediments and perhaps even to specific organisms of the community (*2*). Using a colorimetric method, Schwendinger and Erdman (*3*) made a survey for sterols and reported positive tests for them in a series of Recent sediments, varying from freshwater to deep marine. They stated that high sterolic concentrations of 60 to 300 parts per million in their samples make sterols possible precursors for some of the compounds found in petroleum. Others (*4*) think that sterols or their degradation products are major contributors to the optical activity of petroleum because much of this activity is confined to that fraction of compounds having 27 to 30 carbon atoms. We now report the finding of several specific sterols from marine sediments from two different marine environments.

The bottom meter of a three-meter