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December 1, 1969

Professor Joshua Lederberg
Department of Genetics
Stanford University Medical Center
Stanford, California 94305

Dear Professor Lederberg:

Thank you for your letter of November 10 and the copy of your excellent commentary entitled "The big fuss over MSG." I was particularly pleased to read your commentary because it focuses on aspects of MSG research which go beyond the current controversy over MSG as a food additive.

I do not have a literature check list of analogous effects of other amino acids and, in fact, I do not know of anyone who has loaded infant animals with individual amino acids and then carefully examined the central nervous system for acute neurotoxicity. In the course of my own studies I have administered a good sampling of amino acids in massive oral doses by feeding tube to 10 day old mice (glycine, leucine, methionine, phenylalanine, lysine, arginine, serine, alanine, proline, aspartic acid and glutamic acid) and have found that of these amino acids only glutamic and aspartic acid are capable of inducing neuronal necrosis in the hypothalamus. The lesion induced by aspartate is identical to the one associated with glutamate treatment. Interestingly enough, glutamine, the amide form of glutamate induces only a tiny lesion when given in massive doses (probably by conversion locally to glutamate). GABA, even at doses which are both massive and lethal induces no hypothalamic changes. An additional compound, sodium glutarate, which is structurally identical to glutamate, except for having no amino group, is also unable to produce the hypothalamic lesion at massive doses. We have some additional studies under way at present in hopes of further clarifying these intriguing questions of specificity and mechanism of action.

Enclosed are some reprints of my published work on glutamate and the developing central nervous system.

Sincerely,

John W. Olney

John W. Olney, M.D.

JWO:hme