Effects of a New Isoquinolinone Derivative on Induction of Action Potential Burst in Central Snail Neuron

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Abstract

The effects of 7-bromo-1,4-dihydro-2-phenyl-4,4-bis(4-pyridinylmethyl)2H-isoquinolin-3-one dihydrochloride (BDPBI) on induction of action potential bursts were studied pharmacologically on the RP4 central neuron of the giant African snail (Achatina fulica Ferussac). The effects of m-3M3FBS, a phospholipase activator and HTMT, a histamine (H1) receptor agonist, on the neuron were also tested. The RP4 neuron showed spontaneous firing of action potential. Extracellular application of BDPBI (150 micromol/l) reversibly elicited bursts of potential (BoP) on the neuron. m-3M3FBS and HTMT also elicited BoP on the RP4 neuron. The BoP elicited by BDPBI were blocked by U73122 (6 micromol/l), a compound commonly used as a phospholipase C (PLC) inhibitor. Neomycin (3.5 mmol/l), a high-magnesium solution (30 mmol/l), replacing the physiological sodium ion with lithium ion or adding diphenhydramine, chloropheniramine decreased the BoP elicited by BDPBI. The BoP elicited by BDPBI were not inhibited after administration with (1) prazosin, propranolol, atropine, d-tubocurarine, hexamethonium, haloperidol, cimetidine, (2) calcium-free solution, (3) high-potassium (12 mmol/l) solution, and (4) pretreatment with KT-5720. The BoP elicited by HTMT was not inhibited after administration of diphenhydramine or chloropheniramine. Voltage-clamped studies revealed that BDPBI decreased the amplitudes of calcium and steady-state outward currents while it did not alter the amplitude of the fast inward current. No negative slope relationship of the steady-state current voltage relationship was found in BDPBI-treated neurons. It is concluded that BDPBI reversibly elicited BoP in the central snail neuron. The effect was not due to (1) the extracellular calcium ion fluxes, or (2) the activation of cholinergic, adrenergic or histamine receptors. The BDPBI-elicited BoP were dependent on the phospholipase activity in the neuron.