Effect of HgCl$_2$ on Acetylcholine, Carbachol, and Glutamate Currents of Aplysia Neurons

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SUMMARY

1. Using conventional two-microelectrode voltage-clamp techniques we studied the effects of inorganic mercury (HgCl$_2$) on acetylcholine-, carbachol-, and glutamate-activated currents on Aplysia neurons. Hg$^{2+}$ was applied with microperfusion.

2. Acetylcholine and carbachol activated an inward, sodium-dependent current in the anterior neurons of the pleural ganglion. The medial neurons gave a biphasic current to acetylcholine and carbachol, which was outward at resting membrane potential. The faster component was Cl$^-$ dependent and reversed at about $-60$ mV, while the slower component was K$^+$ dependent and reversed at greater than $-80$ mV.

3. Hg$^{2+}$ (0.1–10 $\mu$M) caused a dramatic increase in the acetylcholine- and carbachol-induced inward current in anterior neurons and the fast Cl$^-$ current in medial neurons. With only a 1-min preapplication of Hg$^{2+}$, the acetylcholine- or carbachol-activated sodium or chloride currents were increased to 300% and the effect was only partly reversible. The threshold concentration was 0.1 $\mu$M Hg$^{2+}$.

4. Contrary to the effects on sodium and chloride currents, concentrations of 0.1–10 $\mu$M Hg$^{2+}$ caused a complete and irreversible blockade of K$^+$-dependent acetylcholine and carbachol currents. The block of the potassium current was...
relatively fast and increased with time. The concentration of HgCl$_2$ that gave a half-maximal blockade of the carbachol-activated potassium current was 0.89 μM. The chloride-dependent current elicited by glutamate on medial neurons was increased by HgCl$_2$ as well.

5. These results suggest that actions at agonist-activated channels must be considered as contributing to mercury neurotoxicity. It is possible that the toxic actions of Hg$^{2+}$ on synaptic transmission at both pre- and postsynaptic sites are important factors in the mechanism of Hg$^{2+}$ toxicity.

**INTRODUCTION**

Mercury present in the environment, upon entering biological organisms including man, causes a variety of toxic actions on different organs. The brain is a particularly important site of mercury action. Mercury is taken up by nervous tissue (Clarkson, 1972) and persists in the brain for a long time (Rustam and Hamdi, 1974; Vallee and Ulner, 1972). Mercury is neurotoxic and causes irreversible damage to animals and man, both in its inorganic form and after undergoing bioconversion to methylmercury (Alberts et al., 1988; Chang, 1977). A variety of effects of mercury on central nervous tissue has been reported, many of which are probably secondary to the strong affinity of mercury and some other metals for –SH groups of proteins (Passow et al., 1961). Mercury inhibits Na/K-ATPase in the brain (Anner, 1992; Magour, 1987) and modulates messenger RNA metabolism (Kuznetsov and Richter, 1987). Mercury induces a dramatic increase in the Ca$^{2+}$ permeability of the sarcoplasmic reticulum (Abramson et al., 1983). At the neuromuscular junction both mercury and methylmercury first stimulate release of synaptic vesicles, recorded as miniature end-plate potentials, and subsequently inhibit such release (Atchinson, 1986; Juang, 1976; Manalis and Cooper, 1975; Miyamoto, 1983). Similar actions of inorganic and organic mercury compounds have been observed when measuring release of labeled serotonin from synaptic vesicles (Oudar et al., 1989). Mercuric ions have been shown to be potent antagonists at one class of excitatory amino acid receptor, the kainate receptor, expressed in Xenopus oocytes (Umbach and Gundersen, 1990), and have also been demonstrated to have actions at γ-aminobutyric acid receptors (Arakawa et al., 1991). Mercury produces an unique inward current on buccal neurons of Aplysia (Weinreich and Wonderlin, 1987). In Helix neurons mercury has been shown to inhibit the excitatory actions of acetylcholine and serotonin and to alter both voltage-activated inward and outward currents (S.-Rózsa and Salánki, 1990, 1991). In neurons of the marine mollusk, Aplysia, mercury irreversibly blocks the voltage-activated calcium channels at concentrations which do not greatly affect membrane potential or resistance (Büsselberg et al., 1991).

In the central nervous system of mollusks, acetylcholine can evoke both excitatory and inhibitory effects (Tauc and Gerschenfeld, 1961) by independently influencing sodium, chloride, or potassium permeabilities of the membrane (Kehoe, 1972b). Increases in K$^+$ and Cl$^-$ permeability result in an inhibitory or hyperpolarizing action, and receptors inducing both permeability changes may be