Mg^{2+} is added simultaneously with the thiol, dissociation does not occur and enzymatic activity is retained. Evidence to be published elsewhere indicates that Mg^{2+} not only protects the enzyme from inactivation by the thiol but also interacts with the dissociated subunits after all catalytic activity has disappeared.

SIDNEY SHIFRIN
BARBARA J. GROCHOWSKI
SAMUEL W. LUBORSKY

National Cancer Institute,
National Institutes of Health,
Bethesda, Maryland 20014.

Received January 19; revised March 19, 1970.

1 Craven, G. R., Steers, jun., E., and Anfinsen, C. B., *J. Biol. Chem.*, **240**, 2468 (1964).
2 Reithel, F. J., Newton, R. M., and Eagelson, M., *Nature*, **210**, 1265 (1966).
3 Shifrin, S., and Steers, jun., E., *Biochim. Biophys. Acta*, **133**, 463 (1967).
4 Zipser, D., *J. Mol. Biol.*, **7**, 113 (1963).
5 Karlsson, U., Koorajian, S., Zabin, I., Sjöstrand, F. S., and Miller, A., *J. Ultrastruct. Res.*, **10**, 457 (1964).
6 Weber, K., Sund, H., and Wallenfels, K., *Biochem. Z.*, **339**, 498 (1964).

Tay-Sachs Disease is Probably not Increasing

RECENTLY, Shaw and Smith[1] have discussed the question of heterozygote advantage for the Tay-Sachs gene in Jewish populations with reference to our published computations[2] and more generally. Their estimate of 5·3 per cent advantage over normal homozygote, based on trial values in a discrete model, is better than our value of 4·6 per cent from a very rough continuous approximation. But they seem to imply that we also accepted another estimate of 1·3 per cent advantage; this value was mentioned only to indicate how little heterosis would be required simply to cancel deaths of the recessive homozygotes.

Just before their article appeared, we wrote to the authors to express our doubt that the Tay-Sachs gene frequency is still increasing, as they suggest. It seems likely that an actual increase of gene frequency under selection was occurring where the frequency of the disease was high—in Eastern Europe, especially in Poland. But there are no longer any Ashkenazi ghettoes where selection for heterozygotes presumably was strong, as actual reproductive data seem to show. And the presumed biological advantage is no longer demonstrable in young, American-born, families with Tay-Sachs disease, suggesting that the ecological circumstances which conferred such advantage no longer prevail[2]. Further, we have evidence that the frequency of Tay-Sachs disease was far from uniform in populations of European Ashkenazi Jews[3]. There is nothing to support the notion that heterozygotes have greater fitness in North America, Britain or Israel. The point might be worth investigating in Russia.

NTINOS C. MYRIANTHOPOULOS
ALFRED F. NAYLOR

National Institute of Neurological Diseases and Stroke,
National Institutes of Health,
Bethesda, Maryland.

STANLEY M. ARONSON

State University of New York,
Downstate Medical Center,
Brooklyn.

Received May 5, 1970.

1 Shaw, R. F., and Smith, A. P., *Nature*, **224**, 1214 (1969).
2 Myrianthopoulos, N. C., and Aronson, S. M., *Amer. J. Human Genet.*, **18**, 313 (1966).
3 Aronson, S. M., Herzog, M. I., Brunt, P. W., McKusick, V. A., and Myrianthopoulos, N. C., *Trans. Amer. Neurol. Assoc.*, 117 (1967).

Brain Damage in Infant Mice following Oral Intake of Glutamate, Aspartate or Cysteine

STRIKING degenerative changes in the infant mouse retina after subcutaneous treatment with monosodium glutamate (MSG) were reported by Lucas and Newhouse in 1957[1]. Other studies[2–6] established that the process of retinal degeneration induced by MSG treatment is a remarkably acute and irreversible form of neuronal pathology. Recently it was found that a similar process of acute neuronal necrosis occurs in several regions of the infant mouse brain after subcutaneous treatment with MSG, and that animals treated with high doses in infancy tend to manifest obesity and neuroendocrine disturbances as adults[7,8]. The arcuate nucleus of the hypothalamus is an area particularly vulnerable to glutamate induced damage in infant animals of several species (mice and rats[7], rabbits and chicks and the rhesus monkey[9]). In mice, which have been studied more extensively for MSG induced disturbances than other species, the infant animal suffered hypothalamic damage from a relatively low subcutaneous dose (0·5 g/kg of body weight)[7].

Table 1

Test compound	Dose (g/kg)	Number treated	Number affected	Necrotic hypothalamic neurones
Intubated, no treatment	—	10	0	0
MSG	0·25	10	0	0
MSG	0·50	23	12	7
MSG	0·75	16	13	13
MSG	1·00	19	19	25
MSG	2·00	7	7	40
L-Glutamic acid	1·00	4	4	23
Monosodium L-aspartate	1·00	4	4	26
L-Glutamate/L-aspartate	0·50/0·50	8	8	27
Monosodium-glutarate	3·00	4	0	0
NaCl	3·00	4	0	0
L-Glycine	3·00	2	0	0
L-Serine	3·00	2	0	0
L-Alanine	3·00	2	0	0
L-Leucine	3·00	2	0	0
DL-Methionine	3·00	2	0	0
L-Phenylalanine	3·00	2	0	0
L-Proline	3·00	2	0	0
L-Lysine	3·00	2	0	0
L-Arginine	3·00	2	0	0
L-Cysteine	3·00	4	4	57

Each of the listed compounds was given in 10 per cent aqueous solution except L-glutamic acid, L-leucine, DL-methionine and L-phenylalanine which were given in 2·5 per cent aqueous solution because of their poor solubility in water. Because a large volume of fluid was needed to deliver high doses of L-leucine, DL-methionine and L-phenylalanine, only half the dose was given orally and the remainder subcutaneously. All of the other compounds were given orally. Sources of L-glutamic acid and MSG were purity checked by thin layer chromatography. Figures in the necrotic hypothalamic neurone column represent averages for each dose level.

Because of the widespread practice of weaning human infants on foods which are not only rich in natural glutamate content but may contain substantial quantities of glutamate (MSG) added for flavouring[10,11], it is important to establish whether damage to the infant central nervous system could follow from oral as well as from parenteral administration of glutamate[12]. We describe here experiments which demonstrate hypothalamic damage in infant mice following relatively low oral doses of glutamate, and also report that orally administered aspartate and cysteine can induce retinal and hypothalamic damage.

Seventy-five Webster Swiss albino mice, 10 to 12 days old, were given single oral doses of a 10 per cent aqueous solution of MSG at one of 5 dose levels (0·25, 0·5, 0·75, 1·0 or 2·0 g/kg). Ten control animals were intubated but given no treatment, and an additional 46 were given single oral doses of other test compounds, as shown in Table 1. Accurate dosage control was ensured by use of an improvised flexible gastric tube inserted gently through the mouth and oesophagus into the stomach. About 5 h after