

The Effect of Mercurials on Amino Acid Transport and Rubidium Uptake by Isolated Rat Brain Microvessels

IVAN TAYARANI, JEANNE-MARIE LEFAUCCONNIER AND JEAN-MARIE BOURRE

*INSERM U26, Hopital Fernand Widal, 200 Rue du Faubourg Saint Denis,
75010 Paris, France*

ABSTRACT: The present studies were undertaken to investigate the *in vitro* effects of mercuric chloride ($HgCl_2$) and methylmercury chloride (CH_3HgCl) on the uptake of [3H]alanine, [3H]phenylalanine, [3H]glutamic acid, [^{14}C]alpha-methylaminoisobutyric acid, and Rubidium (^{86}Rb), as well as on the activity of gamma-glutamyl transpeptidase (γ -GTP) in rat brain microvessels. Similar patterns of inhibition of uptake by capillaries of amino acids and ^{86}Rb were observed in the presence of both mercury compounds. Marked inhibition of uptake was seen at concentrations of 10^{-5} and 10^{-4} M of both compounds, but the uptake was not inhibited at concentrations less than 10^{-5} M. Capillary γ -GTP activity was not influenced by either $HgCl_2$ or CH_3HgCl , suggesting that this enzyme does not play any role in the transport of the amino acids studied in these experiments. The results indicate that the main toxic effect of mercury compounds is inhibition of amino acid transport. The concentration at which mercury exerts its inhibitory effect in this study is similar to that estimated to have been present in the brains of victims during the Minamata epidemic.

Key Words: Brain Microvessels, Amino Acid, Methylmercury, Mercuric Chloride, Rubidium

INTRODUCTION

The toxic effects of organic and inorganic mercury compounds have been well documented. One of the major targets of mercury is the central nervous system, in which mercury intoxication produces morphological alterations (Jod, 1971). Observations of the leakage of dyes from the blood stream into the parenchyma of the brain (Steinwall and Klatzo, 1969; Steinwall and Olsson, 1969; Steinwall and Snyder, 1969; Chang and Hartman, 1972; Ware *et al.*, 1974) suggested that mercury impairs the blood-brain

barrier (BBB). Disturbances in BBB function provoked by mercury diminish the uptake of amino acids by the brain (Cavanagh and Chen, 1971; Pardridge, 1976; Dawson *et al.*, 1983; Hervonen and Steinwall, 1984), disrupt protein synthesis (Yoshino *et al.*, 1966; Verity *et al.*, 1977; Omata *et al.*, 1978; Cheung and Verity, 1985), and cause cerebral edema and neuronal necrosis (Callagher and Lee, 1980). Both mercurials are known to inhibit enzymes containing sulfhydryl groups, such as ATPase (Henderson *et al.*, 1979; Rajanna and Hobson, 1985). The inhibition by mercury compounds of BBB-associated enzymes, such as adenosine

Please send requests for reprints to Dr. Ivan Tayarani.

Accepted: June 8, 1987